A STUDY ON THE EVALUATION OF SERUM URIC ACID LEVELS IN ESSENTIAL HYPERTENSION AT COIMBATORE MEDICAL COLLEGE

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April – 2012

CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON THE EVALUATION OF SERUM URIC ACID LEVELS IN ESSENTIAL HYPERTENSION AT COIMBATORE MEDICAL COLLEGE"** is the bonafide original work of **Dr. S.P.SANTHOSH KUMAR** in partial fulfilment of the requirements for M.D. Branch-I (General Medicine) Examination of the Tamil Nadu Dr. M.G.R. Medical University to be held in April 2012.

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The dissertation is submitted to the Tamil nadu Dr. M.G.R. Medical University, towards the partial fulfilment of requirement for the award of M.D. Degree (Branch – I) in General Medicine.

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Dr. S. P. Santhosh Kumar.

LIST OF ABBREVIATIONS

AAP	4- Amino antipyrine
AICAR	Aminoimidazole Carboxamide Ribotate
AMP	Adenylic acid
APRT	Amido Phosphoribosyl transferase
ATP	Adenosine triphosphate
BP	Blood Pressure
CO_2	Carbon dioxide
CV	Cardio vascular
CVD	Cardio Vascular Disease
DBP	Diastolic Blood Pressure
EDTA	Ethelene diamine tetra acetic acid
GFR	Glomerular Filtration rate
GMP	Guanylic acid
H2O2	Hydrogen peroxide
HF	Heart Failure
HPRT	Hypoxanthine phosphoribosyl transferase
HTN	Hypertension
IHD	Ischemic Heart Disease
IMP	Inosine Monophosphate
JNC	Joint National Committee
LV	Left Ventricle
LVH	Left ventricular hypertrophy
MI	Myocardial infarction
MRI	Magnetic resonance imaging
NHANES	National health and nutrition survey
PRA	Phosphoribosylamine
PRPP	Phosphoribosyl pyrophosphate
SAICAR	Succinylaminoimidazole Carboxamide Ribotate
SBP	Systolic blood pressure
SUA	Serum uric acid
TBHB	2,4,6- tribromo- 3- hydroxy benzoic acid

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ABSTRACT

Back ground & objectives

The association of raised serum uric acid levels with various cardiovascular risk factors has often led to the debate of whether raised serum uric acid levels could be an independent risk factor in essential hypertension. Hence, we carried out a study to examine the possibility of hyperuricemia causing hypertension, to see if there is a relationship between the serum uric acid levels and severity & if they had duration of hypertension.

Methodology

The study was carried out in Coimbatore Medical College Hospital, the study period was of 12 months from December 2010 to November 2011. A total of 400 patients were studied of which 200 were cases and 200 were controls.

The patients were included if they satisfied the JNC VII criteria for hypertension. They were excluded if they were having any other condition known to cause raised serum uric acid levels & secondary hypertension.

Results

The study showed that serum uric acid levels were raised in patients with hypertension in comparison to normotensives. The Mean SUA levels between cases and controls were 6.1125 ± 1.5662 and 5.6695 ± 1.3323 respectively with t-value = 3.05, p-value = .002441.

SUA levels in the stages of hypertension showed a mean serum uric acid level in stage 1 hypertension of 5.5979 ± 1.4046 and stage 2 hypertension of 6.2750 ± 1.5836 with the t-value of 2.65 and p-value = 0.0087 which was significant.

SUA level in patients with hypertension < 5 years was 5.175 ± 1.1188 and those with ≥ 5 years was 6.9779 ± 1.4175 with the t-value of 9.93 and p-value = 0.0001 which was also significant.

Interpretation & Conclusion

Based on the study carried out, we concluded that SUA can be used as an early biochemical marker to determine the severity and duration of hypertension.

Key words: Serum Uric Acid; Hypertension; JNC VII; Hyperuricemia.

Introduction

INTRODUCTION

Hypertension is an important, increasing medical and public health problem. Worldwide prevalence estimates for hypertension may be as much as 1 billion individuals and approximately 7.1 million deaths per year may be attributable to hypertension.[1]

The WHO reports that suboptimal blood pressure (>115 mm of Hg Systolic BP) is responsible for 62% of cerebrovascular disease and 49% of ischemic heart disease. In addition, suboptimal blood pressure is the number one attributable risk for death due to myocardial infarction, stroke, congestive heart failure, peripheral vascular disease and end stage renal disease throughout the world.[1]

Approximately 30% of adults are still unaware of their hypertension, more than 40% of individuals are not on treatment, and two thirds of hypertensive patients are not being controlled to BP levels less than 140/90 mm of Hg.[1]

Uric acid, which serves no biochemical function other than being an end product of purine metabolism, was first discovered in 1776. A Swedish chemist ***Scheele*** isolated it from a urinary tract stone. In 1797, a British chemist ***Wallaston*** detected uric acid in a tophus

which was removed from his own ear. About 50 years later ***Alfred Baring Garrod***, a British physician showed by chemical isolation that uric acid was abnormally high in gouty patients.

In subsequent studies Garrod formulated a rational relationship between hyperuricemia and symptomatology of gouty patients.

Association between hypertension and hyperuricemia was recognized when a family with a unique and unfortunate pedigree attended Hammer Smith hospital in

1957. The father and six of the seven siblings of a patient had hyperuricemia, while his mother and all his siblings had hypertension.[1] This raised the question whether a raised serum uric acid was common in patients with hypertension.

Studies of uric acid levels and the development of hypertension have generally been consistent, continuous, and of similar magnitude. Hyperuricemia is also common among adults with prehypertension, especially when microalbuminuria is present. The observation that hyperuricemia precedes the development of hypertension indicates that it is not simply a result of hypertension per se.

Several multivariate analytical studies have thrown light that an elevated uric acid level is an independent risk factor for cardiovascular disease after controlling for the contribution of established risk factors like age, obesity, smoking, Diabetes mellitus, alcohol consumption and physical inactivity.[2] Such convincing data from a developing country like ours is poorly known. This study was done to determine whether raised serum uric acid levels were an independent risk factor for developing hypertension in our Indian subcontinent.

Aims and Objectives

AIMS AND OBJECTIVES

- To study the relationship between serum uric acid levels and essential hypertension.

- To study the relationship between serum uric acid levels and duration of hypertension.

- To study the relationship between serum uric acid levels and severity of hypertension.

Review of Literature

REVIEW OF LITERATURE

HYPERTENSION

Hypertension is the third leading killer disease in the world and is responsible for 1 in every 8 deaths. About 1 billion people are affected by hypertension worldwide.[3] The prevalence of hypertension is known to increase with age. Over 50% of individuals aged 60 to 69 and over 75% of those aged 70 years and older are affected. Recent Framingham Heart Study reported that lifetime risk of developing HTN is approximately 90% for men and women who are normotensive at 55-65 years old and survived to the age of 80-85 years.[4]

Studies have shown that BP is an independent risk factor for CVD. This relationship is independent, consistent and continuous. Observations involving more than 1 million individuals have shown that death from both CVD and stroke increases progressively and linearly from BP levels of as low as 115mm systolic and 75 mm diastolic upwards. The increased risks are present in all age groups ranging from 40 to 89 years old. For every increment of 20 mm hg systolic or 10mm diastolic there was a doubling of mortality from both ischemic heart disease and stroke.[5]

Evidence also warrants greater attention to the importance of SBP as a major risk factor for CVD. The rise in SBP continues throughout life, in contrast to DBP, which rises until approximately 50 years age, tends to level off over the next decade, and may remain same or fall later in life. Clinical trials have demonstrated that control of isolated systolic hypertension reduces total mortality, CV mortality, stroke and HF events.[6, 7]

MECHANISMS OF HYPERTENSION

1. INTRAVASCULAR VOLUME

The initial elevation of blood pressure in response to vascular volume expansion is related to an increase of cardiac output; however, over time, peripheral resistance increases and cardiac output reverts toward normal. The mechanism for the "pressure-natriuresis" phenomenon may involve a subtle increase of glomerular filtration rate, decreased absorbing capacity of the renal tubules, and possibly hormonal factors such as atrial natriuretic factor.[8]

2. AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system maintains cardiovascular homeostasis via pressure, volume and chemoreceptor signals. Adrenergic reflexes modulate blood pressure over the short term and adrenergic function, in concert with hormonal and volume-related factors, contributes to the long-term regulation of arterial pressure.[8]

3. RENIN-ANGIOTENSIN-ALDOSTERONE-SYSTEM

The renin-angiotensin-aldosterone system contributes to the regulation of arterial pressure primarily via the vasoconstrictor properties of angiotensin II and the sodium-retaining properties of aldosterone.

Angiotensin II is a potent pressor substance, the primary trophic factor for the secretion of aldosterone by the adrenal zona glomerulosa, and a potent mitogen stimulating vascular smooth-muscle cell and myocyte growth. Independent of its hemodynamic effects, Angiotensin II may play a role in the pathogenesis of atherosclerosis through a direct cellular action on the vessel wall.[8]

Aldosterone also has effects on non-epithelial targets. Independent of a potential effect on blood pressure, aldosterone may also play a role in cardiac hypertrophy and CHF.

RENIN - ANGIOTENSIN - ALDOSTERONE SYSTEM

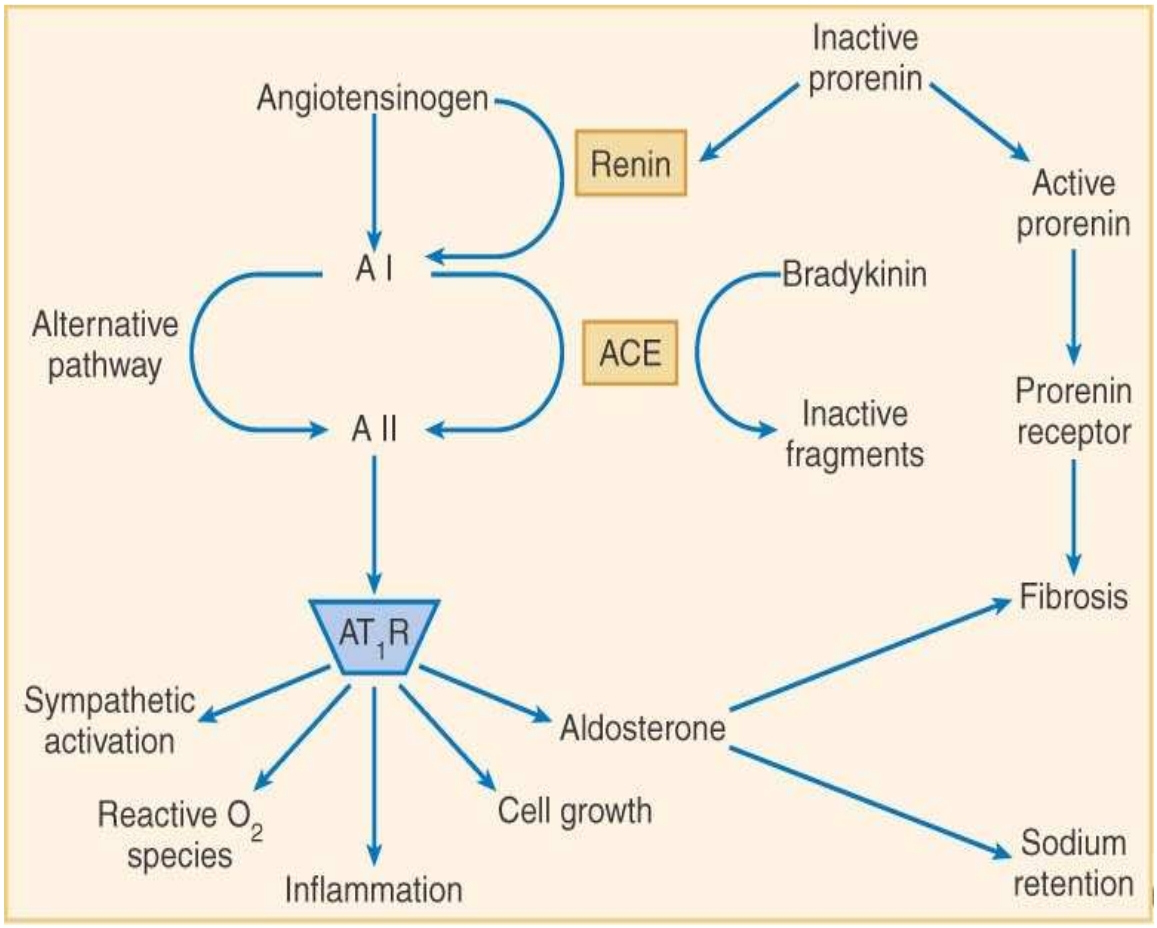

Fig.1-Renin Angiotensin Aldosterone system

Pathologic patterns of left ventricular geometry have also been associated with elevations of plasma aldosterone concentration in patients with essential hypertension, as well as in patients with primary aldosteronism.

PATHOLOGIC CONSEQUENCES OF HYPERTENSION

1. Heart

Hypertensive heart disease occurs as a result of structural and functional adaptations leading to left ventricular hypertrophy, diastolic dysfunction, CHF, abnormalities of blood flow due to atherosclerotic coronary artery disease and microvascular disease and cardiac arrhythmias. Diastolic dysfunction is an early consequence of hypertension related heart disease and is exacerbated by left ventricular hypertrophy and ischemia.[9,10]

Hypertension places increased tension on the left ventricular myocardium that is manifested as stiffness and hypertrophy, which accelerates the development of atherosclerosis within the coronary vessels. Abnormalities in Left Ventricular Function- the earliest functional changes in hypertension are in left ventricular diastolic dysfunction, with lower E/A ratio and longer isovolumic relaxation time.[9]

Left Ventricular Hypertrophy- Hypertrophy as a response to the increased afterload associated with elevated systemic vascular resistance can be viewed. Variety of dysfunctions accompany LVH, including lower coronary vasodilatory capacity, depressed left ventricular wall mechanics, and abnormal left ventricular diastolic filling pattern.[10]

Congestive Heart Failure- The various alterations of systolic and diastolic function seen with LVH can progress into congestive heart failure. A 20mm hg increment in systolic blood pressure conferred a 56% increased risk of CHF in the Framingham cohort.

When haemodynamically challenged by stress, persons with hypertension are unable to increase their end diastolic volume, because of decreased left ventricular relaxation and compliance. Consequently, a cascade begins, in which left ventricular

end diastolic blood pressure rises, left atrial pressure increases and pulmonary edema develops.[11]

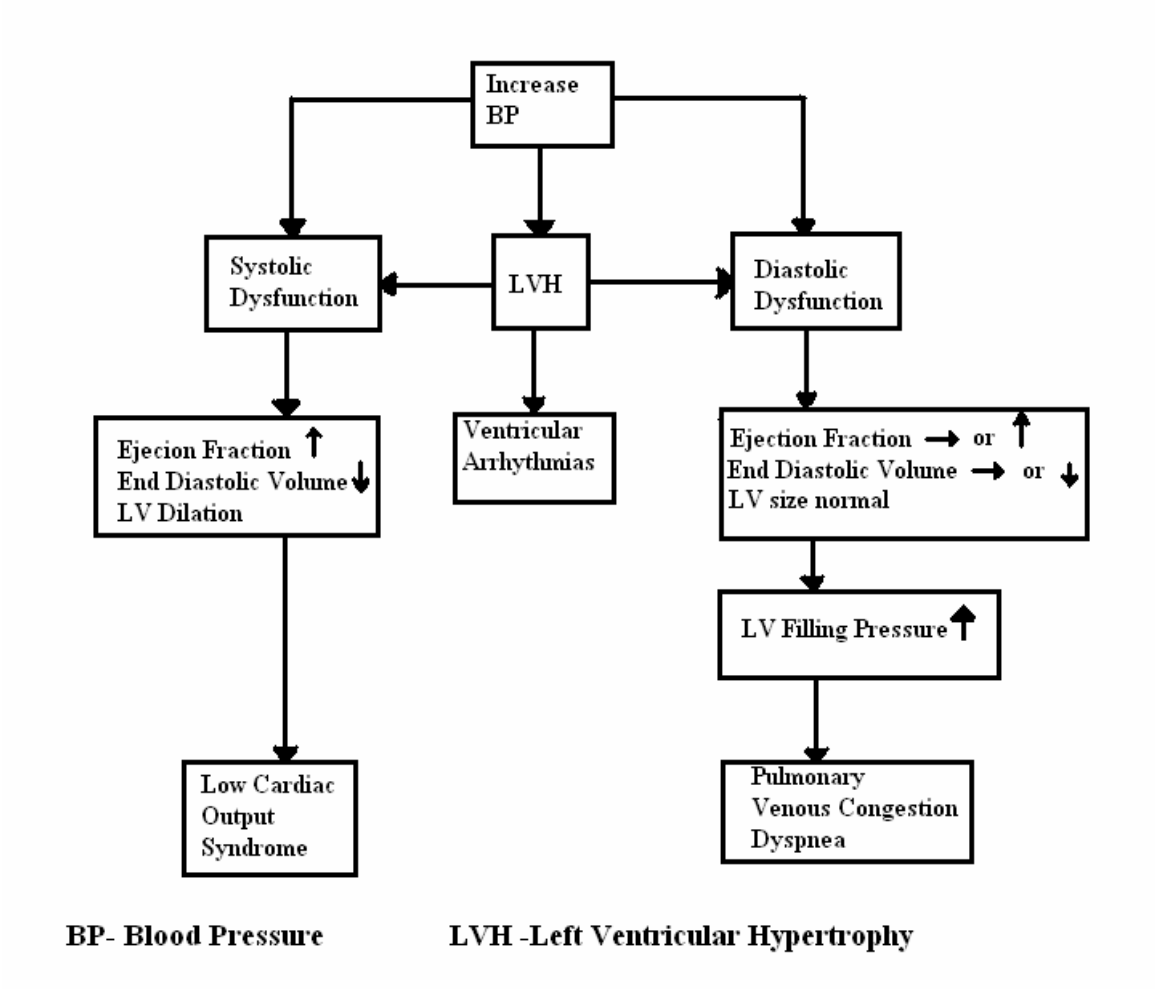

Fig.2-Consequences of systolic and diastolic dysfunction related to hypertension(26)

Coronary Heart Disease- Hypertension is a major risk factor for myocardial infarction and ischemia. Acute rise in blood pressure may follow the onset of ischaemic pain; the blood pressure often falls immediately after the infarct if pump function is impaired. Once MI occurs, the prognosis is affected by both the pre-existing and the subsequent blood pressure. The prevalence of silent MI is

significantly increased in hypertensive subjects, and they have a greater risk for mortality after an initial MI.[12]

2. Brain

Hypertension is an important risk factor for brain infarction and haemorrhage. The incidence of stroke rises progressively with increasing blood pressure levels, particularly systolic blood pressure in individuals >65 years.(8). Hypertension is also associated with impaired cognition in an aged population. Hypertensive encephalopathy is related to failure of auto regulation of cerebral blood flow at the upper pressure limit, resulting in vasodilatation and hyperperfusion. Untreated hypertensive encephalopathy may progress to stupor, coma, seizures, and death within hours.[13]

3. Kidney

Hypertension is a major risk factor for renal injury and ESRD. The increased risk associated with high blood pressure is graded, continuous and present throughout the entire distribution of blood pressure above optimal. Renal risk appears to be more closely related to systolic than to diastolic blood pressure.

