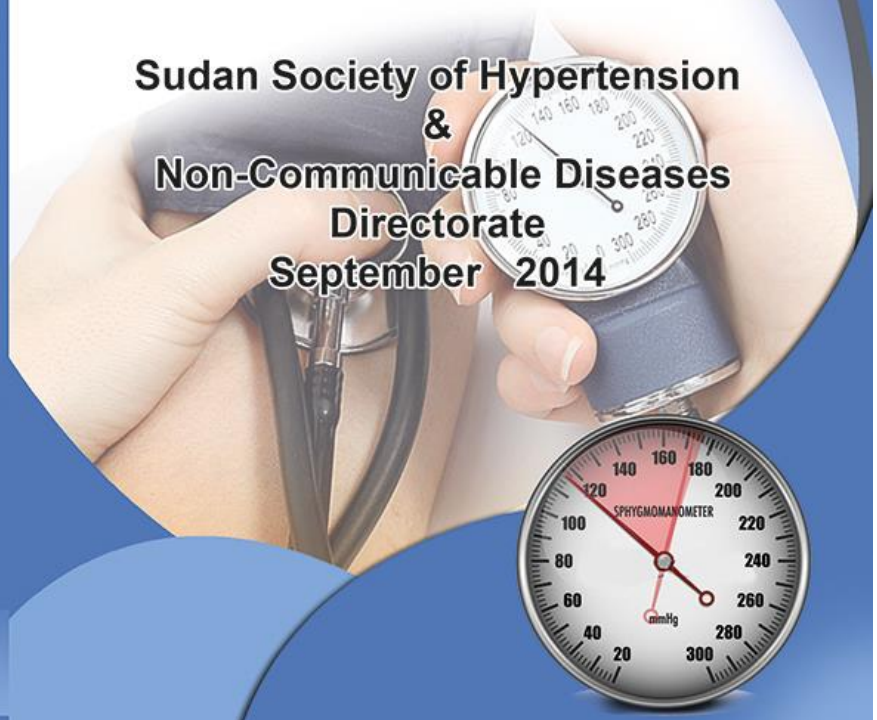
Sudan Guidelines for the Management of Systemic Hypertension in Adults

2ND Edition

Sudan Society of Hypertension
&
Non-Communicable Diseases Directorate

September 2014



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Contents :

1-Introduction

Hypertension has the highest prevalence among the major non communicable diseases in Sudan (prevalence of 23.6% in Khartoum state), among adults (25 - 64 years) (2). Hypertension accounts for 1.3% of the outpatient visits and is one of the10 leading causes of death in Sudan (3).

Sudan guidelines for management of systemic hypertension in adults is the effort of the first working party of Sudan society of hypertension, the federal ministry of health-non communicable disease department, the consultative councils of medicine and cardiology . These guidelines were adopted from the:

1- Joint national committee reports JNC7 and JNC8

2- WHO/ISH (international society of hypertension) clinical guidelines for the management of hypertension

3- ESC/ESH (European society of cardiology/ES of hypertension) 2013 for management of arterial hypertension guidelines

The main modifications from the above guidelines are shorter intervals for diagnosis and follow up. Lower thresholds of intervention were placed and that is due to late patient presentation to healthcare facilities as well as
irregularity of routine follow up in Sudanese patients

1.1Target of the guidelines

To provide an accessible and comprehensive resource document for management of hypertension for health care professionals (Doctors, Nurses, pharmacists and all paramedical personnel) in public and private sectors.
The guideline is aimed to be simple, practical and educational.

1.2-Objectives of the guidelines

1. To promote the primary prevention of hypertension and its cardiovascular complications by life style modification of high risk groups.

2. To increase the detection of under-diagnosed hypertension by routine screening and increase awareness of hypertension among the public.

3. To improve the treatment and control of hypertension to optimal levels.

4. To reduce the risk of cardiovascular disease of treated hypertensive patients by pharmacological and non-pharmacological measures

2- Summary of the Recommendations

1-Measurement of blood pressure (BP) should be carried out regularly in all persons above 18 years of age even if they are asymptomatic. The reading should be confirmed by the mean of two or more appropriate measured using a validated machine

2-If hypertension is suspected on the first visit confirm the DIAGNOSIS:
a- If systolic blood pressure (SBP) 140-159 and /or diastolic blood pressure (DBP) 90-99mmHg (stage 1) measure the BP every week for one month and initiate therapy after one month follow up after the diagnosis

b- If systolic blood pressure (SBP) >160 and /or diastolic blood pressure (DBP) 100mmHg (stage 2) measure the BP twice per week for two weeks and initiate therapy after two weeks follow up after the diagnosis

c- If severe hypertension systolic BP>180 and or diastolic BP>120 immediate treatment is recommended

3-Assessment by focused history and examination should be performed to rule out secondary causes of hypertension and to assess for target organ damage (TOD).

4-Baseline investigations of a hypertensive patient include a complete blood count (CBC), renal function (RFT), urinalysis, fasting blood sugar (FBS),ECG and fasting lipid profile.

5-The risk of developing cardiovascular disease (CVD) can be estimated using either the categorical classification or the WHO risk prediction charts (if available).

6- The goal BP level is <150/90 for people 60 years and older and<140/90for all people between 18-59 years including those with co morbidities such as DM, CKD or CVD according to JNC 8

7-Life-style modifications should be recommended for all people with hypertension and pre-hypertension. (120-139/80-89)

8- The use of calcium channel blockers (CCBs) or thiazide diuretics is recommended as first line therapy unless there are compelling indications or contraindications for specific classes of antihypertensive drugs

9--Combination therapy should be used when BP is >20/10 mmHg above the goals.

10- Unless contraindicated, low-dose aspirin (75-100 mg/ day) is recommended for all people needing secondary prevention of ischemic CVD, and primary prevention in people with hypertension over the age of 55 years or who have a 10-year CVD risk ≥30% by using the WHO charts or moderate risk by using the categorical classification,

11-Statin therapy is recommended for all people with high BP complicated by CVD, irrespective of baseline total cholesterol or low-density lipoprotein (LDL) levels. Similarly, statin therapy is also recommended for primary prevention in people with high BP who have a 10-year CVD risk ≥20%, moderate risk or those more than 65 years of age

12-Advice is provided on the clinical management of hypertension in specific patient groups. These include the elderly, patients with diabetes mellitus, chronic kidney disease, in pregnancy and hypertension and surgery

13-A policy for follow-up care and modification of management plan at primary and specialist care level is provided in these guidelines.

