Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with hsCRP and Uric acid levels: A Cross-Sectional Study.

A Dissertation submitted in partial fulfillment of

M.D (General Medicine) branch I Examination of the Tamil Nadu

Dr. M.G.R. UNIVERSITY, CHENNAI

To be held in 2015

BONAFIDE CERTIFICATE

This is to declare that the dissertation entitled "**Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with hsCRP and Uric acid levels: A Cross-Sectional Study.**" is the bonafide original work done by **Dr. Muthukumaran. P.**, towards the M.D. Branch- I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai to be conducted in 2015.

Candidate

Dr.Muthukumaran .P.

Postgraduate Registrar,

Christian Medical College,

Vellore - 632004

C E R T I F I C A T E

This is to certify that the dissertation entitled "**Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with hsCRP and Uric acid levels: A Cross-Sectional Study.**" is the bonafide original work of **Dr. Muthukumaran. P.**, towards the M.D. Branch- I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai to be conducted in 2015.

Principal

Dr. Alfred Job Daniel

Professor,

Christian Medical College,

Vellore - 632004

C E R T I F I C A T E

This is to certify that the dissertation entitled "**Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with hsCRP and Uric acid levels: A Cross-Sectional Study.**" is the bonafide original work of **Dr. Muthukumaran. P.**, towards the M.D. Branch- I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai to be conducted in 2015.

Guide

Dr. O C Abraham,

Professor of Medicine,

Department of Medicine – I,

Christian Medical College,

Vellore – 632004.

C E R T I F I C A T E

This is to certify that the dissertation entitled "Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with hsCRP and Uric acid levels: A Cross-Sectional Study." is the bonafide original work of Dr. Muthukumaran. P., towards the M.D. Branch- I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai to be conducted in 2015.

Head of Department

Dr. Anand Zachariah,

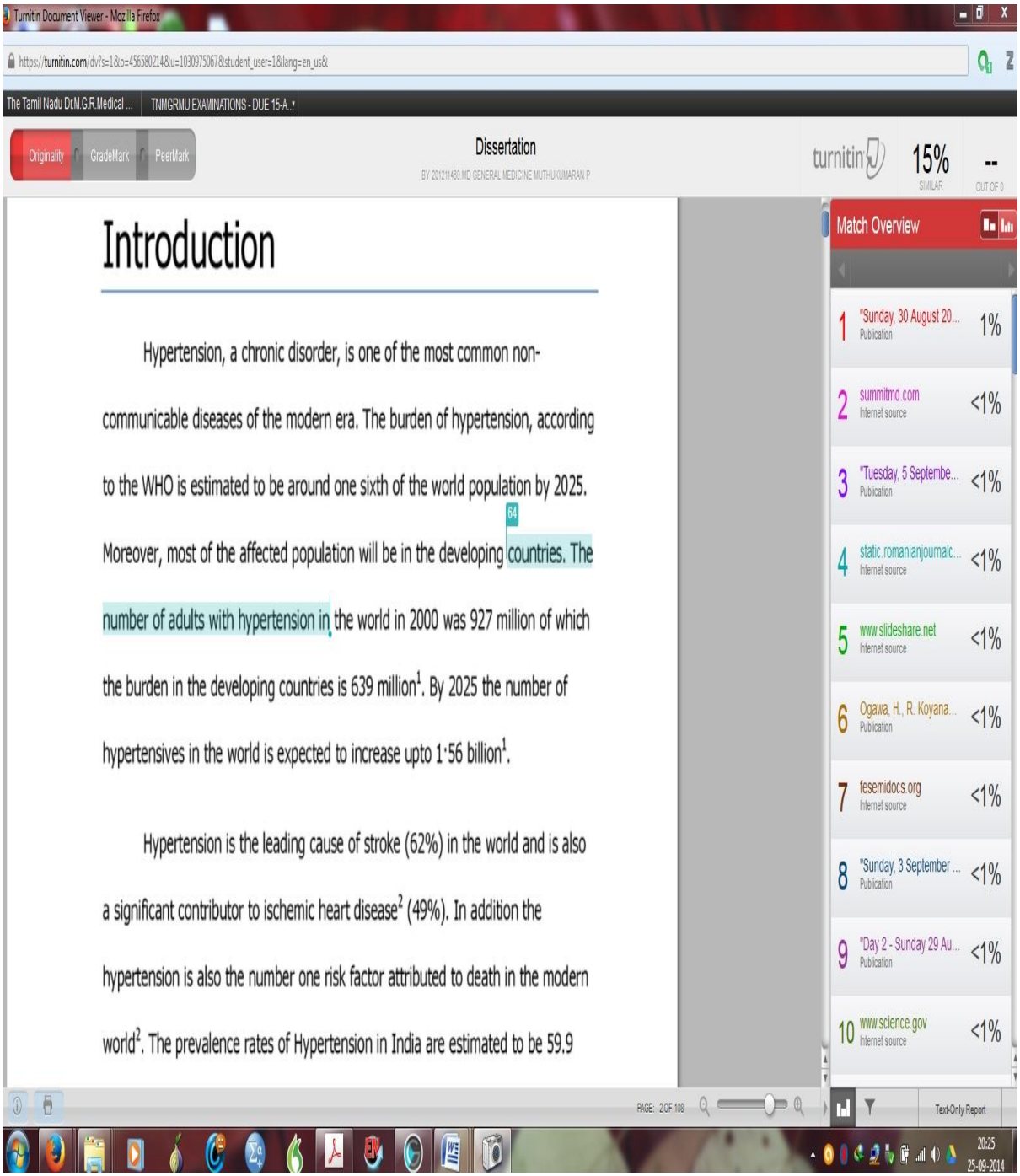
Professor and Head of Medicine,

Department of Medicine- I,

Christian Medical College,

Vellore – 632004.

Anti-Plagarism Software Report



turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201211460.md General Medicine MU...
Assignment title:	TNMGRMU EXAMINATIONS
Submission title:	Dissertation
File name:	Final-withoutbiblio.docx
File size:	904.62K
Page count:	108
Word count:	17,882
Character count:	99,138
Submission date:	25-Sep-2014 08:02PM
Submission ID:	456580214

Institute Research Board Approval Form

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Glas) (EDIN)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

November 25, 2013

Dr. P. Muthukumaran
PG Registrar
Department of Medicine
Christian Medical College
Vellore 632 002

Sub: **Fluid Research grant project:**
Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with HsCRP and Uric acid levels: A Cross-Sectional Study.
Dr. P. Muthukumaran, PG Registrar, Medicine, Dr. O.C. Abraham, General Medicine, Dr. Manjeera Jagannati, Dr. Ronald Albert Benton Carey, Dr. Thomas Isiah Sudarsan, Dr. Samuel G. Hansdak ,Dr. K.G.Selvaraj, Biostatistics.

Ref: IRB Min. No. 8487 [OBSERVE] dated 09.10.2013

Dear Dr. P. Muthukumaran,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with HsCRP and Uric acid levels: A Cross-Sectional Study." on October 9, 2013.

The Committees reviewed the following documents:

1. IRB application form
2. Curriculum Vitae' of Drs. P. Muthukumaran, O.C. Abraham, Manjeera Jagannati, Ronald Albert Benton Carey, Thomas Isiah Sudarsan, Samuel G. Hansdak, K.G.Selvaraj.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Glas) (EDIN)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

3. Data Collection form
4. Algorithm
5. Patient Information & Consent form (English, Hindi & Tamil)
6. No of documents 1-5

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on October 9, 2013 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. Paul Ravindran	PhD, Dip RP, FCCPM	Professor, Radiotherapy, CMCH.	Internal, Clinician
Dr. Susanne Abraham	MBBS, MD	Professor, Dermatology, Venerlogy & Leprosy, CMCH.	Internal, Clinician
Dr. T. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMCH.	Internal, Clinician
Dr. Simon Rajaratnam	MBBS, MD, DNB (Endo), MNAMS (Endo), PhD (Endo), FRACP	Professor, Endocrinology, CMCH.	Internal, Clinician
Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMCH.	Internal, Clinician
Dr. Ranjith K Moorthy	MBBS M Ch	Professor, Neurological Sciences, CMCH.	Internal, Clinician
Dr. Chandra Singh	MS, MCH, DMB	Professor, Urology, CMCH.	Internal, Clinician
Dr. Visalakshi	MPH, PhD	Lecturer, Dept. of Biostatistics, CMC.	Internal, Statistician

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Glas) (EDIN)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Dr. Denise H. Fleming	B. Sc (Hons), PhD	Honorary Professor, Clinical Pharmacology, CMCH.	Internal, Scientist & Pharmacologist
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. Ebenezer Ellen Benjamin	M.Sc, PhD	Professor, Maternity Nursing, CMCH.	Internal, Nurse
Dr. Vathsala Sadan	M.Sc, PhD	Professor, Community Health Nursing, CMCH.	Internal, Nurse
Rev. Joseph Devaraj	B.Sc, BD	Chaplaincy Department, CMCH.	Internal, Social Scientist
Mr. C. Sampath	B. Sc, BL	Advocate, Vellore, CMC	External, Legal Expert
Mrs. Pattabiraman	B. Sc, DSSA	Social Worker, Vellore	External, Lay person
Dr. Nihal Thomas	MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin), FRCP (Glasg)	Secretary IRB (EC)& Dy. Chairperson (IRB), Professor of Endocrinology & Addl. Vice Principal (Research), CMC.	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Glas) (EDIN)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Fluid Grant Allocation:

A sum of 38,960/- INR (Rupees Thirty Eight Thousand Nine Hundred and Sixty only) will be granted for 1 year.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

MINISTERED UNTO BUT TO MINISTER
CHRISTIAN MEDICAL COLLEGE
VELLORE
INDIA

CC: Dr. O.C. Abraham, General Medicine, CMC

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Acknowledgements

Right at the outset, I would like to thank my guide, Dr. O C Abraham from the bottom of my heart for his painstaking and meticulous efforts to guide me throughout the entire process of doing this dissertation. His inputs from the conceptualization to the writing of this dissertation have been extremely valuable and have helped me learn the art of doing a study. Without his support, I do not know if this dissertation would have ever seen the light of the day. I'm extremely thankful to sir for helping me throughout the study and also for teaching and making me understand that medicine is more than a science – It's an art to perfect.

Next I would like to thank Dr. Manjeera who also has been very instrumental in helping me from the stages of writing up to the research committee to the final stages of writing this dissertation. It was her detailed and meticulous comments and suggestions which have helped me a lot. I would also like to thank her for the time spent even at odd hours reviewing my work and for always being helpful when I needed support.

Then I would also like to thank Dr. Samuel George Hansdak for his guidance and his help in conducting the study. I am extremely grateful to him for letting me use the Medicine IV office for recruiting my patients and allowing me unfettered access to see and examine the study patients in the office. I would also like to thank him for the inputs into the development of the study concept and for being a constant source of encouragement during the study period. I would also like to thank my co-investigators Dr. Thomas Isiah Sudarsan and Dr. Ronald Albert Benton Carey who have reviewed the study from the beginning and have offered me many helpful insights.

I would also like to thank the secretarial staff in the Medicine IV office Ms. Maheswari and Ms. Ruth for helping me with organizing the patients. Without them it would have been impossible to recruit the patients. I thank them for the kindness and the efforts they took to pacify the patients who had waited for me when I was caught up with work elsewhere.

Finally, I want to thank my own colleagues in the department of medicine who have been extremely helpful in the recruitment of the patients. If it wasn't for their referral to me of all the new hypertensive patients, I would have never managed to get the patients recruited into my study.

I would also like to thank the whole Department of Medicine with all my friends and my teachers who have made this study possible and have helped me in various stages. Without them this study would not have been possible. And I would also like to thank all the patients who had made this study possible. It was because of their patience and their support; I was able to complete this study.

I would also like to thank my dad who has been my source of inspiration and my mom who has been my pillar of strength for so many years. And it's their unending love and support that has made it possible for me to reach the place I'm right now. And finally before I finish, I would like to thank the Almighty for his benevolent grace, for without which nothing would have been possible.

Table of Contents

Abstract

Title of the Abstract	: Prevalence of asymptomatic cardiac and renal damage in treatment naïve adult patients with Systemic Hypertension and its co-relation with hsCRP and Uric acid levels: A Cross-Sectional Study.
Department	: Department of General Medicine
Name Of The Candidate	: Dr. Muthukumaran. P.
Degree and Subject	: M.D. (General Medicine)
Name of the Guide	: Dr. O C Abraham

Objectives:

To look at the prevalence of asymptomatic cardiac and renal damage in newly diagnosed treatment naive adult patients with systemic hypertension and to study the co-relation between inflammatory markers, hsCRP and uric acid, with the asymptomatic organ damage in hypertensives.

Methods:

The study recruited 98 hypertensives who presented to the medicine OPD and were willing to participate in the study. The patient data was collected with a questionnaire and the blood pressure, height, weight and abdominal circumference were measured in these patients. The blood investigations including fasting glucose, creatinine, electrolytes and lipid profile were done in these patients. The patients also underwent electrocardiography and echocardiography with the documentation of M-Mode values. The albumin creatinine ratio, eGFR and the LV Mass index were also subsequently calculated in these patients.

Results

The prevalence of microalbuminuria was 31.9% and the prevalence of Left ventricular Hypertrophy was 29.59% of the study population. The uric and hsCRP were not related to asymptomatic organ damage when analysed. The hsCRP was however very significantly related to body mass index ($p=0.000$) and abdominal circumference ($p=0.003$) on bivariate analysis. This association of hsCRP to elevated body mass index and abdominal circumference might be due to its association with the metabolic syndrome.

Conclusion

Almost one third of the newly detected hypertensives in the study population had evidence of asymptomatic cardiac and renal damage. However, the asymptomatic cardiac and renal damage was not related to elevated inflammatory markers in these patients. The elevated hsCRP in the study population might be related to an underlying metabolic syndrome.

Keywords

Microalbuminuria, LV Mass Index, Asymptomatic organ damage, newly detected hypertension, prevalence of asymptomatic organ damage.

Introduction

Hypertension, a chronic disorder, is one of the most common non-communicable diseases of the modern era. The burden of hypertension, according to the WHO is estimated to be around one sixth of the world population by 2025. Moreover, most of the affected population will be in the developing countries. The number of adults with hypertension in the world in 2000 was 927 million of which the burden in the developing countries is 639 million[1]. By 2025 the number of hypertensives in the world is expected to increase upto 1·56 billion[1].

Hypertension is the leading cause of stroke (62%) in the world and is also a significant contributor to ischemic heart disease[2] (49%). In addition the hypertension is also the number one risk factor attributed to death in the modern world[2]. The prevalence rates of Hypertension in India are estimated to be 59.9 and 69.9 per thousand males and females, respectively in urban areas and 35.5 and 35.9 per thousand males and females respectively in the rural areas. Thus we know that it's a disease of urbanization[3].

Furthermore, with the estimated prevalence of hypertension being very high in India, it is necessary to study the complications associated with hypertension among the Indian population. Hypertension has a very prolonged asymptomatic period. However, it is during this period when the silent end organ damage happens without the patient developing any clinical manifestations. Most of the times, Hypertension is diagnosed when the patients present with complications. The long latent period between the development of asymptomatic

organ damage and the clinical manifestation gives us ample time to initiate measures to prevent the development of target organ damage.

There are no studies which have regarded the prevalence of asymptomatic organ damage in patients presenting with systemic hypertension for the first time. Further, the presence of asymptomatic organ damage also plays a vital role in patients with stage I Hypertension where the treatment of the condition varies based on the presence or absence of organ damage. Hence this study was undertaken to study prevalence of asymptomatic organ damage in systemic hypertension at the time of presentation. This will give us valuable data regarding the need to assess end organ damage at the first presentation of hypertension. This is particularly important in our country given the fact that the screening programs for non-communicable diseases in our country are virtually non-existent. The burden to the society due to the complications of hypertension can be reduced by early diagnosis and regular screening programs at the community level.

Why Uric acid?

Uric acid has been linked to hypertension in early 1800s[4]. But the concept of uric acid as a factor producing hypertension was conceptualized by studies done in 2000 on rats[5]. The High uric acid levels were found to induce changes in the endothelium, which ultimately lead to Systemic hypertension. Uric acid has since been proven as an independent risk factor for the development of hypertension and increased uric acid levels has been implicated in the development of complications[6].

A meta-analysis of data taken from multiple trials done on hypertensive patients to study the cardiovascular outcomes with uric acid levels showed that for every standard deviation increment of uric acid there was a significantly increased cardiovascular risk. This increase in the cardiovascular risk was equal to that of the increase caused by elevated blood pressure and elevated total cholesterol[7].

Uric acid causes cardiovascular damage due to various pathophysiological mechanisms. The elevated levels of serum uric acid increase the proliferation of the vascular smooth-muscle cells[5]. The elevated uric acid also suggests that there is an activation of an inflammatory pathway as the process of formation of uric acid results in the generation of many free radicals. In addition, uric acid is formed from purine analogues, the degradation of which is increased when there is a destruction of nucleated cells, which includes all the inflammatory cells. The elevated uric acid also by itself causes activation of inflammatory pathways[8].The other mechanism by which uric acid causes cardiovascular damage is by promoting platelet activation[9].

Uric acid has also been shown to be a good surrogate marker to diagnose tissue ischemia and is also associated with endothelial dysfunction[10]. High uric acid levels have also been shown to play a role in the development of atherosclerotic lesions[11]. The main pathophysiological mechanism by which uric acid causes hypertension is postulated to be the renal ischemia which occurs secondary to hyperuricaemia. This reduction in the renal blood flow causes hypertension by renal salt conservation and the activation of the Renin-Angiotensin-Aldosterone System.

Why HsCRP?

HsCRP has evolved as the most reliable marker of vascular inflammation and is considered the prototype downstream marker of inflammation. Out of all the inflammatory markers studied in hypertension, including IL-6, IL-1ß and TNF-α, HsCRP was found to be the most sensitive and specific marker associated with hypertension. This association was well proven in many studies on Hypertension[12].

There is a continuous(linear) relationship between the HsCRP and the Blood pressure[13].And the risk of developing hypertension increases with increasing HsCRP levels.

HsCRP may also predict the risk of developing hypertension in patients who are normotensive and the risk increases significantly in those with elevated HsCRP[14]. King *et al.* showed that prehypertensive population (Systolic BP 120-139 mm Hg and/or diastolic BP 80-89 mm Hg) had a significant number of people with elevated HsCRP compared to normal individuals[15] (27.4% *vs*. 19.8%; $p<0.05$).

In addition, CRP is also shown to down regulate endothelial Nitric Oxide synthase(eNOS) mRNA transcription in the endothelium. This results in a decrease in the release of nitric oxide both basally and on stimulation[16]. Also, reduced nitric oxide at the endothelial level is postulated to be an important step in the development of Hypertension, atherosclerotic events and in vascular catastrophes[17].

Rationale

From the above it is very clear that there is a need to study the prevalence of asymptomatic organ damage in India, though we have a huge burden of hypertensives considering that India has one sixth of the world population. The screening programs for noncommunicable diseases are in their infancy in our country. This makes it important to study the prevalence of asymptomatic organ damage in patients who present with hypertension for the first time.

The role of inflammatory markers in hypertension is not very well studied in our population, though there is enough evidence to implicate HsCRP and Uric acid levels in hypertension. This study was done to study the prevalence of asymptomatic target organ damage in the Indian population and the feasibility of using Uric acid and HsCRP as surrogate markers to predict target organ damage in newly diagnosed Hypertensives.

AIMS OF THE STUDY

Aims of the study

1. To assess the prevalence of asymptomatic organ damage in patients with Hypertension.

2. To assess the role of inflammatory markers in causing the asymptomatic organ damage in patients with hypertension.

OBJECTIVES OF THE STUDY

Objectives of the study

Primary Objective

- To study the prevalence of asymptomatic cardiac and renal damage in adult patients with treatment naïve systemic hypertension according to ESC 2013 criteria

Secondary objectives

- To study the factors associated with asymptomatic cardiac and renal damage.
- To determine the sensitivity and specificity of hsCRP and Uric acid to predict the asymptomatic cardiac and renal damage
- To determine the variations in asymptomatic cardiac and renal damage in patients with varying levels of hsCRP / Uric acid at the time of diagnosis.
- To determine the variations in the asymptomatic target organ damage with respect to mean resting heart rate.

REVIEW OF LITERATURE

Review of literature

The pandemics which have ravaged the world have been changing from time immemorial. The initial pandemics in the undeveloped world where predominantly infectious. The pandemics of influenza, plague and smallpox is very well-known. The other major causes of death before the Industrial Revolution where famine and floods and other natural disasters. This era has represented a change in the fundamental way the humans have conquered the elements of the nature. The quest for supremacy of humankind over the nature has brought with it its own set of challenges. One of the modern pandemics which we face today is the burden of noncommunicable diseases which have been brought about by the unhealthy lifestyle, sedentary activities, dietary changes, and the reduction in the amount of manual labor due to the increase in the machines. All this has contributed much to the modern day epidemics of diabetes mellitus, hypertension and coronary artery disease.

Hypertension befits an important recognition amongst these pandemics. The amount of population suffering from hypertension is really immense The global burden of hypertension in 2000 was estimated to be around 26.4 percentage of the adult population and it was estimated 972 million people were hypertensives. This number was predicted to grow to 1.56 billion people by 2025[18]. The rapid rise in the incidence of hypertension can be attributed to increased screening and unhealthy lifestyle practices.

The world health report 2002 states that suboptimal blood pressure is a leading cause of stroke and it is also an important risk factor for cardiac failure[2]. Hypertension is one of the leading causes of Disability adjusted life years (DALY's). The organ damage caused due to hypertension can lead to disastrous consequences and most of them are not treatable once they occur. The best way to manage hypertension is to detect hypertension early and to institute treatment to prevent the development of complications.

Definition of hypertension:

Hypertension has been defined as the systolic blood pressure of ≥ 140 mmHg and/or diastolic pressure ≥ 90 mm Hg, according to the European Society of hypertension guidelines 2013. This definition of hypertension almost parallels itself with the definition given by other authorities like the JNC 7. This definition of hypertension, however, needs to be taken with deliberate caution. It has been known that any blood pressure is about 115/75 has been associated linearly with increased target organ damage[2]. However, it is at the cutoff of 140/90 that the treatment of blood pressure with antihypertensives produces significant changes in morbidity and mortality and hence this is chosen as the cutoff for elevated blood pressure or hypertension.

Normal blood pressure is defined as a blood pressure of less than 120/80. The value between the normal blood pressure and hypertension is defined as a pre-hypertensive stage where these people are at risk of end organ damage and for transformation into hypertensives with progressive elevation of blood pressure.

The definition of blood pressure also brings into account the staging of hypertension. The hypertension has been staged in many different ways. Here in the study, we follow the European Society of hypertension grading of hypertension for the sake of uniformity. The table showing the grade of hypertension is given below (Table 1.).

Table 1. Grading of Hypertension

Grade	Systolic BP (mm Hg)		Diastolic BP (mm Hg)
Grade I	140-159	And / Or	90-99
Grade II	160-179	And / Or	100-109
Grade III	≥180	And / Or	≥ 110

The Global Burden of Hypertension

The burden of hypertension across the world according to the 2000 estimates was around 26.4% of the world population[2]. Hypertension was alone responsible for around 7.6 million premature deaths, accounting for 13.5% of the global total deaths [19]. It was also responsible for 92 million disability adjusted life years DALY's contributing to around 6% of the global disability adjusted life year DALY' [19]. It was also responsible for 54% of the stroke patients making it the number one cause of stroke and around 47% of patients with ischemic cardiac disease[2]. And paralleling the global trends in hypertension, which was more in the

developing countries, 80% of the disease burden occurred in the developing world[19].

In a study done in east Asian population, diastolic blood pressure co-related well with the increased risk of developing a stroke and ischemic heart disease and the reduction of the diastolic blood pressure by 7% when it is above 95mm Hg resulted in a significant reduction in the incidence of stroke and ischemic heart disease[20].

A recent study done in rural China, which included 16,364 residents showed the prevalence of hypertension was around 43.8% and only around 26.2% were aware that they had hypertension and only 22% were on treatment. Out of all the hypertensives only a mere 3.9% achieved adequate blood pressure control[21].

The Indian Burden of Hypertension.

The diseases in the world have gone through an epidemiological transition. The transition not only occurs in the type of diseases but also among the group of disorders. The initial cardiovascular disorders prevalent among the Indian population were the infective disorders like the rheumatic heart disease, however, with the epidemiologic transition the lifestyle diseases like hypertension and ischemic heart disease predominate Indian scenario and most of the South Asian countries including China[22].

In India cardiovascular diseases caused approximately 2.3 million deaths in 1990 and the number is expected to double in the next 30 years. Hypertension is

directly responsible for more than half of all stroke deaths in India and a quarter of all ischemic cardiac deaths in India[23]. The prevalence of hypertension in India has been increasing very steadily. It is increased from approximately 1 to 5% in the 1950s to 12 to 15% in the 90s[20]. The prevalence of hypertension is much higher in the urban population, compared to the rural population, however the gap is getting smaller and smaller as the years go on. This is probably due to the change in lifestyle of the population.

Most of the studies on hypertension in India are from the western India. One of the studies done in western India assessed 2122 subjects, who were more than 20 years of age and it showed the prevalence of hypertension was around 30% in men and 33% in women. By JNC V criteria and a multivariate analysis showed that age, higher BMI and smoking were independently associated with prevalence of hypertension. The prevalence of hypertension was also found to increase along with the age in both men and women[24].

A recent study in Chennai showed the crew prevalence of hypertension overall in Chennai was around 21.1% and an age standardized prevalence of around 17%. The study also showed hypertension were significantly associated with age, body mass index and glucose intolerance. The high prevalence hypertension in an urban city of South India shows that hypertension is a very common in the south indian population[25].

Another study done in Kerala showed the prevalence of hypertension was around 18.9% between the ages of 25 to 64 and 33.5% between the ages of 45 to 64 years. The prevalence was higher in males than in females in the younger

population, while it evened out as the age of the population increased. Central obesity was found to be a very strong predictor of hypertension in these patients[26].

End organ damage due to hypertension

End organ damage in hypertension is a major cause of morbidity and mortality. The end organs usually affected by hypertension are the heart, the kidney, and the blood vessels. The hypertensive end organ damage in the heart manifests as the hypertrophy of the left ventricle, which leads progressively to a left ventricular systolic and diastolic dysfunction. The hypertensive damage of the kidney leads to the microalbuminuria in the early stages due to intraglomerular hypertension and sustained blood pressure elevation leads to hypertensive nephrosclerosis and eventually to chronic kidney disease. The hypertensive damage to the endothelium of the blood vessels initially leads to the stiffening of the vessel walls. This is reflected by an increase in the central aortic stiffness which is measured by the carotid-femoral pulse wave velocity. Long-term hypertension is also known to cause the increase in the carotid intimal medial thickness. The thickening of the blood vessels leads to a decrease in the compliance of the vessel and is responsible for the vascular events in hypertension[27].

Asymptomatic organ damage in hypertension:

The asymptomatic organ damage has been defined in the ESC guidelines for a few years now. The concept of asymptomatic damage derives itself from the fact that there is a long latent period between the development of hypertension

and the end organ damage, which is a serious cause of morbidity and mortality. Hence, it's imperative to identify people who have developed subclinical target - organ damage to treat them to reverse the condition and to prevent the development of complications.

The asymptomatic organ damage is characterized by the measurement of microalbuminuria, hypertrophy by electrocardiography or echocardiography, the carotid intimal medial thickness and the carotid femoral pulse wave velocity. All these four indicators of asymptomatic organ damage have been independently linked to cardiovascular risk in patients with hypertension. Hence, it's imperative in clinical practice to look for the markers in patients with hypertension, to categorize the cardiovascular risk and to effectively manage them.

Prevalence of Asymptomatic Organ damage in Hypertension:

The prevalence of subclinical target organ damage was found initial study to be very high. The incidence of left ventricle hypertrophy was around 46%, the prevalence of carotid abnormalities was around 31% and the prevalence of microalbuminuria was around 12%[28]. This is very high when compared with the normal population. The prevalence of very high levels of organ damage in newly detected hypertensives highlights the importance of identifying and treating them at the earliest possible time to prevent the development of complications. The Subclinical target organ damage was not related to age nor to the duration of hypertension before diagnosis. The organ damage is however related to body

mass index, serum triglycerides and in women with higher serum uric acid levels.[28]

Microalbuminuria in Hypertension

Microalbuminuria is a very early and are very sensitive marker of renal damage not only in patients of diabetes mellitus but also in patients with essential hypertension. Microalbuminuria is an independent predictor of cardiovascular events in hypertensive patients. Microalbuminuria along with elevated inflammatory markers like HsCRP have been shown to be elevated in patients with metabolic syndrome and this probably denotes a high-risk population who were more prone to end organ damage. From JNC 7 microalbuminuria has been incorporated as one of the major cardiovascular risk factors[29,30].

In a cohort study done between 1994 and 1999 which compared the microalbuminuria in patients with diabetes and in patients without diabetes and looked for the relative risk for all-cause death and hospitalization for congestive cardiac failure showed that the relative risk in patients with and without diabetes mellitus did not show any difference. The risk of cardiovascular events was similar in those with diabetes mellitus and in those without diabetes mellitus, even after adjusting for all other cardiovascular risk factors[31].

In another study revealed microalbuminuria and peripheral arterial disease as risk factors for increased cardiovascular disease and all-cause mortality. It was found that the relative risk of microalbuminuria was 3.2 when compared to the relative risk of peripheral artery disease which was 2.4 in causing an increased cardiovascular mortality. The study also showed that the results were independent

even after adjusting for age, sex, diabetes, hypertension, HDL and triglycerides, body mass index, smoking habits and pre-existing ischemic heart disease.This study showed that the risk is high for microalbuminuria to cause an increase in the cardiovascular mortality. Microalbuminuria and peripheral artery disease were found to be mutually independent risk factors for increasing cardiovascular mortality[32].