The atherosclerotic, hypertension-related vascular lesions in the kidney primarily affect the preglomerular arterioles, resulting in ischemic changes in the glomeruli and postglomerular structures like renal tubules and collecting ducts. Glomerular pathology progresses to glomerulosclerosis, and eventually the renal tubules may also become ischemic and gradually atrophic.

Clinically, macroalbuminuria (a random urine albumin/ creatinine ratio > 300 □g/mg) or microalbuminuria (a random urine albumin / creatinine ratio 30-300 □g/mg) are early markers of renal injury.[8]

Microalbuminuria in hypertensive patients has been correlated with left ventricular hypertrophy and carotid artery thickness.[14]

4. Peripheral Arteries & Eyes

Hypertensive patients with arterial disease of the lower limbs are at increased risk for future cardiovascular disease. The ankle-brachial index is an useful approach for evaluating Peripheral Arterial Disease and is defined as the ratio of noninvasively assessed ankle to brachial (arm) systolic blood pressure. An ankle-brachial index < 0.90 is considered diagnostic of Peripheral Arterial Disease.

Vascular changes in the fundus of the eye reflect both hypertensive retinopathy and arteriosclerotic retinopathy. The hypertensive retinal changes are graded by the **Keith – Wegner – Barker classification** as

Grade 1 Mild to Moderate narrowing or sclerosis of the arterioles.

Grade 2 Moderate to marked narrowing of the arterioles. Local and or generalized narrowing of arterioles. Exaggeration of light reflex.

Grade 3 Retinal arteriolar narrowing and focal constriction, retinal edema, Cotton wool patches, haemorrhages.

Grade 4 Grade 3 + Papilloedema.

5. Hypertension during Pregnancy

In about 12% of first pregnancies in previously normotensive women, hypertension appears after 20 weeks (gestational hypertension) and in about half this will progress to preeclampsia when complicated by proteinuria, edema or hematological or hepatic abnormalities, which in turn, increase the risk of progress to eclampsia, defined by the occurrence of convulsions. Women with hypertension predating pregnancy have an even higher incidence of preeclampsia and a greater

likelihood of early delivery of small-for-gestational age babies. Preeclampsia is of unknown cause but occurs frequently in primigravid women and in pregnancies involving, either men or women who were the product of a pregnancy complicated by preeclampsia, supporting a genetic role.[15]

DEFINING HYPERTENSION

The best operational definition for hypertension is "the level at which the benefits (minus the risks and costs) of action exceed the risks and costs (minus the benefits) of inaction."[16]

From an epidemiologic perspective, there is no obvious level of blood pressure that defines hypertension. The multiple Risk Factor Intervention Trial (MRFIT), which included > 350,000 male participants, demonstrated a continuous and graded influence of both systolic and diastolic blood pressure on CHD mortality. Cardiovascular disease risk doubles for every 20-mmHg increase in systolic and 10-mmHg increase in diastolic pressure. Among older individuals, systolic blood pressure and pulse pressure are more powerful predictors of cardiovascular disease than diastolic blood pressure.[8,17]

CLASSIFICATION OF BLOOD PRESSURE

Based on the seventh report of the **Joint National Committee** on prevention, detection, evaluation and treatment of high blood pressure **(JNC VII report)** BP is classified into the following stages :

Classification of BP	Systolic BP (mm of Hg)	Diastolic BP (mm of Hg)
Normal	< 120	<80
Prehypertension	120 - 139	80 - 89
Stage 1 hypertension	140 - 159	90 - 99
Stage 2 hypertension	≥160	≥100

Table.1- Classification of BP for Adults > 18 years old

In contrast with the classification provided in the JNC VI report, a new category designated prehypertension has been added and stages 2 and 3 have been combined.[17]

Patients with prehypertension are at increased risk for progression to hypertension; those in the 130/80 to 139/89 mm hg BP range are at twice the risk to develop hypertension as those with lower values.[18]

ACCURATE BLOOD PRESSURE MEASUREMENT

The accurate measurement of BP is the sine qua non for successful management. The equipment, whether aneroid, mercury or electronic, should be trained and regularly retrained in the standardized technique, and the patient must be properly prepared and positioned. The auscultatory method of BP measurement should be used.

Persons should be seated quietly for at least 5 minutes in a chair (rather than on an examination table), with feet on the floor, and arm supported at heart level. Caffeine, exercise and smoking should be avoided for at least 30 minutes prior to measurement.

Measurement of BP in the standing position is indicated periodically, especially in those who report symptoms consistent with reduced BP on standing. An appropriately sized cuff (cuff bladder encircling at least 80% of the arm) should be used to ensure accuracy. At least two measurements should be made and the average recorded.

For manual determinations, palpated radial pulse obliteration pressure should be used to estimate SBP. The cuff should then be inflated 20 to 30 mm Hg above this level for the auscultatory determinations. The cuff deflation rate for auscultatory readings should be 2 mm Hg per second. SBP is the point at which the first of two or more Korotkoff sounds is heard (onset of phase 1), and the disappearance of Korotkoff sound (onset of phase 5) is used to define DBP.

In certain conditions like Aortic Regurgitation, the diastolic BP will be 0 mm Hg and the appearance of muffled sound is taken as diastolic BP. Care should be taken while measuring BP in elderly patients as there will be auscultatory gap.

The key messages of JNC – VII are:[17]

- In those older than age 50, SBP of greater than 140 mm Hg is a more important cardiovascular disease (CVD) risk factor than DBP.
- Beginning at 115/75 mm Hg, CVD risk doubles for each increment of 20/10 mm Hg.
- Those who are normotensive at 55 years of age will have a 90 life time risk of developing hypertension.

Initial Blood Pressure, mm Hg*	Follow-Up Recommended +
Normal	Recheck in 2 years
Prehypertension	Recheck in 1 year
Stage 1 hypertension	Confirm within 2 months#
Stage 2 hypertension	Evaluate or refer to source of care within 1 month. For those with higher pressures (eg., > 180/110 mm Hg), evaluate and treat immediately or within 1 week depending on clinical situation and complications.

Table.2-Recommendations for Follow-Up based on Initial Blood Pressure Measurements for Adults without Acute End Organ Damage (JNC-7)

* If systolic and diastolic categories are different, follow recommendations for shorter time follow up (e.g, 160/86 mm Hg should be evaluated or referred to source of care within 1 month).

+ Modify the scheduling of follow-up according to reliable information about past BP measurements, other cardiovascular risk factors, or target organ disease.

Provide advice about lifestyle modifications.

CLASSIFICATION OF HYPERTENSION:

Patients with arterial hypertension and no definable cause are said to have *Primary or essential or idiopathic hypertension.* Individuals in whom a specific structural organ or gene defect is responsible for hypertension are defined as having a *secondary form of hypertension.*[19]

Classification of Arterial Hypertension:

- Systolic hypertension with wide pulse pressure

1. Decreased compliance of aorta (arteriosclerosis)
2. Increased stroke volume
3. Aortic regurgitation
4. Thyrotoxicosis
5. Hyperkinetic Heart Syndrome
6. Fever
7. Arteriovenous fistula
8. Patent Ductus Arteriosus

- Systolic And Diastolic Hypertension

(Increased peripheral vascular resistance)

I. Renal

A. Chronic Pyelonephritis

B. Acute and chronic glomerulonephritis

C. Polycystic kidney disease

D. Renal artery stenosis or renal infarction

E. Other severe renal diseases (arteriolar nephrosclerosis, diabetic nephropathy, etc.,)

F. Renin-producing tumors

II. Endocrine

A. Oral Contraceptives

B. Adrenocortical Hyperfunction

1. Cushing's disease and syndrome
2. Primary hyperaldosteronism

3. Congenital or hereditary adrenogential syndromes.

C. Pheochromocytoma

D. Myxedema

E. Acromegaly

III. Neurogenic

A. Psychogenic

B. Increased intracranial pressure (acute)

C. Familial Dysautonomia (Riley-Day Syndrome)

D. Polyneuritis (acute porphyria, lead poisoning)

E. Spinal cord section (acute)

IV. Miscellaneous

A. Coarctation of aorta

B. Increased intravascular volume (excessive transfusion, Polycythemia Vera)

C. Polyarteritis Nodosa

D. Hypercalcemia

E. Medications e.g. Glucocorticoids, Cyclosporine..,

V. Unknown etiology

A. Essential hypertension (>90% of all cases of hypertension)

B. Toxaemia of pregnancy

C. Acute intermittent porphyria

GENETIC CONSIDERATIONS:

Essential hypertension is almost certainly **a polygenic disorder,** involving multiple genes, each having small effects on blood pressure. [20]

NATURAL HISTORY OF UNTREATED HYPERTENSION:

Both the rising SBP and falling DBP levels logically are associated with an increased risk for atherosclerotic vascular diseases. The resultant widened pulse pressures have been widely reported to be the best prognostic indicator of cardiovascular risk. However, an analysis of data from one million adults in 61 prospective studies found that, for predicting mortality from both stroke and coronary artery disease, the SBP is slightly more informative than DBP and that pulse pressure is much less informative.[21]

SYMPTOMS AND SIGNS:

Uncomplicated hypertension is almost always asymptomatic, so that patient may be unaware of the consequent progressive cardiovascular damage for as long as 10 to 20 years.

Symptoms often attributed to hypertension- Headache, tinnitus, dizziness and fainting may be observed just as commonly in the normotensive population. Many symptoms attributable to the elevated BP are psychogenic in origin, often reflecting hyperventilation induced by anxiety over the diagnosis of a lifelong, insidious disease that threatens well being and survival.[22]

When symptoms do bring the patient to the Physician, they fall into three categories. They are related to

(1) the elevated pressure itself

(2) the hypertensive vascular disease and

(3) the underlying disease, in the case of secondary hypertension.

Though popularly considered a symptom of elevated arterial pressure, headache is characteristic of only severe hypertension. Most commonly such headaches are localized to the occipital region and are present when the patient awakens in the

morning but subsides spontaneously after several hours. Other complaints that may be related to elevated blood pressure include dizziness, palpitations, easy fatigability, and impotence.

Complaints referable to vascular disease include epistaxis, hematuria, blurring of vision owing to retinal changes, episodes of weakness or dizziness due to transient cerebral ischemia, angina pectoris, and dyspnoea due to cardiac failure. Pain due to dissection of aorta or to a leaking aneurysm is a rare presenting symptom.

Examples of symptoms related to the underlying disease in secondary hypertension are polyuria, polydipsia, and muscle weakness secondary to hypokalemia in patients with primary aldosteronism or weight gain, and emotional lability in patients with Cushing's syndrome. Patients with pheochromocytoma may present with episodic headaches, palpitations, diaphoresis, and postural dizziness.[23]

ASSOCIATION OF HYPERTENSION WITH OTHER CONDITIONS:

1. Obesity

Hypertension is more common among obese individuals and adds to their increased risk of IHD especially if it is abdominal/visceral in location as a part of the metabolic syndrome. In the Framingham Study the incidence of hypertension was increased 46 % in men and 75 % in female who are overweight defined as a body mass index of 25.0 to 29.9 compared to normal weight persons.[24]

2. Physical Inactivity

Physical fitness can help prevent hypertension and persons who are already hypertensive can lower their BP by means of regular aerobic exercise. The relationship may involve a restoration of age related declines in endothelium dependent vasodilatation.[25]

3. Alcohol Intake

Alcohol in large amounts (more than 2 portions a day and even more so when drunk in binges), alcohol increases BP and arterial stiffness. The pressor effect of larger amounts of alcohol primarily reflects an increase in cardiac output and heart rate, possibly a consequence of increased sympathetic nerve activity.

Alcohol also alters cell membrane and allows more calcium to enter perhaps by inhibition of sodium transport.

4. Smoking

Cigarette smoking raise blood pressure, probably through the nicotine induced release of nor-epinephrine from adrenergic nerve endings.

Smoking also causes an acute and marked reduction in radical artery compliance, independent of the risk of the increase in blood pressure.

5. Sleep Apnea

Snoring and sleep are often associated with hypertension, which may in turn be induced by increased sympathetic activity and endothelin release in response to hypoxemia during apnea.

Relief of sleep apnea may alleviate hypertension.[26]

6. Hematological Findings:

Higher haematocrits are found in hypertensive persons and associated with abnormal left ventricular filling on echocardiography.[27]

7. Hypercholesterolemia:

Hypercholesterolemia frequently coexists with hypertension at least in part because it impairs endothelium dependent vasodilatation. Lipid lowering therapy restores the bioavailability of nitric oxide, reduces arterial stiffness and lowers BP.[28]

8. Hyperuricemia

Raised serum uric acid concentrations in the blood are commonly encountered in essential hypertension. Although the raised serum uric acid and episodes of gout are occasionally attributable to therapy, asymptomatic hyperuricemia not infrequently precedes the diagnosis and treatment of essential hypertension.

The hyperuricemia observed in untreated hypertension may reflect the decrease in renal blood flow and early hypertensive nephrosclerosis. However, antihypertensive drug regimens, especially those including diuretics, do confound the link between hypertension-associated morbidity and mortality.

Epidemiological evidence to support the contention that uric acid is an independent risk factor for hypertension- associated morbidity can be gleaned from a multivariate analysis of 1988-94 data on 3900 hypertensive people from the public-use database of the US National Health and Nutrition Survey (NHANES III). It showed that raised serum uric acid was associated with significantly higher sex-adjusted risk of heart attack and stroke.

Hypertensive people with raised serum uric acid had a significantly higher relative risk (RR) for both heart attack and stroke.[29] The NHANES III data supports the hypothesis that uric acid is an independent risk factor for hypertension-associated morbidity and mortality.

The renal handling of uric acid may provide a physiological clue to why hypertension-associated morbidity is closely linked to serum uric acid. It is well established that serum uric acid increases as arterial blood pressure rises and is associated with a reduction in renal blood flow.

High serum uric acid concentrations may increase sodium reabsorption at nephron sites proximal to the distal tubule, and it has been proposed that metabolic

perturbations such as hyperinsulinaemia may mediate some of the effects of hypertension.

Hyperuricaemia may represent a multimetabolic syndrome in which insulin-mediated renal haemodynamic abnormalities lead to hypertensive renal damage. It seems safe to say that hyperuricaemia in hypertension may be an early indicator of hypertensive cardiorenal disease, which is commonly associated with a multimetabolic syndrome.[30]

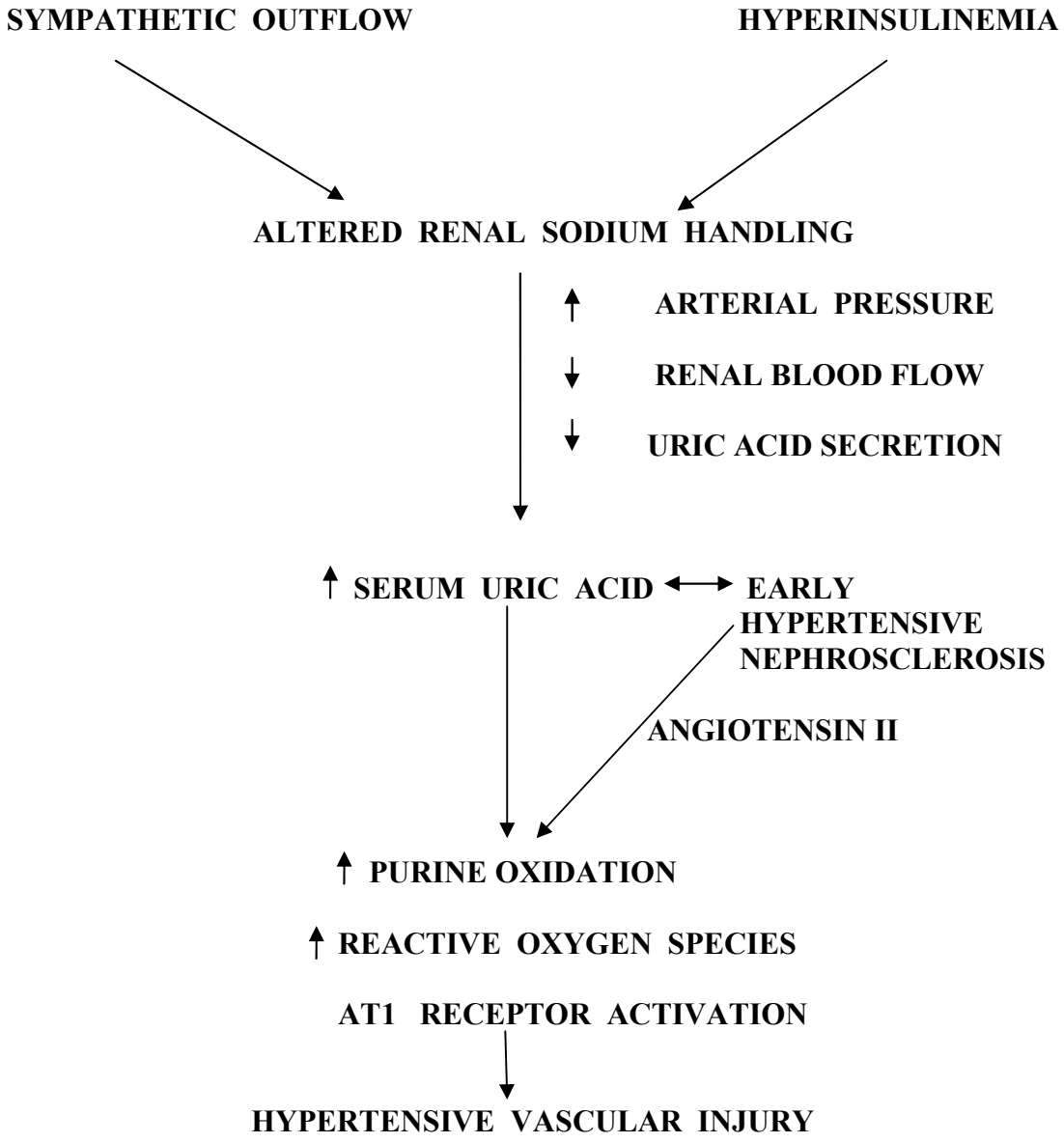

Figure 3 - Interaction between renal pathophysiology of hypertension and uric acid biochemistry

URIC ACID METABOLISM

Uric acid is the final breakdown product of purine degradation in humans. Urates, the ionized forms of uric acid, predominate in plasma extracellular fluid and synovial fluid, with ~98% existing as monosodium urate at pH 7.4.[20]

The pH of urine greatly influences the solubility of uric acid. Although purine nucleotides are synthesized and degraded in all tissues, urate is produced only in tissues that contain xanthine oxidase, primarily the liver and small intestine. Urate production varies with the purine content of the diet and the rates of purine biosynthesis, degradation, and salvage. Normally, two-third to three-fourth of urate is excreted by the kidney, and most of the remainder is eliminated through the intestine.

