INDIAN GUIDELINES ON HYPERTENSION-IV

2019

EDITOR-IN-CHIEF
Dr. Siddharth N. Shah

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Preamble

Hypertension is a major contributor to cardiovascular morbidity and mortality worldwide and in India. In view of our special geographical and climatic conditions, ethnic background, dietary habits, literacy levels and socio-economic variables, there are some areas of significant differences in disease manifestation and management which need to be addressed by us. With this in mind, the Association of Physicians of India (API), Cardiological Society of India (CSI), the Indian College of Physicians (ICP), and the Hypertension Society of India (HSI) developed the “FIRST INDIAN GUIDELINES FOR THE MANAGEMENT OF HYPERTENSION - 2001.”

The second Indian guidelines were published in 2007. The third Indian Guidelines on Hypertension (IGH-III) were published in 2013. The fourth edition of the Indian Guidelines on Hypertension (IGH-IV) is being published now in 2019. There has been significant change in the management of hypertension in the last 6 years since the last edition. Notable ones are: change in definition of hypertension by the ACC/AHA which we are not adopting and are persisting with the earlier definition, changes in target BP to be achieved after the SHIFT trial, greater use of home blood pressure monitoring (HBPM) and ambulatory blood pressure monitoring (ABPM), reduced interest in renal angioplasty and renal denervation therapy due to recent data and an increased use of spironolactone for resistant hypertension. In addition we have new epidemiological data on hypertension and hypertension mediated organ damage (HMOD), which has also been included. Significant changes have appeared in other guidelines released in 2017 and 2018 and we needed to look at the literature which an Indian perspective and thus provide guidelines for Indian physicians for management of hypertension. These guidelines have been prepared as a reference for treating physicians. The current level of practice patterns based on evidence-based medicine have been presented. The intention is not to cover the topic of hypertension in totality but to give useful information based on literature after Medline and Embase search and evaluation of some of the latest guidelines from other national bodies like the Australian guidelines (2016), ACC/AHA guidelines (2017), Canadian hypertension guidelines (2017) and the European ESC/ESH guidelines (2018). The primary aim of these guidelines is to offer balanced information to guide clinicians, rather than rigid rules that would constrain their judgment about the management of individual adult patients, who will differ in their personal, medical, social, economic, ethnic and clinical characteristics. These guidelines do not include hypertension in children and adolescents.

Methodology

In consonance with the first, second and third guidelines, a revised format was evolved by the Core committee which was then reviewed by 15 eminent referees. Their comments were included and following that these were sent to 150 physicians and specialists from across the country whose inputs have been incorporated. Like the previous guidelines, this document has also been studied, reviewed, and endorsed by the Cardiological Society of India (CSI), Hypertension Society of India (HSI), Indian College of Physicians (ICP), Indian Society of Nephrology (ISN), Research Society for Study of Diabetes in India (RSSDI) and Indian Academy of Diabetes (IAD).

We hope these guidelines will help the practicing physicians to address to this very important public health problem. Treatment of essential hypertension is a life-long commitment and should not be stopped even when the blood pressure (BP) is stabilized without consulting the physician.

The core committee recognizes that the responsible physician’s judgment and decision remains paramount for individual adult patients.
What is New in Indian Guidelines on Hypertension – IV

- The title of “Indian Guidelines on Hypertension (IGH - IV)” will be used for the 2019 guidelines henceforth.
- The health related toxic effects of mercury are recognized world over and mercury sphygmomanometers are being replaced by aneroid and digital oscillometric sphygmomanometers.
- The change is inevitable and Indian physicians should also move towards using these devices and wean off the use of mercury sphygmomanometers.
- HBPM should be encouraged for better patient involvement and compliance. Reliable oscillometric devices should be used.
- HBPM correlates better with HMOD than the office recordings.
- Masked hypertension also needs to be diagnosed and recognized like the white coat hypertension we have been more familiar with.
- The diagnosis of hypertension will be blood pressure of ≥140/90 for office BP.
- HBPM and ABPM readings are lower than office readings. The diagnosis by HBPM and by mean daytime ABPM will be pressure of ≥135/85 and a 24 hour mean ABPM of ≥130/80.
- The latest data in India shows that presently the prevalence in urban areas is 33.8% and in rural areas, it is 27.6% with an overall prevalence of 29.8%.
- Prevalence of hypertension is increasing in India as against some other nations since our longevity is increasing.
- The levels of control of blood pressure are very low at 20% in urban and 11% in rural population. Large public health measures need to be undertaken to improve this.
- Special features of hypertension in India have been included and discussed for the first time (Table 5).
- ACEIs and ARBs are the preferred agents in young (<60) and CCBs and diuretics are the preferred agents in those >60 years.
- Combination therapy in single pill is encouraged for better compliance. >70% patients need combination of drugs for control of blood pressure.
- We should start with a two drug combination, preferably in a single pill for stage 2 hypertension.
- The value of beta-blockers as first line agents in hypertension has receded and these are now recommended as agents for use in specific indications.
- For routine patients these are no longer recommended as first line agents.
- Some combinations are preferred. ACEIs/ARBs in combination with CCB’s is considered a first line combination.
- Diuretics may be used as third agent in combination.
- Treatment of hypertension even in octogenarians (more than 80 years) has been showed to be beneficial (newer data) and is recommended.
- After the recent SPRINT study and the HOPE III study the threshold for starting antihypertensive therapy and the target blood pressure has been lowered as compared to the IGH III guidelines.9-10
- The threshold for starting antihypertensive drugs should be 140/90 in most patients.
- In patients of Coronary Artery Disease (CAD) and Heart Failure (HF), antihypertensive therapy may be started beyond 130/80. Target blood pressure of <130/80 should be achieved specially in those less than 60 years.
- In elderly, the target can be between 130-140 / 80-90 and it needs to be individualized.
- Chronic kidney disease (CKD) is a common comorbidity and has been explained.
- Awareness and diagnosis of this entity will help recognize the high risk hypertensive individuals.
- Obstructive sleep apnea (OSA) and its clinical implications have also been included.
- Patients with HFpEF derive significant benefit with good blood pressure control and target of <130/80 should be achieved just as in HFRE.
- Statins are beneficial in hypertensive individuals with dyslipidemia and should be used based on the findings of the HOPE III study.
- Aspirin has no role as a prophylactic agent in hypertension.
Definition and Classification

**Definition**

There is a continuous relationship between the level of blood pressure and the risk of complications. Starting at 115/75 mmHg, CVD risk doubles with each increment of 20/10 mm Hg throughout the blood pressure range. Risk of CV death increases two fold if BP rises to 135/85, fourfold if BP rises to 155/95 and eightfold at 175/105. All definitions of hypertension issued by various international bodies are arbitrary. There is some evidence that the risk of cardiovascular events in Asian Indians is higher at relatively lower levels of BP. Recently, the ACC/AHA guidelines have changed the definition of hypertension to 130/80. However, the European guidelines and many others maintain the earlier definition of 140/90. The Indian guidelines IV will continue with the previous definition of 140/90 and also the staging that we followed in the IGH III guidelines.

So, hypertension in adults age 18 years and older is defined as systolic blood pressure (SBP) of 140 mm Hg or greater and/or diastolic blood pressure (DBP) of 90 mm Hg or greater or any level of blood pressure in patients taking antihypertensive medication.

**Classification**

Although the classification of adult blood pressure is somewhat arbitrary, it is useful for clinicians who make treatment decisions based on a constellation of factors along with the actual level of blood pressure. Table 1 provides a classification of blood pressure for adults (age 18 and older). This classification is for individuals who are not taking antihypertensive medication and who have no acute illness and is based on the average of two or more blood pressure readings taken at least on two occasions, one to three weeks apart, after the initial screening. In addition to classifying stages of hypertension on the basis of average blood pressure levels, clinicians should specify presence or absence of target organ disease and additional risk factors.

The positive linear relationship between SBP and DBP and cardiovascular risk has long been recognized. This relationship is strong, continuous, graded, consistent, independent, predictive and etiologically significant for those with and without coronary heart disease. For persons over age 50, SBP is more important than DBP as a CVD risk factor. SBP is more difficult to control than DBP. SBP needs to be as aggressively controlled as DBP. When SBP and DBP fall into different categories, the higher category should be selected to classify the individual’s blood pressure.

The definition and classification of hypertension is based on office readings by the physicians. The HBPM may be taken in account for staging and therapy of the patient. More recently, the SPRINT study used automatic office blood pressure (AOBP) recording which is not always feasible and so not recommended routinely by us. AOBP readings are 10-15 / 5-7 mm Hg lower than the office BP readings that we routinely use for definition of hypertension. The classification of hypertension will still largely be based on office recordings by the physician and will be as in Table 1.

We now feel that HBPM should also be used for definition and follow up of patients. White coat hypertension is diagnosed when office blood pressure (OBP) readings are high and home BP is normal. Masked hypertension indicates normal office BP and high home BP readings. Incidence of white coat hypertension is 10-15% and that of masked hypertension is 5-10%. Recording of OBP and HBPM both are important for recognizing these entities. A recent study (2018) comparing ABPM with Clinic BP which included 63,000 subjects over 10 years has shown ABP measurements are a stronger predictor of all cause and CV mortality than clinic BP. White coat hypertension which was present in 25% is not benign. Masked hypertension (seen in around 8%) was associated with a greater risk of death than sustained hypertension (Table 2 and Figure 1).

The cut off levels for defining hypertension for the OBP, HBPM and ABPM are given in Table 3.

Table 1 : Classification of blood pressure for adults age 18 and older

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic (mm Hg)</th>
<th>Diastolic (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal**</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;130</td>
<td>&lt;85</td>
</tr>
<tr>
<td>High-normal</td>
<td>130-139</td>
<td>85-89</td>
</tr>
<tr>
<td>Hypertension***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160-179</td>
<td>100-109</td>
</tr>
<tr>
<td>Stage 3</td>
<td>≥180</td>
<td>&gt;110</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>140-159</td>
<td>&lt;90</td>
</tr>
<tr>
<td>Grade 2</td>
<td>≥160</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>

**Not taking antihypertensives and not acutely ill; **Optimal blood pressure with respect to cardiovascular risk is below 120/80 mm Hg. However, unusually low readings should be evaluated for clinical significance; ***Based on the average of two or more blood pressure readings taken at least on two visits after an initial screening.

Table 2 : Patterns of Blood Pressure

<table>
<thead>
<tr>
<th>Ambulatory / Home BP</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP</td>
<td>True normotension</td>
<td>Masked hypertension</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>White coat</td>
</tr>
</tbody>
</table>

Table 3 : Diagnosis of Hypertension

<table>
<thead>
<tr>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP</td>
<td>≥140</td>
</tr>
<tr>
<td>Self/Home BP (mean)</td>
<td>≥135</td>
</tr>
<tr>
<td>Ambulatory BP</td>
<td>Day (mean)</td>
</tr>
<tr>
<td></td>
<td>Night (mean)</td>
</tr>
<tr>
<td></td>
<td>24 hr (mean)</td>
</tr>
</tbody>
</table>
Epidemiology of Hypertension

Global

Cardiovascular disorders (CVD) are the leading cause of morbidity and mortality worldwide. They account for an estimated 17.5 million deaths annually, more than 75% of which occur in lower middle-income countries (LMIC). While the deaths rates due to CVD have declined in several high-income countries (HIC), the trend has not been the same in LMIC. South Asia (India, Pakistan, Bangladesh, Nepal, Sri Lanka), that represents one of the most densely populated regions in the world, experienced an increase of 73% in healthy life-years lost due to ischemic heart disease between 1990 and 2010, compared to a global increase of 30%. Moreover, South Asians have been shown to experience their first myocardial infarction (MI) almost 10 years earlier compared to people from other countries. This increase is largely due to increasing prevalence of risk factors like hypertension, diabetes and dyslipidemia.

As per the World Health Statistics 2018, of the estimated 57 million global deaths in 2016, 41 million (71%) were due to non-communicable diseases (NCDs). The largest proportion of NCD deaths is caused by cardiovascular diseases (44%). In terms of attributable deaths, raised blood pressure is one of the leading behavioral and physiological risk factor to which 12.8% (7.5 million deaths per year) of global deaths are attributed. Hypertension is reported to be the fourth contributor to premature death in developed countries and the seventh in developing countries.

Globally, over 1 billion adults have hypertension and will escalate to 1.5 billion in the decade ahead. Earlier reports also suggest that the prevalence of hypertension is rapidly increasing in developing countries and is one of the leading causes of death and disability. While mean blood pressure has decreased in nearly all HICs, it has been stable or increasing in most African and LMICs. The prevalence of raised blood pressure in 2008 was highest in the WHO African region at 36.8% (34.0–39.7).

The Global Burden of Diseases (GBD); Chronic Disease Risk Factors Collaborating Group had reported 25-year (1980-2005) trends in mean levels of body mass index (BMI), systolic BP and cholesterol in 199 high-income, middle-income and low-income countries. Mean SBP declined in high and middle-income countries but increased in low-income countries and is now more than in high-income countries. The India specific data was similar to the overall trends in low-income countries.

National

The prevalence of hypertension in the late nineties and early twentieth century varied among different studies in India and ranged from 2-15% in Urban India and 2-8% in Rural India. The prevalence increased over six decades to 25% in urban and 15% in rural India. There have been many small, single centre studies on prevalence of hypertension from 1963-2010 from rural and urban India. These studies in 70’s and 80’s had a threshold of 160/90 for diagnosis of hypertension. Subsequent studies have had 140/90 as the cut off. These studies show increasing prevalence of hypertension over these six decades in our country. The increase was greater in urban than in rural areas in the earlier studies (Figure 2).

The latest data shows that presently the prevalence in urban areas is 33.8% and in rural areas, it is 27.6% with an overall prevalence of 29.8%. Thus, there has been a significant rural urban convergence as seen with other risk factors in the last two decades due to the changing lifestyle of the ruralites. Various factors of economic progress might have contributed to this rising trend, such as increased life expectancy, urbanization and its related lifestyle changes including increasing salt intake. Another factor that may contribute is the increased awareness and detection.

India with a population of 1.32 billion is experiencing an increase in CV diseases mainly due to uncontrolled hypertension. In a meta-analysis of multiple cardiovascular epidemiological studies, it was reported that prevalence rates of CAD and stroke have more than trebled in the Indian population. In the INTERHEART and INTERSTROKE study, hypertension accounted for 17.9% and 34.6% of population attributable risk for CAD and stroke respectively.

### Figure 2: Increasing trend in hypertension prevalence in India in urban (top panel) and rural (bottom panel) populations according to cross sectional regional studies from 1990’s to date. The increase is greater in urban (R² = 0.101) compared to rural (R² = 0.046) studies. Size of bubbles corresponds to number of participants in each study.
As per the Registrar General of India and Million Death Study investigators (2001-2003), CVD was the largest cause of deaths in males (20.3%) as well as females (16.9%) and led to about 2 million deaths annually. The Global Status on Non-Communicable Diseases Report (2011) has reported that there were more than 2.5 million deaths from CVD in India in 2008, two-thirds due to coronary artery disease and one-third to stroke. These estimates are significantly greater than those reported by the Registrar General of India and shows that CVD mortality is increasing rapidly in the country. CVD is the largest cause of mortality in all regions of the country. According to WHO absolute number of CVD related deaths in India have been increasing and were 1.93 million in year 2000, 1.96 million in 2005, 2.25 million in 2010 and 2.48 million in 2015. Deaths from IHD were 0.91 million in 2000, 1.06 in 2005, 1.28 in 2010 and 1.45 million in 2015, respectively.35

Hypertension in India has some special features such as; onset occurs relatively early in life, a rural-urban divide in prevalence, clustering of multiple cardiovascular risk factors and a significant seasonal variation of BP (Table 5). Also, the average BP in general population has been rising in the last two decades as against a decrease seen in some western countries. The awareness of hypertension is 42% in 2005, 25% in 2010 and 25% in rural individuals. Only 20% of urbans and 11% of rurals have control of BP. This is much less than the figures in other nations like in the US where awareness, treatment and control are 81, 74 and 53%, respectively.35

There are large regional differences in cardiovascular mortality in India among both men and women. The mortality is highest in south Indian states, eastern and north eastern states and Punjab while it is the lowest in central Indian states of Rajasthan, Uttar Pradesh and Bihar.

