CCDSI

Clinical Cardio & Diabetic Society of India

CCDSICON B & J 2024

Theme : "OPTIMISING CARDIO METABOLIC HEALTH FOR ALL"

8th Annual Conference of CCDSI

Date : 21st, 22nd & 23rd June 2024

E-'BULLETIN' ON HYPERTENTION

Dr. A K Virmani
Chief Advisor

Dr. Satish Prasad
Chief Editor

CCDSI
Clinical Cardio Diabetic Society of India

CCDSICON (B&J)-2024

8th Annual Conference of Clinical Cardio & Diabetic Society of India
(Bihar & Jharkhand)

Theme : "OPTIMISING CARDIO METABOLIC HEALTH FOR ALL"

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THE INSIDE VIEW

I Professor Dr Abhay Narain Rai, Founder President CCDSI would like to congratulate Dr Satish Prasad, Editor of e-Bulletin on Hypertension for his devotion, dedication and hard work in publishing the e-Bulletin in such a short time It will be released 21st June 2024, during the Inaugural function of CCDSICON B&J 24 at Jamshedpur.

I am sure e-Bulletin on Hypertension will not only update and enlightened us but change our vision in management of Hypertension.

I would also like to thank Dr A K Virmani Dean Elect and Immediate Past President CCDSI for taking initiative and keen Interest in publication of e-Bulletin on Hypertension.

Dr Abhay Narain Rai
Founder President
CCDSI

To
The Editor
Dr Satish Prasad Ji

It gives me immense pleasure to write a message for this e-bulletin on hypertension. We know that the medical science is the ever changing science. So it is our duty to incorporate newly learnt lessons in standardized form for our practicing physicians. CCDSI is doing this for years now. And I hope this e-bulletin on hypertension will also be very informative for our members.

I congratulate the editorial team for their great efforts.

With warm regards
Dr Mritunjay Kumar Singh
Secretary
CCDSI

From the Desk of Advisor - "E-Bulliten" on Hypertension

From the desk of Dean Elect,

Indian College of Cardiology and Metabolic Diseases,

Immediate Past President, CCDSI

Dear

Dr. Satish Prasad, EDITOR, E-Bulletin on Hypertension.Im very pleased to know that you will be releasing the e-bulletin dedicated to the topic of hypertension during the CCDSI B&J, State Annual Conference from 21st to 23rd June, 2024, at Jamshedpur. I also congratulate you that you've taken up this responsibility on my request and you've shown total dedication and commitment in advancing our understanding and management of this pervasive and often silent condition, which affects millions globally.Hypertension, or high blood pressure, remains one of the most significant risk factors for cardiovascular disease, stroke, and kidney failure. Despite advances in medical science and technology, the prevalence of hypertension continues to rise, necessitating ongoing education, research, and innovation in both prevention and treatment strategies.This issue brings together a collection of articles that address various aspects of hypertension, from the latest clinical guidelines and treatment modalities to the role of lifestyle modifications in managing blood pressure. We have also included insights into the genetic and environmental factors contributing to hypertension, as well as emerging therapies and their potential impact on patient outcomes.Our contributors are esteemed experts in the field, and their work underscores the complexity of hypertension management and the necessity for a multidisciplinary approach. I am confident that their research and perspectives will provide valuable knowledge and inspire further discussion and investigation among our readership.I extend my heartfelt gratitude to our authors, reviewers, and editorial team for their dedication and hard work in bringing this issue to fruition. It is through their collective efforts that we continue to push the boundaries of what we know and improve the lives of those affected by hypertension. Thank you for your continued support and engagement with our e-bulletin. Together, we can make strides in combating hypertension and enhancing cardiovascular health worldwide.Sincerely,

Dr. Anil Kumar Virmani

MD, DRM, FICP, FIACM, FACP,
FRSSDI, FICCMD, FDI, FISH, CCIO,

From the Desk of Editor - "E-Bulliten" on Hypertension

It gives me immense pleasure and also a sense of responsibility to edit this e Bulletin on Hypertension. This is the brainchild of Dr A.N. Rai,the founder President of CCDSI.I convey my heartfelt gratitude to Dr. A. K. Virmani for motivating me for this job and a constantly guiding .Since the dawn of 20th century Hypertension has been recognized as an important cardiovascular disorder. Hypertension had spread even to the developing countries like pandemic. Despite all research guidelines and technologies the feedback from the real world is not encouraging as very few patients are reaching the target blood pressure .The WHO theme for 2024: "Measure your BP accurately, control it and live longer" is very relevant in practical sense.This book covers almost all the important topics related to Hypertension covering all age groups and different situations and complications of hypertension which clinicians come across. All articles are authored by experts keeping the Indian perspective in the background. Artificial intelligence and it's role in managing Hypertension, BP variability, role if obesity & exercise in Hypertension are highlighted. We hope this effort will be helpful to address a spectrum of questions related to Hypertension. I would like to thank my family and my wife Padma, especially for the cooperation. A special thanks to all the esteemed authors for their excellent articles, an outcome of their devotion and commitment .Our efforts will be only successful if you read it and give your feedback for improvement in future.

Thanks and regards,
Dr Satish Kumar Prasad,
MD (Med),
DCHEx. Head (medicine unit),TMH.
Org.Sec, CCDSI(B/J)2024.

From the Desk of Chairperson - "E-Bulliten" on Hypertension

I am extremely happy and exited for the release of "E-Bulletin" on Hypertension.

Hypertension is a threat to the whole society of minkind. This bulletin will help us is updating our knowledge and its application to the society.

My heartfelt congratulation to Dr. A. K. Virmani, Chief Advisor, Dr. Satish Prasad, Chief Editor for their sincerity and passion in publishing the bulletin.

I also congratulate Dr. A. K. Paul for the editing the bulletin in a nice way.

With my Best Wishes

Dr. Umesh Khan
Chairman CCDSICON-2024

From the Desk of Editing - "E-Bulliten" on Hypertension

I am privileged and honourd in Editing this bulletin.

Hope this editing with cherish us.

My heartfelt thanks & congratulation to Dr. A. K. Virmani, Chief Advisor, Dr. Satish Prasad Chief Editor, our chairman Dr. Umesh Khan & the organising committee for the passion and attitude in every field.

My regards and best wishes for grand success.

Dr. A. K. Paul
Chief Co-ordinator
& Press Media Souvenir

BEST HYPERTENSION GUIDELINES IN INDIA

By - Dr. Umesh Khan
MD (MED), FICCMD , CHAIRMEN, CCDSI (BIHAR & JHARKHAND)

The guidelines for hypertension provides a framework for diagnosing , evaluating and treating high blood pressure to reduce the risk of cardiovascular events such as heart attack & strokes.

Guidelines from American college for cardiology (**AIC)** & the American heart association (**AHA**) are globally follows, However in India , the management of hypertension is guided by protocols established by the **Indian council of medical research & hypertension society of India.**

These guidelines are designed to address the specific healthcare needs & challenges in India, taking into account local epidemiology , resources & healthcare practices.

Key guidelines for hypertension Management in INDIA -

A) ICMR Guideline Blood pressure classifications :

a) Normal
systolic <120 ml of Hg
diastolic < 80 ml of Hg

b) Prehypertension
systolic- 120-139 ml of Hg
diastolic - 80-89 ml of Hg

c) Stage 1 Hypertension
systolic - 140-159 ml of Hg
diastolic - 90- 99 ml of Hg

d) Stage 2 Hypertension
systolic >160 ml of Hg
diastolic > 100 ml of Hg

Diagnosis

- Multiple blood pressure recording on different occasions.
- Use of validated devices and proper measurement techniques.

Management : Lifestyle modifications

- Diet - emphasise a low sodium diet , rich in fruits , vegetables and low fat diary (similar to capital dash diet)
- Physical activity at least 30-45 minutes of moderate intensity exercise most days in a week.
- Weight management : Aim for a healthy BMI (18.5 to 24.9)

- Alcohol : Limit consumption
- Smoking : advise cessation

Pharmacological treatment

- Initiate treatment for stage 1 hypertension with additional consideration of cardiovascular risk factors or target organ damage.
- Start treatment for stage 2 hypertension regardless of other risk factors.
- Common first line medication include thiazide diuretics , AVE inhibitor , ARB , Calcium channel blockers and beta blockers

FOLLOW UP & MONITORING

- Regular follow up to monitor blood pressure and treatment adherence
- Encourage home monitoring of blood pressure
- Special consideration for populations with diabetes, chronic kidney disease and pregnant women.

HYPERTENSION SOCIETY OF INDIA GUIDELINES : these are aligned with ICMR recommendation but may provide additional practical tips and special considerations. Emphasise public health measures such as screening programmes and community awareness to improve hypertension control at a population level.

CONCLUSIONS : ICMR guidelines , complemented by the **HSI guidelines** , offer the most comprehensive and contextually appropriate framework for managing hypertension in India.
Both **ICMR & HSI** Guidelines are considered highly reliable and relevant for Indian populations. They provide evidence based recommendations tailored to specific healthcare challenges in India.

Hypertension and Exercise

Dr Mayura Kale (Mumbai), Dr Suresh Purohit (Mumbai), Dr Vinay Dhandania (Ranchi)

Hypertension, defined as systolic blood pressure (SBP) of 140 mm Hg or greater or diastolic blood pressure (DBP) of 90 mm Hg or greater, affects 32.6% women and 38.7% men over the age of 20 years in India. It is anticipated that it will affect up to one-third of the adult population worldwide by 2025. Hypertension is the leading cause of mortality, accounting for 13.5% of all deaths.

Hypertension is an important risk factor for end-stage renal disease, coronary artery disease, congestive heart failure, and stroke. Despite pharmacologic advances, there is often inadequate BP control in many individuals.

There is an increased interest in lifestyle interventions, including exercise for the treatment and prevention of hypertension. Unfortunately, exercise prescription is underused by clinicians, due uncertainty of its effectiveness and ambiguity about exercise prescription determinants (duration, intensity, and frequency)

The World Health Organization and International Society of Hypertension, the Indian Society of Hypertension advocate increased physical activity as a first-line intervention for preventing and treating patients with prehypertension and as a adjuvant treatment strategy for patients with stage 1 or stage 2 hypertension. Consequently, prehypertension can be prevented from progressing and medications prescribed to treat stage 1 hypertension can be reduced.

Physical activity refers to any bodily movement involving skeletal muscles and energy expenditure. Exercise is a subset of physical activity that is “planned, structured, and repetitive and has as a final or an intermediate objective of improvement or maintenance of physical fitness”. Cardiorespiratory fitness is another term for aerobic fitness and is most commonly measured by V02 max (the maximum volume of oxygen that can be used).

There is a pandemic of physical inactivity. There is strong evidence for the association between physical inactivity and mortality, risk of cancer, depression, dementia and other chronic illnesses. The WHO guidelines state that a minimum of 150 minutes of moderate intensity physical activity or 75 minutes vigorous intensity physical activity per week are required for health. They emphasise a reduction in sitting time and replacing this with any physical activity. Significantly, strength training on at least two days per week is also recommended for all adults. The 2018 European Society of Hypertension guidelines recommend 30 minutes of moderate intensity physical activity on five to seven days per week in addition to resistance training on two to three days per week.

1. Exercise and BP lowering

1.1 Acute physiologic response to exercise

Aerobic exercise increases cardiac output (CO) and redistributes it to maintain perfusion of active muscles. Increased CO leads to raised systolic BP (SBP), while decreased peripheral vascular resistance (PVR) causes fall in diastolic BP (DBP). This facilitates perfusion of large muscle groups. A rise in SBP of more than 7to 10 mm Hg for every 1 metabolic equivalent task unit (MET), or failure of DBP to drop more than 15 mm Hg during aerobic exercise, is a strong predictor of developing hypertension. These patients are prone for fatal cardiovascular events.

In resistance exercise both SBP and DBP increase as a result of rise in arterial pressure to overcome the resistance to muscle perfusion caused by elevated intramuscular pressure and due to the pressor reflex. Improperly performed resistance exercise can cause in appropriate rise in SBP and DBP.

1.2 Postexercise physiologic response:

There is a hypotensive response lasting up to 22 hours after exercise and is cause d by reduced norepinephrine levels and thus by inhibition of sympathetic activity and reduction in circulating angiotensin II, adenosine, and endothelin levels. These changes lead to decreased PVR and increased baroreflex sensitivity .Hypotension is also caused by the vasodilator effect of prostaglandins and nitric oxide. Duration and type of exercise, age, ethnicity, and the individual's clinical status and physical fitness influence the hypotensive response.

1.3 Chronic physiologic response to exercise:

Physical activity has pleotropic benefits. The vascular changes include increased vascular length, increased lumen diameter, increased number of precapillary sphincters, and neoangiogenesis. Physical activity reduces C-reactive protein and inflammatory cytokines levels. Exercise mediated enhanced baroreceptor sensitivity, decreased norepinephrine level, reduced PVR, improved insulin sensitivity exert antihypertensive effect. Aerobic exercise decreases left ventricular mass and wall thickness, upregulates central antioxidant concentrations, reduces arterial stiffness, improves endothelial function. Exercise can lower BP in the long term and enhance the action of antihypertensive drugs.

2. Aerobic exercise (AE)

Examples of AE include speed walking, jogging, running, dancing, cycling, and swimming. AE consists of regular, purposeful movement of joints and large muscle groups. Regular AE has been shown to reduce resting BP and BP reactivity to stressors. High intensity interval training (HIIT) is shown to be more effective in BP reduction than moderate intensity continuous training (MICT) in younger individuals while both were equally effective in older individuals, though MICT is clearly preferable in older individuals for safety purpose.

3. Resistance exercise

In dynamic resistance (DR) training, effort is performed against an opposing force accompanied by purposeful movement of joints and large muscle groups with a goal of progressively increasing muscle strength. It involves concentric or eccentric contraction of muscles. Examples of DR exercise are weight lifting, training with resistance-training machines, squats, push-ups etc. Isometric resistance (IsR) exercise involves sustained static contraction of muscles with no change in the length of the involved muscle groups and without joint movement exa. Isometric hand grip, seated position against a wall.

Overall, evidence suggests that DR exercises can lower BP by a modest degree, especially in stage 1 hypertension, with no evidence of harm. Patients with stage 2 hypertension should be treated pharmacologically before beginning training.

There is a clear but small cardiovascular benefit of IsR training including modest improvements in BP. However, the cardiovascular health risks associated with the transient elevation in BP that occurs during muscle contractions need to be more clearly established. IsR exercises have not been studied in very high-risk or unstable cardiovascular patients or individuals with more severe stages of hypertension.

If the resistance training program increases the DBP more than 20 mm Hg over baseline or the DBP rises above120 mm Hg, the program should be reviewed.

4. Concurrent resistance (CR) training

CR is a combination of aerobic and DR training. A meta-analysis of 68 trials reported that CR training is as useful as aerobic exercise for the for reducing BP in people with hypertension

5. Yoga and Mindfulness

Yoga is known to help reduce stress and likely to reduce blood pressure. It results in decreased sympathetic nervous system activity and simultaneously increases the parasympathetic activity. Yoga includes physical postures (asana), controlled breathing (pranayama), and meditation (dhyana) can be recommended as a relevant lifestyle modification. Although there is limited evidence on the direct impact of mindfulness on hypertension control, Indian Society of Hypertension recommends these practices to patients to ensure a comprehensive lifestyl e modification strategy.

Cornelissen and Smart carried out a meta-analysis to include dynamic aerobic endurance , dynamic and isometric resistance, and combined resistance-endurance training .It involved 93 trials (105 endurance/AE, 29 DR, 14 combined, and 5 IsR groups), with 5223 participants (3401 exercise and 1822 control). SBP was reduced after endurance (–3.5 mmHg; 95% CI –4.6 to –2.3), DR (–1.8 mmHg; 95% CI –3.7 to –0.011), and IsR (–10.9 mmHg; 95% CI –14.5 to – 7.4) but not after combined training. Reductions in DBP were seen in all four modalities examined. IsR training was the most effective modality reported. This review showed that AE has the strongest research base, with 105 endurance groups included, and aerobic exercise will reduce BP among normotensive, high normal and hypertensive groups; greatest BP reductions are among individuals with hypertension

6. Choosing the appropriate type of exercise

Meta analysis by Cornelissen and Smart and American College of Sports Medicine review concluded the following:

Endurance training, DR training, IsR training, and combined training significantly reduce SBP and DBP.

AE might be superior to DR training in men with hypertension only.

AE results in an average reduction of 5to 7 mm Hg in both SBP and DBP for up to 22 hours regardless of the exercise intensity.

AE results in an average chronic reduction in BP of 7.4/5.8 mm Hg for patients with hypertension that does not respond to drugs and of 2.6/1.8 mm Hg for patients with normalized BP irrespective of drug type.

Larger BP reductions were seen after moderate- to high-intensity AE for less than 210 minutes per week versus 210 minutes per week or longer.

Longer unsupervised exercise programs lead to decreased adherence and therefore less reduction in BP.

AE, DR training, and combined training are equivalent in lowering BP in normotensive and prehypertensive persons.

Resistance training has a favourable but less meaningful chronic effect on BP than aerobic exercise does.

7. Exercise prescription.

Exercise prescription in patients with hypertension should be individualized. The prescription should include frequency, intensity, time, and type (Table 1). As part of the initial treatment, AE is recommended in patients with stage 1 hypertension with no evidence of cardiovascular disease (CVD) or other complications. . In patients with diabetes, CVD, or stage 2 or 3 hypertension, or other risk factors (advanced microvascular/macrovascular complications of diabetes) drug therapy should be initiated before starting an exercise program.

