A STUDY ON A COMPARATIVE ANALYSIS ON SERUM URIC ACID LEVELS IN THE SPECTRA OF HYPERTENSION

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CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON A COMPARATIVE ANALYSIS ON SERUM URIC ACID LEVELS IN THE SPECTRA OF HYPERTENSION"** is the bonafide work of Dr. K. BHARADHWAJ, in partial fulfillment of the university regulations of Tamil Nadu Dr. M.G.R. University, Chennai, for MD (Branch I) General Medicine examination to be held in April 2013**.**

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DECLARATION

I, **Dr. K. BHARADHWAJ,** hereby declare that, I carried out this work entitled **"A STUDY ON A COMPARATIVE ANALYSIS ON SERUM URIC ACID LEVELS IN THE SPECTRA OF HYPERTENSION"** at Govt. Kilpauk Medical College Hospital, under the guidance of **Prof. Dr. T. Ravindran MD,** Professor of Medicine. I also declare that this bonafide work has not been submitted in part or full by me or any others for any award, degree or diploma to any other University or Board either in India or abroad.

This is submitted to The Tamil Nadu Dr. M.G.R. University, Chennai, in partial fulfilment of the university rules and regulations of for MD degree examination in General Medicine (Branch I) to be held in April 2013.

Place: Chennai

Date:

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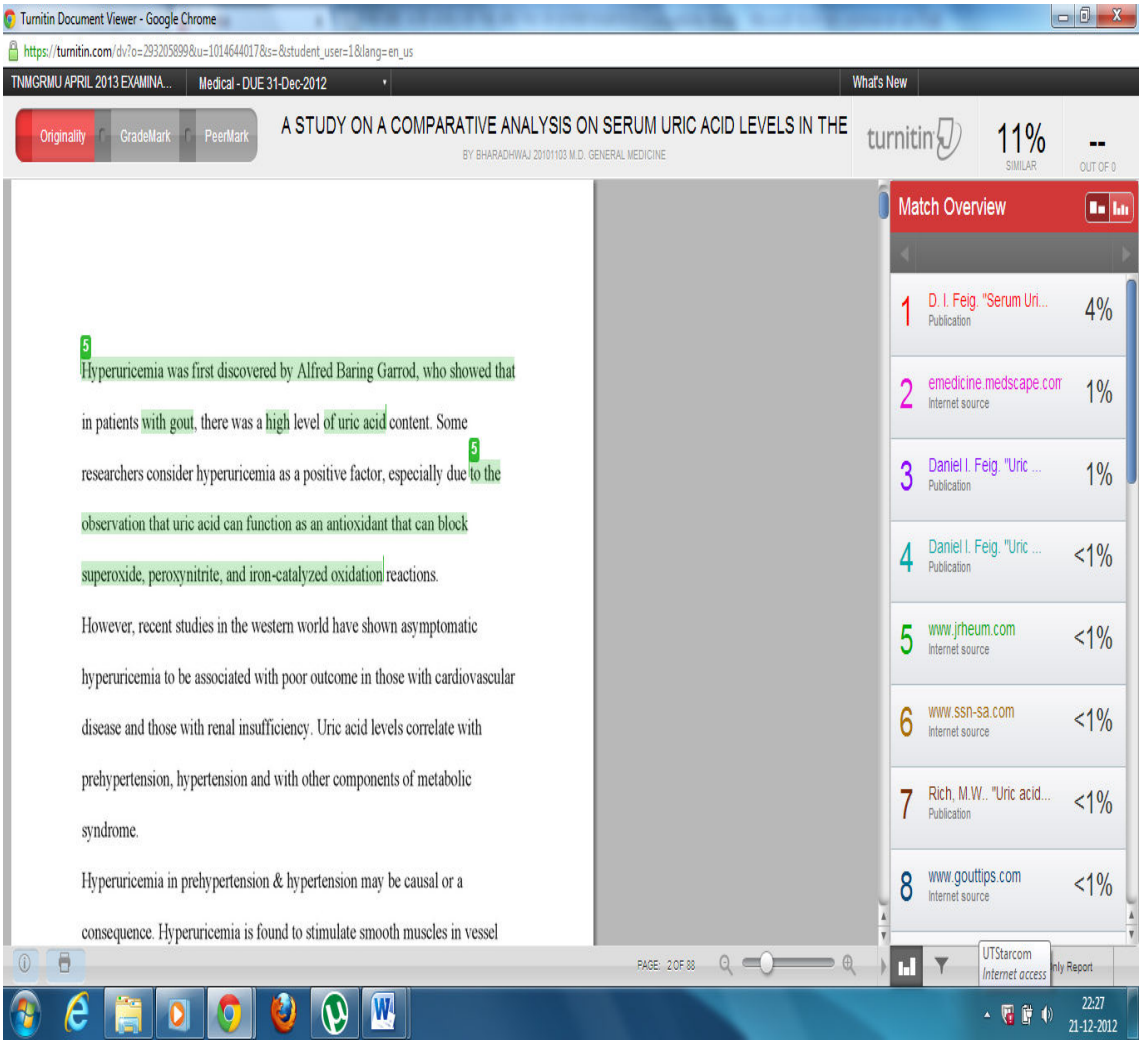

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INTRODUCTION

Hyperuricemia was first discovered by Alfred Baring Garrod [(1)], who showed that in patients with gout, there was a high level of uric acid content. Some researchers consider hyperuricemia as a positive factor, especially due to the observation that uric acid can function as an antioxidant that can block superoxide, peroxynitrite, and iron-catalyzed oxidation reactions.

However, recent studies in the western world have shown asymptomatic hyperuricemia to be associated with poor outcome in those with cardiovascular disease and those with renal insufficiency [(2)]. Uric acid levels correlate with prehypertension, hypertension and with other components of metabolic syndrome.

Hyperuricemia in prehypertension & hypertension may be causal or a consequence. Hyperuricemia is found to stimulate smooth muscles in vessel wall and induce endothelial dysfunction which plays a critical role in pathogenesis of hypertension. Hypertension can, in turn, induce renal dysfunction resulting in reduction in GFR and renal urate excretion. Though studies show elevated uric acid levels in both the Prehypertensive and hypertensive groups, studies analysing the correlation of uric acid levels among the Prehypertensive and hypertensive groups are few. Also a

quantitative correlation may act as a marker of severity of endothelial dysfunction in these subjects [40]. Hence studies are required to quantitate the levels of uric acid among both Prehypertensive and hypertensive groups (with stage I & II as sub groups) and see if higher levels of uric acid are found as BP levels become higher.

Though ample amount of literature and studies supporting the causal role of hyperuricemia in hypertension is available, studies in this regard are lacking in the Indian scenario. The present study is undertaken to generate credible information and evidence concerning this topic.

REVIEW OF LITERATURE

HYPERTENSION

Hypertension is one of the most commonly encountered diseases in the outpatient setting with an estimated prevalence of 30 %. Starting from as low as 115/75 mmHg, the mortality from cardiovascular disease can increase by almost upto 200% for every rise of BP by 20/10 mmHg. This truly places a tremendous burden on the health care sector and hence the perennial interest in Hypertension- the various aetiologies, its pathophysiology and various drug targets to control blood pressure. The problem with this disease is that it many a times remains silently hidden inside the unaware patient and shows its ugly head as one of its severe complications usually as a result of end organ damage. Approximately one-third of adults are unaware of their hypertensive status and almost 66% fall short of their target blood pressure [(11)].

HISTORY:

The understanding of hypertension has evolved since the time of William Harvey (1578–1657), who was the first to describe the blood circulation in his famous book "*De motu cordis*". Stephen Hales, an English clergyman, a botanist and a part time chemist, first made the published measurement of blood pressure in 1733, by sacrificing his mare and

cannulising its arteries. Thomas Young in 1808 and Richard Bright in 1836 were the first to describe Hypertension as a disease. However, what truly revolutionized the diagnosis of hypertension was the invention of sphygmomanometer (*sphygmos*, pulse; *manos*, scanty; *metron, measure*) by Scipione Riva-Rocci in 1896. This eased the procedure of evaluation of BP in outpatient settings. In 1905, Nikolai Korotkoff identified that there was disappearance of sounds on deflating the cuff from a higher pressure and marked the systolic pressure using a stethoscope. Hypertension was often classified into "malignant" and "benign" in the early 20th century. However it was increasingly recognised in the 1950s that the latter was not innocuous as it sounds. Over the next few years, increasing evidence accumulated from various studies, that even lower grades of hypertension increased death and cardiovascular disease, and that these risks increased in a predictable fashion with rising blood pressure across the spectrum of blood pressures. It is interesting that historically the treatment primarily consisted in reducing the quantity of blood either by bloodletting or by the usage of leeches to suck out blood [3-6].

DEFINITION:

For epidemiologic and practical reasons, hypertension is currently defined as a systolic pressure of ≥140 mm Hg and/or a diastolic blood pressure of ≥90 mm Hg. This is based on the mean of two or more blood

pressure measurements in a person in two or more visits ideally a month apart. This value is reduced to 130 and 80 respectively for patients with DM and CKD [8]. However Blood pressure is a continuous variable with a correspondingly variable cardiovascular risk, and hence using definitive numbers is purely on convenience and is arbitrary. It would probably be better to describe systemic hypertension as a progressive cardiovascular syndrome characterized by the presence of elevated BP to a level that places a person at increased risk for vital organ injury secondary to vascular pathology.

CLASSIFICATION:

The "**Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure"** has, over years, studied patterns of hypertension and given the classification and guidelines in the management of hypertension. The latest is the seventh report of JNC [7] and the classification of hypertensive groups holds two primary changes over their sixth; one is the introduction of a new sub group called pre-hypertension, as it was becoming clearer that risk for cardiovascular disease started at much lower values that was previously considered. The second is the merger of what was previously considered as stage 2 & 3 into a single stage, as management of either one is similar.

The present classification reads thus:

BP Classification	SBP mm Hg	DBP mm Hg
Normal	120	and 80
Prehypertension	120–139	or 80–89
Stage 1 hypertension	140–159	or 90–99
Stage 2 hypertension	160	or 100

Some other terms of significant interest are:

Pseudo hypertension refers to the falsely elevated blood pressure measured on sphygmomanometer due to the stiffening of the vessel wall. This can be identified by Osler's manoeuvre, where the artery remains palpable despite an absent pulse, on inflation of cuff.

Malignant hypertension is one where the elevated blood pressure is associated with end organ damage, as in rapid deterioration of renal function, retinal haemorrhages or optic nerve involvement, left ventricular failure, myocardial ischemia, or cerebrovascular accident. These changes are independent of the blood pressure value, but usually the measured blood pressure is above 180/110 mm Hg.

BLOOD PRESSURE MEASURING TECHNIQUE is of vital importance to accurately identify those at risk, and ones requiring treatment. Ideally the patient is to be seated comfortably with arms supported at the level of heart. It is advisable that the patient avoids caffeine, exercise and smoking at least 30 minutes before the measurement. An appropriate cuff

with bladder encircling atleast 80% of arm circumference is to be used. The cuff is inflated 20 to 30 mm Hg beyond the level where radial pulse is not felt and then deflated at the rate of 2 mm Hg/ sec. Appearance of Korotkoff sound 1 & disappearance of sound 5 are taken as SBP and DBP [11]. Nowadays Ambulatory Blood Pressure Monitoring (ABPM) is increasingly being used, especially in cases of white coat hypertension, borderline hypertension, resistant hypertension, and in those on antihypertensive drugs with symptoms suggestive of hypotension.

EPIDEMIOLOGY:

Worldwide prevalence for hypertension is found to be as high as 1.1billion individuals, and every year as many as 7.1 million people die due to various complications of hypertension. The World Health Organization reports that more than 60% of cerebrovascular disease and almost 50% of ischemic heart disease are due to suboptimal BP (115 mm Hg SBP) which also happens to be the most common attributable risk for death across the world.

In India, 57% of all stroke deaths and 24% of CAHD deaths can be attributed to hypertension [9]. There has been a steady increase in the prevalence of hypertension in rural India over time. Recent studies have shown a much higher prevalence of hypertension among urban adults:

	MEN	WOMEN
JAIPUR(2002)	36	37
TRIVANDRUM(2000)	36	31
MUMBAI(1995)	44	45
CHENNAI(2001)	14	14

Pooling the data, it seems hypertension is present in nearly a quarter of the urban and a tenth of rural Indians, which translates to an approx. 31.5 million hypertensive people in rural and 34 million in urban localities. 70% of them would be Stage I hypertension.

GENETIC CONSIDERATIONS:

Although a rare Mendelian form of hypertension is identified in a few subgroups, majority of population have a multifactorial aetiopathology for development of hypertension which includes familial, environmental, and dietary factors among others.

Some of the genes that have been implicated, as in studies using rats and human genome [(11)] include:

- Genes that encode for components of the RAS system
- Angiotensinogen and ACE polymorphism
- The α-Adducin gene that causes increased sodium reabsorption in

tubules. These three genetic components are involved in influence of dietary sodium. Others include genes for β_2 adrenoceptors, AT_1 receptor and aldosterone synthase.

AETIOLOGICAL CLASSIFICATION:

This could be either [12]

A. Essential Hypertension

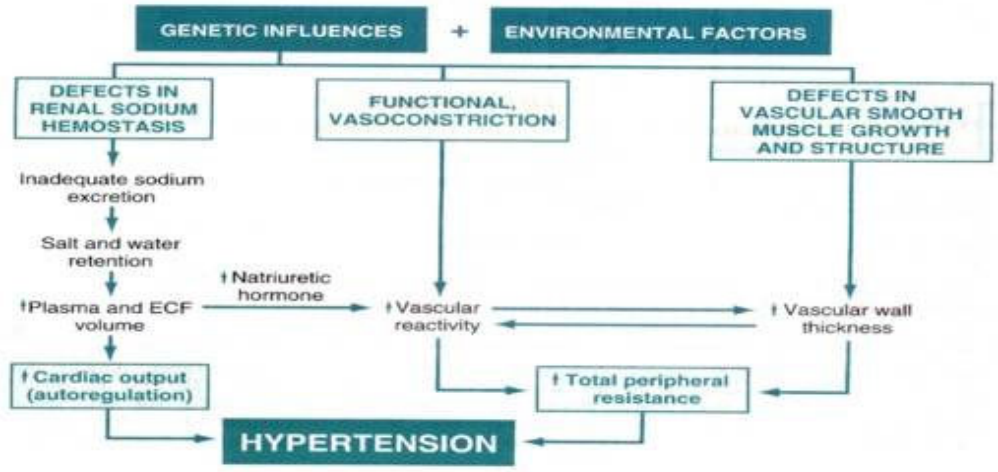
B. Secondary Hypertension:

- **Kidney disease**
- **Endocrine causes**
- **Cardiovascular states**
- **Neurological disorders**
- **Rare Mendelian forms of HT** (glucocorticoid remediable Hypertension, 17α- and 11β hydroxylase deficiency, Liddle's syndrome, PCKD, Pheochromocytoma etc.)

PATHOPHYSIOLOGY OF HYPERTENSION:

The multiple mechanisms involved in hypertension signify an abnormality in the normal regulation of blood pressure. Blood pressure is primarily a function of cardiac output and peripheral vascular resistance [12]. Indeed, it is a complex trait that is determined how various factors- dietary, environmental, demographic, genetic interact to influence these two factors.

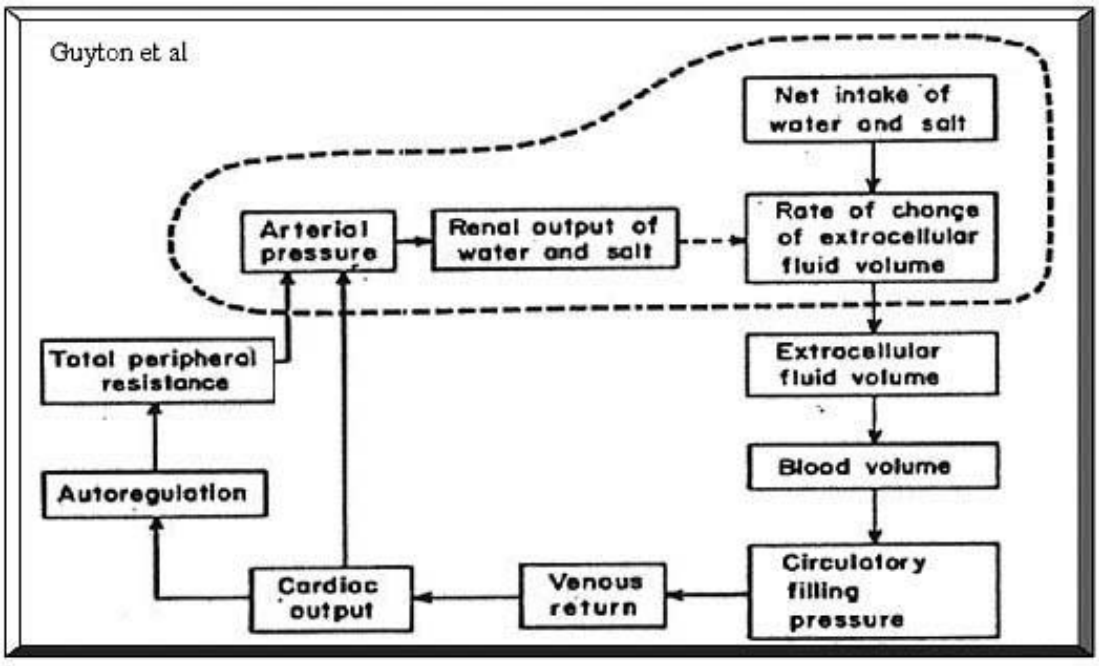
Cardiac output depends on the total blood volume which is in turn influenced by total body sodium. Total peripheral vascular resistance is a function at the level of arterioles and is under the influence of both humoral& neural factors-vasoconstrictors (ATI, Endothelin, catecholamine), vasodilators (NO, Kinins, PG). Other factors include pH, adrenergic system and hypoxia.