In the Islington Diabetes survey, microalbuminuria was found in 23% of newly diagnosed diabetic subjects and in 9.4% of non-diabetic subjects. It was found that there was a weak correlation between microalbuminuria and systolic and diastolic pressures. The coronary artery disease was found in 74% percentage of subjects with microalbuminuria. Even after adjusting for these factors, including diabetes, impaired glucose tolerance, systolic and diastolic blood pressures, smoking, age, sex, ethnic origin and BMI, urine microalbuminuria demonstrated an increased risk for development of coronary artery disease. The odds ratio was 6.38 for development of coronary artery disease. The study also showed microalbuminuria was an independent predictor for the development of coronary artery disease[33].

The life study, which was done in an elderly population with left ventricle hypertrophy and were assigned to receive losartan or atenolol. The study showed that for every tenfold increased in urine microalbuminuria the hazard ratios increased very markedly. For every tenfold increase in microalbuminuria, the cardiovascular mortality increased by 97.7%, stroke by 51%, and myocardial

infarction by 45% and all-cause mortality by 75%. The results were independent of whether the patients were diabetic or non-diabetic[34].

In the third Copenhagen city heartstudy, whichh was conducted in between 1990 to 1994 and followed up till 1999. The population included men and women between 30 to 70 years of age and they had microalbuminuria estimated. During the follow-up 192 patients had died due to coronary artery disease out of a total of 276 deaths, which was found in the study population. Microalbuminuria in the upper quartile was associated with an increased risk of coronary artery disease(RR 2.0, 95%CI - 1.4-3.0) and death (RR 1.9, 95% CI 1.5-2.4). This association was independent of age, creatinine clearance, dyslipidaemia, hypertension or diabetes[35].

Another study done in Denmark involved identifying patients with hypertension between 1983 and 1984 and had a quantification of urine microalbumin at the time of the study. They were followed up for a period of 10 years and ischemic heart disease in them was studied using national hospital and death certificate registers. The study showed that microalbuminuria was very strongly associated with ischemic heart disease with the relative risk of 3.5 when adjusted for all other risk factors. The study also showed that borderline hypertensive patients were also at increased risk of developing ischemic heart disease[36].

All the above studies show that microalbuminuria is an increased risk factor for development of coronary artery disease and is an independent predictor for cardiovascular risk irrespective of whether patient is diabetic or not. The studies

also showed even in the general population urinary microalbuminuria is associated with an increased cardiovascular risk. Thus the identification of microalbuminuria and treatment of microalbuminuria is of extreme importance in the management of hypertension.

In a recent study done in Tamil Nadu the prevalence of microalbuminuria in hypertensives was studied. The study included a majority of patients with stage II hypertension and 64 percentage of the population had microalbuminuria. There was also a significant association between the different hypertensive grades and the microalbuminuria. The study showed that microalbuminuria in hypertensives is not a rare entity[37].

Reduction in microalbuminuria causes reduction in the cardiovascular risk

In the LIFE study, the patients were divided post hoc into 4 strata based on urine microalbumin. The urinary microalbumin was estimated at the baseline and at 1 year of enrollment into the study. The study patients were divided into 4 groups based on microalbuminuria as (1) The Low baseline/low 1 year, (2) Low baseline/High 1 year, (3) High base line/Low 1 year and (4) High baseline/high 1 year. Among the four groups the incidence of the cardiovascular eventswase 5.5%, 8.6%, 9.4% and 13.5% respectively. The results conclusively showed that there was a stepwise reduction in the risk with the decrease in the microalbuminuria. This is independent of all the other factors which could confound the results[38].

Left ventricular hypertrophy in hypertension

Left ventricular hypertrophy is one of the commonest complications associated with the patients with hypertension. The incidence of left ventricular hypertrophy ranges between 16 to 74% in echocardiographic studies and from 1 to 44% in ECG studies.

A comprehensive review of 20 studies with 48,545 participants, which are published between 1962 to 2000 showed that the adjusted risk of future cardiovascular events associated with LVH was found to be between 1.5 to 3.5 with the weighted mean risk ratio of 2.3. The all-cause mortality in the same study was found to be 1.5 to 8 with a mean risk ratio of 2.5. The study showed that there was a trend towards was cardiac outcomes with left ventricular hypertrophy[39].

In a study published in 2000, 1925 hypertensives with no complications underwent an echocardiogram for calculating the LV mass and an ambulatory blood pressure monitoring. They were followed up for a period of four years. During follow-up there were 181 major cardiovascular events. The study participants were divided based on the LV mass into five quintiles separately for both men and women. The study showed that in men and women the cardiovascular event rates vary between .8/100 patient years in the lowest quintile to 4.3/100 patient years in the highest quintile. These results were independent of all the other risk factors and further there was a risk even below the current upper limit of normal for the LV mass in the study subjects. The study showed that there

was a significant risk associated with LV hypertrophy in patients with hypertension[40].

The increased LV mass is also associated with the risk of sudden cardiac death in patients with hypertension. In a study done with 50 hypertensive patients with LVH and 50 normotensive controls the incidence of non-sustained ventricular tachycardia was significantly increased in patients with left ventricular hypertrophy. This was also associated with high prevalence of ST-T abnormalities on the electrocardiography. The clinical importance of these non-sustained ventricular tachycardia was not known .However the significant number of patients showing non-sustained ventricular tachycardia might lead us to say that it might be the cause of fatal arrhythmia in these patients[41].

In another study published in 1986, the study was done on 140 men with uncomplicated hypertension to understand the risks of left ventricle hypertrophy and cardiovascular events. The study included both echocardiographic and electrocardiographic criteria for detection of left ventricular hypertrophy. The study showed that morbid cardiovascular events occurred in patients with LV hypertrophy at the rate of 4.6 per 100 patient years when compared to the patients with normal ventricular size where the incidence was 1.4 per 100 patient years. The electrocardiography showed very few patients with left ventricle hypertrophy and was not found to be of any predictive value. Multiple logistic regression showed that LV mass index was the best independent predictor of future cardiovascular events[42].

Reduction of left ventricle hypertrophy and outcomes:

The reduction in left ventricle hypertrophy has been associated with improved outcomes in patients with hypertension. There are multiple studies which have shown that as the LVH decreases the risk of adverse cardiac events also decreases substantially in this population.

In one of the studies published in 2002, thousand 326 patients with systemic hypertension who had ECG evidence of LVH were recruited from the Nordic countries, the United States and United Kingdom. These patients were randomly assigned to receive either losartan or atenolol with hydrochlorothiazide as second antihypertensive agent. They were followed up for a mean duration of 4.7 years. The results showed that the cardiovascular outcomes were reduced by 25% with losartan when compared to atenolol. The patients who got losartan had lower cardiovascular mortality and low total mortality. Losartan decreased the ECG left ventricular hypertrophy more than atenolol. The study showed that losartan was much superior to beta-blockers in treating patients with left ventricular hypertrophy and hypertension[43].

Another study, which looked that losartan and atenolol in causing regression of left ventricular hypertrophy was the LIFE study. The study included a total of 960 patients with essential hypertension and LVH on screening electrocardiogram. Of the 960 patients, 457 were treated with losartan and 459 were treated with atenolol. The participants with followed up for more than one year to study LV mass index. The losartan-based therapy reduced the LV mass index by 21.7 g/m^2 compared to 17.7g/m^2 in the atenolol group. This was found

to be statistically significant. This also showed that angiotensin receptor blockers are much better than beta-blockers in causing regression of left ventricular hypertrophy[44].

The 4E- left ventricular hypertrophy study was done to study the effects of eplerenone, enalapril and the combination of enalapril/eplerenone. The study was done in 202 patients with left ventricle hypertrophy and hypertension. The change in LV mass was studied with MRI. The change in LV mass from baseline was significant in all the groups. However enalapril alone (-19.9 g/m^2) reduced LV mass more than eplerenone (-14.5 g/m^2) but the combination of enalapril with eplerenone (-27.2g/m^2) reduced the LV mass to the maximum. The study showed that the combination of eplerenone with enalapril was much better than either one of them in causing the regression of left ventricular hypertrophy[45].

Another large study, which looked at the effect of ACE inhibitors on the regression of left ventricular hypertrophy, was the HOPE study. The study included 676 patients with left ventricle hypertrophy into two arms the ramipril group and the placebo group. There was also 7605 patients did not have left ventricle hypertrophy, 3814 in the ramipril group and 355 in the placebo group. At the end of the study 8.1 percentage of patients in the ramipril group had a development or persistence of left ventricle hypertrophy and 9.8 percentage in the placebo group had developed of left ventricle hypertrophy. The patients in the ramipril group also had increased regression of left ventricular hypertrophy compared with the placebo group. Both of these results were statistically significant. The effects of ramipril were also found to be independent of the blood

pressure changes. The patients in the ramipril group also had decreased cardiovascular death, myocardial infarction and congestive cardiac failure. The study against shows the regression of left ventricle hypertrophy reduces the incidence of morbid cardiovascular complications[46].

Another meta-analysis looked at the effect of various medications in reversal of left ventricle hypertrophy in essential hypertension. This study showed that the decline in left ventricle mass was directly proportional to the decline in blood pressure and longer the duration of antihypertensive therapy. The study also showed after adjustments for the different durations of treatment the left ventricular mass decreased the maximum with ACE inhibitors (13%), followed by calcium channel blockers (9%), followed by beta-blockers (6%) and diuretics (7%). There are similar tendencies for decrease with relation to the left ventricle wall thickness also[47].

Patterns of left ventricular geometry in patients with systemic hypertension

Left ventricular hypertrophy is one of the cardinal manifestations in patients with hypertension. The left ventricular hypertrophy is one of the adaptive changes which occurs in the natural history of hypertension. The initial well-known component of hypertensive organ damage was the left ventricular hypertrophy. However, as time progressed by people also realized that hypertension also causes multiple other geometries based on the hemodynamic stressors which are present in the individual. Based on this concept, the LV geometries were described as normal, concentric remodeling, concentric hypertrophy and eccentric

hypertrophy. The diagnoses of these geometries were made on the basis of an echocardiogram. The LV mass index and the relative wall thickness help define the of the various LV geometries (Table 2).

Table 2. Left ventricular geometries in Hypertension

Parameter	LV Mass Index	Relative Wall Thickness
Normal	Normal	Normal
Concentric remodelling	Normal	**Increased**
Eccentric remodelling	**Increased**	Normal
Concentric Hypertrophy	**Increased**	**Increased**

Both LV mass index and relative wall thickness are calculated from readings got from the M-mode in the echocardiography. The formula for calculating both these indexes are described in the methodology separately.

Pathophysiology of the various LV geometries

The various LV geometries are considered to be adaptive changes in the heart due to the various changes in the haemodynamic status of the patients in hypertension.

In patients with concentric remodelling, the remodelling occurs without the thickening of the wall of the chamber and the chamber becomes more elliptical. This adaptive remodeling causes the LV to pump more efficiently and maintain the

cardiac output. Concentric remodeling occurs predominantly in patients with increased afterload and with a reduced venous return or preload[48].

The second LV geometry is the eccentric remodeling, this happens when the LV mass increases and the thickness of the walls compared to that of the internal diameter of the LV remains constant. This shows that there is an increased venous return with a reduced afterload. This results in a dilatation of the left ventricular chamber to accommodate the increased venous return. This is essentially the remodeling that occurs due to volume overload[48].

The third LV geometry is one which is well described and is the most serious adverse prognostic factor in patients with hypertension. It is the concentric hypertrophy of the left ventricle. This happens in patients with an increased afterload and increased venous return. This results in an increase in the absolute LV mass and also an increase in the thickness of the left ventricular wall compared to the internal diameter of the left ventricle. This is the classical geometry associated with patients with hypertension[48].

All of the three ventricular geometries are associated with increased cardiovascular risk. However the highest risk is in patients with concentric hypertrophy. The patients with eccentric hypertrophy and concentric remodelling have an intermediate risk for cardiovascular events in patients with hypertension[48].

In a study done in 43 asymptomatic hypertensive patients and 43 normal individuals who were well matched showed that there was a significant difference in left ventricular mass and relative wall thickness in patients with hypertension.

The LV mass, relative wall thickness and absolute wall thickness were increased significantly in patients with hypertension[49].

In a study published in 2001, the LV geometry in patients with and without hypertension was studied. The patients were evaluated for systolic and diastolic function is with M-mode echocardiography. The patients were divided into four groups as normal LV geometry, concentric remodelling, eccentric hypertrophy and concentric hypertrophy. The LV systolic function as measured by mid-wall fractional shortening was found to be decreased in patients with concentric remodelling and concentric hypertrophy of the heart. The LV diastolic function as measured by the iso-volumetric relaxation time was also decreased in the above groups. In a multivariate analysis systolic blood pressure, end-systolic wall stress and relative wall thickness were independently found to be related to reduction in mid-wall fractional shortening[50].

Carotid Intimal medial Thickness and Hypertension

A Study was done in Iowa in a representative cohort of people were followed from childhood to the age group of 33 to 42 years which consisted of 346 men and 379 women. The study measured the carotid intimal medial thickness in all these patients are 12 points. A medical questionnaire was also completed and the rest factor analysis was done. The study showed that in men who LDL-cholesterol HDL cholesterol and diastolic blood pressure were predictive of the increased carotid intimal medial thickness[51].

In a study published in 2002, a study was done to study the association between carotid intimal medial thickness and left ventricular mass index in

children who were referred with elevated blood pressure. The study was conducted in 32 subjects who were untreated new referrals to pediatric hypertension clinic. The LV mass index is calculated by M-mode echocardiography measurements and the carotid artery duplex ultrasound were performed in these patients. The results showed that the prevalence of LVH and increased carotid intimal medial thickness was around 41% and 28% respectively. The subjects with an increased carotid intimal medial thickness had a higher LV mass index (46.8 g/m^2 vs 31.4g/m^2). Carotid intimal medial thickness also positively correlated with body mass index interventricular septal thickness and posted wall thickness. All the results in a study were adjusted for age, sex and BMI[52].

The Rotterdam study a case-control approach was done among 7983 patients is more than 55 years. At the base line between March 1990 to July 1993 there was a baseline carotid intima medial thickness, which was measured and stored on videotape. Determination of incident myocardial infarction and stroke was predominantly based on hospital discharge records. A total of 98 myocardial infarction and 95 strokes occurred before 1994. The intimal medial thickness was measured in all the case subjects and a sample of thousand 373 patients who did not have a myocardial infarction. The results showed that the stroke risk increased with an increasing intimal medial thickness. For the myocardial infarction the odds ratio was around 1.43(95% CI 1.16 to 1.82). The study showed that there was an increased risk from both cerebrovascular events and coronary events with increased carotid intimal medial thickness[53].

The European Lacipidipine study of atherosclerosis was prospective, randomized, double-blind multinational trial which was published in 1998. The study compared for your treatment based on a calcium antagonist lacidipine with atenolol on development of carotid artery wall alterations in patients with mild to moderate hypertension. The study cohort included 2259 patients. The carotid intimal medial thickness was measured at 12 sites and was expressed as the mean that these sites. A multivariate analysis was done to find the clinical variables which correlated with increased carotid intimal medial thickness. The carotid intimal medial thickness was found to be correlated in the following order with age, 24-hour ambulatory pulse pressure, sex, LDL-cholesterol, serum triglycerides, smoking and systolic blood pressure. This also shows that carotid intimal medial thickness is found to correlate well with patients with hypertension and they predict the risk of end organ damage[54].

Another study, verapamil in atherosclerosis and hypertension study was done to see the effect of verapamil and chlorthalidone on carotid intimal medial thickness in patients with hypertension. The study 498 hypertensive patients from Italian centers were randomized to either verapamil or chlorthalidone. A B mode ultrasound scan was done at baseline and at three months, 12 months, 24 months, 36 months and at 48 months of treatment. The carotid will medial thickness was measured at six sites and the mean maximal thickness was used for analysis. The study showed that the slope a decrease in the carotid intimal medial thickness was much higher in patients in the verapamil group (-0.082mm) versus the chlorthalidone group (0.037mm/year) and the value was statistically

significant. The study showed that calcium channel blockers were more effective in reducing the carotid intimal medial thickness in patients with hypertension[55].

In a study published in 2005, blood pressures, lipid profile, carotid intimal medial thickness in adolescents with and without obesity were measured. The study showed that 24 hour blood pressure, daytime and nighttime systolic BP was high in the obese adolescents. Obese subjects also had elevated triglycerides and low HDL when compared to the non-obese adolescents. The obese adolescents were also found to have higher mean carotid intimal medial thickness than the nonobese adolescents. The study again showed BP and lipid profile were very closely related to the carotid intimal medial thickness[56].

In another study which was done in Sweden, carotid intimal medial thickness and occurrence of the carotid plaque were studied in adult men with borderline systemic hypertension along with age-matched normotensive controls. The B mode ultrasound was used to assess intimal medial thickness. The study showed that there was a slight increase in the carotid intimal medial thickness in the borderline hypertensive group (0.73 vs 0.69mm $p=0.07$). The difference was seen better in the right carotid artery (0.72 vs 0.67mm $P<0.05$). The incidence of the carotid plaque was also higher in the borderline hypertensive group, 26% versus 16% in the control group. The other determinants in the study, which are shown to be significantly related to the carotid intimal medial thickness were age and HDL cholesterol[57].

In another study done in Finland which included 1224 Eastern Finnish men between the ages of 42 to 60 years to look the determinants of carotid intimal

medial thickness. The study showed that the maximum carotid intimal medial thickness varied between .48 mm to 4.09mm. The regression analysis showed that the carotid intimal medial thickness was related to age, blood pressure, smoking and LDL cholesterol concentration. The study also shows the importance of blood pressure in contributing to an increased carotid intimal medial thickness[58].

In a recent study done in Beijing published in 2014 a total 3324 patients were enrolled in the study and 2895 people with carotid ultrasound were analyzed. The study showed that the incidence of carotid mean intimal thickness, maximum carotid intimal thickness and the incidence of coronary plaque all increased in proportion to the blood pressure ($p<0.01$). These values were significant even after adjusting for diabetes, hypercholesterolaemia, elevated HSCRP, smoking, age, obesity and sex. The study against shows the importance of hypertension in causing accelerated atherosclerosis manifesting as an increased carotid intimal medial thickness[59].

Carotid femoral pulse wave velocity and Central aortic stiffness

One of the other important predictors of asymptomatic organ damage in hypertension is the increase in the Central Aortic stiffness. This is considered one of the earliest events in the vascular changes which are caused due to hypertension. The increase in the arterial stiffness leads to the increase in the cerebrovascular disease and the coronary artery disease in patients with

hypertension. The carotid femoral pulse wave velocity is the measurement of the central aortic stiffness.

It is measured in many different ways. There are commercially available systems which can measure carotid femoral pulse wave velocity. However, it can also be measured with an echocardiography machine which records ECG concurrently. However, since measurement with an echocardiography machine will occur in two different cardiac cycles, if the heart rate is irregular then the values will be incorrect.

Many studies have shown the importance of the carotid femoral pulse wave velocity in determining the risk in patients with hypertension. Below are a few studies which have shown the importance of carotid femoral pulse wave velocity in predicting the risks in patients with hypertension.

In a study done in France, 710 patients with essential hypertension were recruited and the factors influencing aortic pulse wave velocity was studied in the population. The atherosclerosis alterations were defined on the basis of clinical events. The patients who had no clinical events, cardiovascular risk estimation with the use of the Farmingham equation was done. The study showed that a higher pulse wave velocity was associated with a higher atherosclerosis alteration even after adjusting for all the confounding factors. Further, patients with higher cardiovascular risk, according to the Farmingham equation were found to have increased pulse wave velocity. The odds ratio of being in the high cardiovascular mortality group (>5% for 10 years) for the patients in the upper quartile of the pulse wave velocity was 7.1% (95% CI 4.5-11.3). A pulse wave velocity > 13 m/s

was found to be strongest independent predictor of cardiovascular mortality. The study shows that the aortic pulse wave velocity significant contributor to cardiovascular mortality in patients with hypertension[60].

In a study done in France just published in 2000, 1290 subjects with normal blood pressure or elevated blood pressure were divided into three groups based on the calculated creatinine clearance. All these patients also had the blood pressure, aortic pulse wave velocity measured. The study showed that in the 112 patients with hypertension the aortic pulse wave velocity correlated significantly with creatinine clearance even after adjusting for confounding factors. The increase in stiffness of the aorta was also associated with a significant decrease in the GFR. This assumes significance in view of the well-known fact that in patients with end-stage renal disease central aortic stiffness is very high. Central aortic stiffness might also predict early renal dysfunction in patients with hypertension[61].

There are many studies which have shown aortic pulse wave velocity is an independent risk factor for cardiovascular mortality but they were all indirect measures. In a study done in France in 2000 it was decided to study the relationship between aortic stiffness and cardiovascular mortality in hypertensive patients directly. The study included 1980 patients who had at entry measurement of carotid femoral pulse wave velocity. These patients were followed up over a mean of 112 ± 53 months. The logistic regression analysis was done to estimate relative risk of cardiovascular deaths and it was found that carotid femoral pulse wave velocity has an odds ratio of 2.35 (95% CI 1.76 to 3.14, $p<0.0001$) for the development of cardiovascular events. The study also showed carotid femoral

pulse wave velocity were significantly associated with all-cause and cardiovascular mortality independent of age, diabetes and a previous history of cardiovascular disease. The study showed that carotid femoral pulse wave velocity was a strong and an independent predictor of cardiovascular mortality in a cohort of hypertensive patients[62].

In another longitudinal study done in France and published in 2002, 1045 hypertensives were evaluated with carotid femoral pulse wave velocity to document the aortic stiffness. The risk assessment was done with a farmingham risk score and they were followed up for a period of 5.7 years. The coronary events and all cardiac events served as the outcome variables. During follow-up there were 53 coronary events and 97 totalled cardiovascular events. In a univariate analysis, the relative risk of developing a cardiovascular event increased with the increasing level of pulse wave velocity. This was statistically significant even after adjusting for multiple risk factors[63].

The aortic stiffness is not only a predictor of cardiovascular events, but also has a role in predicting the development of cerebrovascular disease. In a longitudinal study which included 1715 essential hypertensive patients with no prior history of cardiovascular or cerebrovascular disease, the carotid femoral pulse wave velocity was recorded at baseline. These patients were then followed up for a period of 7.9 years. During follow-up there was an occurrence of 25 fatal strokes. The pulse wave velocity predicted the occurrence of stroke in this population. There was a relative risk increase of 1.72 (95% CI 1.48-1.96, $p<0.0001$) for every standard deviation increase in pulse wave velocity. This

increase in risk persisted even after adjusting for all the classical risk factors for developing a stroke[64].

The reason for the development of stroke in hypertension is supposedly due to the cerebral small vessel disease. In a study done in the Netherlands it was decided to study the effect of central aortic stiffness to the development of small vessel disease in patients with hypertension. 167 hypertensive patients with no history of cardiovascular, cerebrovascular disease with untreated hypertension were admitted into the cohort. These patients had the measurement of blood pressure, carotid femoral pulse wave velocity and the volume of white matter intensities and the lacunar infarcts an MRI. The multivariate analysis done showed that the pulse wave velocity even after been adjusted for sex, age, mean arterial pressure, heart rate and brain volume was significantly associated with the volume of white matter hyperintensities (regression coefficient: 0.041 - 95% Confidence Interval: 0.005 to 0.078; $p<0.05$). The study showed that aortic stiffness is also a predictor of cerebral small vessel disease in patients with hypertension[65].

The effect of aortic stiffness in patients in patients with hypertension is very well-known. However, it is important to also know if with treatment with antihypertensives will improve arterial stiffness in these patients and cause reduction in the morbidity and mortality. A few studies were done in this regard.

One of the studies which was published in 2001 looked at the effect of perindopril on aortic stiffness in patients with hypertension. A total of 2187 patients were enrolled in the study. 1703 patients completed the study. The

patients were treated for six months with perindopril 4 mg which was increased to 8 mg if the blood pressure was not controlled. If the blood pressure was not still controlled, then a diuretic was added. The study showed that there were significant decreases in the carotid femoral pulse wave velocity obtained at two months and six months with the initiation of therapy with perindopril (-1.1 ± 1.4 m/s). The study showed that treatment of hypertension with ACE inhibitors might result in a favorable change in the aortic stiffness[66].

Another study was done in Poland to look at the effect of calcium channel blockers, ACE inhibitors and ARB's on the aortic stiffness. The study included 118 patients were randomized to either of the three groups. The group one was treated with amlodipine, the group two was treated with quinapril and the group three was treated with losartan. The aortic femoral pulse wave velocity was measured at baseline, at three months and at six months. The blood pressure decreased equally in all the three groups. Among the patients with comparable blood pressure values, there was a significant decrease in the pulse wave velocity in the quinapril treated patients when compared to the baseline. The other two groups did not show a significant decrease. The study showed that ACE inhibitors are the best drugs to reduce the aortic stiffness in patients with hypertension[67].

Looking at all the studies which looked at the carotid femoral pulse wave velocity, we now come to the conclusion that carotid femoral pulse wave velocity is a significant predictor of cardiovascular and cerebrovascular risk in patients with hypertension. It is an independent predictor of mortality in these patients. The treatment of hypertension especially with ACE inhibitors produces a decrease in

the Central aortic stiffness. However, further studies need to be done if this reduction in the carotid femoral pulse wave velocity will translate into a reduction in the cardiovascular and cerebrovascular risk.

Hypertension and uric acid

Serum uric acid is often considered as a predictor of cardiovascular risk. Normally, uric acid peaks in men are higher when compared to women. The other conditions were uric acid increases are in patients with insulin resistance, metabolic syndrome and dyslipidaemia. Uric acid is excreted by the renal tubules and any reduction in the GFR causes a reduction in the unit excretion and increases the uric acid levels. The diuretics also increase uric acid levels by promoting uric acid reabsorption.

The serum uric acid is elevated in around 25% of the hypertensive patients[68]. The pathophysiological mechanisms behind the increased uric acid level in hypertension are described below.

1. Hypertension causes a decrease renal blood flow which will stimulate the reabsorption of uric acid.

2. The decrease in the local tissue perfusion increases the production of lactate and lactate competitively blocks the uric acid secretion in the proximal tubule.

3. Ischaemia itself increases the uric acid synthesis.

4. When ischemia occurs, ATP is degraded to adenine and xanthine and this causes the increased uric acid production.

5. During ischemia, there is also an increased production of xanthine oxidase[69].

All these factors lead to the increase in serum uric acid in patients with hypertension.

Serum uric acid is also implicated in the development of pro-inflammatory state. Uric acid causes endothelial dysfunction by causing an impact nitric oxide release from the endothelium. Uric acid also causes increased platelet adhesiveness and causes activation of platelets, which may also be a part of endothelial dysfunction caused by uric acid[70].

Uric acid also directly causes vascular smooth muscle proliferation in the laboratory conditions. The urate which enters the endothelial cell through the organic and transporters causes the up-regulation of the platelet derived growth factor A and the PDGF alpha receptor mRNA. Uric acid also stimulates a synthesis of monocyte chemoattractant protein-1 in the vascular smooth-muscle cells interact. MCP-1 plays a very important role in atherosclerosis[71, 8].

Uric acid was studied in rats in a study in Mazzali et al. They caused hyperuricaemia in one set of rats by feeding them with and uricase inhibitor and another set of rats were used as controls. The hyperuricaemic rats developed hypertension over a period of three weeks while the control rats were normotensive. A direct relationship was found between blood pressure and uric acid levels. The kidneys under light microscopy were normal, however immunohistochemical stains showed and ischemic type of injury and macrophage infiltration. The rats, which were hyperuricaemic also exhibited an increase in the juxtaglomerular renin and reduced nitric oxide synthase in the macula densa[5].

Various studies have been done which evaluated the Association between hypertension and uric acid levels. One of them was the Olivetti heart study. It was a longitudinal study which looked for these factors for coronary artery disease at the Olivetti factory in Italy. The patients were screened at baseline, at five years and at 12 years follow-up. The study showed that serum uric acid were significantly related to age, systolic blood pressure, diastolic blood pressure, total cholesterol, BMI and triglycerides. Logistic regression analysis showed that elevated serum uric acid levels was associated with an increased risk for development of hypertension (RR - 1.23 CI - 1.07-1.39 p=0.011) after adjustments for the confounding factors[72].

In another study, which was done in the Farmingham study participants. The serum uric acid levels were tracked in the 3329 subjects who had no hypertension at the base line. At four years follow-up from the baseline 458 persons developed hypertension. The rates of incidence of hypertension increased progressively from 9.8 % in the lowest quartile of uric acid to 15.6% in the highest quartile of uric acid. The odds ratio was 1.17 with a 95% confidence interval of 1.01 to 1.23. The study showed the uric acid level was an independent predictor of hypertension incidence[73].

The Osaka health survey looked at the Association of serum uric acid with risk of hypertension and type II diabetes. The study enrolled 6356 Japanese men aged 35 to 60 years who at the time of enrollment had normal blood pressure, normal glucose tolerance and no history of diabetes or hypertension. They were followed up for a period of 61716 person years. There were 639 confirmed cases

of hypertension and 454 confirmed cases of diabetes. The serum uric acid level was significantly associated with the risk of developing hypertension. The risk of development of hypertension in the fifth quintile of uric acid was 2.01 (CI 156-2.60). The increased uric acid level was not associated with the development of diabetes. The study again showed elevated serum uric acid level was a risk factor for development of hypertension[74].

The other study that supports the causal role of uric acid in causing hypertension is the normative ageing study published in 2006. The study had enrolled to 2280 men and had data for 2062 men for analysis. 892 men had developed hypertension over 21.5 years of follow-up. The uric acid significantly and independently predicted the development of hypertension in both age-adjusted and multivariate analysis[75].

The above-mentioned studies show that uric acid significantly related to hypertension and also causes of pro-inflammatory state which increases the risk for cardiovascular and cerebrovascular diseases also. Uric acid has a causal role in hypertension and also plays an important role in the renal damage in hypertension by causing arteriolar damage to the kidney and finally resulting in nephrosclerosis and causing microalbuminuria. Uric acid has therefore a causal as well as a pathogenetic role in the worsening of systemic hypertension. These factors make uric acid and interesting target to see if it is elevated in patients with asymptomatic organ damage.