The kidneys clear urate from the plasma and maintain physiologic balance by utilizing specific organic anion transporters (OATs) including urate transporter 1 (URATI) and human uric acid transporter (hUAT). URAT1and other OATs carry urate into the tubular cells from the apical side of the lumen. Once inside the cell, urate must pass to the basolateral side of the lumen in a process controlled by the voltage-dependent carrier hUAT.

Until recently, component model has been used to describe the renal handling of urate / uric acid. The methods are

(1) Glomerular filtration,

(2) Tubular reabsorption

(3) Secretion, and

(4) Postsecretory reabsorption.

URAT1 is a novel transporter expressed at the apical brush border of the proximal nephron. Uric acid compounds directly inhibit URAT1 on the apical side of the tubular cell (so-called cis-inhibition).[20]

The total-body urate pool is the net result between urate production and excretion.

Urate production is influenced by dietary intake of purines and the rates of de novo biosynthesis of purines from nonpurine precursors, nucleic acid turnover, and salvaging phosphoribosyl transferase activities. The formed urate is normally excreted by urinary and intestinal routes.

Hyperuricemia can be caused by increased production, decreased excretion, or a combination of mechanisms. When hyperuricemia exists, urate can precipitate and deposit in tissues as tophi.

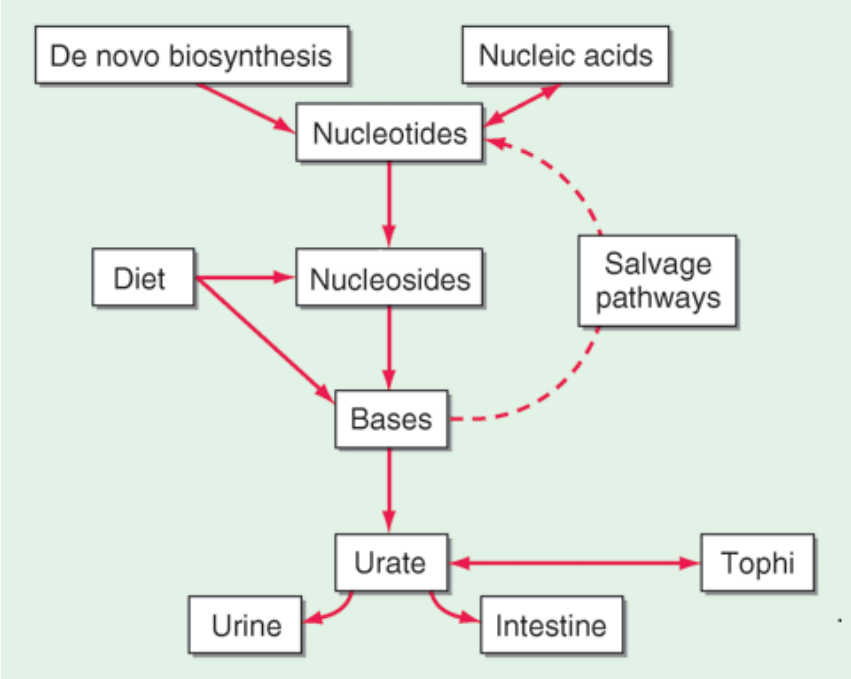

Fig.4-URIC ACID TURNOVER AND METABOLISM

HYPERURICEMIA

Hyperuricemia may be ***defined as a plasma (or serum) urate concentration >420 umol/L (7.0 mg/dL).*** This definition is based on physicochemical, epidemiologic, and disease-related criteria. Physicochemically, hyperuricemia is the concentration of urate in the blood that exceeds the solubility limits of monosodium

urate in plasma, 415 umol/L (6.8 mg/dL). In epidemiologic studies, hyperuricemia is defined as the mean plus 2 standard deviations of values determined from a randomly selected healthy population. When measured in unselected individuals, 95% have serum urate concentrations <420 umol/L (7.0 mg/dL).

Finally, hyperuricemia can be defined in relation to the risk of disease. The risk of developing gouty arthritis or urolithiasis increases with urate levels >420 umol/L (7.0 mg/dL) and escalates in proportion to the degree of elevation.

Hyperuricemia is present in between 2.0 and 13.2% of ambulatory adults and somewhat more frequently in hospitalized individuals.[31]

Causes of Hyperuricemia

Hyperuricemia may be classified as *primary* or *secondary* depending on whether the cause is innate or is the result of an acquired disorder. However it is useful to classify hyperuricemia in relation to the underlying pathophysiology, i.e., whether it results from increased urate production, decreased excretion, or a combination of two.

Classification of Hyperuricemia by Pathophysiology

1) Urate overproduction

a. Primary idiopathic
b. HPRT deficiency
c. PRPP synthetase overactivity
d. Hemolytic process
e. Lmphoproliferative diseases
f. Myeloproliferative diseases
g. Polycythemia vera
h. Psoriasis
i. Paget's disease

j. Glycogenosis III, V, and VII

k. Rhabdomyolysis

l. Exersice

m. Alcohol

n. Obesity

o. Purine-rich diet

2) Decreased Uric acid Excretion

a. Primary idiopathic

b. Renal insufficiency

c. Polycystic kidney disease

d. Diabetic insipidus

e. Hypertension

f. Acidosis

   i. Lactic acidosis

   ii. Diabetic ketoacidosis

g. Starvation ketosis

h. Berylliosis

i. Sarcoidosis

j. Lead intoxication

k. Hyperparathyroidism

l. Hypothyroidism

m. Toxaemia of pregnancy

n. Bartter's syndrome

o. Down syndrome

p. Drug ingestion

i. Salicylates (>2g/d)

ii. Diuretics

iii. Alcohol

iv. Levodopa

v. Ethambutol

vi. Pyrazinamide

vii. Nicotinic acid

viii. Cyclosporine

3) Combined Mechanism

a. Glucose-6- phosphatase deficiency

b. Fructose-1- phosphate aldolase deficiency

c. Alcohol

d. Shock

INCREASED URATE PRODUCTION

Diet provides an exogenous source of purines and, accordingly, contributes to the serum urate in proportion to its purine content. Strict restriction of purine intake reduces the mean serum urate level by about 60 umol/L (1.0 mg/dL) and urinary uric acid excretion by approximately 1.2 mmol/d (200 mg/d). Because about 50% of ingested RNA purine and 25% of ingested DNA purine appear in the urine as uric acid, foods high in nucleic acid content have a significant effect on the serum urate level. Such foods include liver, "sweetbreads" (i.e., thymus and pancreas), kidney, and anchovy.

Endogenous sources of purine production also influence the serum urate level. De novo purine biosynthesis, the formation of a purine ring from nonring structures, is an 11-step process that results in formation of *inosine monophosphate* ***(IMP).*** The

first step combines *phosphoribosylpyrophosphate* ***(PRPP)*** and *glutamine* and is catalyzed by *amidophosphoribosyltransferase* ***(amidoPRT).*** The rates of purine biosynthesis and urate production are determined, for the most part, by this enzyme. **AmidoPRT** is regulated by the substrate **PRPP**, which drives the reaction forward, and by the end products of biosynthesis (IMP and other ribonucleotides), which provide feedback inhibition.

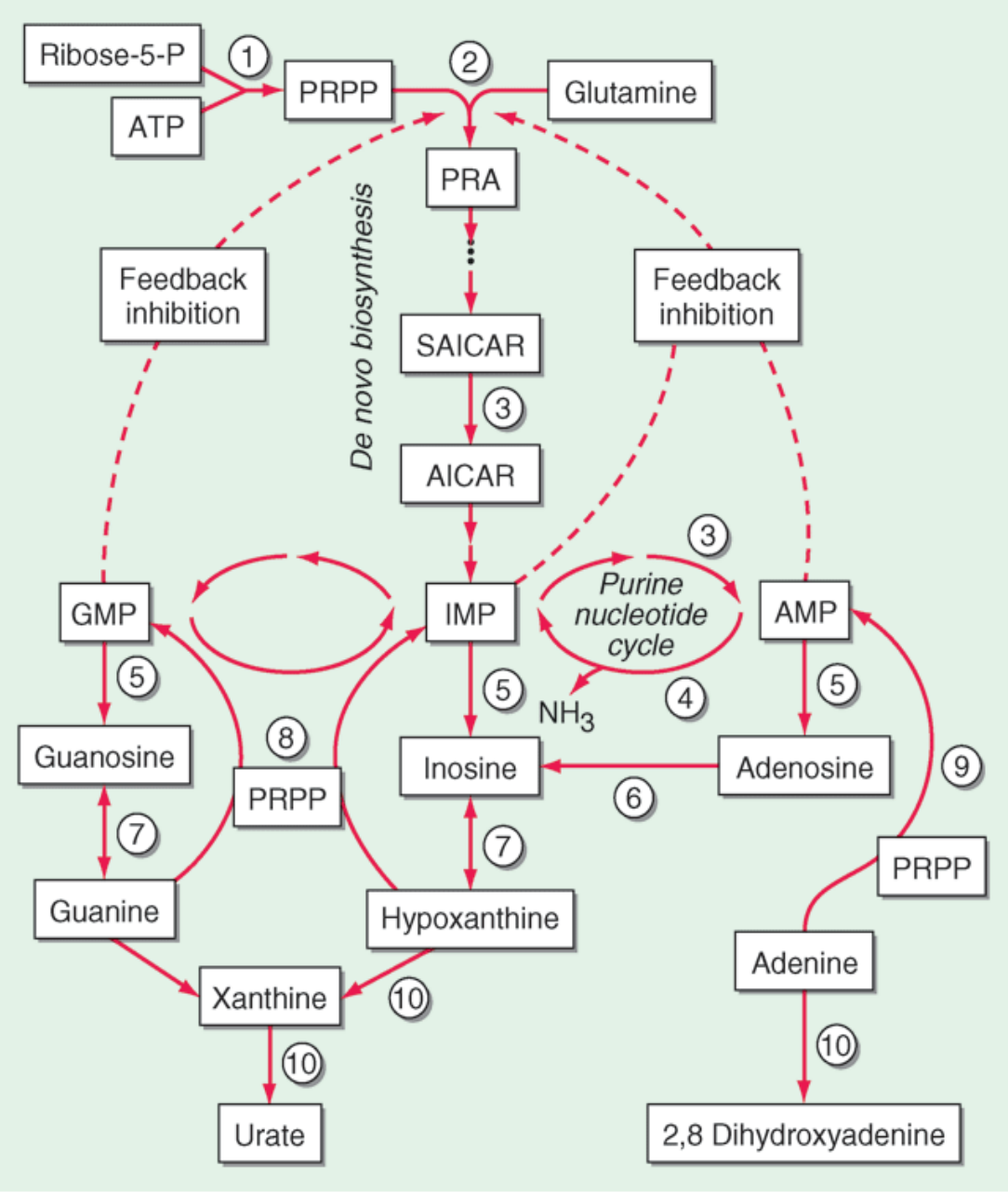

Fig.5- De novo biosynthesis and metabolism of Purine nucleotides

1. Phosphoribosylpyrophosphate(PRPP) synthetase
2. Amidophosphoribosyltransferase (amidoPRT)
3. Adenylosuccinate lyase
4. (myo-)adenylate (AMP) deaminase
5. 5'-nucleotidase
6. Adenosine deaminase
7. Purine nucleoside phosphorylase
8. Hypoxanthine phosphoribosyltransferase (HPRT)
9. Adeenine phosphoribosyltransferase (APRT)
10. Xanthine oxidase

A secondary regulatory pathway is the salvage of purine bases by *hypoxanthine phosphoribosyltransferase **(HPRT).*** **HPRT** catalyzes the combination of the purine bases hypoxanthine and guanine with **PRPP** to form the respective ribonucleotides **IMP** and guanosine monophosphate **(GMP)**. Increased salvage activity thus retards de novo synthesis by reducing PRPP levels and increasing concentrations of inhibitory ribonucleotides.[31]

Serum urate levels are closely coupled to the rates of de novo purine biosynthesis, which is driven in part by the level of **PRPP**, as evidenced by two inborn errors of purine metabolism. Both increased **PRPP** synthetase activity and **HPRT** deficiency are associated with overproduction of purines, hyperuricemia, and hyperuricaciduria.

An X-linked disorder that causes an increase in activity of the enzyme **PRPP** synthetase leads to increased **PRPP** production and accelerated de novo biosynthesis. **PRPP** is a substrate and allosteric activator of amidoPRT, the first enzyme in the de novo pathway.

HPRT deficiency is also X-linked and enhances urate biosynthesis in two ways. PRPP is accumulated as a result of decreased utilization in the salvage pathway and, in turn, provides increased substrate for **amidoPRT** and de novo biosynthesis. In addition, decreased formation of the nucleoside monophosphates, **IMP** and **GMP**, via the salvage pathway impairs feedback inhibition on amidoPRT, further enhancing de novo biosynthesis.

Accelerated purine nucleotide degradation can also cause hyperuricemia, i.e., with conditions of rapid cell turnover, proliferation, or cell death, as in leukemic blast crises, cytotoxic therapy for malignancy, hemolysis, or rhabdomyolysis. Nucleic acids released from cells are hydrolyzed by the sequential activities of nucleases and phosphodiesterases, forming nucleoside monophosphates, which in turn are degraded to nucleosides, bases and urate.

Hyperuricemia can result from excessive degradation of skeletal muscle ATP after strenuous physical exercise or status epilepticus and in glycogen storage diseases types III, V, and VII. The hyperuricemia of myocardial infarction, smoke inhalation and acute respiratory failure may also be related to accelerated breakdown of ATP.[31]

Decreased Uric Acid Excretion

Over 90% of individuals with sustained hyperuricemia have a defect in the renal handling of uric acid. In hyperuricemia with gout the renal defect is evidenced by a lower than normal ratio of urate clearance to glomerular filtration rate (or urate to insulin clearance rate) over a wide range of filtered loads. As a result, gouty individuals excrete approximately 40% less uric acid than nongouty individuals for any given plasma urate concentration.

Uric acid excretion increases in gouty and nongouty individuals when plasma urate levels are raised by purine ingestion or infusion, but in those with gout, plasma

urate concentrations must be 60 to 120 umol/L (1 to 2 mg/dL) higher than normal to achieve equivalent uric acid excretion rates.[31] Altered uric acid excretion could theoretically result from decreased glomerular filtration, decreased tubular secretion, or enhanced tubular reabsorption. Decreased urate filtration does not appear to cause primary hyperuricemia but does contribute to the hyperuricemia of renal insufficiency.

Although hyperuricemia is invariably present in chronic renal disease, the correlation between serum creatinine, urea nitrogen, and urate concentration is poor. Uric acid excretion per unit of glomerular filtration rate increases progressively with chronic renal insufficiency, but tubular secretory capacity tends to be preserved, tubular reabsorptive capacity is reduced, and extrarenal clearance of uric acid increases as renal damage becomes more severe. Decreased tubular secretion of urate causes the secondary hyperuricemia of acidosis.

Diabetic ketoacidosis, starvation, ethanol intoxication, lactic acidosis, and salicylate intoxication are accompanied by accumulations of organic acids (β-hydroxybutyrate, acetoacetate, lactate, or salicylates) that compete with urate for tubular secretion.

Hyperuricemia may be due to enhanced reabsorption of uric acid distal to the site of secretion. This mechanism is known to be responsible for the hyperuricemia of extracellular volume depletion that occurs with diabetes insipidus or diuretic therapy.[31]

Combined Mechanisms

Both increased urate production and decreased uric acid excretion may contribute to hyperuricemia. Individuals with a deficiency of glucose-6- phosphatase, the enzyme that hydrolyzes glucose-6-phosphate to glucose, are hyperuricemic from

infancy and develop gout early in life. Increased urate production results from accelerated ATP degradation during fasting or hypoglycemia. In addition, the lower levels of nucleoside monophosphates decrease feedback inhibition of amidoPRT, thereby accelerating de novo biosynthesis. Glucose-6-phosphatase-deficient individuals may also develop hyperlacticacidemia, which blocks uric acid excretion by decreasing tubular secretion.

Patients with hereditary fructose intolerance caused by fructose-1-phosphate aldolase deficiency also develop hyperuricemia by both mechanisms. In homozygotes, vomiting and hypoglycemia after fructose ingestion can lead to hepatic failure and proximal renal tubular dysfunction. Ingestion of fructose, the substrate for the enzyme, causes accumulation of fructose-1-phosphate. This action results in ATP depletion, accelerated purine nucleotide catabolism, and hyperuricemia. Both lactic acidosis and renal tubular acidosis contribute to urate retention. Heterozygous carriers develop hyperuricemia, and perhaps one-third develop gout. The heterozygous state has a prevalence of 0.5 to 1.5%, suggesting that fructose-1-phosphate aldolase deficiency may be a relatively common cause of familial gout.[31]

Alcohol also promotes hyperuricemia by both mechanisms. Excessive alcohol consumption accelerates hepatic breakdown of ATP and increases urate production. Alcohol consumption can also induce hyperlacticacidemia, which blocks uric acid secretion. The higher purine content in some alcoholic beverages such as beer may also be a factor.