The Renal regulation of blood pressure occurs:

- Via the RAAS (Renin Angiotensin Aldosterone System), the kidney modulates the sodium homeostasis and peripheral vascular resistance.
- The kidney also produces various vasodilators like NO and prostaglandins which counterbalances the effects of angiotensin.
- With fall in ECF, the GFR falls, and sodium reabsorption occurs in proximal tubules.

As previously mentioned, there is an inverse relationship between renal perfusion pressure and proximal sodium reabsorption. If this were to be true in all cases, this pressure natriuresis should cause profound volume depletion in the hypertensive patients which doesn't happen in most of the patients. This suggests that in all hypertensive patients, there is a shift in the pressure natriuresis curve in such a manner that a higher perfusion pressure is needed to achieve the required level of natriuresis. This was studied by **Guyton et al** who postulated that the shift in the pressure natriuresis curve is fundamental pathophysiological abnormality that is responsible for all forms of hypertension [13].



According to him, “the most important mechanism in determining the long term control of blood pressure is the renal fluid- volume feedback mechanism” i.e. kidney regulates arterial pressure by altering the excretion of salt and water through kidney, thereby maintaining the circulatory volume and cardiac output. Any change in BP leads to an alteration of sodium and water excretion. When this feedback mechanism gets deranged, hypertension results and is, in essence, the fundamental mechanism governing long term hypertensive states due to any cause.

In all hypertensive states, an intrinsic natriuretic abnormality exists, so that sodium cannot be excreted at normal BP and hence the hypertension essentially becomes necessary to induce pressure natriuresis. Thus hypertension becomes a protective phenomenon as it induces kidney to undergo diuresis, thereby restoring normal salt and water homeostasis. This also explains why patients with salt- sensitive hypertension (where there is an underlying problem in sodium excretion) usually doesn’t manifest with fluid overload state.

Renin-Angiotensin-Aldosterone

Renin, an aspartyl protease is synthesized from its precursor, prorenin, in the renal afferent renal arteriole. Prorenin may be secreted

directly into the circulation or may be activated within secretory cells and released as active renin. The primary stimuli for renin secretion are:

1. Decreased sodium chloride concentration sensed at macula densa, a part of Juxtra Glomerular Apparatus [14],
2. Decreased pressure sensed in renal afferent arteriole (baroreceptor mechanism), and
3. Stimulation of β_1 adrenoceptors.

Conversely, renin secretion increases due to either ACE or angiotensin II receptors blockade. Active renin cleaves Angiotensinogen into Angiotensin I which on further metabolism in liver, is converted to Angiotensin II by Angiotensin- Converting Enzyme (ACE).

Renin-secreting tumours are one of the examples of renin-dependent hypertension. These include benign hemangiopericytomas, Wilms' tumour & renin-producing carcinomas in lung, liver, pancreas, colon, and adrenals. Renovascular hypertension is another renin-dependent hypertension. Renal artery obstruction leads to decreased renal perfusion pressure, which in turn stimulates renin secretion. Over time, due to secondary renal damage, this may become less renin dependent.

Angiotensin II is a potent vasopressor, the primary tropic factor for aldosterone secretion by the zona glomerulosa, and a growth factor for

vascular smooth muscle cell and myocyte growth and contributes to modeling and repair. Excessive angiotensin II may accelerate atherosclerosis, cardiac hypertrophy, and renal failure and thus may be a target for therapy to prevent target organ damage.

Aldosterone synthesis is dependent on AT II, potassium, and ACTH to a smaller extent. Aldosterone is a potent mineralocorticoid that causes an increase in reabsorption of sodium by amiloride-sensitive epithelial sodium channels (ENaC). Its activation induces structural and functional alterations in the kidney, heart and blood vessels, causing nephrosclerosis, myocardial ischemia and vascular inflammation and remodeling. Animal models have shown that high circulating aldosterone levels can stimulate cardiac fibrosis and left ventricular hypertrophy, and that spironolactone (an aldosterone antagonist) prevents it.

Autonomic Nervous System

The ANS helps in maintaining cardiovascular homeostasis via volume, pressure, and chemoreceptor signals. Adrenergic reflexes modulate short term BP, and adrenergic function, along with hormonal factors, contributes to the long-term regulation. In the kidney, activation of α_1-adrenergic receptors increases renal tubular reabsorption of sodium. Activation of myocardial β_1 receptors increases cardiac output by positive

chronographic and inotropic action. β_1 Receptor activation also stimulates renin synthesis.

Several reflexes modulate blood pressure on very short term basis. One of them is the arterial baroreflex which is mediated by sensory nerve endings in the arch of aorta and carotid sinus. With increase in arterial pressure, these receptors are activated and the net effect is a reduction in sympathetic outflow, causing hypotension and bradycardia. Sympathetic outflow is found to be higher in hypertensive than in normotensive individuals. It plays a role in obesity-related hypertension and Obstructive sleep apnoea syndrome. Pheochromocytoma is the most explicit example of hypertension secondary to increased catecholamine production.

Vascular Mechanisms

Vascular radius and compliance of resistance arteries are important determinants of arterial pressure. Small reduction in lumen size can significantly increase resistance. Hypertensive patients have stiffer arteries, and hence patients with arteriosclerosis usually have high SBP and wide pulse pressures due to decreased vascular compliance. Recent evidence suggests that arterial stiffness has independent predictive value in cardiac events.

Effects of Hypertension on organ systems [11]

Hypertension is an independent predisposing factor for CAHD, CCF, peripheral arterial disease (PAD) and renal disease.

CARDIOVASCULAR SYSTEM

Hypertensive heart disease is the commonest cause of death in this group. Structural and functional adaptations of vascular system lead to LVH, CHF,CAHD and cardiac arrhythmias. Left ventricular hypertrophy increases the risk for CHD, CCF, stroke, and sudden death. Aggressive control of hypertension can partly reverse LVH and reduce cardiovascular risk.

CCF may be either systolic dysfunction, diastolic dysfunction, or both. Diastolic dysfunction is seen often in this subgroup. Patients with diastolic heart failure have a normal EF which is a measure of systolic function. Cardiac catheterization is used to assess diastolic function. Other non-invasive methods, includes echocardiography and radionuclide angiography.

CEREBROVASCULAR SYSTEM

Hypertension is the strongest risk factor for cerebrovascular accident (CVA). Lack of proper management of hypertension increases the incidence of both thromboembolic and haemorrhagic strokes.

Hypertension also is associated with earlier onset of dementia in elderly. This may be due either to large vessel ischemia or Lacunar Infarcts. Whether antihypertensive therapy can retard the progress of the cognitive dysfunction requires further studies.

Autoregulation refers to the maintenance of cerebral blood flow over a wide pressure range (mean arterial pressure of 50–150 mmHg). In patients with malignant hypertension, failure of autoregulation of cerebral blood flow leads to vasodilation and hyperperfusion, and in turn, encephalopathy. Untreated, this can progress to stupor, coma, seizures, and death. Other neurologic syndromes that may be associated with hypertension are, space occupying lesions, benign intracranial hypertension and uremic encephalopathy.

PERIPHERAL ARTERIES

Blood vessels are a target organ for atherosclerotic disease due to hypertension. Hypertension with PAD is a marker for future CVD. Intermittent claudication is the classic symptom of PAD. The ankle-brachial index (ABI) is a useful for evaluating PAD and is defined as the ratio of noninvasively assessed ankle to brachial SBP. An ABI <0.90 is considered diagnostic of PAD.

KIDNEY

The kidney has a causal and effect relationship in hypertension. Primary renal disorders are the commonest cause of secondary hypertension. As analysed in the pathophysiology, various mechanisms play a role in kidney-related hypertension. This includes

- A dysfunction in sodium excretion,
- Excessive renin secretion, and
- Over activity of sympathetic nervous system.

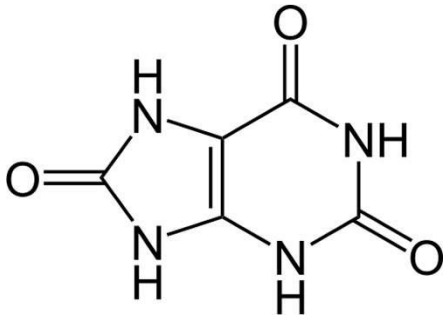
Conversely, hypertension is a major risk factor for kidney injury and End Stage Renal Disease. The increased risk is present throughout the range of blood pressure above optimal level. This appears related to SBP rather than to DBP. Proteinuria is a reliable marker of assessing the severity of CKD and predicts its progression. Patients with higher levels of proteinuria (>3 g/24 h) have a rapid rate of progression than do those with lower levels. Atherosclerotic, hypertension-related vascular lesion primarily affects pre glomerular arterioles leading to ischemic changes in the glomeruli and post glomerular capillaries. Glomerular hyperperfusion plays a role in glomerular injury. Similar to brain, loss of autoregulation of renal blood flow at the afferent arteriole occurs, resulting in transmission of high pressures to unprotected glomeruli with resultant hyperfiltration, and focal segmental glomerular sclerosis. There occurs a vicious cycle of renal injury and loss of

nephron leading to more severe hypertension, glomerular hyperfiltration, and further renal damage. This can progress to glomerulosclerosis, and over a period of time, the renal tubules also become ischemic and atrophic.

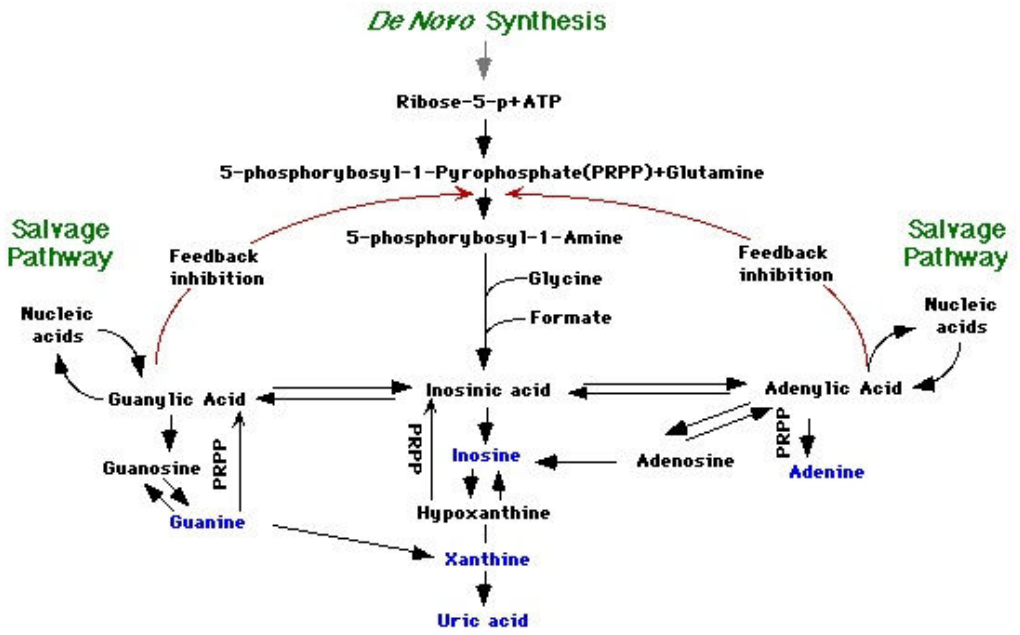
Macro albuminuria (an ACR >300 mg/g) or micro albuminuria (a urine ACR 30–300 mg/g) are early pointer of kidney injury and are also risk factors for disease progression and CVD. Serum uric acid is also found to be elevated in patients with hypertension, as well as in prehypertension and this study is done in this regard.

URIC ACID

Uric acid is a heterocyclic compound of carbon, nitrogen, oxygen, and hydrogen with the formula $C_5H_4N_4O_3$ [15].



It is a by-product of purine metabolism and is formed by the action of xanthine oxidase. Exogenous purines also make up a considerable part of uric acid and this is absorbed in the intestines. In humans, the total uric acid content is about 1.2 g and it is excreted in the kidneys



Uric acid is degraded in most mammals by urate oxidase or uricase, to allantoin, which is excreted in the urine. However, about 10 million years ago, loss of function mutations in genes coding for this enzymes occurred in humans. Hence, we have higher uric acid levels (> 2 mg/dL) than most mammals [18, 19]. The wide range in serum uric acid (upto 12 mg/dL) in humans is determined by the balance between consumption of urate rich diet (such as high protein diets, alcohol consumption, physiological and pathological states with high cell turnover, or defects in purine metabolism), and uric acid elimination by renal and extra renal routes. A reduction in glomerular GFR increases serum urate levels, though a compensatory increase in gastrointestinal excretion also occurs. Increased

net tubular absorption also causes hyperuricemia [16]. The low solubility of uric acid in water is responsible for the development of gout.

Uric acid is a potent reducing substance and hence, a good antioxidant, which makes up almost 50% of the oxidizing capacity of serum. In human blood plasma, the reference range of uric acid is 3.5 mg/dL to 7.4 mg/dL (214- 494 μmol/L) for men and 2.2-6.7 mg/dL for woman (137-393 μmol/L) [17]. Values above these are considered to be hyperuricemia. Hyperuricemia is not diagnosis per se, but is associated with a variety of medical conditions.

PATHOPHYSIOLOGY

Renal uric acid excretion [20]: About 90% of the uric acid filtered through the glomeruli is reabsorbed. There is a four step renal handling of uric acid.

Step1: 100% filtration at glomeruli

Step 2: 98-100% pre secretory reabsorption at proximal convoluted tubule (PCT) by active transport

Step 3: 50% secretion of reabsorbed urate at PCT

Step 4: 40-50% post-secretory reabsorption

Finally, around 5-10% uric acid is excreted through urine, as final net absorption is 90-95%.

Urate secretion can be correlated with its concentration in serum because a minimal rise in the latter results in a substantial rise in the former.

Increased uric acid levels in serum occur due to:

- decreased excretion (under excretors),
- increased production (over producers), or
- Both mechanisms.

Overproducer status is determined by total excretion over 1000mg/day and under excretors, below 600mg/day on a normal purine diet. A single urine sample for uric acid/creatinine ratio is also diagnostic of overproducer when the value is more than 0.5(normal is <0.5). The causes are presented later in the discussion.

Urate Transporters [20, 21]:

There are two main renal transporters of the organic acid transporter (OAT) family:

- URAT 1 is highly specific and localized to the apical brush border of proximal tubular lumen. Probenecid and benzbromarone increase urate excretion by inhibiting URAT 1 and other OATs.

- GLUT 9 exists in two isoforms, GLUT 9L and GLUT 9S, located at the proximal tubular epithelial cells. GLUT 9 is also a transporter for

glucose and fructose and thus has a role in dietary influences of glucose and fructose on hyperuricemia and gout. GLUT 9 is also inhibited by uricosuric agents like probenecid and benzbromarone.

Other transporters are:

- UAT 1- associated with luminal secretion of urate
- ABCG 2
- NPT 1, NPT 4- Sodium-dependent phosphate co-transporter

Endogenous regulators of urate transport are:

- Insulin
- Leptin
- Adiponectin
- Oestrogen
- Uratin

ASYMPTOMATIC HYPERURICEMIA

EPIDEMIOLOGY:

It is defined as a serum urate level greater than 6.8 mg/dl, a level at which MSU remains soluble in serum at 37˚C; beyond which there is super saturation of body fluids and a possibility of deposition in various tissues. This level has been rounded off to 7.0 mg/dl in men and 6 mg/dl in women.

Asymptomatic hyperuricemia is not equivalent to gout. It is common and found in about 5 to 8% of adult males [22]. It is more common in Phillipinos and south East Asians. The prevalence rate of asymptomatic hyperuricemia in USA is estimated at 2.1-13.1%.The risk of gouty arthritis and Urolithiasis increases with duration and severity of hyperuricemia. Clinical gout develops in only about 12% of patients with urate levels between 7.0 and 7.9 mg/dl over a 14 year period.

When serum uric acid level is greater than 9.0 mg/dl, the probability of progression to clinical gout is six times.

Hyperuricemia is more common in men than women and the basal value increases with age.

AETIOLOGY:

The cause of hyperuricemia can be classified based on the pathophysiological mechanism underlying them i.e., uric acid under excretion, uric acid over production, and combined causes.

UNDEREXCRETION:

- Idiopathic
- Familial juvenile gouty nephropathy: It is a rare condition which is characterized by gradually worsening kidney function. Renal biopsy

shows glomerulosclerosis and tubulointerstitial pathology**.**

- Renal Disorders: Disorders of Kidney function is one of the more common causes. In CKD, the uric acid level starts rising as the creatinine clearance≤ 20 mL/min, due to a decrease in urate clearance as retained organic acids compete for secretion**.**
- Metabolic Syndrome [23, 24].
- Drugs: These include diuretics, pyrazinamide, ethambutol, levodopa, aspirin, cyclosporine, nicotinate, and fluorinated anaesthetics.
- Hypertension
- Acidosis: Including lactic acidosis, DKA, alcoholic ketoacidosis, and starvation ketosis. This is due to the fact that these organic acids formed in aforementioned conditions compete with urate for tubular secretion.
- Preeclampsia and eclampsia: Hyperuricemia is a constant finding and used in diagnosis.
- Hyperparathyroidism
- Sarcoidosis
- Pb Toxicity (chronic)
- Hypothyroidism

INCREASED PRODUCTION:

- Idiopathic
- HGPRT deficiency (Lesch- Nyhan syndrome): It is an inherited X-linked disorder. HGRPT is the key enzyme in the conversion of hypoxanthine to inosinate, where Phospho Ribosyl PyroPhosphate serves as the phosphate donor. The deficiency of this enzyme causes an accumulation of Phospho Ribosyl PyroPhosphate , which increases the production of purine and hence increased urate production. It is characterized by gout, uric acid nephrolithiasis, chorea, mental retardation and self-mutilation.
- Partial deficiency of HGPRT (Kelley-Seegmiller syndrome): X-linked disorder with gouty arthritis, kidney stones, and mild cognitive deficits.
- Increased PRPP synthetase function: An uncommon disorder with symptoms similar to the previous condition
- Increased nucleic acid turnover: seen in haemolytic anaemia of any cause and tumours such as Hodgkins- & Non Hodgkins Disease, leukaemia or myeloma
- Tumour lysis syndrome: This is caused by rapid cell lysis of chemo sensitive tumour cells on starting therapy. It is one of the oncological emergencies.

