A DISSERTATION ON

A STUDY ON THE PREVALENCE OF INCREASED LEFT VENTRICULAR MASS & PROTEINURIA IN NEWLY DIAGNOSED HYPERTENSIVE PATIENTS

Submitted to

THE TAMILNADU
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BONAFIDE CERTIFICATE

Certified that the dissertation titled **"A STUDY ON THE PREVALENCE OF INCREASED LEFT VENTRICULAR MASS AND MICRO PROTEINURIA IN NEWLY DIAGNOSED HYPERTENSIVE PATIENTS"** is a bonafide work of the candidate **Dr. LAKSHMI THAMPY .M.S.,** post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai – 10, done under my guidance and supervision, in partial fulfillment of regulations of **The Tamilnadu Dr. MGR Medical University** for the award of M.D. Degree Branch I (General Medicine) during the academic period from May 2006 to March 2009.

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ETHICAL COMMITTEE OF
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Venue: Dean Chamber, Date: 3.1.2008

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TO WHOMSOEVER IT MAY CONCERN

Dear Sir / Madam

Sub: Internal Medicine – MD PG's Dissertation Ethical Committee – Reg.

Ref: Requisition from H.O.D. Medicine.

This is in reference to the letter dated 2.1.2008 regarding Ethical committee meeting clearance with regard to the following topics

Sl.No	Name of the Post Graduate	Dissertation Topic
1	Dr. R.Ramprasad	A study on Prevalence and Risk Factors of Diabetic Nephropathy in Newly Detected Type 2 Diabetic Patients
2	Dr. V.Sakthivadivel	A study on Cardiac abnormalities in HIV infected individuals
3	Dr. K.S.Gopakumar	A study on Subclinical Hypothyroidism in females over 50 years of age
4	Dr. T.Karthikeyan	Inflammatory profile in Acute Myocardial Infarction

5	Dr. Maliyappa Vijay Kumar	A study on Prevalence of Microalbuminuria in HIV patients not on ART and Correlation with CD4 count
6	Dr. D.Radha	High sensitivity C - reactive protein as a determinant in the outcome of Acute ischemic stroke
7	Dr. Lakshmi Thampy M.S	A Study on the prevalence of increased LV mass & Proteinuria in newly diagnosed Hypertensive patients.
8	Dr. Manu Bhasker	A study on the effect of Intravenous Metoprolol along with Thrombolysis in Acute Myocardial infarction
9	Dr. P.Mohanraj	Evaluation of Lipid Profile in patients with non diabetic Chronic Kidney Disease Stage 3,4 and 5
10	Dr. P.Dhanalakshmi	A study On Metabolic Syndrome in Young Ischemic Stroke
11	Dr. V.Murugesan	A study on Electrocardiographic and Echocardiographic changes in Chronic Obstructive Airway Disease
12	Dr. M.Seetha	Effect of Right ventricular infarction on the immediate prognosis of Inferior wall Myocardial Infarction

We are glad to inform you that at the EC meeting held on 3.1.08 on the above topics were discussed and **Ethically approved**.

DEAN

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We confirm that no member of the study team is on the Ethics Committee and no member of the study team voted.

The trial will also follow the Ethics Guidelines for Bio-Medical Research On Human subjects issued by ICMR, New Delhi and will not involve any expense to the Government and will not be detrimental to the normal functioning of the Institution.

The study will also satisfy the revised order issued by the Government of Tamil Nadu, Health and Family Welfare Department G.O.MS.No:319, H & FW, Dept. dated 30.11.2001.

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CONTENTS

INTRODUCTION

Hypertension is defined as any one of the following

Systolic blood pressure $\geq$ 140mmHg

Diastolic blood pressure $\geq$ 90mmHg

Taking any anti hypertensive Medication[1]

Hypertension is a major cause of morbidity and mortality. The heart, arterial vessels, brain, kidney and retinal vasculature are major target organs adversely affected by high blood pressure. In adults there is a continuous incremental risk of target organ damage across levels of both systolic and diastolic blood pressure. The multiple risk factor intervention trial (MRFIT) which included >3.5 lakh male participants, demonstrated a continuous and graded influence of both systolic and diastolic blood pressure on CHD mortality extending down to systolic blood pressure of 120mmHg. Cardio vascular disease risk doubles for every 20-mmHg systolic and 10-mm Hg diastolic rise in blood pressure.[3]

WHO/ ISH guidelines have indicated the following manifestations of target organ damage as factors influencing prognosis[2]

1. Left ventricular hypertrophy
2. Radiological evidence of atherosclerotic plaque
3. Proteinuria / slight elevation of plasma creatinine concentration
4. Generalised / focal narrowing of the retinal arteries

Left ventricular hypertrophy is an independent risk factor to cardiovascular morbidity and mortality in hypertensive individuals[4]. .Identification of various geometric patterns of LV hypertrophy further stratifies cardiovascular risk.[5, 6]

Microalbuminuria is a specific integrated marker of cardiovascular risk and target organ damage in primary hypertension and one that is suitable for identifying patients at higher global risk[7]. [11] Microalbuminuria is considered as strong, early and independent marker of increased cardiovascular risk in hypertension[8] and risk is proportional to urine albumin excretion starting below conventional MAU threshold.

In hypertensive Patients, Micro-Albuminuria has significant association with concentric and eccentric LV hypertrophy[10]. Urine albumin creatinine ratio positively correlate with LV mass, systolic BP, age, pulse pressure and endocardial and mid-wall shortening but not to diastolic filling parameters.[10]

Micro-albuminuria confers a four fold increased risk of Ischemic heart disease among hypertensive or borderline hypertensive subjects [13]

Micro-albuminuria is associated with atherogenic cardiovascular risk factors, endothelial dysfunction, impaired aortic mechanics and increased LV mass.[14,16,17,18] Proteinuria, in hypertensive renal disease[17,18,19,20] may accelerate the decline of renal function and also amplify the risk of vascular disease. Losartan Intervention for end point reduction in hypertension Study (LIFE study) indicates that changes in urine albumin excretion under antihypertensive treatment parallel those of ECG determined LV mass. Determination of albuminuria can become a useful tool in evaluation of global cardio vascular risk [21].

AIM:

1. To study different cardiac geometry in newly diagnosed hypertensives.

2. To correlate proteinuria and LV mass in hypertensives.

REVIEW OF LITERATURE

Affecting one billion people worldwide and 118 million in India, systemic hypertension remains the most common, readily identifiable and reversible risk factor for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection and peripheral arterial diseases. The global burden of hypertension is projected to affect 1.5 billion persons, one third of world's population, by the year 2025.

Hypertension currently is defined as a usual BP of 140/90mm Hg or higher, or BP levels from which the benefits of pharmacological treatment have been definitively established in randomized placebo-controlled trials Studies have shown continuous positive relationships between the risk of coronary artery disease and stroke deaths with systolic or diastolic BP down to values as low as 115/75 mm of Hg. CAD is the most common cause of death from hypertension.