COMPLICATIONS OF HYPERURICAEMIA

Hyperuricaemia and Gout:

The most recognized complication of hyperuricemia is *gouty arthritis*. In the general population the prevalence of hyperuricemia ranges between 2.0 and 13.2%, and the prevalence of gout is between 1.3 and 3.7%. The higher the serum urate level, the more likely an individual is to develop gout. In one study, the incidence of gout was 4.9% for individuals with serum urate concentrations >540 umol/L (9.0 mg/dL) compared with 0.5% for those with values between 415 and 535 umol/L (7.0 and 8.9 mg/dL). The complications of gout correlate with both the duration and severity of hyperuricemia.

Hyperuricaemia and Renal System:

Hyperuricemia also causes several renal problems:

1. Nephrolithiasis;
2. Urate nephropathy, a rare cause of renal insufficiency attributed to monosodium urate crystal deposition in the renal interstitium; and
3. Uric acid nephropathy, a reversible cause of acute renal failure resulting from deposition of large amounts of uric acid crystals in the renal collecting ducts, pelvis, and ureters.

Hyperuricaemia and Syndrome X:

Syndrome X is characterized by abdominal adiposity with visceral adiposity, impaired glucose tolerance due to insulin resistance with hyperinsulinaemia, hypertriglyceridemia, increased low density lipoprotein cholesterol, decreased high density lipoprotein cholesterol, and hyperuricemia.

Hyperinsulinaemia reduces the renal excretion of uric acid and sodium. Not surprisingly,

hyperuricaemia resulting from euglycaemic hyperinsulinaemia may precede the onset of type 2 diabetes, hypertension, coronary artery disease, and gout in individuals with syndrome X.[31]

Increased SUA levels in Hypertension

The mechanisms underlying the increase in SUA and its potential prognostic implications in patients with essential hypertension are still not completely known. Uric acid, a final product of purine metabolism, is bound 5% to plasma proteins, is freely filtered at the glomerulus as a function of renal blood flow, is 99% reabsorbed in the proximal tubule, secreted by the distal tubule, and subjected to considerable postsecretory reabsorption. Fractional secretion of uric acid is about 7% to 10%. A direct association exists between SUA and renal vascular resistance in subjects with essential hypertension.[32]

Uric acid is also commonly associated with hypertension. It is present in 25% of untreated hypertensive subjects, in 50% of subjects taking diuretics, and in >75% of subjects with malignant hypertension.

The increase in serum uric acid in hypertension may be due to the decrease in renal blood flow that accompanies the hypertensive state, since a low renal blood flow will stimulate urate reabsorption.

Hypertension also results in microvascular disease, and this can lead to local tissue ischemia.[33] In addition to the release of lactate that blocks urate secretion in the proximal tubule, ischemia also results in increased uric acid synthesis. With ischemia, ATP is degraded to adenine and xanthine, and there is also increased generation of xanthine oxidase. The increased availability of substrate (xanthine) and enzyme (xanthine oxidase) results in increased uric acid generation as well as oxidant (O_2^-) formation. The finding that ischemia results in an increase in uric acid levels

may also account for why uric acid is increased in preeclampsia and congestive heart failure.[34]

Other factors may also contribute to why uric acid is associated with hypertension, including alcohol abuse, lead intoxication, obesity and insulin resistance and diuretic use.

The observation that an elevated uric acid is associated with subjects at cardiovascular risk may account for why hyperuricemia predicts the development of cardiovascular disease in the general population, in subjects with hypertension and in subjects with preexisting cardiovascular disease. Hyperuricemia also predicts stroke in diabetic and nondiabetic subjects and predicts the development of hypertension and renal disease in the general population.[35,36] Also, hyperuricemia is a novel, independent risk factor for heart failure.[37]

HISTORY OF URIC ACID AND HYPERTENSION

The concept that uric acid may be involved in hypertension is not a new one. In fact, in the paper published in 1879 that originally described essential hypertension, Frederick Akbar Mohamed noted that many of his subjects came from gouty families. He hypothesized that uric acid might be integral to the development of essential hypertension.[38]

Ten years later, this hypothesis re-emerged when Haig[39] proposed low-purine diets as a means to prevent hypertension and vascular disease. In 1909, the French academician Henri Huchard noted that renal arteriolosclerosis (the histological lesion of hypertension) was observed in three groups: Those with gout, those with lead poisoning, and those who have a diet enriched with fatty meat. All of these groups are associated with hyperuricemia.[40] The association between elevated serum uric acid and hypertension was observed and reported repeatedly in the 1950s to 1980 but received relatively little sustained attention because of the lack of a mechanistic explanation.[41-43]

Twenty-five to 40% of adult patients with hypertension have hyperuricemia (> 6.5 mg/dl), and this number increases dramatically when serum uric acid in the high-normal range is included.(19,20) In preeclampsia, the correlation between elevated serum uric acid and hypertension is > 70%.[44]

Despite these observations, the lack of a causal mechanism led to mild elevations of serum uric acid being largely ignored in medical practice. The strength of the relationship between uric acid level and hypertension decreases with increasing patient age and duration of hypertension, suggesting that uric acid may be most important in younger subjects with early-onset hypertension.[43]

Cross-sectional studies have consistently noted that more than a quarter of patients with untreated hypertension have elevated serum UA.[45,46] Serum UA levels have also been associated cross-sectionally with BP[43,47,48] and longitudinally with hypertension incidence [49-53] and future increases in BP.[54]

Mild hyperuricemia in the Rat - an animal model for essential hypertension

The study of mild hyperuricemia required an animal model before the lack of any mechanistic detail that had plagued the hypothesis over 100 years could be addressed. In the late 1990s, Johnson and Colleagues[55] developed a model using a pharmacologic inhibitor of urate oxidase, oxonic acid, that allows the study of sustained mild hyperuricemia.

When fed 2% oxonic acid in their standard diet, Sprague-Dawley rats have an increase of mean serum uric acid concentrations from 0.5 to 1.4 g/dl to 1.7 to 3.0 mg/dl. During a 7-wk treatment period, systolic BP increases an average of 22 mmHg. The increase in BP can be prevented entirely by the co-administration of the xanthine oxidase inhibitor allopurinol or by the uricosuric agent benziodarone, indicating linearly related to the rise in uric acid ($r = 0.77$).

Histologic evaluation of the renal tissue of the hyperuricemic, hypertensive rats reveals an expansion of the vascular smooth muscle and narrowing of the lumina of the afferent arterioles leading to endothelial dysfunction.[56] It is interesting that the development of arteriolosclerosis can be prevented using allopurinol to control uric acid levels. However, hydrochlorothiazide, which normalizes BP without lowering serum uric acid, does not prevent the development of arteriolosclerosis, indicating that uric acid, not hypertension, is the causative stimulus.[46,57]

These experimental results indicate that mild hyperuricemia induces renal inflammation, activation of the renin-angiotensin system and down regulation of nitric

oxide production, all of which are potentially important pathways that lead to uric acid-mediated hypertension. In short, mild hyperuricemia leads to an irreversible salt-sensitive hypertension over time. Recent in vitro studies also have elucidated the possible mechanism of uric acid-mediated arteriolosclerosis. Primary human vascular smooth muscle cells (HVSMC) are induced to proliferate by addition of uric acid to the growth medium in a dose-dependent manner.[58]

The human smooth muscle cells express the urate-transport channel URAT1 as evidenced by both Northern and Western analyses. Consistent with this observation, cultured HVSMC rapidly take up C-urate and blockade of this uptake by probenecid attenuates the uric acid-mediated induction of proliferation in a dose-dependent manner.[59] Signaling studies have revealed further the possible mechanism by which urate uptake leads to HVSMC proliferation.[58,60,61]

The effect of uric acid on vascular smooth muscle cells (VSMC)

Uric acid is taken up through the probenecid-sensitive urate transport channel URAT1. This leads to mitogen-activated protein kinase activation and extracellular signal-regulated kinase 1 and 2 phosphorylation. In turn, transcription factors NF-k□(nuclear transcription factor) and AP1 are activated leading to increased cyclo-oxygenase-2 (COX-2) expression and activity. The COX-2 product Thromboxane A2 mediates increased expression and elaboration of platelet derived growth factor (PDGF) and monocyte chemoattractant protein-1 (MCP-1), which induce VSMC proliferation and macrophage infiltration respectively.[58,60,61,62]

REMNANT KIDNEY MODEL

Various studies have investigated the effect of uric acid on multiple mechanisms of progressive renal injury. In the remnant kidney model, hyperuricemic remnant kidney rats (caused by addition of 2% oxonic acid to their diets) had higher BP, greater proteinuria, and higher serum creatinine.[63,64] Addition of oxonic acid to cyclosporine treatment led to higher uric acid levels, more severe arteriolar hyalinosis, macrophage infiltration, and tubulointerstitial damage compared with rats that were treated with cyclosporine alone.[65] Furthermore treatment of cyclosporine-exposed rats with allopurinol improves GFR and in human liver transplant patients who were receiving cyclosporine, treatment with allopurinol resulted in improved renal function.[66,67]

RECENT EPIDEMIOLOGY: A CHANGE IN PERSPECTIVE

Before 1990, only Khan et al.[51] had reported that an increased serum uric acid is an independent risk factor for hypertension; however, it had been noted that 25 to 40% of adults with hypertension have serum uric acid > 6.5 mg/dl and >60% have a serum uric acid > 5.5 mg/dl and that there was a linear relationship between serum uric acid and systolic BP.[68]

Three reports indicated that serum uric acid is an independent risk factor for hypertension were published in the 1990s[53,68,69] and many more were published in the past 10 yrs.[70-72]

Author	Year published	Study size	Follow-up	Relative Risk
Kahn et al.(27)	**1972**	**10000 males**	**5 Years**	**2 - fold risk**
Selby et al.(26)	**1990**	**2062 adults**	**6 Years**	**3 - fold risk**
Hunt et al.(29)	**1991**	**1482 adults**	**7 Years**	**2 - fold risk**
Jossa et al.(25)	**1994**	**619 males**	**12 Years**	**2 - fold risk**
Taniguchi et al.(42)	**2001**	**6356 males**	**10 Years**	**2 - fold risk**
Masuo et al.(30)	**2003**	**433 males**	**5 Years**	**+27 mmHg in systolic BP per each 1-mg/dL change in uric acid**
Nakanishi et al.(28)	**2003**	**2310 males**	**6 Years**	**1.6 - fold risk**
Nagahama et al.(49)	**2004**	**4489 adults**	**13 Years**	**1.7 - fold risk**
Alper et al.(43)	**2005**	**577 children**	**11 Years**	**Increased risk**
Sundstrom et al.(44)	**2005**	**3329 adults**	**4 Years**	**1.6 fold risk**

Table.3-Studies on Relative Risk for Hypertension in Hyperuricaemia

SIR BRADFORD HILL'S CRITERIA FOR URIC ACID AS A CAUSAL FACTOR IN HYPERTENSION[73]

1. **Strength**. In most studies an elevated uric acid predicts approximately a 2-fold increase in the frequency of hypertension after 5 to 10 years.[74-82]

2. **Consistency**. An elevated uric acid was found in all 9 studies to be predictive for hypertension.[74-82]

3. **Specificity**. The risk for developing hypertension with an elevated uric acid level remains after controlling for other cardiovascular risk factors.[75-82]New onset essential hypertension in adolescents is also associated with an elevated uric acid (UA $\geq$ 5.5 mg/dL) in the vast majority (about 90%) of cases; whereas it is present in only 30% of secondary hypertension and is rare in normotensive and white-coat hypertensive adolescent subjects.[83]

4. **Temporality**. An elevated uric acid often precedes the development of hypertension, both in children and in adults.[74-82]

5. **Dose-dependent**. The relationship of serum uric acid to future hypertension is continuous and dose-dependent.[74-82]

6. **Plausibility**. A biological mechanism has been found by which raising uric acid may cause hypertension.[84-87]

7. **Coherence**. The increase in hypertension frequency with Westernized diets corresponds to the rise in the frequency of hyperuricemia and gout.[88]

8. **Experiment**. Experimental hyperuricemia causes hypertension in rats; preventing the rise in uric acid prevents the development of hypertension.[84-86]

Koch's Postulates for Uric Acid as a Causal Factor of Hypertension

1. An elevated uric acid predicts the development of hypertension (see Table.3).[74-81]
2. An elevated uric acid is observed in 89% of new onset essential hypertension in adolescents and the level of uric acid correlates closely (r = 0.8) with the systolic BP.[83]
3. Raising serum uric acid in rats results in the hemodynamic, pathological, and clinical characteristics of essential hypertension in humans.[84-86]
4. A plausible biological mechanism has been shown in which uric acid induces a salt-resistant hypertension by inhibition of endothelial function and activation of the renin-angiotensin system, and a later salt-sensitive renal dependent hypertension by inducing microvascular disease[84-86]; these changes are consistent with studies of hypertension in humans.[87]
5. Lowering uric acid in hyperuricemic rats prevents or treats new onset hypertension in rats.[84]. Pilot studies in humans also suggest lowering uric acid may lower BP in new onset essential hypertension in adolescents.[89]
6. The recent evaluation of a subset of the Framingham Heart Study found that serum uric acid level was an independent predictor of hypertension and BP progression over as little as 4 years.[72]

Uric acid and essential hypertension in children

In adolescents, the association between elevated serum uric acid and the onset of essential hypertension is even more striking. The Moscow Children's Hypertension study found hyperuricemia (> 8.0 mg/dl) in 9.5% of children with normal BP, 49% of children with borderline hypertension, and 73% of children with moderate and severe hypertension.[90]

The Hungarian Children's Health Study followed all 17,624 children who were born in Budapest in 1964 for 13yrs and found that significant risk factors for the development of hypertension were elevated heart rate, early sexual maturity and hyperuricemia.[91]

Gruskin compared adolescents (13 to 18yrs of age) who had essential hypertension with age-matched healthy control subjects and who had normal BP. The hypertensive children had both elevated serum uric acid (mean > 6.5 mg/dl) and higher peripheral renin activity.[92]

Feig and Johnson observed that the mean serum uric acid level (± SD) in control subjects and children with white coat hypertension were nearly identical but slightly higher in secondary hypertension (4.3 ±1.4 mg/dl, respectively; P = 0.80) but very high in children with primary hypertension (6.7 ±1.3 mg/dl; P = 0.004) [38]. There was a tight, linear correlation between the serum uric acid levels and the systolic and diastolic BP in patients who were referred for evaluation of hypertension (r = 0.8 for systolic BP and r = 0.6 for diastolic BP).[48]

Among patients who were referred for evaluation of hypertension, a serum uric acid > 5.5 mg/dl had an 89% positive predictive value for essential hypertension, whereas a serum uric acid level <5.0 had a negative predictive value for essential hypertension of 96%.[48]

Evidences linking uric acid and hypertension

1. An elevated uric acid level consistently predicts the development of hypertension.[51-53,68,69]
2. An elevated uric acid level is observed in 25-60% of patients with untreated essential hypertension and in nearly 90% of adolescents with essential hypertension of recent onset.[48]
3. Raising the uric acid level in rodents results in hypertension with the clinical, hemodynamic, and histologic characteristics of hypertension.[55]
4. Reducing the uric acid level with xanthine oxidase inhibitors lowers blood pressure in adolescents with hypertension of recent onset.[67]

The identification of a biological mechanism by which uric acid could cause hypertension in humans has led to a renewed interest in the role of uric acid in hypertension. Indeed, there are now 10 studies that have examined whether an elevated uric acid level predicts the development of hypertension, and all found uric acid predictive.

The Bogalusa Heart study, found that uric acid levels in childhood predict the development of diastolic hypertension 10 years later.

The second study, from the Framingham group[72], also found uric acid to predict the development of hypertension. This latter study is all the more remarkable as it was performed in an older population (mean age of 50) in which they first eliminated 25% of their subjects because they already had hypertension or gout, thereby removing a large proportion of their target population.

PROPOSED MECHANISM FOR URIC ACID MEDIATED HYPERTENSION IN HUMANS

Excessive intake of fructose or purine-rich meats or exposure to low doses of lead may result in chronic hyperuricemia.[93]

Mothers with high uric acid levels that are the result of diet or conditions such as preexisting hypertension, obesity, or preeclampsia may transfer uric acid into the fetal circulation through the placenta, which may ultimately contribute to intrauterine growth retardation (IUGR) and a reduction in nephron number.

Among babies born with a low nephron number, hyperuricemia may develop in childhood because of genetic or environmental factors.

Chronic hyperuricemia would stimulate the renin-angiotensin system and inhibit release of endothelial nitric oxide contributing to renal vasoconstriction and possibly increasing blood pressure.

Persistent renal vasoconstriction may contribute to arteriolosclerosis and the development of salt-sensitive hypertension, even if the hyperuricemia is corrected. Thus in the later stage, hypertension becomes salt sensitive but resistant to uricosuric therapy i.e., even after the correction of higher serum uric acid levels, there will be persistant hypertension which will be amenable to conventional anti-hypertensive therapy.