- Glycogenoses III, V, and VII

COMBINED CAUSES

- Alcohol [24]
- Strenuous exercise with dehydration: Exercise may lead to increased cell destruction and decreased excretion due to mild volume depletion.
- Aldolase B deficiency
- Glucose-6-phosphatase deficiency (von Gierke disease)

HYPERURICEMIA AND GOUT

Hyperuricemia is the biochemical precursor of gout. Gout is an inflammatory response to monosodium urate monohydrate (MSUM) crystal deposition in the joints due to alteration in body urate milieu.

New findings have revealed that urate crystals can engage an intracellular pattern recognition receptor, the macromolecular NALP3 (cryopyrin) inflammasome complex which can result in interleukin 1 (IL-1) beta production [25]. This causes inflammation. Inhibition of this pathway may be a target for hyperuricemia-induced crystal arthritis.

Molecular basis of the inflammatory response

Microcrystal shedding

↓

Pro inflammatory coating (IgG, complements)

↓

Interaction with tissue macrophages, fibroblasts, mast cells etc.

↓

Activation of membrane signalling molecules (TLR, CD-14)

↓

Release of cytokines (IL-1, TNF-α) & chemokines

↓

Activation of endothelial cell adhesion molecules

↓

Emigration, attraction and activation of neutrophils

↓

Phagocytosis of crystals by neutrophils

↓

Delayed neutrophil apoptosis by CSF, IL-1, IL-6 etc.

It commonly occurs in men over 40 years of age. The incidence is raising over the last decade due to increased consumption of foods rich in purine, fructose containing and alcoholic beverages. Most frequent presentation is arthritis of first metatarsophalangeal joint [(26)]. Articular gout may be acute, intercritical or chronic tophaceous gout. Diagnosis is confirmed by visualization of negatively birefringent MSU crystals in synovial fluid under polarized light microscopy or demonstration of MSU in tophi.

HYPERURICEMIA & KIDNEY DISEASE

Three types of kidney diseases occur with hyperuricemia and gout:

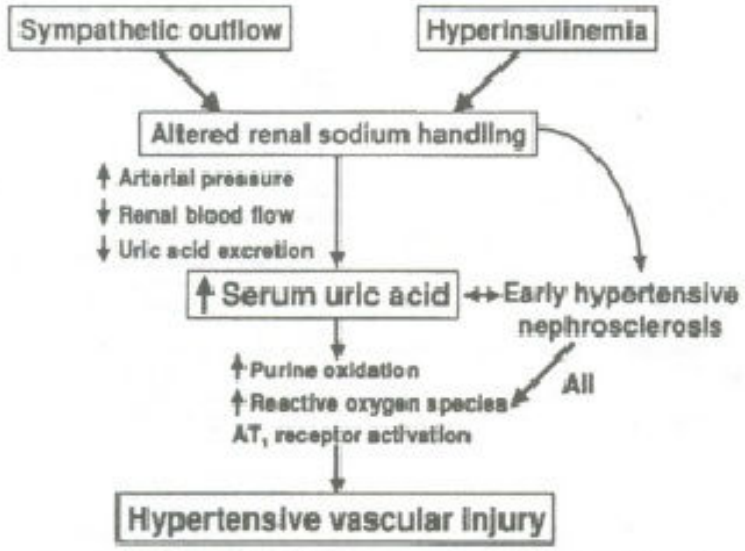
- Urolithiasis- Uric acid acting as nidus for calcium oxalate stone
- Urate nephropathy- Late manifestation of severe hyperuricemia due to deposition of MSU crystals in the medullary interstitium and pyramids, leading to CRF and ESRD.
- Uric acid nephropathy- Due to precipitation of uric acid in renal tubules or collecting ducts causing obstruction. It is usually seen in the setting of tumour lysis syndrome, in those with severe dehydration and acidosis.

HYPERURICEMIA AND CARDIOVASCULAR DISEASE

Multiple studies have confirmed the relationship between hyperuricemia, gout, CVD and metabolic syndrome [27]. The NHANES III-USA has shown that serum urate more than 6 mg/dl is an independent risk factor for CAD and serum urate more than 7 mg/dl is an independent risk factor for stroke.

Uric acid has long been considered a part of the dysmetabolic syndrome or a risk factor of other coronary disease markers like dyslipidemia, glucose intolerance, hypertension and renal disease. In patients with CCF, hyperuricemia correlates with increased mortality and

indicates the needs for aggressive management of the problem. This has also been proved in angiographically confirmed CAHD who had hyperuricemia had a 5 fold risk of mortality. If there is an increase of serum uric acid by 1 mg/dl, prospective studies show a 26% increase in mortality due to CAD.



Postulated link between alterations in uric acid metabolism and pathophysiology of hypertension. Adapted from Ward, Lancet 1998;352:670-1

Richard J. Johnson et al [18, 19] reviewed the epidemiologic evidence and potential mechanisms for this association. The various studies that were included and showed a significant role of uric acid in CVD are:

Hyperuricemia Predicts Cardiovascular Events in Patients With Pre-Existing Cardiovascular Disease

Study	Univariate Correlation With Events	Independent Predictor in Multivariate Analyses
Coronary Drug Project Research Group, 1976	Yes	No
French Canadian Study, 1973	No	Not done
Atherogene Study, 2002	Yes	Yes
The Heart Institute of Spokane, 2002	Yes	Yes

Hyperuricemia Predicts Cardiovascular Events: Studies of the General Population

Study	Length of Follow-Up, y	Univariate Correlation With Events	Independent Predictor in Multivariate Analyses
Framingham			
1985[5]	26	Yes	No
1987[7]	30	Yes	Yes (women)
1988[8]	32*	Yes	Yes
1999[9]	17.3†	Only women	No
Honolulu Heart (Japanese American men)			
1975[5]	2	Yes	Yes
1995[5]	20	Yes	Yes
1996[6]	21	Yes	Yes (in alcohol abstainers)
Chicago Heart Association Detection Project			
1979	5	Yes	Yes (only women)
1989[9]	11.5	Only women	Yes (only women)‡
NHANES I			
1995[5]	13.5	Yes	Yes (only women)
2000[5]	16.4	Yes	Yes
ARIC (Atherosclerosis Risk in Communities Study)			
2000	6	Only women	No
British Regional Heart Study (adult males)			
1997[7]	16.8	Yes	No
Social Institute of Finland			
1982[7]	5	Yes	No
Gothenburg			
1988	12	Yes	Yes‡
MONICA (Monitoring Trends and Determinants in Cardiovascular Diseases)			
1999	8	Yes	Yes‡
CASTEL (Cardiovascular Study in the Elderly)			
1993	7	Yes	Yes‡

*Subanalysis of men with gout.
‡For all-cause mortality.
†Includes original participants of the Framingham Study who took part in the 13th biennial exam and participants of the Framingham Offspring Study.

Some of the mechanisms postulated for the same in various groups are:

Uric Acid Is Increased in Groups at Cardiovascular Risk

Group	Mechanism
Postmenopausal women and men	Estrogen is uricosuric
African Americans	Unknown
Renal disease	Decrease in GFR increases uric acid levels
Diuretics	Volume contraction promotes urate reabsorption
Obesity/insulin resistance	Insulin increases sodium reabsorption and is tightly linked to urate reabsorption
Hypertension	Urate reabsorption increased in setting of increased renal vascular resistance; microvascular disease predisposes to tissue ischemia that leads to increased urate generation (from adenosine breakdown) and reduced excretion (due to lactate competing with urate transporter in the proximal tubule); some hyperuricemic hypertension may be due to alcohol ingestion or lead intoxication
Alcohol use	Increases urate generation, decreases urate excretion

GFR indicates glomerular filtration rate.

They concluded that hyperuricemia had a potential role as a marker of CVD and its co morbidities especially Hypertension and Kidney disease.

HYPERURICEMIA & METABOLIC SYNDROME

A study conducted by **Ford et al** to analyse the role of uric acid in metabolic syndrome [29] concluded that in the paediatric age group, hyperuricemia was associated with the metabolic syndrome and its components and CRP. Several other studies have showed similar results.

HYPERURICEMIA & HYPERTENSION

Role of Uric Acid in Hypertension- The History

In 1879, Frederick Akbar Mohamed noted in his paper on essential hypertension, that many of the hypertensive patients had a familial history of gout. He hypothesized that uric acid could be associated with development of essential hypertension [30]. After ten years, Haig [31] identified that low-purine diets prevented hypertension and vascular disease. In 1909, Henri Huchard, a French academician observed renal arteriolosclerosis, a pathological hallmark of hypertension, in three groups: Those with gout, those with high fatty meat and those with lead poisoning. All three groups were found to have been associated with hyperuricemia. This association was observed in many studies and reported from 1950s but with no mechanistic explanation, not much importance was attached to it. Uric acid was no longer done as a part of routine laboratory investigations in the early 1980s.

Animal Model for Hyperuricemia- The problem!!

As with any other study, an animal model was required to test the hypothesis. The biggest problem in this, stems from the fact that while the enzyme urate oxidase is present in animals including most mammals, it is absent in humans and the great apes, which means that the normal serum uric acid levels in potential study models range between 0.5- to 1.5 mg/dl range (this is about 3.6 to 7.1 mg/dl in humans), and any additional uric acid that is administered in the diet or given intravenously gets rapidly metabolized to allantoin without any alteration of serum levels. The solution for this would be an uricase knockout animal; but when they were bred, they developed urate nephropathy and died of kidney failure within 3 months. Hence their use in studying chronic hyperuricemia was lost [10].

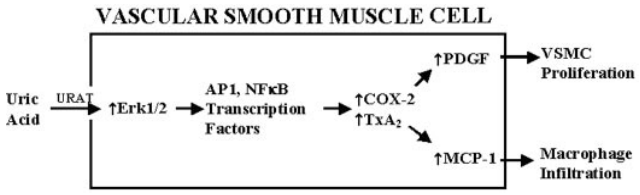
In the end of 20th century, Johnson and colleagues [32, 33] were able to develop an animal model using an inhibitor of urate oxidase that produced a rat with sustained mild hyperuricemia. When 2% oxonate is added to the diet, these rats have their mean serum uric acid concentrations raised from 0.6-1.5 g/dl to 1.8-3.1 mg/dl. Over the same 7 weeks, systolic BP increases by about 22 mmHg. This hypertension is prevented when allopurinol or benziodarone, a uricosuric agent are co administered, identifying uric acid as the cause of elevated BP. Histology of the tissue from rat's kidney reveals narrowing of the lumina of the afferent arterioles and an expansion

of the vascular smooth muscles (arteriolosclerosis) which is the pathognomonic of essential hypertension in humans. The development of arteriolosclerosis can be stopped using allopurinol to control hyperuricemia; hydrochlorhiazide on the other hand normalizes BP without lowering urate levels in blood and doesn't prevent the same indicating that uric acid, is the causative stimulus, not hypertension in itself.

The mechanisms by which hyperuricemia leads to hypertension have been studied using rat models. Direct staining of renal tissue for renin has shown that hyperuricemia causes staining in about 62% of juxtaglomerular apparatus, in comparison with less than 41% in the other study group. The histological study identified infiltration of renal parenchyma with macrophage, which means that increased uric acid levels in serum induces a pro inflammatory state in the kidney. Also, more than 48% reduction in total nitrate levels is noted during mild hyperuricemia. These results indicate that slight rise in uric acid levels causes activation of RAS, induces renal inflammation & CAUSES downregulation of production, all of which are probable pathways for uric acid–mediated hypertension.

Some studies also have identified a probable reasoning for arteriolosclerosis induced by uric acid. Addition of uric acid to the growth medium induces Primary Human Vascular Smooth Muscle cells (HVSMC)

to proliferate in a dose-dependent manner [36- 38]. These cells express the urate-transport channel URAT1. The uric acid causes phosphorylation of kinases which in turn, activates transcription factors. The resultant increase in prostaglandins activates a) Platelet Derived Growth Factor leading to smooth muscle cell proliferation, and b) Monocyte Chemoattractant Protein-1that causes macrophage infiltration. This is depicted in the figure below.



Role of uric acid in endothelial dysfunction

It is well known that endothelial dysfunction predicts early onset of cardiovascular events. For assessment of endothelial function, **Zoccali et al** evaluated endothelial function (by intra-arterial infusion of acetylcholine (ACh) and compared with markers of cardiovascular risk such as C-reactive protein [CRP], insulin resistance, serum creatinine, and UA. They concluded that significant correlation exists between UA and endothelial dysfunction [39].

Role of Uric Acid in Progressive Renal Injury:

Uric acid–mediated arteriolopathy and interstitial inflammation

provide us with a mechanism that explains progressive renal dysfunction. In a study done by **Daniel et al**, the influence of uric acid on various possible mechanisms of progressive renal injury was analysed [10]. Two representative systems considered in this study were the remnant kidney model and cyclosporine nephropathy model in the rats. In the former, unilateral nephrectomy and ligation of the main branches renal arteries on the other side is done. The hyperuricemic remnant kidney rats (to whom 2% oxonic acid was added to diet) had higher BP, higher serum creatinine & greater proteinuria. An increase in glomerulosclerosis and interstitial fibrosis was noted compared to the normal remnant kidney model. Similar results were observed in the cyclosporine nephropathy model wherein addition of oxonic acid to cyclosporine treatment caused higher uric acid levels, with arteriolar hyalinosis, tubulointerstitial damage & macrophage infiltration. Also, allopurinol improves GFR in the latter model, as well as in human liver transplant patients receiving cyclosporine.

URIC ACID AS A BIOMARKER OF HYPERTENSION

A lot of studies have shown the association of hyperuricemia and hypertension. Some of these with the relative risk of hypertension as predicted by them are depicted in the table below:

Serum uric acid and relative risk of hypertension

STUDY	YEAR	POPULATION	RELATIVE RISK
Kahn et al	1972	10,000 males	2-fold risk at 5 years
Selby et al	1990	2,062 subjects	2-fold risk at 6 years
Hunt et al	1991	1,482 adults	2-fold risk at 7 years
Jossa et al	1994	619 males	2-fold risk at 12 years
Taniguchi et al	2001	6,356 males	2-fold risk at 10 years
Masuo et al	2003	433 males	1.0-mg/dL increase in serum uric acid predicts a 27-mm Hg elevation in systolic blood pressure at 5 years
Nakanishi et al	2003	2,310 males	1.6-fold risk at 6 years
Nagahama et al	2004	4,489 adults	1.7-fold risk at 13 years
Alper et al	2005	679 children	Increased risk at 11 years
Sundstrom et al	2005	3,329 adults	1.6-fold risk at 4 years

URIC ACID- A PREDICTOR OF FUTURE HYPERTENSION?

Various studies done in the recent past have shown that serum uric acid may predict development of hypertension in future. The study by **Khan et al.** was one of the conclusive ones that showed that "an increased serum uric acid is an independent risk factor for hypertension [(41)]. **Klein et al** showed that "there was a linear relationship between uric acid levels in serum and SBP irrespective of race [(42)]. There were more than two reports published in the last decade of 20th century that indicated serum uric acid as an independent risk factor for hypertension [(43-45)], and five others published from 2000 to 2005 [(46-50)]. 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" [(49)]. **Krishnan et al** studied the risk of developing hypertension in a follow-up study in men with normal blood pressure, without diabetes/glucose intolerance or metabolic syndrome with baseline hyperuricemia (serum uric acid 7.0

mg/dL) and observed that men normal Blood pressure with asymptomatic hyperuricemia had more than 70% risk for developing hypertension compared with those who did not [50]. Increase in serum uric acid by 1 mg/dl was associated with more than 8% increase in the risk for developing hypertension

URIC ACID IN PAEDIATRIC AGE GROUP:

A significant association has been established between elevated serum uric acid and onset of essential hypertension in the adolescents. A **Hypertension Study** in Russia identified hyperuricemia (>8.0 mg/dl) in almost 10% of children with normal BP, nearly half of the children with borderline hypertension, and three- fourths of children with severe hypertension [51]. **A study in Hungary** included all the children born in its capital city and followed them up for thirteen years and identified significant risk factors for the development of hypertension, which were: tachycardia, sexual maturity at a younger age, and increased uric acid levels [52]. However, these studies didn't categorize the study group by underlying cause of hypertension, and hence the relationship between levels of uric acid and hypertension might be skewed by ascertainment bias. In a small study, **Gruskin et al** compared essential hypertension of children in age group of 12- 18 years with healthy controls with normal BP [53]. The hypertensive group had an elevated serum uric acid with a higher

peripheral renin activity.

Hyperuricemia- To treat or not to??

As presented, the results from various animal and human studies strongly implicate uric acid as one of the factor in the onset of essential hypertension in and also as a potential contributor to progressive renal injury [(10)]. The animal models have also presented a mechanism wherein uric acid leads to various pathological changes in kidney such as afferent arteriolosclerosis, in hypertension. Arteriolosclerosis is irreversible and as shown in some studies, this hypertension becomes uric acid independent over a period of time. This possibly explains why xanthine oxidase inhibitors, such as allopurinol and uricosurics have not been found to be useful as antihypertensive agents. This also leads us to identify their potential use in the primary prevention of essential hypertension in selected populations. These data, however, are to be interpreted cautiously as we do not as yet have human clinical trial data to conclusively prove the use of uric acid–lowering agents as a potential antihypertensive agents, agents which prevent development of hypertension, or agents that attenuate progressive renal injury, like ACEI. Until then, the use of allopurinol or uricosuric agents is not warranted in asymptomatic hypertensives. With various clinical trials under way, the use of uric acid–lowering regimens may find a place in the treatment of hypertension.