3--Definitions , classification , types and causes of Hypertension

What is Blood pressure?
Blood pressure is the lateral force applied by the blood on the arterial walls.
The systolic figure reflects the force of the left ventricle as it contracts in systole. The diastolic figure reflects the pressure of the blood during the brief time between "beats," the ventricular diastole.

3.1- Definition of hypertension:

Hypertension is defined as that level of arterial blood pressure associated with doubling of long-term cardiovascular risk.

- Office BP of ≥140/90 mm Hg,
- daytime ambulatory measurements of ≥135/85 m Hg Or nocturnal measurements of ≥120/70 mm Hg

3.2- Classification

Table 1 Classification of hypertension

Classification	Systolic BP (mmHg)	Diastolic BP(mmHg)
Normal	<120	And <80
Pre hypertension	120---139	And /or 80---89
Stage 1	140---159	And /or 90—99
Stage 2	>160	And /or>100

Simplified from JNC7 (6) Note: SBP> 180 and/or DBP>120 :severe hypertension

• **Pre Hypertension:** This group of patients is at an increased risk for progression to hypertension and has significantly greater risk to develop future cardiovascular events than those with normal blood pressure. Therefore, they should be identified and managed separately.

Clustering of cardiovascular risk factors (e.g., diabetes, dyslipideamia, obesity, and impaired glucose tolerance) is more prevalent in this group than in individuals with normal blood pressure. (1)

• **Isolated systolic Hypertension(ISH):** is defined as high systolic pressure more than 140) with normal diastolic pressure (<90). (1)

3.3- Types of Hypertension: (1, 6)

1- Primary hypertension: is defined as systemic hypertension of unknown cause that affects more than 95% of patients.
2- Secondary hypertension: affects less than 5% of the patients and is due to an underlying disorder.

3.4Causes of secondary hypertension (table 2)

Table 2 Causes of secondary hypertension

Causes of systolic and diastolic hypertension	Renal	Acute Glomerulonephritis, - chronic nephritis- polycystic kidney disease- diabetic nephropathy- hydronephrosis- renal artery stenosis - Intrarenal vasculitis- renin-producing tumours- renoprival-primary sodium retention (Liddle syndrome, Gordon syndrome).
	Endocrine	Acromegaly-Hypothyroidism-Hyperthyroidism-Hypercalcaemia (hyperparathyroidism)-adrenal syndromes -Cushing syndrome-primary
		aldosteronism-congenital adrenal hyperplasia-apparent Mineralocorticoid excess (liquorice)-Pheochromocytoma-Extra-adrenal chromaffin tumours. Carcinoid
	exogenous hormones	Estrogen, Glucocorticoids, Mineralocorticoids,, sympathomimetics, Tyramine containing food, Monoamine oxidase inhibitors
	Pregnancy-induced hypertension	
	neurological disorders	Increased intracranial pressure (brain tumours, encephalitis, and respiratory acidosis) Sleep apnoea, Quadriplegia, Familial dysautonomia.
	Drugs	NSAID- OCP(oral contraceptive bill)- Steroids
Causes of Systolic hypertension	-Increased Cardiac output	Aortic valve insufficiency, Arteriovenous fistula ,Patent ductus arteriosus, Thyrotoxicosis, Paget's disease of bone-Beri-beri, hyperkinetic circulation
	Rigidity of the aorta	

4- Measurement ,Diagnosis of Hypertension and initial assessment of the hypertensive patient

4.1- BP measurement technique and devices:
The person whose BP is about to measured; should be seated quietly for at least 5 minutes in a chair with the arm supported at the heart level. Caffeine, exercise, and smoking should be avoided for at least 30 minutes prior to measurement. No exogenous adrenergic stimulants e.g. nasal decongestants should be administered before measuring the blood pressure. (1)

• Use an appropriately sized cuff (cuff bladder encircling at least 80 percent of the arm) and the length should be one and half times the arm circumference to ensure accuracy. The examiner should have a larger and a smaller bladder available for fat and thin arms, respectively table(3)

Table (3) Correct cuff sizes based on mid-arm* circumferences

Arm circumference (cm)	Bladder size (cm)
<33	13 X 24 (regular cuff)
33- 42	17 X 32 (large cuff)
>42	20 X 42 (thigh cuff)

• Inflate by 20 mmHg above the systolic BP (determined by the pulse) and deflate by 3 mmHg every second, Korotkoff sounds should be heard at least every 2 mmHg gradation of the mercury column.

• Take the mean of at least two measurements spaced by 1–2 minutes. Additional measurements might be needed if the first two are quite different (more than 5 mm Hg difference) and until the two readings are similar.(8)

• Measure BP in both arms at first visit and take the higher value as the reference one.

• Take multiple measurements routinely in patients with irregular pulse (e.g. atrial fibrillation) and in older patients with systolic hypertension.

• Use phase I and V (disappearance) Korotkoff sounds (8) to identify systolic and diastolic BP respectively. If the phase V goes to zero, phase IV (muffling) should be used to identify the diastolic blood pressure.

• Use a mercury sphygmomanometer or validated electronic or aneroid device. Make sure various parts e.g. rubber tubes, valves, amount of mercury, are kept in proper order. (1)

• Measure BP regularly in all persons above 18 years of age even if they are normotensive.

• Encourage the patients to monitor their BP at home and record the reading.

Korotkoff Phase I: begins with the sudden appearance of a faint, clear, tapping or thumping sound that gradually increases in intensity .**Phase II**: **phase II** begins when the sounds change to a loud "swishing" murmur. Phase III: the beginning of **Phase III** occurs when the sounds assume a loud, distinct, knocking quality. These sounds are less intense than those of Phase I. **Phase IV**: begins when the sounds suddenly become muffled and have a faint murmur-like or "swishing" quality. **Phase V:** begins when silence develops."

4.2 Mean arterial pressure (MAP)

Clinical significance of MAP:
MAP

- It is considered to be the perfusion pressure of organs in the body.

- Greater than 60 mmHg is believed to be enough to sustain the organs of an average person.