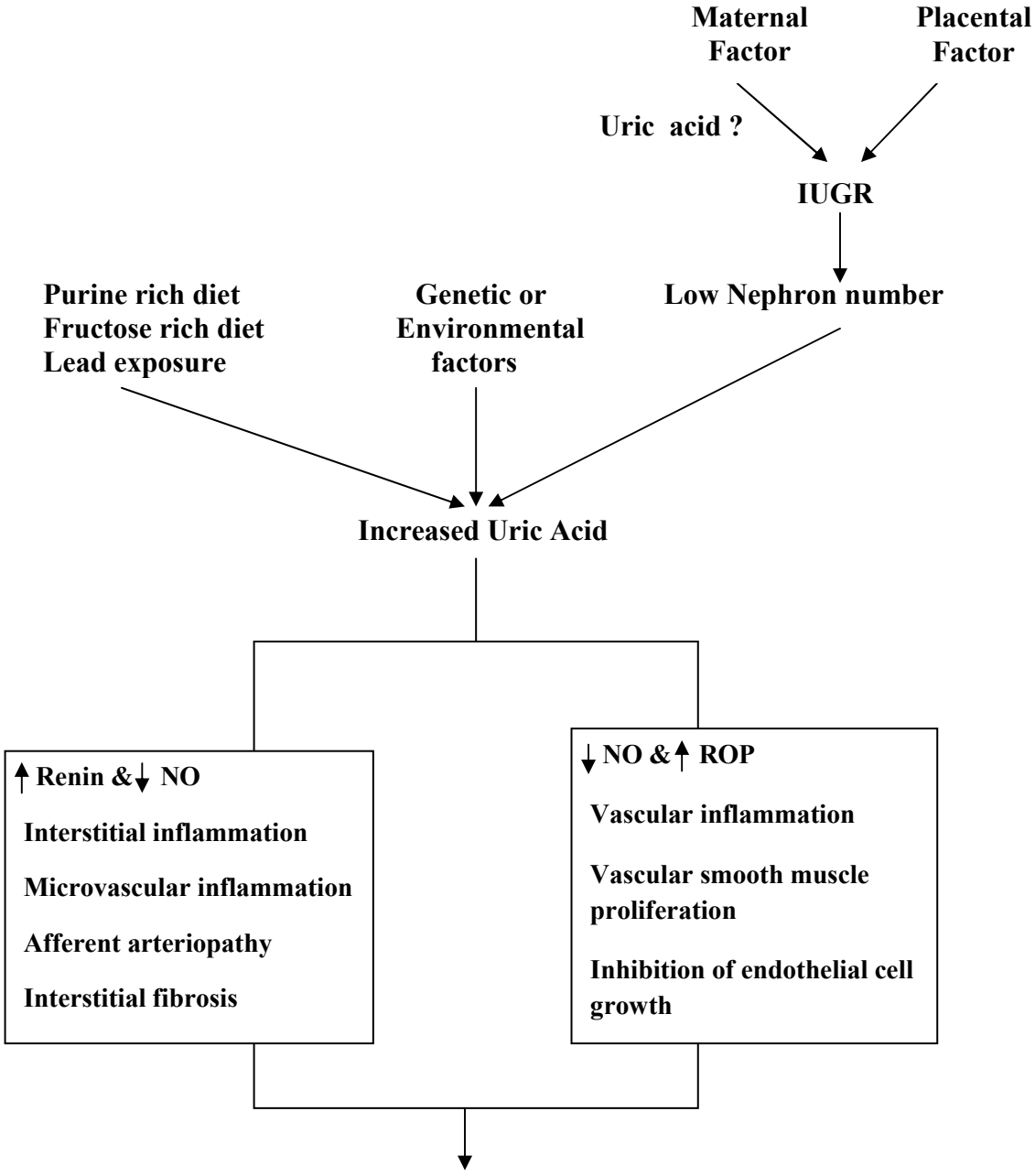

Fig.6-Mechanism of Uric acid mediated Hypertension

Materials and Methods

MATERIALS AND METHODS

Study Setting

Coimbatore Medical College Hospital, Coimbatore. The collaborative department was Department of Biochemistry, Coimbatore Medical College.

Study design

Case – control study

Period of study

December 2010 to November 2011.

Ethical Committee Approval

The study was approved by the Ethical Committee, Coimbatore Medical College, Coimbatore.

Patient Population

Cases

Two hundred adults aged between 20-80 years were selected for the study from the Hypertension OPD of Coimbatore Medical College Hospital. They were studied for Serum Uric acid levels.

Controls

Normotensive controls (n = 200) aged between 20-80 years were selected for the study and evaluated for clinical and laboratory data.

Both males and females were included for the study. All subjects and controls had normal renal function (Renal biochemistry, USG Abdomen).

Both groups are matched for both age and sex.

Inclusion Criteria

1. Age group between 20 to 80 years.

2. Both sexes were included.

3. Stage 1 and stage 2 Hypertension according to JNC-VII without any target end organ damage.

Exclusion Criteria

1. Hypertensive patients with Target End Organ damage
    a) Hypertensive Heart disease as evidenced by Left Ventricular hypertrophy on ECG- voltage criteria / Hypertensive crisis / Malignant Hypertension.
    b) Hypertensive Nephropathy
    c) Hypertensive Retinopathy
2. Diabetes Mellitus – Type 1 and Type 2 or metabolic syndrome
3. Patients with Chronic kidney disease.
4. Hypertensive Patients with known Cerebro vascular disease.
5. Hypertensive Patients with coronary Artery disease – Myocardial Ischemia or Infarction.
6. Patients with long term drug intake like steroids, Anti-Tuberculous Treatment (ATT), diuretics, antimetabolite or chemotherapy drugs.
7. Patients who were regularly consuming alcohol – Alcohol dependence subjects – Evidenced by History, liver function tests and USG Abdomen.
8. Patients with Lympho or Myelo-proliferative disorders.
9. Patients who had chronic liver disease and metabolic disorders.
10. All causes of secondary Hypertension.
11. Psoriasis / Gout.
12. Patients in whom BMI >30.

Consent

The study groups identified by the above criteria (inclusion and exclusion) were first informed about the nature of the study. Participants willing for the study were selected after getting an informed and written consent from them.

Thus, a total of 200 patients were taken up for study who satisfied the inclusion and exclusion criteria. Similarly, 100 age and sex matched subjects were kept as control.

There was no conflict of interest and financial support was Nil. Urinary excretion and urate clearance were not done, only serum uric acid levels were analysed.

Patient profile

Selected socio-demographic, clinical and laboratory data were collected from the cases and controls and recorded in proforma.

1. Socio-demographic profile

- Age
- Sex
- Occupation.
- Cardiovascular risk factors – smoking, family history

2. Clinical profile

- Body weight
- Height
- Body mass index
- Waist circumference
- Pulse
- Systolic and diastolic blood pressure – Average of 3 BP measurements
- Clinical examination

3.Laboratory Data

Laboratory analyses, performed in Biochemical laboratory at the Coimbatore Medical College Hospital, Coimbatore included blood tests for **the evaluation of renal parameters, fasting blood sugar, serum electrolytes, uric acid, lipid profile, thyroid function tests.**

- **Complete urinalyses** were performed by the pathological faculty.
- **ECG** was taken for all the subjects and controls to rule out coronary artery disease and left ventricular hypertrophy.
- **Fundus examination** was done for all subjects to rule out Hypertensive Retinopathy.

Data collection and measurements:

The clinical examination consisted of a medical history, a physical examination, blood pressure measurement and anthropometric measurements. Laboratory data included measurement of fasting serum uric acid levels and other parameters like Blood haemogram, Renal function tests (blood urea, serum creatinine), Electrocardiogram, Chest X-ray, Lipid profile (Total cholesterol, triglycerides, HDL-cholesterol, LDL- cholesterol), urine for protein and sugar.

The patients were asked to fast for 12 hours and to avoid smoking and heavy physical exercise for more than 2 hours before the examinations. After a 5 min rest in a quiet room, systolic and diastolic blood pressures were measured in the sitting position twice at an interval of a five minutes on the right arm with a standard mercury sphygmomanometer on three separate occasions.[(94)]

Anthropometric measurements included height and body weight, which were measured while the subject was wearing light clothing without shoes. The body mass index was calculated as the weight in kilograms divided by the height in m^2.

HYPERTENSION

Hypertension was defined according to the JNC VII classification of hypertension as those with **SBP of < 120 mm hg** and **DBP of < 80 mm hg** as **normal**, those with **SBP of 120- 139 mm hg** or **DBP of 80 - 89 mm hg** were labelled **pre-hypertensive** were not taken up for the study, those with **SBP 140 - 159 mm hg or DBP of 90 - 99 mm hg were labeled as having Stage 1 hypertension**, and those with **SBP ≥ 160 mm Hg or DBP ≥ 100 mm hg were labeled as Stage 2 hypertension.**

Method of Uric Acid estimation

Principle

The principle for the determination of Serum Uric Levels was devised by Trivedi and Kabasakalian with a modified Trinder peroxidase method using TBHB.

$$\text{URIC ACID} + O_2 + H_2O \xrightarrow{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O_2$$

$$H_2O_2 + \text{4- AAP} + \text{TBHB} \xrightarrow{\text{Peroxidase}} \text{Quinoneimine} + H_2O$$

The Sample used was unhemolyzed serum or plasma separated from the cells as soon as possible. Recommended anticoagulants are heparin and EDTA. Uric acid is stable in serum or urine for 3 days at 20 - 25o C. The intensity of chromogen (**Quinoneimine**) formed is proportional to the uric acid concentration in the sample when measured at 510 nm (510 -550nm) on biochromatic analysers against reagent blank.

Reference Values for SUA levels -

In Males : 3.4 - 7.0 mg/dL

In females : 2.4 - 6.0 mg/dL

STATISTICAL ANALYSIS

Data was entered in Microsoft excel spread sheet and analyzed statistically using SPSS 10.0 software package. Significance testing of the difference between means was done by **unpaired 2 tailed student 't'-test for independent samples**, and correlations were assessed by Pearson coefficient. Significance was considered, if the 'p' value was below 0.05.

Observations and Results

OBSERVATIONS AND RESULTS

During the 12 month study period from December 2010 to November 2011 a total of 400 patients were studied of which 200 patients were cases who were categorized into Stage 1 or Stage 2 hypertension (base on JNC VII classification) and 200 were controls who were patients without hypertension or any other condition known to cause raised serum uric acid levels.

AGE DISTRIBUTION:

AGE GROUP	CASES	CONTROLS
20 - 29	2	3
30 - 39	19	20
40 - 49	53	52
50 - 59	69	67
60 - 69	51	52
70 - 79	6	6

Table.4- AGE DISTRIBUTION OF CASES AND CONTROLS

Among the studied population, three-fourth of people fall in the age groups between 40 – 69 years of age.

Only one-fourth of people fall in the extreme ages of studied population.

All the age groups in both cases and controls were matched well with subtle variations.

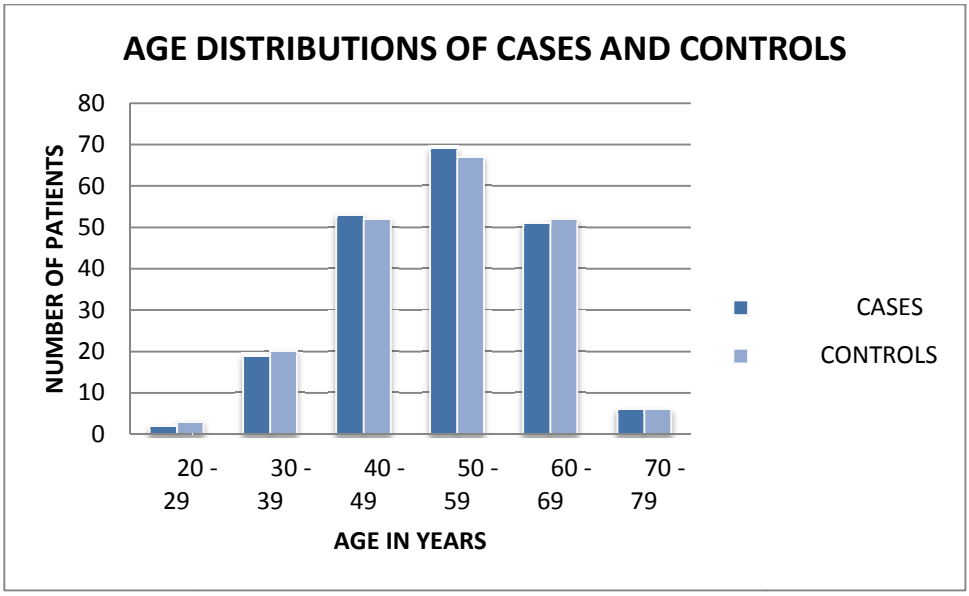

Fig.7-AGE DISTRIBUTION AMONG CASES AND CONTROLS

SEX DISTRIBUTION

CATEGORY	MALES	FEMALES
CASES	143	57
CONTROLS	145	55

Table.5-Sex Distribution of Cases and Controls

Among the cases, total number of male patients were 143 and total number of female patients were 57.

Among the controls, total number of male patients were 145 and total number of female patients were 55.

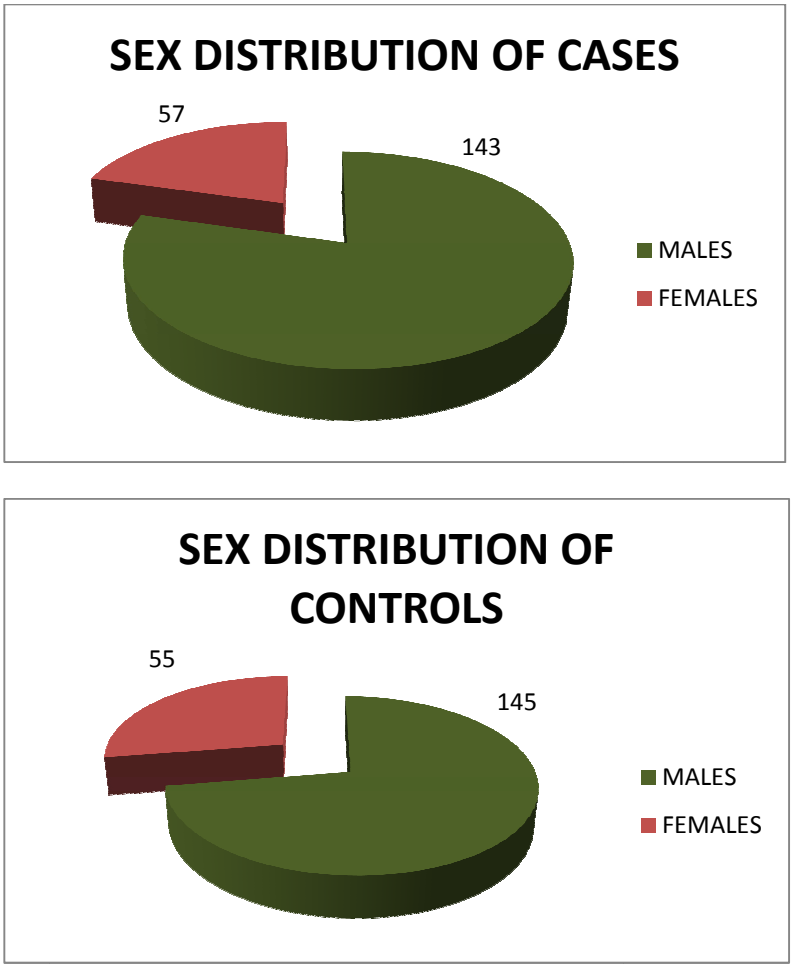

Fig.8-Sex Distribution of Cases and Controls

The Serum Uric Acid levels in male cases ranged from 3.2 mg/dl to 9.8 mg/dl and in female cases ranged from 3.8 mg/dl to 9.6mg/dl.

The Serum Uric Acid levels in male controls ranged from 3.0 – 8.4 mg/dl and in female controls ranged from 2.8 – 8.2 mg/dl.

SUA LEVELS BETWEEN CASES AND CONTROLS

The total number of cases were 200 (both male and female), the data analysis of the cases showed the mean SUA level to be 6.1125 with a standard deviation of 1.5662 (6.1125 ± 1.5662).

The total number of controls were 200 (both male and female), the data analyzed showed a mean SUA level of 5.6695 with a standard deviation of 1.3323 (5.6695 ± 1.3323).

CATEGORY	NUMBER	SUA MEAN ± SD (mg/dL)
CASES	200	6.1125 ± 1.5662
CONTROLS	200	5.6695 ± 1.3323

t-value = 3.05

p value = 0.002441

Table.6-Mean SUA Levels between Cases and Controls

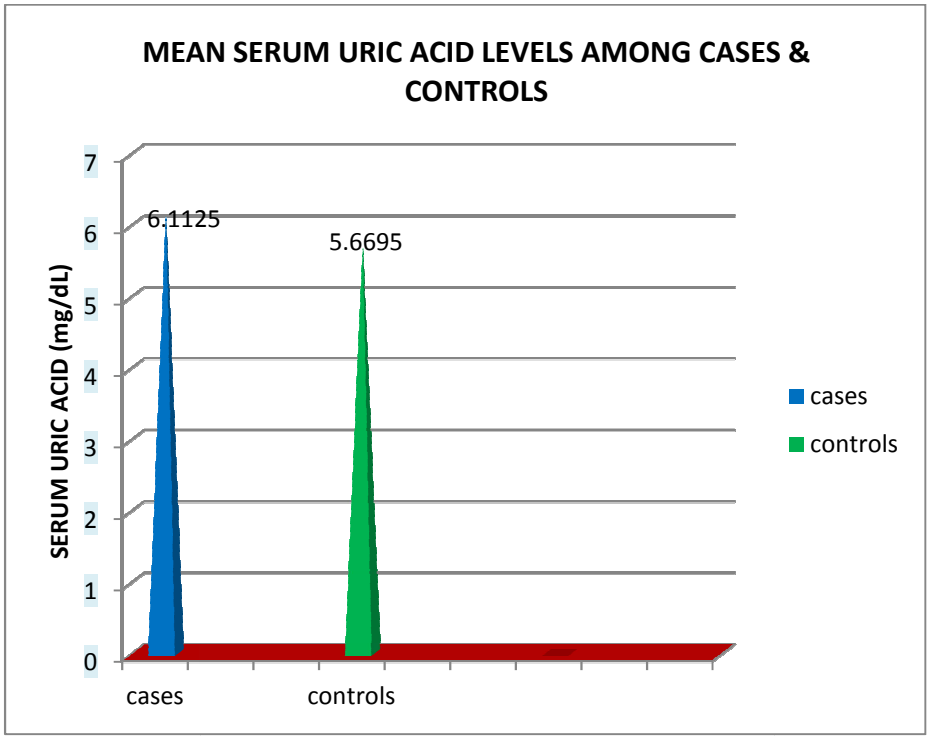

Fig.9-Mean SUA Levels between Cases and Controls

The t-value was found to be 3.05 and **the p value = 0.002441 which was significant**. This showed that there was a significant rise in serum uric acid levels in patients with hypertension when compared to normotensives.