Inflammatory markers in hypertension

Hypertension is being considered a chronic low-grade inflammatory state. This is because hypertension is associated with an increase in the level of various inflammatory markers. There have been many studies which had looked at inflammatory markers in hypertension. The most studied ones are HsCRP, interleukin 6, interleukin one beta and TNF alpha. These are the inflammatory markers which have been shown to consistently be elevated in many trials which have been done in patients with hypertension.

HsCRP in patients with hypertension

HsCRP is the most important downstream marker of inflammation. It is associated with hypertension and it's the most sensitive and specific marker as of now in patients with hypertension[12].

CRP is shown to induce the expression of MMP1. MMP1 causes plaque instability. CRP also up regulates interleukin 8 in aortic endothelial cells and it causes Major Chemoattractant protein – 1 (MCP-1) mediated chemotaxis. CRP also attenuates endothelial progenitor cell survival and differentiation by inhibiting nitrous oxide[76].

CRP also decreases eNOS mRNA transcription and upregulates diverse adhesion molecules, causing a pro-inflammatory and a pro-atherosclerotic state. CRP also up regulates NFKB signaling and causes decreased survival of endothelial progenitor cells. It also augments the angiotensin I receptor in the vascular

smooth-muscle cells. All these together make CRP an important marker to identify endothelial dysfunction[77].

In a study done in 2000, 506 men with coronary heart disease or non-fatal MI along with 1025 controls who were free of any cardiovascular disease were selected from 5661 men who had given blood samples between 1978 to 1980. The results show that compared with the men with the lowest tertile of C-Reactive protein, the men in the highest tertile of C-Reactive protein had an odds ratio of 2.134 developing an acute coronary event[78].

In the patients who had been enrolled in the Farmingham Study, in 1980 to 1982 had CRP levels measured during follow-up. During the next 12 to 14 years, 196 strokes occurred in the population. The highest CRP quartile at baseline had two times the risk of an ischemic stroke independent of the age of the person. Thus the study showed that CRP is an independent predictor of an embolic disease and stroke in patients[79].

In the CAPTURE trial with studied the intervention of adding abciximab before and during coronary intervention in refractory and stable angina the investigators also look for long-term cardiovascular complications. They are studied using troponin T and CRP at baseline. It was found that elevated CRP at baseline was associated with an increased risk for subsequent cardiovascular events[80].

In another study published in 2003, a prospective cohort study that had begun in 1992 was taken and CRP was done on the baseline samples provided in 1990. These individuals who are normotensive were followed up over a period of

more than 7.8 years. During follow-up out of the 20525 female professionals 5365 women developed hypertension. The risk of developing hypertension in the highest quintile of CRP was 2.5 times the risk associated with the lowest quintile of CRP. The study showed that there was a significant risk of developing hypertension in patients with elevated CRP levels[13].

In another study by King et al, the relationship of CRP in blood pressure across a range of blood pressure categories including the pre-hypertension was studied. The data were collected from 1988 to 1994 from the third National health and nutrition examination survey. It was found that prehypertensive subjects had higher prevalence of elevated CRP than normal people(27.4% versus 19.8%, $p<0.05$). CRP and the blood pressure also positively correlated across a wide range of blood pressure categories even after adjusting for potential confounders[15].

There is also an increasing evidence to say that CRP plays an increasing role in the atherogenesis in blood vessels. CRP binds with the lipoproteins and activates the complement pathway. CRP has often found deposited in the arterial wall in the atherosclerotic lesions. Thus CRP might play an important role in atherogenesis[81].

CRP also modulates the roles of various chemokines including MCP-1 which causes atherosclerosis. It also causes an inhibition of the stimulated and basal Nitric oxide release and contributes to the arterial stiffness[16,82]. CRP also induces the peripheral blood monocytes to synthesize tissue factor and causes the increase in the procoagulant and the pro-inflammatory state[83].

Thus HsCRP and uric acid play important role in modulating the inflammatory pathways and thereby causing hypertension. The increased inflammatory markers are also associated with increased morbidity and mortality in the patients with hypertension. They also associated with increased end organ damage in the patients with hypertension.

.

Materials and Methods

Materials and Methods

Inclusion Criteria

1. Age : 30 to 60 years.
2. SBP>140mm Hg or DBP>90 mm Hg. (2 readings on 2 separate occasions)

Exclusion Criteria

1. Patients on antihypertensives or statins.
2. Patients with any acute febrile illness.
3. Patients with connective tissue disorders.
4. Patients with history suggestive of secondary hypertension.
5. Patients with autoimmune disorders.
6. Patients with tuberculosis.
7. Patients with malignancies.
8. Patients with pregnancy related hypertension.

The patients included in the study were selected between the age of 30 to 60 years to exclude patients with secondary hypertension. The exclusion criteria also excluded patients on antihypertensives or statins as they have been shown to

cause a reduction in inflammatory markers like HsCRP. The patients with acute febrile illness, connective tissue disorders, autoimmune disorders, malignancies, active tuberculosis were excluded as they will also have elevated inflammatory markers. Patients with pregnancy related hypertension were excluded as they will form the vulnerable population.

Methodology

Patients presenting to the medicine outpatient department with a diagnosis of newly detected hypertension and satisfying the inclusion criteria and who are willing to participate in the study were recruited in the study after obtaining a signed informed consent. The recruitment was carried out between November 2013 and August 2014. The patients who were found to be hypertensive for the first time and was not on antihypertensives were recruited. Those of them who had diabetes, pregnancy, fever and other diseases like tuberculosis, malignancies were excluded. In the patients who were included in the study, the blood pressure was checked twice at least one hour apart on two separate occasions each. If the blood pressure measurements taken two hours apart was elevated, then the patients were included in the study.

The patients who were included in the study were initially screened for evidence of any secondary hypertension with a questionnaire. The basic demographic data, the blood pressure measurements and the height, weight

, the abdominal circumference recollected at the time of inclusion. The patients were also evaluated to see if they have any signs of secondary hypertension like a cushingoid habitus, the subclavian bruit, to see if there are any differences in

pulses between the four limbs, any signs of thyroid disease and abdominal murmurs. Any patients who had history suggestive of secondary hypertension were excluded from the study.

The patients who had been included in the study were then asked to report back after doing the blood and urine investigations, and the ECG and the echocardiography tests. The information was then gathered from the hospital information system and was entered in the study.

The patients were then informed about their status of asymptomatic organ damage, according to the ESC 2013 criteria and they were further referred to the medicine OPD for management of their hypertension and any end organ damage if present.

Since it was a cross-sectional study, the patients were not followed up any further for the study. They were, however, followed up and managed in the medicine OPD's after the initial assessment, data collection and information given to the patients regarding their cardiac and renal status.

Type of study: cross-sectional study

Institutional Research Board (IRB) Clearance

The study was submitted to the institutional research committee for the review of the study methodology and to address any ethical issues in the study. The study was presented to the IRB review committee on 9.10.2013, IRB Minute Number: 8487. There were a few suggestions regarding the study, which were

incorporated into the study, and the final permission was granted on 25.11.2013 to conduct the study.

STUDY DEFINITIONS

Hypertension

Hypertension is defined as values ≥140 mmHg systolic blood pressure and/or ≥90 mm Hg diastolic blood pressure.

1. The clinical criteria for hypertension is average of 2 or more seated blood pressure readings during each of the two or more hospital visits at least one week apart.

2. Hypertension is clinically defined as the blood pressure at which the institution of therapy produces significant changes in morbidity and mortality.

3. The office pressure measurement of blood pressure is considered the gold standard for diagnosis and treatment of hypertension

Staging of hypertension

Staging of hypertension was done according to ESC 2013 criteria[84] (Table 3).

Table 3. Grading Of Hypertension

Hypertension Grade	Systolic Blood	Diastolic Blood

	Pressure		Pressure
Grade I	140 - 159 mm Hg	And / Or	90-99 mm Hg
Grade II	160 - 179 mm Hg	And / Or	100-109 mm Hg
Grade III	≥ 180 mm Hg	And / Or	≥ 110 mm Hg

Measurement of blood pressure

1. Make the patient said calmly for 3 to 5 minutes before recording blood pressure.
2. Take at least one to two blood pressure readings spaced 2 to 3 minutes apart and if they are grossly different than consider taking one more reading and consider the average of two readings which are closer to each other.
3. Consider taking repeat blood pressure measurements in patients with irregular heart rate example atrial fibrillation.
4. The width of the blood pressure cuff should be at least 40% of the circumference of the arm the length of the cuff should cover at least 80% of the circumference of the arm being measured.
5. The measurements should be taken with the cuff and the level of the heart.
6. While using the auscultatory method, the Korotkoff phase I is taken as the systolic blood pressure and Korotkoff phase II is taken as the diastolic blood pressure.

7. Blood pressure during the first visit is checked both upper limbs to detect any subtle variations in the blood pressure. If there are minimal differences in the blood pressure between the bilateral upper limbs the highest blood pressure recorded is taken as the blood pressure.

8. To measure the heart rate for at least thirty seconds after the second blood pressure measurement to document the same.

The blood pressure was measured in all patients with a Heine Gamma G5 aneroid Sphygmomanometer.

Abdominal circumference measurement:

The abdominal circumference was measured at the narrowest point between the lower border of the lowest rib and the upper border of the iliac crest. The readings were done with the standard measuring tape in centimeters. The minimum reading possible was 1 mm. The values were rounded to the nearest centimeter.

Height and weight measurement

Height was measured with a standard measuring scale pasted on the wall with the readings in centimeter. Sensitivity of the scale was 1 cm.

Weight was measured on a digital scale with sensitivity of 1 g. The readings obtained were rounded off to the nearest kilogram.

Markers of Asymptomatic organ Damage

Table 4. Asymptomatic Cardiac Damage[84]

ECG Criteria	**Sokolow-Lyon index (SV1 + RV5 >3.5 mV)**
	Modified Sokolow-Lyon index (largest S-wave + largest R-wave >3.5 mV)
	Cornell voltage QRS duration product (>244 mV*ms)
ECHO Criteria	LV Mass Index (LVMI) Men >115g/m^2; women >95g/m^2
	Relative Wall Thickness (RWT) > 0.42

Table 5. Asymptomatic Renal Damage[84]

Chronic Kidney Disease with eGFR 30–60 ml/min/1.73 m^2 (BSA)
Albumin–creatinine ratio >29 mg/g (preferentially on morning spot urine)

Table 6. Types of Left Ventricular geometry[48, 84]

Left Ventricular Geometry	**LV mass Index**	**Relative Wall Thickness**
Normal Geometry	Men: <115 g/m^2 Women: <95 g/m^2	<0.42
Concentric Remodelling	Men: <115 g/m^2 Women: <95 g/m^2	≥0.42
Eccentric Hypertrophy	Men: ≥ 115 g/m^2 Women: ≥ 95 g/m^2	<0.42
Concentric Hypertrophy	Men: ≥ 115 g/m^2 Women: ≥ 95 g/m^2	≥0.42

The formulae used in calculation of various indices in the study:

1. Body mass index (kg/m^2) = weight in kilograms / height in $meters^2$

2. Mean Systolic blood pressure (mm Hg) = (SBP1+SBP2+SBP3+SBP4) /4

(SBP1, SBP2, SBP3, SBP4 are discrete systolic blood pressure readings taken individually as described in the procedure)

3. Mean Diastolic Pressure (mm Hg) = (DBP1+DBP2+DBP3+DBP4)/4

(DBP1, DBP2, DBP3, DBP4 are discrete diastolic blood pressure readings taken individually as described in the procedure)

4. Mean Heart Rate (bpm) = (HR1+HR2+HR3+HR4)/4

(HR1, HR2, HR3, HR4 are heart rate readings taken along with the 4 blood pressure readings.)

5. Body Surface Area[85] (m^2) = 0.20247 x $Height(m)^{0.725}$ x $Weight(kg)^{0.425}$

6. Sokolow Lyon Criteria[86] (mV) : S wave in V1 + R wave in V5 > 3.5 mV

S wave in V1 – Amplitude of S wave in V1 lead in mV, R wave in V5 – Amplitude of R wave in V5 Lead in mV

7. Modified Sokolow- Lyon Criteria (mV): largest S-wave + largest R-wave > 3.5 mV

Largest S wave – Amplitude of largest S wave in the precordial leads. Largest R wave – Amplitude of the largest R wave in the precordial leads.

8. Cornell Voltage product Criteria[87] (mV . ms):

[(R wave aVL + S wave in V3) x QRS duration] >244 mV · ms [For Men]

[(R wave aVL + SV3 + 0.8 mV) × QRS duration] > 244 mV · ms [For women]

R Wave aVL – Amplitude of the R wave in Lead aVL, Swave in V3 – Amplitude of the S wave in Lead V3, QRS Duration – Duration of the QRS complex in the ECG.

9. LV Mass[88] (g) = 0.8{1.04[([LVEDD + IVSd +PWd]3 - LVEDD3)]} + 0.6

LVEDD – Left ventricle End diastolic diameter in mm, IVSd – Interventricular septal thickness in Diastole in mm, PWd – Posterior Wall thickness in diastole in mm.

10. LV Mass Index[88] (g/m^2) = LV Mass (in gm) / Body Surface area (BSA in m^2)

11. Relative Wall Thickness[88] = (2*PWd) / LVEDD

PWd – Posterior Wall thickness in diastole in mm, LVEDD – Left ventricle End diastolic diameter in mm.

12. **eGFR[89] ($ml/min/1.73m^2$) = 175 x (Creat)-1.154 x (Age)-0.203 x (0.742 if female) x (1.212 if African American)**

Creat – Serum Creatinine in mg/dl, Age – Age in years

Methodology adopted in doing various Biochemical investigations in the study

Investigation Name	Method used
Fasting Glucose	Hexokinase Method
Total Cholesterol	CHOD-PAP (Cholesterol Oxidase - phenol + aminophenazone) method
LDL Cholesterol	CHE/CHO/POD Direct Method
HDL Cholesterol	Enzymatic
Serum Sodium	Ion Selective Electrode, indirect
Serum Potassium	Ion selective Electrode, Indirect
Serum Creatinine	Jaffe's Method, Compensated
Serum HsCRP	Nephelometry
Serum Uric Acid	Enzymatic uricase-Peroxidase method
Urinary Microalbumin	Immunoturbidometry

Statistical Analysis

Statistical Analysis

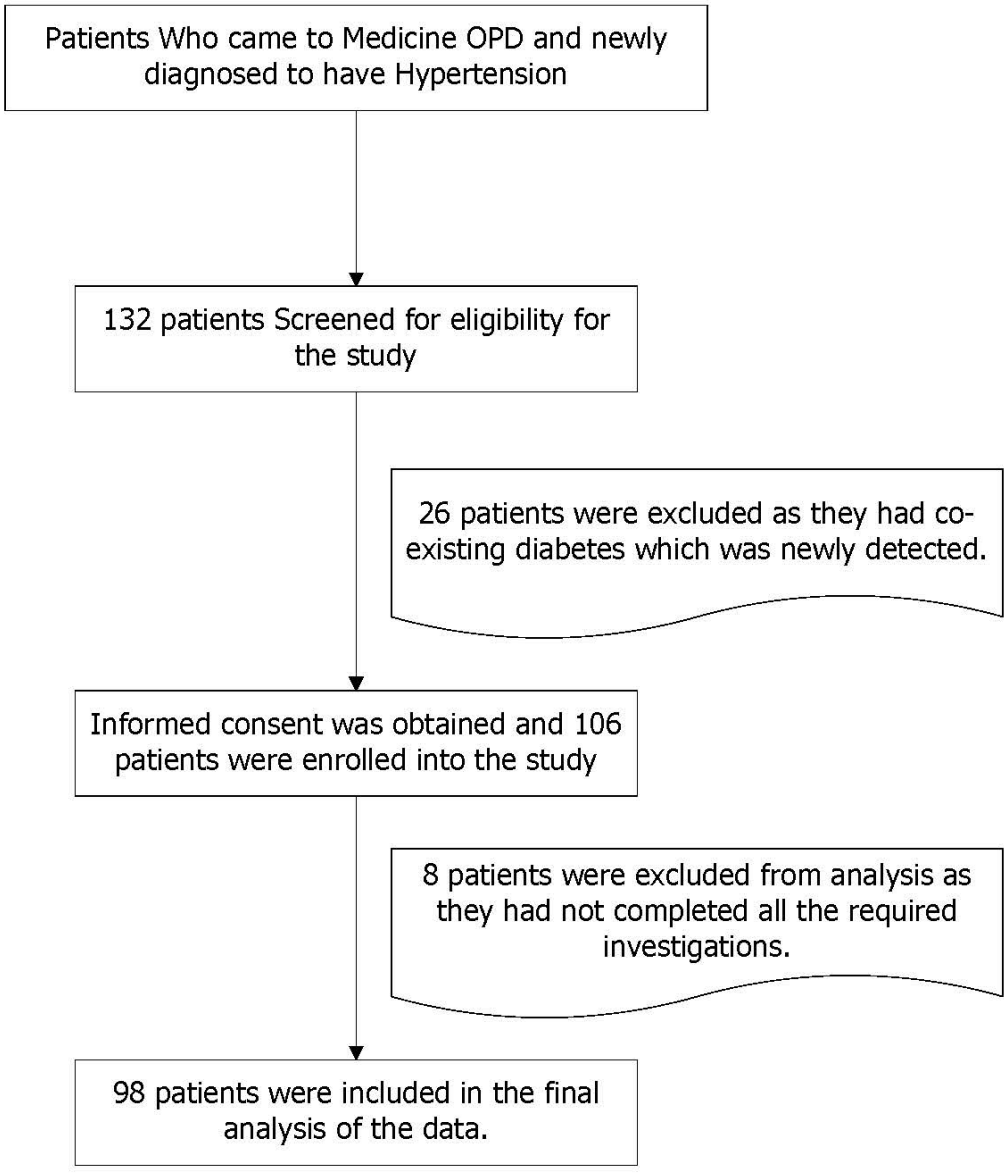
The statistical analysis was performed in this study as below.

- The prevalence of the asymptomatic organ damage was calculated using the formula
- **Prevalence = Number of patients with the problem at a given time**

  Total population included in the study

- The evaluation of HsCRP and Uric acid with the asymptomatic organ damage will be done by dividing the HsCRP and Uric acid into tertiles and comparing the asymptomatic organ damage between the tertiles with Analysis of Variance (ANOVA)
- A Univariate and Multivariate analysis will be done to see if there is any co-relation between the risk factors and the inflammatory markers, HsCRP and Uric Acid.
- All the statistical analysis was done using SPSS Software version 21 by IBM Corporation.

Study methodology



Results

Results:

The total number of patients recruited in the study was 106. Of the 106 included patients only 98 had complete data and they were included in the analysis. The rest of the patients were not included in the analysis as they had incomplete data.

Demographic characteristics.

Of the 98 patients, 57 were males and 41 were females (Figure 1). They were from diverse backgrounds. The population included predominantly patients from Tamilnadu, Andhra Pradesh, Bihar, Jharkhand, West Bengal and Bangladesh as they were the most common population catered in the hospital.

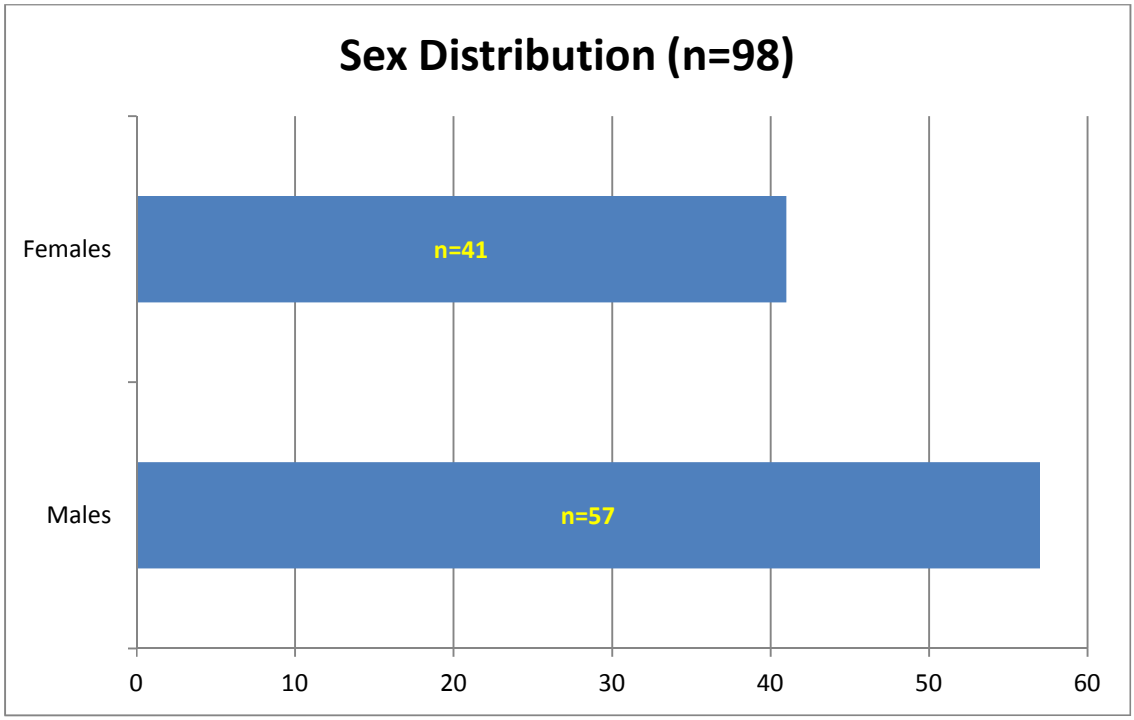


Figure 1. Sex Distribution

Mean age of presentation was 47.03 years and the Standard deviation was 8.3 years. The minimum and the maximum ages in the study were 30 years and 61 years respectively (Figure 2).

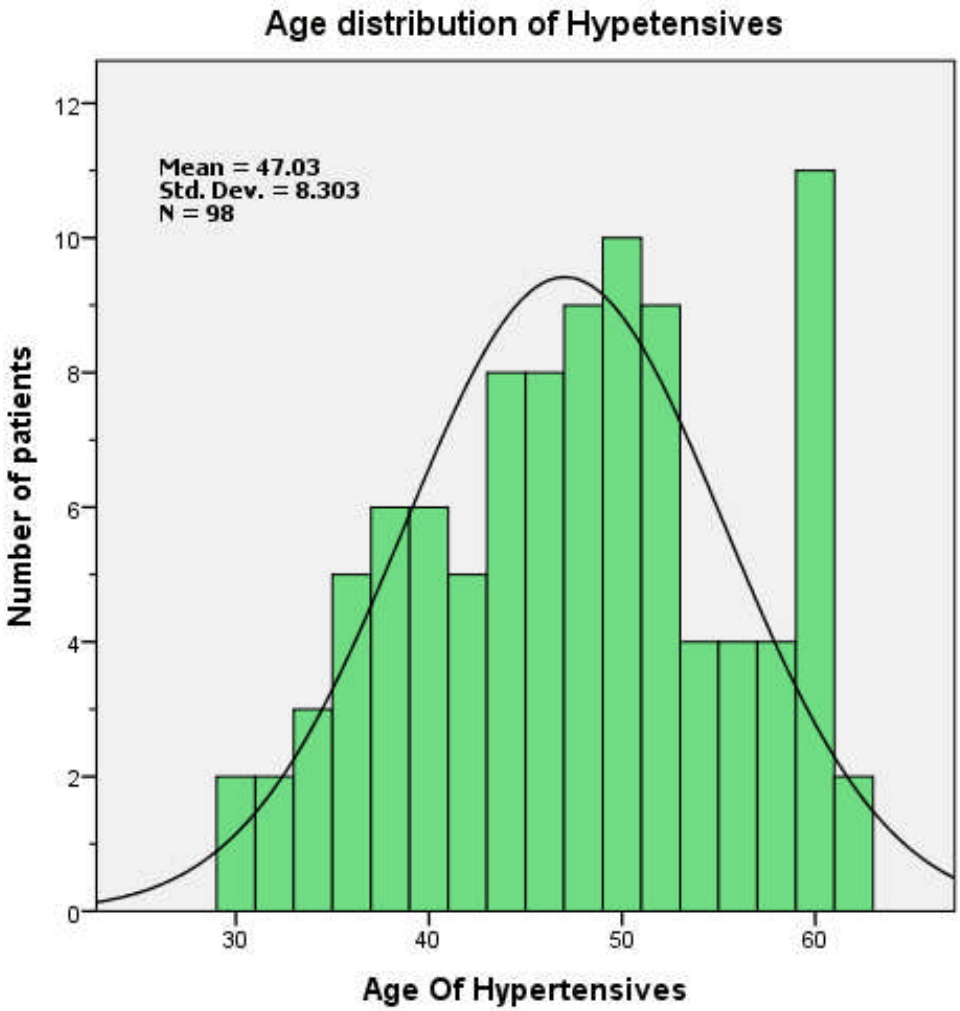


Figure 2. Age Distribution of hypertensives with normal curve

Past History In patients with Hypertension

Among the patients who were included in the study, 39 (39.8%) had a family history of hypertension or coronary artery disease in the first degree relative.

Of the population studied, 3.1% (n=3) had a family history of dyslipidemia in a first degree relative. Around 22.2% (22) were smokers or have had a significant smoking history in the past. Of the studied population, 31.3% (n=31) had clinical symptoms of snoring or a history of obstructive sleep apnea, but none of them were on any treatment for the same. 1 patient (1%) had a history of low birth weight present (Figure 3).

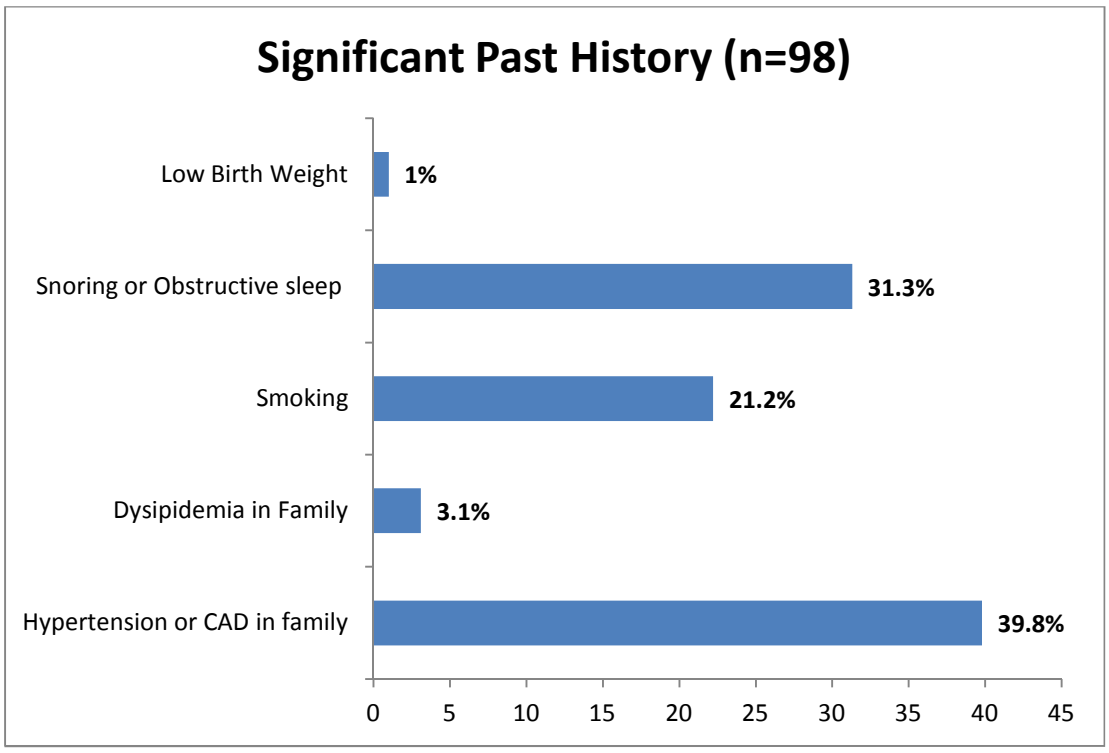


Figure 3. Significant Past History.

History Suggestive of Secondary Hypertension

Any history of secondary hypertension was also studied in the population. Only 2% had a family history of Chronic kidney disease but they were all related to diabetes in the individuals.

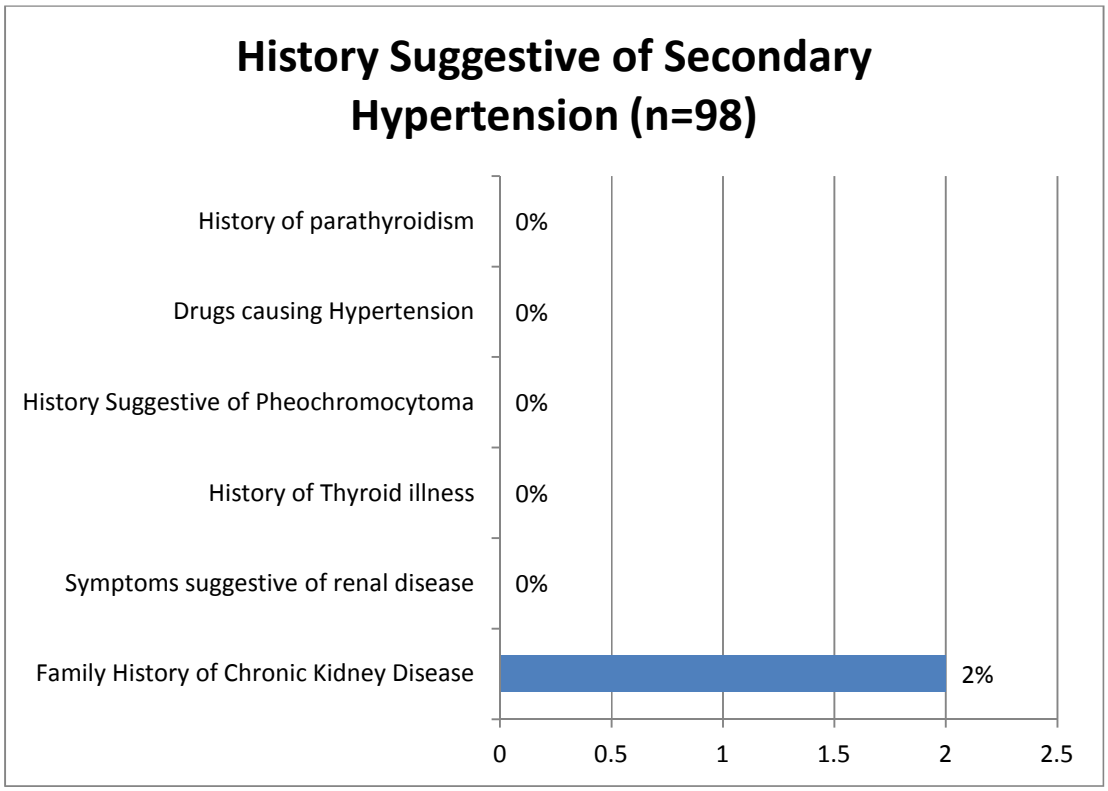


Figure 4. History Suggestive of Secondary Hypertension

The people included in the study didn't have any symptoms related to the renal disease, recurrent urinary tract infections or hematuria in the past. None of them had any history suggestive of a thyroid illness nor were taking any anti-thyroid medication or thyroxine supplements. None of them had any symptoms suggestive of a pheochromocytoma like repetitive episodes of sweating, headache, anxiety, palpitations. None of the patients studied had episodes of tetany or weakness suggestive of a parathyroid dysfunction.

