JULY-SEPTEMBER 2016 ▪ VOL. 1 ▪ ISSUE NO. 1

CLINICAL JOURNAL OF HYPERTENSION

OFFICIAL PUBLICATION OF

Hypertension Society of India

www.hsindia.org

EDITOR-IN-CHIEF
Dr. Siddharth N. Shah

CLINICAL
Journal of Hypertension

Official Publication of
Hypertension Society India

Vol. 1, Issue No. 1 • July-September 2016

Contents

Governing Body

Editorial

Hypertension: The Growing Trend

Siddharth N Shah[1]

I have great pleasure in presenting before you the renewed version of "Clinical Journal of Hypertension" an official publication of Hypertension Society of India. The earlier journal "Hypertension India" was discontinued in view of objection from Indian Newspaper Association for the title of the journal. I am sure you all will welcome the new format of the journal.

High Blood Pressure is a major public health problem in India and its prevalence is rapidly increasing in India. Current estimates puts the incidence of hypertension to 20-40% in urban area and 12-17% in rural areas of India and one in three adults suffer from hypertension "a Silent Killer". The prevalence of hypertension in India is more than 82 million persons suffering from it, even more than other co-morbid conditions like diabetes, obesity, dyslipidemia and kidney disease. It is projected that 213 million Indians will suffer from Hypertension by 2025 of these 25-30% will be from urban areas and 15-18% from rural population. Thus bridging the gap between urban and rural divided in view of rapid urbanization. Hypertension is one of the common non communicable diseases.

High blood pressure is ranked as the third most important risk factor for attributable burden of disease in south Asia 2010[1] and is directly responsible for 7% of all stroke deaths and 25% of all coronary heart disease deaths in India.[2] The WHO rates high blood pressure as one of the most important cause of premature death worldwide.[3] It is important to note that only 35.6% treated patients had their B.P. under control.[4] Thus Hypertension is an important public heath challenge in both economically developing and developed countries. In recent studies in two rural areas, the prevalence of hypertension was 14.1% among 1005 subjects selected using systematic random sampling method.[6] Hypertension was significantly higher in individuals more than 35 years and significantly higher in those who take alcohol and subject with raised total cholesterol level.

In many of the cases of hypertension, the etiologies is undetermined and is attributable to genetic causes. One needs to look at various other reported causalities/association of hypertension. Factors like insulin resistance hyperuricemia, obesity, dietary salt, alcohol

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consumption, anxiety, and its relation to hypertension have been published.

Looking at the existing burden of disease, the Indian Government has initiated the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke for prevention and Control of disease at community level.[7]

This issue of the Clinical Journal of Hypertension includes the contribution made by eminent faculty of HSICON 2016. The article on theme "Home Blood Pressure Monitoring" by Dr. A. Muruganathan describes his experience during the last one year in propogating the concept of Home Blood Pressure monitoring for all. The article on hypertension and hyperuricemia by Dr. B.R. Bansode enumerates pathophysiology of hyperuricemia and its effect on hpertension and the recent trials published on this subject. Dr. G.S. Wander in his scholarly style has discussed the impact of various trials on hypertension in the last one year. The article by Dr. Shashank Joshi on "Salt Sensitivity in Hypertension" discusses the ever important debated role of salt in Hypertension. The journal also includes original articles and abstract presented during the conference at HSICON 2015 at Indore.

It is our endeavor to increase the awareness of hypertension through this journal. An urgent need is to document and assess the burden of hypertension. Also studies to determine the cause which is considered as "Silent Killer" should be undertaken and published. I appeal to all the members of the Hypertension Society of India to contribute to the journal. I assure you my best editorial assistance in fast tracking, peer reviewing and publishing your contribution for the journal.

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Scientific Programme

Friday 19th August, 2016

2.00 pm	**Workshop 1 : Blood Pressures Monitoring** *Mentor:* **Dr. G.S. Wander** Introduction: **Dr. G.S. Wander** B.P. Instruments and Monitoring: **Dr. Santosh Salagre** Home Blood Pressure Monitoring: **Dr. Nihar Mehta** Ambulatory BP Monitoring: **Dr. Dilip Kirplani** 2D ECHO in Hypertension: **Dr. B.R. Bansode** Discussion	**Workshop 2 : Diabetes - Monitoring** *Mentor:* **Dr. S.D. Mehtalia** Introduction Diabetes monitoring Urine, Blood: **Dr. Tejas Shah** Home Blood Glucose Monitoring: **Dr. Vijay Negalur** C.G.M.S.: **Dr. Manoj Chawla** Insulin Infusion Pump: **Dr. Jayanta Panda** Discussion

3.30 pm	TEA BREAK	
4.00 pm - 4.20 pm	*Chairpersons:* **Dr. R.R. Singh, Dr. Jyotirmoy Pal, Dr. Palaniappan**	
	Home Blood Pressure Monitoring - One Year Experience	**Dr. A. Muruganathan**
4.20 pm - 4.40 pm	*Chairpersons:* **Dr. M.P.S. Chawla, Dr. Kunal Kothari, Dr. A.R. Vijaykumar**	
	1st National Hypertension Conference Oration	
	Ten Commandments of Hypertension Management	**Dr. G.S. Wander**
4.40 pm - 5.00 pm	*Chairpersons:* **Dr. V. Parameshwara, Dr. N.R. Rau, Dr. Milind Nadkar**	
	HOLD Concept and Conceptualisation	**Dr. Siddharth N. Shah**
5.00 pm - 5.20 pm	*Chairpersons:* **Dr. B.B. Thakur, Dr. Ashok Taneja, Dr. Pritam Gupta**	
	Lifestyle Management in HOLD	**Dr. Y.P. Munjal**
5.20 pm - 5.40 pm	*Chairpersons:* **Dr. Sukumar Mukherjee, Dr. Mangesh Tiwaskar, Dr. K.C.Mehta**	
	Uric Acid and Hypertension	**Dr. B.R. Bansode**
5.40 pm - 6.30 pm	*Chairpersons:* **Dr. A.M. Argikar, Dr. R. Chandni, Dr. Charu Jani**	
	Clinical Case Discussion	**Dr. Falguni Parikh**
6.30 pm	**PANEL DISCUSSION:** Initiation and Continuation of Hypertensive Therapy	
	Moderator: **Dr. G.S. Wander**	
	Panelists: **Dr. Ramesh Dargad , Dr. Y.P. Munjal, Dr. Nihar Mehta, Dr. Sukumar Mukherjee**	
7.30 pm	DINNER	

Saturday 20th August, 2016

9.00 am - 10.30 am	**Workshop 3 : Lipid Guidelines**	**Workshop 4 : Obesity**
	Mentor: **Dr. R.C. Khokhani**	*Mentor:* **Dr. Shashank Joshi**
	Discussant	Discussant
	Introduction: **Dr. R.C. Khokhani**	Introduction: **Prof. Shashank Joshi**
	Total Cholesterol and LDL Cholesterol: **Dr. R. Agarwal**	Challenges in Diet for Obesity: **Dr. Soumitra Ghosh**
	HDL Cholesterol: **Dr. Bhavesh Vajifdar**	Meal Replacers in Obesity: **Dr. Shilpa Joshi**
	Hypertriglyceridemia: **Dr. Vijay Surase**	Non-Invasive Management of Obesity: **Dr. Geetaa Shah**
	Other Lipid Parameters: **Dr. Sadanand Shetty**	Peri-operative Management of Bariatric Surgery **Ms. Vaishali Shah & Ms. Anuja Khambkar**
	Management Challenges All panellist : Case Discussion	O.S.A. and Obesity: **Dr. Nimish Shah**
	Concluding remark: **Dr. R.C. Khokhani**	Discussion

10.30 am - 11.00 am TEA BREAK

11.00 am - 11.20 am *Chairpersons:* **Dr. Y.S.N. Raju, Dr. Sukumar Mukherjee, Dr. Isaac Moses**

U.N. Mehta Torrent Oration

Common Pitfalls in the Diagnosis and management of Hypertension — **Dr. M. Maiya**

11.20 am - 11.40 am *Chairpersons:* **Dr. B.B. Rewari, Dr. D.P. Singh, Dr. Jai Bhagwan**

Best Practices in Hypertension 2016 — **Dr. P.C. Manoria**

11.40 am - 12.00 pm *Chairpersons:* **Dr. Shashank Joshi, Dr. Alaka Deshpande, Dr. Agam Vora**

DEBATE

All obese patients must undergo Bariatric Surgery

For: **Dr. Shashank Shah**

Against: **Dr. Soumitra Ghosh**

12.00 pm - 12.30 pm *Chairpersons:* **Dr. Sudhir Mehta, Dr. N.P. Singh, Dr. P.K. Sinha**

Masked Hypertension — **Dr. G. London**

12.30 pm - 01.00 pm *Chairpersons:* **Dr. Kamlesh Tiwari, Dr. Rajesh Upadhyaya, Dr. J.L. Pungalia**

Clinical Relevance of High Intensity Statins — **Dr. Peter Toth**

01.00 pm - 02.00 pm LUNCH

Saturday 20th August, 2016

02.00 pm - 03.30 pm	**Insulin Symposium** *Chairpersons:* **Dr. R.B. Phatak, Dr. S. Jayaram, Dr. S.M. Bandookwala**	**Workshop 5 : Resistant Hypertension** *Mentor:* **Dr. Ashok Kirpalani**
02.00 pm - 02.30 pm	Getting to the heart of the matter: Implications of LEADER results: **Dr. John Wilding (UK)**	**Discussant**
02.30 pm - 02.50 pm	Evolution of premix insulins - A leap from human premix to modern co-formulations: **Dr. Piya Ballani Thakkar**	To define resistant hypertension; differentiate between resistant and refractory, and show various ways of ruling out white coat: **Dr. Ashok Kirpalani**
02.50 pm - 03.10 pm	Difference in risk of hypoglycaemia with Basal Insulins - The Verdict is out: **Dr.Anil Bhoraskar**	To enumerate renal diseases and renovascular. Who should be investigated and how for reno-vascular disease: **Dr. N.P. Singh**
03.10 pm - 03.30 pm	**Panel Discussion**	To enumerate adrenal diseases, who should be investigated, limitations of.hormone assays, which tests are now obsolete, nuclear imaging and limitations relating to pheo and Conn's.also who should be operated and how to follow up: **Dr. N.F. Shah** Drug therapy of renal parenchymal diseases. Choices and precautions. Pls also discuss sleep apnoea: **Dr. Alan Almeida** Renovascular intervention trials, current status of BAT and renal denervation: **Dr. Gérard London** Table discussion by Q&A by moderator with audience sending written questions

03.30 pm - 04.00 pm	TEA BREAK	
04.00 pm - 04.20 pm	*Chairpersons:* **Dr. R.R. Chaudhary, Dr. R.K. Bansal, Dr. S. Chakraborty** Hypertension and Stroke	**Bhupendra Chaudhary**
04.20 pm - 04.40 pm	*Chairpersons:* **Dr. S.V. Kulkarni, Dr. R.K. Goyal, Dr. Rakesh Gupta** Azilsartan in Hypertension- What's New	**Dr. Jamshed Dalal**
04.40 pm - 05.00 pm	*Chairpersons:* **Dr. A.M. Bhagwati, Dr. Munish Prabhakar, Dr. S. Arulrhaj** Does Legacy Effect exist in Hypertension	**Dr. Dheeraj Kapoor**
05.00 pm - 05.20 pm	**GUEST LECTURES** *Chairpersons:* **Dr. A.N. Rai, Dr. Sandhya Kamath, Dr. S.B. Ganguly** Hydroxychloroquine in Diabetes	**Dr. Rajeev Chawla**
05.20 pm - 05.40 pm	*Chairpersons:* **Dr. Iqbal Bagasrawala, Dr. Snehal Tanna** Are DPP4 made different following CVOT Trials	**Dr. Shashank Joshi**
05.40 pm - 06.10 pm	*Experts :* **Dr. Jamshed Dalal, Dr. Vijay Negalur** Life after EMPAR-REG : Dialogue with Expert	**Dr. Viraj Suvarna**

6.10 pm - 6.30 pm	*Chairpersons:* **Dr. G.S. Sainani, Dr. Vikram Londhey, Dr. Anupam Prakash**	
	Siddharth N. Shah - Epidemiology Oration	
	The Value of Echocardiography in the Management of Systemic Hypertension : Immense yet Underutilized	**Dr. Ravi R. Kasliwal**
6.30 - 7.00 pm	**Presidental Oration**	
	Salt Sensitivity in Hypertension	**Dr. Shashank Joshi**
07.15 pm	**Inauguration of 2nd HOLD Conference**	
9.00 pm	Entertainment Programme & Dinner	
9.00 pm	e-Hypertension Live Web Cast (Grand Salon)	

Sunday 21st August, 2016

9.00 am
10 .30 am

Workshop 6 : Diabetic Foot

Mentor: **Dr. Vijay Vishwanathan**

Discussant

Introduction Modern Management of DFU: **Dr. Vijay Vishwanathan**

Evaluation: **Dr. Dakshata Padhye**

Neuropathic Foot: **Dr. Benny Negalur**

Vasculopathy: **Dr. Ragini Maheshwari**

Prosthesis: **Dr. Vijay Vishwanathan**

Discussion: **Dr. Banshi Saboo**

Challenges in Management

Chairpersons: **Dr. Girish Mathur, Dr. A.K. Mukherjee, Dr. Altamas Shaikh**

Beta Blockers in Hypertension : **Dr. Amit Saraf**

Alpha Blockers in Hypertension: **Dr. R.K. Jha**

Pioglitazone in Diabetes: **Dr. Vijay Panikar**

10.30 am - 11.00 am TEA BREAK

11.00 am - 11.30 am *Chairpersons:* **Dr. Dilip Kirplani, Dr. Hemal Shah, Dr. Rohini Handa**
Anti-hypertensive Medication in Diabetic Kidney Disease — **Dr. G. London**

11.30 am - 11.50 am *Chairpersons:* **Dr. Anita Jaiswal, Dr. Shibendu Ghosh, Dr. R.M. Chhabra**
Ophthalmic Manifestation of Lipids, Hypertension and Diabetes — **Dr. Yash Shah**

11.50 am - 12.10 pm *Chairpersons:* **Dr. Rakesh Sahay, Dr. N.K. Soni, Dr. Mahesh Marda**
Consensus on Injectable therapies in routine outpatient care of type 2 diabetes in India : Outcomes from CID 2015 — **Dr. Rajiv Kovil**

12.10 pm - 12.30 pm *Chairpersons:* **Dr. K.K. Parekh, Dr. R.N. Sarkar, Dr. A.P.Misra**
Diabetes and Hypertension - Double Whammy — **Dr. Siddharth N. Shah**

12.30 pm - 01.00 pm **P.J. Mehta Oration - Award Session**
Judges: **Dr. Falguni Parikh, Dr. Kunal Kothari, Dr. R. Chandni**

01.00 pm - 01.45 pm **PANEL DISCUSSION : After Metformin What?**
Moderator: **Dr. Shashank Joshi**
Panelists: **Dr. R.K. Sahay, Dr. Vijay Panikar, Dr. Banshi Saboo, Dr. Mangesh Tiwaskar, Dr. Siddharth N. Shah**

01.45 pm - 02.00 pm Valedictory Session

02.00 pm LUNCH

Presidential Oration

Salt Sensitivity in Hypertension

Shashank R Joshi

INTRODUCTION

Salt and Sodium has been intensely studied for its role in human physiology and impact on human health. In particular, excessive dietary salt consumption over an extended period of time has been associated with Hypertension apart from other adverse health effects.Salt chemically is defined as any combination of an acid and base resulting in formation of an ionic compound (examples KCl, KBr, NaSO4, etc.). Common edible salt is composed of sodium chloride NaCl (table salt) is the ionic combination of the cation (Na+) and anion (Cl-). Salt is found naturally in seawater (around 3%), in mineral deposits (halite) and in natural bodies of water (lakes, streams). Salt can be mined from underground deposits, either by rock salt mining or vacuum evaporation. It can be evaporated from seawater (sea salt, fleur de sel) or other bodies of water. Sodium is necessary for life for osmo-regulation, maintaining "water balance" and nerve transduction and other biological functions. Human body contains about 250 grams of salt (3 or 4 full salt shakers).