BLOOD PRESSURE VARIABILITY AND ITS DETERMINANTS

a. Racial

In hypertension, target organ damage and salt insensitive hypertension more common in US blacks.

b. Smoking

Cigarette smoking transiently raise BP by 10 to 20mm Hg with every cigarette, thereby elevating the day time BP in habitual smokers Smoking is associated with impaired coronary vasodilatation and inflammatory prothrombotic state. Moreover, rise in blood pressure is associated with intimal tear; all together contributing for premature atherosclerosis and coronary spam.

c. Exercise

Habitual physical inactivity is associated with markedly increased risk of developing hypertension, in part because of weight gain.

d. Diet

Excess consumption of calories and salt is associated with hypertension. Diets low in fresh fruit and potassium is associated with increased risk.[25] Inter induvidual variability in BP responses to dietary sodium loading and sodium restriction indicates a genetic underpinning.

e. Obesity

Obesity initially raises BP by increasing renal tubular reabsorption, impairing pressure natriuresis and causing volume expansion[26] followed by progressive renal dysfunction

Obesity is associated with

a) Increased heart rate and cardiac output [27,28]

b) Concentric and eccentric cardiac hypertrophy [29,33]

c) Impaired systolic and diastolic function [30]

d) Endothelial dysfunction and arterial stiffness [31,32]

f. Genetics

Fourteen genes involved in Mendelian form of hypertension have been suggested; mostly involving renal handling of salt and water; ACE polymorphism being a prominent example.

JNC – 7 STAGING OF OFFICE BLOOD PRESSURE[34]

Blood pressure stage	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Normal	<120	<80
Pre Hypertension	120-139	80-89
St.1 Hypertension	140-159	90-99
St.2. Hypertension	≥160	≥100

CLASSIFICATION OF BLOOD PRESSURE ACCORDING TO ESH (2003) [(24)]

Category	Systolic	Diastolic
Optimal	<120	<80.
Normal	120-129	80-84.
High Normal	130-139	85-89.
Grade I Hypertension	140-159	90-99.
Grade II Hypertension	160-179	100-109.
Grade III Hypertension	≥180	≥110.
Isolated Systolic Hypertension	≥140	<90.

ESH – European Society of Hypertension

In ESH classification, staging of BP into grade 2 and 3 (stage II of JNC) better convey the concept of a continuous increase in risk with an increase in blood pressure. As prehypertensive patients are considered to have high normal BP according to ESH classification, medicalisation of millions of people avoided [(23)].

HAEMODYNAMIC SUBTYPES

a) Diastolic hypertension in middle age seen in middle aged men with weight gain,[35] due to elevated peripheral resistance with inappropriately normal cardiac output.

b) Combined systolic diastolic hypertension.

c) Isolated systolic hypertension in older adults - After 60 years of age ISH is the most common[36] form, defined as systolic BP higher than 140mmHg and diastolic BP lower than 90mmHg. ISH is due to stiffening of central aorta and rapid return of reflected pulse waves from periphery.[37]

d) Isolated systolic hypertension in young adults - Due to increased cardiac output and a stiff aorta; presumably reflecting an overactive sympathetic nervous system.[38]

Pulse pressure, is due to the force imparted to the arterial blood column by left ventricular contraction. Pulse pressure after sixth decade of life is a surrogate risk marker of central artery stiffness [62]; which is an independent risk factor for cardiovascular disease[63.]

NATURAL HISTORY OF ESSENTIAL HYPERTENSION

Essential hypertension is a heterogenous disorder. The probability of developing a morbid cardiovascular event with a given arterial pressure may vary by as much as twenty fold depending on whether associated risk factors are present or not. Most untreated adults with hypertension will develop further increase in their arterial pressure with time. Further more it has been documented that untreated hypertensives are associated with a shortening of life by 10-20 yrs usually related to an acceleration of an atherosclerotic process with rate of acceleration in part related to the severity of the hypertension.

Even individuals with relatively mild disease left untreated for 7-10 years have a high risk of developing significant complication. Nearly 36% will exhibit atherosclerotic complication and more than 50% will have end organ damage related to hypertension itself eg. Cardiomegaly, retinopathy and renal insufficiency. Thus even in its mild form, hypertension is a progressively lethal disease if left untreated.

Natural history of the disease for long range is available from series Natural course must come from data collected prior to the availability of effective treatment. Two such long series have been reported one by Perera

(1995) and other by Bechgaard. (Perera followed 500 patients with causal diastolic pressures of 90 mm Hg (or) higher, 150 from before onset and 350 from an uncomplicated phase until their death.)

(Data from Perera G.A. Journal of Chronic disease 1955, 1:33-42).

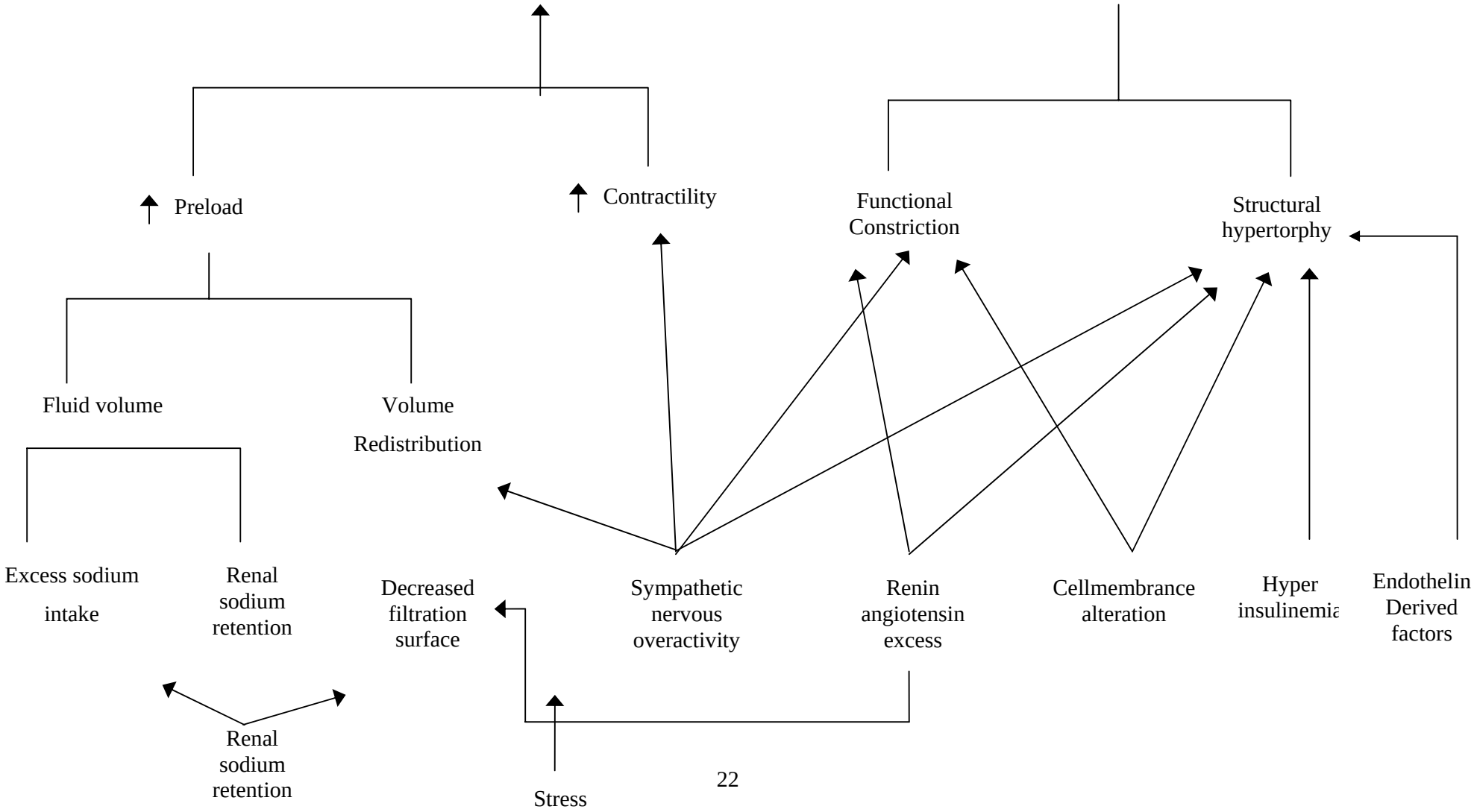
Complications	% Affected	Mean Survival after onset (yrs)
Cardiac Hypertrophy (X-ray)	74	8
ECG	59	6
CCF	50	4
Angina	16	5
Cerebral Encephalopathy	2	1
Stroke	12	4
Renal Proteinuria	42	5
Elevated BU	18	1
Accelerated Phase	7	1