None of the population studied were on the drugs which are known to cause hypertension like oral contraceptive pills, vasoconstrictive nasal drops, glucocorticoids or mineralocorticoids and Non steroidal anti-inflammatory drugs (NSAIDS).

Symptoms at Presentation

The symptoms with which the patients presented to us were also studied in this study. The symptoms were divided into the four major symptom complexes into symptoms suggestive of cardiac involvement, symptoms suggestive of nervous system involvement, symptoms suggestive of renal involvement and the symptoms suggestive of peripheral arterial disease.

Nervous System Complaints at presentation

The symptoms at presentation were analyzed to see the profile of the patients present. The most common complaint was Vertigo with 46.9% (n=46) patients complaining of it. The headache was present in 41 patients (41.83%) and was the next commonest nervous system complaint in the studied population. The other complaint was blurring of vision or impaired vision in 11.22% (n=11) patients. None of the patients studied complained of Transient ischemic attack or stroke or Carotid revascularisation (Figure 5).

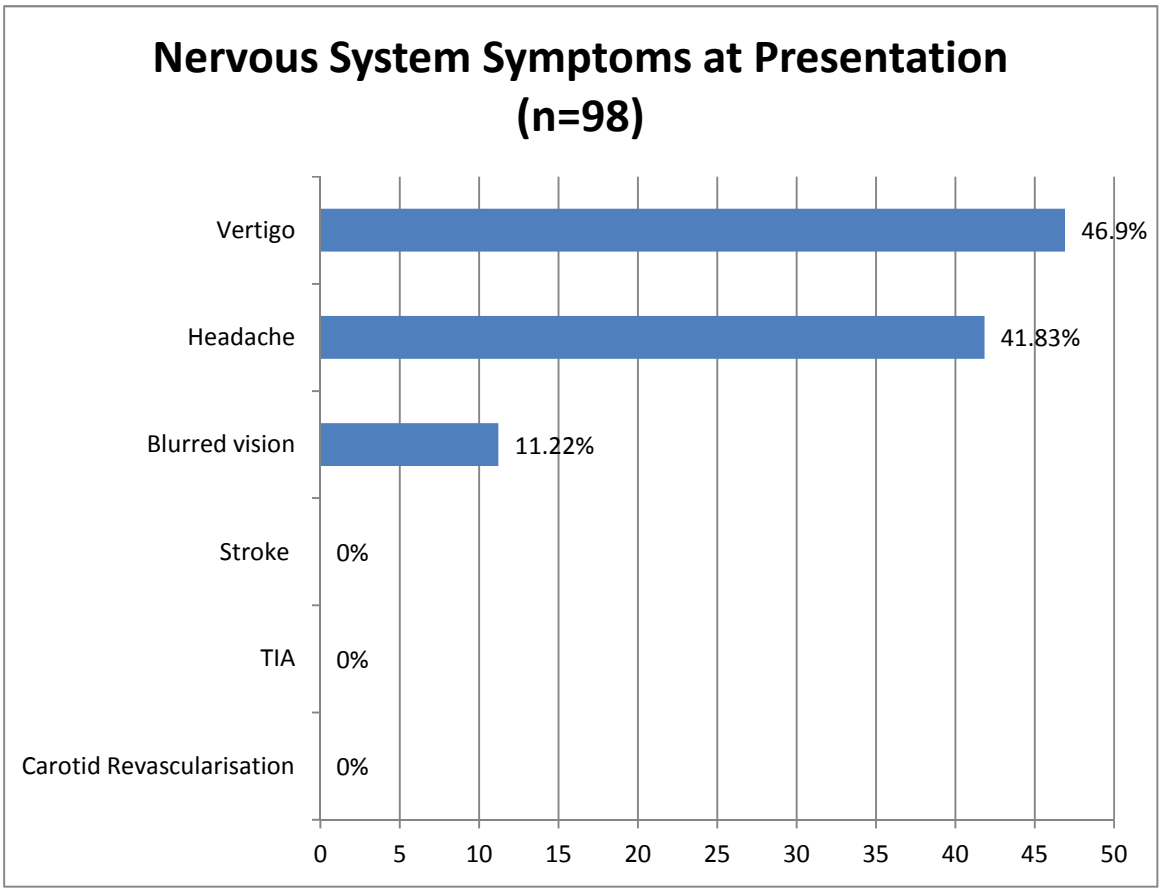


Figure 5. Nervous System Complaints at Presentation

Cardiovascular Symptoms at Presentation

The cardiac symptoms studied were angina, shortness of breath on exertion, pedal edema, myocardial infarction, history of coronary revascularisation, palpitations and arrhythmias. The most common cardiac complaints were shortness of breath and pedal edema. Almost 43.87% (n=43) of the patients in the study complained of shortness of breath on exertion. And almost a same number of patients (n=43) complained of the pedal edema at the time of presentation. 11 patients (11.22%) complained of palpitations at the time of presentation (Figure 6).

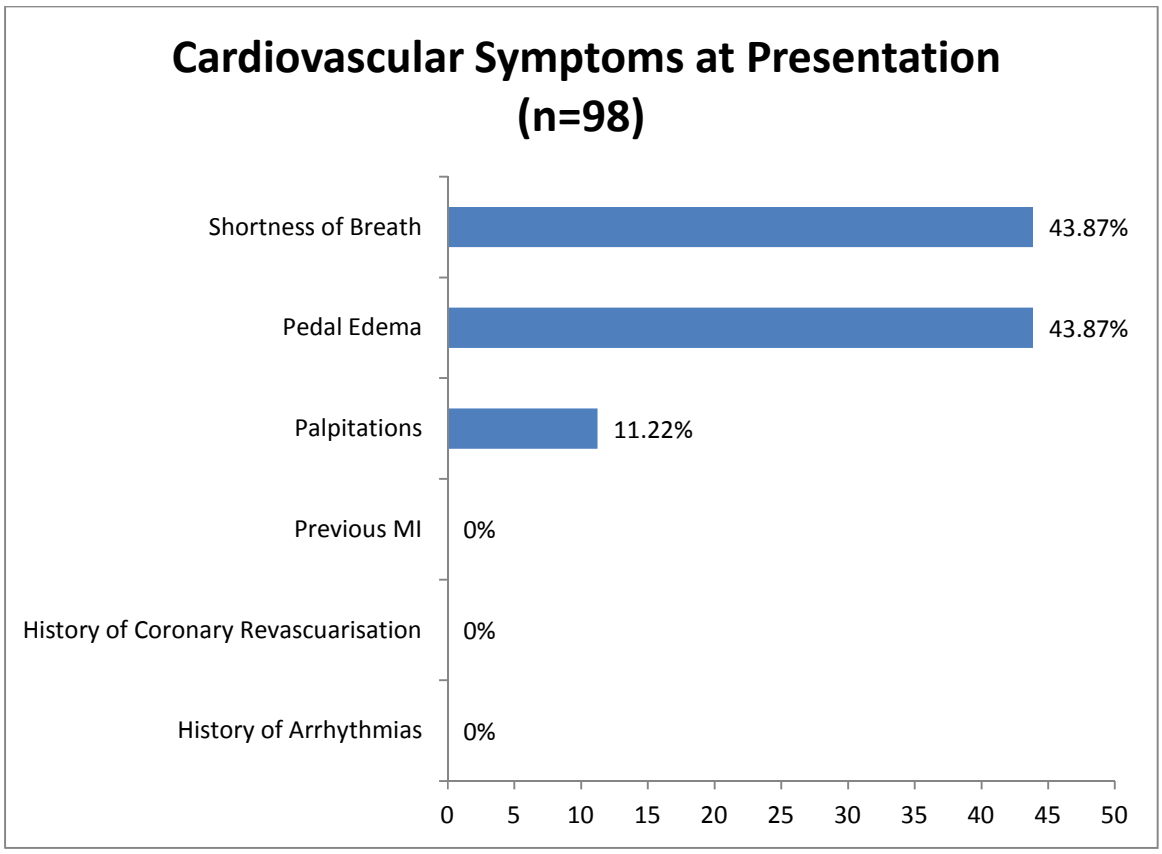


Figure 6. Cardiovascular Symptoms at presentation

The renal symptoms were also assessed in patients who were studied. 2% (n=2) of the patient studied had increased thirst and 1 patient (n=1) complained of nocturia. None of the patients studied complained of hematuria or nocturia.

Only 1 patient (n=1) complained of Intermittent claudication pain in the legs. None of the patients studied complained of the cold extremities and none of the patients had a history of revascularisation.

The patients enrolled in the study were examined for any signs of secondary hypertension, including features of Cushing's syndrome, features of neurofibromatosis, abdominal murmurs, precordial murmurs, radiofemoral delay and large differences between upper limb and lower limb blood pressures. None of the patients studied had any of the following signs which would have suggested a secondary cause of hypertension rather than a primary cause.

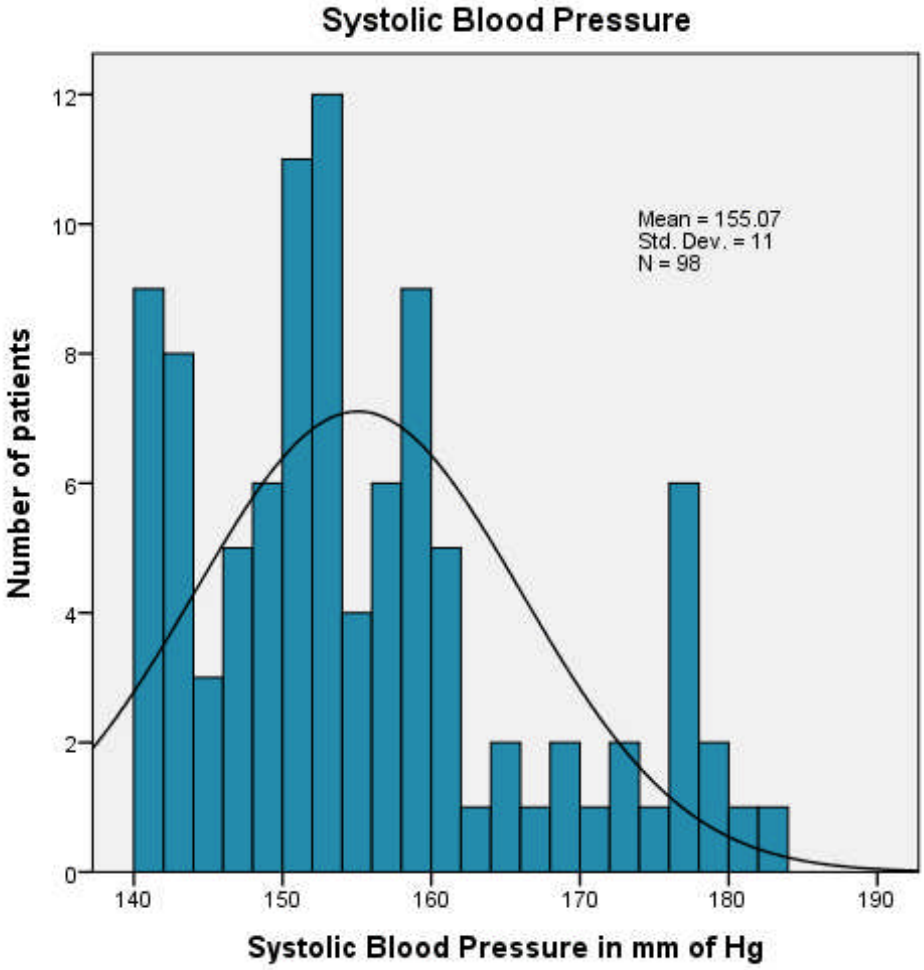


Figure 7. Distribution of Systolic Blood pressure

Mean systolic blood pressure in the studied population was 155 mm of Hg with a standard deviation of 11 mm of Hg (Figure 7). The Mean diastolic blood

pressure in the studied population was 93.94 mm of Hg with a standard deviation of 5.14 mm of Hg (Figure 8). The Mean heart Rate was around 87 beats per minute with a standard deviation of 10 beats per minute. All the values were normally distributed among the study individuals.

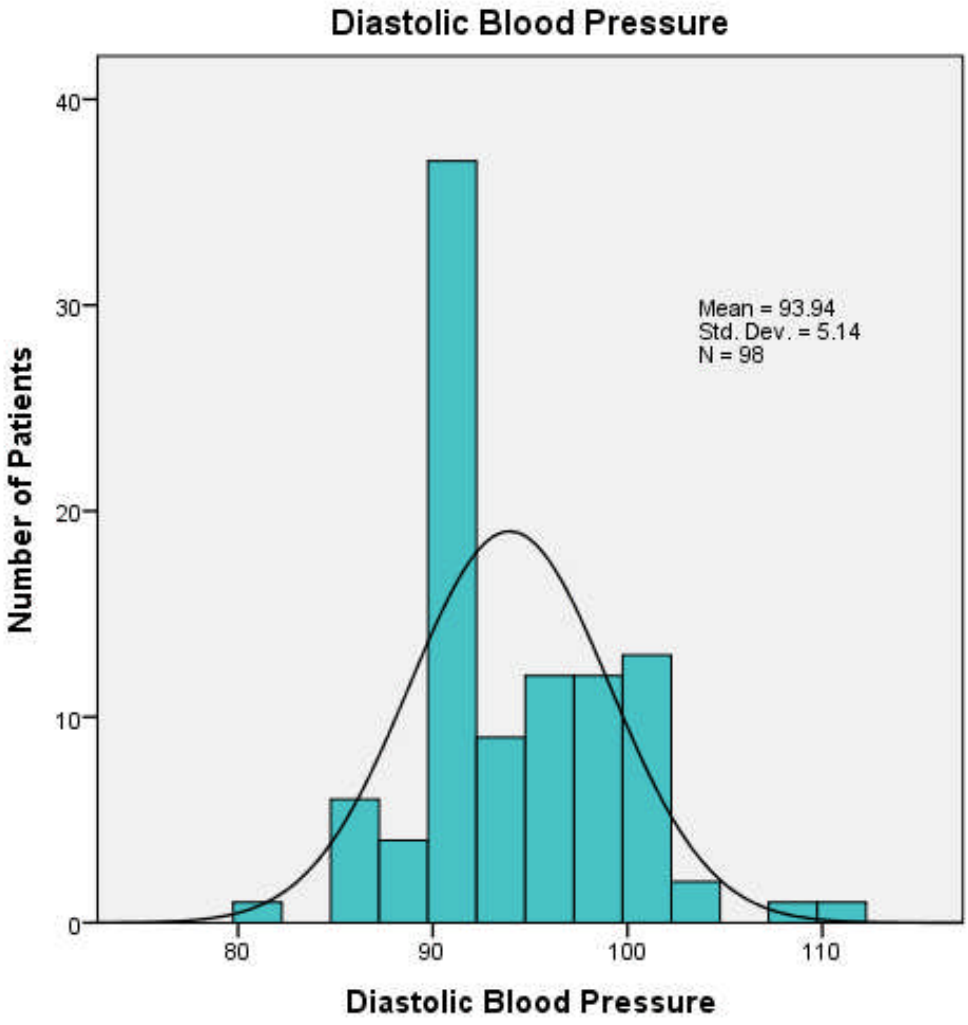


Figure 8. Distribution of Diastolic Blood pressure

The Mean height of the population studied was 162.49 cm with a standard deviation of 9.5 cm. The mean weight of the studied population was 68.55 kgs with a standard deviation of 12.385 kgs. The mean abdominal Circumference of

the population was 89.20 cm with a standard deviation 11.65 cm. Body Mass index on average was 25.93 Kg/m^2 with a Standard Deviation of 5.20 Kg/m^2. The average Body surface area was 1.72 m^2 with a standard deviation of 0.25m^2. All the values were distributed normally in the population (Table 7).

Table 7. Baseline Clinical parameters

Parameter	Mean (SD)
Height (in cm)	162.49 (9.5)
Weight (in Kg)	68.55 (12.39)
Body Mass Index (in Kg/m^2)	25.92 (5.20)
Abdominal Circumference (in cm)	89.20 (11.65)
Body Surface Area (in m^2)	1.72 (0.26)

Clinical Signs Elicited on Examination of the patient

The patients were also examined clinically to elicit symptoms and signs related to hypertension and its complications. The patients had been evaluated for any motor weakness; fundus examination was done to look for hypertensive retinopathy; the cardiovascular system examination was done to look for S3, S4, any murmurs, pedal edema, and by basal crepitations and the carotid arteries were auscultatated to look for any murmurs. All peripheral pulses were examined to rule out any peripheral arterial disease.

Hypertensive retinopathy

Out of the 98 patients, 72 (73.46%) of them had a normal fundus examination, 22 (22.44%) of them had hypertensive retinopathy grade 1 and 4

(4.08%) of them had hypertensive retinopathy grade 2. None of the patients examined had grade 3 or grade 4 retinopathy (Figure 9).

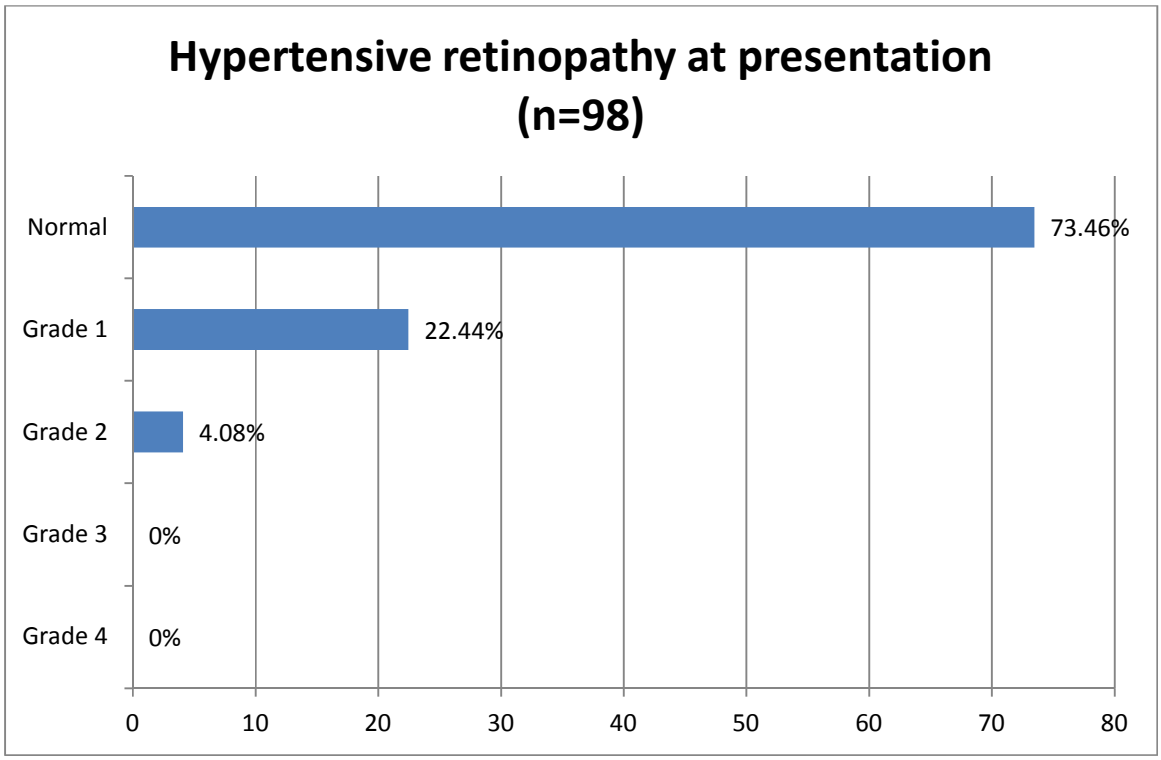


Figure 9. Prevalence of Hypertensive retinopathy in Study Population.

Cardiovascular Signs at presentation

The evaluation of the cardiovascular signs at presentation showed that pedal edema was a commonest sign which was elicitable in around 57 (58.16%) of the patients studied. Two patients (2%) of the study population had an S4 on auscultation and Three patients (3 %) had an Ejection systolic murmur at the apex (however an echocardiogram done on the same patient did not show any valvular lesions) (Figure 10).

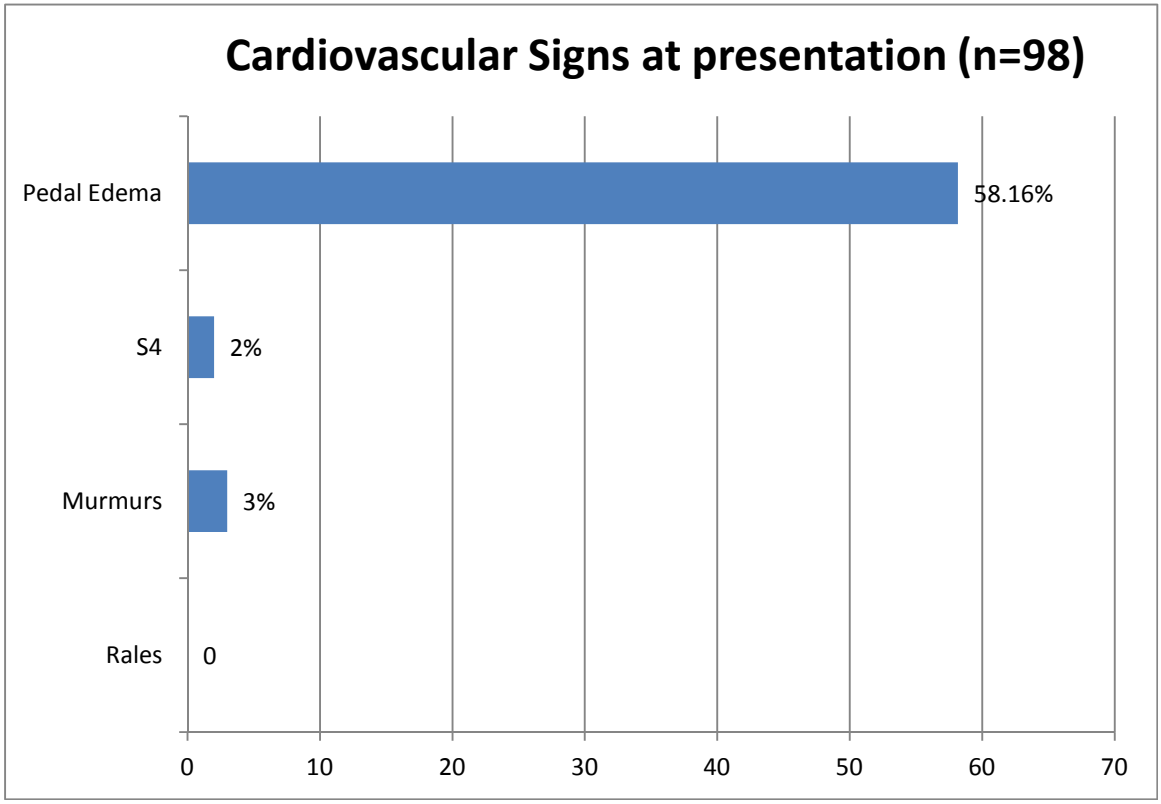


Figure 10. Cardiovascular Signs at presentation

Only one patient(1%) had asymmetry in the pulse volume felt in both feet. And only one patient (1%) had an audible bruit in his right carotid artery.

Baseline Blood investigations

All the patients who were involved in the study underwent estimation of baseline by chemical parameters and the parameters which indicated the underlying organ damage. The blood tests which were done in the patients include hemoglobin, fasting blood glucose, fasting lipid profile, serum sodium, serum potassium, serum creatinine, serum HSCRP, serum uric acid. Patients also underwent an electrocardiogram and an echocardiogram. The M-mode

measurements of LV end diastolic diameter (LVEDD), posterior wall thickness in diastole (PWDd), interventricular septum thickness in diastole (IVSd) and ejection fraction were recorded the data entry sheet. The urine albumin creatinine ratio was also estimated in the early-morning sample in the patients included in the study.

The mean hemoglobin of the population studied was 13.39 gms% (SD 1.73 gms%). The mean blood glucose was below the diabetic range in the population with the mean of 102.23mg/dl (SD 19.57 mg/dl). The Low-density lipoprotein was 116.04 mg/dl (SD 30.41 mg/dl). The serum sodium and potassium levels were also measured and they were within normal limits in all the study population.

The mean creatinine level was 0.77mg/dl (SD 0.19 mg/dl). The hsCRP had a lot of values which were outliers especially if it was elevated. Hence a median and interquartile range was used to describe the data. The median hsCRP was 2.31 with an interquartile range of 0.89-5.2. The mean serum uric acid was 5.0 mg/dl with a standard deviation of 1.3 mg/dl (Table 8).

Table 8. Baseline Investigations

Investigation	Mean	(SD)
Hemoglobin (gms%)	13.39	(1.73)
Fasting Glucose (mg/dl)	102.23	(19.57)
Total Cholesterol (mg/dl)	180.85	(39.31)

Low Density Lipoprotein (mg/dl)	116.04	(30.41)
High Density Lipoprotein (mg/dl)	41.99	(10.21)
Serum Sodium (mEq/l)	138.02	(2.60)
Serum Potassium (mEq/l)	4.17	(0.38)
Serum Creatinine (mg/dl)	0.77	(0.19)
Serum HsCRP (mg/l)	4.26	(4.91) **Median – 2.31** **Interquartile Range – 0.89 -5.2**
Serum Uric Acid (mg/dl)	5.0	(1.3)

Electrocardiographic Data

The 12 lead electrocardiogram was done in all patients were included in the study. They electrocardiogram was recorded and stored in the hospital information system and was analyzed to look for the various indices of detecting LVH.

Electrocardiogram was evaluated for left ventricular hypertrophy with the use of three criteria - The Sokolow Lyon criteria, the modified Sokolow Lyon criteria and the Cornell voltage product criteria.

The results showed that the Sokolow Lyon criteria was positive in 9 patients (9.2%) of the study population. The modified Sokolow Lyon criteria was

positive in 20 patients (20.4%) of the study population. The Cornell voltage product criteria was positive in 7 patients (7.1%) of the study population.

Criteria	Number Satisfied (Percentage)
Sokolow Lyon Criteria	9 (9.2%)
Modified Sokolow Lyon criteria	20 (20.4%)
Cornell voltage product criteria	7 (7.2%)

Echocardiographic criteria

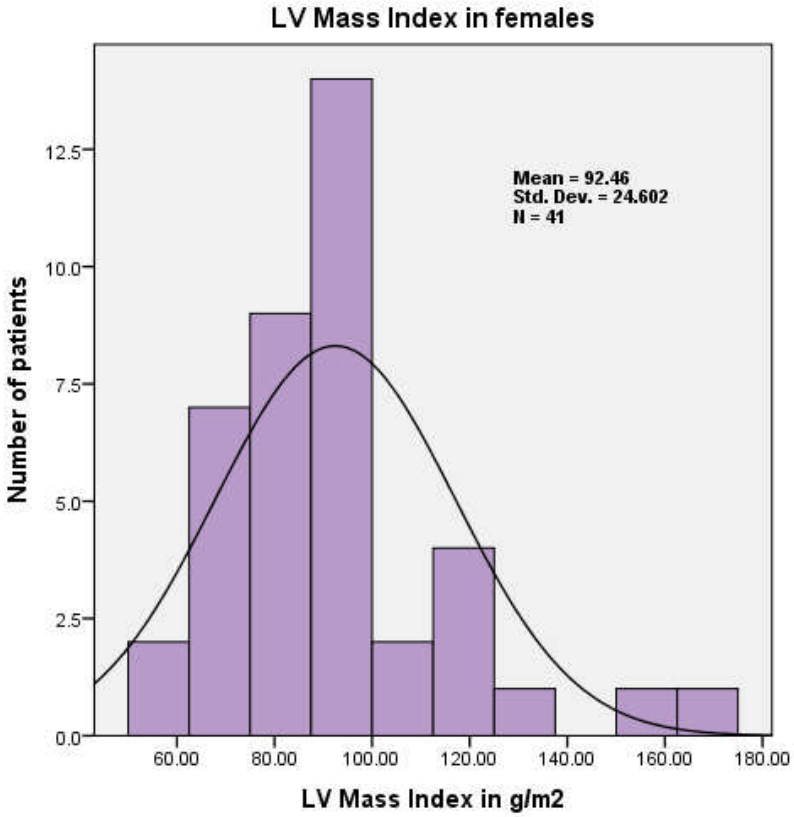


Figure 11. Figure 11. Distribution of LV mass Index in Females

All the patients were enrolled in the study were evaluated using an echocardiogram. The M-mode observations and ejection fraction were recorded in all the patients. The results of the following listed below.