The human body has evolved to balance salt intake with need through means such as the renin-angiotensin system. The well-known effect of sodium on blood pressure can be explained by comparing blood to a solution with its salinity changed by ingested salt. Artery walls are analogous to a selectively permeable membrane, and they allow solutes, including sodium and chloride, to pass through (or not), depending on osmosis. When salt is ingested, it is dissolved in the blood as two separate ions :- Na+ and Cl−. The water potential in blood will decrease due to the increase solutes, and blood osmotic pressure will increase. While the kidney reacts to excrete excess sodium and chloride in the body, water retention causes blood pressure to increase.

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HISTORY OF SALT

Salt is essential for human life, and saltiness is one of the basic human tastes. The tissues of animals contain larger quantities of salt than do plant tissues. Salt is one of the oldest and most ubiquitous food seasonings, and salting is an important method of food preservation. Salt has been used in foods throughout and before history for more than 8000 years. It has had politically and economically important place in human history. Salt was scarce in most areas until recently and important as a traded commodity also used as currency, in fact the world "salary" comes from salt. The word "salary" comes from the Latin word for salt because the Roman Legions were sometimes paid in salt, which was quite literally worth its weight in gold. In Britain, the suffix "-wich" in a place name means it was once a source of salt, as in Sandwich and Norwich. The Natron Valley was a key region that supported the Egyptian Empireto its north, because it supplied it with a kind of salt that came to be called by its name, natron. There is more salt

in animal tissues such as meat, blood and milk, than there is in plant tissues. Nomads who subsist on their flocks and herds do not eat salt with their food, but agriculturalists, feeding mainly on cereals and vegetable matter, need to supplement their diet with salt. With the spread of civilization, salt became one of the world's main trading commodities. Some of the earliest evidence of salt processing dates to around 8,000 years ago, when people living in an area in what is now known as the country of Romania were boiling spring water to extract the salts; a salt-works in China dates to approximately the same period. Salt was prized by the ancient Hebrews, the Greeks, the Romans, the Byzantines, the Hittites and the Egyptians. Salt became an important article of trade and was transported by boat across the Mediterranean Sea, along specially built salt roads, and across the Sahara in camel caravans. The scarcity and universal need for salt has led nations to go to war over salt and use it to raise tax revenues. Salt is also used in religious ceremonies and has other cultural significance.

SALT AND HUMAN HEALTH

The relationship between dietary salt intake and the development of hypertension has been the subject of continuing debate for decades. Despite abundant epidemiological, experimental, and interventional observations demonstrating an association between salt intake and blood pressure, skepticism still remains regarding how a high salt intake can be mechanistically linked to an increase in blood pressure. This skepticism is partly due to the heterogeneity in the blood pressure responses to increases in salt intake in humans. Our inability to explain why salt raises blood pressure in some individuals described as 'salt sensitive', but not in others, termed as 'salt resistant', has hampered the development of a comprehensive theory as to how a high salt intake causes high blood pressure in salt sensitive subjects. Extensive studies have been conducted to identify the pathophysiological mechanisms responsible for the heterogeneity of responses to increased.

The DASH-Sodium study was a sequel to the original DASH (Dietary Approaches to Stop Hypertension) study. Both studies were designed and conducted by the National Heart, Lung, and Blood Institute in the United States, each involving a large, randomized sample. While the original study was designed to test the effects of several varying nutrients on blood pressure, DASH-Sodium varies only in salt content in the diet. Participants were pre-hypertensive or at stage 1 hypertension, and either ate a DASH-Diet or a diet reflecting an "average American Diet". During the intervention phase, participants ate their assigned diets containing three distinct levels of sodium in random order. Their blood pressure is monitored during the control period, and at all three intervention phases. The study concluded that the effect of a reduced dietary sodium intake alone on blood pressure is substantial, and that the largest decrease in blood pressure occurred in those eating the DASH eating plan at the lowest sodium level (1,500 milligrams per day). However, this study is especially significant because participants in both the control and DASH diet group showed lowered blood pressure with decreased sodium alone. In agreement with studies regarding salt sensitivity, participants of African descent showed high reductions in blood pressure.

SALT SENSITIVITY

The simplest definition of salt sensitivity of blood pressure (SSBP) states that it is a physiological trait present in rodents and other mammals, including humans, by which the blood pressure (BP) of some members of the population exhibits changes parallel to changes in salt intake. In animals, the trait has been inbred such that the salt-sensitive (SS) ones will sustain increases in BP with salt loading and decreases with salt depletion, whereas the salt resistant (SR) ones will not. In humans, the trait is normally distributed; therefore, the distinction between SS and SR members of the population has been made by

choosing an arbitrary magnitude of the salt-induced change in BP to define the groups. Regardless of possible causation by abnormalities of sodium handling, the SS phenotype is not usually characterized by alterations in salt balance (eg, impaired natriuresis or expanded plasma volume) but rather by a hypertensive response to maintain it. In an unselected population, SSBP is a continuous, normally distributed quantitative trait. As with any other trait with these characteristics, there is the issue of whether population members with the largest and smallest quantities of the trait represent the randomness of its distribution or are qualitatively different from the population at large. The Gaussian distribution of population BP is probably the result of a random mixture of pro-hypertensive and antihypertensive genes and genetic variants in a heterogeneous population interacting with environmental factors (eg, diet), physiological characteristics (eg, aging), and clinical features (eg, renal function). Research on SSBP in humans is more complex than that in animal rodent strains. The reason is that methodological issues such as random error in BP measurements and physiological issues such as the multiple sources for BP variability may confound the assessment of the BP responses to salt loading or salt depletion. Therefore, defining an individual as SS or SR depends on the selection of arbitrarily chosen cut offs for the magnitude of the BP changes. Environmental factors substantially affect whatever the genetic component may be for SSBP in humans. Additionally, despite the unquestionable influence of environmental factors in the determination of SSBP in humans, estimates of its heritability have been as high as 74% in blacks and 50% in Chinese subjects, both higher than those for hypertension. However we do not have evidence base whether the Asian Indian subjects have heritability like the Chinese or African American populations and is now an area we are investigating. An important issue is the clinical significance of the SSBP phenotype. There was increasing understanding that it represents an abnormality. The reasons were that it contradicts the basic physiological tenet that salt balance can be maintained by natriuretic and anti-natriuretic systems independently of BP, it occurs less frequently than salt resistance in normal subjects, and is associated with several forms of human and experimental hypertension.

Studies of salt sensitivity in rats were pioneered by Dahl, inspired by ecological and epidemiological studies of the association of salt intake with human hypertension. Dahl et al selected Sprague-Dawley rats with the highest BP response to a high-salt diet (facilitated by triiodothyronine administration) and mated them with equally responsive siblings. After few generations, an SS strain with a consistent hypertensive response to a high-salt diet was created. Contrary to common belief, this was not a pure inbred strain because its descendants were also outbred with other SS Sprague-Dawley rats as a result of breeding problems and small litters. Additionally, Sprague-Dawley rats without a hypertensive response to a high-salt diet were inbred to produce the SR strain. From the creation of these strains and the demonstration that a donor SS kidney transplanted into an SR rat conferred SSBP to the recipient (and vice versa), a major role for a renal abnormality was hypothesized as the factor determining the phenotype. Later, Rapp and Dene developed the fully inbred DS/Jr and DR/Jr strains that have subsequently been used by most researchers. The original SS and subsequent DS/Jr rats developed fulminant hypertension when exposed to a high salt (8%) diet and died by the age of 8 weeks. They had a plethora of vascular lesions, renal fibrosis, and cardiac hypertrophy. Several investigators reported a variety of physiological abnormalities contributing to hypertension in DS/Jr rats, among them differences in cellular ion transport and concentration, enhanced sympathetic activity and blunted baroreflexes, reduced renal medullary blood flow, disturbed balance between vasoconstrictors and vasodilators with a special role for nitric oxide (NO), enhanced oxidative stress, and

activated Rac1 GTPase mineralocorticoid receptor interaction.

Research into the possible physiological mechanisms determining SSBP has been driven mostly by a conceptual framework derived from the work of Guyton and co-workers. The major tenet of such framework is that one or many mechanisms that normally regulate the adaptation of the cardiovascular system to a salt load must be impaired in SSBP. This somehow leads to the need for the whole animal to raise BP to excrete the salt load via pressure natriuresis. The result is that an SS animal or human being will be able to maintain a normal salt balance at the expense of developing hypertension, the main feature of SSBP. Obviously, the putative defect can involve a variety of mechanisms. Activation of a natriuretic system required to excrete a salt load (eg, natriuretic peptides, renal eicosanoids) may be impaired, or conversely, lack of physiological suppression of an anti-natriuretic system in response to a salt load (eg, ineralocorticoid or renal transport activity) might be the culprit. Evidence for a genetic basis of salt sensitivity has come from heritability estimates in family studies. Miller et al examined the change in BP between random-sodium and low sodium diets among white US families and found a higher correlation in monozygotic pairs compared with sibling pairs: 0.72 for systolic BP (SBP), 0.62 for diastolic BP (DBP), and 0.68 for MAP in monozygotic twins compared with 0.50, 0.33, and 0.36, respectively, for siblings. Svetkey et al used an established inpatient protocol253 to examine the change in BP between intravenous sodium loading and furosemide induced volume depletion in black US families and found evidence of heritability, although effects of variable family sizes contributed to variation in estimates. Additional evidence was provided by the description of an association of salt sensitivity with haptoglobin phenotypes. The BP response to a change in salt (sodium chloride) intake is not uniform. Different types of study designs have been used to identify subgroups of the population whose BP response to salt is greater (or lesser) than other subgroup responses. Studies include small, brief challenge studies, feeding trials, and meta-analyses of trials. Factors that might influence the BP response to salt include sex, age, adiposity, race-ethnicity, and clinical conditions (hypertension, diabetes mellitus, and chronic kidney disease). For several factors, evidence is insufficient to make strong conclusions because individual studies were not designed to test the effects of salt reduction simultaneously in a comparator group. For example, a few trials have tested the effects of salt reduction in patients with diabetes mellitus, but none tested the effects concurrently in patients without diabetes mellitus. Additionally, most meta-analyses that aggregate published data across studies rather than analyzing individual-level data are poorly suited to identify subgroups that are SS because of potential residual confounding. In contrast, in some studies, the effects of salt were examined in both sexes, in blacks (versus whites), across the age span in adults, and over a broad range of BPs.

In summary, a strong and consistent body of evidence has documented that on average blacks compared with whites have a greater BP response to a change in salt intake and that this finding is independent of baseline BP level. Likewise, individuals with hypertension have a greater BP response to a change in salt than individuals without hypertension, and older individuals have a greater BP response than younger adults. The effects of salt reduction depend on concurrent diet. The effects of salt on BP are greater in the setting of a low-potassium intake and in the setting of poor-quality diet compared with the DASH diet. A less consistent body of evidence suggests that women might be more SS than men and that overweight individuals are more SS than normal-weight individuals. The effects of salt reduction in Asians and in individuals with diabetes mellitus or chronic kidney disease have been tested in few studies, in which salt reduction lowered BP. However, the absence of comparator groups precludes strong statements about whether these groups are more SS than corresponding

groups without the factor. Current methods for determining SSBP are labor intensive and therefore costly; thus, they are rarely if ever undertaken outside the clinical research arena. Two areas of research seeking easily obtainable surrogate markers for SSBP have developed recently, one based on analysis of BPs and heart rates from ambulatory monitors and the other based on excretion of proximal tubular cells or renal exosomes. A group of Italian researchers hypothesized that characteristics in a 24-hour ABPM would reflect SSBP in individuals on habitual salt intake. Other investigators had measured beat-by-beat BP and pulse rate variability in 34 essential hypertensive subjects studied during 1 week of low- and high salt diets and determined by sophisticated spectral analysis methods that SSBP was associated with lesser baroreflex sensitivity and higher pulse interval power. In other words, pulse rate and SSBP increased in parallel in their SS patients but were unaffected by salt intake in SR individuals. Continued research on hemodynamic characteristics that are surrogates of SSBP such as those conducted with ABPM techniques may conceivably provide a biomarker, particularly with incorporation of predictive variables into multivariate models that achieve high sensitivity and specificity compared with direct measurement of SSBP with currently accepted techniques. Additionally, an easily obtained biomarker from urine samples might be developed from continued research on properties of urine renal tubular cells or exosomes. Emerging novel knowledge about the storage of sodium in tissue compartments and the study of possible differences in such storage between SS and SR animals or humans, coupled with the ability to use magnetic resonance imaging techniques to measure such storage, may also lead to the development of a radiological marker for the SSBP phenotype.

Almost five decades ago, Guyton and Coleman proposed that whenever arterial pressure is elevated, pressure natriuresis enhances the excretion of sodium and water until blood volume is reduced sufficiently to return arterial pressure to control values. According to this hypothesis, hypertension can develop only when something impairs the excretory ability of sodium in the kidney. However, recent studies suggest that nonosmotic salt accumulation in the skin interstitium and the endothelial dysfunction which might be caused by the deterioration of vascular endothelial glycocalyx layer (EGL) and the epithelial sodium channel on the endothelial luminal surface (EnNaC) also play an important role in nonosmotic storage of salt. These new concepts emphasize that sodium homeostasis and salt sensitivity seem to be related not only to the kidney malfunction but also to the endothelial dysfunction. Further investigations will be needed to assess the extent to which changes in the sodium buffering capacity of the skin interstitium and develop the treatment strategy for modulating the endothelial dysfunction.

Thus "Salt sensitivity" is estimated to be present in 51% of the hypertensive and 26% of the normotensive populations. The individual blood pressure response to salt is heterogeneous and possibly related to inherited susceptibility. Although the mechanisms underlying salt sensitivity are complex and not well understood, genetics can help to determine the blood response to salt intake.

Salt reduction is a WHO goal globally now.A modest reduction in salt intake for 4 or more weeks causes significant and, from a population viewpoint, important falls in BP in both hypertensive and normotensive individuals, irrespective of sex and ethnic group. With salt reduction, there is a small physiological increase in plasma renin activity, aldosterone and noradrenaline. This will likely lower population BP and, thereby, reduce cardiovascular disease. The current recommendations to reduce salt intake from 9-12 to 5-6 g/d will have a major effect on BP, but are not ideal. A further reduction to 3 g/d will have a greater effect and should become the long term target for population salt intake..It is found that, compared with usual salt intake, reduced salt intake significantly

reduced diastolic blood pressure in men and women.