Morbid Events in 196 Mild Hypertensives given Placebo for 7 yrs USPHS study 1977 (United States Public Health Service Hospital Study)

Total events	Rate / 100	
HT events	**53.1**	
CVA		3.1
LVH		12.8
LVH by ECG		18.9
Cardiomegaly		11.7
Retinopathy		4.6
Rental Insufficiency		1.0
CCF		1.0
Atherosclerotic	28.6	
MI		7.1
Death		2.0
Other Coronary Disease		18.9
Arterial Insufficiency		0.5
Treatment Failure		12.1

BLOOD PRESSURE = CARDIAC OUTPUT X PERIPHERAL RESISTANCE

HYPERTENSION = INCREASED CO AND / OR INCREASED PR.



TARGET ORGAN DAMAGE

Left Ventricular Hypertrophy:-

In Hypertension, Left Ventricle undergoes hypertrophy as a compensatory mechanism to reduce wall stress and maintain pump function in the face of the increased after load. LVH is an important, independent predictor of mortality and morbidity. [39, 40.]

At which point LV mass cease to be compensatory and becomes deleterious in hypertension is not known, but the concept of inappropriate LV mass or excess mass beyond that predicted based on gender, body height and haemodynamic burden has been introduced to better address this issue [41] [42] [43] Hypertension induces change in both contractile and supportive compartments of the heart that are maladaptive and detrimental.[44]

Different patterns of adaption reflect the variable impact of preload on the LV due to changes in blood volume and venous compliance.

Concentric Remodelling; with normal LV mass and increased relative wall thickness is a consequence of volume overload from pressure natriuresis cancelling out the effect of pressure overload.[47] (Eccentric hypertrophy results from concomitant pressure and volume overload).

Concentric Hypertrophy is induced by pure pressure overload due to replication of sarcomeres in parallel: [45] associated with thickening of septal and posterior walls.

Patients with LV hypertrophy are more likely to exhibit kidney damage, and increased carotid intima media thickness. [48] The risk of target organ damage can be further stratified by LV geometric pattern; the risk being highest with concentric and intermediate with eccentric hypertrophy.[49] Concentric remodelling; as well, is an independent predictor of increased cardiovascular risk in hypertensive patients. [47] The higher levels of blood pressure and neurohormonal activation likely explain risk of target organ damage.

Concentric LV hypertrophy is associated with the greatest renal dysfunction and is likely to potentiate the decline in glomerular filtration rate with aging. [50]

The close association between concentric geometry and cardiovascular events likely explained by a number of factors,-

Abnormal diastolic filling

Lower myocardial contractility

Higher risk of arrhythmia

Associated myocardial fibrosis

Coronary Insufficiency

HAEMODYNAMICS AND CARDIAC PERFORMANCE ASSOCIATED WITH LV GEOMETRY IN HYPERTENSION

	Normal LV	**Concentric Remodelling**	**Concentric Hypertrophy**	**Eccentric Hypertrophy**
Prevalence	52%	13%	8%	27%
LV Mass	-	-	↑	↑
Relative wall Thickness	-	↑	↑	-
Blood Pressure	↑	↑	↑↑↑	↑↑
Stroke Index	-	↓	-	↑
Cardiac Index	-	↓	-	↑
Total Perepheral Resistance	↑	↑↑↑	↑↑	-

LVH AND RISK OF CARDIOVASCULAR EVENTS

Reference	No.	LVH criterion	End point	N/100Pt /yr	
				With LVH	**Without LVH**
Castlie et al 1986	140	LVMI >125g/m/m^2	Death/MI/stroke	4.6	1-2
Levy et al 1989	3220	LVMI >116g/m^2	Death/CV events	2 2.3	0.8 1.4
Koren et al 1991	280	LVMI>125g/m^2	Death/CV events	1.4 6.3	0.1 2.2
Partrey et al 1990	104	Wall Thickness >1.4cm	Death	15.3	4.8

Different studies; as shown above, have shown marked increase in mortality and morbidity in patients with LVH.

RENAL DYSFUNCTION

A pivotal part of the renal body fluid feedback control system for long term blood pressure regulation is renal pressure natriuresis mechanism, whereby increased renal perfusion pressure lead to significant increase in sodium and water excretion.

Impaired renal pressure natriuresis in seen in all forms of hypertension including essential hypertension. The shift of pressure natriuresis can be caused by intrarenal disturbances that increases tubular re-absorption or reduce renal blood flow and glomerular filtration or extra renal disturbances like increased sympathetic nervous system activity or excessive formation of anti – natriuretic hormones like aldosterone. With long- standing hypertension, structural damage in the kidney may further shift pressure natriuresis and exacerbate hypertension.

Segmental Hyalinosis of Inter lobular arteries and efferent arterioles reflect earliest hypertension induced intrarenal lesion. In early phase, capillary wall thickening and basement membrane thickening occurs which leads to focal and segmental glomerulosclerosis in malignant hypertension; ischemic collapse of glomerular tuft occurs. Benign hypertension is chara cterised by media thickening while malignant nephrosclerosis predominantly affect the intimal space.

Microalbuminuria and proteinuria are common in hypertensive disease. It may accelerate the decline of renal function and also amplify the risk of vascular disease. Microalbuminuria is also an independent risk factor for cardiovascular disease; even in general population microalbuminuria predict a small fall in creatinine clearance during 7years of follow up in patients with essential hypertension

Micro albuminuria has been defined as urine albumin excretion of 30 -300mg /24 hr OR 20-200µg/minute OR Albumin- creatinine ratio - 30 - 300µg/ mg of creatinine OR Protein Creatinine ratio > 30mg/ g in the first voided morning sample. Control of hypertension is the single most effective intervention for those with proteinuria.