Table 1.Exercise prescriptionFrequency3 to 5 days per weekIntensityModerate, VO2max should be 40% to 70%, equivalent to 3 to 6 METs Time Atleast 30 minutes of continuous or accumulated (eg, 3 intervals of 10 minutes) exercise/ day Type Aerobic exercise supplemented by resistance training and Yoga and pranayam

Pre-participation screening depends on the intensity of the planned exercise and the patient's global cardiovascular risk.

(Table 2)

Table 2 Pre-participation screening Planning a vigorous exercise program (≥60% VO2max or ≥6 METs) in pts with stage 1 hypertension Patients with cardiovascular risk factors or stage 2 hypertension planning for moderate intensity exercise (40% to 60% VO2max or3 to 6 METs)All patients with documented CVD, whatever the level of exercise intensity

Table 3. Absolute Contraindications to exercise.

Recent myocardial infarction or electrocardiography changesComplete heart blockAcute congestive heart failureUnstable anginaUncontrolled severe hypertension (BP ≥180/110 mm Hg)Other systemic/local contraindications

8. Conclusion

Substantial evidence emphasizes the role of moderate-intensity AE in preventing hypertension and managing stage 1 hypertension. There is sufficient evidence that DR training, if done properly, contributes to lowering both SBP and DBP. Pre-participation examination is always preferred in patients with hypertension especially in patients with stage 2 hypertension, and those with CVD or diabetes and its complications. Individual preferences and long term adherence should be considered at the time of prescribing exercise.

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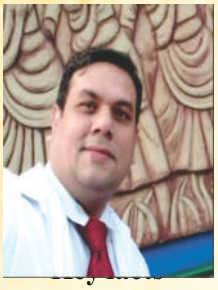

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"Measure Your Blood Pressure Accurately, Control It, Live Longer!".

- **An estimated 1.28 billion adults aged 30–79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries.**
- **An estimated 46% of adults with hypertension are unaware that they have the condition.**
- **Less than half of adults (42%) with hypertension are diagnosed and treated.**
- **Approximately 1 in 5 adults (21%) with hypertension have it under control.**
- Hypertension is a major cause of premature death worldwide.
- **One of the global targets for noncommunicable diseases is to reduce the prevalence of hypertension by 33% between 2010 and 2030.**

Today every 3rd person in urban area suffers from hypertension. Literatures suggest that interventions targeted to reduce the blood pressure below the level of 140/90 mm of Hg reduce such risk substantially [1]. In recent years, there has been a sharp rise in the magnitude of the problem of hypertension across the world. Globally 7.5 million deaths are attributable to hypertension which constitutes about 12.8 % of all deaths, which in turn accounts for more than fifty million disability adjusted life years (DALYS) or 3.7% of total DALYS [1]. Regarding the burden of the disease, the overall prevalence among adults aged 25 years or above was around 40% globally, while in India it was more than one fifth of the total population of that age group [2].

It has been estimated that a rise in systolic BP by only 5 mm of Hg would result in approximately 25% increase in the chances of fatal stroke and fatal myocardial infarction [3].

Accurate measurement of BP is essential both to estimating CVD risk and to guiding management of high BP. Avoiding common errors can lead to correct diagnoses and speed time to treatment, improving BP control rates.

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
Stage 1 Hypertension	130-139 mm Hg	or	80-89 mm Hg
Stage 2 Hypertension	≥140 mm Hg	or	≥90 mm Hg

To Eliminate Inaccurate Readings, Position Your Patient Properly

Common positioning problems can lead to inaccurate BP measurement can have a serious impact on the numbers you use to diagnose and determine treatment. These evidence-based tips can help ensure correct positioning in the clinical setting:

Use Proper Technique

- Use a validated, calibrated measurement device.
- Be sure the patient's arm is supported on a surface at the correct height.
- Place the middle of the cuff on the patient's upper arm.
- Use the correct cuff size. The recommended "ideal cuff" should have a bladder length that is 80% and a width that is at least 40% of the arm circumference, i.e., "Length to Width" ratio of at least 2:1. [4-6]
- Use either the stethoscope diaphragm or bell for auscultatory reading.

Measurement of B.P.

• Patient seated quietly for at least 5minutes in a chair, with feet on the floor and arm supported at heart level.

• The use of an automated device is preferred as these can effectively eliminate variances created with a human observer.[7]

• At the first visit, take readings from both arms. Take subsequent readings from the arm that gave the higher reading.

• Separate repeated measurements by 1–2 minutes

• If you use the auscultation method, prefer a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20–30 mm Hg above this level to determine BP.

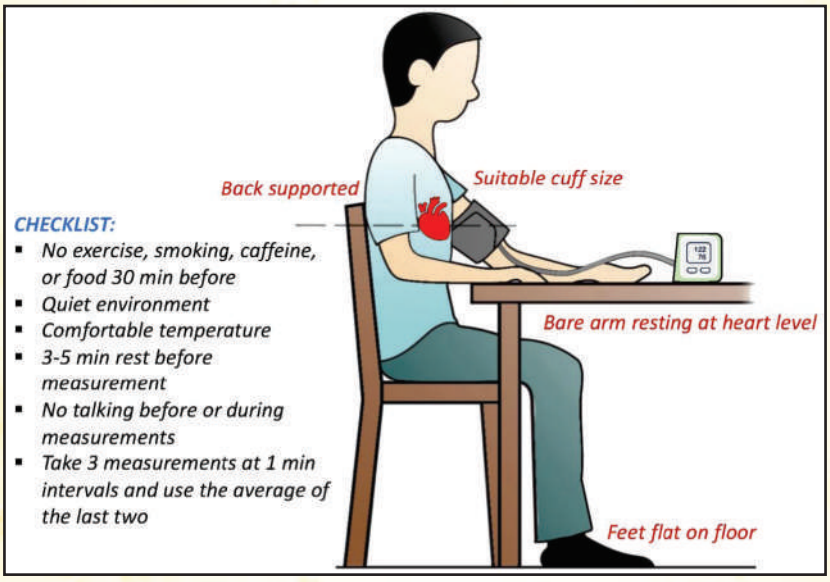
• If you use the auscultation method, deflate the cuff pressure 2 mm Hg per/second, and listen for Korotkoff sounds.

• Record both SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number.

• Use an average based on ≥2 readings obtained on ≥2 occasions to estimate your patient's BP.

Do's

- Void bladder before measurement.
- Sit with your back straight and supported.
- Keep feet flat on the floor and legs uncrossed.
- Take5 min rest before measurement.
- Keep electronic devices away.
- Support arm on a flat surface, at the level of the heart.
- Measure 3 times with at least 1 min difference between measurements and calculate the average of the 3 readings.



Don'ts

• Do not take tea, coffee, or caffeinated drinks within 30 min of measurement of BP.

• Do not exercise within 30 min.

• Do not smoke within 30 min.

• Do not wear tight clothes.

- Don't talk or move during the measurement.
- Don't measure over the clothes.

Approximate error in BP readings due errors of position or method of measurement:

To conclude we must remember that Hypertension is a major cause of morbidity and mortality and needs to be treated. It is an extremely common condition; however, it is still under-diagnosed and undertreated. Accurate measurement of BP is of prime importance in management and reduction of morbidity and mortality. Hypertension is easy to diagnose and easy to treat. Aim of the management is to save the target organ from the deleterious effect. Lifestyle modification should always be encouraged in all Hypertensive patients.

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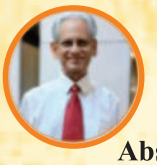

Evolving Hypertension Landscape in India: Latest Updates and Management Approaches

Dr N K Das, MD, DM (cardiology), Jamshedpur, India

Abstract

Introduction: Hypertension, a leading cause of cardiovascular diseases, stroke, and kidney disease, is a growing public health concern in India. This study explores the evolving landscape of hypertension in India, examining recent epidemiological trends, risk factors, and management strategies.

Materials and Methods: A comprehensive literature review was conducted using peer-reviewed journals, government reports, and global health databases. Key terms such as "hypertension in India," "epidemiology," "management," and "public health" guided the search. Relevant studies were analyzed to extract data on prevalence, risk factors, research updates, and management approaches.

Results: The prevalence of hypertension in India has reached approximately 30% of adults, with higher rates in urban areas due to lifestyle factors like high salt intake, physical inactivity, and stress. Gender and age differences show higher prevalence in older adults and a slightly higher rate in men. Recent research, including the India Hypertension Control Initiative (IHCI), provides insights into hypertension awareness, treatment, and control. Innovations in diagnostic tools, such as mHealth technologies and telemedicine, enhance early detection and management. Effective management includes lifestyle modifications and pharmacological treatments using diuretics, ACE inhibitors, ARBs, calcium channel blockers, and beta-blockers.

Conclusion: Despite advancements, challenges remain in awareness, diagnosis, treatment adherence, and healthcare infrastructure, particularly in rural areas. Enhanced screening programs, strengthened primary healthcare, increased public awareness, and continued research are essential. Comprehensive and integrated approaches are crucial to reducing the hypertension burden in India and improving public health outcomes.

Introduction :

Hypertension, or high blood pressure, is a significant public health issue worldwide, with a particularly profound impact in developing countries like India. Characterized by persistently elevated blood pressure, hypertension is a major risk factor for cardiovascular diseases, stroke, and kidney disease. In India, the prevalence of hypertension has been steadily increasing, driven by a combination of urbanization, lifestyle changes, and genetic predisposition. This study explores the current landscape of hypertension in India, recent updates in its epidemiology, and the strategies employed in its management.

Materials and Methods :

This manuscript is a comprehensive review of current literature on hypertension in India. Data sources include peer-reviewed journals, government health reports, and global health databases. Key terms such as "hypertension in India," "epidemiology," "management," and "public health" were used in the literature search. The selected studies were analyzed to extract relevant information on prevalence, risk factors, recent research updates, and management approaches.

Results :

Epidemiology of Hypertension in India

Prevalence and Demographics

The prevalence of hypertension in India has been rising over the past few decades. According to a study published in The Lancet Global Health, approximately 30% of adults in India have hypertension, with a higher prevalence observed in urban areas compared to rural regions (1). This urban-rural divide can be attributed to lifestyle factors such as higher salt intake, obesity, stress, and physical inactivity prevalent in urban settings.

Age and Gender Differences :

Hypertension prevalence increases with age, and older adults are more likely to be diagnosed with the condition. A study in the Journal of Human Hypertension indicated that men have a slightly higher prevalence of hypertension compared to women, although this gap narrows post-menopause due to hormonal changes in women (2).

Risk Factors for Hypertension in India

Lifestyle Factors

Several lifestyle factors contribute to the high prevalence of hypertension in India. These include:

Diet : High salt intake, low consumption of fruits and vegetables, and high-fat diets are common dietary patterns that increase the risk of hypertension (3).

Physical Inactivity: Sedentary lifestyles, particularly in urban areas, contribute to weight gain and elevated blood pressure.
Alcohol and Tobacco Use: Excessive alcohol consumption and tobacco use are significant risk factors for hypertension (4).
Socioeconomic Factors
Socioeconomic status plays a crucial role in the prevalence of hypertension. Lower socioeconomic groups often have limited access to healthcare, unhealthy living conditions, and higher levels of stress, all of which contribute to higher hypertension rates.
Genetic Predisposition
Genetic factors also play a role in hypertension. Studies have shown that individuals with a family history of hypertension are at a higher risk of developing the condition (5).
Recent Updates in Hypertension Research in India
Advances in Epidemiological Research
Recent research hascx focused on understanding the epidemiology of hypertension in India more comprehensively. Large-scale surveys like the India Hypertension Control Initiative (IHCI) have provided valuable data on the prevalence, awareness, treatment, and control of hypertension across different states (6).
Innovative Diagnostic Tools
Advancements in diagnostic tools have improved hypertension detection. Automated blood pressure measuring devices, mobile health (mHealth) technologies, and telemedicine are
becoming increasingly popular, facilitating early diagnosis and monitoring, especially in remote areas (7).
Management of Hypertension in India
Lifestyle Modifications
The cornerstone of hypertension management involves lifestyle modifications. Key recommendations include:
Dietary Changes: Reducing salt intake, adopting the DASH (Dietary Approaches to Stop Hypertension) diet, and increasing the intake of fruits, vegetables, and whole grains.
Physical Activity: Encouraging regular physical activity, such as brisk walking, cycling, and swimming.
Weight Management: Promoting weight loss and maintaining a healthy weight.
Reducing Alcohol and Tobacco Use: Encouraging the reduction or cessation of alcohol and tobacco use (8).
Pharmacological Treatment
Pharmacological treatment is essential for patients with moderate to severe hypertension or those who do not respond adequately to lifestyle changes alone. Common classes of antihypertensive drugs used in India include:
Diuretics: Help reduce blood pressure by eliminating excess sodium and water from the body.
ACE Inhibitors and ARBs: Prevent the narrowing of blood vessels, thereby lowering blood pressure.
Calcium Channel Blockers: Relax blood vessels and reduce heart rate.
Beta-Blockers: Reduce heart rate and the force of the heart's contractions (9).
Integrated Care Models
Integrated care models that combine lifestyle interventions, pharmacological treatment, and regular monitoring have proven effective in managing hypertension. The IHCI, for example, emphasizes a collaborative approach involving healthcare providers, patients, and community health workers to ensure comprehensive care (10).
Public Health Initiatives
Several public health initiatives have been launched to address the growing burden of hypertension in India. These include:
National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS): Aims to reduce the burden of non-communicable diseases, including hypertension, through early detection, diagnosis, and treatment.
Ayushman Bharat: A government scheme that provides comprehensive healthcare coverage, including hypertension management, to economically vulnerable populations (11).

Challenges in Hypertension Management

Awareness and Diagnosis

One of the significant challenges in managing hypertension in India is the low level of awareness and diagnosis. Many individuals with hypertension are unaware of their condition, often due to the lack of regular health check-ups and screening programs (12).

Treatment Adherence

Adherence to hypertension treatment is another major challenge. Factors contributing to poor adherence include the cost of medications, side effects, lack of awareness about the importance of consistent medication use, and cultural beliefs (13).

Healthcare Infrastructure

India's healthcare infrastructure, particularly in rural areas, faces significant challenges. Limited access to healthcare facilities, shortage of trained healthcare professionals, and
inadequate availability of essential medications hinder effective hypertension management (14).

Future Directions

Enhanced Screening Programs

To improve hypertension management, there is a need for enhanced screening programs that can identify at-risk individuals early. Community-based screening initiatives and the use of mHealth technologies can play a crucial role in this regard.

Strengthening Primary Healthcare

Strengthening primary healthcare systems is essential for effective hypertension management. Training primary healthcare providers, ensuring the availability of essential medications, and integrating hypertension care into primary healthcare services can significantly improve outcomes (15).

Public Awareness Campaigns

Increasing public awareness about hypertension, its risk factors, and the importance of regular health check-ups is crucial. Mass media campaigns, community health education programs, and school-based interventions can help raise awareness and promote healthy behaviors.

Research and Innovation

Continued research and innovation in hypertension management are vital. Developing cost-effective diagnostic tools, exploring new therapeutic options, and understanding the genetic and environmental factors contributing to hypertension can pave the way for better management strategies (16).

Conclusion

The landscape of hypertension in India is evolving, with rising prevalence posing significant public health challenges. While advancements in research, diagnostic tools, and management strategies offer hope, there is a need for comprehensive and integrated approaches to address this growing burden. Strengthening healthcare infrastructure, enhancing public awareness, and
fostering innovation are critical steps toward effective hypertension management in India. By adopting these measures, India can improve the health outcomes of millions and reduce the burden of hypertension-related complications.

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"Hypertension and Various Risk Factors"

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Abstract:
Hypertension is one of the most significant health burdens in present day societies, affecting 25–35% of the population. Due to increasing life expectancy, incidence of hypertension is likely to increase in the future. Despite the wide range of available non-pharmacological and pharmacological blood pressure lowering approaches, hypertension is poorly controlled worldwide with a substantial impact on morbidity and mortality. Therefore, early detection in the form of screening for hypertension and associated risk factors can help identify high-risk groups, which can result in timely treatment and management of risk factors.

Introduction:
According to the Joint National Committee 8 (JNC8), normal blood pressure is a systolic BP < 120 mmHg and diastolic BP < 80 mm Hg. Hypertension is defined as systolic BP level of ≥140 mmHg and/or diastolic BP level ≥ 90 mmHg. The grey area falling between 120–139 mmHg systolic BP and 80–89 mmHg diastolic BP is defined as "prehypertension" [1, 2].
Although prehypertension is not a medical condition, but individuals with prehypertension are at more risk of developing hypertension [3]. To lower the risk of prehypertension progressing to hypertension, modification of lifestyle or behaviours is necessary.