Salt Rich Foods in India to be avoided

- Preserved foods like: Pappads, pickles, dried fish etc
  - *Namkeen bhujiya, dalmoth, mathri, sev, farsan chaat-pakori,* french fries,
  - Convenience foods are high in sodium : instant foods, TV Dinners
  - Salted nuts, potato chips, popcorn, salted crackers, biscuits and Crisps.
- Salted butter, and processed cheese
- Frozen foods
  - Sea fish, cured meats, sausages, ham, and bacon
  - Instant cooked cereals and commercial salad dressings
- Pastries, cakes, and ice creams

TIPS TO REDUCE SALT IN DIET

- For seasoning of foods, herbs, spices, lemon, lime, vinegar or salt-free seasoning blends make a better choice than table salt.
- In rice and other cereal preparations like roti, poori, do not mix salt. Avoid the use of salted rice, salted porridge, and other salted cereal mixes.
- Avoid packaged mixes, canned soups, or broths— they generally have a high sodium content.
- Use fresh vegetables. Avoid the use of canned vegetables as they contain salt preservatives.
- Substitute fruits, salad, and fresh vegetables for salted snack foods.
- Limit the use of foods packed in brine such as pickles, pickled vegetables, and olives.
- Use little or no sauces: avoid tomato ketchup, soy sauce, MSG, mustard sauce, and *chutney.*
- Use fresh poultry, fish and lean meat, rather than the canned, smoked or processed types.

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Review Article

Hypertension and Hyperuricemia

BR Bansode

INTRODUCTION

To unravel the major mechanism linking hyperuricemia to hypertension has been a long-standing clinical and basic science quest. It has been now established that the early appearance of hyperuricemia is a reliable predictor of later development of hypertension. In adults with essential hypertension the comorbidity of hyperuricemia is very common.[1]

Recently there has been a growing interest in serum uric acid as an independent risk factor for incident hypertension. Few studies have evaluated the effect of hyperuricemia on blood pressure control in hypertensive patients. A recent meta-analysis also reported a direct correlation between hyperuricemia and incident hypertension.[2]

Hyperuricemia often accompanies metabolic syndrome, hypertension, diabetes, dyslipidemia, chronic renal disease, and obesity, and the serum uric acid level is known to vary significantly depending on meals, lifestyle, gender, and previous use of diuretics.[6]

Uric acid (UA) is the end product of purine metabolism. Humans are more susceptible to hyperuricemia than other mammals because of the loss of urate oxidase activity during human evolution. The relationship of hyperuricemia with cardiovascular diseases (CVDs) has received more and more attention for many years.[5]

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The interactions between serum uric acid (sUA) and other potential metabolic comorbidities increase the risk of gout development. General obesity in women and hypertriglyceridemia in men may potentiate an sUA effect for gout development. There was a synergistic effect seen between hyperuricemia and overweight, general obesity, or central obesity for gout development.[7]

Alcohol consumption has long been considered as a risk factor for chronic disease; the relationship to cardiovascular disease (CVD) is complex and involves at least two dimensions: average volume of alcohol consumption and patterns of drinking.[9]

In recent years, there has been a growing interest in in hyperuricemia and gout with comorbid complication of hypertension. In gout patients with known cardiovascular disease, a large well-powered study is underway, designed to quantify the occurrence of major adverse cardiovascular events emerging during long-term management.[1]

Hyperuricemic patients with hypertension are more likely to have uncontrolled BP despite successful treatment with antihypertensive agents. In particular, the risk of uncontrolled BP related with hyperuricemia was prominent in hypertensive patients without metabolic syndrome. Uric acid levels need to be considered in strategies for BP control in hypertensive patients, even with good adherence to antihypertensive medications.[2]

A randomized, placebo-controlled, double-blind, interventional study, which targeted

young obese patients with prehypertension, demonstrated that an inhibitor of uric acid production (allopurinol) and an accelerator of uric acid excretion (probenecid) both lead to decreased blood pressure.[6]

The mechanism through which alcohol raises blood pressure remains elusive. Several possible mechanisms have been proposed such as an imbalance of the central nervous system, impairment of the baroreceptors, enhanced sympathetic activity, stimulation of the renin-angiotensin-aldosterone system, increased cortisol levels, increased vascular reactivity due to increase in intracellular calcium levels, stimulation of the endothelium to release vasoconstrictors and loss of relaxation due to inflammation and oxidative injury of the endothelium leading to inhibition of endothelium-dependent nitric oxide production. Loss of relaxation due to inflammation and oxidative injury of the endothelium by angiotensin II leading to inhibition of endothelium-dependent nitric oxide production is the major contributors of the alcohol-induced hypertension.[10]

MECHANISM

How hyperuricemia influences hypertension: Activity of the distal nephron epithelial sodium channel (ENaC) is an important determinant of sodium balance and blood pressure. Uric acid could modulate blood pressure in two different ways. One way is by direct regulation, and the second way would be via hyperuricemia effects on ENaC expression and function, which would indirectly result in elevated plasma aldosterone, since the activation of the renin system was observed in the hyperuricemic individuals.

In humans it is seen that hyperuricemia is associated with a number of effects on the vascular endothelium, vessel walls, and kidney parenchyma. UA can functionally upregulate XO, which is a key enzyme in purine metabolism. XO-derived reactive oxygen species and oxidative stress may play an important role in the negative effect of UA on the cardiovascular system. UA can exert, along with extracellular antioxidant activity, an intracellular pro-oxidant effect.

As a consequence, hyperuricemia has a detrimental effect on the vascular endothelium and may cause endothelial dysfunction that plays a key pathophysiologic role in the development and progression of atherosclerosis since it loses the ability to protect the vascular system by reducing its anti-atherosclerotic and antithrombotic actions. UA also stimulates proliferation of the smooth muscle cells of the vascular system through activating the renin-angiotensin system and inhibiting the synthesis of nitric oxide, and finally can impair arterial function and cause arterial stiffening, a risk factor for hypertension and cardiovascular and cerebrovascular events.

Meanwhile, epidemiological studies support high SUA as a precursor of type 2 diabetes, in which SUA increases insulin resistance via inhibiting the synthesis and bioavailability of nitric oxide, promoting oxidative stress and production of tumor necrosis factor α, or via a direct cytotoxic effect on the pancreatic β-cell.[5]

STUDY IN HUMANS

A systematic review has studied data available in MEDLINE, Embase, and the Chinese Biomedical Literature Database, which also suggests that hyperuricemia could slightly increase the risk of cardiovascular diseases and diabetes in patients with hypertension.

17 studies were selected for review which had investigated the prognostic effect of SUA on hypertensive patients with a follow-up duration of more than 1 year and a sample size larger than 100, including both cohort studies and nested case-control studies and randomized controlled trials (RCTs).[5]

A recently published retrospective observational study based on a registered database found that allopurinol use was associated with a significantly lower risk of both stroke (HR=0.50; 95% CI, 0.32–0.80) and cardiac events.

Several meta-analyses have also suggested beneficial effects of UA-lowering therapy in

slowing the progression of chronic kidney disease and reducing left ventricular mass in patients with ischemic heart disease, type 2 diabetes mellitus, and left ventricular hypertrophy.[5]

Clinical Trials

Relationship between uric acid and blood pressure in different age groups (Jae Joong Lee,; Jeonghoon Ahn,; Jinseub Hwang,; Seong Woo Han,; Kwang No Lee Published: 15 July 2015) A total of 45,098 Koreans who underwent health examinations at Korea Association of Health Promotion with no history of taking drugs related with UA and/or BP were analyzed for determining the relationship between serum UA and BP.

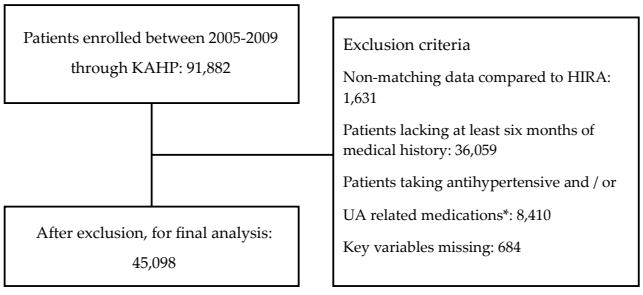

Fig. 1:Flow diagram of the study protocol. *Non-antihypertensive medications which could affect serum UA levels were excluded including allopurinol, benzbromarone, colchicine, febuxostat, rasburicase, probenecid, diuretics, ethambutol, cyclosporine, diazoxide, aspirin, levodopa, and nicotinic acid. KAHP, Korea Association of Health Promotion; HIRA, Health Insurance Review and Assessment Service; UA, uric acid

Study 1

Independent Impact of Hyperuricemia on the Future Risk of Hypertension: A Systematic Review and Meta-Analysis, A systematic review of 18 prospective cohort studies representing data from 55,607 participants and 13,025 incident hypertension cases, Boston

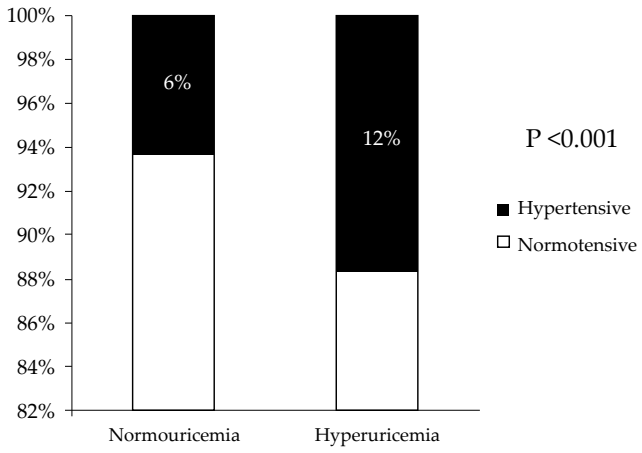

Fig. 2:Prevalence of hypertension in hyperuricemia. A significant difference between normouricemic and hyperuricemic patients was seen among the total subjects who were enrolled ($p < 0.05$)

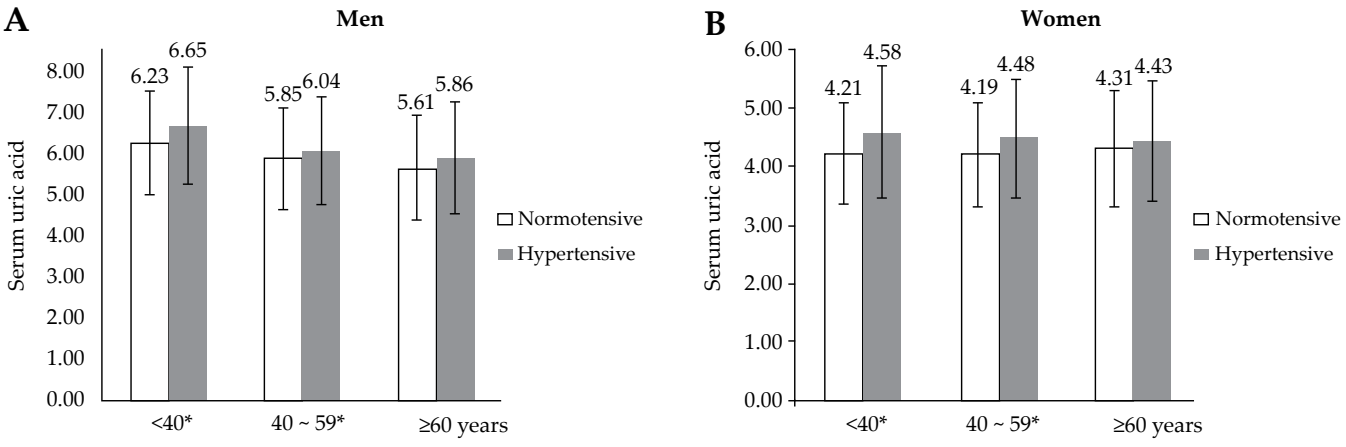

Fig. 3:Serum uric acid levels in different age/gender groups. *Indicates groups with significant differences ($p < 0.05$) between normotensive and hypertensive patients. (A) Men. (B) Women

Medical Canter.

Purpose: To study pathogenetic role of uric acid in hypertension, but it remains unknown whether these findings apply to adult populations where the larger disease burden exists. We conducted a systematic review and meta-analysis to determine if hyperuricemia was associated with incident hypertension, particularly in demographic subgroups.

Methods: A systematic review of major electronic databases: (1) prospective cohort studies without age restrictions; (2) at least 1 year of follow-up; (3) sample sizes of at least 100 subjects; and (4) inception cohorts free of hypertension

Conclusion: Hyperuricemia is associated with an increased risk for incident hypertension, independent of traditional hypertension risk factors. Risk for future hypertension appears more pronounced in hyperuricemic younger individuals and women and appears diminished in US-based studies and studies conducted more recently [11].

Study 2

Relationship between uric acid and blood pressure in different age groups, study of 91,882 patients, Korean study

Purpose: to study the relationship between serum UA and BP in different age groups

Methods: Analysis of more than 45000 Koreans who underwent health examinations for determining the relation between serum UA and BP

RESULTS

A significant difference between normouricemic and hyperuricemic patients was seen among the total subjects who were enrolled ($p < 0.05$).

The strength of the relationship between serum UA and BP is more dominant in the younger age groups and decreases during the aging process as the duration of hypertension gets longer.

It was seen that hypertension was developed by UA-mediated renal vasoconstriction resulting from a reduction in endothelial levels of nitric oxide, with activation of renin-angiotensin system. Microvascular renal disease independently was caused by UA over time, inducing the development of hypertension. Hyperuricemia increased the relative risk of hypertension by approximately 30% in men under 60 and by 2.6 fold in women under 40.[12]

Study 3

The Relationship between Uric Acid and Hypertension in Adults in Fako Division, SW Region Cameroon, 297 adults, Cameroonian population

Purpose: Study was carried out to investigate the relationship between uric acid and hypertension in Cameroonian adults

Methods: Inclusion of of individuals with hypertension (20 years and above) who were asked to complete a structured questionnaire that contained information on general state of health, physical activity, smoking, alcohol consumption and dietary patterns. Fasting blood samples were then collected for the measurement of uric acid, glucose, lipids and creatinine

Conclusion: There was a significant association in the prevalence UA concentration with BP category and Age showed a significant negative correlation with uric acid. Uric acid must be added to the list of conventional risk factors for hypertension. significant correlation between uric acid and triglycerides. Triglycerides have been linked to insulin resistance which promotes hypertension through renal tubular sodium reabsorption, augmentation of the sympathetic nervous system reactivity and activation of the renin–angiotensin system. Given that uric acid can also induce the Renin-angiotensin system it is possible that they both have an additive effect on the blood pressure response [13].

Study 4

Uric Acid and the Development of Hypertension, The Normative Aging Study, 2280 men from Boston

Purpose: To examine the relationship between uric acid level and the development of hypertension

Methods: Cox proportional hazards model was used to examine the relationship between baseline serum uric acid level and the development of hypertension adjusting for age, body mass index, abdominal circumference, smoking, alcohol, plasma triglycerides, total cholesterol, and plasma glucose. At each study visit, an examining physician measured seated blood pressure. The examining physician recorded the use of medication for the treatment for hypertension. The Cornell Medical Index assessed alcohol consumption. A trained interviewer obtained smoking history.