CORONARY MICRO CIRCULATION ABNORMLITIES

In hypertensive patients with LVH, structural and functional alterations in the small coronary vessels, increasing ventricular wall stress and alterations in the rheological properties of blood inhibit the ability of the coronary micro circulation to regulate over all coronary blood flow. [52]

CORONARY VESSEL PATHOLOGY IN LVH

Rarefaction of arterioles – Inadequate growth of coronary micro vascular bed limit myocardial perfusion in the presence of pressure – over load myocardial hypertrophy. [9]

Medial wall thickening – Pressure overload with coronary arterial hypertension cause vascular medial hypertrophy with decreased lumen diameter and increased ratio of media thickness to lumen diameter.

Perivascular and Interstial fibrosis

There will be increased vascular and perivascular deposition of collagen in LVH.

Increased vascular water content

A 10% to 15% increase in vessel wall water content is seen which produce thickening of the vascular walls.

Endothelial dysfunction

An impaired endothelial dependent relaxation occurs before the development of overt hypertension.

Along with the above changes, there is alteration of coronary auto regulation and flow reserve with LVH.

As in Framingham heart study, the Prevalence of silent MI was significantly increased in hypertensive subjects and they were also more susceptible for mortality. After initial myocardial infarction there is increased mortality when diastolic BP is lower below 80mm Hg. This J-Shaped curve probable reflects a reduction in perfusion pressure through the coronary vessels either narrowed or having impaired vasodilator reserve in the hypertrophied myocardium.

COMPETING RISK FOR DIFFERENT CARDIOVASCULAR DISEASE OUT COMES IN HYPERTENSION.

A Recent analysis of Framingham heart study participants who experienced new - onset hypertension had shed light on the risks for CVD associated with hypertension. In women and older men with new onset hypertension, stroke and heart failure were the most common first events,

while in younger men, hard CHD events. These results may have important implication for primary preventive strategies.

LV MASS REGRESSION

Regression of LV mass with effective BP reduction has been in demonstrated in about 400 studies.

In TOMHS, total cardiovascular events were reduced along with. LV mass regression. [64] Mid-wall fractional shortening, a sensitive indicator of intrinsic myocardial systolic performance, appears to improve with LV mass regression as well as stroke volume also improves.

LIFE study showed marked LV mass regression and proteinuria reduction in patients treated with losartan as compared with atenolol.

TOMHS study shown as benefit of exercise on LV mass regression along with pharmalogical therapy.

Reduction of left Ventricular Mass Indexed By Surface Area With Different Antihypertensive Drugs[65]					
	Angiotensin Receptor Antagonists	**Calcium Antagonists**	**Angiotensin converting Enzyme Inhibitors**	**Diuretics**	**Beta Blockers**
Mean(%)	13	11	10	8	6
95% Cl	8 to 18%	9 to 13%	8 to 12%	5 to 10%	3 to 8%

GUIDELINES OF BLOOD PRESSURE MEASUREMENT

The mercury sphygmomanometer is still considered the gold standard for BP measurement in the clinic

The patient should be seated comfortably, uncover the location of cuff placement, with the legs uncrossed, the back and arm supported such that the middle of the cuff on the upper arm is at the level of the right atrium.
BP measurements are influenced by the position of the arm in relation to the position of the chest. There is progressive increase in pressure of about 5-6mmHg as the arm is moved down from the horizontal to vertical position.

2005 AHA RECOMMENDATION

ARM CIRCUMFERENCE	CUFF	BLADDER WIDTH	BLADDER LENGTH
22-26cm	small adult	10cm	24cm
27-34cm	Adult	13cm	30cm
35-44cm	Large adult	16cm	36cm
45-52cm	Adult thigh	16cm	42cm

The cuff should be inflated to 10mmHg above the systolic pressure by palpatory method and deflated at a rate of 2-3mm Hg/ sec. American Heart Association and British Hypertension Society recommend fifth phase of Korotkoff sounds to be recorded as diastolic pressure.

METHODOLOGY

STUDY METHOD

Cross - Sectional Study

SUBJECTS AND METHODS

Fifty newly registered patients at hypertension clinic in Government Royapettah Hospital between February 2008 - July 2008 formed the material of the study.

INCLUSION CRITERIA

1. Newly detected patient with systolic BP $\geq$ 140 mm hg and/or diastolic BP $\geq$ 90 mmhg in atleast 2 visits.
2. Age more than 40 years.
3. No clinical or lab evidence of heart failure, renal failure, coronary artery disease, valvular heart disease, secondary hypertension, hyperlipidemia, overt proteinuria, urinary tract infection.

In all these patients, history of substance abuse, comprehensive clinical examination and appropriate imaging and bio-chemical evaluation done.

BLOOD PRESSURE

BP recordings were taken with well-calibrated mercury sphygmomanometer and proper cuff size was selected so that bladder encircled atleast 2/3rd of arm about one inch above the right cubital fossa. Two measurements were taken on two different occasions while sitting comfortably with back supported. PhaseV of Korotkoffs sound was taken as diastolic BP.

ECHO CARDIO GRAPHIC EXAMINATION

Echocardiography examination was performed at Department of Cardiology GRH, Chennai by an observer, unbiased of patient status. Two – dimensional guided M-mode echocardiography was done standard parasternal and apical view observed with patient supine in left lateral position.

The left ventricular in cavity dimension (LVIDD) Inter ventricular septal thickness (IVSD) and left ventricle posterior wall thickness. (LVPWD) in diastole were measured. All measurements were done on frozen image. All patients had good quality images suitable for measurement and interpretation.

CALCULATION

Relative wall thickness.

$$- \frac{\text{Septal wall thickness + Posterior wall thickness}}{\text{LV end – diastolic diameter}}$$

LV mass was derived using formula by devereux and associates

LV mass (grams) =

$0.8 \times 1.04 [(ivsd + lvidd + pwtd)^3 – (lvdd)^3] +0.6$

IVSd - inter ventricular septal thickness at end - diastole.

LVIDd - Left ventricular mass internal dimension at end - diastole

PWTd - Posterior wall thickness at end – diastole.

Left Ventricular mass index was inferred by calculating LV mass for body surface area taken as. $1.73m^2$

Reference value of LVMI

43 – 88 - for women

49 – 102 - for men.

PROTEINURIA MEASUREMENT

The morning spot urine sample protein – creatinine ratio has been measured using turbidimetric method (sulpho salicylic acid method) after ruling out overt proteinuria and cellular deposits. This method has an analytical sensitivity of 10mg/l.

Concentric LV hypertrophy was considered

If RWT > 0.43 and LVH

Eccentric LV hypertrophy was considered

If RWT $\leq$ 0.43 and LVH.

Concentric remodelling was considered

If RWT $\geq$ O.43 and normal LVMI.