- Is normally between 70 to 110 mmHg and if falls significantly below this level for an appreciable time; end organs will not get enough blood flow and will become ischemic

- Can be determined from: MAP= (CO×SVR) + CVP

- Where: CO is cardiac output.SVR is systemic vascular resistance.CVP is central venous pressure and usually small enough to be neglected in this formula.

- At normal resting heart rates MAP can be approximated using the more easily measured systolic and diastolic pressures, SP and DP:

$$MAP \simeq DP + \frac{1}{3}(SP - DP)$$ or equivalently

$$MAP \simeq \frac{2}{3}(DP) + \frac{1}{3}(SP)$$ or equivalently

$$MAP \simeq \frac{(2 \times DP) + SP}{3}$$ or equivalently

$$MAP \simeq DP + \frac{1}{3}PP$$ Where PP is the pulse pressure, SP − DP

At high heart rates MAP is more closely approximated by the arithmetic mean of systolic and diastolic pressures because of the change in shape of the arterial pressure pulse. (9, 10)

4.3- Diagnosis of hypertension

Uncomplicated hypertension is usually asymptomatic (1)
Anticipate hypertension in adults when the average of two or more SBP is ≥140 mmHg and/or DBP is ≥90 on at least two subsequent visits
Inform patients clearly that a single elevated reading does not constitute a diagnosis of hypertension but is a sign that further observation is required. (1)
Recommended response when hypertension is suspected during the first visit

Table (4) recommended response during first visit

Initial BP measurement (mmHg)	Recommended response
Normal or optimal	Recheck every year if the age above 40 years
Pre hypertension SBP 120-139 and/or DBP 80-89	Recheck every 6 months
Stage 1 SBP 140-159 and/or DBP 90-99	Check every week for one month
Stage 2 SBP>160- and/or DBP>100	Confirm with two readings every week for two weeks

4.4 Indications for Ambulatory Blood Bressure monitoring

*If feasible, ambulatory or home BP monitoring should be considered in the following situations:

1- Suspected white coat Hypertension.
2-suspected episodic Hypertension
3-Hypertension resistant to increased medication
4-Symptomatic patients on antihypertensive medications
5-Autonomic dysfunction
6- Large variation in B.P. values
7- To evaluate whether antihypertensive therapy is moderating early morning B.P. surge
8- Elevated office B.P. in pregnant women with suspected pre-eclampsia
9-to establish non dipper status or nocturnal Hypertension: Blood pressure is, on average, lower during the night (sleep) than during the day (waking hours) by approximately 10–20%. Night–day systolic blood pressure :
Extreme dippers (ratio ≤ 0.8), Dippers (0.8 < ratio ≤ 0.9),
Non dippers (0.9 < ratio ≤ 1.0) . Reverse dippers or risers (ratio > 1.0)

4.5- Initial assessment of newly diagnosed hypertensive patient

The treatment of Hypertension should be tailored to each patient according to the initial assessment:

Table (5) Initial assessment of newly diagnosed hypertensive patient

1)Assessment 0f Causes	1-Drugs: e.g.NSAID's.oral contraceptive pills and steroids 2-Renal parenchymal and Reno - vascular disease (abdominal or loin bruit) Palpation of enlarged kidneys (e.g. polycystic kidney) 3-Endocrine disease: pheochromocytoma, Conn's syndrome, Cushing syndrome 4-Coarctation of the aorta (radio-femoral delay or weak femoral pulses)
2)Assessment of risk factors for cardiovascular diseases	1-Systolic and diastolic BP levels.Levels of pulse pressure (in the elderly) 2-Age: (> 55 years for males and >65 years for females). 3-Smoking 4-Dyslipideamia:Total cholesterol 5.0 mmol/l (190 mg/dl) 1. LDL-C: 3.0 mmol/l (115 mg/dl) a. HDL-C: Male: 1.0 mmol/l (40mg/dl), b. Female: 1.2 mmol/ (46 mg/dl) 2. TG: 1.7 mmol/l (150 mg/dl) 5-Diabetes Mellitus: Impaired glucose tolerance (Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dl) 6-Abdominal obesity (Waist circumference >102 cm (M), >88 cm (W)) 7-Family history of premature CVD: Male at age , 55 years; Female at age ,65 years) (2)
contributory factors	1-Overweight, 2-Lack of exercise 3-Excess alcohol intake (>3 units/day) – 4-Excess salt intake 5-Environmental stress 6-Tobacco use 7-Diet
Target Organ Damage	Eye: impaired vision Fundal hemorrhages or exudates, papillodema Brain: headache, vertigo, transient ischemic attacks, sensory or motor deficits. dementia, carotid bruits Heart: palpitation, chest pain, shortness of breath, swollen ankles ,left ventricular hypertrophy(LVH) and/or LV strain on ECG, heart failure ,Myocardial infarction, angina, CABG or angioplasty, Peripheral vascular disease Kidney: proteinuria, haematuria, generalized body swelling and encephalopathy due to uremia Peripheral arteries: cold extremities, intermittent claudication , Absence, reduction, or asymmetry of pulses, cold extremities, ischemic skin lesions
Drug contraindications	The treatment of hypertension should be tailored to each patients according to the initial assessment.(1)
Investigation	1-Urine strip test for Albumin and blood.RFT.FBS.CBC,Fasting Lipid Profile and ECG

4.6 Assessment of the risk of 10 year risk of cardiovascular disease morbidity and mortality

The two methods of calculating the risk of cardiovascular disease morbidity and mortality in the coming 10 years are:

- **WHO/ISH risk prediction charts**
- **Categorical method**

1- The WHO/ISH risk prediction charts annex (2).

We highly recommend the use of WHO risk chart since it can give more precise assessment of cardiovascular risk

The WHO/ISH risk prediction charts indicate 10-year risk of a fatal or nonfatal major cardiovascular event (myocardial infarction or stroke), according to age, sex, blood pressure, smoking status, total blood cholesterol and presence or absence of diabetes mellitus for WHO epidemiological sub-regions D annex (2).

There are two sets of charts one can be used in settings where blood cholesterol can be measured and the other set is for settings in which blood cholesterol cannot be measured.

Each chart can only be used in countries of the specific WHO epidemiological sub-region, in Sudan the recommended chart is the East Mediterranean region chart (EMRC)(1).