The mean LV end diastolic diameter was 43mm (SD 5.6mm). The mean posterior wall thickness in diastole was 10.69mm (SD 1.49mm). The mean interventricular septum thickness in diastole was 12.15mm (SD 10.34mm). The mean ejection fraction was 57.09% (SD 2.54%). The average relative wall thickness was 0.49 (SD 0.10) (Table 9). The average LV mass index in males was 98.84 g/m^2 (SD 24.61 g/m^2)(Figure 12). The average LV mass index in females was 92.46 g/m^2 (SD 24.60 g/m^2) (Figure 13).

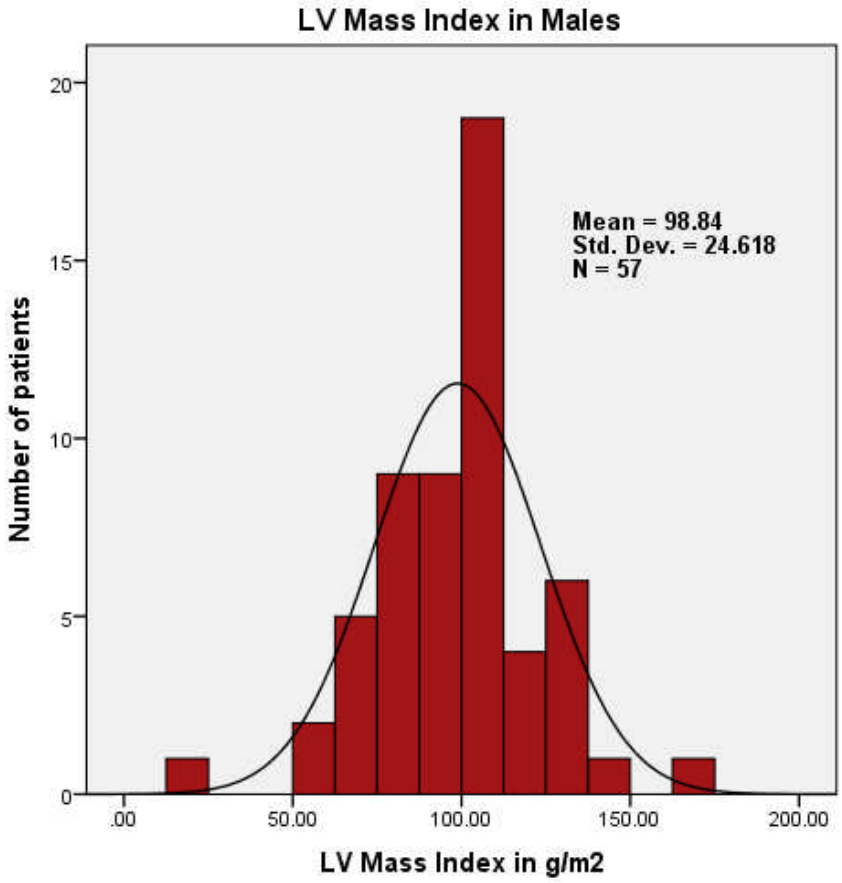


Figure 12. Distribution of LV mass Index in Males

Table 9. Echocardiographic Parameters

Echocardiographic parameter	Mean (SD)
LV end diastolic diameter in diastole (mm)	43 (5.6).
Posterior wall thickness in diastole (mm)	10.69 (1.49).
Interventricular septum thickness in diastole (mm)	12.15 (10.34).
Ejection fraction (%)	57.09% (2.54%)
LV mass index – Male (in g/m^2)	98.84 (24.61)
LV mass index – Female (in g/m^2)	92.46 (24.60)
Relative wall thickness	0.49 (0.10)

Renal parameters

Renal parameters that were assessed to identify in organ damage was microalbuminuria and estimated GFR, which was calculated by the abbreviated MDRD formula.

The mean estimated GFR was 106.90 ml/min/1.73m^2 with a standard deviation of 27.81ml/min/1.73m^2. The mean albumin creatinine ratio in the studied population was 48.27 mg/g. However, this value was confounded by the presence of a few outliers which were huge. Hence the median and the interquartile range were calculated. The median albumin creatinine ratio was 14.35mg/g. The interquartile range was between 4.77mg/g to 49.30mg/g.

Table 10. Predictors of Renal Damage

Parameter	Mean (SD)
eGFR (abbreviated MDRD)	106.90 (27.81)
Urine Albumin Creatinine Ratio	48.27 (103.67) Median – 14.35 mg/g Interquartile Range – 4.77 – 49.3 mg/g

Prevalence of asymptomatic cardiac damage

The prevalence of asymptomatic cardiac damage was calculated with the electrocardiographic and the echocardiographic criteria. If the patient had the presence of the LV hypertrophy, either by an echocardiographic criteria or electrocardiographic criteria, then they were classified as having asymptomatic cardiac damage. The electrocardiographic criteria used where either of Sokolow Lyon criteria, modified Sokolow Lyon criteria or the Cornell voltage product criteria being positive. The echocardiographic criteria used for classifying LV hypertrophy was the LV mass index.

The total prevalence of asymptomatic cardiac damage in the population studied was 29.59% (n=29). All the patients who had left ventricular hypertrophy by Electra cardiogram were found to have LV hypertrophy by LV mass index criteria in echocardiography. Echocardiography proved to be a very sensitive tool to pick up left ventricular hypertrophy (Table 11).

Table 11. . Prevalence of Asymptomatic Cardiac Damage

ELECTROCARDIOGRAPHIC CRITERIA	Prevalence % (Number of patients)
1. Sokolow Lyon Criteria	9.2% (9)
2. Modified Sokolow Lyon Criteria	20.4% (20)
3. Cornell Voltage Product Criteria	7.1% (7)
ECHOCARDIOGRAPHIC CRITERIA	
1. LV mass Index	29.59% (29)

Prevalence of asymptomatic renal damage

The prevalence of asymptomatic renal damage was calculated by the following criteria. If any patient had a urine albumin creatinine ratio ≥ 30mg/g in the early-morning spot urine sample or if any patient had an estimated GFR < 60ml/min/1.73m^2. (Table 12)

The prevalence of asymptomatic renal damage in the studied population was 31.9% (n=30).

Table 12. Prevalence of Asymptomatic Renal Damage

Criteria	Prevalence % (number of patients)
eGFR <60 ml/min	0 % (0)
Albumin Creatinine Ratio ≥ 30mg/g	31.9 % (30)

HsCRP and Risk Factors

Table 13. HsCRP tertiles and Risk Factors

HsCRP and Risk Factors				
Parameter	**Tertile 1** Mean (SD)	**Tertile 2** Mean (SD)	**Tertile 3** Mean (SD)	**P**
Number of patients	33	33	32	
Mean Systolic Pressure (in mmHg)	154.64(11.6)	158.4(12)	152 (8)	0.059
Mean Diastolic Pressure (in mm Hg)	92.71(4.6)	92.61(4.8)	92.8 (5.2)	0.007
Mean Heart rate (in bpm)	86.33(11.6)	88.5(10.42)	86.2(8.1)	0.587
Body mass Index in (Kg/m2)	23.6(5.2)	26.15(4.1)	28.06 (5.2)	0.002
Total Cholesterol (in mg/dl)	183.2(45.5)	186.5(39.56)	178.75 (32.6)	0.901
Low Density lipoprotein (mg/dl)	113.77(36.4)	115.79(26.5)	118.6 (27.85)	0.812
High Density lipoprotein (mg/dl)	42.33(10.6)	42 (8)	41.63 (11.86)	0.962
Serum Creatinine (in mg/dl)	0.80(0.19)	0.78 (0.15)	0.74(0.22)	0.459

The HsCRP values in the studied population were divided into the three tertiles and the risk factors for organ damage in Hypertension were studied in them. The three tertiles were compared with each other to look for any association with ANOVA. HsCRP was significantly related to the Diastolic blood pressure (p= 0.007) and to Body Mass Index (p=0.002). None of the other studied risk factors had any association with the levels of HsCRP. (Table 13)

HsCRP and Asymptomatic Organ Damage

Table 14. HsCRP tertiles and Asymptomatic organ Damage.

HsCRP Tertiles and Asymptomatic organ damage				
Parameter	**Tertile 1** Mean (SD)	**Tertile 2** Mean (SD)	**Tertile 3** Mean (SD)	**P**
LV Mass Index (in g/m^2)	97.06 (24.2)	101.84 (28.4)	89.40 (19.5)	0.123
Albumin Creatinine ratio (mg/g)	Median-10.2 Interquartile range – 25.45	Median – 12.9 Interquartile range – 42	Median – 26.65 Interquartile range – 80.1	0.698
eGFR (in ml/min/1.72 m^2)	109.54(36.77)	104.99 (16.4)	106.15(27)	0.792

The analysis of the HsCRP tertiles for any association with asymptomatic organ damage as defined by the LV mass Index, Albumin Creatinine Ratio and the eGFR also didn't show any significance.

Uric acid tertiles in Men and Risk Factors

Table 15. Uric Acid Tertiles in Men and Risk Factors.

Uric Acid in Men and Risk Factors				
Parameter	**Tertile 1** Mean (SD)	**Tertile 2** Mean (SD)	**Tertile 3** Mean (SD)	**P**
Number of patients	19	20	18	
Mean Systolic Pressure (in mmHg)	159 (11)	152.8 (10.7)	156.61 (8.603)	0.184
Mean Diastolic Pressure (in mm Hg)	93.16(6.5)	94.33 (4.1)	94.33 (4.2)	0.718
Mean Heart rate (in bpm)	86(10.3)	86.2 (13.7)	90.39 (9.09)	0.420
Body mass Index in (Kg/m^2)	23.72 (3.7)	26.0 (4.4)	24.43(6.3)	0.351
Total Cholesterol (in mg/dl)	170.4(46)	189.8(41)	173.83(37.26)	0.312
Low Density lipoprotein (mg/dl)	109.8(30.8)	122.2(30)	116.22(24.39)	0.414
High Density lipoprotein (mg/dl)	40.9(15.2)	42.75(8.6)	37.50(6.2)	0.324
Serum Creatinine (in mg/dl)	0.86(0.15)	0.92(0.14)	0.84(0.16)	0.403

The Uric acid tertiles were studied separately in men and women as they have different peaks in the normative distribution. The Uric acid levels were again divided into three tertiles in men and women and they were analyzed separately.

The Uric acid level was not significantly associated with any risk factors in the amongst the male patients in the study. (Table 15)

Uric acid tertiles in Men and Asymptomatic Organ Damage

Table 16. Uric acid tertiles in men and Asymptomatic Organ Damage

Uric acid in Men and Asymptomatic organ damage				
Parameter	**Tertile 1** Mean (SD)	**Tertile 2** Mean (SD)	**Tertile 3** Mean (SD)	**P**
LV Mass Index (in g/m^2)	101.31(19.9)	100 (26.4)	94.88(27.76)	0.711
Albumin Creatinine ratio (mg/g)	Median – 21.2 Interquartile range – 26.4	Median – 13.55 Interquartile range – 50.18	Median – 12.1 Interquartile range – 57.65	0.784
eGFR (in ml/min/1.72 m^2)	101.5(23.0)	95.34 (15.9)	110 (46)	0.324

The comparison of the uric acid tertiles with the asymptomatic organ damage in men showed no significant association between the Uric acid levels and the asymptomatic cardiac or renal damage. (Table 16)

Uric acid tertiles in Women and Risk Factors

Table 17. Uric Acid tertiles in women and Risk Factors

Uric Acid in Women and Risk Factors				
Parameter	**Tertile 1** Mean (SD)	**Tertile 2** Mean (SD)	**Tertile 3** Mean (SD)	**P**
Number of patients	15	13	13	
Mean Systolic Pressure (in mmHg)	155.8(14)	152.85 (11.11)	152(8.7)	0.653
Mean Diastolic Pressure (in mm Hg)	93.6(5.2)	94.31 (6.1)	94 (5.05)	0.943
Mean Heart rate (in bpm)	86.4(9.1)	90 (8.8)	83.08 (5.25)	0.104
Body mass Index in (Kg/m^2)	25.76(4.4)	27.52(5.7)	29.69(4.73)	0.129
Total Cholesterol (in mg/dl)	183.8(41.2)	179.69 (35.8)	189.6(28.7)	0.780
Low Density lipoprotein (mg/dl)	101.4(34.47)	119.8 (31.2)	128.31(28.5)	0.082
High Density lipoprotein (mg/dl)	44(10.8)	45.38(9.1)	42.85(6.8)	0.782
Serum Creatinine (in mg/dl)	0.60 (0.08)	0.63(0.11)	0.65(0.12)	0.490

Serum uric acid levels in, the women were studied after dividing them into three tertiles and they were analyzed to see if they co-relate with any of the risk factors for organ damage. The ANOVA however, showed that there was no co-relation with any of the risk factors associated with organ damage in the studied intervals. (Table 17)

Uric acid in Women and Asymptomatic Organ Damage

Table 18. Uric Acid tertiles in Women and asymptomatic organ damage.

Uric acid in Women and Asymptomatic organ damage				
Parameter	**Tertile 1**	**Tertile 2**	**Tertile 3**	**P**
	Mean (SD)	Mean (SD)	Mean (SD)	
LV Mass Index (in g/m^2)	99.86(25.56)	87.76 (24.57)	88.61(23.29)	0.350
Albumin Creatinine ratio (mg/g)	Median – 12.9 Interquartile range – 53.4	Median – 16 Interquartile range – 50.9	Median – 17.8 Interquartile range – 53.9	0.616
eGFR (in ml/min/1.72 m^2)	117.8 (19.1)	112.9 (23.7)	108.85(22.6)	0.555

The Uric acid tertiles when analyzed in women didn't show any co-relation with asymptomatic cardiac or renal damage.

The Uric acid and the HsCRP tertiles when compared with the asymptomatic organ damage with ANOVA showed that there was no co-relation with any asymptomatic organ damage in the study participants.

Discussion

Discussion

The discussion of the results will be done under the following major subheadings. Firstly, the demographics and the baseline characteristics will be discussed. Then we will discuss the primary objectives of the study. This will be followed by discussion of the secondary objectives and finally the discussion of the other parameters, which we found a significant in the study and the ones, which were not.

Basic Demographics and baseline characteristics

Age

The patients in the study were chosen between age groups of 30 to 60 years. This is done primarily because we wanted to recruit patients with essential hypertension and exclude patients who would have a secondary cause of hypertension. We also chose this age group because the previous study by Viazzi et al which studied the effects of uric acid on patients with systemic hypertension had most of the population in the age group of 30 to 60 years. The minimum age of recruitment in the study was 30 years and the oldest patient in the study was 61 years. This helped us to choose the patients who had most likely essential hypertension and not hypertension due to secondary causes.

Baseline Characteristics

The study population was divided into three major groups based on the grade of hypertension for the basis of classification of the patients and study the difference in the basal characteristics and also effects of organ damage the different groups.

Sex

The number of males and females in the study were almost equally distributed. Even after dividing the population into three groups based on hypertensive grade the males slightly outnumbered the females in people with grade 1 hypertension. However, in patients with grade II hypertension the males outnumbered females by a ratio of 2:1. (Table 19)

Table 19. Baseline characteristics of the three groups of Hypertensives.

Parameter	**Hypertension Grade I Mean (SD)**	**Hypertension Grade II Mean (SD)**	**Hypertension Grade III Mean (SD)**
Number	**68**	**27**	**3**
Age (years)	46.71(8.2)	47.63(8.9)	49(6.5)
Males (%)	54.4	70.4%	33%
Mean Systolic Pressure (mm Hg)	149.81(5.7)	165.63(10.44)	179.33(3.055)

Mean Diastolic Pressure (mm Hg)	92.02(3.76)	97.89(5.00)	102(6.9)
Height (cm)	161.87(9.8)	164.37(9.0)	159(7.6)
Weight (Kg)	69.67(11.93)	65.81(13.71)	67.92(8.84)
Body Mass Index (Kg/m^2)	26.51(5.33)	24.37(4.81)	26.71(3.55)
Abdominal Circumference (cm)	101(11.93)	86.63(11.29)	91.67(5.51)

Body Mass Index and Abdominal Circumference

The body mass index in the grade I hypertensives was much higher compared to the grade II hypertensives. This difference is, however unexplained. This might be probably due to the fact that a lot of grade I hypertensives might actually be people who had an underlying metabolic syndrome.

The rest of the clinical variables were comparable between the three different groups of hypertensives.

Baseline Investigation Data

Table 20. Baseline investigations

Parameters	**Hypertension Grade I** **Mean (SD)**	**Hypertension Grade II** **Mean (SD)**	**Hypertension Grade III** **Mean (SD)**
Fasting Blood Sugar (mg%)	103.32(20.67)	98.81(17.51)	108.33(4.7)

Total Cholesterol (mg/dl)	183.38(39.32)	174.3(35.25)	182.33(79.28)
Low density lipoprotein (mg/dl)	118.15(27.8)	116.89(29.87)	60.77(50.9)
High Density Lipoprotein (mg/dl)	41.09(9.664)	44.33(11.74)	41.33(5.7)
Serum Sodium (mEq/l)	138.04(2.6)	138.04(2.54)	137.33(1.15)
Serum Potassium (mEq/l)	4.19(0.35)	4.1(0.46)	4.2(0.34)
Serum Creatinine (mg/dl)	0.728(0.20)	0.78(0.16)	0.65(0.15)
HsCRP (mg/L)	4.96(5.33) **Median: 3.02** **Interquartile range: 6.35**	2.83(3.55) **Median: 1.66** **Interquartile range: 2.11**	1.55(1.37)
Uric Acid (mg%)	5.084(1.24)	4.88(1.46)	4.5(1.11)
Ejection Fraction (%)			
LV Mass Index (g/m^2) **Male** **Female**	93.94(19.9) 95.51 (17.56) 92.06 (22.62)	100.92(31.03) 101.84 (31.50) 98.75 (31.90)	104(55.97) 165 (0) 73.5 (26.16)
Relative Wall Thickness	0.49(0.08)	0.499(0.14)	0.47(0.07)
Albumin-Creatinine Ratio (mg/g)	46.19(73.56) **Median: 15** **Interquartile range: 46.05**	55.67(161.19) **Median: 10.2** **Interquartile range: 43.3**	28.9(27.35) **Median: 16.9**
eGFR (MDRD) ml/min	106(30.80)	108.08(20.02)	116(18.12)

The Baseline investigation data for the different groups of hypertensives and given in the above table (Table 20). From the table, we can see that the Baseline investigations are pretty well matched among all the different groups of hypertensives.

However, on a careful examination between the grade I and grade II hypertensives, **the grade I hypertensives are found to have a slightly increased blood glucose, total cholesterol levels and significantly increased HsCRP level**. When we compare this data along with the fact that these patients who belonged to the grade one hypertension also had an elevated BMI compared to the grade II hypertensives, we come to a conclusion that this **might be due to increased prevalence of metabolic syndrome among the group I hypertensives**.

The HSCRP and the urine albumin creatinine ratio had quite a few outliers which made the mean and standard deviation unreliable methods for comparison. Hence the median and the interquartile range have been provided for the comparison.

This table also brings out an **important fact that the asymptomatic end organ damage is not dependent on the grade of hypertension**. **There was a slight increase in LV mass index in female patients in grade II hypertension compared to females in the grade I hypertension group**. Except for this, there was no significant difference in the eGFR, relative wall thickness and the urine albumin creatinine ratio which is evident from the table among the three different groups.

Primary objective

a. Prevalence of asymptomatic cardiac damage

The prevalence of asymptomatic cardiac damage in a study was 29.59% with 29 of the 98 patients having an elevated LV mass index. This was the most sensitive index to detect the LV hypertrophy in our study. The next most sensitive marker in a study to detect LV hypertrophy was the modified Sokolow Lyon criteria. It picked up 20.4% (n=20) of the patients with LV hypertrophy.

One of the earlier studies to look at the prevalence of LV mass index was studied done in the Italian population by Viazzi et al. The study[28] reported the prevalence of asymptomatic cardiac damage in newly detected hypertensives to be 45%.

In a recent study done in Kashmir published in June 2014, the prevalence of asymptomatic cardiac damage is estimated by the LV mass index was found to be 42% in newly detected hypertensives. This was in contrast to electrocardiographic diagnosis of just 16% in the same population[90].

The LV mass index serves as a very good indicator for predicting the LV hypertrophy in newly detected patients with systemic hypertension.

In a study, the Cornell voltage product criteria had the least sensitivity in the prediction of the LV hypertrophy. However, in a recent study done in Italy it was found to be more sensitive to predict cardiovascular events and it was also found to be more sensitive than the Sokolow Lyon index[91]. However, this might be a difference due to the population in which the study was conducted.

In one of the recent studies published in 2013, the investigators looked at the correlation between LV mass and the Sokolow Lyon criteria in patients with hypertension, aortic stenosis and hypertrophic cardiomyopathy. We postulated that Sokolow Lyon criteria might not only predict structural changes (LV hypertrophy) but also predict the functional changes. They found that Sokolow Lyon index correlated with LV mass index ($p<0.001$) and with the global longitudinal strain ($p<0.001$). They found that the correlation was stronger for the global longitudinal strain in patients with hypertension. The Sokolow Lyon index appears to be a very good indicator to predict both structural and functional left ventricular statuses.

We find that the prevalence of LV hypertrophy in newly detected hypertensives is alarming in almost all the studies which had looked at it. Hence, it's imperative to diagnose it at the time of the patient being diagnosed with hypertension. An echocardiogram at the time of diagnosis should be considered in patients with hypertension, especially in those with other risk factors which increased cardiovascular risk and in patients who are obese where the ECG criteria might not be sensitive.

b. Prevalence of asymptomatic renal damage

The prevalence of asymptomatic renal damage in our study population was around 31.9%. 30 out of the 90 participants in the study had increased urine albumin creatinine ratio. However, none of the patients included in the study were found to have an eGFR < 60ml/min/1.73 m^2.

Urine microalbuminuria in patients who do not have an active urinary infection seem to be a very early marker of hypertension renal damage. And it is at the state, when the renal function is not impaired, the treatment is most effective. Most of the hypertensive societies now recommend routine screening at the diagnosis of hypertension to look for urine microalbuminuria.

In a recent study done in Tamil Nadu, the prevalence of microalbuminuria was studied in patients with essential hypertension. The study showed that 64% of the study population had microalbuminuria. The probable reason for this high incidence of urine microalbuminuria might be because the study population was mostly found to having grade II hypertension and they were recruited from a hospital[37].

The study done by Viazzi et al. the prevalence of microalbuminuria was 12%. However, it is to be taken into account that the study was done in Italy. The screening programs for detection of noncommunicable diseases in Italy are much better than in a developing country like India.

In another study done in Karnataka, the prevalence of microalbuminuria was 26% out of the 100 patients were studied. However, this study did not take in new hypertensives alone. The study included both new and old hypertensives on treatment. The study also showed there was a significant correlation between uric acid levels and the left ventricular hypertrophy the population studied[92].

The prevalence of microalbuminuria in some studies was related to the stage of hypertension, however there is conflicting evidence. Not all studies show this uniform relationship. The prevalence of microalbuminuria also varies

with stage of hypertension and the population being studied. With the onset of hypertension in a person is never being picked up early in a country like India due to lack of good screening programs, it is very difficult to say whether a longer duration of hypertension causes high prevalence urine microalbuminuria.

Microalbuminuria has been traditionally been associated with diabetes mellitus while 24 hour urine protein or urine protein creatinine ratio was used to detect proteinuria in non-diabetic conditions. However, in the recent days it has been found that urine microalbuminuria or the albumin creatinine ratio is much better marker as it detects early proteinuria which can be missed by urine protein creatinine ratio. Hence a lot of guidelines now prefer measuring urine albumin creatinine ratio or the urine microalbumin even in patients with non-diabetic disease[93].

Urine microalbumin or the albumin creatinine ratio is a very simple test to detect early hypertensive injury to the kidney and should be done in all patients diagnosed with hypertension as it is a very cost-effective and simple test. The duration at which to repeat urine albumin creatinine ratio, if it was negative at the time of diagnosis, is undefined. This requires further studies to come up with recommendations.

Secondary outcomes

a. HsCRP and asymptomatic organ damage

One of the secondary objectives was to evaluate serum HsCRP levels with asymptomatic cardiac and renal damage. This was done by dividing the study population into three tertiles based on the serum HsCRP levels.

The ANOVA showed that there was no relationship between asymptomatic organ damage and HsCRP levels. However, there were a few very significant associations.

HsCRP levels were significantly associated with the body mass index , $F_{(2,95)=}$6.625, P=0.002. The HsCRP levels were also significantly related to the diastolic blood pressure, $F_{(2,95)=}$5.280, P=0.007. The systolic blood pressure also showed a trend towards significance with HsCRP Levels, $F_{(2,95)=}$2.920, P=0.059.

These values bring about a very curious question to be answered. All the studies which have been done before have studied the levels of HsCRP and its association with hypertension. The very fact that HsCRP is not associated with asymptomatic organ damage, but is associated with body mass index and diastolic blood pressure makes us think if it was confounded by some other factor.

The association between HsCRP and obesity is very well-known. HsCRP is one of the markers of increased visceral fat. And it also plays an important role in people with metabolic syndrome. Multiple studies have shown the association between obesity and HsCRP.

Study done on obese women showed low levels of adiponectin and it was found that this was associated with an increase in inflammatory markers like HsCRP and interleukin-6. The elevation of these inflammatory markers puts these women in a higher cardiovascular risk[94].

Another study was done in obese women have undergone bariatric surgery (gastric banding) to see the effect on inflammatory markers. The study showed that as the patients lost significant amounts of weight there was a significant decrease in the HsCRP levels in the blood. The HsCRP pregastric banding was 1.33+/-1.21 mg/dl and it reduced to 0.40+/-0.61 mg/dl in post-gastric banding period after the significant weight loss[95].

Both these studies tell us that obesity is significantly related to HsCRP. The studies in hypertension, which showed association of HsCRP to blood pressure needs to be re-looked to see if they were confounded by the obesity in the study subjects.

b. Uric acid levels and asymptomatic organ damage

Serum uric acid was analyzed individually for males and females and they were also divided into three Tertiles. That tertiles of uric acid was compared with markers of asymptomatic organ damage (LV mass index, urine albumin creatinine ratio and eGFR) with ANOVA. There was no significant association between uric acid and any of the markers of asymptomatic organ damage.

The results could be slightly biased as the number of patients in each group was very less as the whole study group had to be divided into males and

females. The study was not sufficiently powered to detect any difference in the asymptomatic organ damage due to elevated levels of uric acid.

A larger study is hence required to look for any statistically significant results.

c. HsCRP and uric acid with Risk factors for hypertension.

HSCRP and uric acid were studied to look for any association with the risk factors for hypertension and asymptomatic organ damage. This was done with the help of a bivariate analysis to look for any statistically significant correlation.

The table below shows the results of the Bivariate analysis.

Table 21. HsCRP and Risk Factors

Variables	**HsCRP**	
	R	P
Age	0.002	.981
Systolic Pressure	-.118	.246
Diastolic Pressure	-.74	.469
BMI	**.356**	**0.000**
Abdominal Circumference	**.295**	**0.003**
Mean Heart rate	0.25	.809
Total Cholesterol	-0.58	.573
LDL	0.26	.803
HDL	-0.85	.570

The bivariate analysis showed the **BMI and the abdominal circumference correlated significantly with the HsCRP levels**. (Table 21)

Table 22. Uric acid and risk Factors

Variable	Males		Females	
	R	**P**	**r**	**P**
Age	-.223	0.96	-0.39	0.811
Systolic Pressure	-0.73	.591	-0.93	0.564
Diastolic Pressure	0.20	.881	0.145	0.366
Heart Rate	0.177	0.187	-0.258	0.103
Abdominal Circumference	0.065	0.631	0.262	0.097
Body Mass Index	0.121	0.369	**0.368**	**0.018**
Total Cholesterol	0.011	0.933	0.078	0.629
LDL	0.042	0.755	0.249	0.116
HDL	-0.269	0.43	-0.150	0.349
Serum Creatinine	0.200	0.228	0.291	0.065
eGFR	-0.038	0.778	-0.286	0.070

The bivariate analysis of uric acid was done separately for males and females. The only significant correlation was between body mass index in females and serum uric acid. This co-relation was not seen between the uric acid tertiles analyzed by ANOVA. This might just be an association which a larger study might be able to tell us better. This is, however an expected correlation which has been very well documented before. (Table 22)

d. Left ventricular geometries in the study population

There are four types of ventricular geometries defined in the patients with systemic hypertension. They are normal LV geometry, concentric remodelling, eccentric hypertrophy and concentric hypertrophy. The four types studied based on the LV mass index and relative wall thickness.

In our study, we found a very significant number of patients with concentric remodelling (57.7%, n=56) of the heart. There were four patients with eccentric hypertrophy and 25 patients with concentric hypertrophy of the left ventricle. Only 12.4% (n=12) had a normal LV geometry in the studied population. (Table 21)

Table 23. Prevalence of Different Left Ventricular Geometries

LV Geometry	
Normal	12.4% (12)
Concentric remodeling	**57.7% (56)**
Eccentric Hypertrophy	4.1% (4)
Concentric Hypertrophy	**25.8% (25)**

Concentric remodelling is considered as one of the adaptations of the heart to increased cardiac overload. The prevalence of concentric remodelling in patients with hypertension varies in various populations and in various studies. Few studies have shown that concentric remodelling actually has an intermediate risk for future cardiovascular events and it is also an independent predictor of

systolic and diastolic dysfunction. However, more studies are needed to quantify the risk of cardiovascular events due to concentric remodelling.

Such a high proportion of patients presenting with concentric remodelling needs a study in India to see if the prevalence is the same or is it lower. We also need long-term cohort studies to see if there are any adverse prognostic events associated with concentric remodelling the Indian population.

Concluding Remarks

Conclusion

1. The prevalence of asymptomatic organ damage in newly detected treatment naive hypertensives in our centre this very high. The prevalence of asymptomatic renal damage was 31.9% (n=30) and the prevalence of asymptomatic cardiac damage was 29.59%(n=29)

2. There was no association between the inflammatory markers, HsCRP and uric acid with asymptomatic organ damage in patients with hypertension, however this leads to be confirmed in a larger trial.

3. There was an association between HsCRP with body mass index and abdominal circumference in the study.

4. There was a very high incidence of concentric remodelling in our population which leads to be further clarified and the consequences have to be studied by following up these patients.