Conclusion: In this analysis, subjects with higher baseline SUA levels also had higher SBPs and DBPs, greater BMI and AC, and higher triglycerides and total cholesterol. In addition, current smokers had lower baseline SUA levels, whereas subjects who drank ≥2 alcoholic drinks per day had higher levels.

This association was independent of age, body size, central adiposity, total cholesterol level, triglyceride level, smoking status and alcohol intake, and glucose level. These results demonstrate that the SUA level is a durable marker of risk for hypertension.[14]

SUMMARY

Prevalence of hyperuricemia is high in patients with hypertension. Serum uric acid is significantly associated with parameters of the metabolic syndrome. Hyperuricemia should be acknowledged and monitored as a risk factor for cardiovascular disease.[4]

Recent observations suggest that the association between uric acid and hypertension may, in fact, represent causation.[7] Uric acid has pro-inflammatory effects on vascular smooth muscle cells that seem to be mediated by intracellular redox pathways.[14]

People with elevated uric acid levels are at an increased risk for the future development of hypertension. Medications that lower uric acid levels in the blood may potentially be useful in the prevention or treatment of hypertension.

ENaC is responsible for the rate-limiting step of sodium reabsorption and thus plays an important role in the maintenance of sodium balance, extracellular fluid volume, and blood pressure.[3]

Elevated SUA or hyperuricemia could increase the risk of subsequent CVDs, all-cause mortality, and new-onset diabetes in hypertensive patients.[5]

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Review Article

Ten Commandments on Hypertension Management

Suraj Kumar[1], Ravina Sharma[2], Gurpreet S Wander[3]

Hypertension is a major contributor to cardiovascular morbidity and mortality in India and worldwide, and is defined when blood pressure is above 140 mmHg systolic and/or above 90 mmHg diastolic. Heart disease, stroke, and renal failure are leading causes of death with hypertension being the predominant risk factor.[1] The gist of the article is to highlight 10 important updated and useful points of hypertension.

1. **Lower Blood Pressure targets are better.**

   SPRINT trial[2] showed that primary composite outcome of cardiovascular disease and death was reduced by 25% and all-cause mortality by27% in patients treated intensively to a systolic blood pressure target of <120 mmHg as compared to patients with target < 140 mmHg. Rates of some serious adverse events, including hypotension and acute kidney injury or failure, were higher in the intensive-treatment group than in the standard-treatment group, but these higher rates appeared unlikely to outweigh the benefits overall. Patients with diabetes, those with prior stroke, and those age <50 years were excluded. SPRINT redefines blood-pressure target goals and challenges to improve blood-pressuremanagement.

2. **Renal Denervation therapy is no better than medical therapy for resistant hypertension**

   Resistant hypertension is defined as failure to achieve a BP goal of <140/90 mm Hg, despite treatment with ≥3 different antihypertensive medication classes at a maximally tolerated dose and, including a diuretic. Earlier SYMPLICITY HTN-1 and HTN-2 studies showed impressive decreases in blood pressure. Three-year follow-up of the SYMPLICITY HTN-1 study revealed a decrease in blood pressure of 32/14 mm Hg and these results surpassed what was achievable with drug therapy.

   SYMPLICITY HTN-3 trial[3] showed that there was no significant difference in patient outcome between renal denervation and a sham procedure among patients with drug resistant hypertension. After 6 months, office systolic blood pressure decreased from baseline to a similar extent in the renal-denervation and sham-procedure groups (P<0.001 for both comparisons of the change from baseline); the difference in the change in blood pressure between the two groups was only −2.39 mm Hg. Thus, in the SYMPLICITY HTN-3 study, renal denervation had no significant effect on office or 24-hour ambulatory systolic blood pressure.

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3. **Spironolactone is an effective add-on therapy for resistant hypertension**

   Despite nearly 50 years of research in hypertension, the optimal drug treatment for resistant hypertension remains undefined. It has been suggested, but not mandated in guidelines, that spironolactone be used as a fourth-line therapy for resistant hypertension.

   The PATHWAY-2[4] showed spironolactone was the most effective fourth-line antihypertensive drug compared with doxazosin and bisoprolol in patients with resistant hypertension. These findings challenge the concept that that resistant hypertension cannot be treated adequately with drug therapies, and suggest that treatments which have a natriuretic action are likely to be the most effective.

4. **Implanting stents for moderately severe obstructive renovascular disease is no better than medical therapy alone**

   Atherosclerotic renal-artery stenosis is a common problem in the elderly and community-based screening suggest that the prevalence among persons older than 65 years of age may be as high as 7%. Clinical trials of renal-artery stenting failed to show benefit with respect to kidney function.[5,6]

   CORAL[7] was a randomized clinical trial to determine the effects of renal-artery stenting on the incidence of important cardiovascular and renal adverse events. In contrast to earlier trials which enrolled patients with mild renal artery stenosis, CORAL trial enrolled patients who had stenosis of at least 60% of the diameter of a renal artery. It replicates the findings of the ASTRAL[5] and STAR[6] trials and establishes that renal-artery stenting is futile for the target population enrolled in the study. Patients who have atherosclerotic disease with a mean renal-artery stenosis of 73%, as assessed visually on angiography, in addition to hypertension while receiving two or more antihypertensive drugs or stage 3 chronic kidney disease, should not undergo renal-artery stenting, because the only tangible consequence is the procedure-related risk of bleeding or vascular complications. Patients should receive medical therapy to control blood pressure and prevent the progression of atherosclerosis. Medical therapy alone was associated with a20% rate of the primary end point at 2 years, which was half the expected rate of 40%.[8]

5. **Tight control of hypertension during pregnancy is beneficial for mother with no harm to the fetus.**

   Chronic hypertension is an important risk factor for pregnancy complications, including, for the fetus or neonate, poor fetal growth, preterm birth, low birth weight, requirement for neonatal intensive care, and death, and for the mother, superimposed preeclampsia and eclampsia, acute renal failure, pulmonary edema, cesarean delivery, placental abruption, stroke, peripartum cardiomyopathy, and death.[9] There is consensus that treatment of hypertension in pregnancy is warranted if blood pressure is high to pose a risk of stroke (i.e., ≥160 mm Hg systolic or either ≥105 mm Hg diastolic) or if there is associated renal or cardiovascular disease.

   Randomized trials of treatment of mild, chronic hypertension in pregnancy have consistently failed to show improvements in major complications.[10] CHIPS[11] was an international, randomized trial comparing less-tight versus tight control of mild-to-moderate non-proteinuric hypertension in pregnancy (diastolic blood-pressure targets, 100 mm Hg and 85 mm Hg, respectively). There was no significant difference between groups in the frequency of the primary outcome, a composite of pregnancy loss or high-level neonatal care for more than 48 hours in the first 28 post-natal days (31.4% vs. 30.7%). The groups also did not differ significantly in the frequency of serious maternal complications, including devel-

opment of preeclampsia, although severe hypertension (≥160/110 mm Hg) was significantly more common in the less-tight-control group. Results were similar for gestational and chronic hypertension.

CHIPS study showed that tight control of hypertension conferred no benefits to the fetus and only a moderate benefit (a lower rate of progression to severe hypertension) for the mother. It also provides reassurance that tight control does not carry major risks for the foetus or newborn.

6. **Lower BP targets of 140 mmHg SBP are better in acute haemorrhagic stroke**

Intracerebral hemorrhage is one of the most devastating forms of stroke. It accounts for 10-15% of strokes in western countries and 20-40% in Asian, African and Latin American populations. The median 1-month case fatality rate is 40%, and only 12 to 39% of patients achieve functional independence. There is no proven effective medical treatment and outcome is determined by the volume and growth of the underlying hematoma. Current ACC/AHA guidelines suggest a target mean arterial pressure of less than 110 mm Hg or a blood pressure of less than 160/90 mm Hg.[12] These guidelines also acknowledge that this blood-pressure target is arbitrary and not evidence-based.

INTERACT-2 trial[13] showed a trend toward a reduction in the primary outcome of death or severe disability, significant improvement in secondary functional outcomes, and reassuring safety data, acute blood-pressure reduction to a target systolic blood pressure of 140 mm Hg or less appears to be a reasonable option for patients with spontaneous intracerebral hemorrhage.

ATACH-2 trial[14] randomized patients with ICH to "standard" 140-179 mmHg blood pressure control versus "intensive" 110-139 mmHg blood pressure control. The treatment to achieve a target systolic blood pressure of 110 to 139 mm Hg did not result in a lower rate of death or disability than standard reduction to a target of 140 to 179 mm Hg, with intensive treatment group more likely to suffer neurologic deterioration within 24 hours (11.0% vs. 8.0%) and a serious adverse event within 3 months (25.6% vs. 20.0%).

In INTERACT2, the mean systolic blood pressure was 150 mm Hg in the first hour in the intensive-treatment group and 164 mm Hg in the standard-treatment group. In ATACH-2, mean minimum systolic blood pressure in the first 2 hours after randomization was 128.9 mm Hg in the intensive-treatment group and 141.1 mm Hg in the standard-treatment group. Thus, the profile of the systolic blood-pressure level in the standard-treatment group in the ATACH-2trial was similar to values observed early in the intensive-treatment group in INTERACT2.

7. **Beta blockers are not sufficiently effective as a primary tool to treat hypertension.**

It was NICE Guidelines[15] that recommended not using b-blockers as first-line treatment for hypertension. Various guidelines differ in the opinion regarding the use of beta blockers as first line treatment. JNC 8 did not include β-blockers in their recommendations for the initial antihypertensive therapy.[16] On contrary, European Society of Hypertension (ESH) Task Force dismissed the classification and ranking of antihypertensive drugs into first, second, or third-line drugs.[17]

B-Blockers are associated with lower mortality and cardiovascular events than placebo when prescribed for patients with heart failure or acute myocardial infarction,[18] but initial therapy of hypertension with b-blockers is not associated with reduced all-cause mortality but is associated with modest reductions in cardiovascular events compared with placebo or no treatment. The lower efficacy of b-blockers could not be explained by a lesser decline in blood pressure level associated with β-blocker

treatment. A slightly lower effectiveness of beta-blockers in preventing stroke[19] has been attributed to a lesser ability to reduce central SBP and pulse pressure. Findings may be also related to delay in regression of left ventricular hypertrophy, carotid intima-media thickness, aortic stiffness, and small artery remodeling. Also, beta-blockers tend to increase body weight and particularly when used in combination with diuretics, facilitate new-onset diabetes in predisposed patients.[20]

8. **Combination of an ACE-inhibitor with a CCB has the best scientific evidence of cardiovascular protection.**

   Despite debate about the first choice for treating hypertension, monotherapy effectively normalizes blood pressure values in only a limited number of hypertensive patients. Adding a second drug is more effective than increasing the dose of the first drug and is associated with fewer side effects. Thus, the aim of combination therapy should always be to both improve BP control and to reduce cardiovascular events.

   Antihypertensive drugs can be effectively combined if they have different and complementary mechanisms of action. Combining ACE-I and CCB is the preferred because of the blocking and stimulating effect the renin-angiotensin system (RAS) respectively.[21] In contrast, some combinations (e.g., calcium antagonists plus diuretics or beta-blockers plus RAS blockers) have no additive BP-lowering effects. BP reduction is not the only mechanism that reduces cardiovascular risk. Scientific evidence indicates that some drug classes are better than others in this respect, and therefore some drug combinations are also better than others. The results of the ASCOT-BPLA[22] and ACCOMPLISH[23] trials suggested that an ACE inhibitor/calcium antagonist combination had better cardioprotective effects.

9. **Lifestyle changes is a important step in the controlling hypertension**

   Despite the availability of multiple effective antihypertensive drugs, hypertension control rates remain poor. Antihypertensive drugs cause side effects prompting some patients to discontinue therapy. As a modifiable risk factor, treatment of prehypertension and hypertension through lifestyle changes is a vital approach.[24] The JNC-8[16] and 2013 ESH/ESC[17] guidelines and the results of trials[25,26]on lifestyle modification for hypertension recommended that lifestyle modification is capable of lowering the blood pressure. In some patients, lowering sodium and alcohol intake, keeping weight in the ideal range, engaging in regular aerobic exercise, and stopping smoking can be sufficient to control high blood pressure. Of the various lifestyle interventions, physical activity and dietary intervention have been shown to diminish the blood pressure and reduce CVD events, which have emerged as the two most effective and physiologically desirable approaches. Barriers to adoption of physical activity recommendations include comorbid conditions that limit physical activity, as well as limited time.[27]

10. **Screening for secondary causes should be performed in patients with unusual presentation.**

    The majority (>90%) of patients will have essential hypertension, while only a minority (<10%) have secondary hypertension. Many forms of secondary hypertension cause "treatment resistant" hypertension. As evaluation is not cost effective, patients with clinical clues suggesting the possible presence of secondary hypertension should undergo a more extensive evaluation. Important clues include severe or resistant hypertension, acute rise in BP in previously stable patient, age < 30 years in non-obese, negative family history patient, malignant or accelerated hypertension. In young patients, renal causes and coarctation of the aorta should be considered and in

older patients, primary aldosteronism, obstructive sleep apnea and renal artery stenosis are moreprevalent. If secondary hypertension is present, the most effective treatment strategy is focused upon the specific mechanism of the hypertension and some of disorders can be cured, leading to partial or complete normalization of the blood pressure.

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Review Article

Home Blood Pressure Monitoring

A Muruganathan[1]

INTRODUCTION

Hypertension is a modifiable risk factor and a predictor of cardiovascular morbidity and mortality. It is important to measure the BP accurately as the diagnosis and future management plans are based on the reading obtained. In order to overcome the limitations of the office blood pressure (OBP) measurement, two other methods are widely used in clinical practice

1. 24 hours Ambulatory Blood Pressure Monitoring (ABPM)
2. Home Blood Pressure Monitoring (HBPM)

WHAT IS HOME BLOOD PRESSURE MONITORING?

Regular measurement of BP by the patient outside the clinical setting either at home or elsewhere is known as HBPM or Self Blood Pressure Monitoring (SBPM).

THE ADVANTAGES OF HOME BLOOD PRESSURE MONITORING

1. Multiple measurements of BP on different days, weeks or months can be made in each individual's usual environment, away from the physician's clinic with HBPM.[1-6]
2. Patient friendly inexpensive and reliable devices / are available (www.dableducational.com)
3. The elucidation of the optimal schedule for home reading (Niiranen et al., 2011)
4. Good Reproducibility – Good Prognostic value.[1-6]
5. Hypertension-induced target organ damage and the risk of cardiovascular events are better predicted than office BP.[7] (Niiranen et al., 2013)
6. Home BP monitoring can detect the white-coat and masked hypertension phenomena and it may be useful in detecting masked hypertension in patients with pre hypertension
7. HBPM helps to identify BP Variability
8. HBPM helps to improve adherence to antihypertensive therapy (Bosworth et al., 2011), especially when used in combination with other approaches such as patient counseling, patient reminders from the healthcare team.[8]
9. HBPM may result in greater BP improvement if the translation of home readings either by memory in the device or by telemonitoring.[9] Data transfer to a remote computer through the internet connection, or telephone (stationary or mobile) helps the physician in making therapeutic decisions, communications to the patients. This avoids additional clinic visits for patients.
10. Home BP monitoring provokes more down-titrations of antihypertensive drugs and overcomes therapeutic inertia and results in the greater change in antihyper-

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tensive medications.