How to use the WHO risk prediction chart

Calculate a score based on several risk factors as a percentage chance, for example, if the score is 30% this means that there is a 30% chance of developing a cardiovascular disease within the next 10 years.

- High risk - if the score is 20% or more. (That is, a 2 in 10 chance or more of developing a cardiovascular disease within the next 10 years.)
- Moderate risk - if the score is 10-20% (between 1 in 10 and 2 in 10 chance).
- Low risk - if the score is less than 10% (less than a 1 in 10 chance) (Risk assessment chart annex (2).

2- The Categorical classification: (can be used when the risk assessment charts are not available.)

According to the stage of the blood pressure and the presence or absence of the following risk factors of cardiovascular disease (see table above); hypertensive patients can be classified into three categories: low risk, medium risk, high risk. (See table below)

Table (6): Stratification of risk to quantify prognosis in hypertensive patient

Risk factor and disease history	Stage 1 : SBP 140-159 and/or DBP 90-99	Stage 2: SBP >160 and/or DBP >100
No risk factors, no TOD	Low risk	Medium risk
1-2 risk factors or TOD	Medium risk	High risk
3 or more risk factors or TOD	High risk	High risk

SBP, systolic blood pressure; DBP, diastolic blood pressure, TOD, target organ damage; *modified from the WHO and JNC 7

5-Treatment of Hypertension

Goals of treatment:

The goal in the treatment of hypertension is to reduce the long term risk of cardiovascular morbidity and mortality. This requires: (1)

- Treatment of modifiable risk factors such as;smoking, dyslipideamia, obesity and Diabetes Mellitus
- Proper management of associated clinical conditions, such as; congestive heart failure, coronary artery disease, transient ischemic attacks
- The goal of BP level is <150/90 for patients 60 years and older and<140/90 for all patients between 18-59 years including those with co morbidities such as DM,CKD or CVD according to JNC 8

Patient involvement:

Hypertension is a lifelong disease and its treatment requires commitment to lifestyle changes, taking regular therapy and regularly
attending follow–up appointments.
Effective involvement starts with:

- adequate explanation of the nature of the disease
- discussion of the risk factors that might lead to its development
- patient involvement in the decision as to whether they should start with lifestyle modification or immediately start drug therapy
- which individual drugs the patient should take
- possible side-effects of antihypertensive medications and the likelihood that the patient may need to take at least two or more medications. (8).

General guidance

- Patients with isolated systolic hypertension have the same risk for developing cardiovascular events as those with high diastolic pressure. Therefore, they should be treated when the diagnosis is confirmed.
- Treating hypertension is associated with decrease in cardiovascular complications, including 35%-40% reduction in stroke incidence, 20%-25% reduction in myocardial infarction and≥ 50% reduction in heart failure.
- Establish a partnership with the patient and involve him/her adequately in formulating the management plan so as to encourage trust and adherence to treatment
- Consider cultural beliefs and individual attitude in formulating a treatment plan
- Involve the whole family to facilitate the adoption of healthy lifestyle and increase adherence to the therapy

6. Plan of management after confirmation Of the diagnosis of pre hypertension and hypertension :

(Table 7) Plan of management after confirmation of pre hypertension and hypertension

Presence or absence of CVD risk factors and diseases	Pre hypertension SBP 120-139 And/ Or DBP 80-89	Stage 1 HTN SBP 140-159 And /Or DBP 90-99	Stage 2 HTN SBP >160 And/ Or DBP >100
No risk factors (Low risk) or (score less than 10%)	Life style change Check BP every 6 months No BP intervention	Lifestyle change + Treatment if persistently high over one month Targeting BP < 140/90	Lifestyle change + Drug treatment if persistently high over two weeks Targeting BP < 140/90
1-2 risk factors (moderate risk) or (score 10-20%)	Lifestyle change + Check BP every 2months No BP intervention	Lifestyle change + Treatment if persistently high over two weeks Targeting BP < 140/90	Lifestyle change + Immediate Drug treatment (consider combination therapy) Targeting BP < 140/90
≥3 risk factors or High risk (score is ≥ 20%) Or DM or established CKD or CVD	Life style change Check every month No BP intervention	Life style change + Immediate drug treatment Targeting BP < 140/90	Life style change + Immediate Drug treatment Targeting BP < 140/90

MODIFIED FROM THE ESH/ESC 2013

6.1 Lifestyle modifications:

Lifestyle modification prevents hypertension, decrease blood pressure, enhance antihypertensive drug efficacy and decrease cardiovascular risk. (1)
The life style measures that should be considered in all patients are:

• **Cessation of smoking:** This the most important lifestyle measure for prevention of cardiovascular and non-cardiovascular diseases, including stroke and coronary heart disease.

• **Weight reduction and physical exercise:** Weight reduction reduces blood pressure in overweight patients by 1.6/1.1 mmHg for every kilogram of weight loss, and also has positive effects on associated risk factors such as DM, hyperlipidemia and left ventricular failure. Weight reduction may be achieved by increase in physical exercise such as brisk walking for at least 30 minutes per day, most days of the week.

• **Reduction of salt intake and other dietary changes:** Reducing sodium intake to 2.4 g sodium or 6 g sodium chloride reduces SBP by 4-6 mmHg. Patients should be advised to avoid salted food, to eat more fish, potassium, fruit and vegetables and to reduce intake of saturated fat. This is achieved by adoption of Dietary Approach to Stop Hypertension (DASH) that is rich in fruits, vegetables and low-fat dairy foods (whole grains, poultry, fish and nuts) and increased amount of potassium, calcium, magnesium, dietary fiber and protein, and is reduced in fats, red meat, sweets and sugar. The combination of low sodium intake and DASH diet is more effective than either alone.

Table 4: Summary of the recommended lifestyle modifications

Modification	Recommendation	Approximate SBP reduction
Weight reduction	Maintain normal body weight	5–20 mmHg/10kg
Adopt DASH	Consume a diet rich in vegetables, fruits, and eating plan low-fat dairy products with a reduced content of saturated and total fat	8–14 mm Hg
Dietary sodium	Reduce dietary sodium intake to no more than sodium chloride 2.4 g sodium or 6 g salt	2–8 mmHg
Physical activity	Engage in regular aerobic physical activity at least 30 minutes daily, most days of the week	4–9 mmHg

6.2 Pharmacological therapy:

General Guidance (1)

• Once the selection of the most appropriate agent for initial therapy has been made; a relatively low dose of a single drug should be started, aiming for a reduction of 5 to 10 mm Hg in blood pressure at each step.