OBSERVATION AND ANALYSIS

AGE DISTRIBUTION

TABLE-I

AGE GROUP	FREQUENCY	PERCENTAGE
40-50	17	34%
51-60	22	44%
>60	11	22%
Total	**50**	**100%**

	N	Mean	Std. Deviation	Std. Error Mean
AGE	50	53.7200	7.10573	1.00490

Majority of patients in the study group were in fifth decade of life (44%)

TABLE- II

SEX	FREQUENCY	PERCENTAGE
Male	30	60%
Female	20	40%
Total	**50**	**100%**

The study group consisted of 30 males and 20 females.

TABLE – III

BMI (Body Mass Index (kg/m^2)	**FREQUENCY**	**PERCENTAGE**
18.5 - 23	23	46%
23 - 30	27	54%
Total	**50**	**100%**

18.5 – 23 = Normal, 23 – 30 over weight, > 30 Obesity

	N	**Mean**	**Std. Deviation**	**Std. Error Mean**
BMI	50	23.56	2.53	.35

In the study group, 23(48%) patients had normal BMI while 27 (54%) were over weight. None of the patients were under nourished or obese.

STAGING OF HYPERTENSION ACCORDING TO JNC – 7

CLASSIFICATION

TABLE- IV

STAGE OF HYPERTENSION	FREQUENCY	PERCENTAGE
I (140-159) / (90-99)	24	48%
II ≥ 160/ ≥100	26	52%
Total	**50**	**100%**

Patient distribution between stage I and stage II were almost equal.

TABLE – V

PULSE PRESSURE	FREQUENCY	PERCENTAGE
<=40	7	14%
41-50	20	40%
51-60	15	30%
>60	8	16%
Total	**50**	**100%**

	N	Mean	Std. Deviation	Std. Error Mean
Pulse Pressure	50	54.80	9.52	1.34

Among the distribution of patients with pulse pressure gradient, 20 patients (40%) had pulse pressure in the range of 41-50, 15 patients (30%) had pulse pressure in the range of 51-60. 7 (14%) and 8 (16%) had pulse pressure below 40 and above 60 respectively.

DISTRIBUTION OF DIFFERENT CARDIAC GEOMETRY IN PATENTS WITH ESSENTIAL HYPERTENSION

TABLE-VI

CARDIAC GEOMETRY	FREQUENCY	PERCENTAGE
Normal Geometry	24	48
Concentric Hypertrophy	7	14
Concentric Remodelling	11	22
Eccentric Hypertrophy	8	16
Total	**50**	**100**

Among 50 Patients, 26 patients (52%) had abnormal geometry, of which 11 patients had concentric remodelling, 8 patients had eccentric hypertrophy and 7 patients had concentric hypertrophy. 24 patients (48%) had normal geometry, having normal relative wall thickness and LV mass.

DISTRIBUTION OF URINE PROTEIN CREATININE RATIO IN MICRO – PROTEINURIA RANGE IN PATIENTS WITHOUT OVERT PROTEINURIA

TABLE-VII

URINE PROTEIN – CREATININE RATIO	FREQUENCY	PERCENTAGE
Positive	18	36%
Negative	32	64%
Total	**50**	**100%**

Positive – Urine PCR > 30 mg/g of Creatinine
Negative – Urine PCR < 30 mg/g of Creatinine

In the study, 18 patients (36%) had urine protein in Mircoproteinuria range as detected by early morning spot urine protein - creatinine ratio.

DISTRIBUTION OF PCR FOR DIFFERENT AGE BMI AND PULSE PRESSURE

PCR		N	Mean	Std. Deviation	Std. Error Mean
Pulse Pressure	Positive	18	60.55	8.72	2.05
	Negative	32	51.56	8.46	1.49

PCR		N	Mean	Std. Deviation	Std. Error Mean
BMI	Positive	18	25.00	2.44	.57
	Negative	32	22.75	2.22	.39

			PCR	Total
		Positive	Negative	
AGE GROUP	40-50	2 (11%)	15 (47%)	17
	51-60	12 (66.7%)	10 (31.3%)	22
	> 60	4 (22.2%)	7 (21.9%)	11
Total		18	32	50

p-value - .02

Positive PCR was distributed in mean pulse pressure of 60 and BMI of 25.

Negative PCR was distributed in mean pulse pressure of 51 and BMI of 22.

Majority of patents with MAU was in age group 51 - 60.

DISTRIBUTION OF LV GEOMETRY FOR DIFFERENT AGE BMI AND PULSE PRESSURE

Geometry group		N	Mean	Std. Deviation	Std. Error Mean
Age	Normal	24	53.29	8.14	1.66
	Abnormal	26	54.11	6.13	1.2

P=0.687 NOT SIGNIFICANT.

Geometry group		N	Mean	Std. Deviation	Std. Error Mean
BMI	Normal	24	22.83	2.38	.48
	Abnormal	26	24.23	2.5	.49

p value -0.05

Geometry group		N	Mean	Std. Deviation	Std. Error Mean
Pulse Pressure	Normal	24	52.91	9.07	1.85
	Abnormal	26	56.53	9.77	1.91

p value- 0.18

For LVH, mean age was 54, BMI was 24 and Pulse Pressure was 56.5.

For Normal geometry mean age was 53, BMI was 22.8 and Pulse Pressure was 52.

ASSOCIATION BETWEEN URINE PROTEIN – CREATININE RATIO & ABNORMAL CARDIAC GEOMETRY

TABLE- VIII - A

PCR	Normal	Abnormal
Positive	3 (16.7%) [12.5%]	15 (83.3%) [57.7%]
Negative	21 (65.6%) [87.5%]	11 (34.4%) [42.3%]
Total	**24**	**26**

p-value = 0.001(Pearson)

Among 18 patients with Micro- Proteinuria, 15 patients (83%) had abnormal cardiac geometry. Among 26 patients with abnormal cardiac geometry, 15 patients (58%) had microproteinuria.

There is significant association between microproteinuria and abnormal cardiac geometry in patients with essential hypertension.

ASSOCIATION BETWEEN URINE PROTEIN CREATININE RATIO AND CARDIAC GEOMETRY IN HYPERTENSION

TABLE – VIII - B

Cardiac Geometry	**Urine PCR**		**Total**
	Positive	**Negative**	
Normal Geometry	3 (12.5%) [16.7%]	21 (87.5%) [65.6%]	24 48.0
Concentric Hypertrophy	6 (85.7%) [33.3%]	1 (14.3%) [3.1%]	7 14.0
Concentric Remodelling	6 (54.5%) [33.3%]	5 (45.5%) [15.6%]	11 22.0
Eccentric Hypertrophy	3 (37.5%) [16.7%]	5 (62.5%) [15.6%]	8 16.0
Total	**18** **36.0**	**32** **64.0**	**50** **100.0**

p- value = 0.00189 (Pearson)

Among 18 patients with microproteinuria both concentric hypertrophy and concentric remodelling have 33.3% prevalence. Both normal geometry and eccentric hypertrophy had 16.7%

prevalence. Among 32 patients without proteinuria, 21 (65.6%) had normal geometry

Among 7 patients with concentric hypertrophy, 6 (85.7%) had microproteinuria.