The increasing prevalence of high normal blood pressure has been seen in many recent studies. It was found to be around 32% in a recent urban study from Central India. In some studies from South India (Chennai) and from Delhi prevalence of high normal blood pressure has been even higher up to 36% and 44% respectively in these regions. The prevalence of hypertension increases with age in all populations. In a recent urban study it increased from 13.7% in the 3rd decade to 64% in the 6th decade.

The Global Burden of Disease Study looked at variations in epidemiological transition across the states of India from 1990-2016. They divided states of India into four epidemiological transition level (ETL) groups on the basis of ratio of DALYs from communicable, maternal, neonatal and nutritional diseases (CMNNDS) and those from NCDs and injuries combined. The states with ratios of 0.56–0.75 in 2016 were considered to have low ETLs (Bihar, Jharkhand, Uttar Pradesh, Rajasthan, Meghalaya, Assam, Chattisgarh, Madhya Pradesh, and Odisha; total population 626 million in 2016), those with ratios of 0.41–0.55 had lower-middle ETLs (Arunachal Pradesh, Mizoram, Nagaland, Uttarakhand, Gujarat, Tripura, Sikkim, and Manipur; total population 92 million), those with ratios of 0.31–0.40 had higher-middle ETLs (Haryana, Delhi, Telangana, Andhra Pradesh, Jammu and Kashmir, Karnataka, West Bengal, Maharashtra, and union territories other than Delhi;
Andhra Pradesh 0.309 33.49 0.37 16.2/10.0 (13.1) 28.3/20.7 (24.5)
Arunachal Prades 0.024 22.67 0.55 21.6/15.0 (18.3) 27.7/21.4 (24.7)
Assam 0.138 14.08 0.62 19.6/16.0 (17.8) 21.3/16.8 (19.1)
Bihar 0.158 11.30 - 9.4/5.9 (7.7) 20.2/20.8 (20.5)
Chandigarh - 97.25 - 13.5/9.1 (11.4) 41.8/31.3 (37.0)
Chhattisgarh 0.180 23.24 0.6 12.7/8.8 (10.8) 17.1/13.5 (15.3)
Delhi - 97.50 0.38 4.2/6.5 (5.9) 27.9/22.4 (25.4)
Goa 0.803 62.17 0.21 13.2/8.5 (10.9) 32.9/26.4 (29.7)
Gujarat 0.477 42.58 0.46 13.0/9.7 (11.4) –
Haryana 0.493 34.79 0.4 16.8/9.2 (13.0) 28.1/20.3 (24.5)
Himachal Pradesh 0.647 10.04 0.3 21.9/12.1 (17.5) 38.5/30.8 (34.7)
Jammu and Kashmir 0.479 27.21 0.34 13.7/11.6 (12.7) –
Jharkhand 0.222 24.05 0.69 12.7/8.0 (10.0) 24.7/18.8 (21.8)
Karnataka 0.42 38.57 0.34 15.4/9.7 (12.6) 25.5/21.0 (23.3)
Kerala 0.911 47.72 0.16 9.5/6.8 (8.2) 41.4/33.0 (37.0)
Madhya Pradesh 0.186 27.63 0.6 10.9/7.9 (10.0) 20.2/20.8 (20.5)
Maharashtra 0.629 45.23 0.33 15.9/9.1 (12.5) 28.2/21.8 (25.1)
Manipur 0.199 30.21 0.42 21.9/14.1 (15.9) 25.7/17.6 (21.7)
Meghalaya 0.246 20.08 0.64 10.4/9.9 (10.2) 22.9/18.3 (20.6)
Mizoram 0.408 51.51 0.53 17.9/9.8 (13.9) 24.5/14.8 (19.7)
Nagaland 0.257 28.97 0.47 23.1/16.0 (19.6) 39.6/31.8 (35.8)
Odisha 0.261 16.68 0.58 12.5/9.0 (10.8) 17.2/15.6 (16.4)
Puducherry - 37.49 - 15.1/9.1 (12.1) 27.3/17.6 (22.4)
Punjab 0.538 68.31 0.29 21.8/15.2 (17.5) 41.4/29.4 (35.7)
Rajasthan 0.324 24.89 0.66 12.4/9.7 (11.4) 23.7/16.5 (20.2)
Sikkim 0.324 24.97 0.45 27.3/16.5 (21.9) 36.2/30.4 (33.5)
Tamilnadu 0.632 48.45 0.29 15.4/9.7 (12.6) 25.5/21.0 (23.3)
Telangana - 48.45 0.38 18.2/10.1 (14.2) 26.5/19.6 (23.1)
Tripura 0.354 26.18 0.45 27.9/16.5 (21.9) 22.4/18.8 (20.6)
Uttarakhand 0.426 22.38 0.46 17.2/9.6 (13.4) 32.2/22.3 (27.4)
Uttar Pradesh 0.122 30.55 0.68 10.1/7.6 (8.9) 20.5/18.2 (19.4)
West Bengal 0.483 31.87 0.33 12.4/10.1 (11.4) 22.6/21.0 (21.8)

Human Development Index (HDI) is a statistic composite index of life expectancy, education, and per capita income indicators, which are used to rank countries into four tiers of human development. Urbanization Index (UI) measures the degree of urbanization of a population. Epidemiological transition index (ETI) was done over 1990-2016 and it reflects the latest trends in prevalence across our vast country. The national family health survey 4 (NFHS-4) and the District Level Household Survey 4 (DLHS-4) have tracked into the older age population of the country. The prevalence of hypertension varies in different regions of the country. This variation is due to social, economic, dietary differences in different parts of the country. The socio economic factors are depicted by the human development index and the urbanization index. Also, the epidemiological transition has been variable in different parts of our country. Table 6 shows state wise distribution of parameters of human development index from Government of India, Epidemiological Transition Index from the GBD study (2016), prevalence of hypertension from the national family health survey 4 (NFHS-4) and the District Level Household Survey 4 (DLHS-4). The GBD study was done over 1990-2016 and it reflects the epidemiological transition index over this period in various states. The socio economic and cultural factors which are different in various states effect the prevalence of hypertension and partly explain the variation in the prevalence across our vast country. The national family health survey 4 (2015-16) (NFHS-4) looked at 6,01,509 households which included 6,99,686 women and 1,03,525 men from 28,853 primary sampling units in 640 districts of the country. The NFHS-4 data shows significant difference in hypertension prevalence across states. A major shortcoming of this study is exclusion of old age adults (>50 years) who have a higher prevalence of hypertension. In the DLHS-4 study the Government of India with registrar general of India has estimated CV risk factors in all states of the country. In this, data on BP measurement and hypertension prevalence are available since 2012 and so reflects the latest trends in prevalence across India. The DLHS-4 survey was undertaken in 2012-2014 and are thus provides the state wise recent data. There is a significant association of state level hypertension prevalence among NFHS-4 and DLHS-4 studies in both men and women suggesting that the high prevalence of hypertension in younger population of NFHS-4 survey has tracked into the older age population of DLHS-4 survey.
The treatment of hypertension is usually lifelong although down regulation of therapy can be done in some. 70% patients in our country are out of pocket paid and have no insurance cover. Even the new Ayushman Bharat Yojana is for the hospital admissions and OPD treatment will continue to be self-paid. Cost of medicines should be an important issue for improving drug compliance in our country as against most western countries where 80-100% of the population is covered by insurance. The wellness clinic which will be set up under the National Health Policy 2017 will take care of timely prevention of non communicable diseases on an OPD basis. India spends only 3.9% of its GDP on health and per capita health expenditure is 63 USD only which is much less than other nations. Cost of therapy thus assumes great relevance for this disease requiring lifelong therapy. The prevalence of hypertension is increasing in India. According to WHO atlas, the average SBP in urban men age 40-49 years was 120.4 in 1942, 125.2 in 1963 and 130 in 1997. An ICMR study estimates that hypertension is responsible for 16% of IHD, 21% of PAD, 24% of AMI’s and 29% of strokes. In another analysis hypertension has been found to be directly responsible for 57% of all stroke deaths and 24% of all CHD deaths in India.

Preventive measures are required so as to reduce obesity by increasing physical activity, decreasing the salt intake of the population and a concerted effort to promote awareness about hypertension and related risk factors.
Measurement of Blood Pressure

Clinic Measurement (Office Blood Pressure Measurement)

- Blood pressure is characterized by large spontaneous variations, therefore the diagnosis of hypertension should be based on multiple BP measurements taken on several separate occasions.
- With increasing awareness about the hazardous effects of mercury on health, the mercury sphygmomanometer should not be used now. We recognize that mercury is a potent toxin, a global priority pollutant and a persistent bio-accumulative. A mercury sphygmomanometer contains 70 to 90 grams of mercury. Health Care Without Harm (HCWH) and the WHO are together leading a global partnership to achieve virtual elimination of mercury-based thermometers and sphygmomanometers.
- Humans are exposed to methylmercury almost entirely by eating contaminated fish, seafood and wildlife that are at the top of the aquatic food chain. It is recommended that physicians should phase out the mercury sphygmomanometers and replace these with aneroid and digital oscillometric devices. Some mercury sphygmomanometers can be kept only for the purpose of calibration.
- The aneroid large dial apparatus is the best for use in the office. It needs calibration every six months since the spring can loosen. Proper maintenance and calibration of the sphygmomanometer should be ensured. The automated office blood pressure (AOBP) equipment has been used recently in the SPRINT trial. These are not cost effective and may not be feasible as the devices of choice. The aneroid and the digital oscillometric sphygmomanometers should be used.
- Use a standard cuff with a bladder that is 12 cm X 35 cm. Use a large bladder for fat arms and a small bladder for children. The bladder should encircle and cover 80% of the length of the upper arm. For measurement, inflate the bladder quickly to a pressure 20 mm Hg higher than the point of disappearance of the radial pulse. Deflate the bladder slowly by 2 mm Hg every second. The first appearance of the sound (Phase I Korotkoff) is the systolic BP. The disappearance of the sound (Phase V Korotkoff) is the diastolic BP. For children and in those with high output states, muffling of the sound (Phase IV Korotkoff) is taken as diastolic pressure.
- Occasionally, thigh BP (popliteal) is lower in the lower limb as compared to the upper limb.

Precautions

The following precautions are required for correct measurement of blood pressure:
- At the initial visit, an average of three readings, taken at intervals of 2-3 minutes should be recorded.
- For confirmation of diagnosis of hypertension, record at least 3 sets of readings on different occasions, except in Stage III hypertension.
- Patients should be asked to refrain from smoking or drinking tea/coffee, exercise for at least 30 minutes before measuring the BP.
- Allow the patient to sit for at least five minutes in a quiet room before beginning BP measurement.
- Measurement should be done preferably in a sitting or supine position. Patient’s arm should be fully bared and supported at the level of the heart.
- Measure the blood pressure in both arms at the first visit and use higher of the two readings.
- In older persons aged 60 years and above, in diabetic subjects and patients on antihypertensive therapy, the BP should be measured in both, supine/sitting and in standing positions to detect postural hypotension.
- If atrial fibrillation is present, additional readings may be required to estimate the average SBP and DBP.
- Occasionally, thigh BP (popliteal) has to be measured with appropriately large cuff, in prone position especially in younger persons with hypertension. Normally thigh SBP is higher and DBP a little lower than the arm BP because of the reflected pulse wave. This is important for suspected coarctation and nonspecific aortoarteritis, where BP is lower in the lower limb.

Home Blood Pressure Measurement

Measurement of blood pressure outside the clinic may provide valuable information for the initial evaluation of patients with hypertension and for monitoring the response to treatment. Home measurement has the advantage that it distinguishes sustained hypertension from “white-coat hypertension”, a condition noted in patients whose blood pressure is elevated in the physician’s clinic but normal at other times.

Validated automated (oscillometric) machines that use the brachial artery (arm) for measurement are reliable where as finger and wrist monitors are inaccurate and are not recommended. Home Blood pressure should be used complimentary to the clinic readings for diagnosis and follow up. Validated and calibrated electronic devices that are reliable should be used. Patients are to be encouraged to make morning and evening recordings for 3-5 days. A mean of these multiple readings reflects the true home blood pressure. Besides providing real life blood pressure readings it also encourages patient compliance and participation in the management. The oscillometric devices may not work well in patients who have atrial fibrillation or other arrhythmias.

Technique

- Caffeine, smoking, alcohol, bathing and exercise should be avoided for at least 30 minutes before the reading is taken.
- The patient should sit calmly with back support, feet flat on floor for 5 minutes before taking a reading. Upper arm should be bare. When taking a reading the arm with cuff should be supported on a firm surface (table or arm-rest) at heart level. The Cuff should fit snugly.
on the arm, about ½ -1 inch above the elbow crease.

- Readings should be taken in the morning before medication and at night. Each time, two readings should be taken, separated by one to two minutes between readings. Take readings twice a day for 7 consecutive days. Discard the readings of the first day. The average of the remaining 12 readings is the Home blood pressure measurement.

For home blood pressure, readings of more than 135/85 mm Hg should be considered elevated.

Home BP Monitoring (HBPM) is easy to use, reproducible and had a higher prediction of target organ damage than Clinic blood pressure. It can be used to distinguish white coat hypertension from sustained hypertension. The home monitoring improves compliance and ensures better blood pressure control. We recommend use of this modality after proper patient education. The patient should be educated not to change medication without consulting their physician.

### Ambulatory Blood Pressure Measurement

It has been found that at least 20-25% of patients diagnosed with stage I-II hypertension (DBP 90-104 mm Hg) are normotensive outside the physician’s clinic.

**Ambulatory blood pressure monitoring (ABPM)** has been found to be clinically useful in the following settings: to identify white-coat hypertension, masked hypertension, nocturnal hypertension (non-dippers), resistant hypertension, episodic hypertension, evaluate the effect of antihypertensive drugs and in individuals with hypotensive episodes while on antihypertensive medication.

For measuring ambulatory blood pressure, a portable monitor is worn on a belt connected to a standard cuff on the upper arm. BP measurements are taken over a 24-48 hour period every 15-20 minutes during the daytime (8 am to 10 pm) and every 60 minutes during nighttime.

BP has a reproducible circadian profile with higher values while awake and mentally and physically active, whereas, much lower values during rest and sleep. Different values have been suggested for definition of hypertension with ABPM for day time average BP (≥135/85 mm Hg) and the night-time average (≥120/70 mm Hg) (Table 7).

Early morning surge in BP for 3 or more hours during transition from sleep to wakefulness, can be an independent risk factor and needs to be managed effectively by addition of a second dose in the evening or a dose of a second class of antihypertensive agent in the evening or a drug with a long half-life.