• Thus, there should be a gradual approach to antihypertensive therapy in order to avoid symptoms related to overly aggressive blood pressure reduction.

• **Individualized therapy:** Perhaps the most crucial factor in the selection process is the presence of one or more concomitant conditions, some that could be worsened by the drug chosen, others that could be improved

• **Drug combinations:** Combinations of smaller doses of two drugs from different classes is better to take advantage of the differences in the dose-response curves for therapeutic and toxic (side) effects
• It is better to choose long acting preparations providing effective, 24-hour control of hypertension in a manner that encourages adherence to the regimen.

6.2.1 Initiation of drug treatment

Is determined by presence or absence of compelling indications for the use of a specific drug:

1-In patients without compelling indications:
• Initiate drug therapy with a:

Thiazide diuretic or Thiazide like diuretic

or

Long acting Calcium channel blocker.

2-In patients with compelling indications:
• Initiate drug treatment according to the condition and this is based on outcome data- from clinical trials

Table 5: Indications and contraindications of antihypertensive drugs

Class of drug	Compelling indications	Possible indications	Caution	Compelling Contraindications
Alpha-blockers	Benign prostatic Hypertrophy		Postural Hypotension Heart failure	Urinary incontinence
ACE inhibitors	Heart failure, LV dysfunction post MI Established CHD Type I diabetic nephropathy secondary stroke prevention	Chronic renal disease type II diabetic nephropathy, proteinuric renal disease	Renal impairment PVD	Pregnancy Reno vascular Disease
ARBs	ACE inhibitor intolerance Type II diabetic Nephropathy Hypertension with LVH Heart failure in ACE-intolérant patients post MI	LV dysfunction post MI Intolerance of other antihypertensive drugs proteinuric renal disease Chronic renal disease, Heart failure	Renal impairment PVD	Pregnancy, Reno vascular Disease
Beta-blockers	MI Angina	Heart failure	Heart failure, PVD Diabetes (except with CHD)	Asthma/COPD, heart block
CCBs (dihydropyridine)	Elderly Isolated systolic hypertension	Elderly, Angina		
CCBs(rate limiting)	Angina	MI	Combination with beta-blockade	Heart block, heart failure
Thiazide/thiazide-like	Elderly,			Gout
diuretics	Isolated systolic hypertension Heart failure, Stroke prevention			

6.2.2 Selection of antihypertensive drugs

The selection on antihypertensive drug is based on the presence or absence of compelling indication as indicated on the table above.

According to JNC 8 any one of these policies can be used :

A. Maximize first medication before adding second : OR

B. Add second medication before reaching maximum dose of first medication OR

C. Start with 2 medication classes separately or as fixed-dose combination.

Steps of combining the drugs are (6)

•Use of a single drug

The use of a single antihypertensive drug increases the adherence to the medication. However the response to the anti-hypertensive drugs is substantially different between patients and the use of single drug will reduce the BP by no more than 7-8%. Therefore, the use of single drug is indicated mainly for patients with mild hypertension (8).

When a single drug is chosen to treat hypertension, it is recommended to start with a low dose and gradually build it up until adequate blood pressure control is achieved. If the patient develops persistent side effects or the control is not achieved; try another drug from another class and if no response then two or three drugs should be combined (1)

•Use of combination therapy

Most of the patients will need to use more than one drug due to the heterogeneity in the pathogenesis of BP elevations and the multiplicity of pathophysiological mechanisms responsible for high levels of BP. Combination therapy should be considered when blood pressure is >20/10 mmHg above the goal. It is generally recommended to use drugs with different modes of action when combination therapy is indicated. Fixed drug combinations are recommended to reduce the number of medications, which may enhance adherence to treatment (1)

The policy of combination therapy that we are recommending in our guidelines is modified from the British Hypertension Society Algorithm (ABCD)

The algorithm is developed to improve the control of hypertension and it is based on the notion that the renin levels are different among different groups of people (Caucasian have high renin / Africans have low renin) (8).

In our guidelines we recommend starting treatment with diuretics or long acting calcium channel blockers (drugs with minimal effect on the renin- angiotensin system) and then to add a drug with strong effect on the rennin- angiotensin system e.g. Angiotensin converting enzyme inhibitors, or angiotensin receptor blocker.

NB: diuretics enhance the effects of beta blockers and ACE inhibitors in Africans.

-FIRST STEP: THIAZIDE DIURETIC OR CCBS (maximum dose) + ACEI or ARB (low dose of 2nd drug)

SECOND STEP: THIAZIDE OR CCBS + ACEI or ARB (max. dose of 2nd drug)

THIRD STEP: THIAZIDE + CCBS + ACEI or ARB (low-. dose of 3rd drug)

FOURTH STEP: THIAZIDE + CCBS + ACEI or ARB or {B- BLOCKER OR a – Blockers OR SPIRONOLACTONE OR OTHER DIURETICS OR CENTRALY ACTING DRUGS}.(max. doses)

Screen for secondary causes if still not controlled. Consider ambulatory BP monitoring

(If there is any compelling indication that prevent following these steps, the patient should be treated accordingly)

6.2.3 Other drugs used in the management of hypertensive patients (Asprin&Statins)

Aspirin: Unless contraindicated, low-dose aspirin (75 --100mg/ day) is recommended for all people needing secondary prevention of ischemic CVD, and primary prevention in people with hypertension over the age of 50 years or who have a 10-year CVD risk ≥30%

Statin: therapy is recommended for all people with high BP complicated by CVD, irrespective of baseline total cholesterol or low-density lipoprotein (LDL)-cholesterol levels. Similarly, Statin therapy is also recommended for primary prevention in people with high BP who are above 65 years or have a 10-year CVD risk ≥20%. The target is to achieve optimal cholesterol lowering (reduction of the total cholesterol by 25% or LDL-cholesterol by 30%)or achieves total cholesterol of 4.0 mmol/l or LDL-cholesterol of 2.0 mmol/l, whichever is the greatest reduction

7-Follow-up of Hypertensive patients

Level of follow up:

All the patients with essential hypertension can receive medical care at primary care level (non-specialist care)

Refer patient to specialist care: (if any of the following criteria is present)

1-Secondary hypertension

2-Age less than 18 years (younger patients may have secondary hypertension which need to be treated under specialist care)

3-Presence of co morbidities such as; DM, heart disease, cerebrovascular disease and kidney disease (e.g. albuminuria)

4-Blood pressure not controlled with the use of three drugs

5-Hyperlipidaemia (a cholesterol level of more than 8 mmol/l).