Among ii patients with concentric remodelling, 6 (54.5%) had microproteinuria.

Among 8 patients with eccentric hypertrophy, 3 (37.5%) had microproteinuria.

Among 24 patients with normal geometry, only 3 (12.5%) had microproteinuria.

ASSOCIATION BETWEEN URINE PCR AND SMOKING

TABLE – IX - A

URINE PCR	SMOKING		
	Yes	**No**	**Total**
Positive	9 (50%) [64.3%]	9 (50%) [25%]	18 36.0%
Negative	5 (15.6%) [35.7%]	27 (84.4%) [75.0%]	32 64.0%
Total	**14** **28.0%**	**36** **72.0%**	**50** **100.0%**

p-value = 0.009 (Pearson)

Among 14 smokers, 9 (64%) had microproteinuria showing a significant association between smoking and microproteinuria

ASSOCIATION BETWEEN LVH AND SMOKING

TABLE – IX - B

		GEOMETRY GROUP		Total
		Normal	**Abnormal**	
SMOKING	No	22 (91.7%)	17 (65.4%)	39
	Yes	2 (8.3%)	9 (34.6%)	11
Total		24	26	50

p value-0.02

Among 11 smoker, 9 (82%) had LVH. While smoker represented 35% of LVH patients. A significant association was seen between smoking LVH.

ASSOCIATION BETWEEN PULSE PRESSURE AND CARDIAC GEOMETRY

TABLE - X

PULSE PRESSURE	CARDIAC GEOMETRY		
	Normal	**Abnormal**	**Total**
<= 40	5 (71.4%) [20.8%]	2 (28.6%) [7.7%]	7 14.0%
41-50	12 (60.0%) [50.0%]	8 (40.0%) [30.8%]	20 40.0%
51-60	4 (26.7%) [16.7%]	11 (73.3%) [42.3%]	15 30.0%
>60	3 (37.5%) [12.5%]	5 (62.5%) [19.2%]	8 16.0%
Total	**24 48.0%**	**26 52.0%**	**50 100.0%**

p-value = 0.04746 (Mantel – Haenszel)

Among 8 patients with pulse pressure >60, (62.5%) had abnormal cardiac geometry out of 15 patients with pulse pressure 51-60, 11 (73%) had LVH. In patients with pulse pressure less than 40 and 40-50, majority had normal cardiac geometry. There is a significant association between widened pulse pressure and abnormal cardiac geometry.

ASSOCIATION BETWEEN CARDIAC GEOMETRY AND STAGE OF HYPERTENSION

TABLE –XI - A

STAGE	Cardiac Geometry		Total
	Normal	**Abnormal**	
I	18 (75.0%) [75.0%]	6 (25.0%) [23.1%]	24 48.0
II	6 (23.1%) [25.0%]	20 (76.9%) [76.9%]	26 52.0
Total	**24** **48.0**	**26** **52.0**	**50** **100.0**

p-value = 0.00024 (Pearson)

STAGE - I – 140 – 159 / 80-89 mmHg STAGE – II - ≥ 160/ ≥ 90 mmHg

Among 26 patients with stage II hypertension, 20 patients (77%) had LVH, while 18 patients (75%) with stage I had normal cardiac geometry. There was a strong positive association between stage II hypertension and LVH.

ASSOCIATION BETWEEN CARDIAC GEOMETRY AND STAGE OF HYPERTENSION

TABLE –XI - B

STAGE	CARDIAC GEOMETRY				Total
	NG	CH	CR	EH	
I	18 (75.0%) [75.0%]	1 (4.2%) [14.3%]	4 (16.7%) [36.4%]	1 (4.2%) [12.5%]	24 48.0
II	6 (23.1%) [25.0%]	6 (23.1%) [85.7%]	7 (26.9%) [63.6%]	7 (26.9%) [87.5%]	26 52.0
Total	**24** **48.0**	**7** **14**	**11** **52.0**	**8** **16**	**50** **100.0**

p – value = 0.00197 (Pearson)

Majority of patients (85.7%) with concentric hypertrophy had stage II hypertension; 87.5% patients with eccentric hypertrophy and 63.6% with concentric remodeling had stage II hypertension.

ASSOCIATION BETWEEN STAGE OF HYPERTENSION AND URINE PROTEIN CREATININE RATIO

TABLE – XII

STAGE	POSITIVE	NEGATIVE	TOTAL
I	5 (20.8%) [27.8%]	19 (79.2%) [59.4%]	24 48.0
II	13 (50.0%) [72.2%]	13 (50.0%) [40.6%]	26 52.0
Total	**18** **36.0**	**32** **64.0**	**50** **100.0**

p- value = 0.03182 (Pearson)

Among 18 patients with micro-proteinuria, 13 (72%) had stage II hypertension. While 13 (50%) of patients with stage II had proteinuria, only 5 (20%) with stage I hypertension had proteinuria.

ASSOCIATION BETWEEN CARDIAC GEOMETRY AND BODY MASS INDEX

TABLE - XIII

BMI	**CARDIAC GEOMETRY**		**Total**
	Normal	**Abnormal**	
<= 23	16 (69.6%) [66.7%]	7 (30.4%) [26.9%]	23 46.0
> 23	8 (29.6%) [33.3%]	19 (70.4%) [73.1%]	27 54.0
Total	**24** **48.0**	**26** **52.0**	**50** **100.0**

p- value = 0.00485 (Pearson)

BMI - < 23 – Normal
23-30 – Overweight

Out of 27 overweight patients 19 (70.4%) have LVH.

Among 26 patients with LVH 19 (73.1%) were overweight

ASSOCIATION BETWEEN BMI AND URINE PROTEIN CREATINE RATIO

TABLE – XIV

BMI	Urine PCR		Total
	Positive	**Negative**	
<= 23	4 (17.4%) [22.2%]	19 (82.6%) [59.4%]	23 46.0
> 23	14 (51.9%) [77.8%]	13 (48.1%) [40.6%]	27 54.0
Total	**18** **36.0**	**32** **64.0**	**50** **100.0**

While 14 patients (77.8%) with microproteinuria were having overweight, the distribution of over weight patients between those with and without proteinuria were equal.

ASSOCIATION BETWEEN URINE PCR AND CARDIAC GEOMETRY IN PATIENTS WITH STAGE II HYPERTENSION

TABLE – XV - A

Urine PCR	Cardiac geometry		
	Normal	**Abnormal**	**Total**
Positive	1 (7.2%) [14.3%]	13 (92.8%) [68.4%]	14
Negative	6 (50.6%) [85.7%]	6 (50%) [31.6%]	12
	7 (27%)	19 (73%)	

Among 26 patients with stage II hypertension, 19 patients (73%) have LVH of which 13 (68.4%) had microproteinuria.

Out of 14 patients (53.8%) in stage II hypertension having microproteinuria, 13 (92.8%) had LVH.

Among 7 patients having normal geometry only 1 (14%) had microproteinuria.