The data recorded from ABPM also identifies patterns of blood pressure variation such as dipping, non-dipping, extreme dipping and reverse dipping (Table 8). While dipping is a normal phenomenon, non-dipping and extreme dipping are associated with increase cardiovascular and cerebrovascular event rates. In the case of reverse dipping, a diagnosis of obstructive sleep apnea should be considered.

**Classification of BP based on ABPM**

ABPM is a better predictor of cardiovascular events and all cause mortality than clinic blood pressure. However, this procedure should not be used indiscriminately in the routine work-up of a hypertensive patient because of its high cost.

**Pulse Pressure**

The Pulse Pressure (SBP-DBP) depends upon factors like arterial stiffness (the cushioning capacity of arteries) and wave reflections - speed of the forward wave (pulse wave velocity or PWV).

MBP is the pressure for the steady flow of blood to peripheral tissues. PP is the consequence of intermittent ventricular ejection from the heart and is influenced by left ventricular ejection fraction and large conduit arteries, mainly the aorta. Factors like arterial stiffness (the cushioning capacity of arteries) and wave reflections – speed of the forward wave (pulse wave velocity or PWV) are also major determinants of PP. In subjects >50 years of age the arterial stiffness and wave reflections become the main determinants of increased SBP and PP.

Novel methods of monitoring central aortic pressure are being developed. The therapeutic approaches available to reduce PP and arterial stiffness with age are ACEIs or ARBs in association with CCBs and/or diuretics.
Evaluation

Evaluating patients with documented hypertension has three objectives:

- To identify known causes of high blood pressure
- To assess the presence or absence of HMOD.
- To identify other cardiovascular risk factors or concomitant disorders that may define prognosis and guide treatment.

Data for evaluation is acquired through medical history, physical examination, laboratory tests, and other special diagnostic procedures.

Medical History

- Duration and level of elevated blood pressure, if known
- Symptoms of coronary artery disease (CAD), heart failure, cerebrovascular disease, peripheral vascular disease and CKD
- Diabetes mellitus, dyslipidaemia, obesity, gout, sexual dysfunction and other co-morbid conditions
- Family history of high blood pressure, obesity, premature CAD and stroke, dyslipidaemia and diabetes
- Symptoms suggesting secondary causes of hypertension
- History of smoking or tobacco use, physical activity, dietary assessment including intake of sodium, alcohol, saturated fat and caffeine
- Socioeconomic status, professional and educational levels
- History of use / intake of all prescribed and over-the-counter medications, herbal remedies, liquorice (Yashtimadhu/Jestamadha), illicit drugs, corticosteroids, NSAIDs, nasal drops. These may raise blood pressure or interfere with the effectiveness of antihypertensive drugs
- History of oral contraceptive use and hypertension during pregnancy
- History of previous antihypertensive therapy, including adverse effects experienced, if any

Table 9: Factors influencing risk of cardiovascular disease

<table>
<thead>
<tr>
<th>Risk factors for coronary artery disease (RF)</th>
<th>Hypertension mediated organ damage (HMOD)</th>
<th>Associated clinical conditions (ACC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 55 years*</td>
<td>Left ventricular hypertrophy detected by ECG and/or echocardiogram</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Male sex</td>
<td>Microalbuminuria/proteinuria and/or elevation of serum creatinine (1.2-2.0 mg/dl)**</td>
<td>Transient ischemic attack</td>
</tr>
<tr>
<td>Post-menopausal women</td>
<td>Urinary ACR (albumin creatinine ratio)**</td>
<td>Ischemic stroke</td>
</tr>
<tr>
<td>Smoking and tobacco use</td>
<td>Ultrasound or radiological evidence of atherosclerotic plaques in the carotids</td>
<td>Cerebral haemorrhage</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Hypertensive retinopathy</td>
<td>Heart disease</td>
</tr>
<tr>
<td>Family history of premature coronary artery disease (Males &lt; 55 years, Female &lt; 65 years)</td>
<td>Ankle Brachial Index (&lt;0.9)</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Increased Waisthip ratio</td>
<td></td>
<td>Angina</td>
</tr>
<tr>
<td>Obesity and Obstructive Sleep Apnoea (OSA)</td>
<td></td>
<td>Coronary revascularization</td>
</tr>
<tr>
<td>High LDL or Total cholesterol</td>
<td></td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Low HDL cholesterol and High triglycerides</td>
<td></td>
<td>Renal disease</td>
</tr>
<tr>
<td>High sensitivity C-reactive protein (hs-CRP)</td>
<td></td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td></td>
<td>Renal failure (serum creatinine &gt; 2.0 mg/dl)</td>
</tr>
</tbody>
</table>

*Coronary artery disease is known to occur 10 years earlier in South Asians than in other ethnic groups.;
**Microalbuminuria 30-300 mg/24hours; ***Albumin-Creatinine Ratio (ACR) ≥22 (M) or ≥31 (F) mg/g creatinine

Physical Examination

- Record three blood pressure readings separated by 2 minutes, with the patient either supine or sitting position and after standing for at least 2 minutes.
- Record height, weight and waist circumference, BMI.
- Examine the pulse and the extremities for delayed or absent femoral and peripheral arterial pulsations, bruits and pedal oedema.
- Look for arcus senilis, acanthosis nigricans, xanthelasma and xanthomas.
- Examine the neck for carotid bruits, raised JVP or an enlarged thyroid gland.
- Examine the heart for abnormalities in rate and rhythm, location of apex beat, fourth heart sound and murmurs.
- Examine the lungs for crepitations and rhonchi.
- Examine the abdomen for bruits, enlarged kidneys, masses and abnormal aortic pulsation.
- Examine the optic fundus and do a neurological assessment.

Laboratory Investigations

- Routine
  - Urine examination for protein and glucose and microscopic examination for RBCs and other sediments.
  - Haemoglobin, fasting blood glucose, serum creatinine, potassium and total cholesterol
  - 12-lead electrocardiogram
- Additional investigations in special circumstances can include
  - Fasting lipid profile and uric acid
  - Urine Albumin Creatinine Ratio
  - Echocardiogram
  - Ultrasound of Abdomen
- Other specific tests to rule out secondary causes of hypertension.
Table 10: Risk stratification of patients with hypertension

<table>
<thead>
<tr>
<th>Stage</th>
<th>Other risk factors and disease history</th>
<th>Blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Stage 1</td>
</tr>
<tr>
<td>I</td>
<td>No other risk factors</td>
<td>Low risk</td>
</tr>
<tr>
<td>II</td>
<td>1-2 risk factors</td>
<td>Medium risk</td>
</tr>
<tr>
<td>III</td>
<td>3 or more risk factors or TOD or diabetes</td>
<td>High risk</td>
</tr>
<tr>
<td>IV</td>
<td>ACC</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

Blood pressure values:
- SBP 140-159 or DBP 90-99
- SBP 160-179 or DBP 100-109
- SBP>180 or DBP>110

Risk strata (typical 10 year risk of stroke or myocardial infarction): Low risk = Less than 15% Medium risk = about 15-20% High risk = about 20-30% Very high risk = 30% or more

where there is a high index of suspicion are described under “secondary hypertension”.

- hs-CRP and microalbuminuria can be used in special circumstances for risk stratification.
- The cost of investigations in the context of the needs of an individual patient and resources available is an important consideration. In patients with essential hypertension where there is a resource crunch, one may be required to initiate therapy without carrying out any laboratory investigations.

Factors Influencing Risk

The overall CV risk prediction has been suggested in some latest guidelines for initiation of therapy at lower blood pressure levels. The American guidelines use pooled cohort equations for calculation of 10 year ASCVD risk. The European guidelines use the Systemic Coronary Risk Evaluation System (SCORE) for the same. We do not have our own risk scoring system for Indians at present. European guidelines suggest a multiple of 1.4 increased risk for south Asians. Even otherwise it has been observed that CV risk is underestimated in Indian patients with the established CVD risk calculator scoring systems. Primarily, age, sex, lipids, smoking habit and presence of diabetes are the five major factors in all these risk score calculation systems. We should recognize the presence of these factors along with the fact that we Indians are genetically at a higher risk for ASCVD with any given level of these risk factors.

Besides calculation of the overall risk by these factors or scoring systems the other two factors affecting the overall risk of the individual are the presence of HMOD and other associated clinical conditions (ACC). The presence of one of these three would decrease the threshold for initiation of drug therapy even at lower levels of BP, in that order. The prognosis of the patients and the choice and need for urgency of therapy, will be dependent on the overall risk stratification as shown in Table 10, depending on the ASCVD risk, HMOD and ACC respectively.
Management of Hypertension

Goals of Therapy

The primary goal of therapy of hypertension should be effective control of BP in order to prevent, reverse or delay the complications and thus reduce the overall risk of an individual without adversely affecting the quality of life. Patients should be explained that the lifestyle modifications and drug treatment is generally lifelong and regular drug compliance is important.

Initiation of therapy

Having assessed the patient and determined the overall risk profile, management of hypertension should proceed as follows:

- In patients with stage I hypertension repeat readings should be taken within 2-3 weeks along with lifestyle modification. Pharmacotherapy needs to be initiated after 1 month.
- BP needs to be recorded in both arms and in lying and standing before initiation of pharmacotherapy.
- In patients with stage II or III hypertension, shorter waiting period (in stage III repeat readings after few hours only) will be desirable.
- Those patients who have evidence of ASCVD and HMOD, pharmacotherapy should be started early.

Targets of therapy

The target blood pressure should be 130/80 amongst those <60 years and 120-130/70-80 in those >60 years. The physiological age should be looked at rather than the chronological age in elderly. In active elderly the targets should be achieved more aggressively. In frail elderly individuals who are not very active and especially those with postural hypotension higher target BP should be accepted. Patient should not be made to feel worse and the risk of falls be kept in mind.

The BP control should not be <120/70 since at pressures lower than this the risk is increased. Recognizing the wide variation of BP readings in any given individual one should aim at having most readings in this range, fully recognizing that some would be beyond it in both directions. These guidelines need to be individualized according to age, activity level, other concomitant diseases and therapies.

Table 11: Blood Pressure Levels: Threshold for treatment and Target BP to be achieved

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Threshold to start treatment (mmHg)</th>
<th>Target BP range (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;65 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High ASCVD risk</td>
<td>140/90</td>
<td>120-130/70-80</td>
</tr>
<tr>
<td>Low ASCVD risk</td>
<td>140/90</td>
<td>130-140/70-80</td>
</tr>
<tr>
<td>Age 65-80 years</td>
<td>140/90</td>
<td>130-140/70-80</td>
</tr>
<tr>
<td>Age &gt;80 years</td>
<td>140-150/90</td>
<td>130-140/70-80</td>
</tr>
<tr>
<td>With other risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>140/90</td>
<td>130-140/70-80</td>
</tr>
<tr>
<td>History of Stroke, TIA</td>
<td>140/90</td>
<td>130-140/70-80</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>140/90</td>
<td>130-140/70-80</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>130/80</td>
<td>120-130/70-80</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>130/80</td>
<td>120-130/70-80</td>
</tr>
</tbody>
</table>

Management Strategy

- Recent evidence suggests that the level of SBP control correlates better with reduction of mortality than the level of DBP control.\textsuperscript{56-57}
- Impressive evidence has accumulated to warrant greater attention to SBP as a major risk factor for CVDs. The rise in SBP continues throughout life. In contrast the DBP, rises until approximately 50 years of age. It tends to level off over the next decade, and may remain the same or fall later in life. Diastolic hypertension predominates before 50 years of age, either alone or in combination with SBP elevation. DBP is a more potent cardiovascular risk factor than SBP until age 50; thereafter, SBP is more important.\textsuperscript{12}
- Trials describe population averages for the purpose of developing guidelines, whereas physicians must focus on the individual patient’s clinical responses.\textsuperscript{58}
- We should be moving to an individualized care in which the patient profile (race, age, risk factors, associated diseases, HMOD) and the BP value will both have an equal effect on choice and need for antihypertensive medications and the targets to be achieved.

Non-pharmacologic Therapy

Life style measures should be instituted in all patients including those who require immediate drug treatment. These include:

- Patient education: Patients need to be educated about the various aspects of the disease, adherence to lifestyle changes on long term basis and need for regular monitoring and therapy.
- Weight reduction: Weight reduction of even as little as 4.5 kg has been found to reduce blood pressure in a large proportion of overweight persons with hypertension.\textsuperscript{59}
- Physical activity: Regular aerobic physical activity can promote weight loss, increase functional status and decrease the risk of cardiovascular disease and all-cause mortality. A program of 30-45 minutes of brisk walking or swimming at least 3-4 times a week could lower SBP by 7-8 mm Hg. Isometric exercises such as weight lifting should be avoided as they lead to pressor effects.
- Alcohol intake: Excess alcohol intake causes a rise in blood pressure, induces resistance to antihypertensive therapy and also increases the risk of stroke.\textsuperscript{60,61}

Alcohol consumption should be limited to no more than 2 drinks per day (24oz beer, 10oz wine, 3oz 80-proof whiskey) for most men and no more than 1 drink per day for women and lighter weight people.\textsuperscript{12}
- Salt intake: Epidemiological evidence suggests an association between dietary salt intake and elevated BP. The total daily intake of salt should be restricted to 6
Table 12: Lifestyle interventions for BP reduction

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Recommendation</th>
<th>Expected systolic blood pressure reduction (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain ideal BMI (20-25 Kg/m²)</td>
<td>5-20 mm Hg per 10 kg weight loss</td>
</tr>
<tr>
<td>DASH* eating plan</td>
<td>Eat diet rich in fruit, vegetables, low-fat dairy products. Eat less saturated and total fat</td>
<td>8-14 mm Hg</td>
</tr>
<tr>
<td>Dietary sodium Restriction</td>
<td>Reduce dietary sodium intake to &lt;100 mmol/day or &lt;6 g salt (sodium chloride)</td>
<td>2-8 mm Hg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Regular aerobic physical activity, e.g. brisk walking for at least 30 min most days</td>
<td>4-9 mm Hg</td>
</tr>
<tr>
<td>Alcohol moderation</td>
<td>Total abstinence preferred and recommended if must then Men ≤ 21 units per week Women ≤ 14 units per week</td>
<td>2-4 mm Hg</td>
</tr>
<tr>
<td>Tobacco</td>
<td>Total abstinence</td>
<td></td>
</tr>
</tbody>
</table>

Table 13: Sodium content of foods per 100 gms – Common Indian diets

<table>
<thead>
<tr>
<th>Sodium Level</th>
<th>Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 mg</td>
<td>Amla, Bottle gourd, Bitter gourd, Brinjal, Cabbage, Lady finger, Colocasia, Cucumber, French beans, Peas, Onion, Tomato, Yam</td>
</tr>
<tr>
<td>25-50 mg</td>
<td>Cow pea, Raisins, Wheat, Semolina, Milk, Grapes, Papaya, Orange, Sapota, Apple, Nut</td>
</tr>
<tr>
<td>50-100 mg</td>
<td>Cauliflower, Reddish white, Black gram, Green gram, Red gr (Arunth Toor) dal, Lentil, Bengal (Chana) gram, Pineapple, Moroccan Apple, Prawns, Beef, Chick</td>
</tr>
<tr>
<td>&gt;100 mg</td>
<td>Fenugreek (Methi), Lettuce (Salad Patta), Water melon, Red gr dal, Tender Liver, Bacon, Egg, Lobster</td>
</tr>
</tbody>
</table>

gms (amounting to 3-4 gms of sodium), however, in hot summer this may be relaxed. Patients should be advised to avoid added salt, processed foods, and salt-containing foods such as pickles, papads, chips, chutneys and preparations containing baking powder. Most breads, cereals, packaged namkeen, readymade soups, canned food, pizzas and Chinese takeaway are also high in salt content. The salt content of some commonly used food items are given in Table 13 for reference.