Frequency of the follow-up visits at PHC level

Regular follow-up intervals according to the stage of Hypertension.

- STAGE 1: Monthly until goal blood pressure is achieved, then every 3 to 6 months.
- STAGE 2: every 2 weeks until goal blood pressure achieved then every 3 months.
- In the presence of co-morbidity as DM or heart disease; the follow up frequency may be increased.

What to do during the follow-up visit

1. Check the blood pressure.

2-Check adherence to medication and life style modification

3- Check for signs and symptoms that indicate the presence of target organ damage (complication) e.g. breathlessness,left ventricular hypertrophy

4-Investigate as required;

- One week after initiating ACEIs : Serum creatinine and electrolytes
- Annual routine investigations: Lipid profile. renal function test and electrolytes
- Other investigations are requested according to the symptoms of target organ damage and the presence of concomitant disease e.g. DM

Decide whether to continue the same management plan or to modify it.

8- Modifying the management plan: (13)

Increase the dose of antihypertensive drugs if adequate response is not achieved.

The increment of the antihypertensive dose depends on the maximum drug effect,

8.1Plan the increment in the doses :

- **Diuretics:** after one month
- **ACEIs** : 2 weeks to 1 month
- **CCBs** : 2 weeks to 1 month
- **ARBs** : 2 weeks to 1 month

8.2Reduction or discontinuation of antihypertensive drugs

If the targeted blood pressure achieved and maintained for a period at least of one year, features in favor of withdrawal are: (1)

- Low blood pressure before and after therapy.
- Control of the blood pressure with a low dose of medicine.
- Patient's willingness to maintain healthy lifestyle.

In above cases; decrease the dose of antihypertensive medications first and then stop them if a good response has been maintained. Keep the patient on regular follow up even after discontinuing the medication to maintain the blood pressure under control.

9-MANAGEMENT OF SEVERE HYPERTENSION

Approximately 1% of hypertensive patients will develop acute elevations in blood pressure at some point in their life.

Types:

1. Hypertensive emergencies OR crises : These conditions are characterized by severe elevations in BP (>180/120 mmHg) complicated by target organ dysfunction (11)
2. Hypertensive urgencies: This term is used for patients with severely elevated blood pressure without acute end-organ damage.

Aims of Treatment:

1- reduce the BP safely to non morbid levels.
2-prevent end organ damage.
3- tackle co morbidities.
4- prevent precipitating ischemic attacks.

Hypertensive emergencies:

Clinical conditions that meet the diagnostic criteria for hypertensive emergencies

1-Hypertensive encephalopathy.
2-Dissecting aortic aneurysm
3-Acute left ventricular failure with pulmonary edema
4-Acute myocardial ischemia
5-Eclampsia
6-Acute renal failure
7-Symptomatic microangiopathic hemolytic anemia

The Clinical manifestations of hypertensive emergencies

• The clinical manifestations are those associated with end-organ dysfunction. Organ dysfunction is uncommon with diastolic blood pressures less than 130 mmHg except in children and in pregnant women [the absolute level of blood pressure may not be as important as the rate of increase].

• **Hypertensive encephalopathy:** gives rise to headache, altered level of consciousness, and/or focal neurologic sign. On physical examination, these patients may have retinopathy with arteriolar changes, hemorrhages and exudates as well as papilledema.

• **Cardiovascular manifestations:** may predominate, with angina, acute myocardial infarction, or acute left ventricular failure

• **Renal manifestation:** in some patients, severe injury to the kidneys may lead to acute renal failure with oliguria and/or haematuria.

• **In pregnant ladies**: the clinical features vary but may include visual field defects, severe headaches, seizures, altered mental status, acute cerebro- vascular accidents, severe right upper quadrant abdominal pain, congestive heart failure, and oliguria. In the vast majority of cases, this process can only be terminated by delivery. The decision to continue the pregnancy or to deliver the baby should be made following consultation between medical and obstetric personnel

• **Aortic dissection** should be considered a likely diagnostic possibility in patients presenting with acute chest pain and elevated blood pressure. Left untreated, about three-quarters of patients with type A dissection die within 2 weeks of an acute episode, but with successful initial therapy the 5-year survival rate increases up to 75%.

Evaluation and management of hypertensive emergencies

clinical evaluation.:

• Measurement of the blood pressure in both arms by a physician.
• Use appropriately sized cuffs in obese patients
• Physical examination should include palpation of pulses in all extremities, auscultation for renal bruits, focused neurologic examination, and a Fundoscopic examination.
• Investigations should include the following:

1) Complete blood count
2) Peripheral blood smear (to exclude a microangiopathic anemia),
3) Electrolytes, blood urea, creatinine,
4) Urinalysis
5) Electrocardiogram.
6) Chest radiograph
7) Head computed tomography (CT) or chest CT in patients with focal neurological deficits or patients with unequal pulses and/or evidence of widened mediastinum on the chest radiograph successively

Initial Therapeutic Approach (11)

• Treat patients with hypertensive emergencies in intensive care unit for continuous monitoring of BP and intravenous administration of an appropriate antihypertensive drug (table 1).

• Reduce Mean Arterial BP by no more than 25 % (within minutes to 1 hour), then if stable, to 160/100–110 mmHg within the next 2–6 hours

• If this level of BP is well tolerated and the patient is clinically stable, implement further gradual reductions toward a normal BP in the next 24–48 hours.

• Avoid excessive falls in blood pressure that may precipitate renal, cerebral, or coronary ischemia. Therefore, short-acting Nifedipine is no longer considered acceptable in the initial treatment of hypertensive emergencies or urgencies.

• Exceptions to the above recommendations are:

- Patients with an ischemic stroke in which there is no clear evidence from clinical trials to support the use of immediate antihypertensive treatment
- Patients with aortic dissection who should have their SBP lowered to <100 mmHg if tolerated
- Patients in whom BP is lowered to enable the use of thrombolytic agents.