11. HBPM helps the health care professional to alter and advice regarding the drugs dose adjustments or addition and help them to determine the onset of problems like dizziness or headaches associated with medication changes.[1-6]
12. The differences between the effect of two antihypertensive drugs in the early morning and evening can be detected by HBPM.[10]
13. Identifying optimal treatment-People may respond to any one drug differently and it is difficult to predict which drug is best for which patient. One way of improving the situation is using HBPM in which patient is given a number of different medication in sequence.[11]
14. HBPM helps in evaluation of resistant hypertension
15. HBPM encourages patient-centered care. The study by Fuchs et al supports these indirect effects of self-monitoring. Participating in HBPM alone improved BP control.[12]
16. Behavioral or lifestyle interventions in patients with chronic conditions improved by encouraging the patient to become actively involved in his or her care. 75% of people who are successful with long-term weight loss report weighing themselves regularly in case of obesity.[1-6]
17. Cost-Effectiveness-There is some evidence that self-monitoring may be cost-effective.[13]

NEED FOR HBPM IN SPECIAL POPULATIONS

Home blood pressure monitoring in patients with diabetes

HBPM can detect masked hypertension in diabetic patients who have a very high (47%) prevalence and are at a higher risk of developing brain and kidney damage.[14-17]

The Elderly

Office BP tends to overestimate the out-of-office BP more in older than in younger people. The variability of systolic home BP readings and the white-coat effect increases with age. HBPM can help to reduce potential hazards of excessive BP reduction in older people. HBPM can also be used to detect orthostatic BP changes if readings are taken with the subject both sitting and standing.[18]

Pregnancy

HBPM can provide multiple readings recorded at the same time of day over prolonged periods of time and can monitor changes in BP during pregnancy. HBPM can detect White-coat hypertension, which is not uncommon in pregnancy and may lead to unnecessary early termination.[18]

Kidney Diseases

For predicting ambulatory hypertension HBPM has been shown to be superior to measurements made in the dialysis unit.[18]

Children

The phenomenon of white-coat hypertension occurs in children just as in adults and HBPM is useful when proper cuff size is used in addition to clinic measurements.[18]

Home Blood Pressure Monitoring for the Evaluation of antihypertensive treatment in clinical trials

Clinic based BP measurements are used for most of the large clinical trials of antihypertensive treatment. Despite HBPM's obvious advantages, it is surprising how little use has been made of home monitoring in clinical trials, which are summarized.[13]

Advantages of HBPM over clinic BP in trials antihypertensive treatments13

- Better correlation with changes of target organ damage
- Smaller sample size

- Evaluation of time course
- No placebo effect
- Estimation of the trough to peak ratio

Advice for Home Blood Pressure Monitoring

All patients undertaking HBPM should receive adequate education and training/ teaching.[19]

DO: take all clothing off upper arm and put cuff on

DO: sit on a chair, back supported, arm on a table at heart level, feet flat on the floor

DO: wait for 5 minutes before taking the first measurement

DO: wait for one minute before taking the second measurement

Table 1: Definition of Hypertension by office and out-of-office blood pressure level[20]

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Office BP	>140	and / or	>90
Ambulatory BP			
Daytime (or awake)	>135	and / or	>85
Nighttime (or asleep)	>120	and / or	>70
24-hours	>130	and / or	>80
Home BP	>135	and / or	>85

DO: record date and time of both measurements on BP log

DO: measure twice a day, morning and evening, on the same arm, same time for 7 days before visit your health care provider

DO NOT: cross your feet

DO NOT: take your BP if you are in a hurry

DO NOT: smoke or drink caffeine 30 minutes before measuring BP

DO NOT: eat a big meal for 2 hours before measuring your BP

DO NOT: talk or watch TV during a measurement

DO NOT: measure your pressure if you are uncomfortable, anxious, stressed or in pain

NICE Guidelines: Hypertension Diagnosis

- Home BP measurement may be used to confirm diagnosis if ambulatory BP monitoring is unsuitable:
- Record BP twice daily in the morning and evening for ≥ 4 days (ideally 7 days) discard first day's measurements)
- Three measurements in the morning & three in the evening are required over the period of two days to accurately diagnose masked hypertension.
- The upper limit of normal for home

Table 2[5]: Prospective Studies Relating Home BP and Office BP to Cardiovascular Events and Mortality

Home BP Schedule							
Study	**Population Studied**	**No. of Subjects**	**Days**	**AM**	**PM**	**Total**	**Outcome**
Ohasama	Population	1789	28	1	0	28	Strokes and Mortality predicted better by HBPM
SHEAF	Treated Hypertensive Patients	4939	4	3	3	24	CV morbidity and mortality predicted better by HBPM
PAMELA	Population	2051	1	1	1	2	CV and total mortality predicted better by HBPM
Belgian	Referred	391		3	0	3	Combined CV events predicted better by HBPM
Didima	Population	662	3	2	2	12	CV events predicted by both HBPM and Office BP

Table 3: Comparison of Main Features of 3 Main Methods of BP Measurement[22]

Features	Office BP	ABPM	HBPM
No. of readings	Low	High	Medium
White coat effect	Yes	No	No
Operator dependency	Yes	No	No
Need of device validation (yes if oscillometric device used)	No	Yes	Yes
Daytime BP	+	+++	++
Nighttime BP and dipping	-	+++	-
Morning BP	±	++	+
24-h BP variability	-	++	±
Long-term BP variability	-	±	++
WCH and MH diagnosis	-	++	++
Placebo effect	++	-	-
Reproducibility	Low	High (24-h average values)	High (average of several values
Prognostic value	+	+++	++
Patient involvement	-	-	++
Need of patient training	-	±	++
Physician involvement	+++	++	+
Patient acceptance	++	±	++
Monitoring of treatment effects	Limited information	Extensive information on diurnal BP profile, cannot be repeated frequently	Appropriate for long-term monitoring, limited information on BP profile
Hypertension control improvement	+	++	+++
Cost	Low	High	Low
Availability	High	Low	High

WCH: White Coat Hypertension; MH: Masked Hypertension

pressure is 135/85 mm Hg. This corresponds to an office blood pressure of 140/90 mmHg

ESC 2013

Evidence

Several national and international guidelines recommend the use of HBPM for hypertension management. TASMINH2 study compared self-monitoring and self-adjustment of medications with standard care and found that at 12 months the treatment cohort had a highly significant (5 mmHg) lower SBP than the control group.[21]

Obtaining measurements outside of the clinical setting for diagnostic confirmation before starting treatment is recommended by The USPSTF.

- Only the CHEP and NICE guidelines currently recommend that a diagnosis can be made based on both ABPM and HBPM
- French and Taiwan guidelines recommend the use of self-monitoring to confirm office BP measurements before the diagnosis is made.

Action plan for Future

An 'adjustable cuff', which may be applicable to all adult arms, in order to avoid the inaccuracy induced by miscuffing to be, produced. We

need to improve the reliability of automated devices with validation of arm cuff and wrist devices with built-in software for arrhythmia indication.[23] Sleep HBP in addition to morning HBP, an automatic HBPM device with the data memory and three automatic measurements of BP during the sleep period [24]. HBPM devices that are more accessible and less expensive than 24-hour ABPM devices can recognise nocturnal dipping. Two devices have been used to obtain three measurements of sleep-time BP: the Omron HEM-5001[25] and the Microlife Watch BNP.[26]

It is recommended that HBPM should be popularized, familiarized to be used as a routine component of BP measurement in the majority of patients with known or suspected hypertension, especially those with coronary heart disease, diabetes, pregnancy, chronic kidney disease, suspected nonadherence, or a substantial white-coat effect.[18] HBPM has to be incorporated into the routine care of hypertensive patients in the same way that home blood glucose monitoring performed by the patient with diabetes.

Patients should be advised to purchase oscillometric monitors that measure BP on the upper arm with an appropriate cuff size and that have been shown to be accurate according to standard international protocols. They should be shown how to use them by their healthcare providers.

CONCLUSION

In India, there are nearly 100 million persons with high BP. In every home, there is a person who has Hypertension. Home Blood Pressure Monitoring is the need of the hour which helps to improve adherence to therapy and the BP control. Even home blood sugar monitoring took nearly 20 years before it became popular. It is expected hopefully that more new models of HBPM with the latest technology would be available in every house just like mobile phones. Healthcare professionals, the medical association should explain the need for HBPM and educate the patients.

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Original Article

A Rare Case of IgA Nephropathy with Polycythemia Vera with Mild Hypertension

Monica Razdan, Shahid Abbas

INTRODUCTION

IgA nephropathy is one of the most frequent forms of glomerulonephritis (GN), firstly described by Berger with male preponderance and high incidence in third decade, the disease is characterized by episodic hematuria or persistent asymptomatic microscopic hematuria with IgA deposition in mesangium.

Table 1: Laboratory investigations

Haemoglobin	17.2 gm%
Red Blood Cell Count	6.35 million per cumm
Platelet Count	3.42 lacs/cumm
White Blood Cell Count	9800/cumm
Blood Urea	94 mg/dl
Serum Creatinine	2.46 mg/dl
TSH	85.4 microunit/L
Serum Triglyceride	254 mg%
Serum Free Lambda	Normal (21.20 mg/L)
Serum Free Kappa	Raised (36.10 mg/L)
UGIEndoscopy	Gastric ulcers with H. Pylori
Serum erythropoietin level	6.36 mIU/mL
24 hrs urine protein	3.27 gm/24hrs
USG whole abdomen	Renal parenchymal changes
JAK2V617F mutation	Negative
2D Echo	EF-40%,Concentric LVH

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Polycythemia vera (PV) is a clonal disorder involving a multipotent hematopoietic progenitor cell in which phenotypically normal red cells, granulocytes and platelets accumulate in the absence of a recognizable physiologic stimulus. PV typically manifests as blood circulation disorder, hypertension and cerebral infarction associated with JAK2 mutationin 95 % of cases but negative value does not rule out the disease. Polycythemia Vera associated with renal disease is clinically rare. We report a case of IgA nephropathy combined with polycythemia vera, hypothyroidism and mild hypertension.

CASE HISTORY

50yr old Indian male, diagnosed case of gastric ulcers with H. pylori 10 yrs back for which he was taking regular medication presented in medicine outpatient department with generalised anasarca which progressesd from face to abdomen and finally to bilateral lower limb, he had decreased urine output with no hematuria. He had persistent azotemia with serum creatinine levels ranging from 1.49 to 2.46, blood Urea from 46 to 94 (mg/dl), mild proteinuria and microscopic hematuria in routine microscopy (Table 1). Sonography revealed renal parenchymal changes with poor corticomedullary differentiation with small sized kidneys, after which he was diagnosed as Chronic Kidney Disease (stage II) 3 yrs back. He had dyspnea (NYHA grade II), chest pain on exertion,his Blood pressure

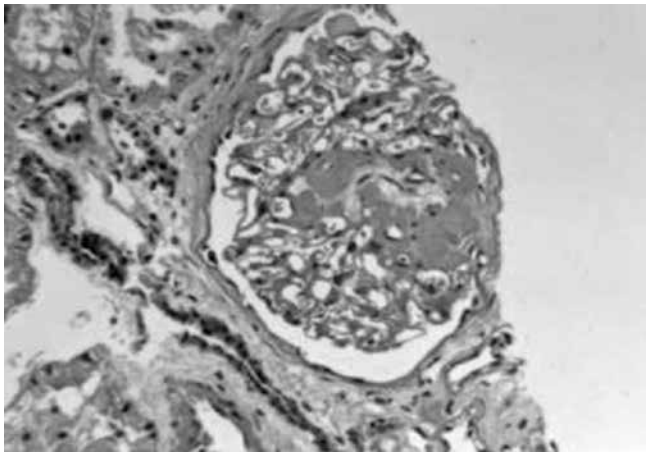

Fig. 1 : Light microscopy microscopy of glomeruli with H&E staining

had consistent higher readings of 140/90 with dull aching headache.

Keeping this in mind his 24 hr urine protein was done which revealed nephrotic range proteinuria (3.27 gm / 24 hrs), microscopic hematuria and lipid profile showed hypertriglyceridaemia with values ranging from 254 to 303 mg/dl,his renal biopsy was done at SAIMS, which showed IgA nephropathy associated with segmental tuft sclerosis involving 3/7 (42.8 %) with M0E0S1T0 score (Figure 1).

He had bilateral lower limb pain with no intermittent claudication, his haemogram showed haemoglobin between 16 to 18 mg/dl,thrombocytosis and mild splenomegaly along with features of erythromelalgia, he got his phlebotomy done for initial 6 months, possible causes of secondary erythrocytosis were ruled out.

He had history of recent onset CVA with right sided hemiparesis, MRI Brain revealed left temporoparietal infarct which recovered gradually.

During the course of the disease he was on medical management wih hydroxyurea, ramipril, statins, aspirin, amlodipine and immunosuppressive drugs and underwent phlebotomy as per medical condition and haematocrit values.

RENAL BIOPSY REPORT

1. IgA nephropathy associated with segmental tuft sclerosis involving 3/7 (42.8%) of sampled glomeruli.
2. MEST scores (Oxford classification of IgA nephropathy)

   Mesangial hypercellularity (M score <0.5): M0

   Endocapillary cellularity (absent): E0

   Segmental sclerosis (present) S1

DISCUSSION

According to current literature there are only 23 cases of PV associated with renal disease, out of which 8 cases showed IgA Nephropahy histologically.

All 8 patients were male with an average age of 47.87 years. All 8 patients presented with hypertension, including 1 case with a hypertension crisis. Among these patients 2 cases underwent steroid therapy, 2 cases received regular phlebotomy and 1 case received mycophenolate mofetil along with antihypertensive, anticoagulant, antiplatelet and bone marrow suppression therapies.

In IgA nephropathy there is a slow progression to chronic kidney failure in 25-30% of cases during a period of 20 years. In 2-3% patients it can also be associated with polycythemia vera as seen in our patient.

Pathogenesis of PV associated with renal disease is not well understood, it may occur as follows. First, PV leads to increases in blood volume and viscosity, thus causing a passive expansion of the capillaries and intimal injury, which results in vascular microthrombi, glomerular capillary occlusion and a reduction in the GFR, thereby leading to tissue ischemia. If the ischemia persists without relief, it is likely to result in chronic renal damage. Second, PV is often associated with hypertension and hyperuricemia, which affect renal microcirculation,thrombocytosis and the abnormal activation of megakaryocytes might be critical factors for glomerular sclerosis. Cytokines and growth factors also play important roles.

After administration of hydroxyurea, ramipril, statins, aspirin and amlodipine, blood cell count, hypertriglyceridemia and blood pressure was normalized, proteinuria regressed while serum creatinine was at around same values since treatment started.

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Original Article

Reference Values for the Six Minute Walk Test

Ashwin Songara, Ravi Dosi, Ashok Bajpai, Mriganka M Misra

INTRODUCTION

The Six Minute walk test (6MWT) is a useful performance based measure of functional exercise capacity in obese individuals. This test measures the distance that a patient can quickly walk on a flat hard surface in a period of 6 minutes (6MWD).[1] Various studies have found reference values for SMWD in healthy individuals but very less is known for healthy obese individuals. The aim of this study is to find reference values for 6MWT in adult obese population.