SUA AND RISK BASED ON SEVERITY OF HYPERTENSION

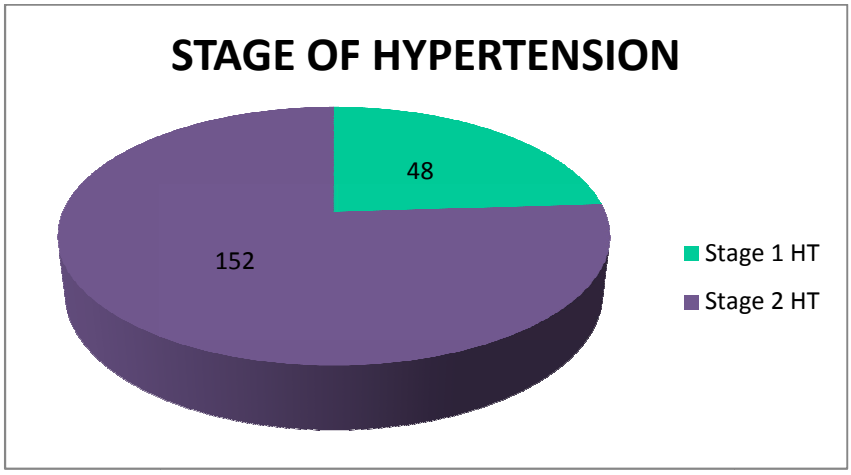

Fig.10-Distribution of stage of HT among cases

The severity of hypertension was divided into stage 1 and stage 2 based on the JNC VII classification of hypertension. In the study done at our hospital the total number of patients assessed to have stage 1 hypertension was 48 patients (both male and female patients) and the total number of patients having stage 2 hypertension was 152(both male and female patients).

Stage of hypertention	Number	SUA MEAN ± SD (mg/dL)
Stage 1	48	5.5979 ± 1.4046
Stage 2	152	6.2750 ± 1.5836

t-value = 2.65

p value = 0.0087

Table.7-Mean SUA among the stages of hypertension

The data analysis for SUA levels in the stages of hypertension showed a mean serum uric acid level in stage 1 hypertension of 5.5979 with a standard deviation of ± 1.4046.

The mean serum uric acid levels in stage 2 hypertensive patient were 6.2750 with a standard deviation of ± 1.5836.

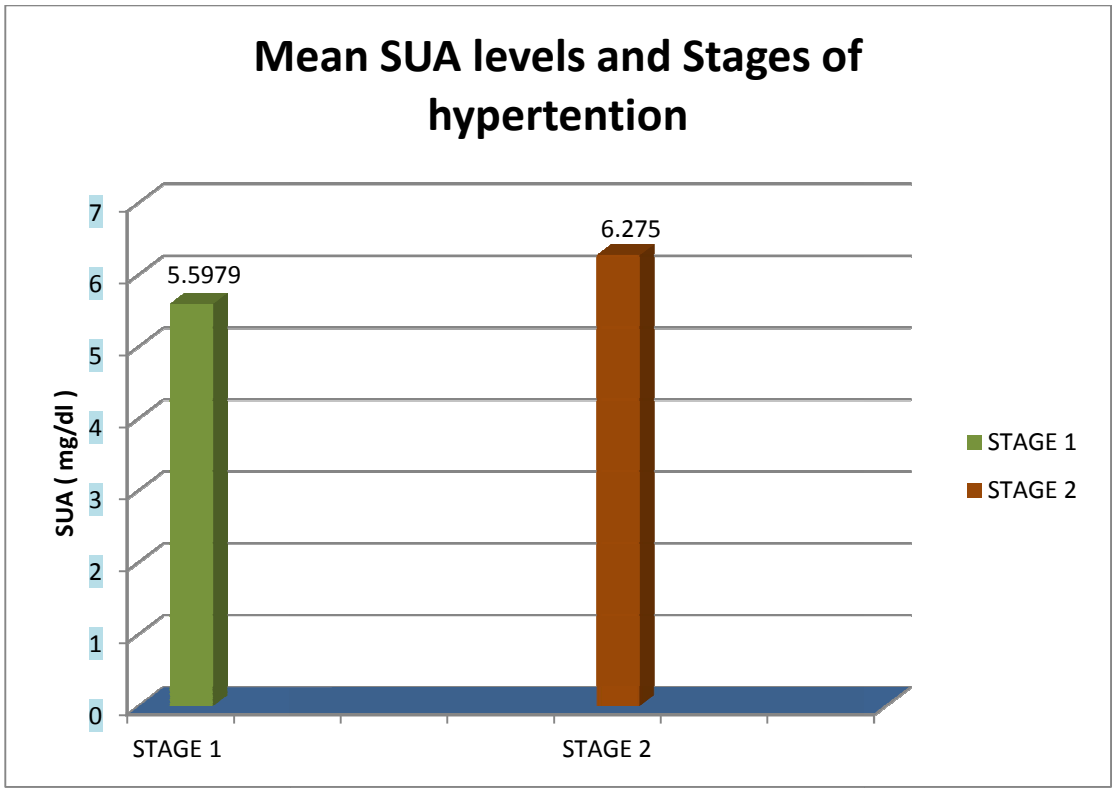

Fig.11-Mean SUA levels and stages of hypertension

The t-value was 2.65 and **a p-value of .0087 which was significant**. The data analysed showed that there was a significant rise in serum uric acid in patients who were having stage 2 hypertension i.e. those with a SBP ≥ 160 and a DBP ≥ 100 mm Hg than those with stage 1 hypertension with a SBP 140- 159 and DBP 90- 99 mm Hg.

SUA AND RISK BASED ON THE DURATION OF HYPERTENSION

The duration of hypertension was divided into 2 categories - those with hypertension for duration of hypertension < 5 years and those with a duration of hypertension≥ 5 years.

The total number of patients with hypertension for duration of < 5 years was 96 and the total number of patients with duration of hypertension ≥ 5 years was 104.

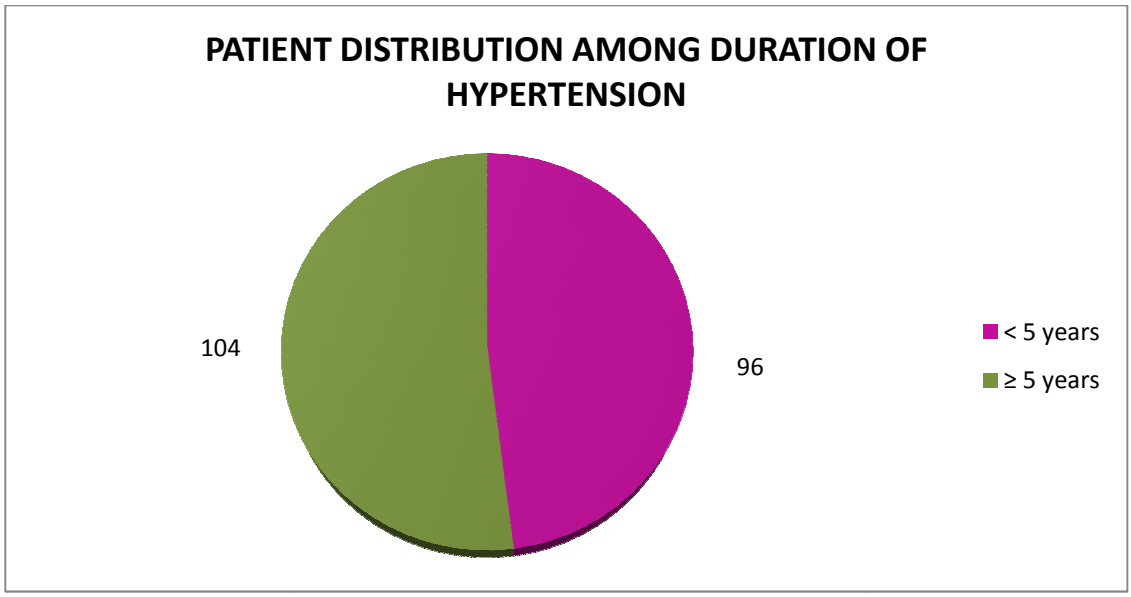

Fig.12-Patient distribution and the duration of hypertension

The mean SUA level in patients with hypertension < 5 years was 5.175 with a standard deviation of ± 1.1188.

The mean SUA level in patients with hypertension ≥ 5 years was 6.9779 with a standard deviation of ± 1.4175.

Duration of hypertension	Number of patients	SUA MEAN ± SD (mg/dL)
< 5 years	96	5.175 ± 1.1188
≥ 5 years	104	6.9779 ± 1.4175

Table.8-Mean SUA levels based on duration of hypertension

t-value = 9.93

p value < 0.0001

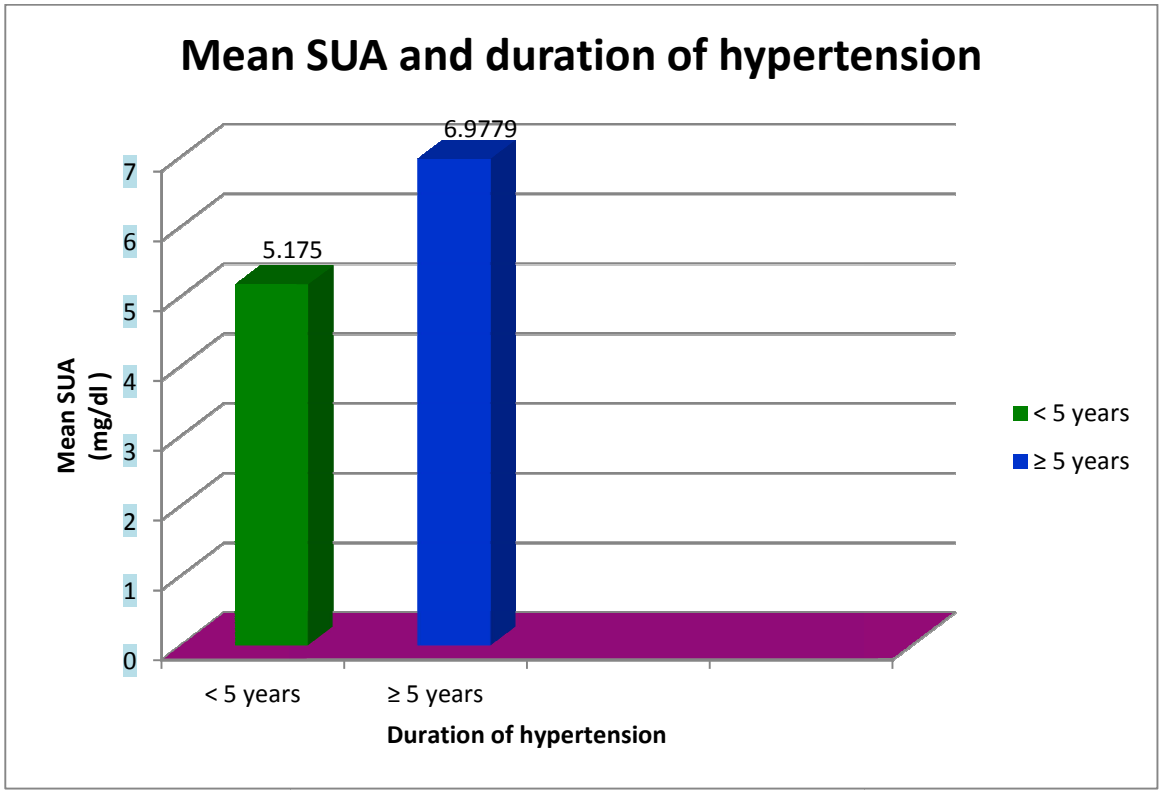

Fig.13-Mean SUA levels based on duration of hypertension

The analyzed data showed a t-value of 9.93 and **a p-value <0.0001** which showed that there is significant increase in SUA levels in patients with hypertension≥ 5 years than those with a duration of < 5 years.

Discussion

DISCUSSION

Elevated SUA levels have been associated with an increased risk for cardiovascular disease. The potential mechanisms by which SUA may directly cause cardiovascular risk include enhanced platelet aggregation and inflammatory activation of the endothelium.[95]

In few studies, the association of SUA with cardiovascular disease was uncertain after multivariate adjustment as in the Framingham Heart Study (1985) and the ARIC study (1996), but in others the association remained certain and significant.

Because elevated serum uric acid is correlated with several risk factors including renal dysfunction, hypertension, insulin resistance, hyperhomocysteinemia and hyperlipidemia, it is debated whether SUA is an independent cardiovascular risk factor.

In the present study the incidence of hyperuricemia in controls was 21% and the incidence of hyperuricemia in cases was 38 %.

Various other studies have also shown that increased SUA levels were seen in hypertensive patients. Kinsey (1961) in his study with 400 hypertensive patients reported a 46 % incidence of hyperuricemia in hypertensives (43). Kolbe (1965) in his study of 46 hypertensive patients found 26 to be having increased SUA levels (56 %).[96]

A. Breckenridge (1966) showed 274 of 470 patients on antihypertensive treatment (58%) had raised SUA levels and 90 of the 333 patients (27%) attending the clinic for the first time had hyperuricemia(1). In a study by C. J. Bulpitt (1975), 48 % male hypertensives and 40 % female hypertensives had their SUA level in the hyperuricemic range.[97]

Ramsay (1979) in his study of 73 men with untreated hypertension had 18 with raised serum uric acid levels (25%).[98] Messerli et al (1980) had an incidence of 72 % raised SUA in their study population of 39 established hypertensives. Messerli and Frohlich et al hypothesized that the frequent presence of hyperuricemia in hypertensive patients reflects underlying renal dysfunction or reduced renal perfusion.[99]

It certainly is possible that uric acid may be an earlier and more sensitive marker of decreased renal blood flow than serum creatinine. It has been recently suggested that since uric acid may play a role in the formation of free radicals and oxidative stress, the increased risk of hypertension in subjects with raised serum uric acid levels might be associated with this increased generation of free radicals. Several observations support this concept of free radical mediated inhibition of endothelium dependent vasodilatation. An antioxidant deficiency in diet which produces hyperuricemia, contributes to the aetiology of hypertension, and the antioxidant drugs also show a blood pressure lowering effect in both diabetic and hypertensive patients.[100]

In a study by Tykarski (1991), he showed SUA concentration and the prevalence of hyperuricemia were significantly higher in hypertensive patients. They further demonstrated that tubular secretion of uric acid was significantly lower in hypertensive patients in comparison with normotensive subjects. There was no difference in pre and post- secretory reabsorption of uric acid. They concluded that high prevalence of hyperuricemia in essential hypertension was caused by impaired renal excretion of uric acid.[101]

Goldstein and Manowitz (1993) showed in an adolescent population that, with age, weight, height and sexual maturity controlled, SUA significantly predicted blood pressure even in adolescents.[102]

Three possible conclusions can be drawn from the association of hypertension with raised SUA levels -.

Hypertension may arise as a result of hyperuricemia,

Hypertension can cause hyperuricemia and

The duration and severity of hypertension is related directly to the SUA levels.

In gouty patients without advanced tophi, however renal failure and hypertension are rare. In a group of 80 patients attending the Hammer Smith hospital gout clinic only 2 were hypertensive. In a study of gouty patients of Northern India by Kumar et al they found that only one out of 30 patients had hypertension.[103] Fessel et al showed no appreciable loss of renal function in patients with gout as compared to normal subjects followed up for 12 years.[104] In a study by Lawrence E Ramsay there was no evidence that hyperuricemia had a deleterious effect on renal function.[98] Canon et al considered that an impairment of renal function will raise the SUA levels more commonly than an increased SUA will cause renal damage.[105]

Hence it is unlikely that hypertension arises as a result of raised SUA levels, but the possibility that uric acid which plays a role in the formation of free radicals and oxidative stress, the increased risk of hypertension in subjects with raised serum uric acid levels might be associated with this increased generation of free radicals. Hence the fact that raised SUA levels can lead to Hypertension cannot be entirely ruled out.

As to the possibility that Hypertension can cause hyperuricemia, it is thought that hyperuricemia can result from either overproduction of uric acid or from under

excretion of uric acid. Overproduction of uric acid can be measured by the rate of incorporation of acid precursors such as Glycine labeled N 15, into the uric acid pool. Such a study carried out in 4 hypertensive patients with raised SUA levels did not show any overproduction of uric acid.

In the study of Breckenridge, excretion of uric acid and uric acid clearance were lower in all hypertensive patients than in the normal group. When the uric acid clearance was expressed per 100ml of glomerular filtrate, there was no significant difference between normal subjects and hypertensive patients who had normal SUA levels, but the difference between those 2 groups and the hyperuricemic hypertensives was significant and they suggested a renal tubular abnormality in the handling of uric acid, the nature of the abnormality was not clear.

Later Messerli et al showed that hyperuricemia in hypertension is due to early renal vascular involvement, namely, Nephrosclerosis. SUA rises because of impaired renal tubular function, which is the main site of regulation of SUA due to nephrosclerosis. Tykarski in his study showed that SUA levels in hypertensives are due to impaired tubular secretion of urate. In the present study incidence and severity of hyperuricemia between cases and controls correlated significantly with the severity of hypertension**.** This correlated with both Kinsey and Breckenridge studies, but according to Cannon et al[105] severity of hypertension had no relation to SUA level.

Our study agrees with the study of Tykarski et al in that there is a positive correlation between SUA and severity of hypertension.[99] As to the possibility as to whether SUA levels was related to the severity and duration of hypertension, Breckenridge[42] in his study showed an increasing incidence of hyperuricemia as the diastolic BP increased in his study, but there was no tendency for hyperuricemia to occur, only with patients with more severe hypertension.

Kinskey also found that hyperuricemia was common in patients with more severe grades of hypertension. **Comparison showed that SUA increased significantly with duration of hypertension in our study**. This was similar to the finding of Tykarski et al who encountered positive correlation between duration of hypertension and SUA in their study.

The PIUMA study demonstrates a strong independent association between SUA and CV risk in initially untreated and asymptomatic adult subjects with essential hypertension, but it is unable to answer the question of whether SUA exerts direct toxic effects. As extensively reviewed by Puig and Ruilope,[106] both uric acid and superoxide radicals are produced for the effect of xanthine oxidase in the late phase of purine metabolism. Superoxide radicals, which may cause tissue and vascular damage[107] are increased in subjects with essential hypertension.[108]

It would be important to clarify whether such increase is due, at least in part, to enhanced xanthine oxidase activity and whether inhibition of this enzyme by allopurinol may reduce CV risk.[109]

In our study we found that there is definite relation in SUA levels between hypertensive patients and normotensive patients and there is a directly proportional relation in the levels of SUA in relation to the duration and severity of hypertension. Hence the possibility of serum uric acid acting by the production of free radicals and causing oxidative stress leading to hypertension and whether the duration and severity of hypertension lead to renal dysfunction in the form of nephrosclerosis leading to higher levels of serum uric acid has to be considered as various other studies have also show to have a positive relation in the SUA levels and hypertension.