Recommended antihypertensive agents for hypertensive crises table (8)

Table (8) antihypertensive agents for hypertensive crises

Condition	Preferred antihypertensive agent
Acute pulmonary edema	nitroglycerin (up to 60 µg/min) and a loop diuretic if needed IV CCBs
Acute myocardial ischemia	Labetalol or Esmolol in combination with nitro-glycerin (up to 60 ug/min)
Hypertensive encephalopathy	Labetalol, Nicardipine, or Fenoldopam
Acute aortic dissection	Labetalol or combination of Nicardipine or Fenoldopam and Esmolol or combination of Nitroprusside with either Esmolol or intravenous Metoprolol
Eclampsia	Labetalol or CCBs, Hydralazine may be used in a non-ICU setting
Acute renal failure, microangiopathic anemia	Hydralazine or CCBs
Sympathetic crisis/cocaine overdose	Verapamil, Diltiazem, or Nicardipine in combination with a benzodiazepine

Hypertensive urgencies :

This term is used for patients with severely elevated blood pressure without acute end-organ damage

• Patients with hypertensive urgencies may benefit from treatment with **an oral, short-acting agent:** such as captopril, (other drugs) followed by several hours of observation.

• **Use alternative approach adjustment in their antihypertensive** therapy, particularly the of combination drugs, or **reinstitution of medications** if noncompliance is a problem

• Check patient with hypertensive urgency in the refer clinic in a week time

• Reduce the blood pressure gradually. The term urgency led to overtreatment which is not without risk.

Figure 1 Management of severe hypertension (11)

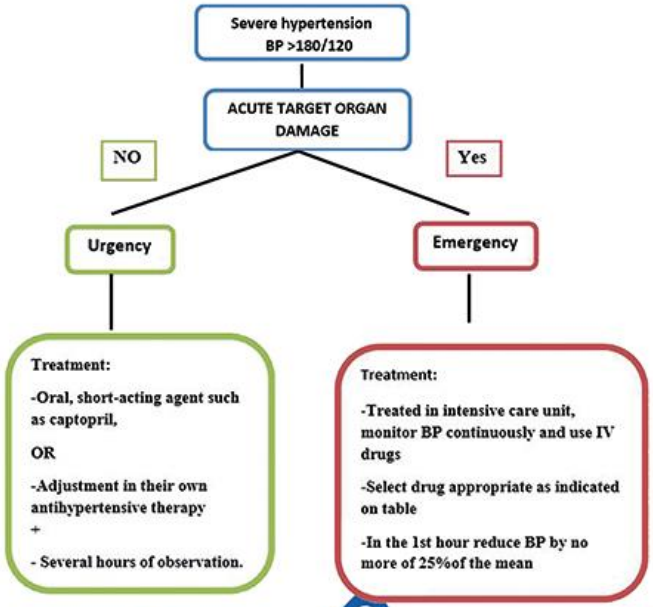


Table (9) Hypertensive emergency drugs

Drug	Dosage	Onset of action	Duration of action	Special indications	Adverse effects
Nitroprusside	0.25–10 µg/kg per min	Instantaneous	1-2 min	Most hypertensive emergencies, caution with highand intracranial pressure cyanide intoxication or azotemia	Nausea, vomiting, twitching, thiocyanate toxicity (AVOID its use for more than 48 hrs to prevent the side effects)
Hydralazine	10–20 mg/ IV 10–50 mg/ IM	10–20 min 20–30 min	1–4 hrs 4–6 hrs	Eclampsia	Tachycardia, flushing, headache, or aggravation of angina
Labetalol	20–80 mg IV Bolus every 10 min, infusion 2 mg/min IV	5–10 min	min 3–6 hrs	Most hypertensive except acute heart failure	Vomiting, burning throat, postural hypotension scalp tingling
Esmolol	250-500 µg/kg per min bolus then 50–100 µg/ kg per min IV infusion may repeat bolus after 5 min or increase infusion to 300 µg/min	1–2 min	10-30 min	Aortic dissection preoperative	Hypotension, nausea, asthma, first degree heart block, heart failure
Nitroglycerin	5–100 µg/min	2–5 min	5–10 min	Coronary ischemia	Tachycardia, flushing, headache IV infusion methaemoglobinoemia
Nicardipine	5–15 mg/h IV	5–10 min	15-30 May exceed 4 hrs	Most hypertensive emergencies except acute heart failure; caution with coronary ischemia	Tachycardia, headache, flushing, local phlebitis
Enalapril	1.25–5 mg every 6 hours	15-30 min	6–12 hrs	Acute left ventricular failure, avoid in acute myocardial infarction	Abrupt fall in BP in high renin states. Variable response
Fenoldopam	0.1–0.3 µg/kg per min	<5 min	30min	Most hypertensive emergency; caution with glaucoma	Tachycardia, headache, flushing Adrenergic inhibitors
Phentolamine	5–15 mg IV bolus	1–2 min	10-30 min	Catecholamine excess	Tachycardia, flushing, headache

Special consideration: Management of hypertension with acute stroke:

The management of BP during an acute stroke remains controversial. BP is often elevated in the immediate post-stroke period and is thought by some experts to be a compensatory physiologic response to improve cerebral perfusion to ischemic brain tissue.
As a result, it has been common practice after acute cerebral infarction to reduce or withhold BP treatment until the clinical condition has stabilized. There still are no large clinical studies upon which to base definitive recommendations.
Nevertheless, it is recommended that: in patients with recent ischemic stroke whose SBP is >220 mmHg or DBP 120–140 mmHg, cautious reduction of BP by about 10–15 %is suggested, while carefully monitoring the patient for neurologic deterioration related to the lower pressure.
If the DBP is >140 mmHg, a carefully monitored infusion of sodium Nitroprusside should be used to reduce the BP by 10–15 % (11).

The use of thrombolytic agents in ischemic stroke is affected by the BP level. SBP >185 mmHg or diastolic pressures >110 mmHg are contraindications to the use of tissue Plasminogen activator (TPA) within the first 3 hours of an ischemic stroke.
Once a thrombolytic agent has been initiated, BP should be monitored closely, especially in the first 24 hrs (11).

Summary of treatment in hypertensive emergencies and urgencies

• The treatment in hypertensive emergencies should be established in an intensive care unit.

• In hypertensive urgencies the recommended action is to reduce the BP within 24 to 48 hours by oral route.