In the Indian context, salt restriction is more important as Indian cooking involves a high usage of salt. Salt intake amongst Indian patients has been found to be high. An ICMR task force study conducted in 13 states documented daily salt intake of 13.8 g per day per person. The SCRIPT study conducted across 4 regions of India showed that a region wise mean daily salt intake in north, east, west and south was 14.1, 9.8, 10.1 and 9.4 g per day respectively. These are much higher than the WHO recommendation of <3 g per day which is also our IGH guideline recommendation.

- Drinking: Smoking or consumption of tobacco in any form is the single most powerful modifiable lifestyle factor for prevention of major cardiovascular and non-cardiovascular disease in hypertensives. Cardiovascular benefits of cessation of smoking can be seen within one year in all age groups. E cigarettes are now available in our country and are being used. These are also harmful and their use needs to be strongly discouraged.
- Yoga and Meditation: Yoga, meditation and biofeedback have been shown to reduce blood pressure in randomized controlled studies from India and the west.

The fall in SBP after yoga therapy has been between 2-6 mm Hg. A recent study from Puducherry shows mean SBP reduction by 4 and 6 mm Hg with lifestyle modification (LSM) and LSM + yoga respectively. Yoga also resulted in reduction of heart rate, waist circumference and lipid levels, all of which reduce CVD prevalence and mortality.

- Diet:
  - Vegetarians have a lower BP compared to meat eaters. This is due to higher intake of fruit, vegetables, fibers coupled with a low intake of saturated fats and not due to an absence of intake of meat protein.
  - Intake of saturated fats is to be reduced since concomitant hyperlipidaemia is often present in hypertensives.
  - Regular fish consumption may enhance blood pressure reduction in obese hypertensives.
  - Adequate potassium intake from fresh fruits and vegetables may improve blood pressure control in hypertensives. Food items with high potassium content that can be beneficial are shown in Table 14.
  - Caffeine intake increases BP acutely but there is rapid development of tolerance to its pressor effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high BP.
  - Recent data from the PURE study shows that high carbohydrate intake (> 60% of energy) was associated with adverse impact on total mortality. In fact higher fat intake was associated with lower risk of total mortality and stroke. Indians consume higher level of carbohydrates than others. Use of carbohydrates should be reduced in diet.
  - The diet should be rich in whole grains, fruits, vegetables and low-fat dairy products and avoid saturated fats.

*DASH= Dietary Approaches to Stop Hypertension

Women ≤ 14 units per week
Men ≤ 21 units per week
- Caffeine intake increases BP acutely but there is rapid development of tolerance to its pressor effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high BP.
- Recent data from the PURE study shows that high carbohydrate intake (> 60% of energy) was associated with adverse impact on total mortality. In fact higher fat intake was associated with lower risk of total mortality and stroke. Indians consume higher level of carbohydrates than others. Use of carbohydrates should be reduced in diet.
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- Diet:
  - Vegetarians have a lower BP compared to meat eaters.72 This is due to higher intake of fruit, vegetables, fibers coupled with a low intake of saturated fats and not due to an absence of intake of meat protein.73
  - Intake of saturated fats is to be reduced since concomitant hyperlipidaemia is often present in hypertensives.
  - Regular fish consumption may enhance blood pressure reduction in obese hypertensives.74
  - Adequate potassium intake from fresh fruits and vegetables may improve blood pressure control in hypertensives. Food items with high potassium content that can be beneficial are shown in Table 14.75
  - Caffeine intake increases BP acutely but there is rapid development of tolerance to its pressor effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high BP.76
  - Recent data from the PURE study shows that high carbohydrate intake (> 60% of energy) was associated with adverse impact on total mortality. In fact higher fat intake was associated with lower risk of total mortality and stroke. Indians consume higher level of carbohydrates than others. Use of carbohydrates should be reduced in diet.77
  - The diet should be rich in whole grains, fruits, vegetables and low-fat dairy products and avoid saturated fats.
Table 14: Foods with high potassium

<table>
<thead>
<tr>
<th>Fruits</th>
<th>Vegetables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amla</td>
<td>Cabbage</td>
</tr>
<tr>
<td>Sapota (Chikoo)</td>
<td>Bitter white gourd</td>
</tr>
<tr>
<td>Peaches</td>
<td>Ladies finger</td>
</tr>
<tr>
<td>Orange</td>
<td>Apple</td>
</tr>
<tr>
<td>Papaya</td>
<td>Cauliflower</td>
</tr>
<tr>
<td>Banana</td>
<td>Spinach</td>
</tr>
<tr>
<td></td>
<td>Potato</td>
</tr>
<tr>
<td></td>
<td>Drumstick</td>
</tr>
<tr>
<td></td>
<td>Tapioca</td>
</tr>
</tbody>
</table>

Table 15: Food items to be avoided in hypertensives

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table salt</td>
<td>Salt preserved foods</td>
</tr>
<tr>
<td>Mono sodium glutamate (Ajinomoto)</td>
<td>Canned foods</td>
</tr>
<tr>
<td>Baking powder</td>
<td>Ketchup and sauces</td>
</tr>
<tr>
<td>Fried foods</td>
<td>Prepared mixes</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Ready to eat foods</td>
</tr>
<tr>
<td>Bakery products :</td>
<td>Highly salted foods</td>
</tr>
<tr>
<td>Biscuits, cakes, breads and pastries</td>
<td>Potato chips, cheese, peanut butter, salted butter, papads</td>
</tr>
</tbody>
</table>

Fat and cholesterol. Such a diet can lower the BP by up to 11 mm Hg if you have high blood pressure. This eating plan is known as the Dietary Approaches to Stop Hypertension (DASH) diet.

Lose extra pounds and watch your waistline

- you may reduce your blood pressure by about 1 millimeter of mercury (mm Hg) with each kilogram (about 2.2 pounds) of weight you lose.
- BMI - Carrying too much weight around your waist can put you at greater risk of high blood pressure.
- 1 tsp of salt (flattened) = 5 g of salt. A hypertensive patient should eat not more than that 5 g of salt in a day.
- adults who consumed more protein, whether from dairy, eggs, meat, or plant sources, had lower blood pressure levels after four years of follow-up. People with the highest protein intake—on average 102 grams a day—saw the biggest benefit, with a 40 percent lower risk of developing high blood pressure.

Avoid

1. Bakery Products (Bread, Biscuits, cakes) – They contain baking powder (Soda bicarb). Instead of bread sandwiches made with thick crisp chapati or bhakri are also tasty. A thick crisp crust of bhakri also makes a good alternate pizza crust. Instead of cheese, low salt paneer is tasty.

Diet Plan for the Day - Total 2300-2500 calories are recommended per day

Early Morning – 2 tbsp of flax seeds / 6-7 badaams (almonds) and 2 pieces (1 piece = ½ a walnut) + 1 cup of tea (Non-diabetics may take about ½ to ¾ spoonful of sugar)

Breakfast – with one cup of tea / coffee.

Upma (Rawa or Daliya – Daliya is recommended because it has more fibre) with mixed vegetables (carrots, peas, capsicum, any other) OR

Egg Omelette with spinach OR 1 stuffed Paratha (Paratha can be made of whole wheat, jowar, ragi, multigrain) with curds OR

Oats in the form of porridge, upma, idli, dosa (should add vegetables in the idli-dosa) 3 home-made idlis or 1 dosa. Instead of rice we can make multigrain idlis, ragi idlis, etc)

Mid-morning

1 fruit – banana, orange, apple, pear, etc

1 cup of Green tea

Lunch

2 medium sized chapatis + 1 soup bowl of vegetable + 1 small bowl of dal + salad + 1 small bowl of rice or pulav (rice can be substituted by one additional chapati for those who have a preference for chapatis) + 1 bowl of chicken or fish (Avoid shell fish).

1 glass of buttermilk or a small bowl of curds to be had one hour after the meal

Snacks with 1 cup of evening tea

1 bowl of Puffed rice, makhanas, unsalted channa-peanuts. Upma or pohe if not already consumed at breakfast. Dhokla (5-6 pieces), khakra

Dinner – can be the same as lunch. Avoid foodstuffs with spices at night.

Thus, the diet in hypertensives should be low calorie, low fat, and low sodium, with normal protein intake. The food items to be avoided in hypertensives are shown in Table 15.

Pharmacologic Therapy

Principles of drug treatment

- Over the past decade, the goals of treatment have gradually shifted from optimal lowering of blood pressure, which is taken for granted, to patient’s overall well-being, control of associated risk factors and protection from future HMOD.
- Achieve gradual reduction of blood pressure. Use low doses of antihypertensive drugs to initiate therapy.
- Five classes of drugs can be recommended as first line treatment for stage 1-2 hypertension. These include: 1) ACE inhibitors, 2) Angiotensin receptor blockers, 3) Calcium channel blockers, 4) Diuretics and 5) Newer β-blockers.
- The Blood Pressure Lowering Treatment Trialists’ Collaboration concluded that treatment with any commonly used regimen reduces the risk of total major cardiovascular events and larger reductions in blood pressure produce larger reductions in risk.
- Choice of an antihypertensive agent is influenced by age, concomitant risk factors, presence of HMOD, other co-existing diseases, socioeconomic considerations, availability of the drug and past experience of the physician.
- Combining low doses of two or more drugs having synergistic
effect is likely to produce lesser side effects. In 70% of patients, goal blood pressure will be achieved with two or more agents only.

- Use fixed dose formulations to improve compliance.
- Drugs with synergistic effects should be combined pertinently to enhance BP lowering effect so as to achieve target BP.
- Use of long-acting drugs that provide 24-hour efficacy with once daily administration ensures smooth and sustained control of blood pressure; which in turn is expected to provide greater protection against the risk of major cardiovascular events and HMOD. Once daily administration also improves patient compliance.
- Although antihypertensive therapy is generally lifelong, an effort to decrease the dosage and number of antihypertensive drugs should be considered after effective control of hypertension (step-down therapy).
- Due to a greater seasonal variation of temperatures in India, marginal alterations in dosages of drugs may be needed from time to time. 82,83
- The commonly used antihypertensive class of agents are discussed further.

**Antihypertensive drugs**

*Angiotensin Converting Enzyme inhibitors (ACE inhibitors)*

ACE inhibitors are effective in lowering blood pressure and are well tolerated. These are first line agents in patients with diabetes, individuals with other metabolic risk factors, post-MI and patients with heart failure. In diabetes mellitus, they retard the onset and progression of renal disease (patients with microalbuminuria and early CKD). The HOPE trial (a primary prevention trial) showed that in high and average risk individuals, use of ramipril reduced overall mortality and cardiovascular endpoints, even with small reductions in blood pressure. 84 As a class, they are metabolically beneficial to other risk factors like dyslipidemia and diabetes. The most common side effect is dry cough. ACE inhibitors are contraindicated in pregnancy. Serum creatinine and potassium should be monitored in patients receiving ACE inhibitors. Ramipril and Perindopril have greater tissue ACE inhibition effect than other agents. Perindopril in combination with Indapamide has been particularly shown to reduce mortality in patients who have survived stroke (PROGRESS trial). 85

*Angiotensin Receptor Blockers (ARBs)*

Angiotensin receptor blockers block the angiotensin II AT1 receptors, and thus prevent the action of angiotensin II. In the LIFE trial, losartan was better than atenolol in reducing the frequency of the primary composite endpoint of stroke, myocardial infarction and cardiovascular death. 86 In theValsartan Antihypertensive Long-term Use Evaluation (VALUE) trial, both valsartan and amlodipine reduced blood pressure in hypertensive patients at high CV risk, but the effects of the amlodipine-based regimen were more pronounced, especially in the early period. 87 These drugs have many features in common with ACE inhibitors, but do not cause an accumulation of bradykinin. Consequently, cough and angioedema are much less likely to occur than with ACE inhibitors. 88 Initially, some fears were raised regarding increase of coronary events with use of these agents, however, these have been disproved ever since. Also, one retrospective meta-analysis suggested increase in neoplasm with ARBs, however no prospective study has suggested this and is generally believed not to be a significant issue at present. In fact, the ONTARGET trial shows telmisartan (80 mg OD) is as effective as ramipril (10 mg OD) in reducing CV events in high-risk individuals in patients with vascular disease or high-risk diabetes. 89 A combination of ACEIs and ARBs should not be used due to increased risk of hypotension and hyperkalemia. In the recent randomized double blind ROADMAP 90 trial involving 4,447 diabetic patients with olmesartan (40 mg OD), the onset of microalbuminuria has been shown to be delayed in patients with type 2 diabetes. A caution of monitoring eGFR change and serum potassium should be added. This monitoring should be after 1 week of initiating this therapy and after each dose increase.

*Calcium Channel Blockers (CCBs)*

The two subgroups of CCBs are dihydropyridines (amlodipine, felodipine, nifedipine, cilnidipine) and non-dihydropyridines (verapamil and diltiazem). Amlodipine is the most commonly used agent in this group. Besides blood pressure lowering effect, they also have antianginal effects and are devoid of metabolic side effects. CCBs are particularly recommended for elderly patients with isolated systolic hypertension. Verapamil and diltiazem reduce heart rate and have negative inotropic effects. In the Nordic trial, 91 diltiazem was shown to be as effective as treatment based on diuretics, β-blockers or both, in preventing the combined primary endpoints of stroke, MI and CV deaths. The findings of the ASCOT-BPLA (Blood Pressure Lowering Arm) study show that an antihypertensive drug regimen starting with amlodipine (adding perindopril as required) is better than one starting with atenolol (adding thiazide as required) in terms of reducing the incidence of all types of cardiovascular events and all-cause mortality, and risk of subsequent new-onset diabetes. 92

Short-acting dihydropyridines (nifedipine) should be avoided. Amlodipine has no effect on heart rate and cardiac contractility, and has been shown to be safe even in the presence of congestive heart failure. 93

**Diuretics**

Diuretics are widely used as first line agents. They are effective and inexpensive. Although high dose diuretic therapy was associated with side effects, currently recommended low dose diuretic therapy is generally well tolerated. Low-dose diuretics have lesser metabolic side effects like worsening of glycemic control, hyperuricemia and dyslipidemia. Diuretics should be used in doses equivalent to 12.5 mg daily of chlorothalidone or hydrochlorothiazide to avoid adverse metabolic consequences. Chlorothalidone is preferred over hydrochlorothiazide as an antihypertensive. 94 Indapamide use has been shown to be associated with minimal metabolic side effects and is a useful agent. Combinations of thiazides and potassium-sparing diuretics (amiloride and triamterene) are available and are effective options. The PATHWAY 3 trial (2016) a double blind randomized trial showed that a combination of amiloride with hydrochlorothiazide prevents glucose intolerance and improves control of BP compared with hydrochlorothiazide alone. Thus, when hydrochlorothiazide is used as a first line agent it should be
Vasodilators

Clonidine Resistant hypertension in α-Centrally acting agents were superior to doxazosin and bisoprolol which showed that spironolactone was used in combination with amiloride.