AIM OF THE STUDY

1. To evaluate for the presence of Asymptomatic Hyperuricemia in Normotensive, Prehypertensive and Hypertensive Population
2. To compare qualitatively and quantitatively, the serum Uric Acid levels in various Hypertensive classification groups.

METHODS & MATERIALS

This study was conducted in the Government Kilpauk Medical College Hospital. Around 150 participants were included in the study. Informed consent was obtained from all individuals. Participants of the study were selected randomly from those attending outpatient clinics in the Department of Medicine, KMCH. Most of the individuals had either come for regular health visits or for problems like epigastric pain, upper respiratory tract infection, myalgia, headache etc. Since the study design has internal comparison among the hypertensive groups, no separate control group was selected.

COLLABORATING DEPARTMENT: Department of Biochemistry

INCLUSION CRITERIA: Normotensive, Pre- Hypertensive and Hypertensive patients (Known and Unknown)

EXCLUSION CRITERIA:

1. Known cases of Hyperuricemia/ Gout
2. Known cases of Leukaemia
3. Patients with malignancies on chemotherapy/ RT
4. Patients with Renal failure
5. Patients with H/O Recent drug intake of ATT/Chronic Alcohol intake/ Diuretics

METHODOLOGY:

The subjects were evaluated for presence of Hypertension and were classified as per JNC VII Recommendation (Normotensive, Pre-Hypertensive, Hypertensive- stage I & II). Other details such as presence of hypertension and diabetes mellitus were noted. Anthropometric measurements were taken for them and BMI was calculated.

Serum Uric Acid, along with fasting blood glucose and serum cholesterol was estimated in these patients. The uric acid was calculated from serum using uricase/ perioxidase method using an autoanalyser. The principle of the method is:

Uric acid in the sample is subjected to coupled reactions described below, such that a coloured complex is formed. This involves reaction between uric acid and uricase which forms allantoin and peroxide. This peroxide reacts with 4- Aminoantipyrine in the presence of peroxidase to form Quinineimine, a coloured complex, which is measured using a spectrophotometry.

All the data were collected on a proforma prepared for this study and was analysed. Hyperuricemia is taken as S. Uric Acid$\geq$ 6.8mg/dl.

RESULT & ANALYSIS

Statistical analysis

Mean values of all parameters in subgroups were calculated by independent sample-t-test. To compare the distributions of dichotomous data viz .gender, presence of hypertension or diabetes and hyperuricemia, Chi-square test was used. Association between Hypertension and hyperuricemia was assessed by logistic regression model. Potential confounders were adjusted for. Pearson correlations were applied to evaluate the correlation between Hypertension and age, sex, height, weight, BMI, blood sugar, cholesterol & uric acid levels. All statistical analyses were performed using the SPSS package .A p-value of less than 0.05 was considered to be statistically significant. The analysis is done for hypertensives and non hypertensives and further study is done among the various hypertensive groups. A total of 150 subjects in the age group of 30-60 yrs attending the outpatient department of our hospital were randomly selected and classified according to their BP into various hypertensive groups. The distribution of these subjects in these hypertensive groups is thus:

Table 1: Distribution of Subjects According to Hypertensive Groups

STAGE OF HT	NO OF SUBJECTS
NORMOTENSION	75
PREHYPERTENSION	25
STAGE I HYPERTENSION	33
STAGE II HYPERTENSION	17

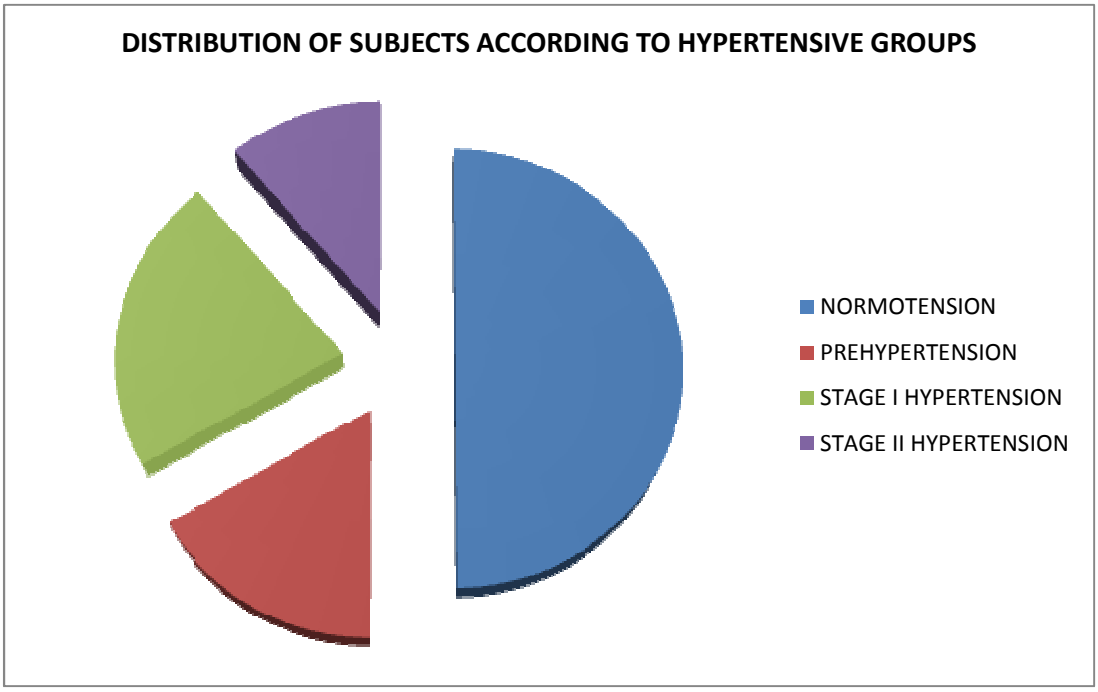


Figure - 1 Distribution of Subjects According to Hypertensive Groups

AGE GROUPS

Table 2 : Distribution in Age Groups

AGE GROUP(NO)	Number of Patients	Percentage
30- 39(1)	39	26
40-49(2)	52	34.7
≥50(3)	59	39.3

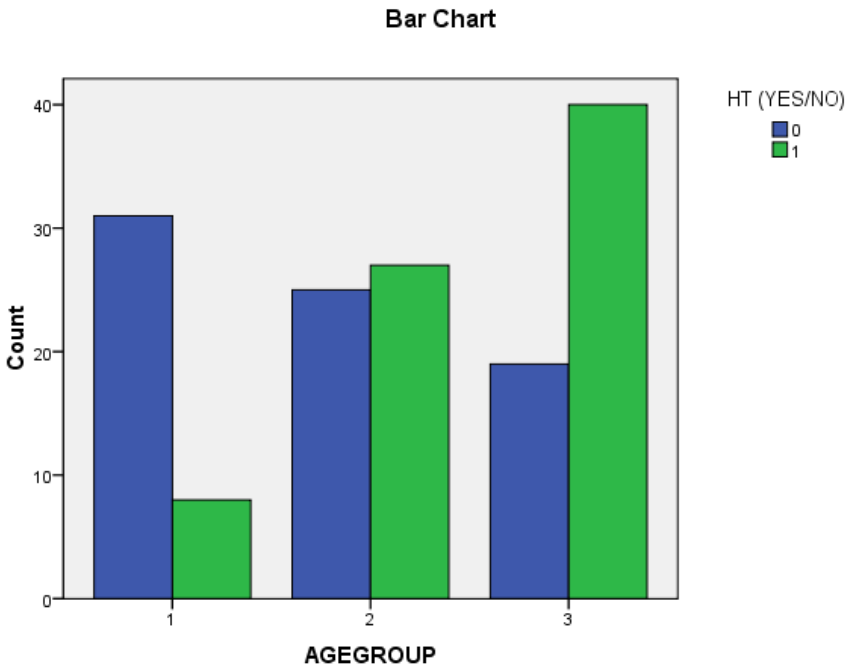


Figure – 2 : Age Distribution

Table 3 : Mean Age

	NUMBER	MEAN AGE
NORMOTENSIVE	75	43
HYPERTENSIVE	75	49.31

Chi square: p= 0.000 < 0.001. There exists a statistical significance between Hypertensive and normotensive subjects with respect to Age group distribution.

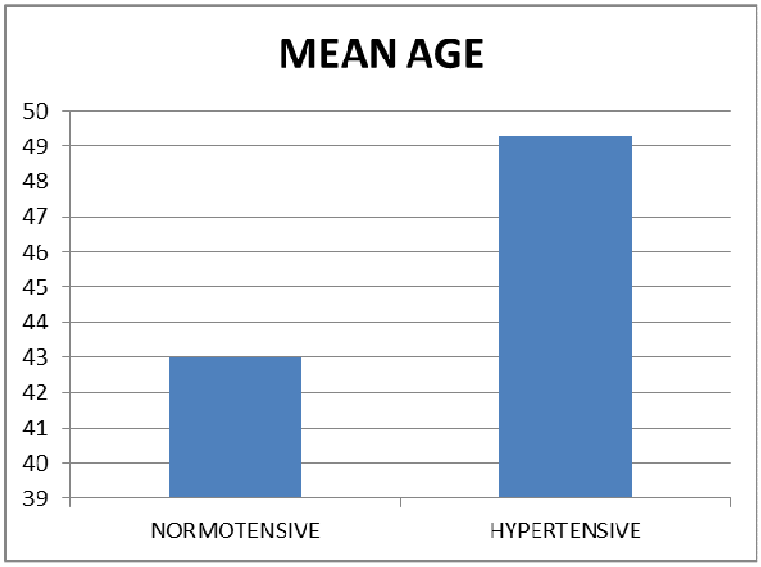


Figure – 3 : Mean Age

COMPARISON WITHIN HYPERTENSIVE GROUPS:

Table 4 : Mean Age among Hypertensive Groups

Hypertensive group	Number	Mean Age
Normotension	75	43.00
Pre Hypertension	25	50.40
Stage I Hypertension	33	49.91
Stage II Hypertension	17	46.53
Total	**150**	**46.15**

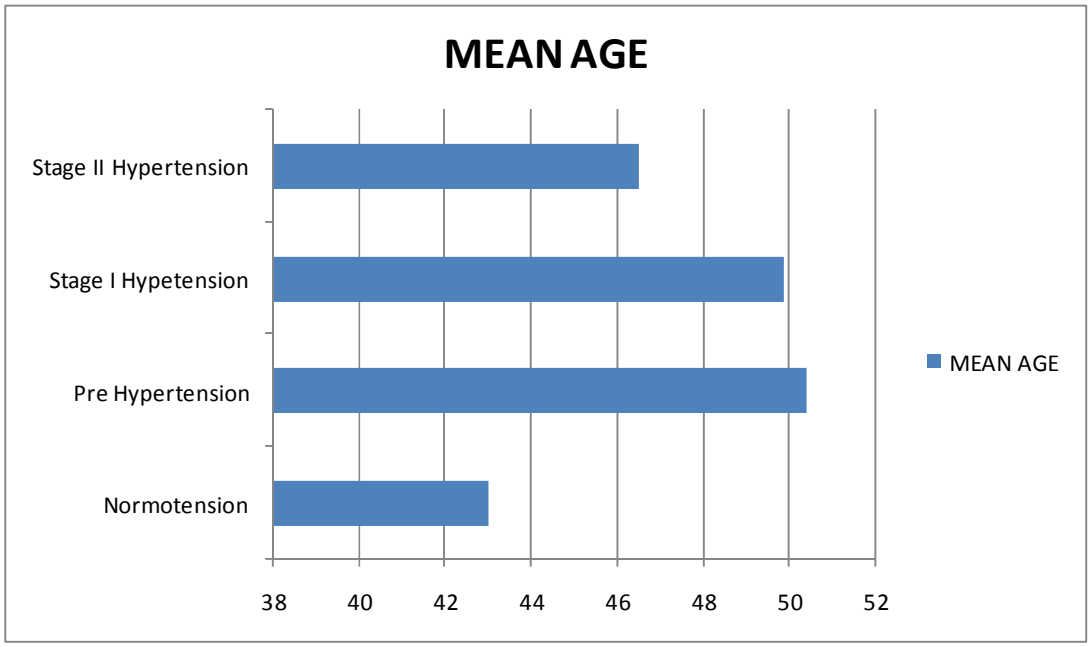


Figure – 4 : Mean Age among Hypertensive Groups

The average age of subjects was lesser in the normotensive group compared to any of the hypertensive subgroups.

SEX GROUPS:

A total of 71 males and 79 females participated in the study.

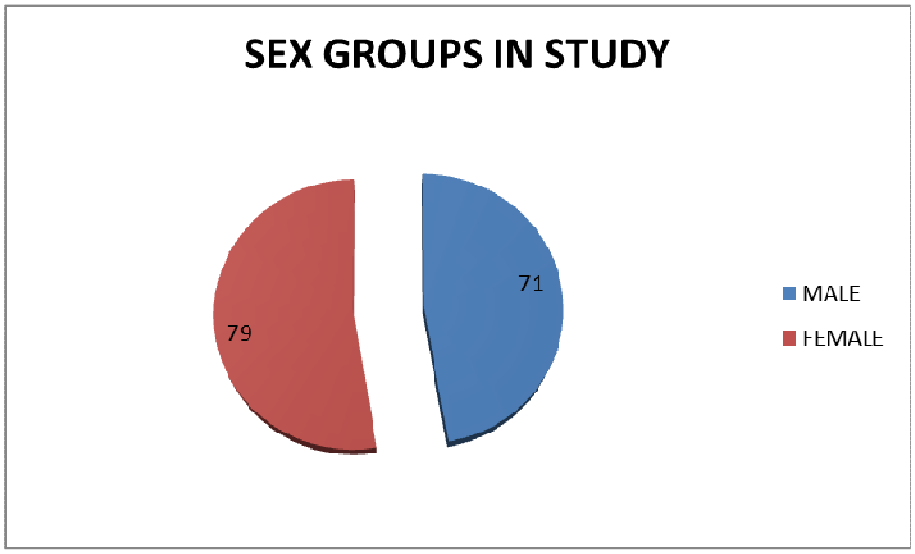


Figure – 5 : Sex Distribution

Table 5: Sex Distribution

	MALES	**FEMALES**
NORMOTENSIVE	41	34
HYPERTENSIVE	30	45

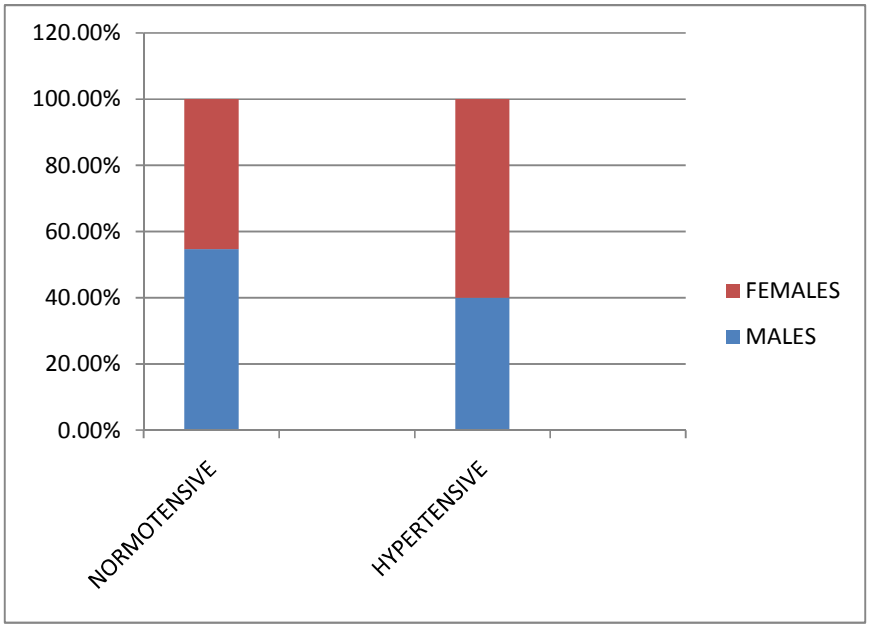


Figure – 6 : Percentage Distribution of Sex Groups

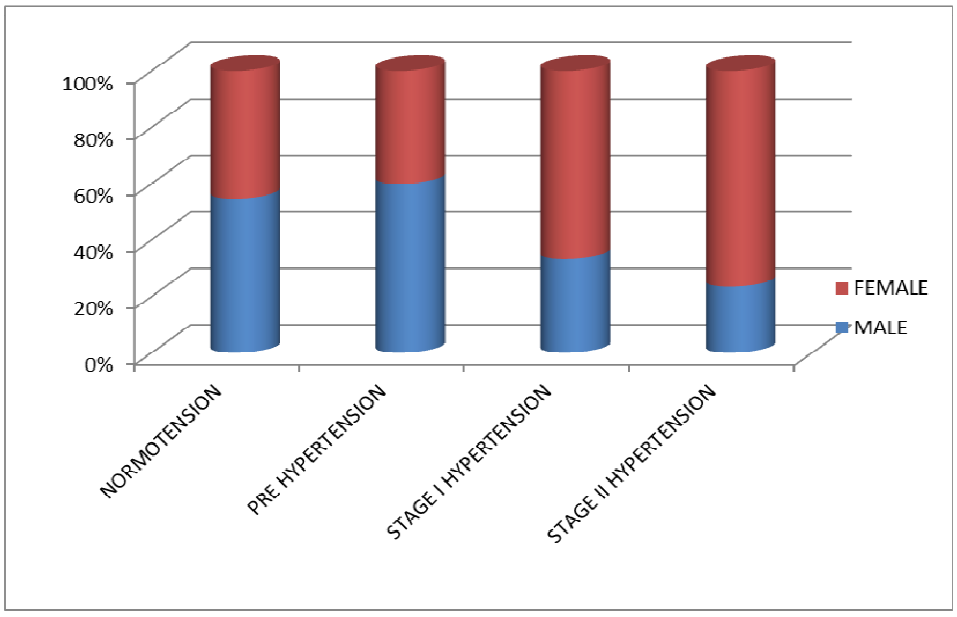


Figure – 7 : Percentage Distribution among hypertensive Groups

Chi square test**: p=0.072 > 0.05** and hence no statistical significance exists between Hypertensive and normotensive with respect to sex distribution