Epidemiology:
Hypertension is one of the leading causes of the global burden, affecting 1.28 billion adults aged 30–79 years worldwide and most of them (two-thirds) living in low- and middle-income countries. Recent epidemiological studies have reported that hypertension is increasing in India with a more rapid increase in rural and young populations. Fifth National Family Health Survey (NFHS-5) and Indian Council of Medical Research-INDIAB surveys have reported that there are substantial geographic variations in hypertension prevalence with greater prevalence in more developed states and districts of the country. There is a high prevalence of young-age hypertension, especially in the less developed states [4]. The incidence of adverse events from hypertension-related cardiovascular disease is significantly greater in India than in more developed countries.
High blood pressure usually does not cause symptoms itself [5] . It is, however, a major risk factor for stroke, coronary artery disease, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia.[6][7][8] It is a major cause of premature death worldwide.[9]

Risk factors:
Both environmental and genetic factors may contribute to regional and racial variations in hypertension prevalence. Obesity and weight gain are strong, independent risk factors for hypertension. It has been estimated that 60% of hypertensives are >20% overweight. Among populations, hypertension prevalence is related to dietary NaCl intake, and the age-related increase in blood pressure may be
augmented by a high NaCl intake. Low dietary intakes of calcium and potassium also may contribute to the risk of hypertension. The urine sodium-to-potassium ratio (an index of both sodium and potassium intakes) is a stronger correlate of blood pressure than is either sodium or potassium alone. Alcohol consumption, psychosocial stress, and low levels of physical activity also may contribute to hypertension.
Although specific genetic variants have been identified in rare Mendelian forms of hypertension (Table 1), these variants are not applicable to the vast majority (>98%) of patients with hypertension. For most individuals, it is likely that hypertension represents a polygenic disorder in which a combination of genes acts in concert with environmental exposures to make only a modest contribution to blood pressure. Furthermore, different subsets of genes may lead to different phenotypes associated with hypertension, e.g., obesity, dyslipidaemia, insulin resistance.
Preliminary evidence suggests that there may also be genetic determinants of target organ damage and vascular disease attributed to hypertension. Family studies indicate significant heritability of left ventricular mass, and there is considerable individual variation in the responses of the heart to

hypertension. Family studies and variations in candidate genes associated with renal damage suggest that genetic factors also may contribute to hypertensive nephropathy. Specific genetic variants have been linked to CHD and stroke.

DISEASE	PHENOTYPE	GENETIC CAUSE
Glucocorticoid-remediable hyperaldosteronism	Autosomal dominant Absent or mild hypokalaemia	Chimeric 11ß-hydroxylase/aldosterone gene on chromosome 8
17α-hydroxylase deficiency	Autosomal recessive Males: pseudo hermaphroditism Females: primary amenorrhea, absent secondary sexual characteristics	Random mutations of the CYP17 gene on chromosome 10
11ß-hydroxylase deficiency	Autosomal recessive Masculinization	Mutations of the CYP11B1 gene on chromosome 8q21-q22
11ß-hydroxysteroid dehydrogenase deficiency (apparent mineralocorticoid excess syndrome)	Autosomal recessive Hypokalaemia, low renin, low aldosterone	Mutations in the 11ß-hydroxysteroid dehydrogenase gene
Liddle's syndrome	Autosomal dominant Hypokalaemia, low renin, low aldosterone	Mutation subunits of the epithelial sodium channel SCNN1B and SCNN1C genes
Pseudo hypoaldosteronism type II (Gordon's syndrome)	Autosomal dominant Hyperkalaemia, normal glomerular filtration rate.	Linkage to chromosomes 1q31-q42 and 17p11-q21
Hypertension exacerbated in pregnancy	Autosomal dominant Severe hypertension in early pregnancy	Missense mutation with substitution of leucine for serine at codon 810 (MRL810)
Polycystic kidney disease	Autosomal dominant	Mutations in the PKD1 gene on chromosome 16
	Large cystic kidneys, renal failure, liver cysts, cerebral aneurysms, valvular heart disease	and PKD2 gene on chromosome 4
Pheochromocytoma	Autosomal dominant (a) Multiple endocrine neoplasia, type 2A Medullary thyroid carcinoma, hyperparathyroidism (b) Multiple endocrine neoplasia, type 2B Medullary thyroid carcinoma, mucosal neuromas, thickened corneal nerves, alimentary ganglioneuromatoses, marfanoid habitus (c) von Hippel-Lindau disease Retinal angiomas, hemangioblastomas of the cerebellum and spinal cord, renal cell carcinoma (d) Neurofibromatosis type 1 Multiple neurofibromas, café-au-lait spots	(a) Mutations in the RET protooncogene (b) Mutations in the RET protooncogene (c) Mutations in the VHL tumour-suppressor gene (d) Mutations in the NF1 tumor-suppressor gene

In the future, it is possible that DNA and epigenetic analyses may predict individual risk for hypertension and target organ damage and will identify responders to specific classes of antihypertensive agents.

Classifications:

High blood pressure is classified as primary (essential) hypertension or secondary hypertension.[10] About 90–95% of cases are primary, defined as high blood pressure due to nonspecific lifestyle and genetic factors.[10]

The remaining 5–10% of cases are categorized as secondary hypertension, defined as high blood pressure due to a clearly identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.[10]

Table 2 – Causes of Secondary Hypertension

Renal	Parenchymal diseases, renal cysts (including polycystic kidney disease), renal tumors (including renin-secreting tumors), obstructive uropathy
Renovascular	Arteriosclerotic, fibromuscular dysplasia
Adrenal	Primary aldosteronism, Cushing's syndrome, 17α-hydroxylase deficiency, 11β- hydroxylase deficiency, 11-hydroxysteroid dehydrogenase deficiency (licorice), pheochromocytoma
Aortic coarctation	
Obstructive sleep apnea	
Preeclampsia/eclampsia	
Neurogenic	Psychogenic, diencephalic syndrome, familial dysautonomia, polyneuritis (acute porphyria, lead poisoning), acute increased intracranial pressure, acute spinal cord section
Miscellaneous endocrine	Hypothyroidism, hyperthyroidism, hypercalcemia, acromegaly
Medications	High-dose estrogens, adrenal steroids, decongestants, appetite suppressants, cyclosporine, tricyclic antidepressants, monoamine oxidase inhibitors, erythropoietin, nonsteroidal anti-inflammatory agents, cocaine

Prevention:

Lifestyle changes are recommended to lower blood pressure. The international guidelines[10 -14] advocate diet/behavioural modification at every stage, both before drug therapy in pre-hypertension or uncomplicated stage-1 hypertension, as well as for high-risk patients and those on medication. They also specifically recommend adoption of the Dietary Approaches to Stop Hypertension (DASH) eating plan.

Recommended lifestyle changes for the prevention of hypertension includes[12]:

- Decrease dietary sodium intake to <6 g of salt (sodium chloride) or <2.4 g of sodium per day.
- Regular aerobic physical activity with moderate intensity (minimum 150 minutes per week)
- Maintain normal body weight for adults (body mass index below 25 kg/m2)
- Limit alcohol consumption (< 14 units /week for men and 10 units/week for women)
- Consume a diet rich in whole grains, fruit, and vegetables, such as the DASH diet
- Stop smoking and Tobacco in any form.
- Stress reduction and management, e.g., by meditation and yoga

Conclusion:

Effective lifestyle modification may lower blood pressure as much as an individual antihypertensive medication. Combinations of two or more lifestyle modifications can achieve even better results. There is

considerable evidence that reducing dietary salt intake lowers blood pressure, but whether this translates into a reduction in mortality and cardiovascular disease remains uncertain.

From a therapeutic point of view, we currently dispose of many effective and well tolerated antihypertensive drugs, device-based approaches in resistant hypertension to modulate sympathetic nervous system like Renal denervation therapy, Baroreflex activation therapy etc but non-pharmacological approaches are always recommended for all individuals with hypertension, regardless of drug therapy.

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"Blood Pressure Variability: how to deal with it"

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Introduction

Blood pressure variability (BPV) refers to the fluctuations in blood pressure (BP) that occur over various time frames, from beat-to-beat to visit-to-visit intervals. BPV has been identified as an independent risk factor for cardiovascular morbidity and mortality, beyond mean BP levels. Understanding BPV's mechanisms, clinical significance, and management is crucial for improving cardiovascular outcomes in hypertensive patients.

Types and Time Frames of Blood Pressure Variability

1. **Short-term BPV :**
   Beat-to-beat variability: This type is measured using continuous non-invasive arterial pressure monitoring or intra-arterial techniques, providing real-time BP changes. It is heavily influenced by the autonomic nervous system (ANS) activity and baroreflex sensitivity, responding to rapid physiological adjustments such as respiration, posture, and emotional stress.

   Minute-to-minute and hour-to-hour variability: Captured through ambulatory blood pressure monitoring (ABPM), these fluctuations are influenced by circadian rhythms, physical activity, and immediate environmental factors.

2. **Long-term BPV :**
   Day-to-night (Diurnal) variability: BP follows a circadian rhythm, typically lower during sleep (nocturnal dipping). A non-dipping or reverse dipping pattern (higher nocturnal BP) is associated with increased cardiovascular risk, including left ventricular hypertrophy and stroke.'

   Day-to-day variability: Assessed using home blood pressure monitoring (HBPM), it reflects BP fluctuations influenced by daily activities, dietary intake, stress, and medication adherence.

   Visit-to-visit variability: Differences in BP readings across clinical visits provide long-term BPV data, affected by factors like medication changes, adherence, and lifestyle factors.

   Mechanisms Underlying Blood Pressure Variability

1. **Neural Mechanisms :** The ANS regulates BP through sympathetic and parasympathetic pathways. Sympathetic nervous system activity increases BP, while parasympathetic activity decreases it. Baroreceptor sensitivity, which decreases with age and certain diseases (e.g., diabetes, heart failure), modulates these rapid BP changes.

2. **Hormonal Influences :**
   Renin-angiotensin-aldosterone system (RAAS): This system influences BP by modulating vascular tone and sodium balance. Dysregulation can lead to increased BPV.

Catecholamines: Hormones such as adrenaline and noradrenaline increase sympathetic activity, causing BP surges in response to stress.

Antidiuretic hormone (ADH) and natriuretic peptides: These hormones regulate fluid balance and vascular tone, contributing to BP variability.

3. **Vascular Factors :** Arterial stiffness, endothelial dysfunction, and vascular compliance are key determinants of BPV. Conditions like atherosclerosis, diabetes, and aging increase arterial stiffness, leading to greater BP fluctuations.

4. **Behavioral and Environmental Factors:** Physical activity, diet (e.g., salt intake), stress, and seasonal variations significantly impact BPV. Interventions aimed at lifestyle modification can modulate these influences.

5. **Measurement Artifacts :** Variability can arise from differences in measurement techniques, devices, observer biases, and patient-related factors such as the "white-coat" effect, where BP readings are elevated in a clinical setting.

Clinical Significance of Blood Pressure Variability

1. **Prognostic Value :** Elevated BPV is an independent predictor of adverse cardiovascular outcomes:

   Stroke: Both short-term and long-term BPV are strongly associated with an increased risk of stroke. Higher BPV indicates greater instability in BP control, leading to cerebrovascular damage.

   Coronary artery disease (CAD): Increased visit-to-visit BPV is linked to higher incidences of CAD. This variability can reflect underlying pathophysiological processes that contribute to atherosclerosis and plaque instability.

   Heart failure and mortality: Patients with higher BPV have a higher risk of developing heart failure and increased mortality rates. This association underscores the importance of stable BP control in improving long-term outcomes.'

2. **Hypertension Management :** Understanding and managing BPV is crucial for effective hypertension treatment:

   Antihypertensive medications: Some drugs are more effective at reducing BPV than others. For example:

   Calcium channel blockers (e.g., amlodipine): Effective in reducing BPV due to their vasodilatory properties.

   Beta-blockers (e.g., carvedilol): Especially those with vasodilatory effects, help stabilize BP by reducing sympathetic nervous activity.

   RAAS inhibitors (e.g., ACE inhibitors, ARBs): These medications reduce BPV by targeting the RAAS, particularly beneficial in combination therapy.'

3. **Target Organ Damage :** Increased BPV is associated with greater damage to target organs:

   Left ventricular hypertrophy (LVH): Higher BPV correlates with increased left ventricular mass, a marker of end-organ damage.

Microalbuminuria: Elevated BPV is linked to renal damage, indicated by the presence of albumin in the urine.

Retinal vascular changes: Fundoscopic examinations reveal microvascular damage associated with BP fluctuations, contributing to conditions like hypertensive retinopathy.

Measurement and Quantification

1. **Ambulatory Blood Pressure Monitoring (ABPM):** ABPM is the gold standard for assessing short-term BPV. It provides a comprehensive 24-hour BP profile, capturing diurnal variations and nocturnal dipping patterns. Key metrics include:

   Standard deviation (SD): Reflects the dispersion of BP readings around the mean.
   Coefficient of variation (CV): The ratio of SD to mean BP, providing a normalized measure of variability
   Average real variability (ARV): The mean of absolute differences between consecutive BP readings, offering a more accurate reflection of variability.

2. **Home Blood Pressure Monitoring (HBPM):** Useful for assessing longer-term BPV, HBPM involves taking multiple readings over extended periods in a naturalistic setting, reducing the "white-coat" effect. Metrics similar to ABPM can be used to assess variability.

3. **Clinical Visit Measurements :** Serial office BP measurements can estimate visit-to-visit variability. Metrics include:

   Visit-to-visit SD: The standard deviation of BP readings across multiple clinical visits, reflecting long-term BP stability. Variability independent of the mean (VIM): A robust measure that accounts for differences in mean BP, providing a more accurate assessment of variability.

4. **Advanced Techniques:**

   Continuous non-invasive arterial pressure monitoring: Provides beat-to-beat BP data, offering insights into rapid BP changes.

   Spectral analysis and time-domain measures : These advanced techniques analyze the frequency and amplitude of BP oscillations, providing detailed information about BP dynamics.

Management Strategies to Reduce Blood Pressure Variability

1. **Pharmacological Interventions:**
   Choosing appropriate antihypertensives: Medications that effectively reduce BPV include calcium channel blockers, beta-blockers with vasodilatory properties, and RAAS inhibitors.

   Combination therapy: Often necessary to achieve optimal BP control and reduce variability. Combining drugs with complementary mechanisms can enhance BP stability.

2. **Non-Pharmacological Interventions:**

   Lifestyle modifications: Dietary changes (e.g., reducing salt intake), regular physical activity, and stress management are crucial in modulating BPV.

Patient education: Enhancing patient understanding of hypertension and the importance of medication adherence can significantly reduce BPV. Self-monitoring of BP using HBPM also empowers patients to participate in their care.

3. **Monitoring and Follow-up:'**

Regular monitoring: Using ABPM and HBPM to track BPV over time allows for timely adjustments in therapy, ensuring sustained BP control.

Integrated care: A multidisciplinary approach involving cardiologists, primary care physicians, and other healthcare providers is essential for comprehensive hypertension management and reducing BPV.

Conclusion

Blood pressure variability (BPV) is a multifaceted and clinically significant aspect of hypertension management, with substantial implications for cardiovascular risk. Elevated BPV has been consistently associated with an increased risk of adverse cardiovascular events, including stroke, coronary artery disease, heart failure, and overall mortality. Understanding the different types and time frames of BPV, from beat-to-beat to visit-to-visit variability, is essential for physician and cardiologists aiming to optimize treatment strategies for hypertensive patients.

The mechanisms underlying BPV are complex, involving neural, hormonal, vascular, behavioral, and environmental factors. The autonomic nervous system, renin-angiotensin-aldosterone system, and vascular stiffness play pivotal roles in modulating BP fluctuations. Recognizing these mechanisms can guide the selection of appropriate therapeutic interventions to reduce BPV.

Clinical measurement and quantification of BPV are critical for accurate diagnosis and management. Tools like ambulatory blood pressure monitoring (ABPM), home blood pressure monitoring (HBPM), and clinical visit measurements provide valuable data on BP patterns and variability. Advanced techniques, such as continuous non-invasive arterial pressure monitoring and spectral analysis, offer detailed insights into BP dynamics.

Effective management of BPV requires a multifaceted approach. Pharmacological interventions, including calcium channel blockers, beta-blockers with vasodilatory properties, and RAAS inhibitors, have been shown to reduce BPV. Combination therapy often enhances BP stability, addressing multiple pathways involved in BP regulation. Non-pharmacological interventions, such as lifestyle modifications and patient education, play a crucial role in modulating BPV. Regular monitoring and follow-up using ABPM and HBPM are essential to track BPV and adjust treatment strategies accordingly.

Integrating care through a multidisciplinary approach involving cardiologists, primary care physicians, and other healthcare providers ensures comprehensive management of hypertension and BPV. By incorporating strategies to reduce BPV into clinical practice, cardiologists can improve prognostic accuracy and tailor interventions to enhance cardiovascular health.

In summary, BPV is a critical factor in hypertension management, with significant implications for cardiovascular risk and patient outcomes. Understanding its mechanisms, accurately measuring and quantifying variability, and implementing effective management strategies are essential for optimizing care in hypertensive patients. Addressing BPV can lead to better control of hypertension, reduction in cardiovascular events, and improved long-term health outcomes for patients.

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Hypertensive Emergencies: How to Manage this Volcano

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Introduction

Hypertensive crises are defined as clinical conditions associated with severe elevations in systolic (more than 180mm Hg) & diastolic blood pressure (above 120 mmHg). Hypertensive emergencies and urgencies are subclasses of hypertensive crises. A hypertensive emergency (HE) is characterized by a rapid increase in blood pressure ((BP) with a systolic value greater than 180 mmHg and/or a diastolic value greater than 120 mmHg and accompanied by acute injury to target organs (neurologic, cardiovascular, renal, retina arteries). This also known as acute hypertension mediated organ damage (A-HMOD) [1]. If there are sudden increases in blood pressure from the lower baseline, lower blood pressure thresholds may also be associated with hypertensive emergencies. Hypertensive urgencies are clinical scenarios where elevated BP is not associated with target organ damage, also known as severe uncontrolled hypertension(U-HTN) [2]. Given the stark differences in management between these two clinical entities, it is imperative to distinguish between hypertensive emergencies and urgencies.