Aldosterone antagonists (Spironolactone, Eplerenone) are the preferred agents as add-on agents to reduce BP in patients with resistant hypertension even without documenting hyperaldosteronemia. The PATHWAY-2 study (2015) was a randomized double blind cross over trial which showed that spironolactone was superior to doxazosin and bisoprolol as an add on agent amongst patients with resistant hypertension who were already on three drugs (ACEI/ARB + CCB + thiazide diuretic). In cases of heart failure and/or renal failure, loop diuretics like Furosemide (40-80 mg), Torsemide (10-40 mg) can be used. Metolazone (2.5-5 mg), is the only thiazide like diuretic which is effective in presence of renal failure.


**Newer β-blockers**

Emerging evidence suggests that β-blockers are losing their pre-eminent place as first-line antihypertensive agents. This is based on the head to head trials where it was found that β-blockers are less effective than ACEIs or CCBs at reducing the risk of diabetes and stroke. This was particularly true in patients taking β-blockers and diuretics. In most of the studies, the β-blocker used was atenolol and in the absence of substantial data on other agents it would not be appropriate to apply this conclusion to all β-blockers. β-blockers reduce central aortic pressure to a lesser extent than other classes and this is additional reason for lack of mortality reduction with their use. They also have limitations in patients with dyslipidemia and impaired glucose tolerance. However, they are used in young hypertensives, those with stable and unstable angina and post-MI patients with hypertension. Agents with intrinsic sympathomimetic activity and highly selective β-blockers such as bisoprolol and nebivolol have lesser metabolic adverse effects. Labelol is an α and β blocker and is the drug of choice for hypertension in pregnancy.

**Other drugs**

α-blockers: Prazosin, terazosin and doxazosin - effectively reduce blood pressure both as monotherapy and in combination. They have a special place in the management of elderly hypertensives with benign prostatic hyperplasia (BPH) and CKD. Since postural hypotension can occur, the dose of α-blockers should be carefully up-titrated. Data from the Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT) shows that patients in the doxazosin-based arm had 25% increase in the cardiovascular events and twice the risk of congestive heart failure. These agents are not to be used as first, second or third line agents. They are

<table>
<thead>
<tr>
<th>Table 16: Guidelines for selecting the most appropriate first-line antihypertensive drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class of drugs</td>
</tr>
<tr>
<td>Diuretics</td>
</tr>
<tr>
<td>Elderly patients</td>
</tr>
<tr>
<td>CCBs</td>
</tr>
<tr>
<td>Angina</td>
</tr>
<tr>
<td>Elderly</td>
</tr>
<tr>
<td>Systolic hypertension</td>
</tr>
<tr>
<td>ACEIs</td>
</tr>
<tr>
<td>Heart failure</td>
</tr>
<tr>
<td>Left ventricular dysfunction</td>
</tr>
<tr>
<td>Post-myocardial infarction</td>
</tr>
<tr>
<td>Significant proteinuria</td>
</tr>
<tr>
<td>ARBs</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Proteinuria</td>
</tr>
<tr>
<td>LV dysfunction</td>
</tr>
<tr>
<td>ACE inhibitor induced cough</td>
</tr>
</tbody>
</table>

Table 17: Guidelines for other drugs

| Class of drugs | Definite indication/s | Possible indication/s | Relative indications |
|---|
| β-blockers (Doxazosin, Prazosin) | Angina | Pregnancy | Heart block |
| Post-myocardial infarction | Diabetes |
| Tachyarrhythmia | |
| Heart failure |
| α-blockers | Prostatic hypertrophy | Glucose Intolerance | Orthostatic hypotension |
| Chronic Kidney Disease | Dyslipidemia |
| Centrally acting agents | Hypertension in Pregnancy | Resistant Hypertension | Acute or Chronic Liver Disease |
| α methyldopa | |
| Clonidine | Resistant Hypertension |
| Vasodilators (Hydralazine) | Resistant Hypertension |
| Coronary Artery Disease |

Dir. 54-65

Verapamil or diltiazem

**Table 16: Guidelines for selecting the most appropriate first-line antihypertensive drugs**

**Table 17: Guidelines for other drugs**
generally used as an add-on therapy in resistant hypertension.

Central acting drugs: α-methyldopa, clonidine and moxonidine have been in use for several years. Methyldopa is an important agent for the treatment of hypertension in pregnancy. Clonidine, though a potent antihypertensive agent, is infrequently used these days due to side effects such as postural hypotension, anticholinergic effects and problem of withdrawal-related rebound hypertension. These agents are used in patients of Chronic Renal Failure (CRF) with resistant hypertension.

Direct vasodilators: Hydralazine and minoxidil - are effective, but some of their side effects (such as tachycardia, headache, and retention of sodium and water) may make it difficult to use them in modern day treatment of hypertension.

Racemic forms: of calcium channel blockers and β-blockers are presently available. However, long-term studies regarding their efficacy and safety are not available.

For a given patient the choice of agent amongst the five classes depends on age, risk factor profile and associated diseases of the patient. Table 16 presents guidelines for selecting the most appropriate antihypertensive drugs. Table 17 shows the commonly used dosages and the various agents in each class. Table 18 delineates the special circumstances in which other agents are used as add on therapy after the first line drugs have been used in combinations. The Table 19 lists some common side effects of these drugs which should always be kept in mind.

### Table 18: Anti-hypertensive drugs and their usual dosage

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dosage (mg/day)</th>
<th>Dosing frequency/Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Hydrochlorothiazide</td>
<td>6.25-12.5</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Chlorthalidone</td>
<td>6.25-12.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Indapamide</td>
<td>1.5-2.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Amiloride</td>
<td>5-10</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Triamterene</td>
<td>50-100</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Spironolactone</td>
<td>25-50</td>
<td>1-2</td>
</tr>
<tr>
<td>β-blockers</td>
<td>Metoprolol</td>
<td>25-100</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Bisoprolol</td>
<td>2.5-10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nebivolol</td>
<td>2.5 - 5</td>
<td>1</td>
</tr>
<tr>
<td>α + β Blocker</td>
<td>Carvedilol</td>
<td>3.125 – 50</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Labetalol</td>
<td>50 -200</td>
<td>2</td>
</tr>
<tr>
<td>CCBs</td>
<td>Amlodipine</td>
<td>2.5-20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Cilnidipine</td>
<td>5 – 10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
<td>90-360</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nifedipine (Long-acting)</td>
<td>10 – 40</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Verapamil</td>
<td>80-240</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Benidipine</td>
<td>4-8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Efonidipine</td>
<td>20-40</td>
<td>1</td>
</tr>
<tr>
<td>Racemic isomers</td>
<td>S-amlodipine</td>
<td>2.5 - 10</td>
<td>1</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Enalapril</td>
<td>2.5-20</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Lisinopril</td>
<td>2.5-20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Ramipril</td>
<td>1.25-10</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Perindopril</td>
<td>2-8</td>
<td>1-2</td>
</tr>
<tr>
<td>ARBs</td>
<td>Losartan</td>
<td>50-100</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Candesartan</td>
<td>8-32</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Valsartan</td>
<td>40-160</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Irbesartan</td>
<td>150-300</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Telmisartan</td>
<td>40-160</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Olmesartan</td>
<td>20 - 40</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Azilsartan</td>
<td>40 - 80</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Fimasartan</td>
<td>60 - 120</td>
<td>1</td>
</tr>
<tr>
<td>α-blockers</td>
<td>Prazosin</td>
<td>2.5-10</td>
<td>2-3</td>
</tr>
<tr>
<td></td>
<td>Doxazosin</td>
<td>1-4</td>
<td>1</td>
</tr>
<tr>
<td>Centrally acting drugs</td>
<td>Clonidine</td>
<td>0.1-0.3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Methyldopa</td>
<td>500-1500</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Moxonidine</td>
<td>0.2-0.4</td>
<td>1-2</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Hydralazine</td>
<td>25-100mg</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Minoxidil</td>
<td>2.5-5mg</td>
<td>1-2</td>
</tr>
</tbody>
</table>

### Table 19: Adverse drug reactions of anti-hypertensive drugs

<table>
<thead>
<tr>
<th>Common side effects</th>
<th>ACE inhibitor</th>
<th>ARB</th>
<th>Calcium channel blocker</th>
<th>Diuretic</th>
<th>B-blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Flushing</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lethargy</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Impotence</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Dry cough</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gout</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Oedema</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Cold hands and feet</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Angioedema</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Combination therapy is the method for effective control of hypertension since a majority of patients will require two or more drugs for sustained and effective control of blood pressure. One often needs to combine different classes of drugs with different mechanisms of action to achieve effective control of blood pressure with minimal side effects. Combinations with additive hypotensive effects will produce greater blood pressure reductions than those obtained with monotherapy. When a subject is in stage 2 or above, therapy can be initiated either with two drugs or as a fixed dose combination. The ACCOMPLISH trial has shown that combination of ACEIs with CCBs is better than a combination of ACEI with diuretic and should be the preferred combination. Younger individuals have high renin...
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Hypertension, hence ACEIs/ARBs or newer β-blockers are preferred; while older individuals have low renin hypertension and hence diuretics or CCBs are preferred as first line agents.

In combination, one out of the two groups A [ACE inhibitor/ ARB] or B [β-blocker] is combined with C [calcium channel blocker] or D [thiazide diuretic] (step 2). In refractory patients, when 3 agents are to be used, A+C+D is a good choice (step 3). The stepped care approach for physicians suggested by the present IGH IV guidelines for combination therapy in hypertension is shown in Figure 4.

Certain drug combinations have synergistic effect and increase the effectiveness of the other agent. However, some combinations are not effective and are thus undesirable and not suggested to be used. These are shown in Table 20.

Drug Interactions

Since multiple drugs are used in hypertensive patients and often these patients have other co-existing conditions, certain common drug interactions should be kept in mind, as shown in Table 21.
Maintenance and Follow-up of Therapy

Once therapy with particular antihypertensive drugs is instituted, patients need to be seen at frequent intervals during the period of stabilization in order to monitor changes in blood pressure and see whether non-drug measures are being strictly followed. At least once in a fortnight, blood pressure should be measured at the clinic or at home. Other CHD risk factors as well as co-existing diseases/conditions should be monitored. The overall risk category of a patient and the level of blood pressure decide the frequency of follow up visits to a large extent. The frequency can be reduced once BP is stabilized and other risk factors are controlled. Tobacco avoidance and alcohol moderations must be promoted vigorously.

Associated Therapies

In order to reduce the overall risk, patients with hypertension need therapies for control of other risk factors for secondary prevention and now with recent available data even for primary prevention. Low dose aspirin should be prescribed to all hypertensives with cardiovascular disease and stroke (secondary prevention). All hypertensive patients with coronary, peripheral, or cerebrovascular disease with LDL levels >100 mg/dL should receive statins as secondary prevention strategies. Hypertensive patients without CV diseases but those in high-risk group should also receive statins for primary prevention as shown in the recently published HOPE III trial. Rosuvastatin 10 mg/day resulted in greater benefit than even antihypertensive drugs in a high risk hypertensive population.10,100,101

Aspirin has no role as a concomitant therapy in patients of hypertension without evidence of ASCVD. Recently, three primary prevention trials the ASCEND, ARRIVE and the ASPREE trial looked at role of aspirin for primary prevention in elderly (ARRIVE and ASPREE) and diabetic (ASCEND) individuals. All three trials were negative for any benefit. Thus, aspirin does not have any role as a primary preventive agent.102-104

Newer Modalities

A novel baroreflex activation therapy has been evaluated recently. It stimulates baroreceptors through an implanted device and has been shown to reduce significant change in BP in patients with resistant hypertension. This therapy is still experimental and has no clinical application as yet.

Renal sympathetic denervation therapy has been evaluated. In this radiofrequency ablation of sympathetic plexus around renal arteries is performed. In the SYMPLICITY hypertension -2 trial,105 it was shown to reduce BP significantly over and above the pharmacological therapy. However, the more recent and meticulously conducted SIMPLICITY III trial has not shown any effect on BP reduction with renal denervation compared to sham controlled placebo therapy. Thus, renal denervation therapy is presently still under evaluation and is not advocated for routine clinical use.
Secondary Hypertension

The prevalence of secondary hypertension is around 5-6% of all hypertensives. Because of low prevalence, routine screening for secondary hypertension is not essential and cost effective. Renal disease constitutes the major group of secondary hypertension.

When to suspect secondary hypertension clinically?
- Absence of family history of hypertension
- Severe hypertension > 180/110 mm Hg with onset at age < 20 years or > 50 years
- Difficult-to-treat or resistant hypertension with significant end-organ damage features
- Combination of pain (headache), palpitation, pallor and perspiration – 4 P’s of pheochromocytoma
- Polyuria, low eGFR, nocturia, proteinuria or hematuria – indicative of renal diseases
- Absence of peripheral pulses, brachiofemoral delay and abdominal or peripheral vessel bruits
- History of polycystic kidney disease or palpable enlarged kidneys
- Cushingoid features, multiple neurofibromatosis
- Significant elevation of plasma creatinine with use of ACE inhibitors

Table 22: The percentage prevalence of various causes of Hypertension

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Primary or Essential</td>
<td>94-95%</td>
</tr>
<tr>
<td>B. Secondary</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td></td>
</tr>
<tr>
<td>Renal parenchymal</td>
<td>2-3%</td>
</tr>
<tr>
<td>Renovascular</td>
<td>1-2%</td>
</tr>
<tr>
<td>Endocirnal</td>
<td>0.3-1%</td>
</tr>
<tr>
<td>Primary aldosteronism</td>
<td></td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td></td>
</tr>
<tr>
<td>Cushing’s Syndrome</td>
<td></td>
</tr>
<tr>
<td>Acromegaly</td>
<td></td>
</tr>
<tr>
<td>Vascular –</td>
<td></td>
</tr>
<tr>
<td>Coarctation of aorta</td>
<td></td>
</tr>
<tr>
<td>Drugs –</td>
<td>0.50%</td>
</tr>
<tr>
<td>Oral Contraceptives</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
</tr>
<tr>
<td>Steroids, Cyclosporine</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>0.50%</td>
</tr>
<tr>
<td>Obstructive Sleep apnoea</td>
<td></td>
</tr>
</tbody>
</table>

Table 23: Staging system and action plan for chronic kidney disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Action†</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
<td>At increased risk for CKD</td>
<td>≥ 90 with risk factors</td>
<td>Screening CKD risk reduction</td>
</tr>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>≥ 90</td>
<td>Diagnosis and treatment. Retard progression of CKD. Treat comorbidities. Cardiovascular disease risk reduction.</td>
</tr>
<tr>
<td>2</td>
<td>Mild decrease in GFR</td>
<td>60-89</td>
<td>Estimate progression</td>
</tr>
<tr>
<td>3</td>
<td>Moderate decrease in GFR</td>
<td>30-50</td>
<td>Evaluate and treat complications</td>
</tr>
<tr>
<td>4</td>
<td>Severe decrease in GFR</td>
<td>15-29</td>
<td>Prepare for renal replacement therapy</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure &lt; 15 or dialysis</td>
<td></td>
<td>Renal Replacement Therapy if uremic</td>
</tr>
</tbody>
</table>

Table 23 notes:
- Estimated GFR (eGFR) using Modification of Diet in Renal Disease (MDRD) formula: GFR (mL/min/1.73 m²) = 186 x (Pcr⁻¹.164 x (age⁻⁰.₂⁰ x (0.742 if female) x (1.210 if African American)); 
- Includes actions from preceding stages; 
- Risk factors: hypertension, dyslipidemia, diabetes mellitus, anemia, systemic lupus erythematosus, chronic analgesic ingestion; 
- Kidney damage as manifested by abnormalities noted on renal pathology, blood, urine or imaging tests.