HEIGHT &WEIGHT:

The mean height and weight of the subjects in various hypertensive groups is shown below:

Table 6 : Mean Height and Weight

		No of subjects	Mean
WEIGHT	Hypertensive	75	66.00
	Non- Hypertensive	75	61.79
HEIGHT	Hypertensive	75	164.29
	Non- Hypertensive	75	163.25

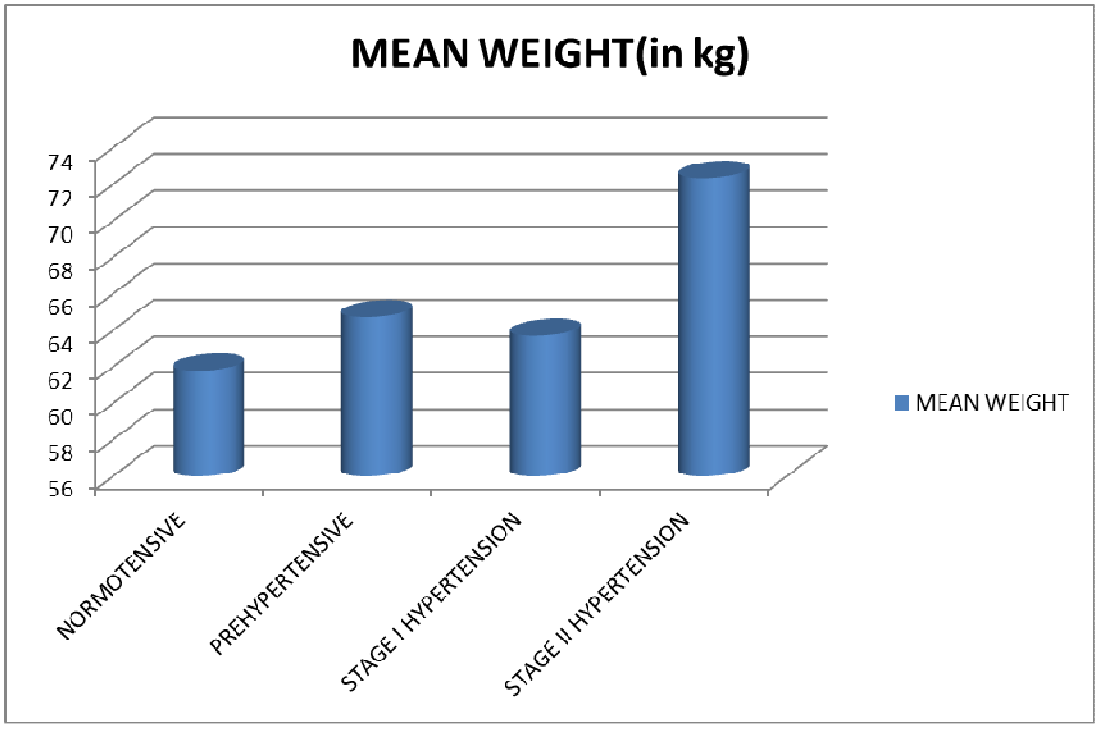


Figure – 8 : Mean Weight of Hypertensive Groups

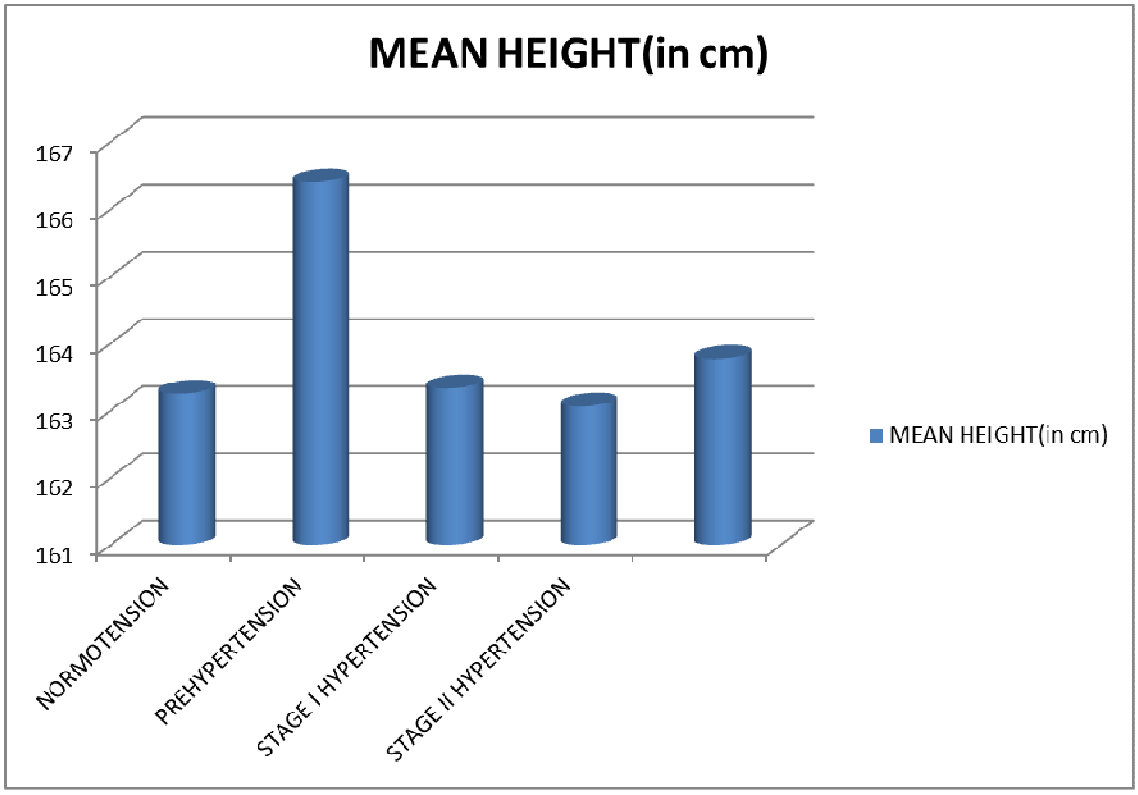


Figure – 9 : Mean Height of Hypertensive Groups

Taking weight into consideration, using chi square test**, p= 0.028 i.e. a** statistical significance exists between hypertensive and normotensive population with respect to weight. However no statistical significance is seen between the groups and height.

On doing post hoc analysis for multiple comparisons within the group, this **significance for weight (p=0.01) existed only between the Normotension and Stage II Hypertension groups**, and not among the other groups.

Table 7 : Post Hoc Analysis of Weight

(I) STAGE OF HT	(J) STAGE OF HT	Level of significance (p value)
0	1	.270
	2	.426
	3	.001
1	0	.270
	2	.737
	3	.036
2	0	.426
	1	.737
	3	.012
3	0	.001
	1	.036
	2	.012

(0- NORMOTENSION; 1- PREHYPERTENSION;

2- STAGE I HYPERTENSION; 3- STAGE II HYPERTENSION)

BMI:

Table 8 : Mean BMI

	No of subjects	Mean BMI
HYPERTENSIVE	75	24.26
NON HYPERTENSIVES	75	22.57

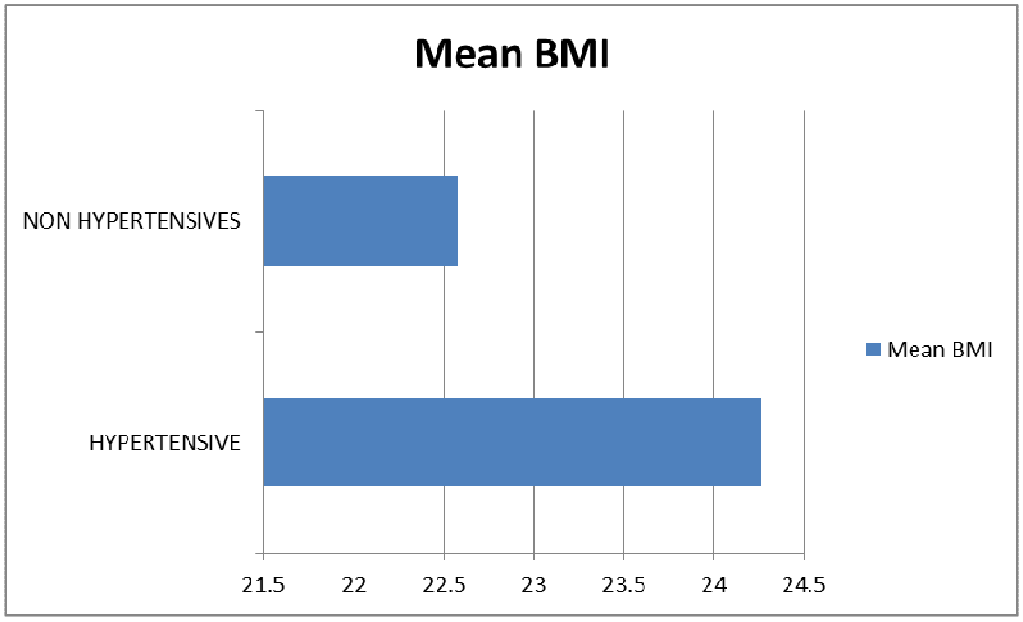


Figure – 10 : Mean BMI

With regards to BMI, P=0.000 i.e. There exists a statistical significance between hypertensive and normotensive patients with respect to BMI levels. In Hypertensive patients, the BMI level is elevated to 24.26 than 22.57 of Normotensive patients.

The Mean BMI among the groups was:

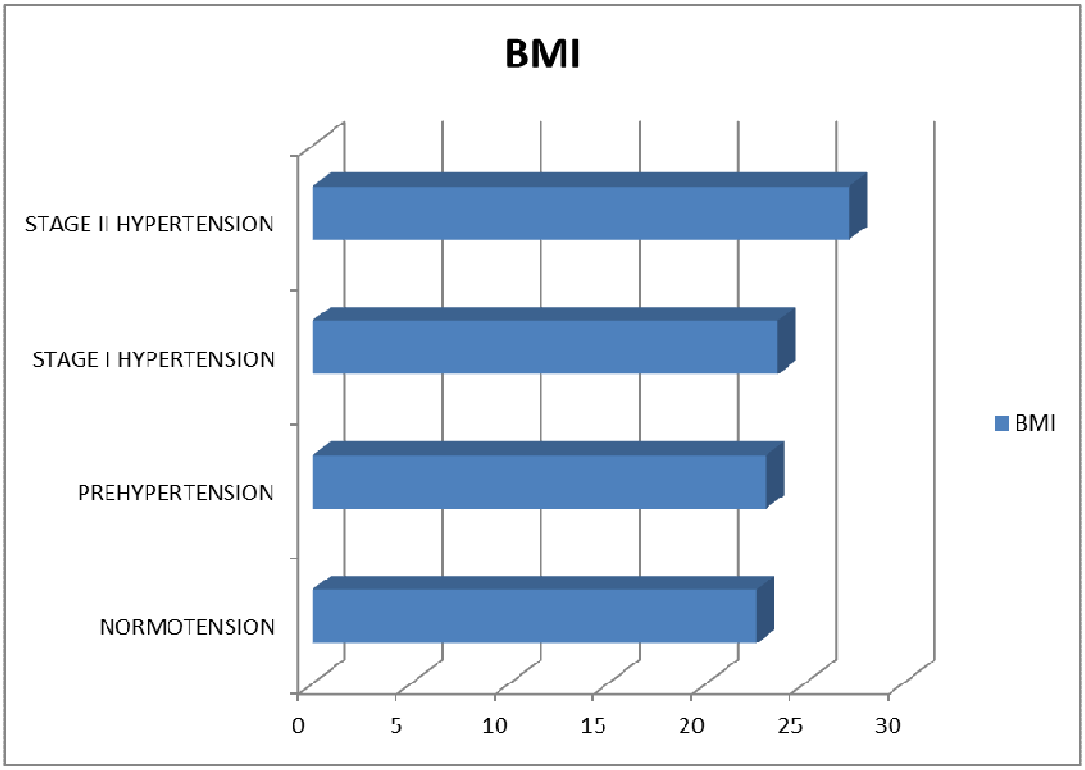


Figure – 11 : Mean BMI of Hypertensive Groups

On post hoc multiple comparative analysis among the hypertensive groups, it is found that this statistical significance (p=0.000) exists between Stage II hypertension and the other groups and not among the others. In other words, there is a significant difference in BMI in patients with stage II Hypertension when compared to that in other hypertensive groups.

Table 9 : Post Hoc Multiple Comparative Analysis of BMI

STAGE OF HT	STAGE OF HT	SIGNIFICANCE (p value)
0	1	.494
	2	.087
	3	.000
1	0	.494
	2	.447
	3	.000
2	0	.087
	1	.447
	3	.000
3	0	.000
	1	.000
	2	.000

(0-NORMOTENSION; 1- PREHYPERTENSION;

2- STAGE I HYPERTENSION; 3- STAGE II HYPERTENSION)

FASTING BLOOD SUGAR:

Table 10 : Mean FBS

	NO OF SUBJECTS	MEAN FBS
HYPERTENSIVE	75	134.60
NORMOTENSIVE	75	117.97

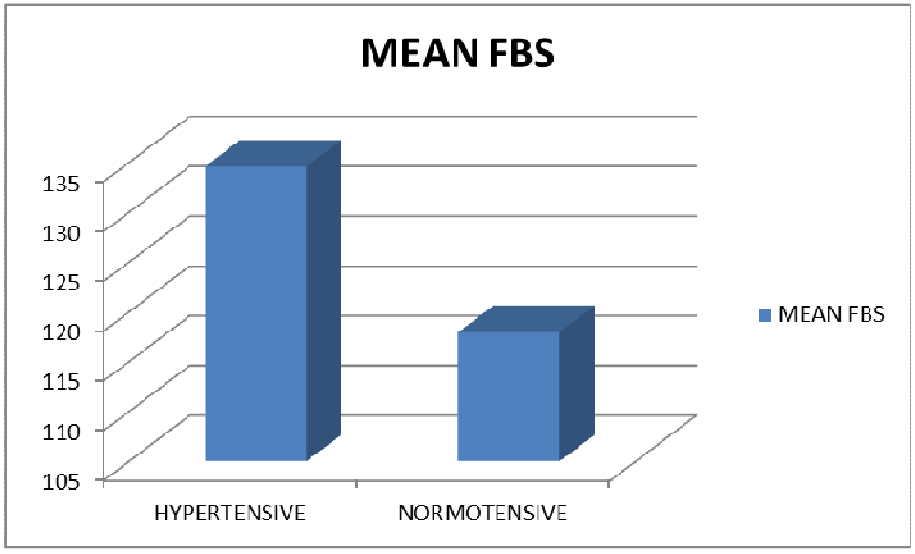


Figure – 12 : Mean FBS

The mean fasting blood sugar value in the hypertensive population is 134.6 mg/dl and is found to be statistically significant compared to the mean fasting blood sugar in normotensive study members (0.009).

An analysis of FBS among the groups shows the following means:

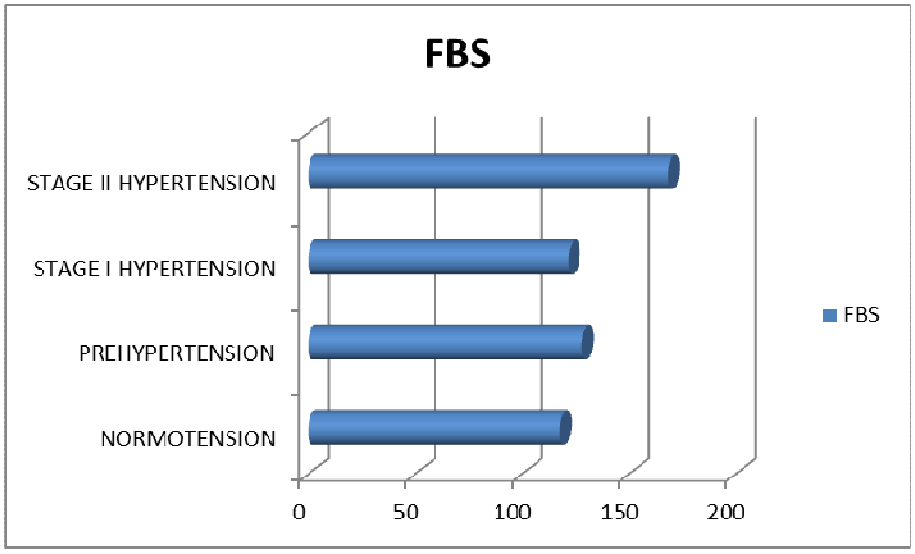


Figure – 13 : Mean FBS of Hypertensive Groups

On post hoc multiple comparative analysis among the hypertensive groups, it is found that this statistical significance exists between Stage II hypertension and the other groups and not among the others.(P=0.000 between stage II Hypertension and normotensives & Stage I Hypertension & P= 0.001 between Stage II Hypertension and pre hypertension groups). In other words, there is a significant difference in FBS in patients with stage II Hypertension when compared to that in other hypertensive groups.