Of all HE presentations, stroke accounts for 38% of clinical presentations. Pulmonary oedema (35%) and coronary syndromes (25%) are the next most common clinical presentations [3]. The one-year mortality rate with HE approaches 80% if treatment is not received [4].

The kind of organ damage, comorbidities, drug pharmacokinetics, and adverse effects all influence the selection of antihypertensive medications and the timeframe for BP reduction [5]. Ideally, HE should be managed in ICU setting with immediate pharmacological and nonpharmacological interventions for lowering BP levels along with specific treatment protocols for the associated clinical conditions (acute coronary syndrome, acute heart failure with pulmonary oedema, acute aortic syndrome, hypertensive encephalopathy, ischemic or haemorrhagic stroke, pre-eclampsia/eclampsia) [6]. U-HTN can be treated by simply ramping up the antihypertensive medication therapy that was previously recommended [7]. Here, blood pressure drops should be achieved gradually and under monitoring so as not to impair organ perfusion [8].

Studies demonstrate that poor compliance to antihypertensive medication therapy, interrupting antihypertensive drugs, abusing illicit and recreational drugs, and inadequate management of common risk factors (smoke, obesity, hypercholesterolemia, diabetes mellitus) are the most common triggers of the sudden elevation of BP [8,9].

Pathophysiology

The target organ tissue experiences hypoperfusion due to increased vascular permeability, platelet and coagulation cascade activation, fibrin clot deposition, and endothelial damage caused by mechanical stress on vascular walls.

Evaluation

Important components of the medical history include the use of illicit or over-the-counter medicines, history of control of blood pressure, and antihypertensive medication should be monitored, both in supine and standing positions, and in both arms to assess the possibility of aortic dissection if it is found to be significantly different [10].Jugular venous distension, crackles, level of consciousness, focal neurological symptoms, and meningeal irritation signs are all part of the physical examination. Blood tests include the complete blood count, ECG, metabolic panel, urinalysis, chest X-ray, and natriuretic and troponin peptides. Computed tomography angiography of the abdomen and thorax is required for acute aortic syndrome.

Differential Diagnosis

1. Acute kidney injury
2. Aortic coarctation
3. Aortic dissection
4. Chronic kidney disease

5. Eclampsia
6. Hyperthyroidism
7. Pheochromocytoma
8. Renal artery stenosis
9. Subarachnoid hemorrhage

Management

Lowering blood pressure in a controlled manner could be the primary goal. Systolic BP should be reduced by no more than 25% in the first hour, then gradually to 160/100 mmHg over the next two to six hours, and finally, over the course of the next 24 to 48 hours, blood pressure should be gradually returned to normal [7]. However, aortic dissection, pre-eclampsia, or pheochromocytoma call for a rapid decrease in blood pressure.

There are many parenteral and oral antihypertensive medications available, but not many studies have compared them to one another. All these medications are generally well tolerated [4,11]. Thus, the kind of hypertensive emergency and the medication's availability are taken into consideration for selecting the drugs for administration. Because of their quick action, ease of titration, and short half-life, intravenous medicines are recommended [2].

The most effective medications for treating HEs include clevidipine, labetalol, esmolol, and nicardipine. For many years, nitroprusside was the recommended choice of treatment; however, nicardipine and clevidipine, which are simpler to titrate and do not pose a risk of cyanide poisoning, also have comparable effectiveness [12,13]. Diuretics are not recommended in HEs.

Nicardipine is a more potent antihypertensive medication in an ICU context than labetalol, with a better side effect profile linked to a lower incidence of bradycardia, atrioventricular block, and hypotension [38]. According to another study, individuals receiving intravenous nicardipine had a higher chance than those receiving intravenous labetalol of reaching the desired blood pressure targets in less than 30 minutes [14].

Both labetalol and nitroprusside adequately lower blood pressure in malignant hypertension; however, labetalol also decreased cerebral vascular resistance. In contrast, sodium nitroprusside reduced systemic vascular resistance instead of cerebral vascular resistance, with a larger rate of reduction in the middle cerebral artery. This suggests that blood flow is preferentially directed to the low resistance systemic vascular bed rather than the cerebral vascular bed [15]. There is insufficient evidence currently to draw the conclusion that a particular intravenous (IV) antihypertensive drug is better than another. Oral medication can begin once the goal blood pressure has been reached.

Hypertensive Encephalopathy

The preferable medications are labetalol or nicardipine because they may be used continuously and prevent significant blood pressure swings, which can interfere with regular blood flow when there is abnormal autoregulation [16]. Because of its venous vasodilatory effect and potential to raise intracranial pressure and exacerbate cerebral oedema, nitroglycerine is contraindicated in hypertensive encephalopathy [15]. Since nitroprusside acts primarily on systemic vascular resistance rather than cerebral vascular resistance and is a more balanced arterial and venous vasodilator, it can be utilized in hypertensive encephalopathy [15]. Cerebral hemorrhage, coma, and death are possible outcomes of untreated hypertensive encephalopathy and posterior reversible encephalopathy syndrome.

Acute Ischemic Stroke

It is not recommended to decrease blood pressure rapidly and substantially over the first 24 hours [17]. To lower the risk of cerebral bleeding, patients undergoing thrombolysis benefit from a quick drop in blood pressure to less than 185/100 mmHg and continued maintenance for at least 24 hours [18]. Maintaining a higher blood pressure, even as high as 220/120 mmHg, is indicated for patients who are not eligible for thrombolysis or thrombectomy to maintain cerebral perfusion with potentially reversible ischemia. A decrease of less than 15% within the first 24 hours is deemed safe and appropriate [19]. The blood pressure should be steadily reduced over the course of the next 24 to 48 hours.

Acute Intracranial Hemorrhage

Current guidelines recommend reducing blood pressure to less than 140 mmHg (but not below 110 mmHg) in patients presenting with hyperacute intracerebral hematoma (symptoms lasting fewer than 6

hours), based on the existing data, as this can reduce the expansion of the hematoma. However, the magnitude of BP drop ought to be limited to 90 mmHg [19].

Acute Coronary Syndrome

When used in conjunction with intravenous beta-blockers, such as labetalol or esmolol [20], which reduce cardiac output and myocardial oxygen consumption [21], intravenous nitroglycerin is up titrated to treat angina while quickly reducing the systolic blood pressure to less than 140 mmHg.

Acute Cardiogenic Pulmonary Oedema

Clevidipine was found to meet the target blood pressure in 71% of patients, compared to 37% of patients receiving nitroglycerin or nicardipine, according to a randomized control study involving 104 patients. Additionally, at 45 minutes, clevidipine was shown to be more successful in alleviating dyspnoea (14). NITURA study demonstrated that individuals with acute pulmonary edema who received urapidil instead of nitroglycerine had a more marked drop in blood pressure and better respiratory and metabolic outcomes [22].

Acute Aortic Syndrome

Medical therapy entails managing chest pain and quickly bringing the systolic blood pressure down to 100 to 120 mmHg while also bringing the heart rate down to fewer than 60 beats per minute [23].

Eclampsia and Severe Pre-Eclampsia

When compared to IV labetalol or IV hydralazine, oral nifedipine has the best therapeutic efficacy in lowering blood pressure during pregnancy [24]. However, there is no discernible difference in the risk of adverse effects between these medications.

Pheochromocytoma/Paraganglioma

The initial line of treatment for BP management is usually an alpha 1 blocking medication, such as doxazosin or phentolamine, followed by a beta-blocker.

Conclusions

Because of its broad spectrum of clinical patterns and potential to adversely affect cerebrovascular and cardiovascular outcomes, hypertensive crises continue to provide a significant problem. To minimize organ damage, treatment for each form of HE should be customized.

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Hypertension in Children and Adolescents

In infants and young children, systemic hypertension is uncommon, with a prevalence of <1% but, when present often indicates an underlying disease process (secondary hypertension). Severe and symptomatic hypertension in children is usually caused by secondary hypertension. In contrast, the prevalence of primary hypertension, mostly in older school-age children and adolescents, has increased in prevalence in parallel with the obesity epidemic. A recent systematic review and meta-analysis reports that approximately 10% of Indian children have prehypertension, 7% have hypertension and 4% have sustained hypertension [1]. The influence of obesity on elevated blood pressure is evident in children as young as 2 to 5-year-old. Approximately 8.4% of Indian children are obese, and up to 10% of obese youth have hypertension [2]. Hypertensive children, more often asymptomatic, may manifest evidence of target organ damage at the first presentation. Up to 40% of hypertensive children have left ventricular hypertrophy, and hypertensive children have increased carotid intima-to-media thickness, a marker of early atherosclerosis. Primary hypertension occurring during childhood often continues into adulthood. Children with BP >90th percentile exhibit a 2.4-fold greater risk of having hypertension as adults. Similarly, almost half of hypertensive adults had a BP >90th percentile as children. Adolescent hypertension is also an independent predictor of both end-stage renal disease and left ventricular dysfunction in middle-aged men.

Background

This guideline will focus on the pediatric population aged 1–17 years (not infants). Hypertension in childhood is a key predictor of risk for hypertension, cardiovascular disease and end organ damage in adulthood. Primary/essential hypertension accounts for the majority of hypertension in children >6 years old and is generally associated with obesity or a family history of hypertension. Secondary hypertension is more common in younger children (<6 years old) with renal disease being the most prevalent cause. This population is at greater risk of hypertensive emergencies due to an underlying condition

Risk factors

These are varied and include, Overweight/obesity, male sex, family history of hypertension, low birth weight/intrauterine growth restriction, prematurity, excess dietary salt intake, physical inactivity, chronic health concerns, e.g. chronic kidney disease and diabetes.

Causes of Hypertension

- Primary Hypertension
- Situational Hypertension
    - Stress, pain, anxiety
- Secondary Hypertension
    - Renal parenchymal disease
    - GN, polycystic kidneys, CKI
    - Cardiac, Vascular
        - Renal artery stenosis, Co-arctation repair (pre and post)
    - Endocrine
        - Diabetes, thyroid disease, CAH, Diabetes, thyroid disease, CAH, Cushings
    - Autoimmune
        - Thrombotic thrombocytopenic purpura,
        - Hemolytic Uremic Syndrome,
        - Henoch-Schönlein Purpura
    - Genetic/Syndromic
        - Neurofibromatosis,

    - Williams Syndrome,
    - Turners Syndrome
  - Malignancy
    - Wilms tumour,
    - neuroblastoma,
    - pheochromocytoma
  - Intracranial pathology
    - Intracranial hemorrhage/stroke,
    - pituitary adenoma,
    - raised ICP
  - Respiratory
    - Chronic lung disease,
    - OSA
  - Drug-induced
    - Corticosteroids,
    - OCP,
    - stimulants

History

It is necessary that a detailed history is elicited for, headache/vomiting, blurred vision, change in mental state, seizures, chest pain/palpitations, shortness of breath, cardiac failure, past history of acute kidney Injury (AKI) etc.

Examination

- Confirm hypertension (See measuring blood pressure section below)
- Vitals: tachycardia, four limb BP for upper and lower limb discrepancy
- Height and weight: obesity, growth retardation
- Signs of end organ damage
  - Fundoscopy: hypertensive retinopathy
  - Cardiovascular: apical heave, hepatomegaly, edema
  - Chronic renal failure: palpable kidneys
  - Focal neurology e.g. facial nerve palsies
- Signs of underlying cause
  - General appearance: Cushingoid, proptosis, goitre, webbed neck (Turner syndrome), elfin facies (William syndrome)
  - Skin: Cafe-au-lait spots, neurofibromas, acanthosis nigricans, hirsutism, striae, acne, rash (vasculitis)
  - Cardiovascular: murmurs +/- radiation, apical heave, reduced femoral pulses, edema, hepatomegaly (CCF)
  - Abdomen: masses, palpable kidneys, flank bruits
  - Genitourinary: ambiguous/virilised genitalia eg CAH

Key points when measuring blood pressure

Ensure the correct cuff size is selected for each patient, favoring a larger rather than smaller cuff (smaller cuff creates artificial hypertension)

- BP cuff width should be 40% of the length of the arm measure from the shoulder tip to the elbow
- Abnormal oscillatory BP measurement needs checking with a manual BP from the child's arm

Screening BP Values Requiring Further Evaluation (90th centile for a child at average height)

Age (years)	Blood pressure (mmHg)			
	Boys		Girls	
	Systolic	Diastolic	Systolic	Diastolic
1	98	52	98	54
2	100	55	101	58
3	101	58	102	60
4	102	60	103	62
5	103	63	104	64
6	105	66	105	67
7	106	68	106	68
8	107	69	107	69
9	107	70	108	71
10	108	72	109	72
11	110	74	111	74
12	113	75	114	75
=13	120	80	120	80

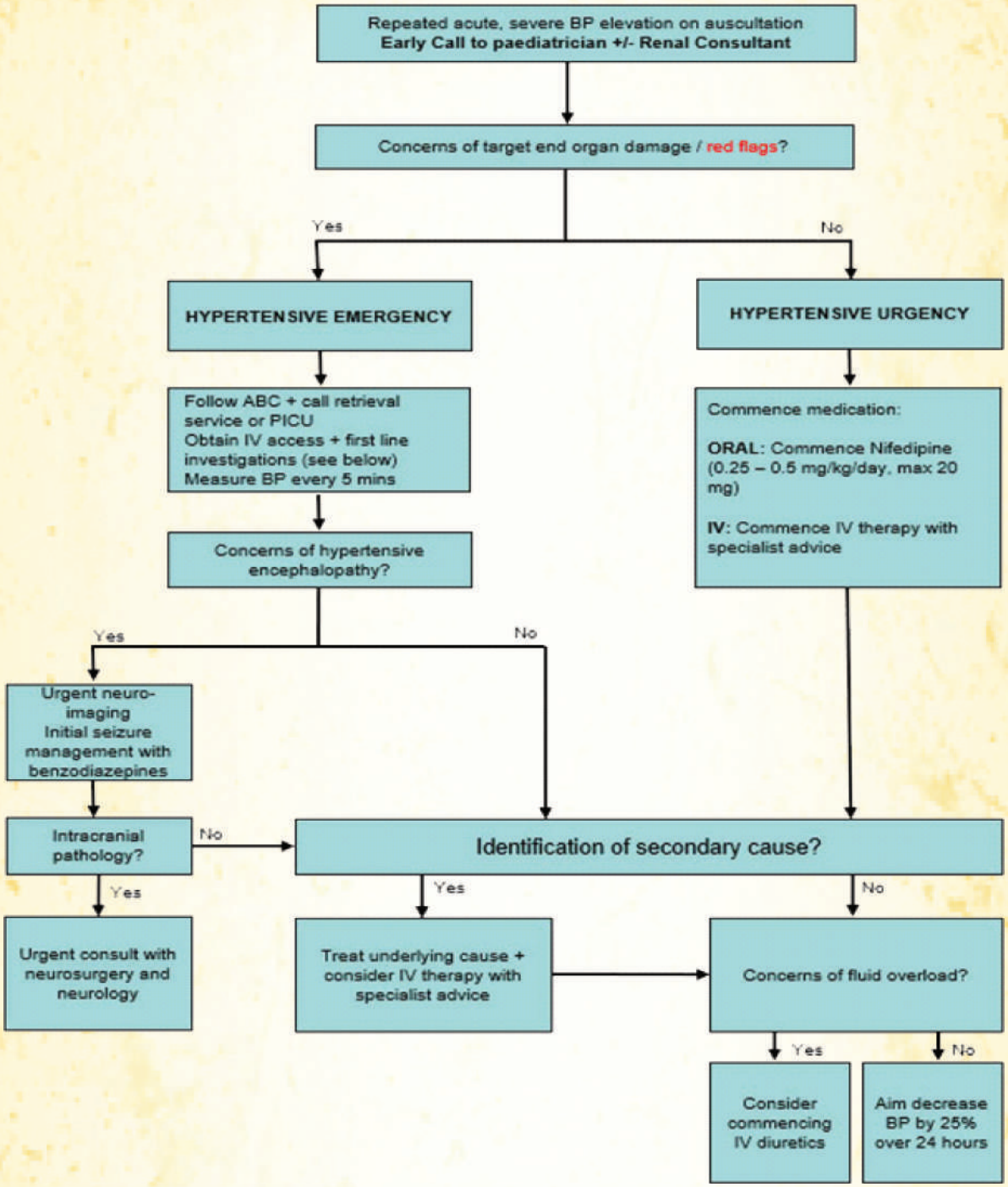
Assessment of severity

Interpreting blood pressure measurement [3]