A. Hypertension in Chronic Kidney Diseases
Hypertension, after diabetes mellitus, is the second leading cause of end stage renal disease (ESRD) and together these entities account for over 60% of ESRD patients. Essential hypertension is an important cause of chronic kidney disease and renal parenchymal disease is a well-established cause of secondary hypertension.

In India diabetic nephropathy contributes to 30% of cases of CKD while hypertensive nephropathy and chronic pyelonephritis each contribute to 10% cases of chronic renal failure.

There are two forms of kidney diseases causing hypertension namely renal parenchymal and renovascular.

- Causes:
  - Renal parenchymal diseases – (Non-diabetic)
    - Chronic glomerulonephritis
    - Chronic interstitial nephritis
    - Analgesic nephropathy
    - Polycystic kidney disease
    - Gout with renal failure
    - Obstructive nephropathy
  - Stages of Chronic Kidney Diseases and Action Plan

The functional stages are based on estimated GFR in CKD with the relevant action plan as below.

Treatment

Therapy with antihypertensives in CKD has been found to not only control BP but also slow down the progression. The Ramipril Efficacy in Nephropathy (REIN), ACEI and progressive Renal Insufficiency (AIPRI) and modification of Dietary Protein in Renal Disease (MDRD) trials established the ability of antihypertensives to slow down the progression of non-diabetic chronic kidney disease.

Threshold for initiation of Anti-Hypertensive Treatment
a. BP 140/90 Hg for patient without proteinuria
b. BP 130/80 for those with proteinuria Target to achieve: BP < 130/80mmHg

In post renal transplant patients, hypertension is an important issue since certain drugs like cyclosporine and erythropoietin used in these patients can aggravate hypertension. At times, combination of multiple drugs including ACEI, ARB, CCB and diuretics may be required for effective BP control.
where BP is still not controlled, clonidine, α methyl dopa or α blockers may be added.

Renovascular
- The most common cause of renovascular hypertension in India is Takayasu’s syndrome (progressive aortoarteritis).116 though atherosclerotic renovascular disease is also being recognised more often now in early patients.
- The most common cause of renovascular disease in Western population are atherosclerotic disease in 60% of elderly population and fibromuscular dysplasia in 35% of young. Atherosclerotic renal artery stenosis patients often have associated cardiovascular disease.
- Rare causes include embolic and tumor, thrombus and extrinsic reasons.
- Takayasu’s disease is a non-specific panarteritis affecting young women. Hypertension is mainly due to renal artery stenosis which can be unilateral or bilateral.116
- Renovascular disease is much more common than renovascular hypertension (RVH).
- Atherosclerotic disease usually involves the proximal segment while fibromuscular dysplasia involves the distal part of renal artery.

Investigations:
- A paraumbilical bruit is heard in 50-60% of patients with renovascular hypertension and 10% cases of essential hypertension. A diastolic renal bruit is more specific than systolic bruit.
- In patients with moderate degree of suspicion of renovascular hypertension, non-invasive tests are recommended initially.
- Wherever there is a high degree of suspicion, direct selective renal arteriography is recommended.
- Colour Doppler Ultrasound (CDUS), CT angiography and MRI angiography are other good and non-invasive modalities. MRI angiography has higher sensitivity (90%) and specificity (92%).
- 99Tc – DTPA and 123I – Hippuran scan are useful non-invasive investigations. These tests give functional status of CKD.
- Conventional angiography, though invasive, is the gold standard. Intra-arterial injection with digital subtraction angiography (DSA) may be used. Once the diagnosis is confirmed, renal angioplasty with stenting shows similar results as medical therapy.

Treatment of renal artery stenosis
Goals are control of BP and preservation of renal function. In general there are three options:
  - Medical
    - Percutaneous transluminal renal angioplasty
  - Surgery
    - Patients with fibromuscular dysplasia benefit from angioplasty or surgical revascularisation. Patients with atherosclerotic renovascular disease do not demonstrate any significant benefit from renal artery intervention but medical therapy is equally effective in these patients.116 as shown in the ASTRAL study published in 2009 and the more recent CORAL study in 2014.117,118 Renal artery stenting does not confer any benefit to prevent clinical events when added to medical therapy in patients of renal artery stenosis with hypertension or CKD.

B. Endocrine causes

Pheochromocytoma
- These chromaffin cell tumors are mostly adrenal.
- These may be extra-adrenal in 15% of the cases and bilateral adrenal in 10% of the cases. 10% of all cases are familial and 10% are malignant.
- Episodic hypertension, postural fall, pallor, throbbing headache, palpitations and perspiration are suggestive clinical features.118

Investigations: Screening tests include plasma and urinary biochemical assay for free catecholamines, metanephrines and vanillylmandelic acid (VMA). These tests have high specificity (99%) and sensitivity (85-90%). Following drugs should be withdrawn for 48 hours before doing these tests: α methyl dopa, β blockers, clonidine, penicillin and certain vegetables. Patients can be continued on CCBs and ACE inhibitors during evaluation.

Tumor localisation: Computed Tomography scan and MRI of the abdomen have greatly simplified tumor localisation; MIBG labelled with I is the most specific way of diagnosing adrenal and extra adrenal pheochromocytomas.119 Other modalities include PET scan using18 F-fluorodeoxy glucose.

- Once localised, surgery should be offered to all the patients. Mortality from surgery is now less than 5%. For pre-operative preparation, control of blood pressure is important and can be achieved with oral phenoxybenzamine 10 mg once daily, to be increased slowly. Oral prazosin and terazosin preferentially block post-synaptic α1-receptors on vessel wall and leave pre-synaptic α 2- receptors. As a result, tachycardia is less of a problem. B-blockers may be given to these patients to control tachycardia and arrhythmias, only after α-blockers have been started. Two third of patients can be operated by minimally invasive surgery. One third require open surgery. Post-operative hypotension and hypoglycemia can be managed by continuous monitoring.120,121

Primary Aldosteronism
- It is due to excess aldosterone secretion by the adrenal cortex secreted generally by adenomas and occasionally
due to bilateral adrenocortical hyperplasia.

- This is suspected in a case of hypertension showing persistent hyokalaemic metabolic alkalosis in the absence of diuretic therapy.

- Plasma Aldosterone to Plasma Renin Activity (PRA) ratio more than 20 to 25 (normal < 10) is 95% sensitive and 75% specific for Primary Hyper Aldosteronism. It is usually diagnosed by imaging techniques.

Cushing's Syndrome

- Hypertension is present in approximately 80% of patients with Cushing’s syndrome.
- Other clinical features include central obesity, hirsutism, polycythemia and pink striae on the abdomen.

- This can be screened by performing early morning serum cortisol levels. Hypertension remits in most patients after successful treatment.

Miscellaneous

- Other important secondary causes include:
  - Oral contraceptives
  - Thyroid disorders, both hypothyroidism and hyperthyroidism

Other causes

- Coarctation of aorta, a congenital disease needs surgical correction
- Sleep apnea syndrome is one of the common causes of reversible hypertension. Polysomnography is diagnostic. No specific drugs have proven superior in sleep apnea but use of C-PAP improves the hypertension

- Acute stressful situations cause intense sympathetic discharge and may temporarily induce hypertension. B blockers are preferred. Common conditions include acute mental stress, hypoglycaemia, acute intermittent porphyria, exposure to cold, burns, perioperative period and post head injury

- Drugs: Non-steroidal anti-inflammatory drugs, sympathomimetic amines, ephedrine, glucocorticoids, cocaine and amphetamines can all cause significant hypertension.
Complications

The complications of hypertension can be considered either hypertensive or atherosclerotic. Although the extent of damage often correlates with the level of blood pressure, it is not always the case. Blood pressure and organ impairment should be evaluated separately. The various complications are as follows:

1. Hypertensive Heart Disease
   - Hypertension has the following effects on the heart: left ventricular hypertrophy, increased risk of coronary artery disease, arrhythmias, congestive cardiac failure (HFNEF and HFrEF) and sudden death. However, the impact of reduction of LVH on reduction of morbidity and mortality is still debated.
   - Most episodes of left ventricular failure in hypertensive patients are associated with diastolic heart dysfunction.
   - Treatment of hypertension can reverse ventricular hypertrophy. However, the usefulness of the classification by Keith, et al and its relevance to current clinical practice. Recent studies show that some of the retinal signs (e.g., hemorrhages, microaneurysms and cotton-wool spots) predict stroke and death from stroke independently of elevated blood pressure and other risk factors.

2. Cerebrovascular Disease
   - Hypertension is the most important modifiable risk factor for all types of atherothrombotic stroke and intracerebral haemorrhage due to rupture of Charcot-Bouchard aneurysms.
   - The relation between the incidence of stroke and blood pressure is continuous. A 5-6 mm Hg reduction in diastolic blood pressure reduces the risk of stroke by 40%. The SHEP (Systolic Hypertension Elderly Program) study showed substantial benefit following control of systolic blood pressure in the elderly.

3. Kidney
   - About 20-25% of renal failure is attributed to uncontrolled hypertension.
   - Development of renal damage is preceded by microalbuminuria, which progresses to overt proteinuria and may further progress to end-stage renal disease.
   - Reduction of proteinuria can be achieved by effective blood pressure control specially with use of ACEIs and ARBs.

4. Retina
   - Hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated blood pressure.
   - The classification of Keith, Wagener and Barker has been widely used. Grade I retinopathy is characterized by copper wire appearance; Grade II by arteriovenous nicking; Grade III by the presence of haemorrhages and exudates; and Grade IV by papilloedema.
   - Grade III and IV retinopathy is seen in long standing uncontrolled hypertension. These changes may regress with effective control of blood pressure.
   - Several reviews of hypertensive retinopathy since 1996 have questioned the usefulness of the classification system by Keith, et al and its relevance to current clinical practice. Recent studies show that some of the retinal signs (e.g., hemorrhages, microaneurysms and cotton-wool spots) predict stroke and death from stroke independently of elevated blood pressure and other risk factors.

5. Large Vessel Disease
   - Hypertension is a risk factor for development of intermittent claudication. It also increases the risk of abdominal aortic aneurysms and aortic dissection. Eighty percent of patients with aortic dissection have hypertension.

6. Hypertensive crises
   - Hypertensive crises are classified as hypertensive emergencies or urgencies.

Hypertensive emergencies (Malignant Hypertension) are characterized by severe elevations in BP (>180/120 mm Hg) complicated by evidence of impending or progressive target organ dysfunction. They require immediate BP reduction (not necessarily to normal) often with parenteral agents over a period of 6-8 hours with constant monitoring, to prevent or limit HMOD. Examples include hypertensive encephalopathy, intracerebral hemorrhage, acute myocardial infarction, acute left ventricular failure with pulmonary edema, unstable angina pectoris, aortic dissection, or eclampsia. IV nitroglycerine is generally used although it is not very effective, but specially useful in patients with ischaemic heart disease and left ventricular failure. The recommended dose is initially 5mcg/min, then titrate by 5 mcg/min at 3 to 5 minute intervals, upto 10 mcg/min. Intravenous enalaprilat is useful in hypertensive emergencies, specially in presence of heart failure. It is used in dosages of 0.625 – 1.25 mg bolus every 6 hours. IV Labetalol is also being used in hypertensive emergencies in a bolus dosage of 2-10 mg and infusion of 2.5-30 mcg/kg/min. IV esmolol has been shown to be specially useful for peri-operative accelerated hypertension. Usual bolus dose is 80-500 mcg/kg over 1 minute followed by an infusion of 50-300 mcg/kg/min. IV nitroprusside is required rarely, in situations like dissection of aorta and subarachnoid haemorrhage with very high blood pressure. It requires intensive care setting and very close monitoring. The dose is 0.3 mcg/kg/min to a maximum of 4 mcg/kg/min. Sublingual captopril can also be used when less rapid reduction is required.

Hypertensive urgencies (Accelerated Hypertension)
are situations associated with severe elevations in BP without progressive target organ dysfunction. Examples include upper levels of stage II hypertension associated with severe headache, shortness of breath, epistaxis, or severe anxiety. The majority of these patients present as noncompliant or inadequately treated hypertensives, often with little or no evidence of HMOD.

The aim should be safe, prompt and gradual lowering of blood pressure with oral medication over a period of 1-3 days. In most urgencies, blood pressure can be controlled with rapidly acting oral medications like calcium channel blockers and ACEI/ARB. Sublingual nifedipine should not be used in hypertensive crises as it can cause precipitous fall in blood pressure, reflex tachycardia and may precipitate renal, cerebral or coronary ischaemia.
Hypertension in Special Situations

Hypertension with Diabetes Mellitus

- 30% to 35% of hypertensive patients are detected to have co-existing diabetes mellitus. Similarly, the prevalence of hypertension is 1.5 to 2 times greater in patients with diabetes mellitus as compared to non-diabetics subjects. Co-existence of diabetes and hypertension leads to increased cardiovascular morbidity and mortality. The progress of type 2 diabetes in India is increasing at a very fast pace and this is likely to also contribute to a significant burden of hypertension.

- Blood pressure should be measured on each visit of the diabetic patient and the procedure for measurement is the same as in ordinary hypertensive patients. In diabetic population it is imperative to measure the blood pressure in supine, sitting and standing positions to exclude the possibility of autonomic neuropathy.

- Some of the earlier trials like UKPDS and HOT showed evidence in favour of treating high normal blood pressure aggressively but subsequently, in the ESH/ESC Guidelines 2007, no definitive data was available to substantiate this. Therefore, it is recommended that in high normal blood pressure, more aggressive lifestyle measures should be followed while a blood pressure of more than 140/90 mmHg should be treated with pharmacotherapy to achieve cardiovascular and microvascular protection. In patients with diabetes, blood pressure targets should be less than 140/80 mmHg.

- In the management of diabetic hypertensives, lifestyle modifications have to be more aggressive.

- Lifestyle measures include weight loss in case of obese, dietary changes like low salt and low fat. Regular exercises form the basis and are applicable at all stages of hypertension.

- It has been proven that it is useful and effective to treat hypertension in people above the age of 65 years. It has been observed that to effectively lower the blood pressure a combination of two or more drugs are required for controlling the blood pressure to target levels. ACEIs in the HOPE trial and ARBs in the ONTARGET trial have emphasised the importance of RAAS blockade to reduce the risk of complications of diabetes, specially microvascular complications and macrovascular complications. Therefore, ACEIs in type 1 diabetes are recommended as the first line drug therapy while ARBs may be used in patients who have type 2 diabetes or who are intolerant to ACE inhibitors.

- β-blockers have been shown to be useful as monotherapy and in combination with ACEI in the ASCOT trial. The combination of amlodipine and perindopril was associated with significantly less incidence of new onset diabetes as compared to the combination of β-blocker and diuretic.

- β-blockers potentially mask hypoglycemic symptoms. β-blockers are falling into disrepute in an ordinary hypertensive patient but in diabetic population with evidence of coronary artery disease and congestive heart failure they may be quite useful. It is recommended that we may use cardioselective β-blockers like nebivolol and carvedilol. α-blockers can also be used as a useful adjunct in the treatment of the above clinical scenario.