Conclusion

CONCLUSION

The study showed *the SUA levels are increased in hypertensives compared to normotensives.* With the results based on the study carried out we concluded that there can be a direct relation between hyperuricemia and hypertension.

Also the study showed that *the SUA levels were significantly increased in patients with Stage-2 hypertension in comparison with those with stage-1 hypertension*, showing that the severity of hypertension also related to the SUA levels.

The study also showed that *the duration of hypertension had a significant impact on the SUA levels,* those with a longer duration of hypertension had significantly raised SUA levels when compared with those of a lesser duration.

Summary

SUMMARY

Serum uric acid levels were measured in 400 patients both outpatient and in-patients attending Coimbatore Medical College Hospital. The 400 patients were divided into 200 cases who were again divided again into categories based on severity of hypertension into stage 1 and stage 2 and duration of <5 years and ≥ 5 years.

The study showed a rise in SUA levels in cases with a highly significant p = 0.002441 when compared to that of controls. The mean serum uric acid in cases and controls were 6.1125 ± 1.5662 and 5.6695 ± 1.3323 respectively.

The incidence of hyperuricemia in case and controls were 38% and 21% respectively.

A positive correlation was found between the severity of hypertension, the patients who were found to be having stage 2 hypertension had an increase in SUA levels which was highly significant p= .0087 when compared with those with stage 1 hypertension. The mean SUA in patients with stage 1 hypertension was 5.5979 ± 1.4046 and those with stage 2 hypertension was 6.2750 ± 1.5836.

We also found a positive correlation between SUA levels and the duration of hypertension patients with a duration of hypertension ≥ 5 years had a significant increase in the SUA levels p= < 0.0001 than those patients with hypertension for a duration of <5 years. The mean SUA in patients <5 years was 5.1750 ± 1.1188 and those with duration of ≥ 5 years was 6.9779 ± 1.4175.

As it has been shown that hyperuricemia is observed in untreated hypertension may be due to a decrease in the renal blood flow and early nephrosclerosis, unexplained rise in SUA levels in Essential Hypertension can be used as a simple biochemical marker in determining the severity and duration of hypertension.

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Annexures

PROFORMA

SERUM URIC ACID IN ESSENTIAL HYPERTENSION

Name : **OP / IP No. :**

Age : **Hospital : CMCH**

Sex : **Unit :**

Occupation : **Date :**

Address :

Presenting Complaint :

Duration of Hypertension :

Treatment History :

Past History : Diabetes mellitus / IHD / Stroke

Family History : Diabetes mellitus / IHD / Stroke

Personal History : Tobacco - Smoking **:** Yes/No

Quantity **:**

Duration **:**

Chewing **:** Yes/No

Quantity **:**

Duration **:**

Alcohol Consumption **:** Yes/No

Quantity **:**

Duration **:**

Diet **:** Veg/Non-Veg

Micturition **:**

Bowel Habits **:**

Menstrual History :

General Physical Examination :

Pallor

Clubbing

Oedema

Cyanosis

Icterus

Xanthoma

Arcus senilis

Tophi

Arthritis

Pulse : Rate **:** /min.

Rhythm **:**

Character **:**

Volume **:**

Condition of vessel wall:

Other peripheral pulses:

BP (**Sitting**) **:** 1. mm Hg (**Standing) :** 1. mm Hg

2. mm Hg. 2. mm Hg

3. mm Hg 3. mm Hg

Respiratory rate: /min **Temperature :** ^{0} F

JVP :

Height : cms. **Weight :** Kgs

BMI :

Systemic Examination :

CVS :

RS :

Abdomen :

CNS :

Fundoscopy :

INVESTIGATIONS:-

Blood Routine : Hb % -

TotalCount -

Differential Count - N %; L %; EMB %

ESR -

Urine Examination : Albumin **:**

Sugar **:**

Microscopy **:**

Blood Sugar : mg/dL

Serum Uric Acid : mg/dL

Serum Urea : mg/dL

Serum Creatinine : mg/dL

Lipid Profile :

Total Cholesterol	mg/dL
LDL Cholesterol	mg/dL
HDL Cholesterol	mg/dL
Triglycerides	mg/dl

ECG :

Chest X-ray :

Comments :

MASTER CHART FOR CASES

Sl. No	Name	Age	Sex	IP/OP No	SBP (mm of Hg)	DBP (mm of Hg)	Duration of Hypertension	Stage of Hypertension	SUA levels (mg/dL)	Category
1	Ganesan	38	M	31313	140	100	<5 Years	Stage 2	5.2	Case
2	Sivaperumal	58	M	6254	140	90	>5 Years	Stage 1	4.2	Case
3	Poongodhai	52	F	25863	130	90	>5 Years	Stage 1	4.6	Case
4	Velmurugan	36	M	21586	150	100	<5 Years	Stage 2	5.2	Case
5	Ramasamy	68	M	3658	166	100	>5 Years	Stage 2	4.8	Case
6	Perumayiammal	65	F	14756	158	90	>5 Years	Stage 2	4.5	Case
7	Devan	44	M	66552	146	102	<5 Years	Stage 2	3.2	Case
8	Krishnamoorthy	63	M	36549	150	90	<5 Years	Stage 2	6.4	Case
9	Veeraiyan	59	M	4526	136	94	>5 Years	Stage 1	4.5	Case
10	Manickam	55	M	26479	162	110	>5 Years	Stage 2	5.4	Case
11	Rajagopal	46	M	1025	170	100	<5 Years	Stage 2	3.6	Case
12	Chinnadurai	41	M	1114	158	106	<5 Years	Stage 2	3.8	Case
13	Fathima	49	F	11889	164	90	>5 Years	Stage 2	6.5	Case
14	Kuppayammal	53	F	42001	170	100	>5 Years	Stage 2	6.0	Case
15	Eswaramoorthy	57	M	52410	134	98	<5 Years	Stage 1	5.2	Case
16	Marudhayi	61	F	56369	178	110	>5 Years	Stage 2	6.4	Case
17	Bakthavatchalam	60	M	57896	162	90	>5 Years	Stage 2	6.7	Case
18	Thangadurai	59	M	23018	146	100	<5 Years	Stage 2	3.8	Case
19	Peer Mohammed	43	M	22594	138	94	<5 Years	Stage 1	3.8	Case
20	Kaaliyappan	55	M	33339	162	100	>5 Years	Stage 2	7.2	Case
21	Subba Gounder	69	M	36533	162	90	>5 Years	Stage 2	7.0	Case
22	Narayanan	64	M	40258	170	110	>5 Years	Stage 2	7.5	Case
23	Ramathal	58	F	46023	130	90	>5 Years	Stage 1	7.4	Case
24	Angamuthu	57	M	65432	150	100	<5 Years	Stage 2	3.9	Case
25	Subramani	51	M	34567	154	96	<5 Years	Stage 2	4.2	Case
26	Murugesan	66	M	36555	160	100	>5 Years	Stage 2	8.2	Case

27	Sadhasivam	69	M	39981	176	90	>5 Years	Stage 2	7.6	Case
28	Selvaraj	53	M	30002	132	94	<5 Years	Stage 1	4.1	Case
29	Mohammed Khan	50	M	5552	144	100	>5 Years	Stage 2	8.0	Case
30	Pangajam	54	F	63215	156	86	>5 Years	Stage 1	7.6	Case
31	Soundammal	46	F	6677	148	100	<5 Years	Stage 2	4.1	Case
32	Sundarapandiyan	48	M	817	156	110	<5 Years	Stage 2	4.1	Case
33	Sivagami	49	F	9365	164	96	<5 Years	Stage 2	4.5	Case
34	Elayappan	58	M	998	180	100	>5 Years	Stage 2	7.8	Case
35	Jaganathan	60	M	47856	176	110	>5 Years	Stage 2	8.8	Case
36	Balaji	39	M	49821	152	104	<5 Years	Stage 2	4.2	Case
37	Aiyamperumal	47	M	55500	160	100	<5 Years	Stage 2	4.4	Case
38	Issakiyammal	39	F	501	130	90	<5 Years	Stage 1	4.2	Case
39	Karunagaran	49	M	2121	132	94	<5 Years	Stage 1	4.6	Case
40	Kalimuthu	57	M	25007	158	102	>5 Years	Stage 2	8.5	Case
41	Meenakshi	61	F	852	168	100	>5 Years	Stage 2	8.6	Case
42	Gopalakrishnan	66	M	7410	148	90	>5 Years	Stage 1	8.4	Case
43	Kondaiyan	47	M	10479	178	110	<5 Years	Stage 2	5.0	Case
44	Rajapandi	56	M	11236	174	100	>5 Years	Stage 2	8.6	Case
45	Marudhamuthu	68	M	68426	182	112	>5 Years	Stage 2	9.5	Case
46	Dhanalakshmi	52	F	24862	130	92	<5 Years	Stage 1	4.8	Case
47	Sivapadham	59	M	3690	130	90	>5 Years	Stage 1	4.5	Case
48	Arputharaj	49	M	31105	166	100	<5 Years	Stage 2	5.5	Case
49	Joseph	46	M	10268	164	100	<5 Years	Stage 2	5.2	Case
50	Kaasirajan	55	M	14598	136	92	>5 Years	Stage 1	4.6	Case
51	Luqman Ahmad	39	M	96321	140	96	<5 Years	Stage 1	5.4	Case
52	Arokiyasamy	57	M	65210	160	100	>5 Years	Stage 2	4.6	Case
53	Savithri	64	F	64852	160	100	>5 Years	Stage 2	5.0	Case
54	Aiyappan	66	M	1597	168	110	>5 Years	Stage 2	5.3	Case
55	Pasupathi	48	M	35793	138	94	<5 Years	Stage 1	5.2	Case
56	Kamaraj	49	M	85210	156	90	<5 Years	Stage 1	5.5	Case
57	Manimegalai	56	F	8789	154	90	>5 Years	Stage 1	5.2	Case

58	Chandra	54	F	95102	160	90	>5 Years	Stage 2	5.2	Case
59	Palanisamy	68	M	75320	168	100	>5 Years	Stage 2	5.2	Case
60	Sethuraman	66	M	98412	166	106	>5 Years	Stage 2	5.2	Case
61	Andiyappan	60	M	78632	162	104	<5 Years	Stage 2	5.5	Case
62	Ramanathan	53	M	74123	158	90	>5 Years	Stage 1	5.4	Case
63	Velayutham	69	M	84265	156	100	>5 Years	Stage 2	5.5	Case
64	Ibrahim	65	M	86212	166	108	>5 Years	Stage 2	7.5	Case
65	Elangovan	47	M	65310	150	90	<5 Years	Stage 1	5.5	Case
66	Allah Pitchai	51	M	40002	170	110	>5 Years	Stage 2	5.8	Case
67	Rasathi	50	F	8014	168	100	<5 Years	Stage 2	5.6	Case
68	Malarkodi	45	F	55632	152	96	<5 Years	Stage 1	5.5	Case
69	Karikalan	61	M	52869	144	90	>5 Years	Stage 1	5.6	Case
70	Ambikeshwaran	47	M	85566	162	96	<5 Years	Stage 2	6.0	Case
71	Selvam	53	M	23478	154	90	>5 Years	Stage 1	5.6	Case
72	Singaravelu	51	M	52019	168	100	>5 Years	Stage 2	6.2	Case
73	Thirupathi	59	M	63570	160	104	>5 Years	Stage 2	6.0	Case
74	Somasundaram	49	M	666	160	100	<5 Years	Stage 2	6.2	Case
75	Thirumoorthi	54	M	526	162	94	<5 Years	Stage 2	6.3	Case
76	Thillaivinayagam	60	M	33612	164	110	>5 Years	Stage 2	7.2	Case
77	Prakasam	62	M	38957	176	100	<5 Years	Stage 2	8.9	Case
78	Vadivel	52	M	6219	170	110	>5 Years	Stage 2	6.2	Case
79	Saroja	50	F	440	166	90	<5 Years	Stage 2	4.0	Case
80	Arokiyamary	57	F	8270	174	90	>5 Years	Stage 2	6.2	Case
81	Manoranjitham	46	F	6951	160	100	<5 Years	Stage 2	4.1	Case
82	Mayilathal	49	F	69532	160	90	<5 Years	Stage 2	4.1	Case
83	Karuppasamy	58	M	11516	180	110	>5 Years	Stage 2	6.2	Case
84	Muthukumar	47	M	10009	168	100	<5 Years	Stage 2	4.2	Case
85	Chenniyappan	53	M	14403	162	100	>5 Years	Stage 2	6.4	Case
86	Nagarajan	52	M	49031	174	106	>5 Years	Stage 2	8.4	Case
87	Muruganandam	48	M	75506	164	102	<5 Years	Stage 2	4.2	Case
88	Govindhan	67	M	23680	170	100	>5 Years	Stage 2	6.5	Case

89	Unnikrishnan	59	M	1005	170	104	>5 Years	Stage 2	6.8	Case
90	Vadivambal	39	F	339	150	90	<5 Years	Stage 1	4.2	Case
91	Mookan	49	M	2458	180	100	<5 Years	Stage 2	4.2	Case
92	Chakravarthy	55	M	15200	170	100	>5 Years	Stage 2	6.5	Case
93	Loganayaki	50	F	45557	168	90	<5 Years	Stage 2	4.2	Case
94	Madheshwaran	40	M	96298	166	98	<5 Years	Stage 2	4.2	Case
95	Kittu	59	M	58262	172	100	>5 Years	Stage 2	6.5	Case
96	Rajendhiran	48	M	13056	174	110	>5 Years	Stage 2	7.2	Case
97	Sakthivel	51	M	17750	168	100	>5 Years	Stage 2	6.9	Case
98	Chinrasu	48	M	17025	156	90	<5 Years	Stage 1	9.2	Case
99	Periyasamy	58	M	19983	170	110	>5 Years	Stage 2	7.0	Case
100	Aasaithambi	53	M	1964	176	100	>5 Years	Stage 2	7.0	Case
101	Mohanasundar	56	M	10253	172	100	>5 Years	Stage 2	6.9	Case
102	Ravichandran	50	M	45019	140	90	<5 Years	Stage 1	4.2	Case
103	Shahin	27	F	16694	164	100	<5 Years	Stage 2	4.2	Case
104	Siluvai	40	M	1991	152	86	<5 Years	Stage 1	4.2	Case
105	Seeniyammal	49	F	4268	160	102	>5 Years	Stage 2	7.2	Case
106	Alagiyanambi	57	M	1616	160	106	<5 Years	Stage 2	4.3	Case
107	Kovendhan	38	M	63284	150	88	<5 Years	Stage 1	4.3	Case
108	Rajarajan	52	M	159	166	104	>5 Years	Stage 2	7.2	Case
109	Sangameshwaran	60	M	753	170	110	>5 Years	Stage 2	7.4	Case
110	Swaminathan	54	M	68420	168	90	<5 Years	Stage 2	4.5	Case
111	Killivalavan	59	M	10215	164	100	>5 Years	Stage 2	7.2	Case
112	Chitrambalam	62	M	65024	172	110	>5 Years	Stage 2	7.3	Case
113	Ramkumar	44	M	90024	164	90	<5 Years	Stage 2	4.5	Case
114	Geetha	33	F	86300	154	86	<5 Years	Stage 1	4.5	Case
115	Peranandham	45	M	54631	160	100	<5 Years	Stage 2	4.6	Case
116	Siddalingam	58	M	79831	170	108	>5 Years	Stage 2	7.4	Case
117	Jayaraman	48	M	56479	162	90	>5 Years	Stage 2	7.4	Case
118	Venkateshwaran	44	M	1236	172	100	<5 Years	Stage 2	4.6	Case
119	Udayageetha	36	F	3215	168	100	<5 Years	Stage 2	4.6	Case

120	Myvizhiselvi	34	F	21478	164	104	<5 Years	Stage 2	4.8	Case
121	Bommusamy	42	M	89632	170	110	<5 Years	Stage 2	4.6	Case
122	Ramalingam	70	M	65214	156	96	>5 Years	Stage 1	7.4	Case
123	Kathiravan	52	M	9988	170	104	<5 Years	Stage 2	4.6	Case
124	Porkodi	55	F	85217	178	110	>5 Years	Stage 2	7.5	Case
125	Suganthi	43	F	86920	162	110	<5 Years	Stage 2	4.6	Case
126	Rangaraj	66	M	23669	152	98	>5 Years	Stage 1	7.5	Case
127	Moorthy	47	M	69874	166	100	<5 Years	Stage 2	4.6	Case
128	Gobinath	41	M	41023	150	100	<5 Years	Stage 2	5.0	Case
129	Vikraman	39	M	35793	156	94	<5 Years	Stage 1	5.0	Case
130	Velusamy	65	M	15970	152	100	>5 Years	Stage 2	7.5	Case
131	Umakanthan	62	M	20201	164	106	>5 Years	Stage 2	7.6	Case
132	Selvamani	61	M	35980	170	118	>5 Years	Stage 2	7.6	Case
133	Balamurugan	51	M	30007	176	98	>5 Years	Stage 2	7.8	Case
134	Jambulingam	64	M	1267	180	110	>5 Years	Stage 2	7.8	Case
135	Mathiyarasi	49	F	10027	148	84	>5 Years	Stage 1	7.8	Case
136	Angammal	59	F	50063	158	100	>5 Years	Stage 2	7.8	Case
137	Nanjundappan	66	M	50997	166	108	>5 Years	Stage 2	7.8	Case
138	Muthupetchi	56	F	5558	156	104	>5 Years	Stage 2	7.6	Case
139	Kayalvizhi	47	F	6147	144	84	<5 Years	Stage 1	4.8	Case
140	Thangavel	57	M	66693	180	112	<5 Years	Stage 2	5.0	Case
141	Karmegam	62	M	70001	180	118	>5 Years	Stage 2	7.6	Case
142	Pulliyappan	67	M	9647	174	110	>5 Years	Stage 2	7.6	Case
143	Mirunalini	53	F	90609	158	108	<5 Years	Stage 2	5.0	Case
144	Boominathan	60	M	4994	160	102	>5 Years	Stage 2	7.6	Case
145	Vellaiyan	48	M	2793	150	90	<5 Years	Stage 1	5.2	Case
146	Lalitha	44	F	6953	164	100	<5 Years	Stage 2	5.2	Case
147	Aravindh	29	M	2040	166	100	<5 Years	Stage 2	5.2	Case
148	Arjunan	32	M	24680	154	90	<5 Years	Stage 1	5.3	Case
149	Sujatha	57	F	16987	168	106	>5 Years	Stage 2	8.0	Case