Blood pressure classification in children and adolescents		
	For children aged 1 to 13 years	**For children aged 13-17 year**
Normal blood pressure	<90th centile	<120/<80 mmHg
Elevated blood pressure	=90th centile to <95th centile or 120/80 mmHg to <95th centile (whichever is lower)	120/<80 to 129/<80 mmHg
Stage 1 Hypertension	=95th centile to <95th centile + 12 mmHg or 130/80 to 139/89 mmHg (whichever is lower)	130/80 to 139/89 mmHg
Stage 2 Hypertension	=95th centile + 12 mmHg, or =140/90 mmHg (whichever is lower)	=140/90 mmHg
Severe Hypertension		
Hypertensive Urgency	>95th centile + 30 mmHg without symptoms/signs of target end organ damage (See Examination)	>180/120 without symptoms/signs of tar organ damage (See Examinati
Hypertensive Emergency	>95th centile + 30 mmHg associated with encephalopathy, e.g. headache vomiting, vision changes and neurological symptoms (facial nerve palsy, lethargy, seizures, coma) +/- target-end organ damage	>180/120 associated with encephalopath e.g. headache vomiting, vision changes and neurological symp (facial nerve palsy, lethargy, s coma) +/- target-end organ dar

Management [3]

Emergency management of severe hypertension



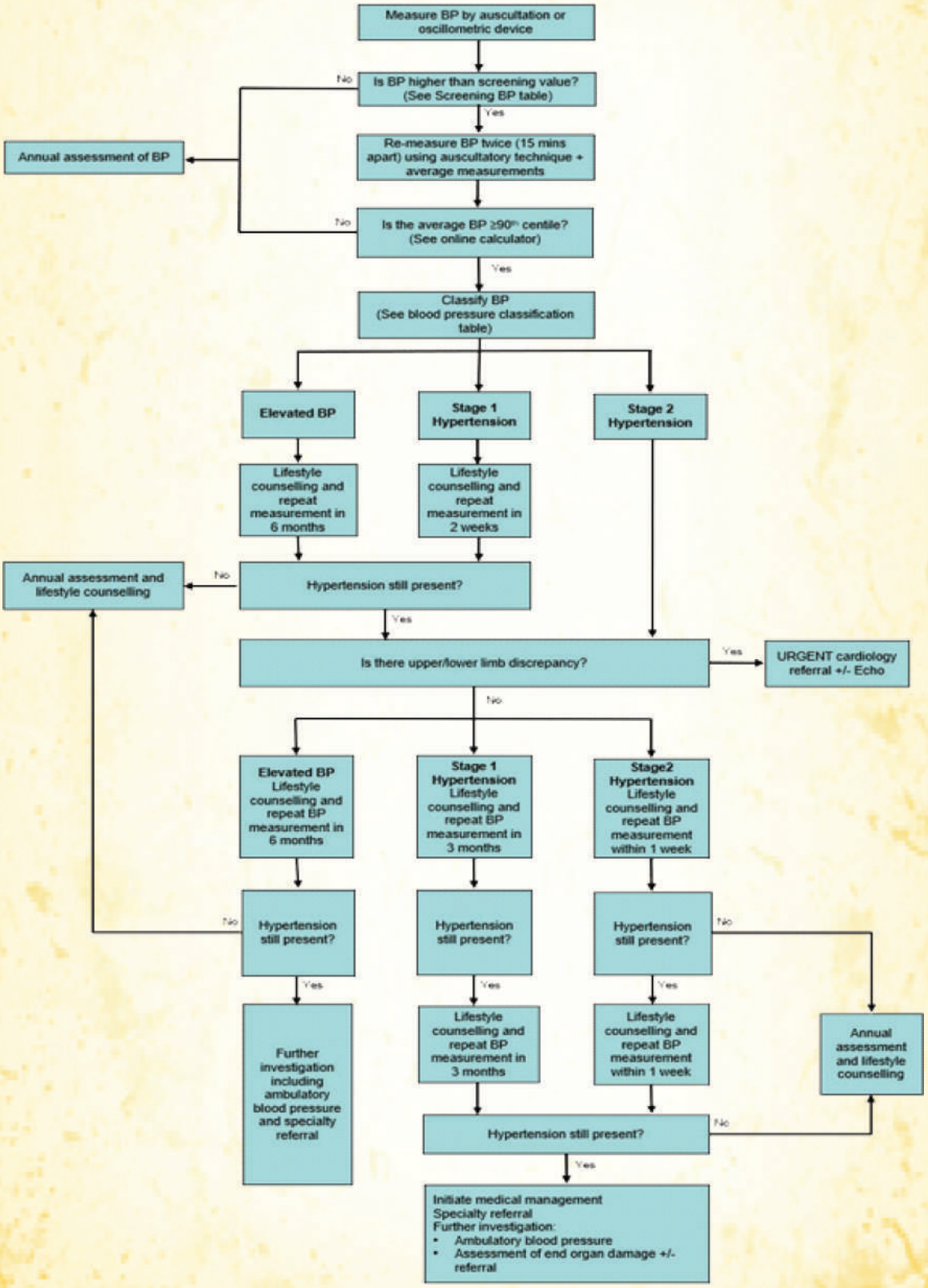
Hypertensive urgency

If medically stable, consider short acting oral agents while investigating cause and start with Nifedipine at 0.25–0.5 mg/kg/day (max 20 mg) and titrate up as required to a maximum of 3 mg/kg/day (max 120 mg)

Hypertensive emergency

It is advisable to start intravenous therapy aiming to gradually reduce BP to the patient's estimated 95th centile while trying to decrease BP by 25% of the original value every 24 hours till target BP reached.

Hypertension without severe symptoms



Investigations

First-line investigations: Urea, Electrolytes and Creatinine, Urinalysis +/- Renal ultrasound, LFT, Hb A1c, fasting lipids particularly in children with BMI >95th centile.

Consider further testing if the child is less than 6 years, concerns for secondary causes on history/examination and abnormal first-line investigations.

Suppressed plasma renin activity or elevated aldosterone renin ratio (ng/dL and ng/mL per hour, respectively) >10, especially in presence of family history of early-onset hypertension or associated hypokalemia highlights need for genetic work up. A new addition is the clear recommendation in favor of echocardiogram vis-a-vis electrocardiogram as it correlates better with left ventricular hypertrophy (LVH)[4]

Further Investigations

- Bloods: FBE, Bicarbonate, renin/aldosterone ratio, TFT, plasma metanephrins, cortisol, fasting glucose
- Urine: microscopy, protein/creatinine ratio, Catecholamines, drug screen
- Imaging: renal doppler ultrasound, DMSA, CTA/MRA
- Other: Echocardiogram, sleep study

Lifestyle counselling and modification

Initiate dietary modifications in the form of diets rich in fresh fruit and vegetables/legumes, fish, poultry, lean red meat and low fat dairy and limit intake of high sodium, fat or sugar containing foods. Weight loss is the primary therapy in obesity-related hypertension. It is recommended that all hypertensive children have a diet increased in fresh fruits, fresh vegetables, fiber, and nonfat dairy and reduced in sodium. The DASH diet is beneficial in lowering BP in adolescents as well as in adults. In addition, regular aerobic physical activity for at least 30-60 min on 3 to 5 days/week along with a reduction of sedentary activities to <2 hour/day is recommended.

Medical management

Children with symptomatic hypertension, stage 2 hypertension without a modifiable risk factor, hypertension, in patients with comorbidities such as diabetes (types 1 and 2) or CKD, and persistent hypertension despite non-pharmacologic measures, should be started with pharmacologic therapy. A single antihypertensive medication at low dose is to be started, if indicated and it can then be increased gradually until the goal BP is achieved. Once the highest recommended dose is reached, or if the child develops side effects, a 2nd drug from a different class can be added. Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), thiazide diuretics, and calcium channel blockers are generally considered acceptable initial agents for use in children. Medications should be commenced if conservative measures have failed, symptomatic hypertension develops, there is stage-2 hypertension with no modifiable risk factors and for hypertension in setting of chronic kidney disease or diabetes.

The choice of antihypertensive agent for a patient should be tailored to the etiology of that patient's hypertension whenever possible. With evidences primarily from adult studies, beta blockers were discouraged as first line anti-hypertensive.

There have been changes in the recommended BP goals for treatment of hypertension in children and adolescents. Data from the SPRINT (SBP intervention) trial group suggests that stricter goals (SBP goal of 120 vs 140 mm Hg) improve cardiovascular outcomes in adults. In children with CKD, the ESCAPE (Effects of Strict BP Control and Angiotensin-Converting Enzyme Inhibition on the Progress of Chronic Renal Failure in Pediatric Patients) trial group showed slower progression of CKD if the 24 hour MAPs

were kept below the 50th percentile on ABPM (Ambulatory Blood Pressure Monitoring) compared to the 50th-95th percentile. It is now recommended that treatment achieves BP <90th percentile for age, or <130/80 mm Hg, whichever is lower. A lower goal based on ABPM (24 hr MAP <50th percentile) is recommended for children and adolescents with CKD. ACEIs or ARBs should be used for children with diabetes and microalbuminuria or proteinuric renal disease [5]

The drugs available for treating hypertension in children are:

1. Aldosterone receptor antagonist: Eplerenone, Spironolactone
2. Angiotensin-converting enzyme inhibitors: Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Quinapril, Ramipril
3. Angiotensin receptor blockers: Candesartan, Losartan, Olmesartan, Valsartan
4. α- and β-Adrenergic antagonists: Labetalol, Carvedilol
5. β-adrenergic antagonists: Atenolol, Bisoprolol, Metoprolol, Propranolol
6. Calcium channel blockers: Amlodipine, Felodipine, Isradipine , Extended-release Nifedipine
7. Central α-agonist: Clonidine
8. Diuretics: Amiloride, Chlorthalidone, Chlorothiazide, Furosemide
9. Vasodilators: Hydralazine, Minoxidil

Key points

1. Severe hypertension requires urgent consultation and management. Hypertension associated with encephalopathy is a medical emergency
2. All hypertension in children requires monitoring and follow-up
3. Blood pressure should be measured annually in healthy children
4. Where possible, abnormal machine BP measurement should be confirmed, preferably with a manual BP, ensuring appropriately sized cuff is used for accurate measurement

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HYPERTENSIVE DISORDERS IN PREGNANCY

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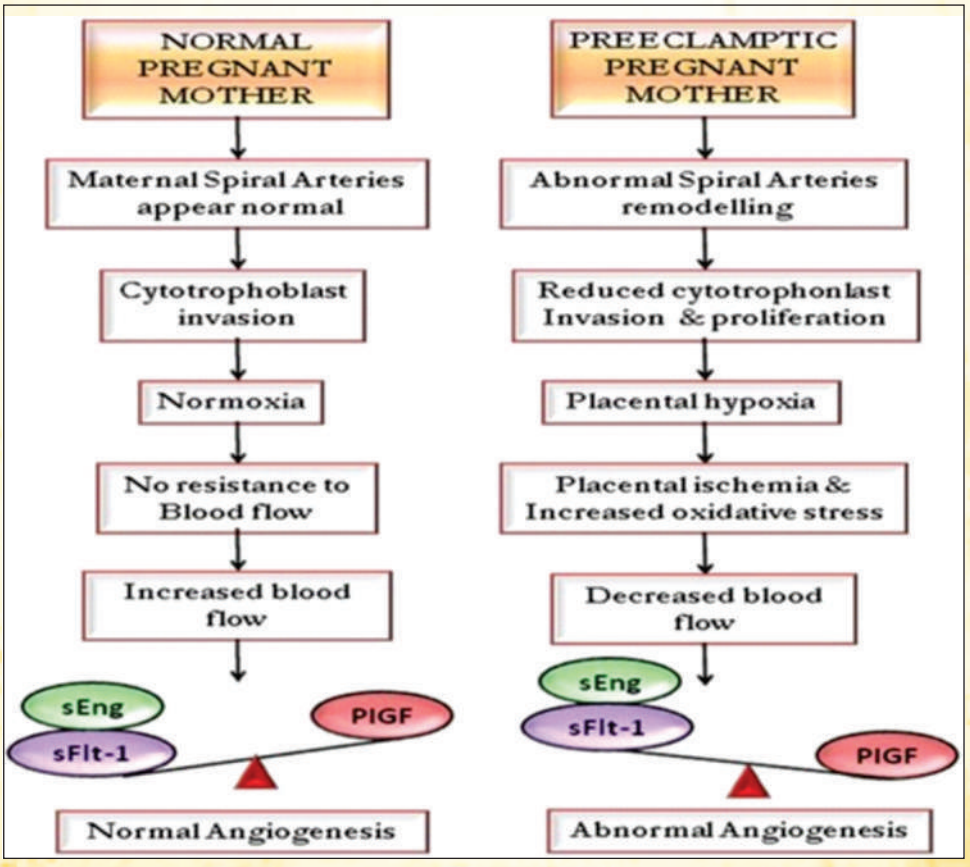
Hypertensive disorders of pregnancy affect 10% of pregnancies and can result in considerable maternal and fetal morbidity and mortality. Women may have chronic hypertension, or develop hypertension during pregnancy. Hypertension in pregnancy is defined as a SBP of ≥ 140 mmHg ; DBP 90 mmHg or above. Severe hypertension is classified as a systolic blood pressure 160 mmHg or above, or a diastolic blood pressure 110 mmHg or above after 20 weeks gestation. This umbrella definition includes chronic hypertension, gestational hypertension and preeclampsia (de novo or superimposed on chronic hypertension).

Hypertensive disorders of pregnancy can be divided into four categories:

- chronic hypertension
- gestational hypertension
- pre-eclampsia and eclampsia
- pre-eclampsia superimposed on chronic hypertension.

The 2019 NICE guidelines classify a woman at **high risk** of preeclampsia if there is a history of hypertensive disease during a previous pregnancy or a maternal disease including chronic kidney disease, autoimmune diseases, diabetes, or chronic hypertension; at **moderate risk** if they are nulliparous, ≥40 years of age, have a body mass index (BMI) ≥ 35 kg/m, a family history of preeclampsia, a multifoetal pregnancy, or a pregnancy interval of more than 10 years. The presence of one high risk factor, or two or more moderate risk factors, is used to help guide aspirin prophylaxis.

PATHOPHYSIOLOGY:



Renal

- proteinuria – spot urine protein:creatinine ratio : 30 mg/mmol or more
- acute kidney injury with serum creatinine >90 micromol/L
- oliguria: <80 mL/4 hours

Haematological

- thrombocytopenia – platelet count <100,000/microlitre
- haemolysis
- disseminated intravascular coagulation

Hepatic

- raised serum transaminases (alanine aminotransferase or aspartate aminotransferase >40 IU/L)
- severe right upper quadrant or epigastric pain

Neurological

- eclamptic convulsion
- sustained clonus (hyperreflexia is commonly found and not diagnostic)
- severe headache
- visual disturbance – photopbia, scotomata, cortical blindness
- stroke
- **Pulmonary oedema Uteroplacental dysfunction** with fetal growth restriction, abnormality on doppler imaging of the umbilical artery, stillbirth**Complications:**
  - Fetal growth restriction: Preeclampsia affects the arteries carrying blood to the placenta. If the placenta doesn't get enough blood, the baby may receive inadequate blood and oxygen and fewer nutrients.
  - Preterm birth: Preeclampsia may lead to an unplanned preterm birthdelivery before 37 weeks. Planned preterm birth is a primary treatment for preeclampsia.
  - Placental abruption: Preeclampsia increases risk of placental abruption.
  - Hemolysis elevated liver enzymes and low platelet count (HELLP) syndrome : This severe form of preeclampsia affects several organ systems. HELLP syndrome is life-threatening to the mother and baby.
  - Eclampsia : Eclampsia is the onset of seizures or coma with signs or symptoms of preeclampsia. Eclampsia can happen without any previously observed signs or symptoms of preeclampsia.
  - Other organ damage : Preeclampsia may result in damage to the kidneys, liver, lung, heart, or eyes, and may cause a stroke or other brain injury. The amount of injury to other organs depends on severity of preeclampsia.

Prediction and prevention:

Numerous options available in first trimester for predicting risk of pre-eclampsia. These include using maternal blood pressure and risk factors or combined prediction models using additional tests of placental growth factor and doppler imaging of the uterine artery. These tests are readily available and consideration needs to be given to how they could be integrated into antenatal care.

Although there is no method of preventing pre-eclampsia, aspirin is recommended for women considered to be at high risk. The ASPRE trial combined first trimester screening and found a 62% reduction in preterm pre-eclampsia at less than 37 weeks gestation in women who took aspirin 75-150 mg daily. Women at high risk require early obstetric review, because starting aspirin before 16 weeks is most effective. If started for pre-eclampsia prophylaxis, aspirin should be continued until 36 weeks gestation. Aspirin reduces the risk of preterm birth, fetal growth restriction and fetal death, but may increase postpartum bleeding. Women with an inadequate dietary calcium intake may have an increased risk of pre-eclampsia. They should aim to achieve the recommended daily allowance (1000 mg daily).

Management of PIH:
Management involves close maternal and fetal surveillance.
Antihypertensive drugs that can be safely used in pregnancy

Antihypertensive drug*	**Class/action**	**Dose**	**Adverse effects**
Labetalol	Beta blocker	100 mg twice a day – 400 mg three times a day	Bradycardia, bronchospasm, headache
Nifedipine controlled release	Calcium channel antagonist	30 mg daily – 60 mg twice a day	Headache (first-dose effect), flushing, tachycardia, peripheral oedema
Methyldopa	Central action	250 mg twice a day – 750 mg three times a day	Depression, dry mouth, sedation, rarely haemolysis and hepatitis
Hydralazine	Vasodilator	25 mg three times a day – 50 mg three times a day	Flushing, headache, lupus-like syndrome
Prazosin	Alpha blocker	0.5 mg twice a day – 5 mg three times a day	Orthostatic hypotension

Severe hypertension urgent management is indicated and drugs are required to rapidly lower blood pressure. An infusion of magnesium sulphate can be considered as it reduces the rate of seizure by 50%

Urgent treatment of severe hypertension* in pregnancy

Drug	Dose	Route	Onset of action	Adverse effects
Hydralazine	5–10 mg	Intravenous bolus repeated after 20 min if blood pressure remains >160/110 mmHg	20 min	Flushing, headache, nausea, hypotension, tachycardia
Labetalol	20–80 mg	Intravenous bolus over 2 min, repeat after 10 min if blood pressure remains >160/110mmHg	5 min	Bradycardia, hypotension, fetal bradycardia
Labetalol	200 mg	Oral	30–45 min	Bradycardia, bronchospasm, headache
Nifedipine	10 mg	Oral	30–45 min	Headache, flushing

* Severe hypertension is 160/110 mmHg or above.