ASSOCIATION BETWEEN URINE PCR AND CARDIAC GEOMETRY IN PATIENTS WITH STAGE I HYPERTENSION

TABLE – XV - B

Urine PCR	Cardiac geometry		
	Normal	**Abnormal**	**Total**
Positive	2 (40%) [11.1%]	3 (60%) [50. %]	5
Negative	16 (84.3%) [88.9%]	3 (15.7%) [50%]	19
	18 75%	6 25%	

Among 24 patients in stage I hypertension, 18 (75%) had normal cardiac geometry only 6 (25%) had LVH and 5 (21%) had microproteinuria.

BINARY LOGISTIC REGRESSION MODEL FOR DIFFERENT FACTORS WITH LVH

FACTORS	CHI- SQUARE	P- VALUE
SEX	1.410	.235
BMI	.078	.78
STAGE OF HTN	**5.5**	**.018**
PP	.34	.55
SMOKING	3.77	.05
AGE	.29	.58

When regression model was applied for studying association between different factors and LVH only staging of hypertension (Stage II) showed a positive association.

BINARY LOGISTIC REGRESSION MODEL FOR DIFFERENT FACTORS WITH MICROPROTEINURIA

FACTORS	CHI- SQUARE	P- VALUE
SEX	0.5	0.47
BMI	2.1	.13
STAGE OF HTN	.002	.96
PP	2.3	.12
SMOKING	2.7	.07
AGE	3.7	.05
CARDIAC GEOMETRY	**4.2**	**.039**

When regression model was applied for studying association between different factors and PCR only Abnormal cardiac geometry showed a positive association.

DISCUSSION

Study was conducted in 50 newly detected hypertensives in the age group of 40-70-years of age with 60% females and 40% male. Most of the patients were in 40-50 years of age group.

Among 30 males, 14 were smokers (46%)

Out of 50 patients, 27 (54%) were having a body mass index consistent with overweight (23-30), 23(46%) were having normal BMI.

As per JNC-7 staging of hypertension, 24 (48%) of patients were in stage I and 26 (52%) were in stage - II

Out of 50 patients, 26 (52%) had unfavourable cardiac geometry. Among patients with unfavourable cardiac geometry, 11 patients (22%) had concentric remodelling, 8 (16%) had eccentric hypertrophy and 7 (14%) had concentric hypertrophy.

The urine protein creatinine ratio was in microalbuminuria range in 18 (36%) patients of which 15 (83%) had abnormal cardiac geometry, 3 (17%) had normal cardiac geometry; showing a significant association between proteinuria and left ventricular hypertrophy in patients with essential hypertension.

Among 14 (48%) patients with smoking habit out of 30 males in the study, 9 (64%) had proteinuria. A significant association was seen between proteinuria and smoking.

A significant association was seen between widened pulse pressure and abnormal cardiac geometry.

Incidence of LVH was more in patients with widened pulse pressure. 11(73%) out of 15(30%) of patients with pulse pressure in the range of 51-60 and 5(62.5%) of 8(16%) with pulse pressure >60 had LVH respectively while LVH was seen in 2 patients (29%) and 8 patients (40%) in patients with pulse pressure range of <40 and 41-50 respectively. Majority of patients in the pulse pressure range of < 40 and 41-50 had normal geometry.

Among 26 patient with stage II hypertension, 20 (77%) had LVH while 6 (25%) of patients with stage I hypertension had LVH.

In patients with proteinuria, 12 (80%) of LVH was in stage II; in patients without proteinuria, 8 (72%) of LVH was in stage II hypertension.

Among 27 overweight patients, (70%) 19 had LVH. out of 18 patients with proteinuria, 14 (78%) were overweight.

Among 24 patients with stage I hypertension, 18 (75%) had normal cardiac geometry and only 5 (21%) had microproteinuria.

Among 26 patients with stage II hypertension, 19 (73%) had LVH of which 13 (68%) had microproteinuria.

PERERA STUDY

COMPLICATION	OUR STUDY	PERERA STUDY
LVH	52%	59%
PROTEINURIA	36%	42%

Our study results are comparable with study by perera et al.

PERERA Study Insisted of 500 Untreated Patients.

USPHS STUDY

COMPLICATION	OUR STUDY	USPHS STUDY
LVH	52%	9%
Renal Dysfunction	36%	1%

In USPHS Study LVH was based on ECG Findings. The study was done in Patients with mild Hypertension, who were treated and followed up with placebo.

Another Study by O.Kumar et al showed Similar Results.

STUDY	TOTAL	PROTEINURIA / LVM
O. Kumar et al	50	44%
Our Study	50	36%

STUDY	TOTAL	LVH
SR Gupta et al	50	74%
Our Study	50	50%

TOD	OUR STUDY	S. A. KHAN et al
Proteinuria	36%	29.3%
LVH	50%	44%

This study results are compared with study done by S. A. Khan et al, Aligarh

LVH By Echo	PROTEINURIA	
	OUR STUDY	S. A. KHAN et al
No	12.5%	11.1%
Yes	57.6%	38.8%

CONCLUSION

Among the fifty patients with newly diagnosed hypertension in the age group of 40-70 years majority were in fifth decade. Among the fifty patients, 26 had left ventricular hypertrophy and 24 had normal cardiac geometry.

In patients with LVH, majority had concentric remodelling, while eccentric hypertrophy and concentric hypertrophy occurred with almost equal incidence.

Among 18 patients with microproteinuria, 15 had left ventricular hypertrophy showing significant association between proteinuria and left ventricular hypertrophy.

Smoking showed significant association with proteinuria.

A significant association was seen between widened pulse pressure and LVH Majority of patients with pulse pressure above 50 had LVH. While most of the patients with pulse pressure < 50 had normal geometry.

Majority of patients (70%) with proteinuria and LVH were in stage-II hypertension.

A significant majority of overweight patients had LVH and proteinuria.

Patients were almost equally distributed between stage I and II Hypertension. Majority of patients had normal cardiac geometry in stage I while stage II patients had LVH of whom majority had microproteinuria.

On applying binary logistic regression model for analysis of association between age, sex, BMI, smoking, pulse pressure, stage of hypertension and LVH; only stage II hypertension had significant association with LVH.

On applying binary logistic regression model for analysis of association between age, sex, BMI, smoking, pulse pressure, LVH and microproteinuria; only abnormal cardiac geometry had significant association with microproteinuria.

Our study has shown a significant association between LVH and microproteinuria in hypertensive patients; in conformance with different studies as quoted above. We can recommend microproteinuria as a screening procedure for target organ damage in newly diagnosed hypertensive patients so as to select our treatment strategy accordingly.