Table 11 : Post Hoc Multiple Comparative Analysis of FBS

STAGE OF HT	STAGE OF HT	Significance (p value).
0	1	.223
	2	.602
	3	.000
1	0	.223
	2	.514
	3	.001
2	0	.602
	1	.514
	3	.000
3	0	.000
	1	.001
	2	.000

(0-NORMOTENSION; 1- PREHYPERTENSION;

2- STAGE I HYPERTENSION; 3- STAGE II HYPERTENSION)

SERUM CHOLESTEROL:

Table 12 : Mean Cholesterol Levels

	NO OF SUBJECTS	MEAN CHOLESTEROL LEVEL
HYPERTENSIVE	75	191.05
NORMOTENSIVE	75	156.80

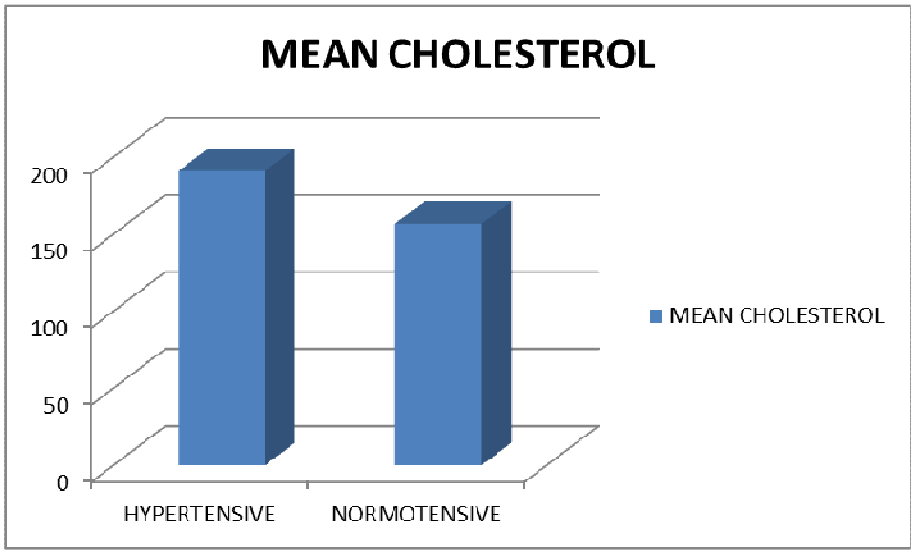


Figure – 14 : Mean Cholesterol Levels

The mean S. Cholesterol level in the hypertensives was 191.05 which is statistically significant (0.000) and higher compared to the levels in the normotensives.

The Mean Serum Cholesterol levels in the various subgroups are:

Table 13 : Mean Serum Cholesterol levels among Hypertensive Groups

	NO OF SUBJECTS	MEAN CHOLESTEROL LEVELS
NORMOTENSION	75	156.80
PRE HYPERTENSION	25	179.84
STAGE I HYPERTENSION	33	172.61
STAGE II HYPERTENSION	17	243.35

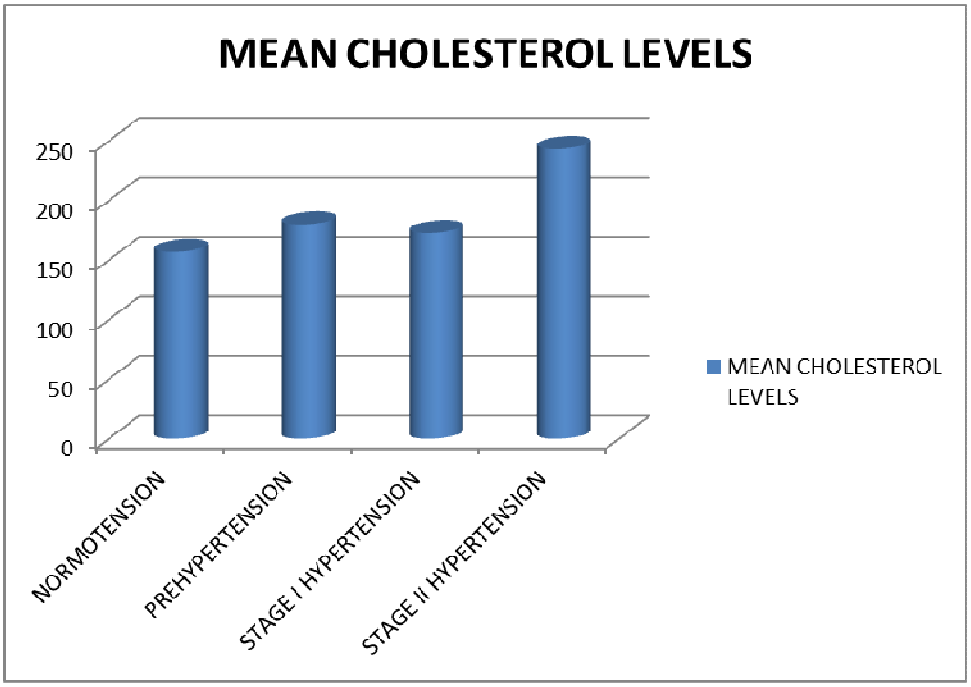


Figure – 15 : Mean Serum Cholesterol levels among Hypertensive Groups

On post hoc multiple comparative analysis among the hypertensive groups, it is found that this statistical significance exists between Stage II hypertension and the other groups (P=0.000) and also between Normotensive and Pre hypertensive group (P=0.005). In other words, there is a significant difference in Serum cholesterol levels in patients with stage II Hypertension when compared to that in other hypertensive groups and between Normotensive and Prehypertensive subjects.

Table 14 : post hoc multiple comparative analysis

(I) STAGE OF HT	(J) STAGE OF HT	SIGNIFICANCE (P VALUE)
0	1	.005
	2	.034
	3	.000
1	0	.005
	2	.441
	3	.000
2	0	.034
	1	.441
	3	.000
3	0	.000
	1	.000
	2	.000

(0-NORMOTENSION; 1- PREHYPERTENSION; 2- STAGE I HYPERTENSION; 3- STAGE II HYPERTENSION)

SERUM URIC ACID:

The primary aim of this study is to look at the levels of uric acid in various hypertensive groups and identify the level of hyperuricemia.

Table 15 : Mean Serum Uric Acid

	NO	MEAN	STANDARD DEVIATION	STANDARD ERROR OF MEAN
HYPERTENSIVE	75	5.55	2.014	0.233
NORMOTENSIVE	75	4.09	1.036	0.120

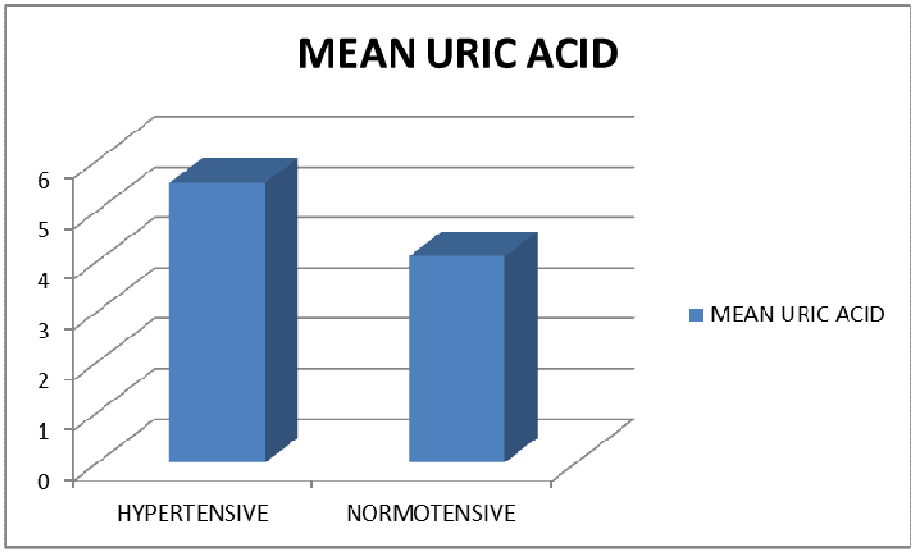


Figure – 16 : Mean Serum Uric Acid

With regards to Serum Uric Acid, P=0.000 i.e. There exists a statistical significance between hypertensive and normotensive patients with respect to BMI levels. In Hypertensive patients, the mean uric acid level is 5.55 compared to 4.09 in Normotensive patients.

Table 16 : Test of Significance

	Levene's Test for Equality of Variances	**t-test for Equality of Means**
Significance(p)	0.000	0.000

Table 17 : Mean Serum Uric Acid among Hypertensive Groups

	MEAN S. URIC ACID
NORMOTENSION	4.09
PRE HYPERTENSION	4.86
STAGE I HYPERTENSION	5.08
STAGE II HYPERTENSION	7.46

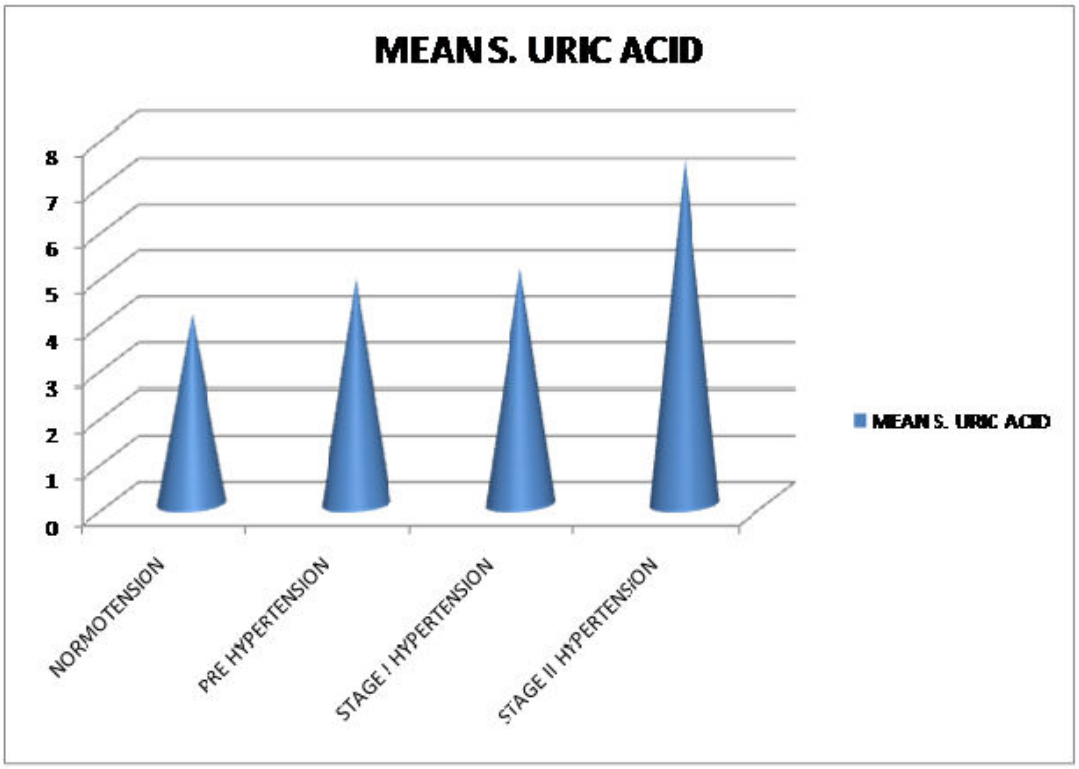


Figure – 17 : Mean Serum Uric Acid among Hypertensive Groups

On post hoc multiple comparative analyses among the hypertensive groups the following findings are present:

a) Serum uric acid is elevated as the level of hypertension increases

b) When compared to normotensive group, there is an elevation in uric acid levels in Stage I & II hypertensives which is statistically significant(p=0.001 & 0.000 respectively)

c) The higher level of serum uric acid levels in the Stage II hypertension is statistically significant across all groups.

Table 18 : Post Hoc Multiple Comparative Analyses of Uric Acid

(I) STAGE OF HT	(J) STAGE OF HT	SIGNIFICANCE(P)
0	1	.022
	2	.001
	3	.000
1	0	.022
	2	.554
	3	.000
2	0	.001
	1	.554
	3	.000
3	0	.000
	1	.000
	2	.000

(0-NORMOTENSION; 1- PREHYPERTENSION; 2- STAGE I HYPERTENSION; 3- STAGE II HYPERTENSION)

HYPERURICEMIA:

Hyperuricemia is taken as S. Uric acid > 6.8 mg/dl

Table 19 : Frequency of Hyperuricemia

Hyperuricemia	Frequency	Percentage
Absent	128	85.3
Present	22	14.7

Out of the 150 subjects, 22 had hyperuricemia.

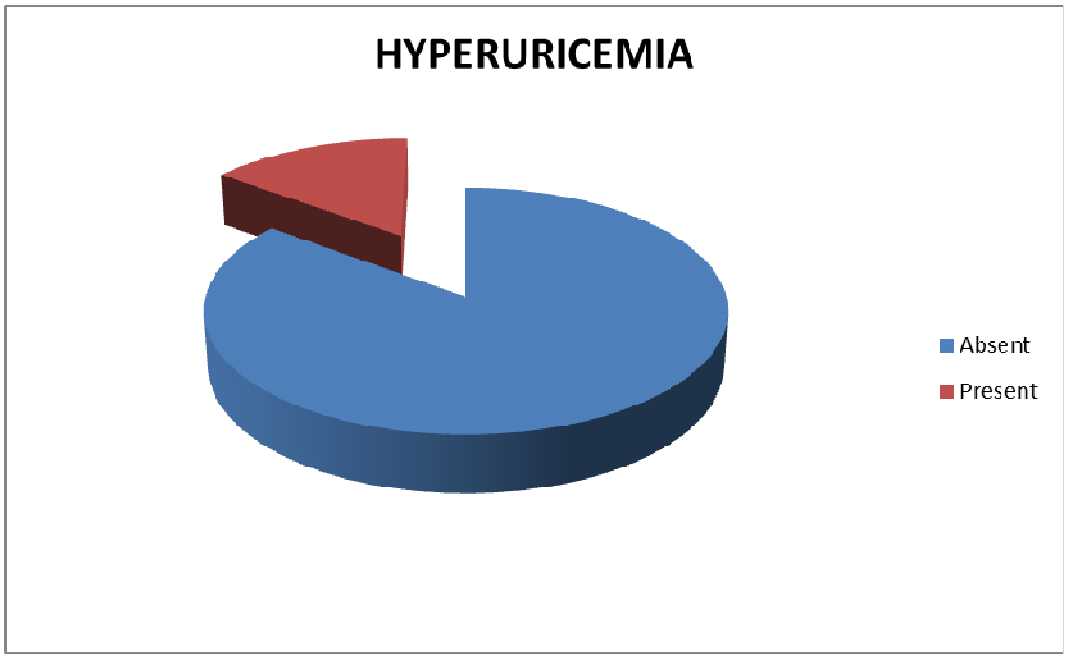


Figure – 18 : Hyperuricemia among Subjects

Table 20 : Distribution of Hyperuricemia among Hypertensive Groups

	UA< 6.8		UA≥6.8	
	NUMBER	**PERCENT**	**NUMBER**	**PERCENT**
NORMOTENSION	74	57.8	1	4.5
PRE HYPERTENSION	23	18	2	9.1
STAGE I HYPERTENSION	27	21.1	6	27.3
STAGE II HYPERTENSION	4	3.1	13	59.1

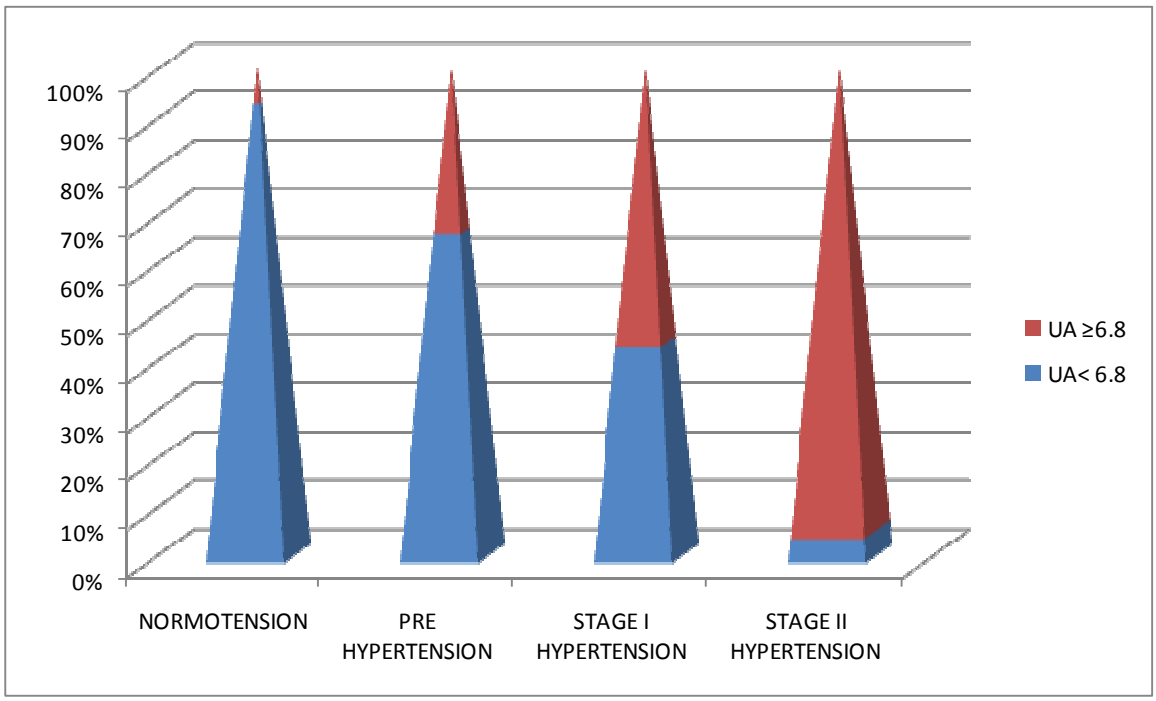


Figure – 19 : Hyperuricemia among Hypertensive Groups

With regards to hyperuricemia, p=0.000 i.e. the correlation between hyperuricemia and hypertension is statistically significant