Seizure prophylaxis and treatment of eclampsia

Drug	Dose	Route	Onset of Action	Adverse effects
Magnesium sulphate	4 g	Intravenous bolus over 20 min followed by 1 g/hour infusion, typically continued for 24 hours	20 min	Flushing, respiratory depression Caution in renal impairment as magnesium is excreted renally and toxicity may occur

Obstetric Management: considering maternal safety we need to deliver the baby taking maturity into consideration if gestational age is ≥37 weeks we go for induction of labor.

Postpartum management : hypertension typically resolves within 12 weeks for women with gestational hypertension or pre-eclampsia. If this does not occur, consideration should be given to investigation for primary or secondary hypertension. Regular monitoring of blood pressure postnatally should occur, with down titration of antihypertensive drugs when the systolic blood pressure drops below 120 mmHg. For women with chronic hypertension, the decision to return to their usual antihypertensive treatment will depend on its compatibility with breastfeeding. It would be reasonable to transition them back to their usual treatment early.

The antihypertensive drugs that are safe in pregnancy are also safe in breastfeeding. Methyldopa is associated with a 30% risk of depression, it is stopped postpartum. ACE inhibitors, particularly enalapril, have very low concentrations in breast milk and are often used during lactation. Angiotensin receptor blockers are not recommended.

Gestational hypertension and pre-eclampsia are associated with a two- to fourfold increase in the future risk of cardiovascular disease. Women may develop hypertension, stroke, diabetes, venous thromboembolic disease or chronic kidney disease. Cardiovascular events such as stroke may occur in middle age. Given these risks, and the cumulative risks associated with several pregnancies complicated by severe pre-eclampsia, or preterm delivery, preconception counselling before future pregnancies is recommended.

Women with a history of hypertension in pregnancy require indefinite follow-up. They are recommended to have annual reviews of blood pressure, fasting lipids and blood glucose. Counselling on a healthy lifestyle and diet, maintenance of an optimal BMI, smoking cessation and regular exercise are essential for optimising long-term health outcomes.

CONCLUSION: Delivery of a healthy baby and maintainance of safe course of pregnancy is the key challenge. Despite the differences in guidelines, there appears to be consensus that severe hypertension and non-severe hypertension with evidence of end-organ damage need to be controlled.

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Obstetric Management: considering maternal safety we need to deliver the baby taking maturity into consideration if gestational age is ≥37 weeks we go for induction of labor.

Postpartum management : hypertension typically resolves within 12 weeks for women with gestational hypertension or pre-eclampsia. If this does not occur, consideration should be given to investigation for primary or secondary hypertension. Regular monitoring of blood pressure postnatally should occur, with down titration of antihypertensive drugs when the systolic blood pressure drops below 120 mmHg. For women with chronic hypertension, the decision to return to their usual antihypertensive treatment will depend on its compatibility with breastfeeding. It would be reasonable to transition them back to their usual treatment early.

The antihypertensive drugs that are safe in pregnancy are also safe in breastfeeding. Methyldopa is associated with a 30% risk of depression, it is stopped postpartum. ACE inhibitors, particularly enalapril, have very low concentrations in breast milk and are often used during lactation. Angiotensin receptor blockers are not recommended.

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Resistant Hypertension (RH)

Dr. Tapan Kumar, MD (Medicine), DNB (Cardiology)

Introduction

Hypertension is the world's leading risk factor for cardiovascular disease (CVD), stroke, disability, and death. Even with steady improvement during the past 30 years in hypertension awareness, treatment, and control rates, a large proportion of hypertensive adults, despite conscientious clinical management, still fail to achieve their recommended blood pressure (BP) treatment targets on three antihypertensive medications or require ≥4 medications to achieve their targets. These individuals, designated as having treatment-resistant hypertension, remain at increased risk for target organ damage, morbidity, and mortality despite ongoing antihypertensive drug therapy.

Definition :
Resistant hypertension is defined as BP that remains above goal (target BP <130/80 mm Hg as per ACC/AHA guidelines[1,2] and <140/90 as per ESC/ESH guidelines) despite three antihypertensive drugs of different classes, with one of them being a diuretic appropriate for renal function and all the drugs are used at maximally tolerable doses.

Resistant hypertension has to be differentiated from pseudo resistance or white coat effect. Adherence to therapy has to be ensured and secondary causes of hypertension have to be excluded before diagnosing RH.

Prevalence :
With the new target BP given by ACC/AHA guidelines which is defined as systolic blood pressure (SBP) <130 mm Hg and diastolic blood pressure (DBP) <80 mm Hg for all adults <65 years of age,[1,2] RH was seen in 19.7% (in USA) with almost 3% of adults taking thiazide like diuretic and 9% taking mineralocorticoid receptor antagonist.[3] In India, according to a study done in JIPMER institute between December 2018 and February 2020, RH was seen in 11% of individuals according to the new target BP definition.

The World Health Organization (WHO) report states that 1.28 billion people between the age of 30 and 79 years are affected by hypertension worldwide and two-thirds of them are from low to middle income countries. The global prevalence is 34% in men and 32% in women, the prevalence being higher in women following menopause.[4]

Pathogenesis :
The pathophysiology of RH is not fully understood. RH has been associated with three major underlying mechanisms which include-fluid retention, sympathetic system activation, and arterial stiffness. Increased aldosterone production, impaired renal natriuresis and excessive salt consumption all contribute to excessive fluid retention.[5]

Clinical substrates :
There are certain specific substrates associated with higher incidence of RH as listed in Table – 1.[6]

TABLE- 1

Black race	Metabolic derangements e.g., hyperuricemia
Male sex	Hyperaldosteronism
Older age	Higher Framingham 10-year risk score
obesity	Obstructive sleep apnoea
Diabetes	Peripheral and carotid atherosclerosis
Chronic kidney disease	Impaired endothelial dysfunction

Diagnosis :

The definition of RH which is previously stated should be fulfilled. The primary role of physician to take a multistep approach to rule out false positive cases.

1. First Step: Rule Out Pseudoresistance[2,7]

The common causes include :

I. Inaccurate measurement of blood pressure- The apt technique to measure BP is to make the patient sit with back supported and feet on the floor for minimum of 5 minutes and then check the BP with appropriate size cuff using either a sphygmomanometer or automated BP machine
II. Poor adherence to antihypertensive therapy.
III. Suboptimal antihypertensive therapy.
IV. Poor adherence to lifestyle and dietary approaches to lower blood pressure.
V. White coat hypertension – is described as a rise in BP when an individual comes to the clinic. The prevalence ranges between 15-40% in outpatients. According to European guideline is defined as office systolic/diastolic BP of 140/90 mm of Hg or more and 24 hour BP is < 130/80 mm of Hg.

2. Second Step: Assessment for Secondary Causes of Hypertension Almost 5-10% of RH patients are associated with secondary hypertension. It is not feasible to screen all patients for secondary hypertension. The common causes are primary aldosteronism, renal parenchymal disease and renovascular disease, and less frequently encountered ones are Cushing syndrome, pheochromocytoma or coarctation of the aorta.[8] comprehensive clinical examination followed by relevant laboratory and radiological tests would identify a cause for secondary hypertension.[9]
3. Third Step: Exclude Interfering Substances.

There are certain drugs and substances which interfere with the regulation of BP and can result in increased BP, these substances/factors need to be excluded (Table 2).[10,11]

TABLE 2: The list of interfering substances and its effect on BP studies.

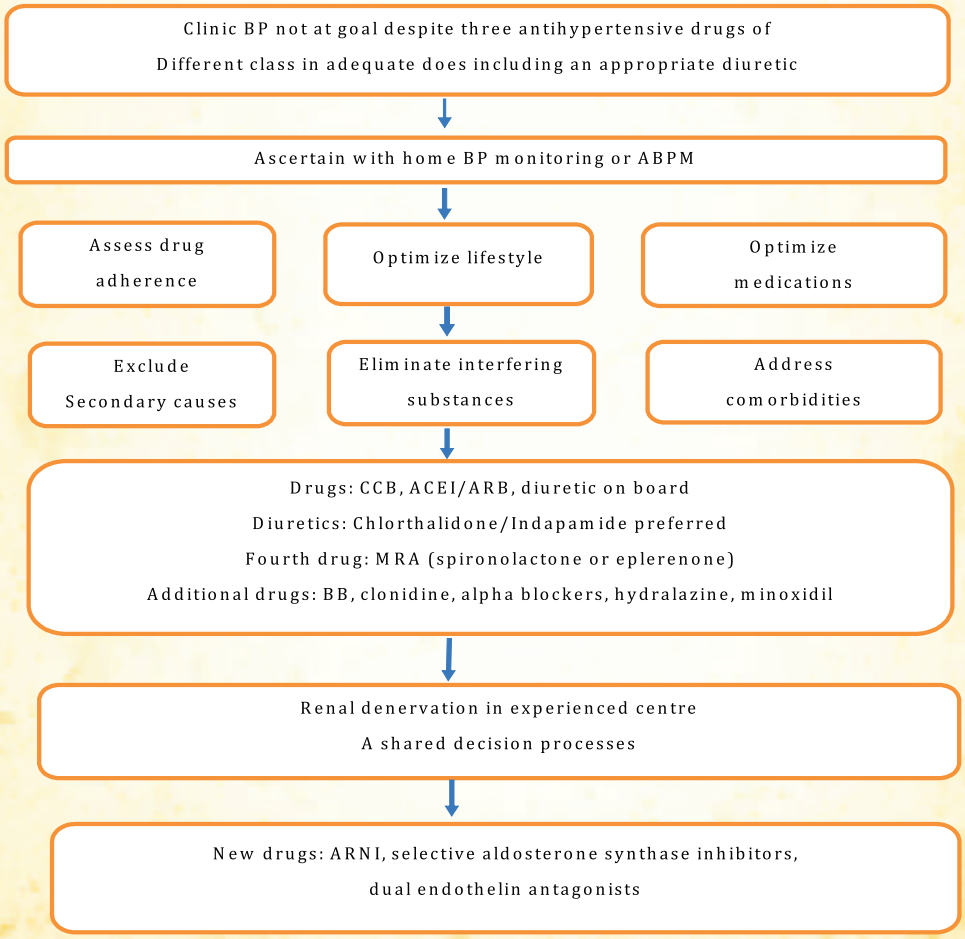
Drugs	NSAID
	Selective COX-2 inhibitors
	Sympathomimetics such as nasal decongestants, OCPs, glucocorticoids, Erythropoietin
	Cyclosporine
Substance abuse	Cocaine and amphetamine
	Alcohol
	Oral tobacco
Diet	Salt intake

Treatment :

The treatment goal is to maintain BP at <130/80 mm Hg according to 2018 AHA guidelines[2] In patients with RH, BP should be reduced <140/90 mm Hg and <130/80 mm Hg, if tolerated.[8] In patients with CKD according to kidney disease: Improving Global Outcomes (KDIGO) recommendation the target BP should be 120 mm Hg systolic or less.[12]

1. Optimization of nonpharmacologic intervention and pharmacological intervention- This includes lifestyle modification in the form of weight reduction, daily exercise, and dietary changes in the form of consumption of food rich in fiber, low salt, less fat, increased potassium intake, smoking cessation, and reduction in alcohol intake. These measures need to be emphasized, enhanced, and reinforced, and this in turn may reduce the number of drugs required to achieve BP control.[13]
2. Optimization of pharmacotherapy - Commonly used antihypertensive drugs in these patients are calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARBs), and diuretics at maximally tolerated dose.[14]
   A mineralocorticoid receptor antagonist (MRA) such as spironolactone has shown significantly favourable effect in controlling BP in RH in ASPIRANT trial. Once a diagnosis of RH is made, a fourth drug is MRAs.[15] In selective cases Beta blockers, alfa blocker, centrally acting alpha adrenergic receptor agonist or direct vasodilators like Hydralazine or Minoxidil can be used judiciously.

Management of resistant hypertension (stepwise approach)



1. Management of comorbidities-Comorbidities are frequent in patients with RH. The common ones are obesity, OSA, and heart failure with preserved ejection fraction. These should be managed appropriately.[16]
2. Device based therapy - Human sympathetic nervous system dysfunction plays an important role in the development and progression of hypertension.[17] Sympathectomy has demonstrated dramatic improvement in BP control and accompanying reduction in cardiac size in different trials.[18] Over the period different approach has been developed to reduce sympathetic outflow and includes.
   I. Catheter-based ablation of renal sympathetic nerves - Different trails has shown mixed result. Post hoc analyses from SYMPLICITY HTN-3 suggest that BP fell in patients with more complete ablation compared with those with lesser degrees of renal nerve ablation.[19] In addition, the DENERHTN trial (Renal Denervation for Hypertension) recently demonstrated a statistically significant reduction in daytime ambulatory SBP.[20]
   II. Electrical stimulation of carotid baroreflex system - This modality electronically activates baroreceptors that signal the brain to orchestrate a multisystemic response and decrease sympathetic overactivity. CALM-FIM_EUR has recently demonstrated in patients with RH that endovascular baroreflex amplification with the MobiusHD device substantially lowered BP with an acceptable safety profile.[21]
   In summary the role of device-based sympatholytic treatments, as with renal denervation and baroreceptor stimulation, awaits clarification.

Prognosis of RH :

Observational studies using the 2008 criteria have shown that patients with RH are at higher risk for poorer outcomes compared with patients without RH.[22] In a retrospective study of >200 000 patients with incident hypertension, those with RH were 47% more likely to suffer the combined outcomes of death, myocardial infarction, heart failure, stroke, or CKD over the median 3.8 years of follow-up.[22]

CONCLUSION :

Resistant hypertension carries a higher cardiovascular and renal risk. While pathophysiology of RH needs to be understood better and, more effective therapeutic strategies have to be developed, it is important in the meantime for the clinician to avoid "clinical inertia", ensure medication adherence, exclude pseudoresistant hypertension, and detect secondary hypertension. Therapeutic lifestyle measures and drug therapy have to be optimized using appropriate diuretics, MRAs, and other drugs. Renal denervation therapy looks promising, has a role and its use should be a shared decision process.

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" HYPERTENSION AND KIDNEY AND VICE VERSA"

Abstract :
Hypertension and chronic kidney disease are closely linked. Patients with chronic kidney disease have hypertension almost universally and uncontrolled hypertension accelerates the decline in kidney function. The pathophysiology of hypertension in chronic kidney disease is complex, but is largely related to reduced nephron mass, sympathetic nervous system overactivation, involvement of the renin-angiotensin-aldosterone system, and generalized endothelial dysfunction. Consensus guidelines for blood pressure targets have adopted a blood pressure <120/80 mm Hg in native chronic kidney disease and <130/80 mm Hg in kidney transplant recipients. Guidelines also strongly advocate for renin-angiotensin-aldosterone system blockade as the first-line therapy. It is therefore important that we continue to investigate the hypertension/renal relationship to better understand the determinants of essential hypertension and to prevent a major cause of end-stage renal disease.
Keywords: hypertension, chronic kidney disease, masked hypertension, ambulatory blood pressure monitor

Introduction

Hypertension is a common finding in individuals with chronic kidney disease (CKD), afflicting 65% to 85% of patients and increasing as kidney function declines.1 The causes of CKD, including salt retention, overt hypervolemia, sympathetic overactivity, and endothelial dysfunction, contribute to this high prevalence. Moreover, uncontrolled hypertension has a graded relationship with cardiovascular disease and remains a leading cause of cardiac morbidity and mortality. In this article, we review the classification of blood pressure (BP), goals of BP reduction, and hypertension management in those with CKD.

ETIOLOGY OF HYPERTENSION IN CKD :

Hypertension is ubiquitous in the chronic kidney disease. Impaired salt excretion leads to increased extracellular fluid volume and consequent hypertension in renal disease. It is assumed that the excess salt and water retention increases the blood flow to the tissues, which sets in motion the phenomenon of autoregulation. The tissue arterioles vasoconstrict, under the influence of various mediators to decrease the excessive blood flow. The resulting vasoconstriction increases the peripheral vascular resistance, resulting in hypertension. The kidney and central nervous system in integrated manner play role in development of hypertension in chronic kidney disease. Recently, more light has been shed on the multitude of factors and pathophysiologic mechanisms that lead to hypertension in the renal disease. The level of blood pressure is most likely determined by the level of the peripheral vascular resistance and volume status in combination. If the peripheral vascular resistance is not appropriately lowered in the face of hypervolemia, hypertension results.