ABBREVIATION

BMI	-	Body Mass Index
LVH	-	Left Ventricular Hypertrophy
MAU	-	Micro Albuminuria
PCR	-	Protein – Creatinine Ratio
LV	-	Left Ventricle
BP	-	Blood Pressure
IVSd	-	Inter-Ventricular Septal Thickness at End - Diastole
LVISd	-	Left Ventricular Cavity internal Dimension at End- Diastole
PWTd	-	Posterior Wall Thickness at End - Diastole
LVMI	-	Left Ventricular Mass Index
RWT	-	Relative Wall Thickness
CVD	-	Cardio Vascular Disease
CAD	-	Coronary Artery Disease

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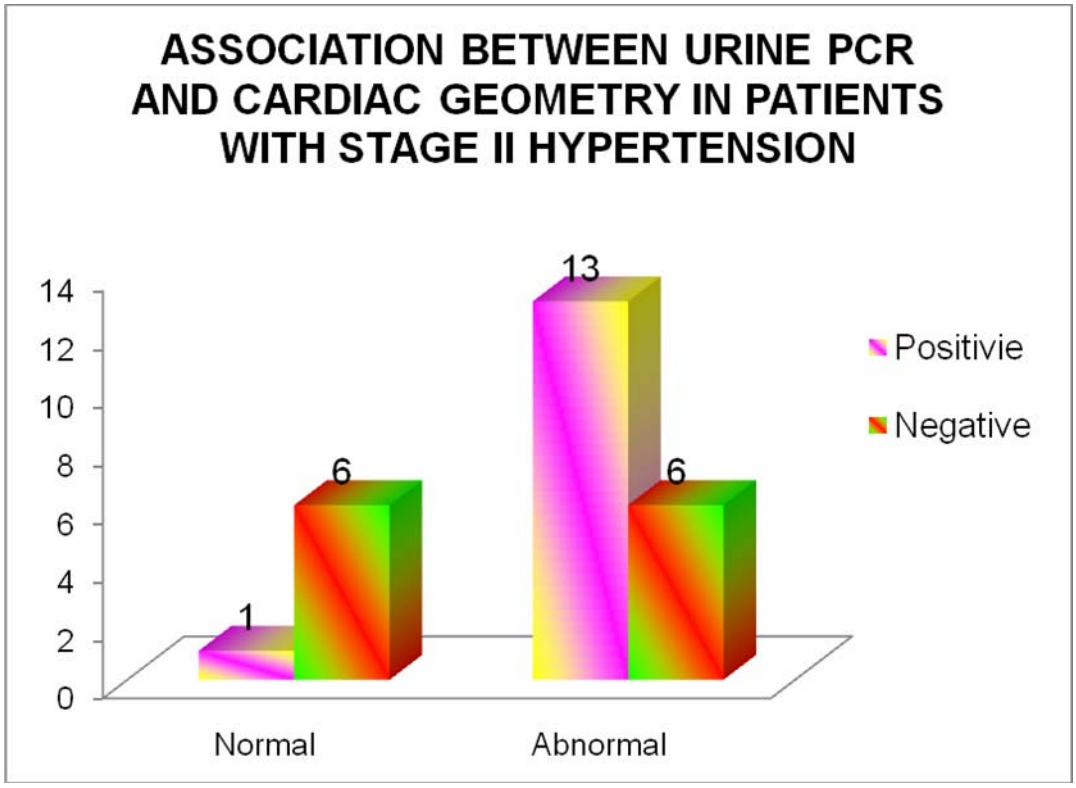
ASSOCIATION BETWEEN URINE PCR AND CARDIAC GEOMETRY IN PATIENTS WITH STAGE II HYPERTENSION
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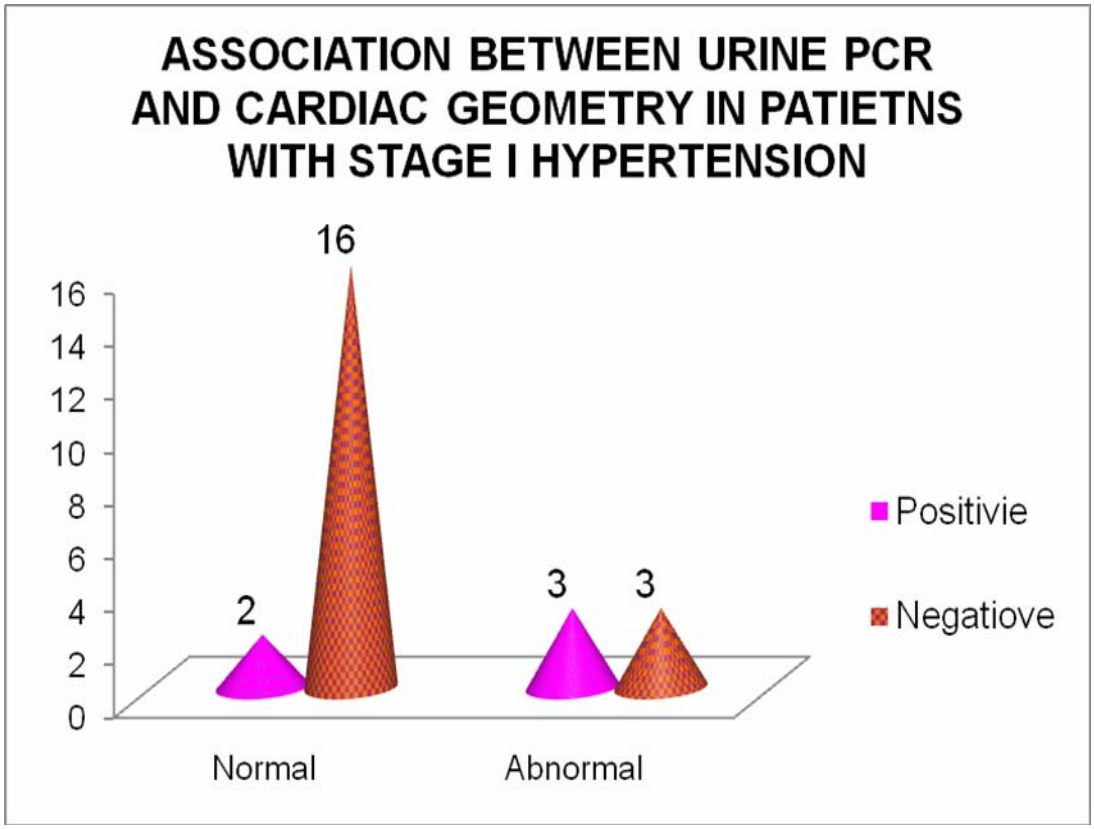
ASSOCIATION BETWEEN URINE PCR AND CARDIAC GEOMETRY IN PATIETNS WITH STAGE I HYPERTENSION
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PROFORMA FOR DATA COLLECTION

Name:		
Age:		
Sex:	Male /Female	

H/o Presenting complaint					
H/o Smoking					
Co-morbidities					
Examination					
Height:		Weight:		BMI:	
Pulse Rate:					
Blood Pressure:					
RS:				CVS:	
Abdomen:				CNS:	

INVESTIGATION						
RBS:		Blood Urea:				
S.Creatinine		S. Sodium/Potassium				
S. Fasting Cholesterol						
Urine	Albumin:		Sugar:		Deposits:	
ECG						
CXR-PAView						

ECHO CARDIOGRAPHY		
LVIDd	IVSTd	PWTd
EF		
Valves/RWMA		
Spot Urine PCR		