CORRELATION OF HYPERURICEMIA WITH VARIOUS PARAMETERS WITH SBP & DBP:

Table 21 : Mean SBP and DBP among Hyperuricemic Subjects

		NO OF SUBJECTS	MEAN BP
SBP	HYPERURICEMIA	22	156.77
	NORMAL	128	122.87
DBP	HYPERURICEMIA	22	97.09
	NORMAL	128	81.91

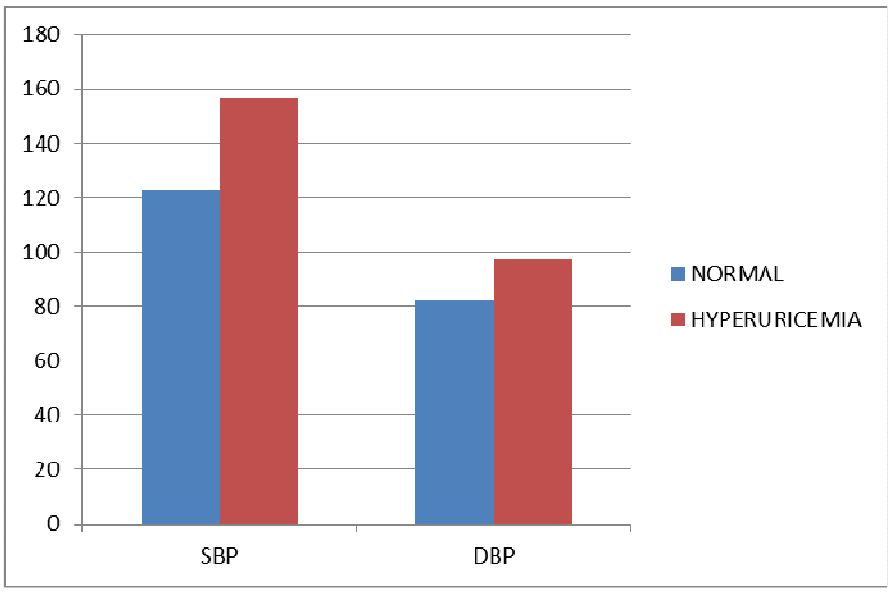


Figure – 20 : Mean SBP and DBP among Hyperuricemic Subjects

With regards to BP values, p=0.000 i.e. the correlation between hyperuricemia and value of BP, both systolic & diastolic is statistically significant. The average SBP & DBP in the hyperuricemic subjects was 156.77 & 97.09 mm Hg, values which almost correlates with Stage II Hypertension.

WITH WEIGHT AND HEIGHT:

Table 22 : Mean Weight and Height among Hyperuricemic Subjects

		NO OF SUBJECTS	Mean
WEIGHT	HYPERURICEMIA	22	70.91
	NORMAL	128	62.69
HEIGHT	HYPERURICEMIA	22	163.73
	NORMAL	128	163.78

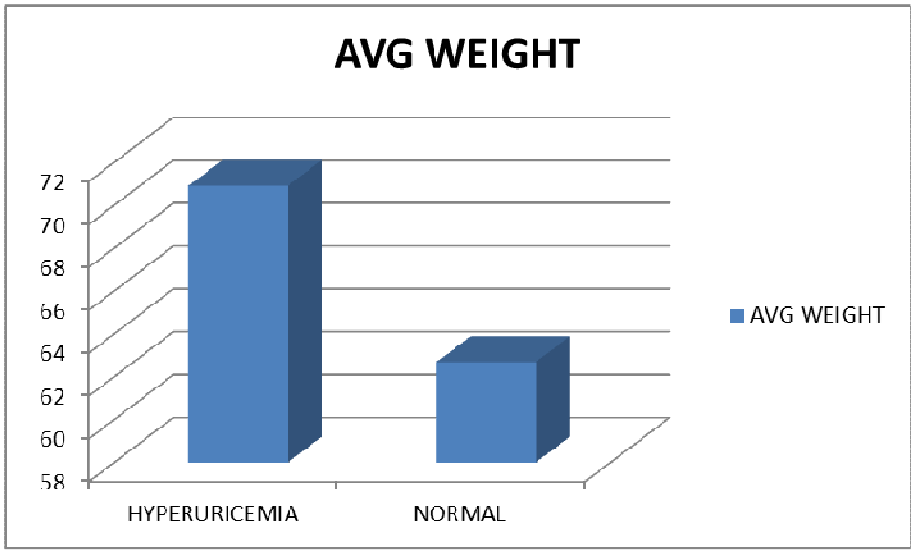


Figure – 21 : Average Weight among Hyperuricemic Subjects

With regards to anthropometric measures:

- For Weight measures, p=0.002 i.e. the correlation between hyperuricemia and weight is statistically significant. The average Weight in the hyperuricemic subjects was 70.79 kg compared to 62.69 kg in the normal group.
- For Height, the correlation is not statistically significant(p=0.9)

WITH BMI:

Table 23 : Mean BMI among Hyperuricemic Subjects

	NO OF SUBJECTS	MEAN BMI
HYPERURICEMIA	22	26.25
NORMAL	128	22.93

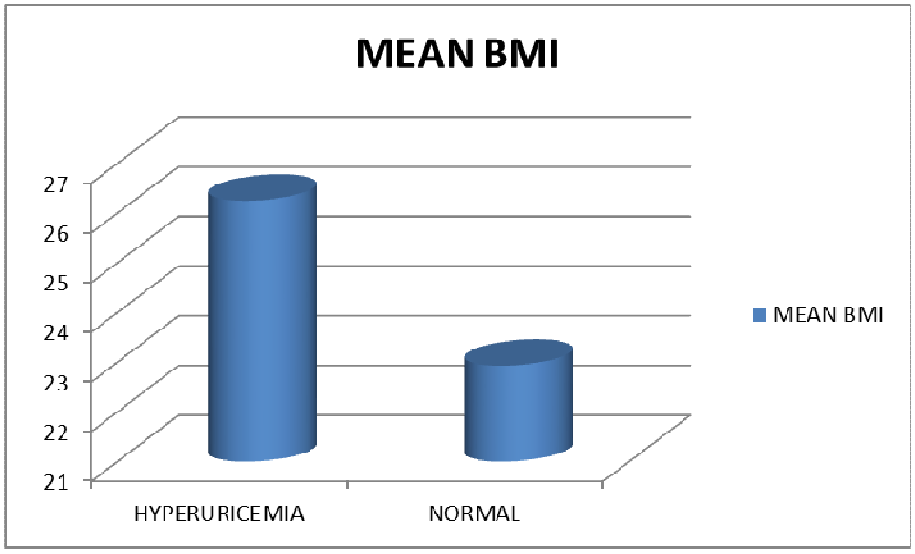


Figure – 22 : Mean BMI among Hyperuricemic Subjects

With regards to BMI, p=0.000 i.e. the correlation between hyperuricemia and BMI, is statistically significant. The average BMI in the hyperuricemic subjects was 26.25 kg, compared to 22.93 kg in normal subjects.

INFERENCES FROM CORRELATIONAL STUDIES:

- Level of hypertension increases with age
- Greater the weight and BMI, higher is the Blood Pressure
- Diabetics and those with high cholesterol levels have higher BP
- There is a strong correlation between levels of uric acid and BP levels. The correlation is strongest for Stage II Hypertension
- Asymptomatic hyperuricemia (UA≥6.8) correlates with advanced age, weight and BMI and higher SBP & DBP.

DISCUSSION

In my study, 150 subjects attending the outpatient department of our hospital for minor ailments were screened. The study group included 71 males and 79 females (47.3% & 52.3%) respectively. The age of the study group was between 30 & 60 yrs, with a distribution of 39.3%, 34.7% & 26.0% when grouped for a decade. Among the 150 subjects, 75 were found to be normotensive while the rest had an abnormal BP. The distribution among the Prehypertensive, Stage I Hypertensive & Stage II Hypertensive groups was 17% 22% & 11% respectively.

The mean age of the study group was 46.15 years. The mean age distribution among the normotensive, Prehypertensive, Stage I Hypertensive & Stage II Hypertensives was 43, 50.4, 49.9 & 46.53 years. Using ANOVA, the age distribution was found to be statistically significant meaning that age correlates with level of blood pressure with normotensive being younger than hypertensives. However, the study also throws an interesting observation that among the hypertensive population, stage II Hypertensives seem to be younger than for lesser levels of hypertension, in the study group. This is a dangerous finding and further studies are needed if this trend exists in the population at large or is just an incidental finding in this

study. There was no correlation found between the sex groups and the development of hypertension.

Analysis of the anthropometric measurements revealed that hypertensives tend to be obese compared to normotensives (66 & 61.29 kg respectively) and this was also statistically significant (p=0.028). Using post hoc analysis, this correlation was found to apply best on comparison of weight between the Normotension and Stage II Hypertension groups, and not among the other groups. However no correlation was made out between height and BP levels. On an expected note, the BMI also was found to be higher in hypertensives (p=0.00). The mean BMI level was 24.26 compared to 22.57 in the normotensive subjects. On post hoc analysis, this correlation was best appreciated between all the hypertensive groups and Stage II hypertensives i.e. these subjects were associated with very high BMI (27.26).

Among the other biochemical parameters, both FBS and serum cholesterol levels were much higher in the hypertensive group (134.60 vs 117.97 & 191.05 vs 156.80 respectively). In this correlation, multiple comparisons among the hypertensive groups were done. With regards to FBS, the difference in the value was significant between stage II hypertension (mean FBS- 168.3 mg/dl) and other groups. With regards to

serum cholesterol, a similar relationship existed (S. Cholesterol in Stage II Hypertension=243.34 mg/dl). In addition, there was also significant difference between the cholesterol levels in normotensive and prehypertension groups.

The major parameter in this study is S. Uric acid & Hyperuricemia. By levene's test & independent t- test, the relation between uric acid levels and hypertension was found to be statistically significant (p=0.00) i.e. **with increasing BP, the mean serum uric acid level also increases**(5.55 mg/dl among hypertensives vs 4.09 mg/dl in normotensive). The mean serum uric acid level among the hypertensive groups in increasing levels of BP is 4.09, 4.86, 5.08 & 7.46(in mg/dl). On post hoc multiple comparative analyses among the hypertensive groups, there was an elevation in uric acid levels in Stage I & II hypertensives which was statistically significant(p=0.001 & 0.000 respectively. The higher level of serum uric acid levels in the Stage II hypertension was statistically significant across all groups.

Hyperuricemia was seen in 22 subjects out of the 150 (14.7%) and was distributed with increasing frequency with increasing BP, with almost 60% of them in Stage II Hypertension. Using Pearson's chi- square test, the relation between hyperuricemia and hypertension was found to be statistically significant (p=0.000). Hyperuricemia was associated with

higher mean SBP (156 mm Hg) & DBP (97 mm Hg), values that almost near the levels of Stage II Hypertension. With regards to anthropometric measure, the correlation between hyperuricemia and weight was statistically significant (p=0.002). The average Weight in the hyperuricemic subjects was 70.79 kg compared to 62.69 kg in the normal group. For Height, the correlation was not statistically significant (p=0.9> 0.05). The correlation between hyperuricemia and BMI, was statistically significant (p=0.000). The average BMI in the hyperuricemic subjects was 26.25 kg, compared to 22.93 kg in normal subjects.

These results are consistent with studies by **Cannon et al** whose studies had analysed the correlation between uric acid and level of hypertension [54]. Their studies have shown that hyperuricemia was observed in 25% of hypertensive subjects who weren't treated, half of those on treatment, and almost all of those with malignant hypertension. Another study by **Bulpitt et al** [55] reported that elevated levels of uric acid were observed in half of hypertensive subjects at the national level.

The data from the First National Health and Nutrition Examination Survey (NHANES I) from NHANES I Epidemiologic Follow-up Study (NHEFS) were analysed in a landmark trial by **Fang et al** [56]. Around 6000 subjects were studied and the correlation between serum uric acid and

cardiovascular risk factors were analysed. Our results were consistent with the findings in their study which showed a significant association between uric acid and factors like blood sugar, serum cholesterol and BMI. Their results are tabulated thus.

Table 1. Characteristics by Quartiles of Baseline Level of Uric Acid*

	Quartiles of Serum Uric Acid, µmol/L									
	Men					Women				
Characteristics	1 (<321)	2 (321-363)	3 (364-416)	4 (>416)	P Value	1 (<238)	2 (238-280)	3 (281-333)	4 (>333)	P Value
No. of subjects	666	674	700	662		859	798	800	767	
Age, y	49.6 (13.9)	46.9 (14.3)	47.8 (13.9)	48.6 (13.8)	<.03	44.6 (13.1)	45.6 (13.5)	48.5 (14.0)	53.7 (13.6)	<.001
Body mass index, kg/m^2	24.0 (3.6)	25.3 (4.5)	26.1 (4.0)	27.6 (4.2)	<.001	23.5 (4.4)	24.4 (4.3)	26.0 (5.4)	29.2 (7.0)	<.001
Blood pressure, mmHg										
Systolic	131.4 (21.1)	132.9 (20.3)	132.5 (19.0)	138.2 (21.7)	<.001	124.7 (21.8)	126.7 (21.9)	131.9 (23.6)	143.4 (26.4)	<.001
Diastolic	83.5 (11.6)	84.7 (11.8)	85.3 (11.6)	89.7 (13.5)	<.001	78.8 (11.4)	80.3 (11.4)	83.3 (12.1)	88.5 (14.6)	<.001
Cholesterol, mmol/L	5.55 (1.11)	5.64 (1.11)	5.66 (1.17)	5.83 (1.19)	<.001	5.51 (1.18)	5.73 (1.21)	5.84 (1.23)	6.23 (1.30)	<.001

*Data are presented as mean (SD). To convert from µmol/L per liter to mg/dL divide by 59.48.

Table 2. Baseline Serum Uric Acid by Medical History, Behavior, Race, and Sex

	White					Black				
	Variable Present		Variable Not Present			Variable Present		Variable Not Present		
Variables	No. of Subjects	Serum Uric Acid Level, µmol/L	No. of Subjects	Serum Uric Acid Level, µmol/L	P Value	No. of Subjects	Serum Uric Acid Level, µmol/L	No. of Subjects	Serum Uric Acid Level, µmol/L	P Value
				Men						
Hypertension	208	393	2178	368	<.001	61	401	255	374	.05
Diabetes	43	357	2343	366	.27	9	343	307	382	.13
Diuretics use	66	415	2276	369	<.001	13	447	292	378	<.001
Alcohol use ≥2 times weekly	1001	384	1385	359	<.001	120	394	196	371	.04
Kidney disease	209	358	2177	367	.09	22	389	294	379	.19
Current smoking	809	363	1522	373	.10	158	378	135	380	.90
				Women						
Hypertension	345	319	2466	284	<.001	116	321	297	307	.21
Diabetes	58	307	2753	288	.05	24	343	389	309	.04
Diuretics use	307	333	2441	282	<.001	58	364	344	301	<.001
Alcohol use ≥2 times weekly	529	297	2282	286	.04	61	321	352	309	.05
Kidney disease	279	298	2532	287	.10	26	312	387	311	.97
Current smoking	742	280	1896	290	.31	148	312	231	309	.10

CONCLUSION

The findings in my study reinstate the analyses done in western world on the correlation between uric acid and hypertension. All hypertensive groups have elevated uric acid levels. The strongest correlation among the hypertensive groups is found in stage II Hypertension. It is also seen that as the stage of hypertension increases, the mean uric acid levels also increase. There is a sudden rise in the mean values from stage I to stage II. This suggests that there might be a significant role of uric acid in pathophysiology of complications of hypertension as it is well established that higher grades of hypertension are associated with greater degree of end organ damage. Asymptomatic hyperuricemia (S. Uric acid≥ 6.8 mg/dl) is significantly associated with all factors making up the components of metabolic syndrome, consistent with similar studies done in this regard. The correlation between serum uric acid levels and hypertension is an important paradigm in the identification of multiple factors involved in the pathophysiology of hypertension. The need for this comes from the fact that hypertension is a major morbidity and mortality factor which is becoming increasingly prevalent in our country. As further studies are in progress, there may come a time when drugs lowering uric acid may play a role in primary prevention of hypertension or secondary prevention of complications.