BP Classification :

An office blood pressure (OBP) of 140/90 mm Hg is thought to correlate with a 24-hour average ambulatory blood pressure measurement (ABPM) of 130/80 mm Hg and a mean home BP of 135/85 mm Hg.2 With the change in hypertension diagnosis thresholds in the 2017 American Heart Association/American College of Cardiology (AHA/ACC) guidelines, an OBP < 120/80 mm Hg is still considered normal, but an OBP of 120–129/ <80 mm Hg is elevated, and an OBP ≥ 130/80 mm Hg is consistent with hypertension.2 An OBP reading of 130/80 mm Hg is thought to correlate with a 24-hour average reading of 125/75 mm Hg, and the recommended 24-hour ABPM targets are: 24-hour mean BP ≤ 125/75 mm Hg, a daytime BP ≤ 130/80 mm Hg, and a nighttime BP ≤ 110/65 mm Hg with appropriate nocturnal dipping.2 When both OBP and ABPM are available, individuals may be classified into one of four groups: controlled (normal office and ABPM), white coat hypertension (elevated office and normal ABPM), masked hypertension (normal office and elevated ABPM), and sustained hypertension (elevated office and ABPM).

Masked hypertension (30–60%) in CKD has a higher prevalence compared to the general population (10–25%).3 In the Chronic Renal Insufficiency Cohort (CRIC) study, 1,502 participants with CKD had ABPM profiles available for review. Masked hypertension was associated with more cardiovascular events and a more rapid decline in kidney function after a mean follow-up of 6.72 years.4 Increasing use of ABPM or home blood pressure monitoring (HBPM) in clinical CKD practice will help confirm treatment responses and perhaps better characterize risk for future target organ damage.

Proper BP Measurement Technique :

"Standardized" Office Blood Pressure Measurement

Routine in-office BP measurements served as the traditional method for hypertension diagnosis and treatment decisions until recent recommendations favoured implementation of standardized practices.2-5 Standardized OBP measurements should include: (1) appropriate cuff size (bladder should encircle 80% of the bare arm); (2) proper positioning (patient's arm should be supported at the level of the heart while seated with back supported, legs uncrossed, and both feet flat on floor); (3) patient preparation (patient should relax for 5 minutes, abstain from caffeine, exercise, and smoking in the preceding 30 minutes, and ensure his or her bladder is empty; and (4) multiple measurements (≥2 readings at least 1–2 minutes apart) in both arms while using a validated device that is appropriately calibrated.2-5 Importantly, these measurements should be done without the white coat provider being in the room.

Many studies have demonstrated the lack of correlation between routine and standardized OBP measurements.6-7-8 Agarwal et al. compared routine versus standardized BP measurements in 275 participants from the Systolic Blood Pressure Intervention Trial (SPRINT). The mean systolic blood pressure (SBP) and diastolic blood pressures (DBP) in routine office measurements were 12.7 and 12 mm Hg higher, respectively, than the standardized measurements performed on the same day.8 Moreover, studies have implicated poor proficiency by medical staff in following standardized BP measurement protocols, therefore re-training should occur on a regular basis.9-10-11

Ambulatory BP Monitoring :

Out-of-office BP measurements should complement standardized OBP measurements and include both ABPM and HBPM. Briefly, ABPM involves the application of an appropriately sized BP cuff to the nondominant arm with BP measurements taken every 20 to 30 minutes for a 24- to 48-hour period. While following their normal daily routine, individuals are instructed to keep their arm still during measurements and to keep a diary of sleep and wake periods.12 ABPM provides a more robust estimate of the 24-hour, daytime and nighttime readings, including BP variables such as dipping and BP decline > 10% during sleep. Both nocturnal hypertension and non-dipping status are prevalent in CKD and are associated with higher risk of cardiovascular morbidity and mortality.13

Goals of BP Reduction and Consensus Targets :

The optimal BP targets for CKD hypertension treatment have evolved as new research accumulates .14 In September 2015, the randomized SPRINT trial stopped before completion—after the interim analysis showed the group assigned to an intensive systolic BP goal < 120 mm Hg had a 25% lower cardiovascular disease risk and 27% lower all-cause mortality compared with the standard group assigned to systolic BP < 140 mm Hg.15 Subsequent guidelines from the AHA/ACC in 2017 recommended a BP goal of <130/80 mm Hg in patients with CKD and those with increased cardiovascular risk. The AHA/ACC chose 130 mm Hg instead of BP < 120 mm Hg due to concerns that routine clinic visit BP measurements are unlikely to be measured in a standardized approach such as that used in the SPRINT trial.16 In addition, there were more hypotensive and acute kidney injury events requiring emergency department visits among participants in the intensive group. Citing these concerns, the 2018 European Society of Hypertension and European Society of Cardiology (ESH/ESC) guidelines recommended a goal of SBP between 130 and 139 mm Hg in CKD hypertension. Newer recommendations from the 2021 Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines have favored more intensive treatment to a SBP of < 120 mm Hg.5 This recommendation followed subgroup analysis that tested the two BP targets (SBP < 120 vs SBP < 140 mm Hg) among 2,600 CKD patients in SPRINT and showed lower composite cardiovascular outcome (HR 0.81; 95% CI, 0.63-1.05) and lower mortality (HR 0.72; 95% CI, 0.53-0.99) after median follow-up of 3.3 years in the intensive arm.18 Fortunately, kidney outcomes such as the development of end-stage kidney disease (ESKD) or a greater than 50% reduction in estimated glomerular filtration rate (eGFR) were not more pronounced between the two groups, with one exception: a more pronounced eGFR decline in the intensive group in the first 6 months (-0.47 vs -0.32 mL/min/1.73m^2/year; $P < .03$), attributed to an acute hemodynamically mediated decline in the renal blood flow, without further appreciable change over the remainder of the study.18

The SPRINT trial differed from three previous trials comparing BP targets in CKD due to heterogeneity in primary outcomes. The Modification of Diet in Renal Disease (MDRD) trial, the African American Study of Kidney Disease and Hypertension (AASK) trial, and the Blood-Pressure Control for Renoprotection in Patients with Non-diabetic Chronic Renal Disease (REIN-2) trial used kidney outcomes (ESKD and reduced eGFR) as primary outcomes instead of cardiovascular outcomes.19,20,21 These studies had few cardiovascular and mortality events, making data synthesis challenging for evidence-based practice guidelines. A meta-analysis performed by Malhotra et al. later examined mortality among CKD subgroups, including these three trials, and showed a lower mortality in the intensive BP control group (HR 0.86; 95% CI, 0.76-0.97; $P = .01$).22 However, intensive BP targets among all four studies showed no benefit for reducing kidney outcomes.23 Taken together, an intensive BP target seems appropriate for reductions in cardiovascular complications, particularly given the higher cardiovascular risk in people with CKD.

The 24-hour ABPM can help ensure BP targets are met by identifying two specific BP phenotypes in hypertensive CKD patients: masked uncontrolled hypertension (MUCH) and white coat hypertension (WCH). MUCH, defined as normal clinic blood pressures but uncontrolled out-of-office blood pressures, is grossly underrecognized. Up to 60% of clinically normotensive CKD patients are uncontrolled out of the office and possibly face increased cardiovascular (CV) risk and accelerated kidney function decline.24,25 Individuals with WCH have uncontrolled clinic blood pressures but normal out-of-office blood pressures and represent up to 30% of clinically uncontrolled hypertensive CKD patients. The diagnostic failure of these two phenotypes have led to under- and overtreatment, respectively.12 Ku et al. showed the clinical relevance of these conditions among 610 participants in the AASK trial, which revealed a U-shaped association between clinic and ambulatory SBP difference and an increased mortality but no ESKD risk.26

Treatment :

Non-pharmacologic

Dietary interventions and daily exercise are adjuncts to pharmacologic therapies and should be the first step to hypertension management. The Dietary Approaches to Stop Hypertension (DASH) diet, which Favors fruits and vegetables over saturated fats, has led to modest BP declines in hypertensive individuals.[27,28] Reducing sodium intake to less than 2 grams daily may lower SBP by 5 to 10 mm Hg, and increasing potassium intake to more than 3 grams daily may be additive in those who are salt sensitive.28,29 However, dietary sodium reduction should not be a universal recommendation as it will have little impact on BP in those with CKD and salt-losing nephropathies.30 More importantly, high potassium content of many of these BP-friendly foods may even provoke hyperkalemia.

Regular exercise should be encouraged to help lower blood pressure and improve CV health in CKD, not to mention its beneficial effects on quality of life. Prior studies suggest that exercise implementation may improve eGFR at 12 months or slow CKD progression.31,32 This effect on eGFR, however, was inconsistent in newer studies.33,34,35,36 To align guidelines, KDIGO and AHA/ACC now recommend "a total duration of 150 minutes of moderate intensity physical activity (resistance or aerobic) per week."5,37 Individuals with CKD that have limited exercise ability due to their comorbidities should perhaps have this exercise target modified accordingly. Weight loss of more than 5 kg can enhance the favourable exercise benefits by lowering the SBP by 5 mm Hg.38 For those with obstructive sleep apnoea, a recent meta-analysis showed nocturnal continuous positive airway pressure treatment can have a modest reduction in SBP by up to 5 mm Hg in the most severe cases.39 This is highly relevant as sleep disturbances and sleep apnoea are extremely common in CKD.40

Pharmacologic :

Antihypertensive medications are almost always needed in patients with CKD. When initiating antihypertensive medication, one should consider starting two drugs from different classes, particularly in those with Stage 2 hypertension (≥ 140/90 mm Hg).2 The typical primary agents are renin-angiotensin-system inhibitors (RAAS), which include angiotensin-converting enzyme inhibitors (ACEi), and angiotensin receptor blockers (ARB), as well as calcium channel blockers (CCB) and diuretics. Beta blockers, on the other hand, lack evidence of benefit, increase risk of new-onset type 2 diabetes, and perhaps should be avoided as first-line therapy unless indicated for cardiovascular disease.41,42 ACEi and

ARBs are the mainstays of CKD hypertension management, particularly in those with albuminuria (urine albumin > 300 mg/d).43 Ruggenenti et al. showed ramipril's salutary effect in slowing eGFR decline among 166 proteinuric patients (> 3 g/d) compared with placebo (0.51 ± 0.09 vs 0.76 ± 0.10 mL/min/1.73 m^2 per month, $P < .03$) in the Gruppo Italiano di Studi Epidemiologici in Nefologia (GISEN) study, or Ramipril Efficacy In Nephropathy (REIN) follow-up study.44 A meta-analysis of 119 randomized controlled trials showed ACEi and ARBs reduced kidney failure by 39% and 30%, and reduced major cardiovascular events by 18% and 24%, respectively, versus placebo.45 The combination of ACEi and ARBs is discouraged because it is associated with higher rates of acute kidney injury (AKI) and hyperkalemia.46 In the ESKD population, dosing adjustment should be considered in those without residual kidney function. For example, lisinopril dosing should be three times weekly instead of daily, preferably after hemodialysis due to potential for being removed with dialysis.47There is less consensus concerning the optimal second-line antihypertensives. Dihydropyridine calcium channel blockers, such as amlodipine, are commonly used as an adjunct to an ACEi or ARB on the basis of their synergistic ability to reduce BP.48 There is also evidence to suggest nondihyropyridine CCBs (eg, verapamil and diltiazem) have a more pronounced antiproteinuric effect and may be a reasonable therapeutic option for proteinuric CKD despite maximal doses of ACEi or ARBs.49 CCBs such as nifedipine should be avoided particularly in those with proteinuria as they may transmit systemic pressures to the glomerular space more readily. Diuretics are also a reasonable second-line therapy choice, especially in those with reduced kidney function and hypervolemia. The prevailing dogma has been that thiazide diuretics lose effectiveness at a lower GFR, and guidelines have recommended changing from a thiazide to a loop diuretic at GFR values below 30 mL/min/1.73 m^2.50 However, the evidence against thiazide use in advanced CKD is weak. A recent randomized control trial showed that, for patients with stage 4 CKD, the addition of chlorthalidone to traditional antihypertensives reduced SBP by 11 mm Hg (95% CI, -13.9 to -8.1) at 12 weeks.51 Chlorthalidone and indapamide are preferred over hydrochlorothiazide due to their longer half-lives and higher potency, and reductions in GFR may be met with increased drug dosages.52 Resistant hypertension, defined as uncontrolled BP despite using three antihypertensive medications, one of which is a diuretic, is common with CKD.53 Prior to diagnosing an individual with resistant hypertension, clinicians should confirm accurate clinic BP measurements as well as use out-of-office BP measurements to exclude pseudo-resistance. Mineralocorticoid receptor antagonists (MRA) such as spironolactone and eplerenone have been found to reduce BP in resistant hypertension.54 However, hyperkalemia may be a concern, particularly when added to a background of ACEi or ARBs in the setting of reduced GFR, as seen with advanced CKD. AMBER trial results showed that use of the oral potassium binder patiromer enabled more patients with resistant hypertension and CKD to continue spironolactone.55 In addition, the recent FIDELIO trial showed that treatment with the nonsteroidal MRA finerenone had lower risks of CKD progression and lower CV events in those with type 2 diabetes and CKD.56Among patients with CV disease and CKD, there may be indications for drugs such as beta-blockers, though dual alpha and beta blockade may be superior in BP reduction due to its additional vasodilatory effect.57 Sodium-glucose cotransporter 2 inhibitors also have been associated with significant reductions in home BP in individuals with type 2 diabetes mellitus, as well as patients with resistant hypertension, and have shown a laudable reduction in kidney disease progression and CV mortality.58

Conclusion :

Hypertension management in CKD lowers incident CV risk and reduces kidney disease progression. Existing guidelines have moved closer to consensus BP targets and place more emphasis on accurate BP measurements and more dependence on home and ABPM. Pharmacologic therapies offer varying degrees of risk reduction in CKD, and lifestyle interventions should be encouraged to augment these health benefits. Most importantly, patient engagement with out-of-office BP measurements, as well as more informed and shared decision making, will lead to long-term successes.

Key Points

- The goal blood pressure for hypertension management in chronic kidney disease is < 120/80 mm Hg to reduce cardiovascular disease risk.
- Masked uncontrolled hypertension is highly prevalent in CKD patients, and out-of-office measurements such as home or ambulatory blood pressure monitoring are needed for diagnosis.

- Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are first-line for hypertension treatment in proteinuric CKD.
- Thiazide and thiazide-like diuretics have a role in hypertension management even in advanced kidney disease.

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Treatment of Isolated systolic hypertension

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Isolated systolic hypertension is common in the elderly population. SBP has a better prediction for the risk of cardiovascular disease as compared to DBP. Hence, treatment of isolated systolic hypertension is beneficial to reduce all-cause mortality and cardiovascular risk, and stroke. The optimal SBP remained unclear, but an SBP goal of less than 140 mmHg and keeping DBP at 70 mmHg or higher are considered appropriate in most patient populations.Randomized controlled trials have shown that thiazide-like diuretics and CCBs are the preferred first-line agents in reducing the risk of stroke and other morbidities in patients with isolated systolic hypertension.The dose of the single oral antihypertensive agent should be titrated to the maximum before initiating a second oral antihypertensive agent.ACEi or ARB is often used in the patient with compelling indications such as heart failure reduced ejection, post-myocardial infarction, diabetes, or chronic kidney disease.A combination of either ACEi or ARB with CCB or a thiazide-like diuretic can be consideredIt is important to note that ACEi should never be used concomitantly with ARB under any circumstances.Blood Pressure Goalsthe optimal SBP in patients with hypertensive disorder remained a controversial topicSHEP and HYVET trials have shown significant benefits of antihypertensive treatment in patients with the goal of SBP less than150 mmHg.[1]The valsartan in elderly isolated systolic hypertension (VALISH) trial showed no significant difference in the primary outcome of sudden death, fatal or nonfatal myocardial infarction and stroke, heart failure death, or other cardiovascular death among patients with strict (less than 140 mmHg) and moderate (140 to 150 mmHg) SBP control.[2]The most recent systolic blood pressure intervention trial (SPRINT) has shown that an intensive SBP target of less than 120 mmHg improved the cardiovascular outcomes and the overall survival compared to the standard SBP target of 135 to 139 mmHg.[3]However, aggressive SBP lowering may be harmful in the elderly and incite more adverse effects such as hypotension, end-organ hypoperfusion (causing acute kidney injury, and intracranial hypoperfusion which may link to cognitive decline), and polypharmacy.It is suggested that a goal blood pressure of less than 130/80 mmHg is appropriate as long as the patient tolerates it.Otherwise, less than 140/90 mmHg is considered reasonable in patients who are in the elderly population and patients with labile blood pressure or polypharmacy.Management strategies should always be patient-centered, with the aim of optimizing blood pressure control and avoiding polypharmacy, especially in the elderly. J-curve Phenomenon [4] [5]Various studies have shown a J-curve association between blood pressure with risk of myocardial infarction and death.Patients with isolated systolic hypertension who receive antihypertensive treatment may precipitously drop their DBP as well.As myocardial perfusion occurs mainly during diastole, an excessive drop in DBP may increase the risk of cardiovascular disease and death Lifestyle modificationsFollowing life style modification can help to control blood pressure.1.Daily aerobic physical activity2.Diets low in salt, total fat, and cholesterol3.Adequate dietary intake of potassium, calcium, and magnesium4.Limited alcohol consumption5.Quit cigarette smoking6.Avoidance of the use of illicit drugs, such as cocaine7.Weight loss for obese patientsBecause of the numerous drugs available to treat hypertension, a consult with a cardiologist is highly recommended if there is any doubt about the

efficacy of the drug. There is ample evidence showing that when systolic hypertension is well treated, the patients have good outcomes with an interprofessional approach to care.[6][7][8] (Level 1) Refrences :1.Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA. 1991 Jun 26;265(24):3255-64. [PubMed]2.Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ., HYVET Study Group. Treatment of hypertension in patients 80 years of age or older. N Engl J Med. 2008 May 01;358(18):1887-98. [PubMed]3.SPRINT Research Group. Wright JT, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, Lewis CE, Kimmel PL, Johnson KC, Goff DC, Fine LJ, Cutler JA, Cushman WC, Cheung AK, Ambrosius WT. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015 Nov 26;373(22):2103-16. [PMC free article] [PubMed]4.Kimm H, Mok Y, Lee SJ, Lee S, Back JH, Jee SH. The J-curve between Diastolic Blood Pressure and Risk of All-cause and Cardiovascular Death. Korean Circ J. 2018 Jan;48(1):36-47. [PMC free article] [PubMed]Kang YY, Wang JG. 5. J-Curve Phenomenon in Hypertension. Pulse (Basel). 2016 Jul;4(1):49-60. [PMC free article] [PubMed]6.Benetos A, Petrovic M, Strandberg T. Hypertension Management in Older and Frail Older Patients. Circ Res. 2019 Mar 29;124(7):1045-1060. [PubMed]7.Ojji DB, Mayosi B, Francis V, Badri M, Cornelius V, Smythe W, Kramer N, Barasa F, Damasceno A, Dzudie A, Jones E, Mondo C, Ogah O, Ogola E, Sani MU, Shedul GL, Shedul G, Rayner B, Okpechi IG, Sliwa K, Poulter N., CREOLE Study Investigators. Comparison of Dual Therapies for Lowering Blood Pressure in Black Africans. N Engl J Med. 2019 Jun 20;380(25):2429-2439. [PubMed]8.Poblete F, Barticevic N, Bastías G, Quevedo D, Vargas I. [Effectiveness of a case management intervention for high blood pressure and type II diabetes in primary health care]. Rev Med Chil. 2018 Nov;146(11):1269-1277. [PubMed]