Clinical implications

1. Almost one third of the patients included in the study had asymptomatic organ damage and this implies that all patients were newly diagnosed with hypertension should be screened for asymptomatic cardiac and renal damage.

2. It is better to screen high-risk patients and obese individuals who present with hypertension for LV hypertrophy with echocardiogram as the electrocardiogram can miss out patients with left ventricular hypertrophy.

3. All patients who are newly diagnosed with hypertension should have in urine albumin creatinine ratio done to screen for asymptomatic renal damage.

Limitations

The sample size was small in the study as the recruitment was done in a tertiary care centre and the number of patients presenting with isolated hypertension was very small. Patients had multiple other comorbidities and hence could not be included in the study.

We suggest repeating the study on a community basis in a cohort so that the patients can be followed up in the inferences can be drawn upon on a continuous basis over the years which will help us manage hypertension in a much better way.

Directions for future research

1. Need for a cohort study on hypertension in India is the need of the day as all the data we have on hypertension is from the west.

2. The left ventricular geometry in Indian population needs to be studied in more detail.

Bibliography

1. The Lancet. Hypertension: uncontrolled and conquering the world. The Lancet. 2007 Aug;370(9587):539.

2. WHO | The world health report 2002 - Reducing Risks, Promoting Healthy Life [Internet]. WHO. [cited 2014 Sep 3]. Available from: http://www.who.int/whr/2002/en/

3. Park K. Textbook of Preventive and Social Medicine. 19th edition. Bansaridas Bhanot; 2007. 309-14. p.

4. Garrod AB. On the Blood and Effused Fluids in Gout, Rheumatism, and Bright's Disease. Medico-Chir Trans. 1854;37:49–60.1.

5. Mazzali M, Kanellis J, Han L, Feng L, Xia Y-Y, Chen Q, et al. Hyperuricemia induces a primary renal arteriolopathy in rats by a blood pressure-independent mechanism. Am J Physiol Renal Physiol. 2002 Jun;282(6):F991–7.

6. Feig DI. Uric Acid and Hypertension. Semin Nephrol. 2011 Sep;31(5):441–6.

7. Gueyffier F, Boissel JP, Pocock S, Boutitie F, Coope J, Cutler J, et al. Identification of risk factors in hypertensive patients: contribution of randomized controlled trials through an individual patient database. Circulation. 1999 Nov 2;100(18):e88–94.

8. Kanellis J, Watanabe S, Li JH, Kang DH, Li P, Nakagawa T, et al. Uric acid stimulates monocyte chemoattractant protein-1 production in vascular smooth muscle cells via mitogen-activated protein kinase and cyclooxygenase-2. Hypertension. 2003 Jun;41(6):1287–93.

9. Rao GN, Corson MA, Berk BC. Uric acid stimulates vascular smooth muscle cell proliferation by increasing platelet-derived growth factor A-chain expression. J Biol Chem. 1991 May 5;266(13):8604–8.

10. Langlois M, De Bacquer D, Duprez D, De Buyzere M, Delanghe J, Blaton V. Serum uric acid in hypertensive patients with and without peripheral arterial disease. Atherosclerosis. 2003 May;168(1):163–8.

11. Patetsios P, Song M, Shutze WP, Pappas C, Rodino W, Ramirez JA, et al. Identification of uric acid and xanthine oxidase in atherosclerotic plaque. Am J Cardiol. 2001 Jul 15;88(2):188–91, A6.

12. Boos CJ, Lip GYH. Is hypertension an inflammatory process? Curr Pharm Des. 2006;12(13):1623–35.

13. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. JAMA. 2003 Dec 10;290(22):2945–51.

14. Saito M, Ishimitsu T, Minami J, Ono H, Ohrui M, Matsuoka H. Relations of plasma high-sensitivity C-reactive protein to traditional cardiovascular risk factors. Atherosclerosis. 2003 Mar;167(1):73–9.

15. King DE, Egan BM, Mainous AG, Geesey ME. Elevation of C-reactive protein in people with prehypertension. J Clin Hypertens Greenwich Conn. 2004 Oct;6(10):562–8.

16. Verma S, Wang C-H, Li S-H, Dumont AS, Fedak PWM, Badiwala MV, et al. A self-fulfilling prophecy: C-reactive protein attenuates nitric oxide production and inhibits angiogenesis. Circulation. 2002 Aug 20;106(8):913–9.

17. Ikeda U, Takahashi M, Shimada K. C-reactive protein directly inhibits nitric oxide production by cytokine-stimulated vascular smooth muscle cells. J Cardiovasc Pharmacol. 2003 Nov;42(5):607–11.

18. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. The Lancet. 2005 Jan 15;365(9455):217–23.

19. Lawes CM, Hoorn SV, Rodgers A. Global burden of blood-pressure-related disease, 2001. The Lancet. 2008 May 9;371(9623):1513–8.

20. A R, C L, S M. Reducing the global burden of blood pressure-related cardiovascular disease. J Hypertens Suppl Off J Int Soc Hypertens. 2000 May;18(1):S3–6.

21. Li H, Meng Q, Sun X, Salter A, Briggs NE, Hiller JE. Prevalence, awareness, treatment, and control of hypertension in rural China: results from Shandong Province: J Hypertens. 2010 Mar;28(3):432–8.

22. Yusuf S, Reddy S, Ôunpuu S, Anand S. Global Burden of Cardiovascular Diseases Part I: General Considerations, the Epidemiologic Transition, Risk Factors, and Impact of Urbanization. Circulation. 2001 Nov 27;104(22):2746–53.

23. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens. 2004;18(2):73–8.

24. Prevalence and determinants of hypertension in the urban pop... : Journal of Hypertension [Internet]. [cited 2014 Sep 8]. Available from: http://journals.lww.com/jhypertension/Fulltext/1995/10000/Prevalence_and_determinants_of_hypertension_in_the.14.aspx

25. Shanthirani CS, Pradeepa R, Deepa R, Premalatha G, Saroja R, Mohan V. Prevalence and risk factors of hypertension in a selected South Indian

population--the Chennai Urban Population Study. J Assoc Physicians India. 2003 Jan 1;51:20–7.

26. Beegom R, Beegom R, Niaz MA, Singh RB. Diet, central obesity and prevalence of hypertension in the urban population of South India. Int J Cardiol. 1995 Sep;51(2):183–91.

27. Bonow RO, MD DLM, MD DPZ, PhD PLM. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, Single Volume: Expert Consult Premium Edition - Enhanced Online Features and Print, 9e. 9 edition. Philadelphia: Saunders; 2011. 2048 p.

28. Viazzi F, Parodi D, Leoncini G, Parodi A, Falqui V, Ratto E, et al. Serum Uric Acid and Target Organ Damage in Primary. Hypertension. 2005 May 1;45(5):991–6.

29. S S, G K. [Microalbuminuria in hypertension]. Nihon Rinsho Jpn J Clin Med. 2004 Jan;62(1):97–102.

30. Pedrinelli R, Dell'Omo G, Bello VD, Pellegrini G, Pucci L, Prato SD, et al. Low-Grade Inflammation and Microalbuminuria in Hypertension. Arterioscler Thromb Vasc Biol. 2004 Dec 1;24(12):2414–9.

31. Gerstein HC, Mann JE, Yi Q, et al. ALbuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA. 2001 Jul 25;286(4):421–6.

32. Jager A, Kostense PJ, Ruhé HG, Heine RJ, Nijpels G, Dekker JM, et al. Microalbuminuria and Peripheral Arterial Disease Are Independent Predictors of Cardiovascular and All-Cause Mortality, Especially Among Hypertensive Subjects Five-year Follow-up of the Hoorn Study. Arterioscler Thromb Vasc Biol. 1999 Mar 1;19(3):617–24.

33. Yudkin J, Forrest R, Jackson C. MICROALBUMINURIA AS PREDICTOR OF VASCULAR DISEASE IN NON-DIABETIC SUBJECTS: Islington Diabetes Survey. The Lancet. 1988 Sep 3;332(8610):530–3.

34. Wachtell K, Ibsen H, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Albuminuria and Cardiovascular Risk in Hypertensive Patients with Left Ventricular Hypertrophy: The LIFE Study. Ann Intern Med. 2003 Dec 2;139(11):901–6.

35. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B, Jensen G, Clausen P, Scharling H, et al. Very Low Levels of Microalbuminuria Are Associated With Increased Risk of Coronary Heart Disease and Death Independently of Renal Function, Hypertension, and Diabetes. Circulation. 2004 Jul 6;110(1):32–5.

36. Jensen JS, Feldt-Rasmussen B, Strandgaard S, Schroll M, Borch-Johnsen K. Arterial Hypertension, Microalbuminuria, and Risk of Ischemic Heart Disease. Hypertension. 2000 Apr 1;35(4):898–903.

37. GM marudhaiveeran, Radhakrishnan S, Alphonse F. Prevalence of microalbuminuria among patients with essential hypertension. Trop J Med Res. 17:76–80.

38. Ibsen H, Olsen MH, Wachtell K, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Reduction in Albuminuria Translates to Reduction in Cardiovascular Events in Hypertensive Patients Losartan Intervention for Endpoint Reduction in Hypertension Study. Hypertension. 2005 Feb 1;45(2):198–202.

39. Vakili BA, Okin PM, Devereux RB. Prognostic implications of left ventricular hypertrophy. Am Heart J. 2001 Mar;141(3):334–41.

40. Schillaci G, Verdecchia P, Porcellati C, Cuccurullo O, Cosco C, Perticone F. Continuous Relation Between Left Ventricular Mass and Cardiovascular Risk in Essential. Hypertension. 2000 Feb 1;35(2):580–6.

41. McLenachan JM, Henderson E, Morris KI, Dargie HJ. Ventricular Arrhythmias in Patients with Hypertensive Left Ventricular Hypertrophy. N Engl J Med. 1987 Sep 24;317(1987):787–92.

42. CASALE PN, DEVEREUX RB, MILNER M, ZULLO G, HARSHFIELD GA, PICKERING TG, et al. Value of Echocardiographic Measurement of Left Ventricular Mass in Predicting Cardiovascular Morbid Events in Hypertensive Men. Ann Intern Med. 1986 Aug 1;105(2):173–8.

43. Kjeldsen SE, Dahlöf B, Devereux RB, et al. Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: A losartan intervention for endpoint reduction (life) substudy. JAMA. 2002 Sep 25;288(12):1491–8.

44. Devereux RB, Dahlöf B, Gerdts E, Boman K, Nieminen MS, Papademetriou V, et al. Regression of Hypertensive Left Ventricular Hypertrophy by Losartan Compared With Atenolol The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Trial. Circulation. 2004 Sep 14;110(11):1456–62.

45. Pitt B, Reichek N, Willenbrock R, Zannad F, Phillips RA, Roniker B, et al. Effects of Eplerenone, Enalapril, and Eplerenone/Enalapril in Patients With Essential Hypertension and Left Ventricular Hypertrophy The 4E–Left Ventricular Hypertrophy Study. Circulation. 2003 Oct 14;108(15):1831–8.

46. Mathew J, Sleight P, Lonn E, Johnstone D, Pogue J, Yi Q, et al. Reduction of Cardiovascular Risk by Regression of Electrocardiographic Markers of Left Ventricular Hypertrophy by the Angiotensin-Converting Enzyme Inhibitor Ramipril. Circulation. 2001 Oct 2;104(14):1615–21.

47. Schmieder RE, Martus P, Klingbeil A. Reversal of left ventricular hypertrophy in essential hypertension: A meta-analysis of randomized double-blind studies. JAMA. 1996 May 15;275(19):1507–13.

48. Ganau A, Devereux RB, Roman MJ, de Simone G, Pickering TG, Saba PS, et al. Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. J Am Coll Cardiol. 1992 Jun;19(7):1550–8.

49. Roman MJ, Saba PS, Pini R, Spitzer M, Pickering TG, Rosen S, et al. Parallel cardiac and vascular adaptation in hypertension. Circulation. 1992 Dec 1;86(6):1909–18.

50. Li L, Shigematsu Y, Hamada M, Hiwada K. Relative Wall Thickness Is an Independent Predictor of Left Ventricular Systolic and Diastolic Dysfunctions in Essential Hypertension. Hypertens Res. 2001;24(5):493–9.

51. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid Intimal-Medial Thickness Is Related to Cardiovascular Risk Factors Measured From Childhood Through Middle Age The Muscatine Study. Circulation. 2001 Dec 4;104(23):2815–9.

52. Sorof JM, Alexandrov AV, Cardwell G, Portman RJ. Carotid Artery Intimal-Medial Thickness and Left Ventricular Hypertrophy in Children With Elevated Blood Pressure. Pediatrics. 2003 Jan 1;111(1):61–6.

53. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common Carotid Intima-Media Thickness and Risk of Stroke and Myocardial Infarction The Rotterdam Study. Circulation. 1997 Sep 2;96(5):1432–7.

54. Zanchetti A, Bond MG, Hennig M, Neiss A, Mancia G, Palu CD, et al. Risk factors associated with alterations in carotid intima-media thickness in hypertension: baseline data from the European Lacidipine Study on Atherosclerosis. J Hypertens July 1998. 1998;16(7):949–61.

55. Zanchetti A, Rosei EA, Palu CD, Leonetti G, Magnani B, Pessina A, et al. The Verapamil in Hypertension and Atherosclerosis Study (VHAS): Results of long-term randomized treatment with either verapamil or chlorthalidone on carotid intima-media thickness. J Hypertens Novemb 1998. 1998;16(11):1667–76.

56. Stabouli S, Kotsis V, Papamichael C, Constantopoulos A, Zakopoulos N. Adolescent Obesity is Associated with High Ambulatory Blood Pressure and Increased Carotid Intimal-Medial Thickness. J Pediatr. 2005 Nov;147(5):651–6.

57. Lemne C, Jogestrand T, Faire U de. Carotid Intima-Media Thickness and Plaque in Borderline Hypertension. Stroke. 1995 Jan 1;26(1):34–9.

58. Salonen R, Salonen JT. Determinants of carotid intima-media thickness: a population-based ultrasonography study in Eastern Finnish men. J Intern Med. 1991 Mar 1;229(3):225–31.

59. W M, Y Y, L Q, B Z, L M, Y Z, et al. [Relationship between high normal blood pressure and carotid artery atherosclerosis in Beijing residents]. Zhonghua Xin Xue Guan Bing Za Zhi. 2014 Jun;42(6):510–4.

60. Blacher J, Asmar R, Djane S, London GM, Safar ME. Aortic Pulse Wave Velocity as a Marker of Cardiovascular Risk in Hypertensive Patients. Hypertension. 1999 May 1;33(5):1111–7.

61. Mourad J-J, Pannier B, Blacher J, Rudnichi A, Benetos A, London GM, et al. Creatinine clearance, pulse wave velocity, carotid compliance and essential hypertension. Kidney Int. 2001 May;59(5):1834–41.

62. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. Aortic Stiffness Is an Independent Predictor of All-Cause and Cardiovascular Mortality in Hypertensive Patients. Hypertension. 2001 May 1;37(5):1236–41.

63. Boutouyrie P, Tropeano AI, Asmar R, Gautier I, Benetos A, Lacolley P, et al. Aortic Stiffness Is an Independent Predictor of Primary Coronary Events in Hypertensive Patients A Longitudinal Study. Hypertension. 2002 Jan 1;39(1):10–5.

64. Laurent S, Katsahian S, Fassot C, Tropeano A-I, Gautier I, Laloux B, et al. Aortic Stiffness Is an Independent Predictor of Fatal Stroke in Essential Hypertension. Stroke. 2003 May 1;34(5):1203–6.

65. Henskens LHG, Kroon AA, Oostenbrugge RJ van, Gronenschild EHBM, Fuss-Lejeune MMJJ, Hofman PAM, et al. Increased Aortic Pulse Wave Velocity Is Associated With Silent Cerebral Small-Vessel Disease in Hypertensive Patients. Hypertension. 2008 Dec 1;52(6):1120–6.

66. Asmar R, Topouchian J, Pannier B, Benetos A, Safar M, on behalf of the Scientific QC. Pulse wave velocity as endpoint in large-scale intervention trial. The Complior(R) study. J Hypertens April 2001. 2001;19(4):813–8.

67. Rajzer M, Klocek M, Kawecka-Jaszcz K. Effect of amlodipine, quinapril, andlosartan on pulse wave velocity andplasma collagen markers in patients withmild-to-moderate arterial hypertension. Am J Hypertens. 2003 Jun;16(6):439–44.

68. Cannon PJ, Stason WB, Demartini FE, Sommers SC, Laragh JH. Hyperuricemia in primary and renal hypertension. N Engl J Med. 1966 Sep 1;275(9):457–64.

69. Johnson RJ. Resurrection of Uric Acid as a Causal Risk Factor in Essential Hypertension. Hypertension [Internet]. 2004 Nov 22 [cited 2012 Sep 14]; Available from: http://hyper.ahajournals.org/cgi/doi/10.1161/01.HYP.0000150785.39055.e8

70. Mustard JF, Murphy EA, Ogryzlo MA, Smythe HA. BLOOD COAGULATION AND PLATELET ECONOMY IN SUBJECTS WITH PRIMARY GOUT. Can Med Assoc J. 1963 Dec 14;89:1207–11.

71. Kanellis J, Watanabe S, Li JH, Kang DH, Li P, Nakagawa T, et al. Uric Acid Stimulates Monocyte Chemoattractant Protein-1 Production in Vascular

Smooth Muscle Cells Via Mitogen-Activated Protein Kinase and Cyclooxygenase-2. Hypertension. 2003 Jun 1;41(6):1287–93.

72. F J, E F, S P, V K, E C, R G, et al. Serum uric acid and hypertension: the Olivetti heart study. J Hum Hypertens. 1994 Sep;8(9):677–81.

73. Sundstrom J. Relations of Serum Uric Acid to Longitudinal Blood Pressure Tracking and Hypertension Incidence. Hypertension [Internet]. 2004 Nov 29 [cited 2012 Sep 14]; Available from: http://hyper.ahajournals.org/cgi/doi/10.1161/01.HYP.0000150784.92944.9a

74. Taniguchi Y, Hayashi T, Tsumura K, Endo G, Fujii S, Okada K. Serum uric acid and the risk for hypertension and Type 2 diabetes in Japanese men: The Osaka Health Survey. J Hypertens July 2001. 2001;19(7):1209–15.

75. Perlstein TS, Gumieniak O, Williams GH, Sparrow D, Vokonas PS, Gaziano M, et al. Uric Acid and the Development of Hypertension The Normative Aging Study. Hypertension. 2006 Dec 1;48(6):1031–6.

76. Venugopal SK, Devaraj S, Jialal I. Effect of C-reactive protein on vascular cells: evidence for a proinflammatory, proatherogenic role. Curr Opin Nephrol Hypertens. 2005 Jan;14(1):33–7.

77. Szmitko PE, Wang C-H, Weisel RD, Almeida JR de, Anderson TJ, Verma S. New Markers of Inflammation and Endothelial Cell Activation Part I. Circulation. 2003 Oct 21;108(16):1917–23.

78. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, et al. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ. 2000 Jul 22;321(7255):199–204.

79. Rost NS, Wolf PA, Kase CS, Kelly-Hayes M, Silbershatz H, Massaro JM, et al. Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. Stroke J Cereb Circ. 2001 Nov;32(11):2575–9.

80. Lenderink T, Boersma E, Heeschen C, Vahanian A, de Boer M-J, Umans V, et al. Elevated troponin T and C-reactive protein predict impaired outcome for 4 years in patients with refractory unstable angina, and troponin T predicts benefit of treatment with abciximab in combination with PTCA. Eur Heart J. 2003 Jan;24(1):77–85.

81. Torzewski J, Torzewski M, Bowyer DE, Fröhlich M, Koenig W, Waltenberger J, et al. C-reactive protein frequently colocalizes with the terminal complement complex in the intima of early atherosclerotic lesions of human coronary arteries. Arterioscler Thromb Vasc Biol. 1998 Sep;18(9):1386–92.

82. Pasceri V, Cheng JS, Willerson JT, Yeh ET, Chang J. Modulation of C-reactive protein-mediated monocyte chemoattractant protein-1 induction in human

endothelial cells by anti-atherosclerosis drugs. Circulation. 2001 May 29;103(21):2531–4.

83. Cermak J, Key NS, Bach RR, Balla J, Jacob HS, Vercellotti GM. C-reactive protein induces human peripheral blood monocytes to synthesize tissue factor. Blood. 1993 Jul 15;82(2):513–20.

84. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013 Jul 21;34(28):2159–219.

85. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. 1916. Nutr Burbank Los Angel Cty Calif. 1989 Oct;5(5):303–11; discussion 312–3.

86. Sokolow M, Lyon TP. The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. Am Heart J. 1949 Feb;37(2):161–86.

87. Molloy TJ, Okin PM, Devereux RB, Kligfield P. Electrocardiographic detection of left ventricular hypertrophy by the simple QRS voltage-duration product. J Am Coll Cardiol. 1992 Nov 1;20(5):1180–6.

88. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification. Eur J Echocardiogr J Work Group Echocardiogr Eur Soc Cardiol. 2006 Mar;7(2):79–108.

89. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999 Mar 16;130(6):461–70.

90. laway M, Dar HA, para KA, Sheikh NA, S.K, Mir mohd. D. PREVALENCE OF CONCENTRIC LEFT VENTRICULAR HYPERTROPHY IN NEWLY DIAGNOSED HYPERTENSIVES BY ECHOCARDIOGRAPHY IN KASHMIR. Int J Recent Sci Res. 2014 Jul;5(7):1262–3.

91. Cuspidi C, Facchetti R, Bombelli M, Sala C, Grassi G, Mancia G. Accuracy and prognostic significance of electrocardiographic markers of left ventricular hypertrophy in a general population: findings from the Pressioni Arteriose Monitorate E Loro Associazioni population. J Hypertens. 2014 Apr;32(4):921–8.

92. Agarwal S, Prabhu VM, * AS, Pinto VJ, Bhat GK, * DM. Correlation of microalbuminuria with cardiovascular morbidity in essential hypertension. Int J Clin Cases Investig. 2014 Jul 1;5(6):67–76.

93. Lamb EJ, MacKenzie F, Stevens PE. How should proteinuria be detected and measured? Ann Clin Biochem. 2009 May;46(Pt 3):205–17.

94. Engeli S, Feldpausch M, Gorzelniak K, Hartwig F, Heintze U, Janke J, et al. Association Between Adiponectin and Mediators of Inflammation in Obese Women. Diabetes. 2003 Apr 1;52(4):942–7.

95. Laimer M, Ebenbichler CF, Kaser S, Sandhofer A, Weiss H, Nehoda H, et al. Markers of chronic inflammation and obesity: a prospective study on the reversibility of this association in middle-aged women undergoing weight loss by surgical intervention. Int J Obes. 2002 May 17;26(5):659–62.

Annexures

Patient Information Sheet

Hypertensive End organ damage Study with HsCRP and Uric acid (HEDS –UP)

PATIENT INFORMATION SHEET

Hypertension is a chronic disorder affecting the human population. Worldwide, the estimated number of adults with hypertension was 972 million in 2000; 639 million live in developing countries like India. Hypertension is the commonest cause of stroke in the word. It is also an important cause of Heart attack and renal Failure in the Indian Population. The prevalence of Hypertension in India is estimated between 17-21% i.e, as high as 1 in 5 people in india are hypertensive in the urban India.

Many a times Hypertension is diagnosed when the patient ends up in hospital with a stroke or heart attack. At this stage the damage that has occurred in the heart or the brain or the kidney is irreversible. This study aims at identifying the persons with very minimal damage to heart or kidneys as they are the earliest organs damaged in Hypertension. This will help us guide the management of Hypertension better.

The information from this study will help other doctors understand the burden of hypertension in our country. It will also help them understand the value of prompt diagnosis and treatment of Hyertension. It will also help us identify whether few blood tests can be used as markers to identify the population with cardiac and renal damage among the hypertensive patients. In turn this will help in mass screening of hypertensive patients for cardiac and renal damage.

If you are willing to participate in this study, you may be asked to review with your doctor 2 weeks after your initial visit for a few blood tests if required for the diagnosis.

By participating in the study you will not be made to incur any added expenses apart from the routine initial investigations. There is no added risk or discomfort of any kind for you by participating in this study. Any personal information about you that is collected as part of this study will be maintained strictly confidential. Participation is entirely voluntary and refusal to participate will not involve any loss of benefit or change in treatment that you receive.

For trial related queries, the principal investigator Dr P. Muthukumaran is to be contacted.

Dr P. Muthukumaran
Department of General Medicine
Email: pmkumaran@gmail.com
9543352184

1st Oct 2013.

Consent Form

Study Title: ***Hypertensive End organ damage Study with HsCRP and Uric acid (HEDS –UP)***

Serial Number: _____

Subject's Initials: _____ **Subject's Name:** _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood / the sheet was read out to me and I have understood the information sheet dated 1st Oct 2013 for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: ____/____/_____

Subject / Representative Name: _____ Signature:

Or

Signature of the Investigator: _____

Study Investigator's Name: _____

Date: ____/____/_____

Signature of the Witness: _____

Date: ____/____/_____

Name & Address of the Witness: _____

Clinical research Form

To study the prevalence of asymptomatic cardiac and renal damage in treatment naïve patients adult patients with Systemic Hypertension and to study the co-relation between HsCRP / Uric Acid with asmptomatic organ damage.

HYPERTENSIVE END ORGAN DAMAGE STUDY With Uric acid and HsCRP (HEDS-UP)

Personal Details							
Serial Number:				Hospital Number:			
Name		Sex		MALE / FEMALE		Age	
Address:				Occupation:			
				Landline No.			
				Mobile Number			
				Email Id.			
Pincode:							

Risk Factors			If yes, Details
a	Family / Personal history of CAD and HTN	Yes / No	
b	Family / Personal history dyslipidemia	Yes / No	
c	Family / Personal history Diabetes	Yes / No	
d	Smoking	Yes / No	
e	family History of Premature CAD	Yes / No	
f	Snoring / sleep apnea	Yes / No	
g	Low Birth weight	Yes / No	

SECONDARY HYPERTENSION			If Yes, Details
a	Family H/O of CKD	Yes / No	
b	H/O renal disease / UTI / Hematuria	Yes / No	
c	Drugs*	Yes / No	
d	Symptoms of Pheochromocytoma#	Yes / No	
e	Episodes of weakness or tetany	Yes / No	
f	Symptoms sugg. of thyroid disease	Yes / No	
# - Repetitive episodes of sweating, headache, anxiety, palpitations			
* - OCP's, Vasoconstrictive nasal drops, Steroids, NSAIDS.			

HISTORY OF ORGAN DAMAGE (encircle symtoms)	
CNS / Eyes	Headache / Vertigo / Impaired Vision / TIA / Stroke / Carotid Revascularisation
Heart	Angina / SOB / Pedal edema / MI / Revasularisation / Palpitations / Arrhythmias
Kidney	Thirst / Polyuria / Nocturia / Hematuria
PAD	Cold extremities / Intermittent claudication / peripheral revascularisation

Blood Pressure (in mmHg)						
BP:	1st	/	HR	/min	Height	cm
Dt:	2nd	/	HR	/min	Weight	kg
BP:	1st	/	HR	/min	Abd. Circ.	cm
Dt:	2nd	/	HR	/min	BMI	kg/m^2
Mean Systolic BP			Mean Heart Rate			/min
Mean Diastolic BP					BSA	m^2

Examination for Secondary Hypertension			
a	Features of cushings syndrome	Yes / No	
b	Skin stigmata of neurofibromatosis	Yes / No	
c	Abdominal murmurs	Yes / No	
d	Precordial murmurs sugg of CoA[1], UED[2]	Yes / No	
e	radiofemoral delay	Yes / No	
f	Large Upper limb diference (CoA, Subclavian stenosis)	Yes / No	
CoA = Coarctation of Aorta, UED = upper extremity disease.			