- The ACCORD trial (2010) has shown benefits of effective BP control in diabetic patients. It shows targeting a SBP of <120 as compared to <140 did not reduce composite outcome in diabetic population. A subgroup analysis of a high risk population like the one in SHIFT trial showed benefit of more tight control in the diabetic population also. Another analysis shows intensive BP treatment benefit was observed amongst patients undergoing standard glycemic controls even amongst those without additional risk factors. The ADVANCE trial and INVEST trial show definitive improvement in the microvascular complications specially on kidneys but their effect on eye and neural complications is questionable. There was a shift towards improvement in macrovascular complications but it did not reach statistical significance.

- The therapy and the targets need to be individualized for each patient depending on age, comorbid conditions, cost factor and socio-psycological factors.

- The drugs which are useful in diabetic pregnant patients who are hypertensive include methyldopa, calcium channel blockers and labetolol. The use of ACE inhibitors/ARBs is contraindicated. Use of diuretics during pregnancy can lead to reduction of plasma volume which can result in low perfusion resulting in decreased fetal growth/fetal damage.

- SGLT2 inhibitors (Empagliflozin, Canagliflozin and Dapagliflozin) have been evaluated recently amongst diabetic patients in three large trials (EMPA-REG, CANVAS Program and DECLARE-TIMI 58). These agents have significant CV benefits and reduce blood pressure. They reduce BP significantly in patients of diabetes or hypertension irrespective of the level of BP. This is a class effect seen with all these three agents. In the EMPA-REG trial there was a 38% relative risk reduction in death from CV causes, 35% risk reduction in hospitalization for heart failure. There is also a significantly reduced progression of kidney disease and renal events with these agents.

Hypertension with Cerebrovascular Disease

- Excessive and sudden elevation of blood pressure is more often associated with cerebral haemorrhage than infarction. Moderate reduction in blood
• In post stroke patients for long term the evidence for reduction in incidence of stroke with control of blood pressure has been consistent. In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence averaging 35% to 40%.12 In stroke survivors with hypertension, blood pressure lowering therapy has been shown to result in 43% reduction in stroke recurrence.

• Hypertensive encephalopathy is an emergency that needs to be identified and aggressively managed.

• In acute cerebrovascular disease, the goal is to gradually reduce the blood pressure and carefully monitor it for the first 24 hours in view of the possibility of transient hypertension.

• Treatment of acute BP elevation in cerebral haemorrhage has been addressed in two recent trials – the INTERACT 2 (2013) and the ATACH II trial (2016) have looked at benefits of intensive BP lowering in patients with acute cerebral haemorrhage. Both these trials show that early intensive lowering to less than 140 as against target of <180 has no mortality benefit although there was some improved functional outcome.151,152

We recommend initiation of antihypertensive therapy and continuous monitoring only when BP is more than 220 systolic and it should be maintained below 180/105 mm Hg.1

• Immediately after the occurrence of an ischemic cerebral infarction, it is appropriate to withhold treatment in patients who present with high blood pressure, unless blood pressure is very high (>220/120 mm Hg). In such patients a cautious reduction in B.P. by 10 to 15% only is suggested.15

• BP should not be aggressively reduced in ischemic stroke patients who are otherwise not candidates for thrombolysis. In patients for thrombolytic therapy, SBP of >185 and DBP of > 110 mm Hg should be actively treated and maintained below 185/105 mm Hg.153

• In post stroke patients for long term the evidence for reduction in incidence of stroke with control of blood pressure has been consistent. In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence averaging 35% to 40%.12 In stroke survivors with hypertension, blood pressure lowering therapy has been shown to result in 43% reduction in stroke recurrence.

• In the PROGRESS TRIAL, the combination of perindopril and indapamide reduced the risk of stroke by 43% among patients who were hypertensive or normotensive. Perindopril alone was not found to have a similar reduction in the risk of stroke. Hence, a combination of a ACEI and a diuretic is preferable.80

### Hypertension in Women

• Some of the side effects of commonly used drugs like ACE inhibitor-induced cough, CCB-induced pedal edema, and diuretic-induced hyponatremia and hypokalemia are seen more often in women than in males.12,154

• Estrogen-progesterone oral contraceptives cause a distinct increase in systolic and to a lesser extent diastolic pressure in virtually all women. Five percent women who use the pill for 5 years develop hypertension. Age, positive family history, history of PIH and obesity are known predisposing factors for pill-induced hypertension.12,150

In more than one half, blood pressure returns to normal when the pill is withdrawn.

• Hormone replacement therapy (low dose estrogen) in post-menopausal women is no longer indicated.

### Hypertension in Pregnancy

Hypertension can affect 5-10 % of pregnancies and remains a major cause of maternal and fetal morbidity and mortality. Maternal risks include placental abruption, stroke, multiorgan failure and disseminated intravascular coagulation. The fetal risks include intruterine growth retardation, prematurity and intrauterine death.

Hypertension in pregnancy is classified as office BP measurements of SBP ≥ 140 mmHg and/or DBP measurements of ≥ 90 mmHg. It is classified as Mild hypertension if BP is 140-159/90-109 mmHg and Severe hypertension if BP is ≥160/110 mmHg.

Hypertension in pregnancy includes four entities

- Pre-existing hypertension/Chronic hypertension: precedes pregnancy or develops before 20 weeks of gestation, and usually persists for more than 6 weeks post-partum
- Gestational hypertension: develops after 20 weeks of gestation, without significant proteinuria and usually resolves within 6 weeks post-partum
- Pre-eclampsia: gestational hypertension with significant proteinuria (>0.3 g/24 h or ≥30 mg/mmol ACR). It is usually accompanied by headache, visual disturbances, abdominal pain, or abnormal laboratory tests, specifically low platelets and/or abnormal liver function. Eclampsia is the occurrence of seizures that cannot be attributed to other causes in a patient with pre-eclampsia.
- Preeclampsia superimposed on Pre-existing hypertension

Hypertension in pregnancy is diagnosed by recording phase IV or V of Korotkoff sounds with the patient lying in a lateral position. The manual auscultation is the method of choice since automated BP machines are unreliable in pregnancy and eclampsia. Ambulatory BP Monitoring is the preferred over Home BP monitoring or office BP measurements.

Investigations during pregnancy include urine analysis, blood count, haematocrit, liver enzymes, serum creatinine and serum uric acid. A urine protein dipstick test showing >1+ warrants evaluation of ACR with values of ≥30 mg/mmol being abnormal. Additional tests include ultrasonography of the kidneys and adrenals and doppler ultrasound of the uterine arteries.

In a 2014 Meta-analysis - evaluated maternal and fetal outcomes in 49 randomized trials of treatment versus no treatment of women with mild hypertension (140-159/90-109 mmHg) during pregnancy, Treatment Did Not Result In Either Fetal Benefit Or Harm. However, antihypertensive therapy Significantly Decreased the incidence of severe hypertension by 40 to 60 %. In a 2015 the CHIPS trial (Control of Hypertension in Pregnancy) - randomly assigned pregnant women with gestational or chronic hypertension to Diastolic Blood Pressure Treatment targets of 85 mmHg (tight control) or 100 mmHg...
Management of hypertension in pregnancy

Amongst lifestyle changes, exercise is recommended with caution. A salt restricted diet is not recommended.

Women with a moderate to high risk of preeclampsia (previous eclampsia, CKD, diabetes mellitus, chronic hypertension, autoimmune diseases, multiple pregnancy, maternal age >40 years) should start on aspirin 100-150 mg from the 12th to 36th week of pregnancy.

In Mild hypertension in pregnancy, initiation of antihypertensive medications is considered if the BP is ≥ 140/90 mmHg along with gestational hypertension or subclinical HMOD or in any patient with BP ≥ 150/95 mmHg. A BP target of < 140/90 is considered if the BP is ≥ 140/90 mmHg in any patient with subclinical HMOD or in any patient with mild hypertension along with gestational hypertension or autoimmune diseases, multiple pregnancy, maternal age >40 years.

In Moderate hypertension in pregnancy, the need for blood pressure lowering medications in elderly hypertensives with no more than an initial 25% decrease, even in situations requiring rapid reduction in blood pressure with medications.

- Targets for BP control are <140/80 mmHg for those aged 55-79 years. However, for those aged >80 years, a systolic BP of 140-145 mmHg is acceptable.

- Long-acting dihydropyridine CCBs, specially amlodipine, are considered to be the drug of choice in these patients. The CCBs are recommended because they have been shown to be effective in reducing mortality and morbidity. Unless there is a compelling indication to use another class of drugs.

- Low dose hydrochlorothiazide, chlorthalidone (6.25 to 12.5 mg per day) or indapamide (1.25-2.5 mg per day) can also be used. Where indicated, these could be combined with ACEIs or ARBs.

- Bilateral atherosclerotic renovascular disease in the elderly must be kept in mind while treatment with ACEIs or ARBs.

- The HYVET trial and HYVET Extension both add evidence of the benefit of BP lowering in the very elderly (octogenarians) patients and the importance of early and sustained antihypertensive treatment even in very elderly people.

Isolated Systolic Hypertension

- Isolated systolic HT is more often seen in the elderly than in the young. The goal of blood pressure control in older patients should be the same as in younger patients (i.e. 140/90 mm Hg). However, an interim value of a systolic blood pressure below 160 mm Hg may be necessary in elderly patients with marked systolic hypertension, especially if they develop symptoms of giddiness and light headedness when their blood pressure is reduced to 140/90 mm Hg.

- Management of isolated systolic hypertension in the elderly is the same as mentioned in the management of hypertension in the elderly.
• Isolated systolic hypertension in the young patients, although uncom- mon, is often successfully treated with lifestyle modification and long-acting β-blockers.

Orthostatic Hypotension

• This is defined as a fall in the BP of more than 20 mm Hg systolic and/or more than 10 mm Hg diastolic in response to moving from supine to standing position within 3 minutes.

• Its prevalence is higher in diabetics, elderly, Parkinson’s disease. It results in symptoms of lightheadedness, giddiness, blurring of vision or syncope. It may be associated with supine hypertension or a lack of compensatory tachycardia suggestive of autonomic insufficiency.

• All antihypertensive drugs may produce OH as a side effect, however this occurs more commonly with diuretics, α-blockers, vasodilators and ACEI. OH will influence the selection and continuation of antihypertensive drugs.

• Low BP per se is of no significance, however, it should be evaluated in the clinical context.

Hypertension with Congestive Cardiac Failure

• Congestive cardiac failure is a common sequel of long standing hypertension and adequate control of BP improves mortality in these patients.

• Heart failure with normal ejection fraction (HFnEF) is an entity which is being increasingly recognized now in elderly hypertensives who present with dyspnea. The prevalence of HFnEF is equivalent to systolic HF. The prognosis is marginally better than systolic HF. Effective and good control of BP is the mainstay of therapy. Diuretics help in symptomatic improvement in these patients. Other agents like β-blockers and positive inotropes are not useful in these patients.176-178

• Several large trials of ACEIs in patients with left ventricular dysfunction due to hypertension have provided evidence of significant reduction of morbidity, secondary to heart failure.179

• Low dose diuretics are also used in hypertension with heart failure, particularly when associated with fluid retention.

• In patients with congestive heart failure stabilized with ACE inhibitors and diuretics, selective β-blockers such as metoprolol, bisoprolol and α-β blocker carvedilol may be used wherever indicated. Use of these β-blockers has been shown to reduce mortality. These agents should be started in low doses and then gradually increased.180,181

• Amlodipine has been found to be safe in treating hypertensive patients with angina and left ventricular failure, when added to ACEIs, low dose diuretics and digoxin. Other calcium channel blockers are not recommended in these patients.1

• In patients with severe hypertension and acute left ventricular failure, blood pressure needs to be brought down rapidly to normal or slightly above normal range. This can be done by administration of intravenous drugs such as furosemide, nitroglycerine, enalaprilat or sodium nitroprusside.

• INTER CHF Heart failure registry shows that 62% of patients with HF have HTN and it is the leading risk factor responsible for it. Other risk factors like dyslipidemia 35%, tobacco use (35%), diabetes (30%), alcohol (14%), CKD (9%), history of MI (21%) are much less common.182

• The ASIAN –HF registry of more than 5000 patients from across Asia with major participation from India shows ACEIs/ ARBs were prescribed to 77%, β-blockers, vasodilators and ACEI.

• The PARADIGM-HF study shows that angiotensin receptor (Valsartan)–neprilysin inhibitor (Sacubitril) - ARNI was superior to Enalapril in reducing the risks of death and of hospitalization for heart failure. This agent should be used amongst those who do not respond optimally to ACEI/ARB.190

Hypertension with Atrial Fibrillation

• Hypertension is an important risk factor for atrial fibrillation. Atrial fibrillation increases the risk of cardiovascular morbidity and mortality by approximately 2 to 5 fold with a marked increase in the risk of embolic stroke. Increased left ventricular mass and enlargement of the left atrium have been identified as independent determinants of new onset atrial fibrillation. Blood pressure control appears to be strictly required when anticoagulant treatment is given because stroke and bleeding episodes are more frequent when systolic blood pressure is >140 mmHg.

• A recent meta-analysis shows that there is reduced incidence of new atrial fibrillation in patients receiving an angiotensin receptor antagonist or ACE inhibitor.

• In another recent metaanalysis191 including almost 12000 patients with systolic heart failure, and therefore at high risk of atrial fibrillation, β-blockers were found to significantly reduce (by about 27%) the incidence of atrial fibrillation. A history of atrial fibrillation and systolic heart failure is therefore a specific indication for using β-blockers. In patients with atrial fibrillation CHA2DS2-VASc score with points as follows (C.CHF 1, H-hypertension 1, A-age >75 years 2, D-diabetes 1, S.prior stroke 2, V-Vascular disease 1, A-age 65-74 years 1, Sc-female sex 1) should be calculated. A score of 1 is “low-moderate” risk and we can consider antiplatelet or anticoagulation depending on patient preference. However, a score of ≥2 is “moderate-high” risk and these patients should be put on anticoagulation for a lifelong period. Vitamin K antagonists - Warfarin or dicoumarol is used in dosages so as to keep the INR between 2-3.192 More recently newer oral anticoagulants (NOACs), dabigatran, rivaroxaban and apixaban are available in India.
Hypertension with Chronic Obstructive Pulmonary Disease

- Hypertension in patients with COPD and bronchial asthma is seen. It is often precipitated by the use of systemic steroids, β-agonists or nasal decongestants. Stress also plays a significant role in the development of hypertension in these patients. It is therefore recommended that the above precipitating factors should be looked for and modified.
- Long acting calcium channel blockers such as amlodipine have been found to be relatively safe drugs in this group of patients.1
- ACEIs have not been found to increase bronchial reactivity in these patients. It is recommended that if cough develops, angiotensin II receptor blockers should be tried as alternative to ACE inhibitors.
- β-blockers and α-β blockers are not routinely recommended as they are known to exacerbate asthma. However, α-blockers can be used as add-on therapy in patients with COPD.193
- Inhaled corticosteroids and ipratropium bromide can be used safely in these patients.