AIMS & OBJECTIVES

1. Correlation of anthropometric measures with SMWD
2. To find the Reference equation to predict the distance walked during SMWT in obese individuals.

SIX MINUTE WALK TEST

There are several modalities available for the objective evaluation of functional exercise capacity. SMWT is a practical & simple test that requires a 100 ft hallway but no exercise equipment or advanced training for technicians. Walking is an activity performed daily by all but the most severely impaired patients. This test measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes. It evaluates the global & integrated responses of all the systems involved during exercise including the pulmonary & cardiovascular systems, systemic circulation, peripheral circulation, neuromuscular units & muscle metabolism.[1]

INDICATION

The strongest indication for the 6MWT is for measuring the response to medical interventions in patients with moderate to severe heart or lung disease.[2] The 6MWT has also been used as a onetime measure of functional status of patients as well as predictors of morbidity & mortality .

METHODS

- Source: The study was conducted on 100 healthy obese individuals (BMI >30 kg/m2) & (65 Male, 35 Female) who visited SAIMS & MOHAK Hospital for multidisciplinary rehabilitation, after oral consent. The 6MWT was performed according to the guidelines of ATS. Baseline blood pressure, heart rate, respiratory rate & oxygen saturation were measured. The total distance walked in 6 minutes was noted.
- Research Design: A prospective study.
- Study Set Up: This study has been conducted at SAMC & PGI and Mohak Hospital, Indore
- Study Duration: The duration of study was 8 months i.e. from October 2014 to May 2015
- Study Tools: History,Examination,Body Mass Index Sphygmomanometer, Pulse Oximeter
- Inclusion Criteria: Healthy Obese individuals of age 20-60 years with BMI>30 kg/m2.
- Exclusion Criteria: Known case of

Pre-existing Cardiovascular or Respiratory disease.

RESULTS

Distance walked during six minute walk test was significantly correlated (by using linear regression method) to age; oxygen saturation at starting of test and BMI unlikely to previous studies gender is not correlated significantly. Reason can be genetically different South Asian population from European Caucasian Populations which were used in previous studies. Between variables SBP was positively correlated with BMI.

"The proposed reference equation is:

6MWT distance = (6.8) O_2 saturation-(4.3) BMI-(0.6) Age-170.64

(Evolved from linear regression coefficient table and model summery R value)

In the multiple regression analysis,age, oxygen saturation and BMI explained 86% of the total variance in 6MWT.The average difference between predicted & measured 6MWT values (11.33 ± 52.98 m) didn't reach the statistical significance & the correlation was significant (R=0.701). Reason can be limitations of study like different encouragement levels and mental status of patients, lung capacities and muscle strength.

CONCLUSION

A reference equation specific for the obese population was provided; it can be used as realistic benchmark in the rehabilitation setting to assess functional capacity, plan exercise intensity & monitor changes over time.

DISCUSSION

1. Troosres et al. found that age, gender, height & weight explained 66% of the 6MWT distance variability in 51 healthy adults.
2. Capodaglio P, et al found significant correlation of age, gender & BMI with 6MWD & deduced a reference equation specific to obese individuals.

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Original Article

Effect of Telmisartan on Lung Volumes, Hematocrit and Arterial Blood Gases alongwith Blood Pressure in Chronic Obstructive Pulmonary Disease with Arterial Hypertension

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) has traditionally been considered a disease of the lungs secondary to cigarette smoking and characterized by airflow obstruction due to abnormalities of both airway (bronchitis) and lung parenchyma (emphysema). However, COPD has important manifestations beyond the lungs, the so-called systemic effects, which include unintentional weight loss, skeletal muscle dysfunction, an increased risk of cardiovascular disease, osteoporosis, and depression, among others. Thus COPD, and emphysema in particular, is nowadays being considered 'a disease with a significant systemic component', if not a 'systemic disease' per se.

The GOLD guidelines 2015 defines COPD as a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.

Abundant evidence of both local and systemic inflammation have been found in patients with COPD. Various mediators such as leukotriene B4 and and TNF-α which induce destructive changes are released from activated inflammatory cells in COPD patients. In addition to inflammation, oxidative stress also plays an important role in the pathogenesis of COPD.

Angiotensin II plays an important role in induction, and persistence of this inflammation and thus Angiotensin receptor blockers (ARBs) which exert ameliorating effects on inflammation, and oxidative stress may very well be useful in the management of COPD.

Also, in COPD, the sympathetic nervous system, as well as the renin–angiotensin system, is activated with possible negative systemic effects on skeletal muscles. Activation of the RAS is associated with the development of secondary erythrocytosis in hypoxaemic patients with COPD . Furthermore, AT1 receptors are highly expressed within the lung and modulate alveolar epithelial cell apoptosis and lung fibroblast growth . Thus there is the possibility that AT1 receptor

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blockers effect haematocrit and lung function in COPD.

Angiotensin II type-1 receptor blockers inhibit the sympathetic and renin– angiotensin systems and might improve skeletal and respiratory muscle strength in patients in whom these systems are activated.

Spirometry

- Spirometry is the most common of the pulmonary function tests (PFTs), measuring lung function, specifically the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled. The following graphs are usually displayed:
- A *volume-time curve*, showing volume (litres) along the Y-axis and time (seconds) along the X-axis
- A *flow-volume loop*, which graphically depicts the rate of airflow on the Y-axis and the total volume inspired or expired on the X-axis

Forced Vital Capacity

Forced vital capacity (FVC) is the volume of air that can forcibly be blown out after full inspiration, measured in liters. FVC is the most basic maneuver in spirometry tests. Patients with obstructive lung disease usually have a normal or only slightly decreased vital capacity. Patients with restrictive lung disease have a decreased vital capacity.

Forced expiratory volume in 1 second (FEV1)

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration.. The FEV1 is reduced in both obstructive and restrictive lung disease. The FEV1 is reduced in obstructive lung disease because of increased airway resistance. It is reduced in restrictive lung disease because of the low vital capacity.

FEV1/FVC ratio

The FEV1/FVC ratio, also called **Tiffeneau-Pinelli index**, is a calculated ratio used in the diagnosis of obstructive and restrictive lung disease It represents the proportion of a person's vital capacity that they are able to expire in the first second of forced expiration.

A derived value of FEV1% is **FEV1% predicted**, which is defined as FEV1% of the patient divided by the average FEV1% in the population for any person of similar age, sex and body composition.

Peak expiratory flow

Also called peak expiratory flow rate (PEFR), it is a person's maximum speed of expiration, as measured with a peak flow meter, a small, hand-held device used to monitor a person's ability to breathe out air. It measures the airflow through the bronchi and thus the degree of obstruction in the airways.

OBJECTIVE

- To assess the effect of an AT1 receptor antagonist, Telmisartan, on lung volumes, hematocrit, arterial blood gases and 24-hour profile of blood pressure (BP) in patients with stable chronic obstructive pulmonary disease and I-II stage arterial hypertension prior to and after 12 weeks of therapy with it.

METHODS

Study design: This is a prospective study

Study set up: The study was conducted in the Departments of Respiratory Medicine and General Medicine at Sri Aurobindo Medical College & Post Graduate Institute.

Size of the study: The study was done on 50 male subjects with stable COPD with I-II stage arterial hypertension, who had come for routine follow up in the Departments of Respiratory Medicine and General Medicine, SAIMS, Indore.

Duration: The duration of the study was 1 year.

Study tools: history, general and systemic examination, hemodynamic parameters, peak expiratory flow rate, Blood investigations, ECG, ABG, pulmonary function test, 2D

Table 1:

Variables	Baseline	After 12 weeks	P value
FEV1 (L)	3.62±0.56	3.96±0.51	0.001
FVC (L)	4.11±0.64	4.13±0.64	0.430
FEV1/FVC	0.88±0.11	0.96±0.13	0.005

ECHO (optional).

INCLUSION CRITERIA

- Patients with a diagnosis of COPD with concomitant I-II stage arterial hypertension.

Diagnosis of COPD made according to symptoms of dyspnea, chronic cough, chronic sputum production, history of exposure to risk factors and age more than 40 years as per GOLD guidelines and confirmed by spirometry, FEV1/FVC<70%.

EXCLUSION CRITERIA

- Patients with other associated co morbidities like diabetes mellitus, malignancy, arthritis, gastrointestinal disorders among others.
- Presence of congenital and valvular diseases, cardiomyopathy of heart or other cardiac illness.
- Patients unable to perform pulmonary function test properly.

RESULTS

Telmisartan, administered in a dose of 40 mg/day, significantly increased forced expiratory volume in 1 second[FEV1] (p0.001) (Table 1), peak expiratory flow rate(PEFR) and showed significant decrease in hematocrit (p0.001) and hemoglobin values (p0.002) (Table 2), decrease in CO2 partial pressure (pCO2) in arterial blood.

It also significantly reduced mean systolic BP ($p < 0.003$) and diastolic BP ($p < 0.003$) during day hours, significantly reduced SBP load ($p < 0.02$) and DBP load ($p < 0.003$) during day hours, and SBP load ($p < 0.02$) during night hours.

Table 2:

	Telmisartan		
	Baseline	After 12 wks	p value
Hematocrit %	46.4±3.6	43.9±4.3	0.001
Hemoglobin g/dl	15.1±1.3	14.2±1.6	0.002
(All Data are presented as mean±SD)			

CONCLUSION

WHO predicts that COPD will become the 3rd leading cause of death and 5th leading cause of disability worldwide by the year 2030. Hence, research regarding newer treatment options for COPD and its associated systemic effects is of utmost importance.

The changes in FEV1, PEFR, haematocrit and CO2 partial pressure(pCO2) in arterial blood following treatment with Telmisartan raises the possibility that well-known group of cardiovascular drugs can produce unanticipated beneficial effects in COPD patients.

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Original Article

Replacement of Amlodipine with Cilnidipine and Assessment of Pedal Edema Alongwith Blood Pressure Control

Anand Baharani, Abhishek Singhai, RK Jha

INTRODUCTION

Hypertension is the most common cardiovascular disease. In India, 29.8% population are suffering from hypertension.[1] Pedal edema is a common adverse effect of amlodipine, a widely used L-type calcium channel blocker (CCB), seen in up to 15% of patients receiving the drug.[2] The usual approach to patients with amlodipine-induced edema involves cessation of amlodipine therapy and substitution with an alternative antihypertensive. Cilnidipine is a third generation L/N-type CCB and is approved for the therapy of essential hypertension. This study was, therefore, planned to determine whether cilnidipine therapy can produce resolution of amlodipine-induced edema while maintaining adequate control of blood pressure.

SUBJECTS AND METHODS

This prospective, observational study conducted at the tertiary care centre of Central India between January 2015 and June 2015. All patients of hypertension who were taking amlodipine and developed amlodipine induced pedal edema were included. Patients with preexisting edema, cor pulmonale, nephrotic syndrome, hypoproteinemia, anemia, pregnant women, varicose veins and patients on drugs such as nonsteroidal anti-inflammatory drugs were excluded from study.

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Study Procedure

Total 50 patients (n = 50) who met the inclusion criteria were recruited in the study. The patients were examined by the consultant physician and blood pressure was measured in right arm, sitting posture by the auscultatory method using standard mercury sphygmomanometer. Two recordings of blood pressure were taken at an interval of 15–20 min by the same consultant. Pedal edema was assessed by clinical method over the medial malleolus of both legs. Presence of pitting edema on either of the legs was considered as positive for the pedal edema.

After initial screening, demographic data, past medical history, family history, and findings of clinical examination were recorded in the case report form. Baseline parameters including clinical evidence of ankle edema, pulse rate, blood pressure, bilateral ankle circumference, and body weight were recorded for all patients. All patients were then initiated on an efficacy-equivalent dose of cilnidipine (5 mg of amlodipine is equivalent to 10 mg of cilnidipine). Amlodipine therapy was stopped on the day of initiating cilnidipine. The patients were followed-up for four weeks. Relevant parameters were then recorded again for all the patients. Data

Table 1: Baseline data

Sr. No.	Parameters	Measurement at baseline (On Amlodipine)Mean ± SD	Measurement after 4 weeks (On Cilnidipine) Mean ± SD	Change in value	p value
1.	Ankle circumference, right (cm)	27.0 ± 1.08	23.07 ±0.99	3.93	< 0.001
2.	Ankle circumference, left (cm)	26.98 ± 1.01	23.08 ± 0.97	3.90	< 0.001
3.	Body weight (kg)	76.7 ± 2.6	72.6 ± 1.8	4.1	<0.001
4.	Pulse rate (bpm)	89 ± 5	87 ± 4	2	0.987
5.	Mean systolic blood pressure (mm Hg)	124 ± 3.8	123.3 ± 2.9	0.7	0.18
6.	Mean diastolic blood pressure (mm Hg)	78.9 ± 2.6	76.8 ± 1.9	2.1	0.12

analysis was done with Statistical Product and Service Solutions (SPSS) Statistics version 17.0 (Chicago IL, USA).

RESULTS

Out of 50 patients included in the study, 22 (44 %) were male. The mean age was 55 years (± 2.6 SD). Mean duration of therapy with amlodipine at the time of inclusion in the study was 12 months. Forty five patients (90%) were receiving 5 mg of amlodipine daily. Baseline hemodynamic data, ankle circumferences, and body weight are detailed in Table 1.

Reassessment after 1 month showed complete clinical resolution of ankle edema in all 50 patients. There was a significant decrease in ankle circumference and body weight. Comparison of hemodynamic parameters revealed a non-significant change in mean arterial blood pressure, and no significant change in pulse rate.

DISCUSSION

A number of mechanisms have been postulated for CCB-induced edema. The principal mechanism involves interference of normal auto-regulatory postural vasoconstrictor reflexes. L-type CCBs like amlodipine directly inhibit pre-capillary vasoconstriction through arteriolar dilatation, thus promoting interstitial edema. Other contributory mechanisms include capillary hypertension and increased microvascular permeability. In contrast to amlodipine which acts primarily through blockade of L-type Ca^{2+} channels, cilnidipine acts through dual blockade of L-type and N-type Ca^{2+} channels.[3] Whereas L-type Ca^{2+} channel blockade produces vasodilation of peripheral resistance vessels akin to amlodipine, inhibition of neuronal N-type Ca^{2+} channels disrupts sympathetic nervous outflow, lowering plasma catecholamine levels, and thereby producing further vasodilatation. This unique mechanism of action results in vasodilation of both pre- and post-capillary resistance vessels reducing capillary hypertension and consequent hyperfiltration of fluid into the interstitium.

CONCLUSION

Cilnidipine is an effective and well-tolerated alternative antihypertensive in patients with amlodipine-induced edema.

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Original Article

Clinic Based Measurement of Central Aortic Systolic Pressure – Practical Utility and Advantages

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BACKGROUND

Central aortic blood pressure is established as a strong predictor of cardiovascular events independent of the brachial blood pressure especially in patients with chronic kidney disease (CKD).Central aortic systolic pressure (CASP) is one of the surrogate marker of large artery stiffness which in turn influences microcirculation of brain and kidney as also the ventricular workload and coronary perfusion.Simple and noninvasive devices are now validated worldwide to measure CASP in outpatient clinics.However there is lack of data on CASP and it`s significance in our Indian subjects.