150	Sivakozhundhu	66	M	10001	162	110	>5 Years	Stage 2	8.2	Case
151	Srilakshmi	67	F	13579	160	100	<5 Years	Stage 2	5.3	Case
152	Masoodh Basha	71	M	32987	150	94	>5 Years	Stage 1	8.0	Case
153	Gandhimathi	49	F	35971	170	108	<5 Years	Stage 2	5.4	Case
154	Santhi	64	F	35550	178	110	>5 Years	Stage 2	8.1	Case
155	Rani	55	F	81309	160	98	<5 Years	Stage 2	5.4	Case
156	Vanithamani	53	F	75553	154	90	<5 Years	Stage 1	5.5	Case
157	Pandurangan	77	M	96227	168	100	>5 Years	Stage 2	8.2	Case
158	Sengamalai	61	M	77625	156	94	>5 Years	Stage 1	8.2	Case
159	Dharmaraj	54	M	90133	150	100	<5 Years	Stage 2	5.5	Case
160	Lakshmanan	68	M	67668	162	100	<5 Years	Stage 2	5.5	Case
161	Ramachandran	60	M	33146	180	110	>5 Years	Stage 2	8.4	Case
162	Chandrasekar	56	M	85625	172	110	<5 Years	Stage 2	5.5	Case
163	Devaki	41	F	8697	144	88	<5 Years	Stage 1	5.5	Case
164	Diana	45	F	99111	158	100	<5 Years	Stage 2	5.5	Case
165	Nalliyappan	66	M	31656	166	96	>5 Years	Stage 2	8.4	Case
166	Prabakaran	55	M	77555	176	104	>5 Years	Stage 2	8.6	Case
167	Kajalakshmi	68	F	56999	180	100	>5 Years	Stage 2	9.0	Case
168	Sanniyasi	64	M	60004	182	114	>5 Years	Stage 2	9.4	Case
169	Kumarasamy	69	M	48927	152	94	<5 Years	Stage 1	5.5	Case
170	Veerapathran	59	M	14501	164	104	>5 Years	Stage 2	8.6	Case
171	Sangeetha	49	F	24510	174	108	>5 Years	Stage 2	9.4	Case
172	Chithra	47	F	34569	160	100	<5 Years	Stage 2	5.5	Case
173	Shanmugam	43	M	54369	160	98	<5 Years	Stage 2	5.5	Case
174	Kalaiarasan	37	M	10566	166	90	<5 Years	Stage 2	5.6	Case
175	Saed Kahn	70	M	395	150	94	>5 Years	Stage 1	4.2	Case
176	Vigneshwaran	35	M	45396	164	106	<5 Years	Stage 2	5.6	Case
177	Poornambigai	47	F	66610	160	100	<5 Years	Stage 2	5.6	Case
178	Hemavathi	32	F	37135	168	108	<5 Years	Stage 2	5.6	Case
179	Maariyappan	61	M	26595	170	110	>5 Years	Stage 2	9.5	Case
180	Kurshad Khan	36	M	29856	154	100	<5 Years	Stage 2	6.2	Case

181	Thilagavathy	45	F	76844	158	100	<5 Years	Stage 2	6.2	Case
182	Mallikarjun	56	M	6851	158	90	>5 Years	Stage 1	5.1	Case
183	Vetrivel	52	M	42119	166	102	<5 Years	Stage 2	6.2	Case
184	Rukmani	42	F	85633	160	100	<5 Years	Stage 2	6.2	Case
185	Deivanai	65	F	84100	170	110	>5 Years	Stage 2	9.6	Case
186	Meiyappan	68	M	86103	180	114	>5 Years	Stage 2	9.8	Case
187	Ramajeyam	72	M	99997	150	96	>5 Years	Stage 1	6.3	Case
188	Anandhan	37	M	77114	154	90	<5 Years	Stage 1	6.5	Case
189	Yellappan	62	M	2244	160	108	>5 Years	Stage 2	7.9	Case
190	Srinivasan	60	M	7418	168	100	>5 Years	Stage 2	8.4	Case
191	Singari	45	F	337	162	106	<5 Years	Stage 2	6.4	Case
192	Lingeshwaran	54	M	111	156	100	>5 Years	Stage 2	4.4	Case
193	Ramesh	31	M	7540	166	100	<5 Years	Stage 2	6.5	Case
194	Ammani	48	F	1090	148	94	<5 Years	Stage 1	7.5	Case
195	Valliyammal	59	F	50505	136	96	>5 Years	Stage 1	3.8	Case
196	Kailash	66	M	42426	148	100	<5 Years	Stage 2	8.0	Case
197	Roselin	39	F	36917	134	90	<5 Years	Stage 1	7.6	Case
198	Kannagi	47	F	11557	144	100	<5 Years	Stage 2	8.9	Case
199	Veeramani	55	M	786	168	96	>5 Years	Stage 2	5.6	Case
200	Kathija	70	F	90090	170	110	>5 Years	Stage 2	6.4	Case

MASTER CHART FOR CONTROLS

Sl. No	Name	Age	Sex	IP/OP No	SBP (mm of Hg)	DBP (mm of Hg)	SUA Levels (mg/dL)	Category
1	Ramalingam	60	M	111	120	82	3.8	Control
2	Sivagami	55	F	1150	126	88	4.2	Control
3	Cheraladhan	54	M	25636	110	80	4.0	Control
4	Arun kumar	41	M	21265	122	76	4.4	Control
5	Sundaram	63	M	23458	130	70	3.0	Control
6	Kasinadhan	52	M	5645	128	74	4.4	Control
7	Kumari	58	F	9283	124	70	4.0	Control
8	Manivannan	38	M	37881	118	70	3.0	Control
9	Ramaiyah	67	M	32431	120	78	4.0	Control
10	Ponnusamy	69	M	53566	116	74	3.2	Control
11	Veerasamy	61	M	70774	114	86	5.0	Control
12	Marikozhundu	57	F	310	110	72	4.5	Control
13	Velankanni	53	F	51423	108	72	3.6	Control
14	Mumtaz	52	F	66111	110	70	5.0	Control
15	Kesavan	48	M	67115	112	70	3.8	Control
16	Jagadesh	44	M	1120	116	70	4.6	Control
17	Sathish	41	M	42133	120	70	4.6	Control
18	Ranjith	24	M	56780	130	76	4.2	Control
19	Srirangan	49	M	41537	132	80	5.3	Control
20	Parasuraman	63	M	57620	136	82	5.6	Control
21	Ramasamy	69	M	115	130	84	6.0	Control
22	Athiyappan	67	M	901	120	76	4.6	Control
23	Sengodan	55	M	506	126	74	5.6	Control
24	Kalimuthu	50	M	59871	120	70	4.6	Control
25	Kamalakannan	40	M	62158	122	76	5.4	Control
26	Thirupathi	38	M	41250	134	80	6.0	Control
27	Sriram	32	M	47111	136	82	5.6	Control
28	Marudhai	65	M	46956	130	88	5.2	Control
29	Gopal	52	M	33119	110	80	5.6	Control
30	Nallathangal	60	F	3141	112	78	5.2	Control
31	Sasikumar	36	M	50507	110	70	5.8	Control
32	Ramesh	28	M	61236	106	70	5.5	Control
33	Nallasamy	78	M	85850	110	70	5.2	Control
34	Srinivasan	70	M	8423	110	74	5.0	Control
35	Sivanesan	56	M	62584	110	76	5.9	Control
36	Thilagavathi	58	F	35425	120	74	5.6	Control
37	Balu	54	M	56842	134	82	5.0	Control
38	Krishnan	60	M	80258	136	80	6.4	Control
39	Eswaran	66	M	15486	130	88	6.6	Control
40	Dilli kumar	35	M	36541	132	80	6.0	Control

41	Gowthaman	55	M	1026	104	68	5.0	Control
42	Malliga	46	F	60150	110	74	6.4	Control
43	Ravi kumar	41	M	81080	120	76	6.2	Control
44	Chandran	39	M	65409	126	80	5.2	Control
45	Gurumoorthi	68	M	7000	120	70	6.8	Control
46	Ilamparithi	47	M	4100	116	74	6.6	Control
47	Kuyilathal	60	F	5069	118	70	5.2	Control
48	Rudhran	30	M	3756	110	74	6.6	Control
49	Manickam	55	M	25401	104	70	6.8	Control
50	Lilly	34	F	45630	102	68	6.8	Control
51	Fathima	48	F	11279	104	70	2.8	Control
52	Kadhar Ali	62	M	1569	100	68	4.0	Control
53	Vinayagam	70	M	56423	100	70	3.6	Control
54	Madhesh	39	M	8684	110	70	3.4	Control
55	Pranesh	41	M	87153	124	76	3.0	Control
56	Veerappan	50	M	1313	130	78	4.2	Control
57	Prabakaran	52	M	17112	136	74	4.0	Control
58	Badrinath	44	M	77066	124	70	7.6	Control
59	Palani	61	M	50454	120	70	3.2	Control
60	Alagusundaram	63	M	8056	122	78	7.6	Control
61	Nallathambi	53	M	5552	134	74	4.0	Control
62	Rajaganapathi	47	M	3496	130	70	3.2	Control
63	Vellaiyammal	45	F	2985	124	70	4.5	Control
64	Banu	48	F	82620	110	80	7.8	Control
65	Senthamarai	39	F	228	100	66	4.2	Control
66	Rasathi	34	F	3570	106	76	3.4	Control
67	Kannan	54	M	1982	108	70	4.4	Control
68	Dinesh	32	M	1108	104	68	8.4	Control
69	Sudhakar	48	M	19841	110	70	4.5	Control
70	Periyasamy	63	M	9051	100	66	4.2	Control
71	Vinayagam	67	M	982	120	72	4.5	Control
72	Abdul Rashid	74	M	1607	110	74	8.2	Control
73	Natarajan	66	M	1987	100	70	4.4	Control
74	Srinivasan	64	M	2703	104	70	4.5	Control
75	Yasodha	48	F	20100	106	70	4.2	Control
76	Nagarajan	59	M	12945	108	72	4.4	Control
77	Padma	63	F	36001	100	70	4.8	Control
78	Mariyappan	54	M	15008	110	68	4.2	Control
79	Thayammal	57	F	60458	120	76	4.4	Control
80	Sudharsanam	49	M	75308	126	72	4.4	Control
81	Varadharaj	53	M	95004	122	70	5.2	Control
82	Siddhaiyan	60	M	6024	132	80	4.2	Control
83	Rangammal	65	F	20147	134	86	4.8	Control
84	Jai Shankar	55	M	63254	124	80	4.8	Control
85	Jayamani	50	F	12035	118	70	4.8	Control
86	Rathinam	52	F	865	120	72	4.2	Control
87	Manohar	40	M	958	126	76	4.2	Control
88	Arunachalam	60	M	3657	100	74	5.6	Control

89	Kalavathi	42	F	2359	138	76	5.2	Control
90	Arumugam	58	M	11599	134	84	4.6	Control
91	Radha	42	F	3357	132	80	5.8	Control
92	Lalitha	56	F	77536	130	70	5.6	Control
93	Elumalai	40	M	88541	124	70	4.4	Control
94	Pavithra	43	F	75520	120	80	5.8	Control
95	Archana	52	F	997	110	64	4.6	Control
96	Prema	41	F	5150	110	70	4.6	Control
97	Manjula	58	F	7466	110	70	6.2	Control
98	Anandhan	55	M	12240	112	70	6.4	Control
99	Ramachandran	62	M	3659	104	66	6.4	Control
100	Kannaiyan	45	M	1227	108	68	4.4	Control
101	Devaraj	48	M	4400	100	70	4.7	Control
102	Uma	50	F	271	102	74	5.8	Control
103	Soman	63	M	40006	100	70	4.8	Control
104	Poornima	40	F	3617	104	70	4.6	Control
105	Govindhan	70	M	1223	106	68	5.2	Control
106	Varadharaj	59	M	69507	104	66	5.6	Control
107	Sumathi	54	F	54027	118	74	5.4	Control
108	Murugesh	45	M	91005	124	70	4.6	Control
109	Renukadevi	37	F	75992	120	70	6.1	Control
110	Rizwan	41	M	65783	134	78	4.6	Control
111	Chinnathambi	47	M	33375	136	80	5.6	Control
112	Indhumathi	39	F	56541	128	82	5.2	Control
113	Rangachari	58	M	65810	122	74	6.2	Control
114	Giridharan	66	M	69341	136	80	6.4	Control
115	Karuppaiyah	54	M	77512	130	80	4.6	Control
116	Pandiyan	48	M	63178	120	74	6.8	Control
117	Noorun Tahira	50	F	36419	110	76	6.2	Control
118	Vadvikarasi	54	F	912	130	78	5.2	Control
119	Vijaya	58	F	4479	110	70	4.6	Control
120	Kamala	66	F	11504	100	68	5.4	Control
121	Muthu	52	M	10127	106	70	4.6	Control
122	Raju	60	M	83657	104	70	5.6	Control
123	Samikannu	47	M	88817	108	70	6.5	Control
124	Samuel	62	M	94019	110	74	4.6	Control
125	Mookan	66	M	43105	120	74	5.2	Control
126	Elavarasan	42	M	4523	110	78	4.6	Control
127	Kandhasamy	60	M	26226	104	72	6.2	Control
128	Ibrahim	64	M	11985	126	80	5.6	Control
129	Saraswathi	54	F	31042	128	80	6.9	Control
130	Selvam	58	M	46028	134	84	6.8	Control
131	Kalaiarasan	34	M	65283	132	86	6.6	Control
132	Meenakshi	64	F	45861	136	86	4.6	Control
133	Saravanan	56	M	1806	104	74	5.6	Control
134	Thangavel	56	M	39420	100	72	6.6	Control
135	Prakasam	66	M	25791	110	70	5.2	Control
136	Ram kumar	48	M	22207	114	70	6.2	Control

137	Sivashankar	42	M	29537	138	84	5.6	Control
138	Karthikeyan	51	M	3549	130	80	6.6	Control
139	Vargheese	60	M	67492	128	80	6.8	Control
140	Rajeshwari	66	F	5128	130	74	5.0	Control
141	Priya	42	F	20156	100	68	5.4	Control
142	Sushila	43	F	35417	106	68	5.6	Control
143	Singaram	53	M	15482	124	70	5.0	Control
144	Mohan	59	M	20567	122	70	5.6	Control
145	Subramani	67	M	9043	120	66	6.2	Control
146	Senthil	45	M	91107	108	70	6.8	Control
147	Appuraj	45	M	46505	100	64	6.4	Control
148	Israel	44	M	20254	110	70	5.6	Control
149	Ragupathi	66	M	98105	116	70	5.0	Control
150	Bhavani	67	F	47100	130	78	6.2	Control
151	Malarvizhi	48	F	60149	138	80	7.2	Control
152	Kulandaivel	75	M	50661	134	82	7.0	Control
153	Mayakkannan	50	M	1019	128	80	6.0	Control
154	Kaasi	60	M	20114	120	78	7.4	Control
155	Sugavanam	51	M	35048	110	70	7.5	Control
156	Sodalaimadan	63	M	71651	120	76	6.0	Control
157	Kuppannan	64	M	47960	126	76	7.4	Control
158	Koodamalai	58	M	29811	130	78	6.0	Control
159	Mathiyarasi	50	F	25189	122	70	6.0	Control
160	Arthanari	48	M	91117	124	70	6.4	Control
161	Thenappan	61	M	44819	120	68	7.0	Control
162	Ponnuthayi	60	F	47335	110	66	7.2	Control
163	Poovayi	57	F	41639	128	70	6.0	Control
164	Karnan	55	M	97111	134	74	7.8	Control
165	Dharman	56	M	96102	100	70	7.0	Control
166	Shenbagam	49	F	1086	120	70	8.0	Control
167	Ibrahim	47	M	1050	128	70	7.6	Control
168	Sethuraman	59	M	81745	128	74	6.4	Control
169	Rajeshwaran	57	M	63218	118	70	8.0	Control
170	Aiyanar	55	M	30018	114	72	7.6	Control
171	Younis Ahmed	56	M	46870	100	68	7.0	Control
172	Thamarai	30	F	61279	112	70	6.0	Control
173	Angamuthu	48	M	775	110	66	6.4	Control
174	Pachamuthu	64	M	940	116	68	7.2	Control
175	Bogar	66	M	1899	138	84	7.0	Control
176	Kanagavalli	38	F	3347	134	80	6.4	Control
177	Pandiyan	30	M	488	132	80	7.6	Control
178	Allikodi	39	F	59217	122	70	8.0	Control
179	Mahendran	28	M	36115	120	72	7.6	Control
180	Gomathy	36	F	19113	126	74	7.2	Control
181	Arulmurugan	44	M	88811	126	70	8.3	Control
182	Moorthy	68	M	77113	128	74	6.0	Control
183	Pichamuthu	61	M	51566	120	78	6.4	Control
184	Gopinath	52	M	56300	110	68	7.6	Control

185	Navukarasu	50	M	67001	106	68	7.2	Control
186	Sakthi	40	M	63611	108	70	8.0	Control
187	Sathiyaseelan	49	M	66410	104	74	6.4	Control
188	Selva kumar	43	M	18636	100	70	6.0	Control
189	Balaji	47	M	10118	106	70	7.6	Control
190	Sagayamary	56	F	52020	126	74	7.2	Control
191	Yoganandham	49	M	59600	118	70	8.0	Control
192	Nirmala	51	F	57116	104	70	8.2	Control
193	Navaneedhan	60	M	96115	108	72	8.2	Control
194	Kasirajan	63	M	20019	106	70	7.6	Control
195	Vijaya	52	F	9194	124	74	7.2	Control
196	Muralirajan	57	M	193	128	78	8.2	Control
197	Manoharan	59	M	85580	134	76	8.2	Control
198	Malarvannan	40	M	61793	138	80	7.2	Control
199	Tamizhselvi	50	F	49317	130	82	3.6	Control
200	Sanjeevi	55	M	1001	136	80	8.0	Control

KEY TO MASTER CHART

Sl.No - Serial number

IP - Inpatient

OP - Out patient

SBP - Systolic blood pressure

DBP - Diastolic blood pressure

SUA - Serum uric acid