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PROFORMA

NAME:

AGE: SEX:

ADDRESS:

OP NO:

PRESENTING COMPLAINTS:

PAST HISTORY:

DRUG HISTORY:

LIFE STYLE HISTORY:

EXAMINATION:

GENERAL:

Built: Pallor: Pedal Oedema: Facial Puffiness:

VITALS:

BP MEASUREMENTS:

I: II: BP (Final):

Stage Of Hypertension (As Per JNC VII):

Pulse Rate:

Weight: Height: BMI:

SYSTEMIC EXAMINATION:

CVS:

RS:

ABDOMEN:

CNS:

MUSCULOSKELETAL:

INVESTIGATIONS:

RANDOM BLOOD SUGAR:

LIPID PROFILE:

S. URIC ACID:

Hyperuricemia: Y or N

ANALYSIS:

MASTERCHART

Name	Age	Sex	Duration of SHT	Duration of DM	SBP 1	DBP 1	SBP 2	DBP 2	SBP Final	DBP Final	Stage of SHT	Weight in Kg	Height in cm	BMI	S.uric acid	Hyperuricemia	FBS	S.cholesterol
DEVI	30	F			100	72	100	72	100	72	NORMO	54	168	19	2.3	N	90	130
UMA MAHESWARI	30	F			110	80	110	80	110	80	NORMO	48	155	20	2.4	N	70	105
SELVI	33	F			100	70	100	70	100	70	NORMO	54	157	22	2.8	N	134	176
BANU	33	F			110	70	110	70	110	70	NORMO	71	165	26	3.4	N	142	167
KALA	33	F			120	80	120	80	120	80	NORMO	48	155	20	4	N	96	134
RENUKA	34	F			100	70	100	70	100	70	NORMO	73	178	23	2	N	80	187
SANTHAKUMARI	34	F			100	78	100	70	100	74	NORMO	78	168	28	4.3	N	120	234
KAMARUNISHA	36	F			120	80	120	80	120	80	NORMO	43	115	19	4.9	N	150	140
TAMIL ILAKIYA	36	F			110	70	110	70	110	70	NORMO	62	163	23	2.5	N	80	179
AMMU	36	F			110	80	110	80	110	80	NORMO	63	165	23	2.5	N	89	142
INDRA	37	F			120	70	120	70	120	70	NORMO	57	155	24	4.1	N	100	134
RAMAYEE	37	F			120	80	120	80	120	80	NORMO	42	156	20	4.2	N	110	156
JAYASREE	38	F			96	66	100	66	98	66	NORMO	64	165	20	2.7	N	115	140
SHALU	38	F		NEW	110	80	110	80	110	70	NORMO	83	175	27	5.1	N	155	219
MUNIAMMAL	39	F			110	80	110	80	110	80	NORMO	51	160	20	4.9	N	109	110
RAMYA	39	F			110	70	110	70	110	70	NORMO	68	172	23	4.6	N	230	180
DHANALAKSHMI	40	F			110	70	110	70	110	70	NORMO	64	165	20	6.9	Y	120	234
JACQUELIN	40	F			110	80	110	80	110	80	NORMO	66	170	23	3.6	N	104	155
HAMSA	42	F			100	78	100	70	100	74	NORMO	48	155	20	4.8	N	120	156
ANJALAI	43	F			110	80	110	80	110	80	NORMO	42	156	20	5.8	N	80	118
USHA	45	F			100	70	110	70	100	70	NORMO	43	115	19	3	N	80	112
ANANTHANAYAGI	45	F			110	80	110	80	110	80	NORMO	64	165	20	4.7	N	148	168
RADHA	45	F			120	88	120	80	120	84	NORMO	83	175	27	5	N	123	165

Name	Age	Sex	Duration of SHT	Duration of DM	SBP 1	DBP 1	SBP 2	DBP 2	SBP Final	DBP Final	Stage of SHT	Weight in Kg	Height in cm	BMI	S.uric acid	Hyperuricemia	FBS	S.cholesterol
CHINNAPONNU	45	F			110	80	110	80	110	80	NORMO	62	163	23	3	N	100	132
THULUKANAM	46	F			110	70	110	70	110	70	NORMO	78	168	28	3.5	N	110	160
RADHIKA	46	F			110	80	110	80	110	80	NORMO	48	155	20	4	N	90	110
JAYALAKSHMI	47	F			110	80	110	80	110	80	NORMO	48	155	20	3.1	N	115	140
THAVASELVI	50	F		15	120	80	120	80	120	80	NORMO	55	155	23	2.5	N	155	146
BADHUR NISHA	50	F			110	80	110	80	110	80	NORMO	60	157	25	3.3	N	90	130
MANMAYA	53	F			110	80	110	80	110	80	NORMO	61	175	20	5	N	89	177
DHANALAKSHMI	53	F		NEW	110	80	110	80	110	80	NORMO	42	156	20	2.5	N	176	156
SORAJA	54	F		15	110	80	110	80	110	80	NORMO	51	160	20	3.6	N	176	155
SAVITHRI	58	F			110	80	110	80	110	80	NORMO	64	165	20	3.1	N	100	150
JAYALAKSHMI	60	F			110	80	110	80	110	80	NORMO	54	150	24	4.7	N	122	268
HARISH	30	M			120	80	120	80	120	80	NORMO	55	155	23	4.4	N	78	154
TIRUMALAI	30	M			110	70	110	70	110	70	NORMO	68	172	23	4.6	N	102	155
SUBBURAYAN	30	M			100	70	100	70	100	70	NORMO	78	168	28	4.2	N	105	150
RAMESH	30	M			110	80	110	80	110	80	NORMO	68	172	22	4	N	90	120
YASEEN	30	M			96	60	100	60	98	60	NORMO	48	155	20	4.3	N	88	120
SAKTIVAL	31	M			110	70	110	70	110	70	NORMO	55	163	21	3.2	N	88	132
DHANANJAYAN	32	M			120	80	120	80	120	80	NORMO	68	172	22	4.6	N	98	175
RAMAKRISHNAN	32	M			100	80	100	80	100	80	NORMO	64	165	20	3.8	N	86	100
PRAKASH	32	M			100	70	100	70	100	70	NORMO	71	165	26	4.2	N	90	150
NAVEEN	33	M			110	80	110	80	110	80	NORMO	67	168	24	4.1	N	107	140
SIVA	36	M			120	80	120	80	120	80	NORMO	55	163	21	4.5	N	100	146
GOVINDAN	38	M			110	80	110	74	110	77	NORMO	64	165	20	5.7	N	90	110
KUMAR	38	M			110	70	110	70	110	70	NORMO	48	155	20	5.5	N	144	178
KUMAR	39	M			120	80	124	80	122	80	NORMO	64	165	20	3.7	N	88	150

Name	Age	Sex	Duration of SHT	Duration of DM	SBP 1	DBP 1	SBP 2	DBP 2	SBP Final	DBP Final	Stage of SHT	Weight in Kg	Height in cm	BMI	S.uric acid	Hyperuricemia	FBS	S.cholesterol
HARRIS	39	M			100	66	100	68	100	67	NORMO	68	172	22	3.8	N	100	150
RAVIKUMAR	40	M			120	80	120	80	120	80	NORMO	61	160	24	6	N	154	168
RAVIKUMAR	40	M			120	80	120	80	120	80	NORMO	42	156	20	4.4	N	80	160
MAYILVAHANAN	41	M	NEW		146	94	146	94	146	94	NORMO	81	168	29	4.7	N	122	170
RAVI	42	M			120	70	120	70	120	70	NORMO	55	163	21	4.8	N	110	160
SIVAKUMAR	42	M			110	80	110	80	110	80	NORMO	66	178	21	3.1	N	98	143
ISMAIL	42	M			120	80	120	80	120	80	NORMO	55	163	21	3.6	N	120	234
SHANKAR	45	M			110	70	110	70	110	70	NORMO	68	172	23	3.8	N	90	130
MUNIUSAMY	46	M			110	80	110	80	110	80	NORMO	55	163	21	5	N	110	123
SRINIVASAN	47	M			120	80	120	80	120	80	NORMO	68	172	22	6.5	N	120	180
BABU	48	M			110	80	110	80	110	80	NORMO	55	155	23	4.4	N	180	150
JAYASEELAN	48	M			110	80	110	80	110	80	NORMO	73	178	23	3.5	N	123	165
ISMAIL	48	M			100	80	100	80	100	80	NORMO	83	175	27	3.8	N	130	150
SATISH	49	M			120	80	120	80	120	80	NORMO	72	160	28	4.7	N	130	179
CHANDRAMOHAN	49	M		2	120	80	120	80	120	80	NORMO	81	168	29	4.5	N	180	187
THOMAS	50	M			100	70	100	70	100	70	NORMO	83	175	27	3.7	N	148	168
ANBUSELVAM	50	M		4	110	80	110	80	110	80	NORMO	51	160	20	4.3	N	155	210
DEVAN	54	M		15	110	80	110	80	110	80	NORMO	59	168	21	4.8	N	190	180
KAMAL	55	M			110	80	110	80	110	80	NORMO	63	165	23	5.2	N	144	178
GANDEEBAN	55	M			120	70	120	70	120	70	NORMO	68	172	23	3.1	N	150	140
SUBRAMANIAM	55	M			110	80	110	80	110	80	NORMO	78	168	28	3.8	N	78	123
ANNAMALAI	56	M			120	80	120	80	120	80	NORMO	66	170	23	2.5	N	130	179
LAKSHMANAN	58	M			120	80	120	80	120	80	NORMO	81	168	29	4.1	N	148	168
SUBRAMANI	60	M			110	70	110	70	110	70	NORMO	66	170	23	6.6	N	98	160
SANTHANAM	60	M		5	120	80	120	80	120	80	NORMO	55	163	21	3.7	N	230	180

Name	Age	Sex	Duration of SHT	Duration of DM	SBP 1	DBP 1	SBP 2	DBP 2	SBP Final	DBP Final	Stage of SHT	Weight in Kg	Height in cm	BMI	S.uric acid	Hyperuricemia	FBS	S.cholesterol
MANIKANNAYYA	60	M			120	88	120	80	120	84	NORMO	68	172	22	4.3	N	110	160
AYYAVU	60	M			120	80	120	80	120	80	NORMO	48	155	20	4.7	N	98	120
BAVANI	33	F			130	90	130	90	130	90	PRE	66	178	21	4.2	N	115	140
LAKSHMI BAI	40	F			130	90	130	90	130	90	PRE	60	160	23	4.2	N	133	177
DURGA DEVI	41	F			130	80	130	90	130	85	PRE	68	172	23	6.2	N	121	188
USHA	45	F		5	130	80	130	80	130	80	PRE	48	154	20	3	N	176	188
ELIZABETH	47	F			130	80	130	80	130	80	PRE	62	158	25	1.9	N	90	160
KASTHURI	57	F			136	80	136	80	136	80	PRE	60	161	24	4.9	N	100	150
PARVATHY	60	F			130	70	130	80	130	75	PRE	62	163	23	3.8	N	110	130
SUSEELA	60	F			132	86	132	86	132	86	PRE	48	155	20	3.1	N	80	122
RADHAMMAL	60	F			130	80	130	80	130	80	PRE	83	175	27	3	N	77	156
VALLIAMMAL	60	F		8	130	80	130	80	130	80	PRE	64	165	20	4.3	N	180	245
SATISH	32	M			130	80	130	80	130	90	PRE	61	175	20	5	N	145	210
MURUGAN	33	M			136	86	132	80	134	83	PRE	83	175	27	6	N	170	220
SATYARAJ	42	M			130	90	130	90	130	90	PRE	64	168	23	4.2	N	90	120
RAVI	46	M			130	90	130	90	130	90	PRE	51	160	20	6.5	N	122	180
GANESH	48	M			130	80	130	80	130	80	PRE	66	170	23	3.9	N	150	140
SEKAR	50	M			130	90	130	90	130	90	PRE	55	163	21	8	Y	190	255
SAHAYA RAJ	50	M			130	80	130	80	130	80	PRE	72	160	28	5.9	N	112	132
KUBERAN	50	M			130	80	130	80	130	80	PRE	83	175	27	4.9	N	130	170
MANI	53	M		5	130	90	130	90	130	90	PRE	66	170	23	4.6	N	180	198
PRAKASH	56	M			130	90	130	90	130	90	PRE	70	175	23	6.1	N	85	198
PALANI	57	M			130	80	130	80	130	80	PRE	55	163	21	5.8	N	110	280
PAZHANISAMY	60	M			130	80	130	80	130	80	PRE	83	175	27	5	N	120	156
RATHINAM	60	M			130	90	130	90	130	90	PRE	64	165	20	6.8	Y	132	221

Name	Age	Sex	Duration of SHT	Duration of DM	SBP 1	DBP 1	SBP 2	DBP 2	SBP Final	DBP Final	Stage of SHT	Weight in Kg	Height in cm	BMI	S.uric acid	Hyperuricemia	FBS	S.cholesterol
NAVIN	60	M			130	80	130	80	130	80	PRE	63	165	23	5	N	108	160
RAJAMANI	60	M		5	130	90	130	90	130	90	PRE	61	160	24	5.2	N	180	200
KAUSALYA	35	F	NEW	12	140	90	140	90	140	90	I	72	160	28	6.6	N	166	198
MARY	40	F	2		150	90	150	90	150	90	I	54	150	24	7.2	Y	123	156
MABHUNISHA	40	F	4		140	100	140	100	140	100	I	51	153	22	3.4	N	80	122
IRUDAYARANI	41	F	NEW		140	100	140	90	140	95	I	54	150	24	4.2	N	110	160
VASUKI	43	F	1		140	90	140	90	140	90	I	84	168	30	5.7	N	133	188
JAYALAKSHMI	45	F	2		140	96	140	96	140	96	I	60	157	25	8	Y	142	244
LOGANAYAGI	45	F	1	3	140	90	140	100	140	95	I	81	168	29	4.8	N	100	143
AARTHI	45	F	NEW	NEW	150	90	150	90	150	90	I	62	159	24	6	N	205	190
KALA	46	F	0		140	80	140	80	140	80	I	63	165	23	6.6	N	132	180
BEAULA	48	F	1		140	100	140	90	140	95	I	83	175	27	6.1	N	120	178
SUJEETHA	48	F	2		140	90	140	90	140	90	I	48	155	20	5	N	99	149
SHANMUGAVALLI	50	F	NEW		130	90	130	90	130	90	I	55	163	21	3.3	N	98	165
FATHIMA	51	F	10		140	90	140	90	140	90	I	66	170	23	6.8	Y	133	187
ELLAMMA	55	F			140	94	136	90	138	92	I	60	157	25	8.8	Y	120	256
KARUPAYEE	55	F	5	5	140	90	140	90	140	90	I	83	175	27	3	N	100	154
KANTHA	55	F	3		140	100	140	90	140	95	I	52	159	20	4.1	N	110	165
DHANALAKSHMI	55	F	2		140	90	140	90	140	90	I	51	157	20	1.9	N	109	151
RAJBHAI	60	F		2	142	80	140	80	141	80	I	72	160	28	8.8	Y	221	240
SUBBAMMA	60	F	4		150	90	150	90	150	90	I	64	165	20	4.3	N	110	165
RUKMANI	60	F	2		140	80	140	80	140	80	I	68	172	22	4.2	N	88	143
RANI	60	F	5		140	90	140	90	140	90	I	60	168	21	4.2	N	98	159
KASTHURI	60	F	5	10	130	90	130	90	130	90	I	50	156	20	2.9	N	108	154
BABU	30	M			140	90	140	90	140	90	I	63	165	23	4.3	N	123	165

VADIVELU	43	M	NEW		150	96	150	90	150	93	I	42	156	20	2.8	N	100	132
SHANMUGAM	45	M	5		150	100	150	100	160	100	I	95	172	32	4.3	N	155	210
SRINIVASAN	46	M	5		140	90	140	90	140	90	I	54	168	19	4.9	N	130	179
KANNIAPPAN	48	M			130	90	130	90	130	90	I	54	164	20	3.7	N	98	167
MOORTHY	54	M			150	100	154	100	152	100	I	67	168	24	5.1	N	116	158
VENKATESH	54	M	NEW		140	90	140	90	140	90	I	64	163	24	4.5	N	144	188
RADHAKRISHNAN	55	M	NEW		146	90	146	90	146	90	I	63	165	23	6.1	N	88	140
BHASKAR	57	M			146	90	140	90	143	90	I	70	175	23	4.4	N	120	156
PATTBIRAMAN	58	M	1		140	90	140	90	140	90	I	54	157	22	4.9	N	125	174
THANGAN	60	M	1		150	90	150	90	150	90	I	83	175	27	6.9	Y	120	180
INDRA	37	F	5	5	160	100	160	100	160	100	II	74	162	28	8.8	Y	210	276
CHOKKAMMA	40	F	4		150	100	150	100	150	100	II	68	172	23	7.3	Y	143	203
RAMYA	44	F	5	8	180	100	180	100	180	100	II	70	158	28	8	Y	210	255
LILLY	48	F	NEW		160	100	160	100	160	100	II	56	157	22	2.6	N	124	144
DEVI	48	F	10	8	200	110	200	120	200	115	II	60	149	28	9.8	Y	258	243
DEVI	49	F	NEW		168	100	162	100	165	100	II	78	168	28	8.7	Y	110	275
KAVITA	50	F			160	100	160	100	160	100	II	81	168	29	8	Y	110	280
JAMUNA	50	F	NEW		170	90	170	100	170	95	II	78	168	28	7.8	Y	123	185
DHANAM	50	F	5		150	110	150	110	150	110	II	70	163	28	6.6	N	140	200
GAYATRI	50	F	8	8	190	110	190	110	190	110	II	70	152	31	10	Y	277	287
AMMU	53	F		NEW	160	100	160	96	160	98	II	83	175	27	7.2	Y	132	266
KUPPU	54	F	3		160	100	160	100	160	100	II	70	158	28	3	N	100	160
CHANDRA	55	F	2		170	100	170	100	170	100	II	60	160	23.5	7.2	Y	160	275
NAGARAJ	30	M	NEW	NEW	180	120	170	110	175	115	II	95	172	32	10.6	Y	208	256
NAZEEMUDIN	37	M	NEW	NEW	170	100	170	100	170	100	II	52	154	21	4.7	N	180	288
CHERAN	42	M	NEW		170	110	170	110	170	110	II	84	168	30	9	Y	146	268
RAJATRATNAM	54	M	2	5	170	110	170	100	170	105	II	81	168	29	7.5	Y	234	276

ETHICAL COMMITTEE APPROVAL CERTIFICATE

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.8139/ME-1/Ethics/2012 Dt:06.09.2012.
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on A comparative analysis on serum uric acid levels in the spectra of hypertension" - For Dissertation purpose submitted by Dr.K.Bharadhwaj, IIIrd year, MD (GM), PG Student, KMC, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE * Kilpauk, Chennai-10. * 14 SEP 2012

CHAIRMAN, 14/9/12
Ethical Committee
Govt.Kilpauk Medical College,Chennai