Signs of Organ Damage (Encircle)	
CNS	Sensory or Motor Symptoms
Retina	Fundoscopic abnormalities
Heart	3rd or 4th heart sounds / Downward displacement of Apex / Cardiac murmurs / rales / pedal edema
PAD	Absence / assymetry or reduction of pulses / Cold extremeties / Ischaemic ulcers
Carotid	Systolic murmurs

Investigations			
HB	gms%	Sodium	mg/dl
Fasting Glucose	mg/dl	Potassium	mg/dl
Total Cholesterol	mg/dl	Creatinine	mg/dl
LDL	mg/dl	HsCRP	mg/L
HDL	mg/dl	Uric acid	mg/dl

ECG			
S wave in V1	mV	R wave in V5	mV
Largest S wave	mV	Largest R wave	mV
R wave in AVL	mV	S wave in V3	mV
QRS duration	ms		

ECG Criteria		Value	Criteria satisfied
a	Sokolow Lyon Index		Yes / No
b	Modified Sokolow Lyon Index		Yes / No
c	Cornell Voltage criteria		Yes / No

ECHO			
LVEDD	mm	LVMI	g/m²
PWd	mm	RWT	
IVSs	mm		
EF	%		

Renal End Organ Damage	
Albumin-Creatinine Ratio	mg/g
Abbreviated MDRD equation (eGFR)	ml/min

S_No	P_Age	P_Sex	P_OCC	H_CH	H_DYS	H_DIAB
1	46	1	injection mould operator	1	0	0
2	56	1	security guard	0	0	0
3	44	0	homemaker	1	0	0
4	40	1	manual labourer	0	0	0
5	39	0	homemaker	1	0	0
6	45	1	business	1	0	0
7	60	1	machine operator	0	0	0
8	59	1	advocate	0	0	0
9	48	1	business	1	0	1
10	60	1	Poen	0	0	0
11	54	1	Teacher	0	0	0
12	59	1	surveyor	0	0	0
13	57	1	agriculture	0	0	0
14	49	1	manual labourer	1	0	0
15	60	1	agriculturer	0	0	0
16	41	0	housewife	0	0	0
17	52	1	social worker	1	0	1
18	40	1	manual labourer	0	0	0
19	35	0	housewife	0	0	0
20	35	0	housewife	1	0	0
21	47	1	civil engineer	0	0	1
22	60	1	retired	0	0	0
23	34	0	housewife	1	0	0
24	50	0	tea stall owner	0	0	0
25	58	1	farmer	0	0	0
26	50	1	farmer	1	0	1
27	51	1	jute mill worker	0	0	0
28	53	1	CHEMICAL FACTORY	1	0	0
29	49	0	housewife	1	0	0
30	55	0	housewife	1	0	0
31	42	0	housewife	0	0	0
32	52	0	food business	0	0	0
33	61	1	retired	0	0	0
34	38	1	business	1	1	0
35	55	0	housewife	0	0	0
36	37	1	Professional	1	0	1
37	37	1	banker	1	0	1
38	42	0	housewife	1	0	1
39	57	0	housemaid	0	0	0
40	48	0	housewife	0	0	0
41	61	0	housewife	1	0	0
42	45	1	salesman	1	0	0
43	48	0	housewife	1	0	1
44	59	0	housewife	1	0	1
45	45	1	rickshaw driver	0	0	0
46	52	1	tailor	0	0	0
47	47	1	agriculture	1	0	0
48	31	0	teacher	1	0	1
49	45	0	housewife	0	0	0
50	31	1	software developer	1	1	0

51	30	1	teacher	0	0	0
52	46	0	manual labourer	1	0	1
53	43	1	agriculture	0	0	0
54	37	1	finance	1	0	1
55	47	1	printing press	1	0	1
56	42	0	housewife	0	0	0
57	33	1	police	0	0	0
58	53	0	govt. service	0	0	0
59	44	1	agriculture	1	0	1
60	49	1	workshop	1	0	1
61	30	1	shopkeeper	0	0	0
62	60	1	retired	1	0	0
63	52	0	compamy worker	0	0	0
64	39	1	driver	1	0	1
65	52	1	manual labourer	0	0	0
66	37	0	teacher	0	0	1
67	38	0	tea shop	1	0	0
68	36	1	teacher	0	1	0
69	59	1	retired	0	0	0
70	47	0	housewife	1	0	1
71	57	0	housewife	0	0	0
72	53	0	housewife	1	0	1
73	47	1	manual labourer	0	0	0
74	51	0	housewife	1	0	0
75	50	1	driver	1	0	1
76	43	0	manual labourer	0	0	0
77	34	1	cloth shop	1	0	1
78	59	0	housewife	0	0	0
79	46	1	petrol bunk	0	0	1
80	43	1	business	0	0	0
81	43	1	mechanic	0	0	0
82	51	0	housewife	0	0	0
83	46	1	teacher	0	0	0
84	50	0	florist0	0	0	0
85	43	1	mechanic	1	0	1
86	49	0	HOUSEWIFE	0	0	1
87	47	0	HOUSEWIFE	0	0	0
88	50	1	Manual labourer	0	0	0
89	52	1	not working	0	0	0
90	50	0	housewife	1	0	0
91	40	0	housewife	0	0	0
92	60	0	nil	0	0	0
93	36	1	flour mill	0	0	0
94	36	1	vegetable business	0	0	0
95	55	0	housewife	0	0	0
96	42	1	carpenter	0	0	0
97	44	1	nil	0	0	0
98	39	0	HOUSEWIFE	0	0	0

S_No	H_SMOK	H_PCAD	H_SSA	H_LBW	H_CKD	H_RD	H_DRUG	H_PHEO
1	0	0	0	0	0	0	0	0
2	1	0	1	0	1	0	0	0
3	0	0	1	0	0	0	0	0
4	1	0	1	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0
8	0	0	1	0	0	0	0	0
9	0	0	0	0	0	0	0	0
10	0	0	1	0	0	0	0	0
11	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0
13	1	0	1	0	0	0	0	0
14	1	0	0	0	0	0	0	0
15	1	0	0	0	0	0	0	0
16	0	0	1	0	0	0	0	0
17	0	0	1	0	0	0	0	0
18	1	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0
23	0	0	0	0	1	0	0	0
24	0	0	0	0	0	0	0	0
25	1	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0
27	1	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0
29	0	0	1	0	0	0	0	0
30	0	0	1	0	0	0	0	0
31	0	0	0	0	0	0	0	0
32	0	0	1	0	0	0	0	0
33	1	0	1	0	0	0	0	0
34	1	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0
36	1	0	1	0	0	0	0	0
37	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0
40	0	0	1	0	0	0	0	0
41	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0
44	0	0	1	0	0	0	0	0
45	0	0	1	0	0	0	0	0
46	1	0	0	0	0	0	0	0
47	1	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0
50	0	1	0	0	0	0	0	0

51	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0
53	0	0	1	0	0	0	0	0
54	0	0	0	0	0	0	0	0
55	1	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0
59	0	1	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0
61	1	0	0	0	0	0	0	0
62	0	0	1	0	0	0	0	0
63	0	0	0	0	0	0	0	0
64	0	0	0	0	0	0	0	0
65	0	0	0	0	0	0	0	0
66	0	0	0	0	0	0	0	0
67	0	0	0	0	0	0	0	0
68	1	0	1	0	0	0	0	0
69	0	0	0	0	0	0	0	0
70	0	0	1	0	0	0	0	0
71	0	0	1	0	0	0	0	0
72	0	0	1	0	0	0	0	0
73	0	0	1	0	0	0	0	0
74	0	0	1	0	0	0	0	0
75	1	0	1	0	0	0	0	0
76	0	0	0	0	0	0	0	0
77	0	1	0	0	0	0	0	0
78	0	0	0	0	0	0	0	0
79	1	0	1	0	0	0	0	0
80	1	0	0	0	0	0	0	0
81	1	0	0	0	0	0	0	0
82	0	0	1	0	0	0	0	0
83	0	0	1	0	0	0	0	0
84	0	0	1	0	0	0	0	0
85	0	0	0	0	0	0	0	0
86	0	0	0	0	0	0	0	0
87	0	0	1	0	0	0	0	0
88	1	0	0	0	0	0	0	0
89	0	0	0	0	0	0	0	0
90	0	0	1	0	0	0	0	0
91	0	0	0	0	0	0	0	0
92	0	0	0	0	0	0	0	0
93	0	0	0	0	0	0	0	0
94	1	0	0	0	0	0	0	0
95	0	0	0	0	0	0	0	0
96	0	0	0	0	0	0	0	0
97	0	0	0	0	0	0	0	0
98	0	0	0	0	0	0	0	0

S_No	H_WT	H_HyTHY	PH_CNS	PH_CVS	PH_RD	PH_PAD	SBP1_1	SBP1_2
1	0	0	0.0	3.0	0.0	0.0	148	146
2	0	0	1.2	3.0	0.0	0.0	150	150
3	0	0	1.2	2.3	3.0	0.0	150	150
4	0	0	0.0	1.2	0.0	0.0	180	186
5	0	0	1.2	3.0	0.0	0.0	150	150
6	0	0	0.0	0.0	0.0	0.0	154	158
7	0	0	1.0	3.0	0.0	0.0	160	160
8	0	0	0.0	1.2	0.0	0.0	160	154
9	0	0	0.0	0.0	0.0	0.0	160	160
10	0	0	1.0	2.3	0.0	0.0	150	152
11	0	0	1.0	3.0	0.0	0.0	150	150
12	0	0	1.2	3.0	0.0	0.0	150	152
13	0	0	1.2	1.3	0.0	0.0	140	140
14	0	0	1.3	3.0	0.0	0.0	140	140
15	0	0	0.0	2.3	0.0	0.0	170	170
16	0	0	1.2	0.0	0.0	0.0	154	158
17	0	0	2.0	2.0	0.0	0.0	160	162
18	0	0	3.0	0.0	0.0	0.0	160	160
19	0	0	1.2	2.3	0.0	0.0	170	180
20	0	0	2.0	2.3	0.0	0.0	140	142
21	0	0	0.0	2.0	0.0	0.0	150	154
22	0	0	0.0	0.0	0.0	0.0	180	174
23	0	0	0.0	3.0	0.0	0.0	140	140
24	0	0	1.2	2.2	0.0	0.0	150	146
25	0	0	2.0	2.3	0.0	0.0	150	170
26	0	0	2.3	2.3	0.0	0.0	180	184
27	0	0	2.0	6.0	0.0	0.0	150	150
28	0	0	0.0	3.0	0.0	0.0	140	150
29	0	0	1.0	0.0	0.0	0.0	144	140
30	0	0	0.0	2.3	0.0	0.0	180	180
31	0	0	1.2	2.3	0.0	0.0	140	140
32	0	0	2.0	2.3	0.0	0.0	144	150
33	0	0	1.0	3.0	0.0	0.0	180	180
34	0	0	1.0	0.0	0.0	0.0	140	140
35	0	0	2.0	2.2	0.0	0.0	140	140
36	0	0	1.0	3.0	0.0	0.0	140	144
37	0	0	1.0	6.0	0.0	0.0	180	180
38	0	0	0.0	3.6	0.0	0.0	180	200
39	0	0	1.2	3.0	0.0	0.0	140	140
40	0	0	1.2	2.5	0.0	0.0	170	180
41	0	0	0.0	2.6	0.0	0.0	150	154
42	0	0	0.0	3.6	0.0	0.0	160	160
43	0	0	2.0	2.0	0.0	0.0	140	140
44	0	0	1.0	2.0	0.0	0.0	174	170
45	0	0	2.3	2.3	0.0	0.0	176	180
46	0	0	3.0	2.5	0.0	2.0	150	150
47	0	0	2.3	5.0	0.0	0.0	164	160
48	0	0	1.0	5.0	0.0	0.0	140	140
49	0	0	0.0	0.0	0.0	0.0	140	144
50	0	0	1.2	2.3	0.0	0.0	150	150

51	0	0	1.2	0.0	0.0	0.0	150	140
52	0	0	2.0	2.0	0.0	0.0	150	150
53	0	0	3.0	3.0	0.0	0.0	150	150
54	0	0	1.0	3.0	0.0	0.0	150	140
55	0	0	0.0	5.0	0.0	0.0	150	150
56	0	0	2.0	0.0	0.0	0.0	140	140
57	0	0	1.2	0.0	0.0	0.0	150	150
58	0	0	2.0	1.2	0.0	0.0	170	150
59	0	0	2.0	2.0	0.0	0.0	160	150
60	0	0	1.0	0.0	0.0	0.0	170	150
61	0	0	0.0	0.0	0.0	0.0	150	150
62	0	0	1.0	0.0	0.0	0.0	150	150
63	0	0	0.0	0.0	0.0	0.0	150	150
64	0	0	1.2	3.0	0.0	0.0	170	150
65	0	0	1.2	0.0	0.0	0.0	170	172
66	0	0	1.0	0.0	0.0	0.0	140	140
67	0	0	1.2	2.3	0.0	0.0	160	170
68	0	0	0.0	5.0	0.0	0.0	150	140
69	0	0	0.0	0.0	0.0	0.0	150	140
70	0	0	2.0	2.5	0.0	0.0	160	160
71	0	0	2.0	2.0	0.0	0.0	150	150
72	0	0	2.0	2.0	1.0	0.0	150	150
73	0	0	2.0	2.0	1.0	0.0	150	152
74	0	0	0.0	2.3	0.0	0.0	160	162
75	0	0	0.0	3.0	0.0	0.0	160	140
76	0	0	1.2	2.3	0.0	0.0	160	156
77	0	0	1.2	0.0	0.0	0.0	150	150
78	0	0	1.0	2.0	0.0	0.0	160	164
79	0	0	2.0	0.0	0.0	0.0	140	160
80	0	0	0.0	0.0	0.0	0.0	150	140
81	0	0	0.0	2.3	0.0	0.0	140	160
82	0	0	3.0	2.3	0.0	0.0	150	150
83	0	0	2.3	2.3	0.0	0.0	170	170
84	0	0	1.2	2.3	0.0	0.0	160	160
85	0	0	0.0	2.5	0.0	0.0	160	160
86	0	0	0.0	0.0	0.0	0.0	140	160
87	0	0	2.3	2.0	0.0	0.0	150	160
88	0	0	1.2	3.0	0.0	0.0	160	162
89	0	0	2.0	0.0	0.0	0.0	140	140
90	0	0	2.0	2.0	0.0	0.0	150	154
91	0	0	1.2	2.3	0.0	0.0	150	150
92	0	0	1.0	0.0	0.0	0.0	180	180
93	0	0	3.0	0.0	0.0	0.0	180	178
94	0	0	1.0	3.0	0.0	0.0	150	152
95	0	0	2.0	0.0	0.0	0.0	170	174
96	0	0	1.0	2.3	0.0	0.0	140	144
97	0	0	0.0	3.0	0.0	0.0	164	164
98	0	0	0.0	0.0	0.0	0.0	150	146

S_No	SBP2_1	SBP2_2	M_SBP	DBP1_1	DBP1_2	DBP2_1	DBP2_2	M_DBP
1	142	140	144	90	90	90	90	90
2	154	152	152	90	90	92	90	90
3	152	150	151	100	100	98	96	99
4	180	170	179	100	104	100	98	101
5	142	154	149	100	100	98	98	99
6	152	150	154	100	100	94	92	97
7	154	158	158	90	90	90	88	90
8	152	154	155	90	90	90	90	90
9	150	156	157	94	98	96	94	96
10	150	154	152	90	94	88	90	91
11	150	154	151	100	100	98	98	99
12	150	150	151	90	90	88	88	89
13	144	142	142	100	100	100	100	100
14	142	140	141	90	86	88	90	89
15	164	172	169	100	88	84	88	90
16	158	162	158	90	90	90	88	90
17	160	162	161	100	98	90	90	95
18	156	158	159	100	100	102	100	101
19	174	180	176	100	100	100	100	100
20	142	140	141	90	94	94	88	92
21	152	156	153	90	92	88	90	90
22	180	176	178	100	100	100	98	100
23	140	144	141	100	96	98	98	98
24	150	152	150	90	90	90	90	90
25	154	156	158	80	80	82	82	81
26	180	182	182	100	98	94	100	98
27	150	154	151	90	84	86	88	87
28	150	146	147	100	90	90	88	92
29	140	142	142	90	90	90	88	90
30	170	174	176	120	100	110	108	110
31	140	142	141	90	92	90	94	92
32	142	150	147	94	94	90	90	92
33	176	170	177	90	100	96	98	96
34	144	140	141	90	90	90	90	90
35	142	144	142	90	90	90	90	90
36	142	144	143	94	90	90	90	94
37	170	174	176	100	90	94	98	96
38	180	178	180	185	100	100	96	98
39	140	142	141	94	96	88	90	92
40	170	174	174	110	100	100	100	103
41	152	154	153	100	90	90	90	93
42	160	162	161	90	90	90	94	91
43	142	144	142	90	90	90	90	90
44	160	160	166	100	100	90	90	95
45	174	174	176	100	100	98	100	100
46	146	144	148	92	90	90	88	90
47	158	156	160	100	100	100	98	100
48	142	140	141	90	92	90	84	89
49	142	140	142	90	90	92	92	91
50	154	150	151	90	90	90	90	90

51	152	154	149	90	90	90	92	91
52	154	152	152	90	90	88	88	89
53	154	152	152	100	90	90	90	93
54	152	150	148	100	100	100	100	100
55	152	154	152	100	90	94	90	94
56	142	144	142	90	90	90	90	90
57	154	152	152	100	90	94	94	95
58	158	156	159	100	90	94	98	96
59	162	156	157	90	90	90	90	90
60	158	156	159	100	90	94	90	94
61	152	154	152	90	96	90	92	92
62	152	146	150	100	98	98	94	98
63	152	148	150	90	90	94	90	91
64	158	154	158	100	100	98	98	99
65	174	170	172	110	110	108	108	109
66	142	140	141	90	96	90	90	92
67	164	166	165	100	102	100	98	100
68	146	144	145	100	90	90	92	93
69	152	148	148	90	90	90	90	90
70	154	152	157	90	90	90	90	90
71	142	146	147	80	90	84	86	85
72	140	146	147	90	84	86	84	86
73	150	154	152	90	100	96	92	95
74	150	150	156	100	92	90	92	94
75	148	146	149	100	96	94	96	97
76	154	156	157	100	100	96	98	99
77	170	174	161	110	100	100	100	103
78	160	170	164	90	104	96	96	97
79	160	160	156	90	90	90	90	90
80	142	144	144	100	90	90	92	93
81	160	160	155	90	90	90	90	90
82	152	150	151	100	90	94	94	94
83	164	168	168	100	100	98	98	99
84	154	158	158	90	100	94	96	95
85	160	156	159	80	90	92	84	87
86	156	154	153	90	80	84	88	86
87	150	154	154	100	100	100	98	100
88	160	162	161	90	90	90	90	90
89	142	140	141	86	90	94	90	90
90	152	150	152	90	90	92	90	91
91	150	148	150	100	100	96	96	98
92	174	170	176	80	90	86	88	86
93	170	164	173	90	90	90	90	90
94	150	150	151	90	90	90	90	90
95	170	170	171	100	104	100	100	101
96	144	140	142	100	100	100	100	100
97	162	162	163	100	100	100	100	100
98	142	144	146	100	98	98	98	99

S_No	HR1	HR2	HR3	HR4	M_HR	HT	WT	ABD_CIRC
1	108	106	98	92	101	165	63	86
2	76	78	72	72	75	170	66	78
3	94	92	96	86	91	168	67	84
4	100	100	92	94	97	168	67	88
5	92	92	88	86	90	151	67	89
6	102	104	88	94	97	158	70	96
7	68	72	72	74	72	172	64	74
8	76	78	72	74	75	161	104	89
9	82	86	80	82	83	168	70	88
10	92	94	92	90	92	168	72	84
11	78	78	74	72	76	172	74	88
12	100	94	92	86	93	168	68	84
13	68	72	82	80	76	170	68	78
14	76	78	74	82	78	155	50	78
15	84	82	81	80	82	166	52	74
16	84	88	84	82	85	148	65	96
17	80	84	82	84	83	175	76	82
18	80	82	84	82	82	165	75	100
19	96	98	96	94	96	140	54	94
20	92	90	90	84	89	164	70	104
21	84	88	82	88	86	176	88	89
22	89	88	84	82	85	172	68	76
23	80	84	82	84	83	154	70	86
24	84	88	84	82	85	156	64	88
25	78	76	74	72	75	171	57	84
26	76	78	74	78	77	168	75	98
27	98	98	88	92	94	166	62	84
28	84	86	84	82	84	175	75	82
29	84	86	88	82	85	160	56	88
30	96	108	100	94	100	153	71	88
31	90	98	94	88	93	156	64	86
32	88	76	88	84	84	150	52	78
33	68	70	72	70	70	161	64	82
34	70	72	76	72	73	171	61	86
35	80	84	82	80	82	165	83	102
36	68	70	72	70	70	166	66	89
37	114	110	112	108	111	173	80	96
38	99	84	86	88	82	158	58	89
39	84	88	84	82	85	150	66	88
40	80	84	82	84	83	153	78	114
41	100	104	100	84	97	142	77	104
42	96	98	96	98	97	164	54	78
43	98	96	88	84	92	153	62	84
44	84	88	82	86	85	154	77	94
45	84	88	88	90	88	167	60	90
46	100	104	102	100	101	171	68	91
47	98	94	88	90	93	178	77	92
48	100	102	94	98	95	158	64	92
49	74	76	72	74	74	150	45	90
50	96	98	94	96	96	165	84	98

51	120	124	114	100	115	148	56	84
52	74	76	72	74	74	154	65	93
53	90	88	88	84	88	165	68	94
54	96	98	94	96	96	178	97	96
55	84	88	84	86	86	168	64	90
56	84	84	86	82	84	153	57	86
57	112	110	104	108	109	178	78	89
58	88	94	82	86	88	150	53	78
59	90	90	92	84	89	172	73	86
60	76	84	82	84	82	166	63	96
61	88	86	82	80	84	168	67	24
62	84	88	82	84	85	155	70	90
63	88	88	82	84	86	157	62	87
64	84	88	78	84	84	179	97	109
65	98	96	94	90	95	172	50	74
66	94	96	98	94	96	157	73	80
67	96	98	94	96	96	160	89	111
68	80	72	84	86	81	165	65	93
69	80	68	72	74	74	165	76	100
70	80	70	74	72	74	157	91	107
71	80	84	76	78	80	165	64	84
72	72	80	68	66	72	145	75	101
73	68	70	74	70	71	175	76	94
74	104	100	88	92	96	160	63	93
75	100	110	98	104	103	179	105	119
76	80	84	88	84	84	160	83	108
77	104	100	102	102	102	160	70	90
78	80	68	72	74	74	155	47	84
79	90	88	84	86	87	170	73	98
80	82	92	84	88	87	164	65	88
81	94	112	100	100	102	165	71	100
82	95	86	84	82	84	146	72	93
83	64	68	70	72	69	172	68	90
84	92	100	100	96	97	150	77	105
85	82	96	92	94	91	180	84	104
86	74	76	72	74	74	136	42	86
87	72	74	74	78	75	160	54	78
88	88	84	88	84	86	170	47	68
89	74	74	72	74	74	170	76	89
90	76	78	76	78	77	155	91	104
91	96	98	94	94	96	158	63	82
92	112	104	102	100	105	152	45	72
93	88	84	82	85	85	164	60	76
94	112	108	102	104	107	172	79	89
95	92	94	92	90	92	152	50	84
96	104	102	100	96	100	170	69	84
97	88	92	92	92	91	167	81	94
98	84	88	84	86	86	157	67	98

S_No	BMI	BSA	PS_CS	PS_NF	PS_AM	PS_PM	PS_RFD	PS_ULD
1	23.14	1.27	0	0	0	0	0	0
2	22.84	1.77	0	0	0	0	0	0
3	30.59	1.61	0	0	0	0	0	0
4	23.74	1.76	0	0	0	0	0	0
5	29.38	1.63	0	0	0	0	0	0
6	28.04	1.72	0	0	0	0	0	0
7	21.46	1.74	0	0	0	0	0	0
8	40.12	2.06	0	0	0	0	0	0
9	24.73	1.79	0	0	0	0	0	0
10	25.51	1.76	0	0	0	0	0	0
11	25.01	1.87	0	0	0	0	0	0
12	24.13	1.77	0	0	0	0	0	0
13	23.53	1.79	0	0	0	0	0	0
14	20.81	1.47	0	0	0	0	0	0
15	18.87	1.57	0	0	0	0	0	0
16	29.77	1.64	0	0	0	0	0	0
17	24.82	1.92	0	0	0	0	0	0
18	27.36	1.85	0	0	0	0	0	0
19	27.55	1.45	0	0	0	0	0	0
20	25.91	1.78	0	0	0	0	0	0
21	28.41	2.07	0	0	0	0	0	0
22	22.99	1.80	0	0	0	0	0	0
23	29.52	1.73	0	0	0	0	0	0
24	26.30	1.67	0	0	0	0	0	0
25	28.73	2.00	0	0	0	0	0	0
26	26.57	1.87	0	0	0	0	0	0
27	22.35	1.69	0	0	0	0	0	0
28	24.47	1.91	0	0	0	0	0	0
29	21.88	1.58	0	0	0	0	0	0
30	30.33	1.74	0	0	0	0	0	0
31	25.07	1.63	0	0	0	0	0	0
32	23.11	1.47	0	0	0	0	0	0
33	24.69	1.69	0	0	0	0	0	0
34	20.80	1.70	0	0	0	0	0	0
35	30.49	1.95	0	0	0	0	0	0
36	23.95	1.74	0	0	0	0	0	0
37	26.73	1.96	0	0	0	0	0	0
38	23.23	1.60	0	0	0	0	0	0
39	29.33	1.66	0	0	0	0	0	0
40	33.32	1.82	0	0	0	0	0	0
41	38.19	1.74	0	0	0	0	0	0
42	20.08	1.57	0	0	0	0	0	0
43	26.46	1.62	0	0	0	0	0	0
44	32.64	1.82	0	0	0	0	0	0
45	21.51	1.67	0	0	0	0	0	0
46	23.26	1.80	0	0	0	0	0	0
47	24.30	1.95	0	0	0	0	0	0
48	25.44	1.67	0	0	0	0	0	0
49	19.87	1.36	0	0	0	0	0	0
50	30.85	1.96	0	0	0	0	0	0

51	25.57	1.52	0	0	0	0	0	0
52	27.49	1.67	0	0	0	0	0	0
53	24.98	1.77	0	0	0	0	0	0
54	30.61	2.19	0	0	0	0	0	0
55	22.68	1.73	0	0	0	0	0	0
56	24.35	1.56	0	0	0	0	0	0
57	24.62	1.96	0	0	0	0	0	0
58	23.73	1.49	0	0	0	0	0	0
59	29.68	1.87	0	0	0	0	0	0
60	22.83	1.70	0	0	0	0	0	0
61	1.77	0.00	0	0	0	0	0	0
62	29.14	1.74	0	0	0	0	0	0
63	25.23	1.65	0	0	0	0	0	0
64	32.86	2.15	0	0	0	0	0	0
65	17.00	1.55	0	0	0	0	0	0
66	29.62	1.78	0	0	0	0	0	0
67	34.77	1.99	0	0	0	0	0	0
68	23.88	1.73	0	0	0	0	0	0
69	27.73	1.86	0	0	0	0	0	0
70	37.04	2.00	0	0	0	0	0	0
71	23.51	1.71	0	0	0	0	0	0
72	35.67	1.74	0	0	0	0	0	0
73	24.65	1.92	0	0	0	0	0	0
74	24.61	1.67	0	0	0	0	0	0
75	32.77	2.28	0	0	0	0	0	0
76	32.58	1.93	0	0	0	0	0	0
77	27.34	1.76	0	0	0	0	0	0
78	19.56	1.42	0	0	0	0	0	0
79	25.26	1.86	0	0	0	0	0	0
80	24.32	1.73	0	0	0	0	0	0
81	26.08	1.80	0	0	0	0	0	0
82	24.34	1.85	0	0	0	0	0	0
83	22.99	1.80	0	0	0	0	0	0
84	34.31	1.79	0	0	0	0	0	0
85	25.93	2.05	0	0	0	0	0	0
86	22.71	1.26	0	0	0	0	0	0
87	21.09	1.55	0	0	0	0	0	0
88	16.26	1.49	0	0	0	0	0	0
89	26.30	1.83	0	0	0	0	0	0
90	37.84	1.98	0	0	0	0	0	0
91	25.24	1.66	0	0	0	0	0	0
92	19.48	1.38	0	0	0	0	0	0
93	22.16	1.65	0	0	0	0	0	0
94	26.57	1.94	0	0	0	0	0	0
95	21.64	1.45	0	0	0	0	0	0
96	23.94	1.81	0	0	0	0	0	0
97	29.04	1.94	0	0	0	0	0	0
98	27.18	1.71	0	0	0	0	0	0

S_No	PS_CNS	PS_FUND	PS_HRT	PS_PAD	PS_CAR	PI_HB	PI_FBS	PI_TC
1	0.0	0.0	5.0	0.0	0.0	12.6	84	197
2	0.0	0.0	5.0	0.0	0.0	14.3	111	157
3	0.0	0.0	5.0	0.0	0.0	13.4	110	167
4	0.0	1.1	0.0	0.0	0.0	16.8	163	146
5	0.0	1.1	0.0	0.0	0.0	13.6	94	204
6	0.0	1.2	5.0	0.0	0.0	12.5	105	162
7	0.0	0.0	5.0	0.0	0.0	13.6	115	150
8	0.0	0.0	0.0	0.0	0.0	15.0	120	179
9	0.0	1.1	0.0	0.0	0.0	16.3	96	179
10	0.0	0.0	5.0	0.0	0.0	15.8	100	234
11	0.0	1.1	0.0	0.0	0.0	14.6	125	170
12	0.0	0.0	5.0	0.0	0.0	13.4	100	115
13	0.0	1.1	5.0	0.0	0.0	15.4	124	211
14	0.0	1.1	5.0	0.0	0.0	13.9	93	217
15	0.0	0.0	5.0	0.0	0.0	18.0	88	149
16	0.0	0.0	5.0	0.0	0.0	12.5	103	204
17	0.0	0.0	5.0	0.0	0.0	15.7	84	191
18	0.0	0.0	5.0	0.0	0.0	13.4	101	161
19	0.0	0.0	5.0	0.0	0.0	12.8	89	165
20	0.0	1.1	5.0	0.0	0.0	11.3	90	141
21	0.0	0.0	5.0	0.0	0.0	14.5	84	179
22	0.0	0.0	5.0	0.0	0.0	11.9	100	175
23	0.0	1.2	5.0	0.0	0.0	13.1	125	155
24	0.0	1.1	5.0	0.0	0.0	12.0	122	168
25	0.0	0.0	5.0	0.0	0.0	13.4	106	162
26	0.0	0.0	3.5	0.0	0.0	13.8	110	126
27	0.0	1.1	0.0	0.0	0.0	12.0	106	290
28	0.0	0.0	0.0	0.0	0.0	14.4	103	170
29	0.0	0.0	0.0	0.0	0.0	11.6	89	166
30	0.0	1.1	0.0	0.0	0.0	12.1	112	148
31	0.0	0.0	0.0	0.0	0.0	11.9	107	159
32	0.0	1.2	0.0	0.0	0.0	13.6	107	173
33	0.0	1.1	5.0	0.0	0.0	13.8	84	197
34	0.0	0.0	0.0	0.0	0.0	12.6	88	258
35	0.0	1.1	0.0	0.0	0.0	13.3	118	265
36	0.0	0.0	5.0	0.0	0.0	13.8	101	180
37	0.0	1.1	5.0	0.0	0.0	14.9	82	175
38	0.0	0.0	0.0	0.0	0.0	14.3	103	273
39	0.0	0.0	5.0	0.0	0.0	11.4	101	175
40	0.0	0.0	0.0	0.0	0.0	11.9	93	170
41	0.0	0.0	5.0	0.0	0.0	10.1	86	177
42	0.0	1.1	0.0	0.0	0.0	13.0	113	135
43	0.0	0.0	0.0	0.0	0.0	12.0	108	139
44	0.0	0.0	0.0	0.0	0.0	11.2	112	129
45	0.0	0.0	5.0	0.0	0.0	13.6	84	128
46	0.0	0.0	5.0	0.0	0.0	14.0	240	179
47	0.0	1.1	5.0	0.0	0.0	15.8	92	136
48	0.0	0.0	5.0	0.0	0.0	13.3	84	191
49	0.0	0.0	0.0	0.0	0.0	11.7	104	189
50	1.0	0.0	5.0	0.0	0.0	15.5	88	168