AIMS AND OBJECTIVES

1. To measure CASP across a cross-section of our patient population and assess the demographic profile using A-Pulse CASP device.
2. To compare and analyse CASP measurements vs brachial blood pressure measurements in patients (pts) with Hypertension and CKD.

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METHODS

Basic demographic and anthropometric data was recorded.Brachial BP was measured by oscillometric method using A-Pulse device (Healthstats International,Singapore,approved by USFDA) in the sitting position.CASP was then measured by applanation tonometry and radial transfer function technique by placing the sensor of the A-Pulse CASP device over the ipsilateral radial artery.

RESULTS

- 90 consecutive subjects (males-60;females-30) with mean age 47.11±14 years were included in the study.
- Subgroups were : Group A- Normotensive healthy volunteers (n=25); Group B – pts with Hypertension without CKD (n=16); Group C – pts with CKD,stage 1-4 (n=27) and Group D –with CKD - 5D,on hemodialysis (n=22).
- In Group A,mean CASP (115 ± 10.8) values across all age groups corresponded to the age censored worldwide reference range,while in groups B,C and D, 51/65 (78%) pts had mean CASP values significantly higher($p<0.05$) than the age censored reference range.
- Subjects with normal Brachial Pulse Pressure (<50 mmHg,n=40) had near normal mean Brachial systolic BP [BASP](124.98 ± 14.27) and CASP (117.35 ± 13),while those with high Brachial Pulse Pressure (>50

mmHg,n=50) had correspondingly higher mean BASP(147.48 ± 14.84) and CASP (136.2 ± 15.36) values when compared to the age censored reference range.In the latter subgroup, younger subjects (age <50 years,n=23) had more significant elevation of CASP (136.73 ± 13.94) than BASP (148.26 ± 13.40) ($p<0.05$).

- 30/55 patients with high BMI (>25 kg/sqm) in younger age group (age < 50 years) had comparable BASP (135.9 ± 16.91),but mean CASP (126.9 ± 15.32) was significantly higher ($p<0.05$) than age censored reference range.
- Literature shows that the mean difference between absolute CASP and BASP values narrows down with advancing age in normal people and this is confirmed in our normal volunteers. In groups B, C and D the mean difference between BASP and CASP was similar (10.8 vs 9.3) in younger (age <50 years, n= 29) versus older (age>50 years= 36) age group; thus emphasizing that younger pts with hypertension and CKD exhibit accelerated vascular ageing.
- Patients (n=22) having longer duration (>5 years) of CKD had significantly higher CASP (136 +17 vs 127+14; p value) as compared to pts (n=27) with lesser duration of CKD (< 5 years).

CONCLUSIONS

- Our study validates the use of A-pulse device for measurement of CASP.
- CASP measurement may be better than BASP measurement in identifying high CV risk early in young and obese individuals.
- Younger patients with hypertension and CKD having high brachial pulse pressure (>50 mmHg) should undergo central BP assessment
- Office based measurement of CASP is a necessary additional tool for thorough cardiovascular risk assessment, especially in patients with CKD.

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Original Article

A Correlation of Left Ventricular Hypertrophy (Eccentric) with Anthropometric Measurements in Obese Adults

Arvind Mittal[1], Pranay Bajpai[2], RK Jha[4], Dolly Joseph[3]

INTRODUCTION

The global epidemic of overweight & obesity- **"globesity".**[1] In 2014, more than 1.9 billion (39%) adults, 18 years and older, were overweight. Of these over 600 million (19%) were obese[2] and Prevalence is increasing not only in the developed countries but also in developing countries like India.[3] Obesity represent a state of ↑ adipose tissue mass.[4] Adipose tissue, recently been recognized as active participant in numerous physiological & pathological process and central adiposity (visceral fat) contributes to chronic subclinical inflammation which is linked to endothelial dysfunction & early development of cardiovascular diseases.[5] Currently overweight and obesity are classified by Body Mass Index (BMI) which is considered as **"Gold Standard"** by WHO as measure of fatness in children and adult .

The Echocardiography (Echo) diagnosis of LVH in obese help to prevent life threatening complication of obesity.[6] LVH is present in a consistent fraction of the obese population and that eccentric hypertrophy prevails over the concentric phenotype. As obesity-related LVH is a powerful risk factor for systolic/ diastolic dysfunction, the prevention/ treatment of obesity may have a strong, favourable impact on incident heart failure.[7] In Obesity the cardiac output is elevated due to increase blood volume causing a chronically elevated preload condition which in turn increases ventricular size, wall stress and left ventricular mass (LVM) leading to development of eccentric ventricular hypertrophy.[8]

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AIMS /OBJECTIVE

To study a correlation of left ventricular hypertrophy (eccentric) with anthropometric measurements of obese adults as an independent prognostic marker for Obesity.

To study LVH as represented by Left Ventricular Mass and its comparison with (a) BMI (Body Mass Index), (b) BSA (Body Surface Area) and (c) WHR (Waist To Hip Ratio).

Inclusion Criteria

1. All patient with age between 20years to 60years
2. Obese as Cases with BMI ≥30kg/m²
3. Non Obese as Controls - with BMI 18.5kg/m² to 24.9kg/m²

Consent was taken from all patients included in study

Exclusion criteria

1. Who were not willing to give consent
2. All diabetic Subjects

3. Patients with history of heart disease
4. All Patient who were overweight - with BMI of 25.0kg/m² to 29.9kg/m²
5. Women with pregnancy

METHODS

All adults patients attending the Medicine OPD of Sri Aurobindo Medical College and Post graduate, Indore, between Sept.2012-May14 were enrolled in the study. Total of 200 patients were included in study, out of them 100 as cases and 100 as controls. It was a prospective cross sectional study. Anthropometric data collection was done for all cases and controls as Weight in Kg, Height in cm, Waist Circumference in cm and Hip Circumference in cm, three readings were taken for each and mean of these readings was taken.Pulse & Blood pressure were recorded for all and FBS, PPBS and ECG was done for all cases and controls . Echocardiography was performed after anthropometric measurements,two dimensional targeted M-mode measurement of LVM as recommended by American Society of echocardiography was done, BSA was calculated by Echo machine (by Du Bois formula =BSA =$0.007184 \times W^{0.425} \times H^{0.725}$)and Left ventricular mass(LVM) was calculated using ASE modified formula also called"The Deverux-Modified ASE Cube Formula"[9] (LVM (g) =$0.8 (1.04(IVSd + LVIDd + PWTd)^3 - LVIDd^3)+0.6$)

Table 1: Mean BMI in Both the Groups

Characteristic	Study group (Mean ± SD)	Control Group (Mean ± SD)
BMI (kg/m²)	42.48 ± 7.35	21.69 ± 3.32

STATISTICAL ANALYSIS AND RESULTS

A total of 200 subjects were included in study. Out of these 200 subjects, 100 were taken in study group which was consisted of obese patients and 100 subjects were taken as control group, which was consisted of non-obese patients. Obesity was defined on the basis of BMI. In both the groups, the mean age was comparable (mean age of cases was 42.5 ± 10.9 and of controls was 47.03 ± 13.28). BMI was higher in cases with mean value of 42.48 ± 7.35 as compared to control with mean value of 21.69 ± 3.32 (Table 1).

In this study, we found that mean waist hip ratio (WHR) was 0.97 ± 0.13 in study group and 0.92 ± 0.07 in control group which was significantly higher in cases as compared to controls with p value of 0.001. Mean body surface area (BSA) was also found significantly higher in study group as compared to control with mean value of 2.19 ± 0.22 & 1.68 ± 0.23 respectively and p value 0.001 (Table-2). We also found that mean Left ventricular mass(LVM) was 222.94 ± 89.25 in study group and 165.17 ± 55.45 in control group which was also significantly higher in cases as compared to controls with p value of 0.001 (Table 3).

In our study, we found that among males LVM was showing positive correlation with BMI with r value 0.339 & p value 0.001 (significant) and also with BSA with r value 0.438 & p value 0.001 (significant) but not with WHR with r value 0.113 & p value 0.236 (insignificant). In females we found that LVM was showing positive correlation with all the three parameters BMI,WHR & BSA with

Table 2: Mean Anthropometric data (WHR & BSA) of both the groups

Characteristic	Study group (Mean ± SD)	Control Group (Mean ± SD)	'Z' test	P value
WHR	0.97 ± 0.13	0.92 ± 0.07	3.39	0.001***
BSA (m2)	2.19 ± 0.22	1.68 ± 0.23	16.02	0.001***

Table 3: Mean LVM in Both the Groups

Characteristic	Study group (Mean ± SD)	Control Group (Mean ± SD	'Z' test	P value
LVM (g)	222.94 ± 89.25	165.17 ± 55.45	5.50	0.001***

Table 4: Correlation between the measures of obesity and Echocardiographic parameters in both the groups (Pooled Data N=200)

Characteristic	Male/Female	BMI r value (P value)	WHR r value (p value)	BSA r value (p value)
LVM(g)	Male	0.339(0.001***)	0.113 (0.236)	0.438(0.001***)
	Female	0.328(0.002***)	0.231 (0.030)*	0.340(0.001***)

r value 0.328 (P value 0.002), 0.231 (p value 0.030) and 0.340 (p value 0.001) respectively (Table-4).

DISCUSSION

In our study of 200 subjects we found that the BMI was significantly higher in the study group 42.48(±7.35)than control group 21.69(±3.32) and this was also supported by *Oliver J et al* in *2009* they also found BMI (37.8 ± 6.9 kg/m^2) higher in cases than in controls (BMI 21.7 ± 1.8 kg/m^2) in their study.[10]

We also found BSA & WHR both were significantly higher in experimental than control group and this was also supported by *Okpara IC et al* in 2009 and they also found that BSA & WHR were significantly higher in the obese subjects than control group ($p<0.05$).[9]

In our study we also found that LVM is significantly higher in study group than control group. Amongst three parameters of anthropometry, significant correlation of LVM was seen with BMI in males & females both, with BSA in males & females both, but with WHR only in females; this was supported by studies done by *Okpara IC et al* in 2009 *& Rider et al* in 2009; showed that BSA, WHR & BMI have a significant positive correlation with LVM.[9,11]

CONCLUSION

WHR and BSA is a equivalent anthropometric marker of Obesity like BMI. LVM estimation is an independent predictor of eccentric LV Hypertrophy in Obesity. Thus, reduction in BMI, marker of Obesity will lead to improvement of Echocardiographic parameters of Obesity and will likely to prevent further cardiovascular morbidity & Mortality.

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Abstracts of 24th HSICON 2015, Indore
22 - 23 August, 2015

The Relationship Between Uric Acid and Hypertension in Adults

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Introduction: Uric acid has been associated with hypertension in many studies involving different populations but little or no information was found on this association in a Indian population. The aim of this study therefore was to correlate serum uric acid concentrations with blood pressure measurements in individuals who are hypertensive, pre-hypertensive and normotensive, and to investigate the possibility of existence of an association between uric acid levels and other risk factors for hypertension.

Material & Methods: A total of 297 adults from Medicine department of SAMC & PGI, Indore participated in the study. Blood pressure, serum uric acid, fasting blood glucose (subjects with ≥ 110mg/dl were excluded), lipids, body mass index and waist circumference were measured.

Results: Individuals who were pre- hypertensive had the highest mean uric acid concentration which was significantly higher than that for normotensives (P<0.0001). There was a significant positive correlation between uric acid with systolic and diastolic blood pressure (P<0.0001; P<0.0001), respectively. A significant positive correlation was also observed between serum uric acid levels with gender, age, triglycerides and life style patterns (P<0.0001).

Discussion & Conclusion: In conclusion we observed a significant positive association between uric acid with both systolic and diastolic blood pressure after controlling for confounding factors. The association was most evident in people with hypertension.

An Interesting Case of Headache

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Background: Pheochromocytomas are catecholamine producing tumors derived from sympathetic or parasympathetic nervous system. These may arise sporadically or inherited as MEN type 2 syndromes. The diagnosis provides a potentially correctable cause of hypertension. The clinical presentation is variable ranging from adrenal incidentaloma to hypertensive crisis with associated cardio or cerebrovascular complications. Incidence 2 to 8 of 1 million persons per year. 0.1 %of hypertensive patients harbour this tumor. Mean age at diagnosis is about 40 years. Presentation is 10% bilateral, 10% extra adrenal, 10%malignant.

Case Report: A 31 years old female patient came with complaints of persistent headache with raised blood pressure. Ultrasound of the abdomn revealed retroperitoneal echogenic lesion. CECT of abdomen and angio showed retroperitoneal mass lesion encasing IVC and aorta. Urine VMA was positive. Free metanephrines were elevated. Technetium 99m scan was done. DTPA scan was done. Patient was operated upon and HPE revealed pheochromocytoma. Post surgery patient blood pressure returned to normal.

Conclusion: This case is being presented to highlight the importance of secondary reversible causes of hypertension and the importance of timely intervention to prevent end organ damage.

An Unusual Cause of Renovascular Hypertension in Young Patient

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Introduction: Entrapment of renal artery by the diaphragmatic crus is a rare cause of renal artery stenosis. This condition should be considered in young hypertensive patients with renal artery stenosis without cardiovascular risk factors. Here we present a case of young boy who presented with hypertension.

Case Report: A 19 year old boy presented with dyspepsia and headache 5 months back, evaluated and found to have high blood pressure in another hospital and referred to our hospital for further workup. On admission he denied any other symptoms. He had no other medical history. His father had hypertension. On examination patient had blood pressure 160/80 mmHg. Other physical examination normal. Full blood count and urea, creatinine and electrolytes are normal. Lipid studies, thyroid function tests, liver function tests, coagulation screening, blood glucose level, complete urine examination were normal. CECT abdomen suggestive of crura of diaphragm impinging on right renal artery. MRI of abdomen suggestive of thickened right crus of diaphragm displacing the right main renal artery anterior and around the crus. A renal doffer ultrasound suggestive of right renal artery stenosis at proximal part. Renal Angiogram was normal. Patient was started on antihypertensives and after discussion among nephrologists patient was discharged on medical treatment.

Conclusion: Compression of a renal artery by the crus of the diaphragm (renal entrapment syndrome) should be investigated in proximal renal artery stenosis in young hypertensive patients without other cardiovascular risk factors, and where fibromuscular dysplasia is unlikely. It requires specific therapeutic management.

An Interesting case of Drug Resistant Hypertension

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Introduction: In certain situations, control of blood pressure could not be obtained by all the possible drugs against various axis of blood pressure despite using adequate and maximal drug dosage. We present a case which posed such difficulty in controlling the blood pressure.

Case Details: A 40 year old male ESRD with hypertension on maintenance hemodialysis, HCV infection treated with interferon alpha 2b, Tuberculous cervical adenopathy by ATT. After few weeks he presented with headache, blurring of vision, generalised seizure with very high BP 250/190 mm Hg, diagnosed as hypertenisive crisis. He was treated with NTG, Nitroprusside, oral Nifedepine, Hydralazine, Alphamethyl dopa at maximal doses. The pressure remained high 250/120 mm Hg. The BP still remained uncontrolled despite adding Minoxidil, Enalapril, Atenolol. But the BP got controlled only after stopping the drug Rifampicin.