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The Double Jeopardy: Understanding the Link Between Hypertension and Diabetes

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Abstract :

Diabetes and hypertension, prevalent chronic conditions, frequently co-occur, significantly amplifying the risk of cardiovascular disease, stroke, and kidney complications. Recent data suggests a global prevalence of roughly 12% and 17% for diabetes and hypertension, respectively. Shared risk factors like obesity and unhealthy lifestyles contribute to this co-occurrence. The high blood sugar in diabetes damages blood vessels, increasing susceptibility to the narrowing caused by hypertension. This creates a vicious cycle, where uncontrolled diabetes worsens hypertension, and uncontrolled hypertension accelerates diabetic complications. Effective management strategies encompass lifestyle modifications (healthy weight, diet, exercise) and medications (blood sugar control, blood pressure control). Collaboration between patients, healthcare providers, and specialists is crucial for optimal health outcomes in individuals facing this double threat.

Introduction:

Diabetes and hypertension, also known as high blood pressure, are two of the most prevalent chronic health conditions worldwide. While concerning on their own, their frequent co-occurrence creates a dangerous synergy, significantly amplifying the risk of severe health complications. This article delves deeper into the intricate relationship between these conditions, exploring the recent epidemiological data, discussing the heightened risks associated with the double threat, and outlining current treatment strategies for effective management.

Epidemiology: A Shared Burden :

Global prevalence of hypertension According to recent WHO data.

An estimated 1.28 billion adults aged 30–79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries

- An estimated 46% of adults with hypertension are unaware that they have the condition.
- Less than half of adults (42%) with hypertension are diagnosed and treated.
- Approximately 1 in 5 adults (21%) with hypertension have it under control.
- Hypertension is a major cause of premature death worldwide.
- One of the global targets for non-communicable diseases is to reduce the prevalence of hypertension by 33% between 2010 and 2030.

The co-existence of diabetes and hypertension paints a concerning global picture. Recent data suggests a staggering prevalence. A 2021 systematic review reported that the overall prevalence of diabetes and hypertension among adults was roughly 12% and 17%, respectively. Notably, these figures represent global averages, and the prevalence can vary significantly depending on factors like geographical location, socioeconomic status, and ethnicity. For instance, a 2020 study investigating the prevalence of diabetes and hypertension in slum residents across South Asia found a concerning trend. The reported prevalence of hypertension ranged from 11.6% to 28.0%, while diabetes prevalence ranged from 8.1% to 31.5%. These findings highlight the disproportionate burden faced by low-resource communities.

Pathophysiological Link: A Vicious Cycle :

Understanding the physiological mechanisms behind the link between diabetes and hypertension is crucial for effective management. Chronically elevated blood sugar levels, a hallmark of diabetes, wreak havoc on the body's blood vessels. High glucose levels damage the delicate endothelial lining of these vessels, making them stiff and inflamed. This impaired vascular function paves the way for hypertension by increasing resistance to blood flow and promoting the narrowing of arteries due to a process called atherosclerosis. Hypertension, in turn, exacerbates the complications associated with diabetes. The persistently high blood pressure further strains the already damaged blood vessels, accelerating the process of atherosclerosis and increasing the risk of cardiovascular events like heart attack and stroke. Diabetic nephropathy, a complication of diabetes characterized by kidney damage, further complicates the picture. The kidneys play a vital role in regulating blood pressure, and their dysfunction in diabetes can contribute to uncontrolled hypertension. This creates a vicious cycle, where poorly managed diabetes worsens hypertension, and uncontrolled hypertension accelerates diabetic complications.

Beyond Cardiovascular Woes: A Multi-Organ Threat :

The detrimental effects of diabetes and hypertension extend far beyond the cardiovascular system. Diabetic retinopathy, a leading cause of blindness, is significantly worsened by poorly controlled hypertension. Hypertension can also accelerate the decline in kidney function in individuals with diabetes, potentially leading to kidney failure. Even the nervous system suffers, with an increased risk of neuropathy, a condition characterized by pain, numbness, and weakness in the extremities.

Management Strategies: A Multifaceted Approach :

Fortunately, effective strategies exist to manage both diabetes and hypertension, significantly reducing the risk of life-threatening complications.

Lifestyle modifications form the cornerstone of successful management. Maintaining a healthy weight through a balanced diet low in saturated fat, added sugars, and salt is crucial. Regular physical activity helps improve insulin sensitivity and reduce blood pressure. Effective stress management techniques are also essential, as stress can exacerbate both conditions.

Pharmacological interventions play a vital role in managing diabetes and hypertension. For diabetes, medications like insulin or oral hypoglycemic agents help control blood sugar levels. For hypertension, various classes of medications are available, with some offering additional benefits for individuals with diabetes. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are two such classes that provide dual protection by lowering blood pressure and reducing kidney damage.

Conclusion: Working Together for Optimal Health :

The co-occurrence of diabetes and hypertension necessitates a comprehensive approach to management. Effective communication and collaboration between patients, healthcare providers, and specialists like diabetologists and cardiologists are essential. Regular monitoring of blood sugar levels and blood pressure, along with adherence to medication regimens and lifestyle modifications, are crucial for successful management. By adopting a proactive approach, individuals with this double threat can significantly reduce their risk of developing debilitating complications and enjoy a longer, healthier life. Emerging research continues to explore the complex interplay between diabetes and hypertension. Understanding these interactions at a deeper level can lead to the development of more targeted treatment strategies in the future. The emotional and psychological toll of managing two chronic conditions should

not be underestimated. Support groups and mental health resources can play a vital role in helping individuals cope with the challenges associated with diabetes and hypertension.

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Artificial intelligence in management of hypertension

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Abstract: Hypertension, usually called essential hypertension, is the leading risk factor of cardiovascular morbidity and mortality (13%) globally. Despite availability of different class of medications and health care facility there are only 14% hypertensive people with systolic blood pressure below 140 mmHg. This is attributed to unawareness among people, unhealthy lifestyle, blood pressure variability and many more factors. There is a big gap in the achievable target and the real figure. Therefore, real-time availability of cardiovascular parameters with the help of wearable devices and its amalgamation with artificial intelligence is going to fill the gap and help in gaining the optimal response.

Keyword: hypertension, AI, ML, BP.

What is AI?

The formal organization of AI as a discipline started in the 1950s when Alan Turing posed the question can machines think?

AI is a technology which enables a machine to simulate human behaviour. It is an interdisciplinary science with multiple approaches that incorporate reasoning (making inferences using data), natural language processing (ability to read and understand human languages), planning (ability to act autonomously and flexibly to create a sequence of actions to achieve a final goal), and machine learning (ML) (algorithms that develop automatically through experience). [1]

ML creates artificial neural networks (ANN) into layers and mimics the human brain in functioning and decision making.

ML has got 4 subtypes which can be utilized based on different clinical parameters and available data: [2]

1-Supervised: In this samples are labelled with an outcome by expert which are used to construct a model that shows connection between inputs and the outcome.

2-Unsupervised: Here we don't have labelled outputs, so its objective is to give an inference from the natural structure within a set of data points.

3-Reinforcement: It shares some features of unsupervised learning, but inputs have come from human experts. It is used in robots and games at present.

4-Deep learning: It is an autonomous, self-teaching system in which algorithms are trained to find patterns then used to make predictions about new data.

Why is AI needed in hypertension?

The prevalence of hypertension among adults is estimated to be 31% globally and 28% in India. [3] With only 14% people with BP below 140/90 mmHg, Majority is uncontrolled with high cardiovascular risk.[4] It has kept high financial burden on the health care system despite the availability of effective treatment regimen and guidelines. Almost 50% of adults with hypertension are unaware of their condition and hence are at potential risk of sudden cardiovascular events (CVE). Even those who appear to have controlled office blood pressure often present to emergency with sudden CVE. Researchers have attributed these events to poor at home or out of the office BP control due to variability depending on physical activity, stresses, and various environmental influences. [5,6]

. Here comes the role of artificial intelligence (AI) in the proper and individualized management of hypertension.

Mechanism of AI in hypertension:

Alternatives to BP monitoring are both cuff-based (wrist-worn inflatable cuffs) and cuffless devices using optical sensors (photoplethysmography-PPG). PPG is commonly used in pulse oximetry for measuring oxygen saturation and pulse waveforms by analyzing the amount of light absorbed or reflected by blood vessels.

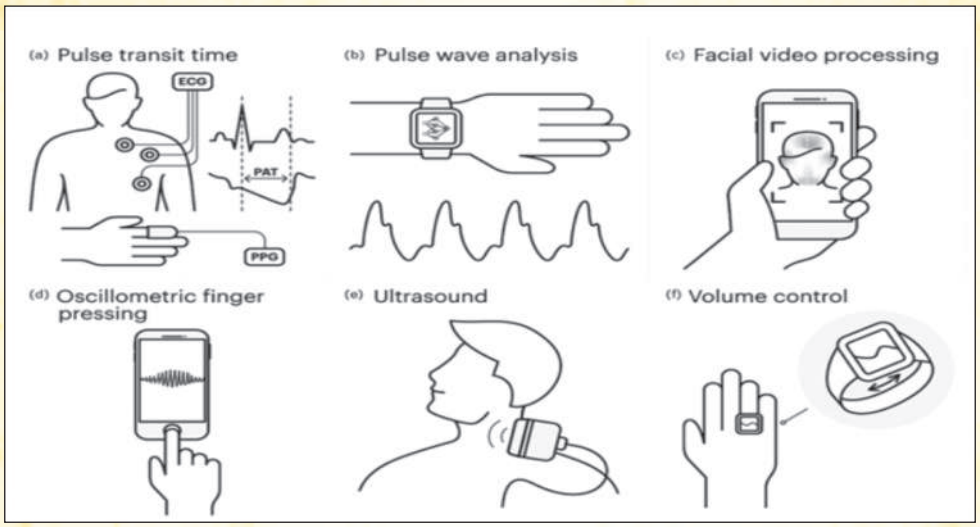

Figure-1: Cuffless wearable blood pressure devices

Irrespective of which of these we use, the signals are pre-processed and then sent for extraction and selection after which the gathered data can be used to feed ML and we get the BP values from the signal. This signal is directly affected by changes in blood volume and provides a variety of parameters that can be used for BP estimation, such as pulse transit time. Seeing the BP records and its variability (short term & long term) dose modification, drug medication and or selection of the best time to administer antihypertensive can be done to obtain optimal response. The data from electronic health records (EHRs), wearable devices, omics (genomics, proteomics, metabolomics etc), and social media is utilized by ML for predictive analyses.

Similarly, deep learning (DL), another type of AI utilizes patterns from various cardiac imaging and electrocardiogram with the help of ANN and that resembles the human brain. [7,8] So, it can perform automated predictive analyses and help in the development of precision medicine.

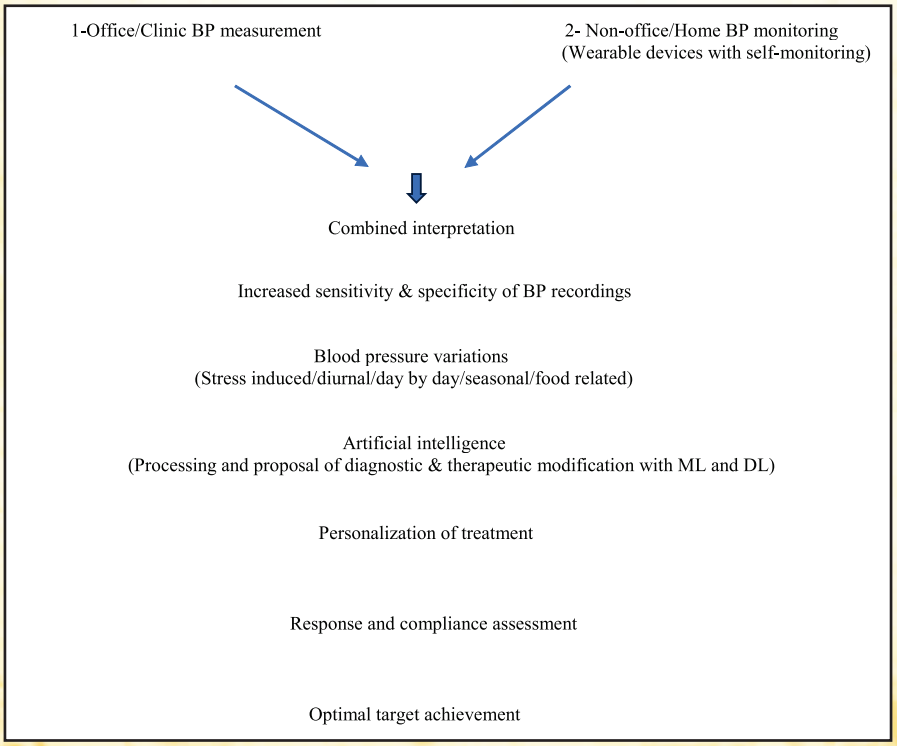

Figure-2: Amalgamation of Office and non-office BP

Application of AI in hypertension:

With the integration of clinical parameters, laboratory reports, effects of ongoing medications, physiological response of the patients, observational data, we can use the AI processing and find out the way to optimal therapy of the individualized target. There are different applications of AI in hypertension.

1- In forecasting hypertension: With the help of available clinical data

Socioeconomic status, lifestyle, environmental impact and the genomics of patients, AI can predict the development of hypertension and so screen judiciously.[9]

2-Accurate diagnosis: It can use demographic profile, vital signs, cardiovascular risk factors and laboratory records to differentiate pseudo hypertension, masked hypertension, and white coat effect.[10]

3-Blood pressure measurement: It has made BP measurement easier which can be done anywhere and anytime. This is done with the help of ML and DL algorithms.[11]

4-Predicting cardiovascular risk: There are various clinical and vitals parameters including cardiac imaging, electrocardiogram and target organ damage that will give a prediction of future risk of cardiovascular events in a hypertensive patient. This is done based on stratification of individuals and their response to therapy.[12]

5-Assessment of barriers to BP control: AI can warn both the patient and the clinician with the prediction of uncontrolled hypertension. It can also inform about the excess salt intake, sedentary habit, drug defaulter and stressors that might be responsible for the uncontrolled BP. This can be done with the remote patient monitoring based on wearable devices.[13]

6-Changing goals of BP levels: It can be predicted with the help of advancing age of the patient, acuteness and chronicity of the blood pressure, target organ damage and adverse events as suggested in various randomized controlled trials.[14]

What are the challenges in using AI?

Although AI is showing positive impact on many healthcare related issues, it also has some of the sensitive questions to be answered.

1. Personal information leak:

With the technology, we also encounter different types and levels of crime like cybercrime and hacking of data, hence we need a robust and highly secured system to safeguard the personal information and data of every individual.

2. Equity issue:

Network issues, nonavailability of tools and so disparities may hamper the functioning. It may lead to inequal distribution of information or delay.

3. Trust issues:

Patients and healthcare providers must have belief in the technology. They will need supervisor and guide to understand the system.

4.Errors:

Machines can make mistakes like human brain, and it is possible that it will not understand its limitations and gives wrong information leading to confusions.

Conclusion:

AI in hypertension is still in its neonatal age but is growing fast. There are many trials going on that may prove its application in novel risk factors that may be contributing to pathophysiology of hypertension. Judicious and secured use of AI may give us prioritized and personalized approach to achieve the desired goal.

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Wisdom lies not on the amount of knowledge acquired
But on the degree of its application

- Swami Vivekanand


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