51	0.0	0.0	1.3	0.0	1.0	9.0	93	123
52	0.0	0.0	5.0	0.0	0.0	13.5	84	158
53	0.0	0.0	5.0	0.0	0.0	13.1	88	196
54	0.0	0.0	0.0	0.0	0.0	15.8	102	167
55	1.0	0.0	5.0	0.0	0.0	14.8	114	147
56	0.0	0.0	0.0	0.0	0.0	13.6	83	235
57	0.0	0.0	0.0	0.0	0.0	14.4	92	220
58	0.0	0.0	5.0	0.0	0.0	7.1	88	131
59	0.0	1.1	5.0	0.0	0.0	8.6	95	91
60	0.0	1.1	5.0	0.0	0.0	14.2	96	161
61	0.0	0.0	5.0	0.0	0.0	14.8	102	149
62	0.0	0.0	5.0	0.0	0.0	14.3	124	143
63	0.0	0.0	5.0	0.0	0.0	12.2	111	165
64	0.0	0.0	0.0	0.0	0.0	15.2	89	124
65	0.0	1.1	0.0	0.0	0.0	13.7	120	201
66	0.0	0.0	5.0	0.0	0.0	12.9	96	203
67	0.0	0.0	5.0	0.0	0.0	11.7	95	186
68	0.0	0.0	0.0	0.0	0.0	14.6	91	214
69	0.0	0.0	0.0	0.0	0.0	15.2	91	188
70	0.0	1.1	0.0	0.0	0.0	11.4	112	179
71	0.0	1.2	0.0	0.0	0.0	13.0	119	146
72	0.0	0.0	0.0	0.0	0.0	13.1	88	204
73	0.0	0.0	0.0	0.0	0.0	15.4	82	253
74	0.0	1.1	0.0	0.0	0.0	13.1	96	207
75	0.0	0.0	5.0	0.0	0.0	14.2	102	206
76	0.0	1.1	5.0	0.0	0.0	11.4	116	228
77	0.0	0.0	0.0	0.0	0.0	12.1	85	204
78	0.0	0.0	0.0	0.0	0.0	12.5	79	167
79	0.0	0.0	5.0	0.0	0.0	14.8	117	223
80	0.0	1.1	0.0	0.0	0.0	15.0	105	123
81	0.0	0.0	5.0	0.0	0.0	14.5	91	182
82	0.0	0.0	5.0	0.0	0.0	13.4	103	162
83	0.0	0.0	5.0	0.0	0.0	13.5	102	243
84	0.0	0.0	5.0	0.0	0.0	9.7	112	144
85	0.0	0.0	2.5	0.0	0.0	15.9	105	263
86	0.0	0.0	0.0	0.0	0.0	12.3	117	185
87	0.0	0.0	0.0	0.0	0.0	11.3	94	202
88	0.0	0.0	5.0	0.0	0.0	12.1	110	133
89	0.0	0.0	5.0	0.0	0.0	14.3	95	236
90	0.0	0.0	5.0	0.0	0.0	14.0	123	236
91	0.0	0.0	1.1	0.0	0.0	13.9	93	200
92	0.0	0.0	5.0	0.0	0.0	12.1	96	201
93	0.0	0.0	0.0	0.0	0.0	11.9	80	121
94	0.0	0.0	5.0	0.0	0.0	15.4	108	225
95	0.0	0.0	0.0	0.0	0.0	12.9	103	260
96	0.0	0.0	5.0	0.0	0.0	14.3	98	202
97	0.0	0.0	5.0	0.0	0.0	12.8	95	151
98	0.0	0.0	0.0	0.0	0.0	12.8	92	201

S_No	PI_LDL	PI_HDL	PI_Na	PI_K	PI_CR	PI_CRP	PI_UA	ECG_SV1
1	130	34	140	4.10	0.93	24.900	5.4	1.3
2	110	28	136	4.90	0.97	0.739	4.3	1.7
3	110	43	135	3.90	0.67	15.000	6.6	0.4
4	106	30	139	4.00	0.77	2.450	4.5	3.0
5	135	59	136	4.10	0.71	1.360	5.9	1.2
6	101	26	139	3.80	0.95	0.779	7.9	1.0
7	90	48	137	3.80	0.88	0.693	5.1	1.0
8	115	44	137	4.40	0.83	2.680	5.6	0.5
9	117	46	142	4.00	0.95	0.710	7.5	1.2
10	151	37	133	4.50	0.86	3.100	7.6	1.1
11	116	44	134	4.10	0.77	3.100	5.3	0.7
12	66	33	129	5.00	0.76	14.300	4.3	0.5
13	156	37	136	4.70	1.01	3.280	5.0	1.0
14	128	61	138	4.30	0.70	0.768	3.8	0.5
15	83	63	137	3.40	0.80	1.030	3.9	2.2
16	135	43	140	4.60	0.48	17.300	5.1	0.5
17	140	38	139	4.10	0.91	1.660	6.6	0.5
18	98	44	140	3.60	0.76	1.010	3.6	2.1
19	94	48	140	4.30	0.57	1.640	2.9	1.0
20	90	40	138	4.40	0.67	4.080	3.4	0.1
21	108	48	140	4.30	0.88	7.130	7.0	1.2
22	129	37	138	4.30	0.91	2.340	4.5	1.1
23	93	34	138	4.30	0.71	4.660	5.4	0.7
24	122	33	135	4.20	0.47	8.280	4.3	0.8
25	100	32	138	3.90	0.96	0.355	4.9	0.3
26	84	38	138	4.60	0.83	0.414	5.5	0.3
27	115	27	137	4.50	0.91	1.680	5.6	0.1
28	120	30	139	4.70	1.00	5.000	4.3	0.8
29	111	43	143	3.80	0.89	4.930	4.4	0.7
30	96	38	138	4.00	0.61	3.080	4.7	1.0
31	97	45	134	4.00	0.56	1.290	2.5	1.5
32	111	65	140	4.10	0.56	0.500	2.5	1.6
33	130	49	142	4.50	1.05	1.310	4.3	0.6
34	118	23	139	4.70	0.73	0.406	3.9	0.6
35	112	32	141	3.90	0.46	0.327	3.6	0.5
36	111	40	139	4.00	0.90	0.699	5.5	0.7
37	101	49	140	3.60	1.14	4.360	5.0	1.0
38	2	48	136	4.00	0.52	1.170	3.3	0.6
39	125	46	141	4.70	0.57	2.950	5.2	0.7
40	103	46	142	4.30	0.55	13.300	5.8	0.7
41	127	36	140	4.50	0.43	13.200	4.2	0.4
42	89	27	140	4.30	1.01	1.020	7.8	0.6
43	86	45	141	4.30	0.72	9.850	4.5	0.6
44	75	41	137	4.20	0.52	3.840	3.8	1.0
45	80	36	135	4.30	0.74	1.910	6.1	0.7
46	121	53	138	4.50	1.24	0.421	5.6	1.2
47	76	51	137	3.80	0.82	2.560	5.9	1.8
48	128	43	143	4.00	0.71	0.882	3.3	1.0
49	106	37	141	3.90	0.67	4.180	4.3	0.5
50	110	41	139	4.00	0.38	0.497	6.5	2.0

51	79	37	137	4.20	0.72	0.168	4.2	0.9
52	84	57	140	4.10	0.48	10.600	2.9	0.5
53	146	31	137	4.20	1.00	7.260	6.1	0.6
54	114	37	137	4.50	0.82	3.120	6.7	0.5
55	98	37	135	4.00	0.84	1.300	4.4	1.0
56	170	39	137	4.50	0.57	13.000	5.2	0.6
57	155	46	139	4.00	0.89	1.260	6.0	0.6
58	73	47	141	3.50	0.58	3.960	4.0	1.8
59	50	34	138	4.50	1.12	1.060	4.3	0.3
60	104	46	141	4.30	0.81	1.840	5.6	0.3
61	87	43	140	4.10	0.87	0.882	7.1	1.2
62	100	34	139	3.70	0.96	2.460	6.3	0.8
63	101	39	139	4.60	0.62	4.620	5.8	0.5
64	77	26	140	4.30	1.18	12.800	5.9	0.2
65	111	87	136	3.80	0.56	4.590	2.9	0.7
66	145	48	140	3.70	0.68	1.240	3.9	0.4
67	125	49	134	4.50	0.70	15.500	3.8	0.8
68	138	36	134	4.10	0.80	1.180	5.6	1.1
69	118	59	136	4.10	1.20	0.655	5.9	1.2
70	114	45	135	4.70	0.54	19.600	5.4	1.2
71	86	21	134	4.30	0.70	5.700	2.9	0.5
72	137	56	135	4.50	0.63	5.040	4.8	0.3
73	188	47	135	4.50	1.00	0.457	5.3	0.6
74	128	66	136	4.50	0.70	1.850	4.0	1.1
75	155	36	135	4.20	0.84	1.690	6.0	1.5
76	130	41	137	4.30	0.89	7.410	6.5	0.7
77	143	38	134	4.60	0.78	3.070	7.2	1.8
78	106	53	134	4.40	0.60	1.340	3.7	0.6
79	119	30	138	4.20	1.16	7.170	4.9	0.4
80	105	44	137	4.50	0.83	14.100	6.2	0.6
81	127	36	139	3.80	1.35	7.680	7.5	1.8
82	184	44	140	4.60	0.86	6.170	5.2	0.4
83	157	46	139	4.00	0.97	1.540	7.2	0.7
84	90	40	139	3.80	0.61	5.010	4.0	0.4
85	180	42	135	4.20	0.81	1.570	3.9	0.5
86	106	31	141	3.50	0.72	6.580	6.4	1.5
87	143	33	134	4.90	0.72	0.340	3.8	1.0
88	166	43	140	4.10	0.81	0.171	3.7	1.1
89	164	53	144	3.90	0.81	8.530	5.0	0.8
90	162	47	139	4.40	0.56	10.700	5.5	1.0
91	148	48	138	3.10	0.60	4.660	3.9	0.9
92	130	49	140	2.70	0.56	0.885	2.5	0.5
93	84	34	139	4.70	0.74	0.475	6.7	1.5
94	133	33	140	4.40	0.73	1.820	6.2	1.3
95	189	53	140	3.80	0.65	0.537	4.0	0.8
96	131	41	136	4.00	0.78	0.898	5.2	1.2
97	97	38	142	4.00	0.93	2.280	4.8	0.9
98	138	36	137	3.80	0.69	0.569	3.6	0.6

S_No	ECG_LS	ECG_RAVL	ECG_QRS	ECG_RV5	ECG_LR	ECG_SV3	ECG_SLI	ECG_MSLI
1	1.3	0.0	70.0	1.9	1.9	0.5	3.2	3.2
2	2.7	0.3	97.0	1.5	1.5	0.9	3.2	4.2
3	0.4	0.6	92.0	0.6	0.6	0.6	1.0	1.0
4	3.0	1.3	108.0	1.8	2.3	2.1	4.8	5.3
5	1.2	0.2	83.0	0.9	0.9	1.1	2.1	2.1
6	1.5	1.3	84.0	1.1	1.7	1.0	2.7	3.2
7	1.0	0.7	83.0	1.5	2.2	1.1	2.5	3.2
8	0.5	0.5	106.0	0.5	0.6	0.6	1.0	1.1
9	1.2	0.2	84.0	1.5	1.9	1.0	2.7	3.1
10	1.1	0.5	90.0	1.6	1.6	1.1	2.7	2.7
11	1.8	0.2	95.0	1.5	1.5	0.6	2.2	3.3
12	1.4	0.5	87.0	1.4	1.8	1.0	1.9	3.2
13	1.3	0.1	116.0	1.7	1.7	1.2	2.7	3.0
14	0.8	0.6	89.0	2.1	2.1	0.6	2.6	2.9
15	2.5	0.0	90.0	1.5	2.6	0.9	3.7	5.1
16	1.3	0.5	84.0	1.0	1.0	0.7	1.5	2.3
17	1.3	0.5	88.0	0.7	1.0	1.0	1.2	2.3
18	2.1	0.4	88.0	1.8	1.8	1.0	3.9	3.9
19	1.0	0.8	70.0	1.8	2.0	0.4	2.8	3.0
20	0.8	0.1	90.0	0.8	0.9	0.8	0.9	1.7
21	1.2	0.2	88.0	1.4	1.5	0.6	2.6	2.7
22	2.2	0.5	79.0	2.0	2.6	2.2	3.1	4.8
23	0.7	0.5	76.0	0.7	0.7	0.2	1.4	1.4
24	1.3	0.4	83.0	1.6	1.6	0.7	2.4	2.9
25	0.3	0.2	83.0	2.0	2.0	0.3	2.3	2.3
26	0.3	0.1	83.0	2.0	2.0	0.3	2.3	2.3
27	0.4	0.8	128.0	0.9	1.0	0.5	1.0	1.4
28	1.2	0.6	103.0	1.2	1.2	1.1	2.0	2.4
29	0.7	0.6	96.0	2.0	2.2	0.3	2.7	2.9
30	1.0	0.3	78.0	1.3	1.5	0.1	2.3	2.5
31	1.5	0.5	81.0	2.0	2.0	0.6	3.5	3.5
32	1.6	0.7	90.0	1.5	1.5	0.6	3.1	3.1
33	1.7	0.5	84.0	1.7	1.7	1.5	2.3	3.4
34	1.4	0.5	99.0	2.2	2.5	1.5	2.8	3.9
35	0.6	0.4	109.0	0.8	1.0	0.2	1.3	1.6
36	1.8	0.2	80.0	1.7	1.7	0.7	2.4	3.5
37	2.2	1.0	98.0	2.0	2.2	1.5	3.0	4.4
38	0.7	0.5	89.0	0.7	0.7	0.7	1.3	1.4
39	0.8	0.4	90.0	1.3	1.5	0.5	2.0	2.3
40	0.8	0.7	87.0	1.7	1.7	0.7	2.4	2.5
41	0.6	0.6	85.0	0.6	0.6	0.8	1.0	1.2
42	0.7	0.4	81.0	2.6	2.6	0.9	3.2	3.3
43	0.9	0.4	96.0	1.4	1.5	0.4	2.0	2.4
44	2.0	0.7	89.0	1.5	1.7	2.0	2.5	3.7
45	1.2	0.2	98.0	1.9	2.0	1.2	2.6	3.2
46	0.8	0.6	83.0	0.6	0.8	0.8	1.8	1.6
47	2.4	0.7	89.0	1.8	2.0	1.5	3.6	4.4
48	1.0	0.9	83.0	1.0	1.0	0.5	2.0	2.0
49	0.8	0.1	102.0	1.7	1.7	0.4	2.2	2.5
50	2.5	0.5	87.0	2.2	2.7	2.5	4.2	5.2

51	1.7	0.2	117.0	2.2	2.2	1.7	3.1	3.9
52	0.8	0.3	88.0	1.2	1.3	0.5	1.7	2.1
53	1.0	0.5	85.0	1.7	1.9	0.5	2.3	2.9
54	1.2	0.5	79.0	0.7	1.2	1.1	1.2	2.4
55	1.4	0.2	76.0	1.3	1.3	1.0	2.3	2.7
56	1.1	0.3	103.0	0.6	0.8	0.6	1.2	1.9
57	1.7	0.3	92.0	1.3	1.3	1.0	1.9	3.0
58	1.9	2.3	122.0	1.1	1.5	1.9	2.9	3.4
59	1.4	0.5	107.0	1.5	1.7	0.6	1.8	2.1
60	0.4	0.3	79.0	1.5	1.6	0.2	1.8	2.0
61	1.9	0.3	92.0	1.9	2.0	1.1	3.1	3.9
62	1.5	0.5	93.0	1.4	1.4	1.5	2.2	2.9
63	0.8	0.1	85.0	1.9	1.9	0.6	2.4	2.7
64	1.0	0.4	89.0	0.4	0.6	1.1	0.6	1.6
65	2.0	0.4	96.0	2.2	3.2	2.0	2.9	5.2
66	1.0	0.4	78.0	0.8	0.8	0.4	1.2	1.8
67	1.0	0.3	76.0	0.8	0.8	0.4	1.6	1.8
68	1.4	0.3	82.0	1.9	1.9	0.8	3.0	3.3
69	1.4	0.4	84.0	1.6	1.9	0.6	2.8	3.3
70	1.5	0.5	97.0	1.9	1.9	1.0	3.1	3.4
71	1.0	0.3	80.0	0.7	0.9	0.5	1.2	1.9
72	0.5	0.1	86.0	1.1	1.1	0.5	1.4	1.6
73	0.6	0.3	80.0	2.0	2.3	0.0	2.6	2.9
74	1.1	0.7	93.0	0.8	0.9	0.3	1.9	2.0
75	1.5	0.1	92.0	1.1	1.6	0.6	2.6	3.1
76	1.0	0.7	82.0	1.2	1.2	0.7	1.9	2.2
77	2.0	0.5	74.0	1.5	1.8	1.0	3.3	3.8
78	1.0	0.1	84.0	2.2	2.2	0.7	2.8	3.2
79	1.2	0.4	95.0	1.5	2.0	1.1	1.9	3.2
80	1.4	0.1	74.0	1.4	1.4	0.7	2.0	2.8
81	1.8	0.8	91.0	2.1	2.1	1.0	3.9	3.9
82	0.8	0.6	88.0	1.1	1.1	0.6	1.5	1.9
83	2.4	0.4	95.0	1.5	2.0	1.6	2.2	4.4
84	0.8	0.8	98.0	0.7	0.8	0.7	1.1	1.6
85	1.5	0.3	95.0	0.8	0.8	0.7	1.3	2.3
86	2.5	1.2	78.0	1.5	1.5	2.1	3.0	4.0
87	1.0	0.6	87.0	1.1	1.6	0.4	2.1	2.6
88	1.1	0.6	89.0	1.6	1.7	0.8	2.7	2.8
89	1.0	0.3	90.0	1.3	1.7	1.0	2.1	2.7
90	1.0	0.4	88.0	1.4	1.7	0.3	2.4	2.7
91	0.9	0.5	106.0	0.7	1.2	0.0	1.6	2.1
92	0.8	0.3	78.0	1.5	1.5	0.5	2.0	2.3
93	4.0	0.2	101.0	2.0	2.0	2.6	3.5	6.0
94	2.3	0.6	81.0	2.2	2.2	1.0	3.5	4.4
95	1.5	2.1	98.0	1.0	1.5	1.5	1.8	3.0
96	2.3	0.9	94.0	1.5	1.5	1.2	2.7	3.8
97	1.2	0.7	95.0	1.7	2.0	1.1	2.6	3.2
98	0.9	0.3	76.0	0.7	0.7	0.6	1.3	1.6

S_No	ECG_CVC	ECG_SLIS	ECG_MSLIS	ECG_CVCS	ECH_LVED	ECH_PWD	ECH_IVS	ECH_EF
1	0.00	0	0	0	46.00	8.80	9.50	57.2
2	116.40	0	1	0	47.00	10.00	11.00	56.9
3	184.00	0	0	0	36.00	10.00	10.00	56.9
4	367.20	1	1	1	43.00	12.00	15.00	52.4
5	174.30	0	0	0	42.00	10.00	9.90	58.4
6	193.20	0	0	0	47.00	11.00	11.00	58.0
7	149.40	0	0	0	29.00	12.00	14.00	57.6
8	116.60	0	0	0	46.00	11.00	11.00	57.9
9	100.80	0	0	0	44.00	9.50	9.90	58.3
10	144.00	0	0	0	38.00	10.00	11.00	56.4
11	76.00	0	0	0	46.00	10.00	9.90	57.6
12	130.50	0	0	0	46.00	13.00	13.00	59.5
13	150.80	0	0	0	46.00	8.50	12.00	44.1
14	106.80	0	0	0	41.00	11.00	11.00	55.8
15	0.00	1	1	0	44.00	11.00	11.00	57.0
16	168.00	0	0	0	46.00	10.00	10.00	57.9
17	132.00	0	0	0	39.00	16.00	17.00	59.0
18	123.20	1	1	0	46.00	12.00	12.00	58.7
19	140.00	0	0	0	41.00	10.00	10.00	56.6
20	153.00	0	0	0	42.00	10.00	10.00	57.3
21	70.40	0	0	0	46.00	11.00	12.00	56.0
22	213.30	0	0	0	43.00	8.00	7.00	58.0
23	114.00	0	0	0	43.00	11.00	10.00	56.9
24	157.70	0	0	0	43.00	10.00	10.00	57.9
25	41.50	0	0	0	46.00	11.00	10.00	57.9
26	33.20	0	0	0	52.00	14.00	14.00	56.0
27	166.40	0	0	0	47.00	9.00	9.00	58.2
28	175.10	0	0	0	41.00	10.00	9.50	59.7
29	163.20	0	0	0	42.00	10.00	9.50	59.7
30	132.60	0	0	0	41.00	9.00	8.00	56.1
31	153.90	1	1	0	49.00	10.00	12.00	55.3
32	189.00	0	0	0	43.00	11.00	12.00	57.2
33	168.00	0	0	0	45.00	11.00	11.00	56.7
34	198.00	0	1	0	43.00	9.90	1.40	57.2
35	152.60	0	0	0	45.00	11.00	12.00	55.7
36	72.00	0	1	0	43.00	11.00	12.00	57.7
37	245.00	0	1	1	49.00	13.00	14.00	59.0
38	178.00	0	0	0	42.00	11.00	10.00	56.0
39	180.00	0	0	0	48.00	11.00	12.00	55.9
40	191.40	0	0	0	43.00	9.50	8.40	58.2
41	187.00	0	0	0	43.00	10.00	11.00	57.9
42	105.30	0	0	0	43.00	11.00	13.00	57.9
43	192.00	0	0	0	41.00	10.00	9.00	57.0
44	311.50	0	1	1	47.00	15.00	16.00	56.9
45	137.20	0	0	0	41.00	10.00	13.00	58.0
46	116.20	0	0	0	38.00	12.00	13.00	59.0
47	195.80	1	1	0	44.00	14.00	16.00	57.0
48	182.60	0	0	0	49.00	11.00	11.00	58.0
49	132.60	0	0	0	41.00	8.40	9.20	59.0
50	261.00	1	1	1	45.00	12.00	11.00	57.9

51	222.30	0	1	0	47.00	11.00	9.00	56.9
52	140.80	0	0	0	43.00	11.00	11.00	57.2
53	85.00	0	0	0	47.00	10.00	111.00	58.5
54	126.40	0	0	0	46.00	12.00	12.00	58.0
55	91.20	0	0	0	43.00	11.00	13.00	58.0
56	175.10	0	0	0	42.00	7.00	9.00	55.7
57	119.60	0	0	0	48.00	12.00	12.00	58.6
58	610.00	0	0	1	47.00	13.00	13.00	56.6
59	117.10	0	0	0	45.00	10.00	10.00	55.7
60	53.50	0	0	0	43.00	10.00	11.00	60.0
61	128.80	0	1	0	43.00	12.00	12.00	57.8
62	186.00	0	0	0	47.00	11.00	11.00	57.5
63	238.00	0	0	0	40.00	10.00	10.00	57.8
64	133.50	0	0	0	44.00	11.00	20.00	56.7
65	230.00	0	1	0	45.00	10.00	11.00	57.8
66	124.80	0	0	0	44.00	9.00	8.70	56.8
67	114.00	0	0	0	40.00	11.00	10.00	56.0
68	90.20	0	0	0	43.00	10.00	10.00	61.2
69	84.00	0	0	0	43.00	8.80	8.40	57.7
70	223.10	0	0	0	40.00	9.20	11.00	56.3
71	128.00	0	0	0	40.00	9.90	11.00	55.5
72	120.40	0	0	0	46.00	11.00	10.00	57.9
73	0.00	0	0	0	47.00	12.00	11.00	56.9
74	167.40	0	0	0	44.00	9.40	11.00	56.5
75	64.40	0	0	0	45.00	13.00	14.00	56.3
76	180.40	0	0	0	41.00	9.50	9.20	57.6
77	111.00	0	0	0	44.00	10.00	10.00	56.8
78	134.40	0	0	0	40.00	10.00	11.00	57.0
79	142.50	0	0	0	46.00	11.00	10.00	57.9
80	59.20	0	0	0	45.00	10.00	12.00	56.0
81	163.80	1	1	0	55.00	11.00	8.80	39.8
82	176.00	0	0	0	40.00	12.00	12.00	58.0
83	190.00	0	1	0	44.00	11.00	11.00	58.8
84	225.40	0	0	0	42.00	11.00	10.00	59.0
85	95.00	0	0	0	47.00	11.00	11.00	57.0
86	319.80	0	1	1	41.00	11.00	13.00	59.7
87	156.60	0	0	0	47.00	9.60	10.00	55.9
88	124.60	0	0	0	41.00	7.00	13.00	57.6
89	117.00	0	0	0	44.00	9.20	9.50	58.3
90	132.00	0	0	0	44.00	11.00	11.00	56.8
91	0.00	0	0	0	34.00	11.00	11.00	57.0
92	124.80	0	0	0	4.00	10.00	11.00	57.8
93	282.80	1	1	0	58.00	14.00	16.00	55.4
94	134.40	1	1	0	48.00	13.00	14.00	57.6
95	431.20	0	0	1	47.00	9.00	8.70	58.0
96	197.40	0	1	0	52.00	11.00	11.00	56.5
97	171.00	0	0	0	51.00	12.00	14.00	58.9
98	68.40	0	0	0	40.00	9.20	9.90	56.3

S_No	ECH_LVMI	ECH_RWT	PI_ACR	PI_EGFR
1	83.00	0.38	98.70	92.97
2	100.00	0.47	21.20	85.09
3	108.00	0.65	6.30	101.63
4	124.00	0.70	17.30	118.93
5	81.00	0.47	54.10	97.40
6	107.00	0.47	67.10	91.12
7	68.00	0.97	4.80	93.89
8	84.00	0.48	14.30	100.79
9	79.00	0.45	2.90	89.93
10	64.00	0.53	2.90	96.41
11	84.00	0.43	2.90	111.90
12	129.00	0.57	48.00	111.58
13	92.00	0.52	14.20	80.92
14	103.00	0.54	13.40	127.40
15	109.00	0.50	2.90	104.80
16	97.00	0.43	10.50	151.48
17	136.00	0.87	0.90	92.99
18	111.00	0.52	1.30	120.73
19	91.00	0.49	94.30	128.29
20	77.00	0.48	29.20	106.46
21	87.00	0.48	12.30	98.66
22	54.00	0.33	57.40	90.33
23	88.00	0.47	17.80	100.15
24	92.00	0.51	14.10	149.08
25	103.00	0.43	27.60	85.51
26	165.00	0.54	16.90	104.23
27	85.00	0.38	12.90	93.36
28	67.00	0.46	28.90	83.08
29	84.00	0.45	167.20	71.65
30	55.00	0.39	9.60	108.23
31	121.00	0.49	8.50	126.18
32	118.00	0.56	3.40	120.82
33	103.00	0.49	4.40	76.32
34	108.00	0.65	2.90	127.80
35	96.00	0.53	8.70	149.90
36	100.00	0.56	162.80	100.92
37	137.00	0.57	7.70	76.82
38	92.00	0.48	60.20	137.44
39	124.00	0.50	12.00	120.32
40	67.00	0.39	173.80	125.38
41	88.00	0.51	66.00	158.66
42	118.00	0.60	24.00	84.90
43	76.00	0.49	15.00	91.89
44	170.00	0.64	839.80	128.28
45	97.00	0.49	12.00	121.57
46	91.00	0.63	1.00	65.07
47	137.00	0.64	46.20	108.48
48	120.00	0.45	209.30	102.05
49	81.00	0.41	2.90	136.34
50	95.00	0.53	15.00	282.94

51	108.00	0.47	1.40	101.09
52	98.00	0.51	13.40	147.99
53	100.00	0.43	2.90	86.68
54	67.00	0.65	2.90	112.36
55	107.00	0.51	6.10	104.10
56	65.00	0.33	18.70	123.63
57	112.00	0.50	58.00	104.63
58	159.00	0.55	19.60	115.58
59	82.00	0.44	29.10	75.70
60	90.00	0.47	75.70	107.65
61	104.00	0.56	401.00	109.51
62	108.00	0.47	7.50	84.92
63	77.00	0.50	2.90	107.43
64	128.00	0.50	31.90	73.04
65	106.00	0.44	29.30	162.84
66	70.00	0.41	16.00	109.10
67	68.00	0.55	6.80	99.53
68	83.00	0.47	11.10	116.00
69	62.00	0.41	4.70	65.86
70	65.00	0.46	24.40	128.60
71	79.00	0.50	12.90	91.67
72	98.00	0.48	2.90	105.06
73	104.00	0.51	5.10	85.13
74	91.00	0.43	48.30	93.76
75	103.00	0.58	8.80	102.80
76	62.00	0.46	14.40	73.57
77	84.00	0.45	31.20	121.10
78	96.00	0.50	2.40	108.75
79	91.00	0.48	224.90	72.04
80	101.00	0.44	66.40	107.47
81	117.00	0.40	123.40	61.31
82	97.00	0.60	13.20	72.29
83	94.00	0.50	58.60	88.56
84	82.00	0.52	99.30	110.34
85	92.00	0.47	22.30	82.02
86	136.00	0.54	300.40	91.50
87	103.00	0.41	2.90	92.28
88	89.00	0.34	2.90	107.21
89	71.00	0.42	155.40	106.36
90	85.00	0.50	76.20	121.79
91	69.00	0.65	29.10	117.68
92	99.00	0.50	10.20	127.43
93	16.00	0.05	2.90	129.21
94	134.00	0.54	3.30	129.21
95	96.00	0.37	1.80	100.58
96	122.00	0.42	2.90	116.01
97	139.00	0.55	52.30	93.81
98	70.00	0.46	45.80	100.67