Hypertension with Coronary Artery Disease

Among all the risk factors documented for pathogenesis of CAD, hypertension is reported to be the major risk factor.133 Blood pressure levels have been shown to be positively and continuously related to the risk of major CAD events.135
- Too rapid lowering of blood pressure, which can cause reflex tachycardia and sympathetic activation, should be avoided in patients with CAD.
- One may have to set the target of BP control even below 130/80 mm Hg but not lower than 120/70. The CLARIFY registry (2016) shows levels below 120 systolic and 70 diastolic were associated with adverse CV outcomes including mortality supporting the existence of a J curve phenomenon.194,195 All other risk factors should be treated appropriately.
- HT in patients with acute coronary syndrome should be treated aggressively.
- β-blockers and CCBs are the drugs of first choice in the management of angina in patients with hypertension associated with CAD.
- β-blockers have been shown to reduce the risks of re-infarction and cardiovascular death by 25% in patients with MI.196
- Amlodipine has been shown to produce subjective and objective improvement in patients with angina.197
- Treatment with amlodipine is associated with fewer hospitalisations for unstable angina and revascularisations in patients with angiographically documented CAD.198
- Verapamil and diltiazem reduce risk of developing MI following non-Q-wave myocardial infarction.199
- After MI, therapy with ACEIs prevents subsequent heart failure and reduces morbidity and mortality.200 ACEIs in combination with digoxin or low dose diuretics, are effective in reducing morbidity and mortality in patients in heart failure.201
- Statins and aspirin are recommended in patients with hypertension associated with CAD.

Hypertension with Dyslipidaemia

Dyslipidaemia often co-exists with hypertension.202
- Lifestyle modifications are of particular importance in such patients as they can lower blood pressure and improve lipid levels.
- The choice of antihypertensive agent should be made after considering the effects on the lipid profile that some of these drugs have.
- ACEIs and calcium channel blockers are lipid neutral drugs and the preferred agents in patients with hypertension in dyslipidemias.
- In high doses diuretics can induce a short-term increase in cholesterol, triglycerides and LDL cholesterol levels. Low dose thiazides do not produce this effect.
- β-blockers without intrinsic sympathomimetic activity (ISA) may increase levels of plasma triglycerides and reduce levels of HDL-cholesterol. Despite this, these have been shown to reduce rate of sudden death, overall mortality and recurrent MI in patients with previous MI.
- Patients with HT and dyslipidaemia warrant lipid lowering therapy (statins) just as for patients with CV disease and diabetes.203

Hypertension with Obesity and Metabolic Syndrome

- Prevalence of obesity and hypertension is increasing. Obesity is almost always accompanied by insulin resistance, hyperinsulinemia, impaired glucose tolerance and dyslipidemia. Truncal obesity is more common in Indian population. Also, abdominal obesity is associated with sodium retention, endothelial dysfunction, microalbuminuria, LVH and elevated markers of inflammation.
- The diagnosis of metabolic syndrome is made when 3 or more of the risk determinants are present (Table 24).
- Compared with Whites, Indian men and women have a higher prevalence of central obesity.205 Anthropometric parameters of Asians are different than those for white Caucasians and blacks. For example, Asian Indians have smaller body size, excess body
Epidemiological studies have
- Thyroid or parathyroid disease
- Obstructive sleep apnea syndrome
- Primary aldosteronism and other mineralocorticoid excess states
- Pheochromocytoma
- Obstructive uropathy
- Cocaine, amphetamines, other illicit drugs
- Inappropriate combinations
- Inadequate doses
- Excess alcohol intake
- Cyclosporine and tacrolimus
- Excess sodium intake
- Volume overload
- Excess sodium intake

- Volume retention from kidney disease
- Inadequate doses
- Nonsteroidal anti-inflammatory drugs and cyclooxygenase 2 inhibitors
- Cocaine, amphetamines, other illicit drugs
- Cyclosporine and tacrolimus
- Tobacco
- Selected over-the-counter dietary supplements and medicines (e.g. liquorice and cough syrups)
- Associated conditions
  - Obesity
  - Excess alcohol intake
- Secondary causes of hypertension
  - Chronic kidney disease
  - Coarctation of the aorta
  - Non-specific aortoarteritis
  - Cushing syndrome and other glucocorticoid excess states including chronic steroid therapy
  - Obstructive uropathy
  - Pheochromocytoma
  - Primary aldosteronism and other mineralocorticoid excess states
  - Renovascular hypertension
  - Obstructive sleep apnea syndrome
  - Thyroid or parathyroid disease

- Dyslipidemia in these patients is characterised by high TG levels and low HDL levels. Such patients require fibrates for control of dyslipidemia.
- On the basis of their favourable metabolic profiles, it would appear that ACEIs, ARBs, CCBs and α-blockers can decrease blood pressure without worsening the metabolic abnormalities that accompany hypertension in obese patients. ACE inhibitors, low-dose diuretics and non-dihydropyridine CCBs are probably the drugs of first choice in this setting. α -blockers have particular advantages in individuals with dyslipidaemia or glucose intolerance and may be considered as add-on agents. Given that control of hypertension in the majority of hypertensive patients is unlikely to be achieved with any single drug alone, the discussion on choice of drug class may be moot. 199,211

Hypertension with Obstructive Sleep Apnea (OSA)
- OSA is now considered a cause of secondary hypertension and is closely associated with obesity.
- The treatment with of OSA with continuous positive airway pressure (CPAP) has been shown to decrease daytime and nocturnal blood pressures. 210

Resistant Hypertension
- Resistant hypertension is defined as the failure to reach goal BP in patients who are adhering to full doses of an appropriate 3-drug regimen of different classes that includes a diuretic. The causes of resistant hypertension are shown in Table 25.

Clinical Approach to Resistant Hypertension
About 12.2% of hypertensive patients have Resistant Hypertension. Ambulatory blood pressure monitoring should be done in these patients in order to classify them as follows:
1. True resistant hypertensives (62.5%)
2. Pseudo or white-coat resistant hypertension (37.5%)

True resistant hypertensive patients are more commonly men, of younger age, with a longer duration of hypertension, smokers, diabetics, HMOD (including left ventricular hypertrophy, impaired renal function, and microalbuminuria) and overall a worse cardiovascular risk profile.

Therefore, it necessary to assess ambulatory blood pressure monitoring for a correct diagnosis and management of true resistant hypertension. 210

Table 25 gives causes of resistant HT2. These causes can be readily identified and treated.

Management of resistant hypertension
Most patients with resistant hypertension need to be referred to specialized hypertension clinics after evaluation of level of compliance. More aggressive salt restriction and elimination of drugs interfering with action of anti-hypertensive agents should be looked at. Subsequently, one should look for secondary hypertension and in case no secondary cause is found these patients need multiple drugs in high dosages. After starting adequate doses of ACEI/ARB + CCB + Thiazide diuretic and making sure of compliance, in case BP is not controlled add MRA (Spironolactone). Table 25 in case BP is still not controlled, an agent out of the choices given in step 5 can be added. Besides combination pharmacotherapy intervention-based treatment modalities such as Renal Sympathetic Denervation Therapy and Carotid Baroreceptor Stimulation therapy were evaluated. However, these have not been found to be of any clinical utility till now.

Renal denervation therapy for resistant hypertension was shown to be of great potential in initial unblended studies. Catheter based renal artery denervation was shown to reduce BP significantly (SIMPLICITY I and II). 213,105 However, a meticulously conducted prospective randomized sham controlled trial in 535 patients showed that there is no significant reduction of SBP in patients with resistant hypertension after renal artery denervation as compared to sham control (SIMPLICITY III). Following this study interest in renal denervation therapy has waned off although a recent study published in circulation showed some benefit with this therapy. 214,215

Table 25: Causes of resistant hypertension

<table>
<thead>
<tr>
<th>Causes of Resistant Hypertension</th>
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<tbody>
<tr>
<td>Volume overload</td>
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<tr>
<td>- Excess sodium intake</td>
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<tr>
<td>- Volume retention from kidney</td>
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<tr>
<td>Drug</td>
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<tr>
<td>- Inadequate doses</td>
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<tr>
<td>- Inappropriate combinations</td>
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<tr>
<td>- Nonsteroidal anti-inflammatory</td>
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<tr>
<td>drugs and cyclooxygenase 2</td>
</tr>
<tr>
<td>inhibitors</td>
</tr>
<tr>
<td>- Cocaine, amphetamines, other</td>
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<tr>
<td>illicit drugs</td>
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<tr>
<td>- Cyclosporine and tacrolimus</td>
</tr>
<tr>
<td>- Tobacco</td>
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<tr>
<td>- Selected over-the-counter</td>
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<tr>
<td>dietary supplements and medicines</td>
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<tr>
<td>(e.g. liquorice and cough syrups)</td>
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<tr>
<td>Associated conditions</td>
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<tr>
<td>- Obesity</td>
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<tr>
<td>- Excess alcohol intake</td>
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<tr>
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<td>glucocorticoid excess states</td>
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<td>- Obstructive uropathy</td>
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<td>- Pheochromocytoma</td>
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<td>- Primary aldosteronism and other</td>
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<tr>
<td>mineralocorticoid excess states</td>
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<td>- Renovascular hypertension</td>
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<tr>
<td>- Obstructive sleep apnea syndrome</td>
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<tr>
<td>- Thyroid or parathyroid disease</td>
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</tbody>
</table>

Fat, and truncal and abdominal adiposity than white Caucasians. 206 In Asians, the BMI cut-offs for overweight (>23.0 kg/m2) and obesity (>25.0 kg/m2) are lower than WHO criteria. These provisional recommendations will need to be revised in the light of further validation of studies and clinical experience. 154,207

Epidemiological studies have consistently shown a tight correlation between body weight and blood pressure, with 70% of hypertension in men and 60% in women being directly attributable to excess adiposity. 208 Essential hypertension is very frequently associated with a decrease in insulin sensitivity. This insulin resistance is very often associated with dyslipidaemia, obesity, hypertension and impaired glucose tolerance, a cluster termed the “metabolic syndrome or the insulin resistance syndrome. 209

Lifestyle modification (diet, exercise) is the cornerstone in management of hypertension in obese individuals.
Abbreviations

ABPM – Ambulatory Blood Pressure Monitoring
ACC – Associated Clinical Conditions
ACC/AHA – American College of Cardiology / American Heart Association
ACCOMPLISH – Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension
ACCORD – Action to Control Cardiovascular Risk in Diabetes
ACEI – Angiotensin Converting Enzyme Inhibitors
ACR – Albumin Creatinine Ratio
ADVANCE – Action in Diabetes and Vascular Disease Perterax and Diamicon MR Controlled Evaluation
AHT – Antihypertensives
AIPRI - ACEI and progressive Renal Insufficiency
ALLHAT – Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial
API - Association of Physicians of India
ARB – Angiotensin II Receptor Blockers
ARRIVE - A Randomized Trial of Induction Versus Expectant Management
ASCEND - A Study of Cardiovascular Events in Diabetes
ASPREE - Aspirin in Reducing Events in the Elderly
ASCOT – Anglo – Scandinavian Cardiac Outcomes Trial
ASCOT-BPLA – Anglo – Scandinavian Cardiac Outcomes Trial – Blood Pressure Lowering Arm
ASIAN-HF - Asian Sudden Cardiac Death in Heart Failure
ATACH II - Antihypertensive Treatment of Acute Cerebral Hemorrhage-II
BHS – British Hypertension Society
BMI – Body Mass Index
BP – Blood Pressure
BPH – Benign Prostatic Hypertrophy
CAD – Coronary artery disease
CCB – Calcium Channel Blockers
CDUS – Colour Doppler Ultrasound
CKD – Chronic Kidney Disease
COPD – Chronic Obstructive Pulmonary Disease
COX-2 – Cyclo-oxygenase – 2
CLARIFY - Prospective observational LongitudinAI Registry of patients with stable coronary artery disease
CMNNDs - Communicable, Maternal, Neonatal and Nutritional Diseases
CPAP – Continuous Positive Airway Pressure
CSI - Cardiological Society of India
CV – Cardio-vascular
CVA – Cerebro-vascular Accident
CVD – Cardio-vascular Disease
DASH – Dietary Approaches to Stop Hypertension
DALYs - Disability Adjusted Life Years
DBP – Diastolic Blood Pressure
DLHIS - District Level Household Survey
DM – Diabetes Mellitus
DSA – Digital Subtraction Angiography
DTPA – Di-ethylene-triamine-penta-acetate
ECG – Electro-cardiogram
ESC – European Society of Cardiology
ESH – European Society of Hypertension
ESRD – End Stage Renal Disease
ETL- Epidemiological Transition Level
GBD- Global Burden of Diseases
GFR – Glomerular Filtration Rate
HBP – Home Blood Pressure Monitoring
HCWH – Health Care Without Harm
HDI -Human Development Index
HDLC – High Density Lipoprotein
HF – Heart Failure
HFpEF – Heart Failure with normal Ejection Fraction
HIC - High-Income Countries
HOPE – Heart Outcomes Prevention Evaluation
HOT – Hypertension Optimal Treatment Study
HSI- Hypertension Society of India
HMOD - Hypertension Mediated Organ Damage
hs CRP – Highly sensitive C Reactive Protein
HT – Hypertension
HYVET – Hypertension in Very Elderly Trial
IAD - Indian Academy of Diabetes
ICP - Indian College of Physicians
IGH – Indian Guidelines on Hypertension
INR - International Normalised Ratio
INTERACT 2 - The Second Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial
INVEST – International Verapamil SR/Trandolapril Study
ISH – Isolated Systolic Hypertension
JNC – Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure
JVP - Jugular venous pressure
KDIGO – Kidney Disease: Improving Global Outcomes
LDL – Low Density Lipoprotein
LIFE – Losartan Intervention for Endpoint Reduction in Hypertension
LMIC- Lower Middle Income Countries
LSM - lifestyle modification
LV – Left Ventricle
LVH – Left Ventricular Hypertrophy
MBP – Mean Blood Pressure
MDRD – Modification of Dietary Protein in Renal Disease
MI – Myocardial Infarction
MIBG – Meta-iodo-benzyl-guanidine
MRI – Magnetic Resonance Imaging
NCD – Non communicable diseases
NFHS - National Family Health Survey
NICE – National Institute for Health and Clinical Excellence
NSAIDS – Non Steroidal Anti Inflammatory Drugs
OBP - Office Blood Pressure
OH – Orthostatic Hypotension
ONTARGET – Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial
OSA – Obstructive Sleep Apnea
PATHWAY – Prevention and Treatment of Resistant Hypertension With Algorithm Guided Therapy
PET – Positron Emission Tomography
PIH – Pregnancy Induced Hypertension
PP – Pulse Pressure
PRA – Plasma Renin Activity
PROGRESS – Perindopril Protection against Recurrent Stroke Study
PURE Study – Prospective Urban Rural Epidemiology Study
PWV – Pulse Wave Velocity
RAAS – Renin Angiotensin Aldosterone System
REIN – Ramipril Efficacy in Nephropathy
RBCs – Red Blood Cells
RF – Risk Factors
RH – Resistant Hypertension
RSSDI – Research Society for Study of Diabetes in India
RVH – Renovascular Hypertension
SBP – Systolic Blood Pressure
SCORE – Systemic Coronary Risk Evaluation System
SPRINT – Systolic Blood Pressure Intervention Trial
SHEP – Systolic Hypertension in Elderly Program
SHIFT – Systolic Heart Failure treatment with the I, inhibitor ivabradine Trial
TG – Triglycerides
TIA – Transient Ischemic Attack
TOD – Target Organ Damage
TONÉ – Trial of Non-Pharmacological interventions in the Elderly
UI – Urbanization Index
UKPDS – United Kingdom Prospective Diabetes Study
VALUE – Valsartan Antihypertensive Long-term Use Evaluation
VMA – Vanillyl-Mandelic Acid


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