Discussion: In this case as the BP could not be controlled with all the drugs at maximum dosage, the possibility of drug intereaction was considered. Among the drugs in use by the patient, Anti Hypertensives, Anti Tb drugs in Renal adjusted dose (INH, RMP, EMB, PYZ), Diuretics, Calcium supplements, H2 blocker drugs, Weekly Inteferon – the hepatic enzyme inducer Rifampicin was considered and stopped. After that BP got controlled.with Nifedipine, ACE inhibitors and Atenolol.

Conclusion: The possibility of drug interaction of anti hypertensive drugs used with the other drugs being used in that patient, to be considered in instances when anticipated therapeutic effect not obtained despite sufficient number of drugs used at adequate and maximal dosage.

Awareness Program for Hypertensive Patients through Counselling by Undergraduate Students

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Objective of Study: To assess the level of awareness about hypertension in patients attending hypertension clinic. To train the undergraduate medical students regarding counseling of hypertensive subjects. Through student – patient interactions create awareness about various aspects of disease in hypertensive subjects.

Methodology: The undergraduate medical students posted in medical unit were trained in various aspects of hypertension by didactic lecture, small group discussion, role plays. The hypertension awareness booklets in Marathi, Hindi, Guajarati and English were given to students as per their mother tongue/ choice. The students were sensitized to key aspects of counseling in hypertensive subjects. Each student interacted with five to six hypertensive patients over a period of eight weeks of posting. The subjects attending hypertension clinic were assessed for the level of awareness about various aspects of hypertension with the help of questionnaire. The pictorial exhibition on hypertension in the hypertension clinic premises was used by students as medium to explain lacunae in awareness/ wrong practices by hypertensive patients. Feedback was taken from students and patients about this awareness program.

Results and Impact: Various key issues related to awareness about the common lifestyle disease, hypertension figured out from this program. The undergraduate students went through direct patient encounters, enabling them to understand the various aspects of the disease and also got practical experience of counseling the patients. The patient's feedback about awareness program was positive and reflected in gaining the awareness through these sessions, sensitizing them about the key issues of life style modifications and chronicity of the disease.

Conclusions: The hypertension clinic or medical outpatient services should have mechanisms to assess the awareness about hypertension. With structured training, undergraduate students can be a useful source in counseling the patients with chronic diseases. Student-patient direct interactions should be enhanced for better understanding of clinical medicine.

Recent Advances in the Pharmacotherapy of Hypertension

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Hypertension is an important risk factor for cardiovascular morbidity and mortality. Blood pressure control with antihypertensive drugs reduces target organ damage and prevents cardiovascular disease outcomes.Different classes of drugs are available for the management of hypertension, but still a significant number of patientssuffering from hypertension have suboptimalcontrol of blood pressure.

Thereforethere is a need for developing new drugs for treatment of hypertension and its comorbidities. Several new compounds drugs based on novel targets for control of blood pressure are being studied and are either in preclinical or in various clinical phases of drug development. These include inhibitors of vasopeptidases, aldosterone synthase and phosphodiesterase 5; agonists of natriuretic peptide

A and vasoactive intestinal peptide receptor 2; and mineralocorticoid receptor antagonist. These are in phase II/III of drug development.Drugs in preclinical phase or phase I include inhibitors of aminopeptidase A, dopamine β-hydroxylase, and the intestinal Na+/H+ exchanger 3; and agonists of components of the angiotensin- converting enzyme 2/angiotensin (1–7)/Mas receptor axis. Moreover some vaccines directed toward angiotensin II and its type 1 receptor are also being developed and are in preclinical or phase I development.

These drugs based on novel approaches look promising but still it is unclear how many of them will be available for the patients after successfully clearing all the phases of drug development.

Keywords: Hypertension, Pharmacotherapy, Novel targets

A Survey of Prevalence, Awareness, Treatment and Control of Hypertension in Indore

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Introduction: Hypertension (HTN) is the leading risk factor for cardiovascular disease and mortality worldwide. A large proportion of these hypertensive patients are unaware of their blood pressure (BP) level and are consequently not treated. In addition, among treated individuals, more than half do not have their BP under control. Our study was thus designed to determine the prevalence, awareness, treatment, and control rates of HTN.

Material and Methods: We conducted a cross-sectional survey in all persons visiting Sri Aurobindo Medical College & PGI, Indore. Inclusion criteria were adults older than 21 years who gave oral consent to participate. Data were collected on demographic variables, socio-economic status, presence of other cardiovascular risk factors, and medication use. BP was measured after at least 10 minutes of rest in the sitting position.

Results: The crude prevalence of HTN in our study was 36.9%. Almost three quarters of subjects aged 65 years and older had HTN. In addition, HTN was more prevalent in patients who smoked, patients with diabetes, patients with higher BMI, and those who were married, divorced, or widowed compared with singles.

HTN awareness was 53. About 49% of patients with HTN were receiving treatment. Treatment rates were higher in older individuals, in those with higher income, in people who were married, in patients who smoked, in patients with diabetes mellitus.

Among "aware" participants, 93% were taking BP-lowering therapy. Among treated participants, 54% had their BP under control during the examination. This translates into an overall 27% control rate when all hypertensive patients were considered (treated and not treated). Overall, only one third of the subjects have an optimal BP defined as <120/80 mm Hg. Optimal BP was more prevalent in women compared with men in all age groups, while pre-HTN and HTN were overall more prevalent in men.

Discussion: It highlights the extent of the epidemic: 35.9% of the study participants were hypertensive, 30% had pre-HTN, and only one third had optimal BP level. The awareness rate was 53% and the overall treatment rate was 48.9% but treatment rate was extremely high (93%) in persons who were aware. BP control was observed in 54% of those who were treated, resulting in an overall 27% control rate when all hypertensive patients were considered.

Conclusions: The results of our study should encourage the development of national programs in India to improve public awareness of HTN and to train public health providers for better screening and treatment of this disease.

Comparative Study of Hypertensive Subjects with Diabetes as Co-Morbidity

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Objective of Study: To study the prevalence, clinical profile, investigations, micro vascular and macro vascular end organ involvement in hypertensive subjects with diabetes as co-morbidity and to compare these findings with hypertensive subjects without diabetes.

Methodology: After institutional ethics committee approval and written informed consent from participants, an observational cross sectional prospective study was conducted in hypertension clinic of tertiary care hospital over a period of one year on 250 hypertensive patients with diabetes as co-morbidity. The results were compared with 122 hypertensive subjects without diabetes.

Summary of Results: The hypertensive diabetic patients were significantly younger (mean age 57.88±10.72 years) than patients with hypertension alone (mean age 63.56±8.79 years) p< 0.0001. These subjects were significantly overweight (p= 0.0002) with significantly high waist circumference (p= 0.0017) reflecting central obesity. The mean diastolic blood pressure was significantly higher (p< 0.0001) in hypertensive diabetic patients. Serum BUN was significantly higher (p< 0.0001) along with higher serum creatinine levels (1.54 mg/dl in hypertensive diabetics as compared to 1.11 mg/dl in hypertensive patients). The macro vascular end organ involvement namely cerebrovascular (14.8% versus 4% in hypertensive subjects without diabetes with p= 0.0015), cardiovascular (15.2% versus 9.8%) and micro vascular end organ involvement namely retinal (33.2% versus 18.8 % with p=0.0059), renal (28% versus 7.3 % p< 0.0001) reflects the increased morbidity and disease burden in hypertensive diabetic subjects.

Conclusions: The younger Indian population is subjecting to morbidity due to co-existence of diabetes in

hypertensive patients. Tight control of blood pressure and blood glucose along with regular screening for early end organ involvement should be meticulously followed in patients with these co-morbidities.

Study of Clinical and Laboratory Profile of Elderly Hypertensive Patients

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Objective of Study: To study the symptoms, clinical signs including anthropometric examination and laboratory work-up of elderly hypertensive patients.

Methodology: After institutional ethics committee approval and written informed consent from participants, an observational cross sectional prospective study was conducted in hypertension clinic of tertiary care hospital over a period of one year on 252 elderly hypertensive patients (age more than 60 years).

Summary of Results: The prevalence of elderly hypertensive patients attending hypertension clinic of a tertiary care hospital was 11.03 %. Females (56.3%) outnumbered males (43.7%) with maximum patients (56.7%) in the age group of 60 to 65 years. Out of 252 elderly Hypertensive subjects 25 (9.9%) were newly diagnosed to have hypertension, 56% out of them had isolated systolic hypertension. 64.2% of study subjects had hypertension for 2 to 10 years duration. Giddiness was the most common symptom (55.8%) followed by headache (35.6%) and 16.3% of patients were asymptomatic. Tobacco chewing or applying masheri was commonest addiction (24.6%). 13.5% of elderly subjects had family history of hypertension. 24.1% of elderly Hypertensives were diabetic, 48.4% subjects had BMI >25, 20.2% had abnormal waist circumference and 89.7% had abnormal waist to height ratio. 31.3% study subjects had dyslipidemia. Cardiac involvement was observed in 5.5%, cerebrovascular in 4 %, retinopathy in 14.3% and renal in 10.4% elderly subjects. Single organ involvement was seen in 39.3% and multiple organs were involved in 40.1 %.

Conclusions: With rise in the population of elderly people, it is imperative to manage hypertension effectively and to regularly screen these patients for associated co-morbidities and the end organ damages.

Study of Microaluminuria as a Predictive Marker of Target Organ Damage in Hypertension

Nikhil Bakhtar, S Inamdar Sir

Introduction: Accurate cardiovascular risk evaluation : Cost effective strategy in treatment of hypertension. Microalbuminuria : an integrated marker of target organ damage. Regression of LVH : parallel decrease in MAU regardless of BP changes

Aims: Prevention of MAU in Hypertension. Correction of MAU.

Methods: Non randomised cross sectional observational study. Duration of 2 months from June 2015 to August 2015. Clinical examination. Routine investigations. Inclusion Creteria: asymptomatic adults aged> 18 years with BP of > 140\90 mm of hg

Results: Mean age of pts having MAU is 56 % in 9-10 age group. Prevalence of MAU increases with increase in age. 63% of male obese had MAU vs 25 % of female obese. 62.5% of pts had retinopathy having MAU. Retinopathy increases with severity of hypertension. ECG changes of LVH : 79.16%. MAU had no correlation with creatinine clearance

Conclusion: MAU is seen in most of the pts of hypertension. MAU had a postivite correlation with (duration and severity of HTN, Male sex, Obesity, Retinopathy & evidence of LVH)

Summary: MAU remains to be a important marker in HTN. An impotant target for early therapeutic intervention in modulating the course of disease.

Prevalance of Amlodipine Induced Gingival Overgrowth at a Tertiary Care Hospital

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Background: This study was carried out with an aim to determine the prevalence of Amlodipine induced Gingival Overgrowth (AIGO), since the prevalence of AIGO remains poorly determined. It is also a concern for both the patient and the clinician due to its unaesthetic appearance and formation of new niches for periodontopathogenic bacteria.

Materials & Methods: This study was a prospective clinical study done at Stanley Medical College over a period of two months and ongoing. Patient known to have systemic hypertension and who have received Amlodipine either singly or in combination with other anti hypertensive drugs for a minimum period of atleast three weeks were screened for the presence of gingival overgrowth. The Gingival Overgrowth was graded for severity based on Carranza's Clinical Score. Patients who were on other drugs known to cause gingival overgrowth and patients known to have certain systemic diseases like leukemia and granulomatous diseases were excluded from the study.

Results: In this ongoing study, the results so far : Of the study population, 76% of the patients were found to have gingival overgrowth, of which there was a 68% female preponderance. 66% of patients were found to be over 50 years of age. No significant correlation was observed between age, gender, drug dosage and prevalence of gingival overgrowth.

Conclusion: Prevalence of Amlodipine Induced Gingival Overgrowth was noted to be higher than that of previously reported.

Prevalence and Risk Factors of Hypertension in Centralised Indian Population Study

Sonam Verma

Objective: Hypertension is a major health problem in developing countries. The aim of the study is to determine the prevalence of hypertension and its associated risk factors in centralised indian population.

Methods: The centralised indian population study is an epidemiological study involving two residential areas in india. Of the total 3399 eligible subjects (age>20yrs), 3262 participated in the study. All the subjects underwent a glucose tolerance test (GTT) and were categorised as having normal glucose tolerance (NGT), impaired glucose tolerance (IGT) or Diabetes Mellitus (DM).

Subjects were classified as hypertensives using the criteria, systolic blood pressure (SBP) > 140mmHg, and/ or diastolic blood pressure (DBP) > 90mmHg and /or treatment with anti hypertensive drugs. Twelve –lead resting electrocardiography (ECG) was performed in 1175 individals and peripheral Doppler studies were done in 50% of the individual.

Result: The overall crude prevelance of hypertension in this population is 21.1% while the age standardized prevelance is 17%. Body mass index (BMI) and waist hip ratio (WHR) were significantly higher in the hypertensive group compared to the non-hypertensive individuals. The prevelance of diabetes and PVD was higher amongst the hypertensive compared to normotensive group.

Conclusion: The prevelance of hypertension appears to be high in centralised indian population and this calls for urgent steps for its prevention and control.

Serum Creatinine as a Risk Factor for Hypertension in Diabetic Nephropathy

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Background: Diabetic nephropathy is the commonest cause of end-stage renal disease (ESRD). The next most common cause is hypertension. The aim of study was to found out the incidence and risk factors associated with hypertension in diabetic nephropathy.

Material and Method: This study was performed in three groups normal controls (232), type 2 diabetics without nephropathy (185) and type 2 diabetics with nephropathy (407). Diabetic nephropathy was clinically defined by the presence of persistent proteinurea of >500mg/day in a diabetic patient in the absence of clinical or laboratory evidence of other kidney or urinary tract disease. Hypertension was categorized based on JNC eight classifications. Detail clinical history was taken from all the patients and controls regarding duration of disease, smoking history etc. Student t test was applied to see the difference in mean values of quantitative data in two groups. Chi Square test was applied to see the difference in frequency of discrete variables in two groups.

Results: 66.3% diabetic nephropathy patients and 51.9% type 2 diabetics without nephropathy were found hypertensive in present study in contrast only 14.7% controls had hypertension. No association of hypertension was found with age and gender in either group. Serum Creatinine and eGFR was found significantly different in hypertensive diabetic nephropathy patients than normotensive. Smoking was not found as a risk factor for hypertension in either group. Serum Creatinine was found as independent risk factor for the hypertension as revealed by multinomial logistic regression analysis.

Conclusion: Serum Creatinine and eGFR were found associated with incidence of hypertension in diabetic nepthropathy.

To Find out Prevalence & Grade of Hypertension Amongst executives

Nikhil Bakhtar

Objective: To find out prevalence & grade of hypertension amongst executives of Indore.

Methods: Data of annual medical check-up of 500 executives was evaluated. Blood pressure was measured as per JNC VI/WHO guidelines.

Results: Overall prevalence of hypertension amongst Indore executives was 37.40% of 50.0% of executives who were hypertensive based on casual reading were later found to have normal or high normal blood pressure.

Conclusion: For all epidemiological surveys, blood pressure must be recorded on at least two subsequent occasions after initial screening.