• In patients with end organ damage rapid but controlled lowering of blood pressure is indicated to limit and prevent further organ damage.

The type of antihypertensive should be selected according to the organ involved.

• Severe hypertension in the setting of an acute ischemic stroke,the blood pressure should be reduced by no more than 10–15% in the first 24 hours.

• In patients with intra cerebral hematomas lowering blood pressure is currently recommended only when the systolic blood pressure is greater than 200 mmHg or the diastolic pressure is greater than 110 mmHg.

• Pregnant patients with systolic blood pressure greater than 180 mmHg or diastolic blood pressure greater than 110 mm Hg, should be treated by the intravenous route keeping the diastolic blood pressure over 90 to avoid fetal distress.

10- Special Groups

Hypertension in the elderly:

Older people show greater BP variability, so multiple measurements on several occasions are mandatory to confirm the diagnosis It is also worth noting that seated and standing measurements be taken during initial assessment and after initiating therapy because of high prevalence of orthostatic hypotension (SBP ≥20 mmHg).
Treatment may need to be titrated to the standing value. Lifestyle measures should be offered to all older people as they have been proven to be effective in reducing BP as they are in younger people.
Thiazide/thiazide-like diuretics are especially effective at lowering BP in older people as are dihydropyridine CCBs.
ARB-based therapy was shown to be more effective than beta blockers based therapy at reducing the risk of stroke and CVS mortality in people with ISH, so beta-blockers should be used when indicated, e.g. post MI, angina or HF. More than one drug can be used and logical combinations are outlined in the ABCD algorithm. (8)

Hypertension and pregnancy:
There is consensus for initiating treatment at BP level 150 – 160 mmHg SBP or 100-110 mmHg DBP or in the presence of target organ damage. There is concern that excessive lowering of BP leads to i ntrauterine growth restriction. Regarding the choice of anti-hypertensive therapy, methyldopa remains the drug of choice. CCBs (esp. long acting form of Nifidipine) and the vasodilator Hydralazine is
commonly used as a second line drug. Labetalol can also be used as second line and esp. for resistant hypertension in third trimester. Beta-blockers frequently less used as it inhibits fetal growth. ACE-inhibitors and ARBs are contraindicated during pregnancy. Thiazide/thiazide-like diuretics should be avoided as much as possible, as theoretically, they have the potential of reducing circulatory blood volume.(8)

Hypertension and diabetes:
The target blood pressure for diabetics with hypertension is <140/90 mmHg and combined therapy is usually needed to achieve this target. ACE-inhibitor or ARBs are the first line therapies. Other drugs that will be required to achieve targeted blood pressure are long acting CCBs, beta blockers and alpha blockers. In patients with renal impairment and/or edema, a loop diuretic may be required as an alternative to, or in addition to, thiazide and thiazide-like diuretics. A precaution to use of thiazides and thiazide-like diuretics is hyperglycemia. (10)

Diabetic nephropathy:
The target B.P is <140/90 mmHg in CKD patients without proteinuria. .Control of BP by using an ACEI slow the rate of decline of renal function and delay progression from the microalbuminuric phase to overt nephropathy. ACE-inhibitors have specific renoprotective properties in patients with incipient or overt type I diabetic nephropathy and are recommended as initial therapy. ARBs can be used as an alternative in patients with a persistent cough due to ACEI treatment.

ACE-hibitors / ARBs should be titrated to the maximum dose. If the goal is not achieved by one medication then combined therapy is required. Drugs that can be used in combined therapy are low dose thiazide/thiazide-like diuretics, CCBs, beta blockers and alpha blockers (8)
In CKD patients with proteinuria more than 500 gms/day;the target B.P is <130/80 mmHg
N.B. Combining ACEI and ARBS should be avoided according to JNC 8

Orthostatic hypotension:
Diagnosed by measuring standing and supine blood pressure; normally there is slight difference between the two measurements but the presence of >20 mmHg difference in systolic or >10 mmHg diastolic blood pressure confirms the diagnosis of orthostatic hypotension. The patient presents with dizziness or fainting on standing, eating or hot bathing. It is associated with the presence of impaired vasomotor reflexes (which are present in elderly), autonomic neuropathy (e.g. DM), and antihypertensive medication and overdiuresis. (1, 8)
Orthostatic hypotension is an obstacle to achieving good blood pressure control and its severity is strongly related to premature death, increased numbers of falls and fractures.
The presence of orthostatic hypotension necessitates slow-dose titration of antihypertensive drugs. Moreover, volume depletion should be avoided and a clear warning should be given to patients. (1, 8)

11. Resistant hypertension

Definition: (14)

Defined as blood pressure that remains above goal in spite of concurrent use of three antihypertensive agents of different classes and if tolerated, one of the three agents should be a diuretic.
All agents should be prescribed at optimal doses (i.e. 50% or more of the maximum recommended antihypertensive dose) Thus, patients whose blood pressure is controlled with four or more medications should be considered to have resistant hypertension

Causes of resistant hypertension (15)

1) Improper blood pressure measurements.

2) Volume overload:

- Excess sodium intake.
- Volume retention from kidney disease.
- Inadequate diuretic therapy.

3) Drug induced or other causes:

-Drugs: NSAIDs use, sympathomimetic (decongestants), oral contraceptive pills, corticosteroids, cyclosporine, erythropoietin

- Cocaine/amphetamine + illicit drugs
- Non-adherence to antihypertensive medication.
- Inadequate antihypertensive doses.
- Inappropriate drug combination.

4) Associated conditions:

- Obesity.
- Excess alcohol.
- Obstructive sleep apnea (present in 50% of hypertensive patients)

Management approach (14):

1. Confirm resistant hypertension diagnosis and check for the following:

- If adequate treatment is prescribed
- If it is the appropriate treatment
- If the patient is taking the pills or not
- If BP is measured correctly

2. Exclude pseudo-resistance through the following:

- Check adherence with prescribed medication
- Obtain home, work or ambulatory BP readings to exclude white coat effect
- Identify and reverse contributing lifestyle factors

3. Increase patients compliance to medication: this can be achieved through:

- Proper education
- Increase the frequency of the follow-up visits
- Encourage self measurement of BP
- Prescribe of drugs that least likely to cause adverse effect
- Prescribe once a day regimen
- Use of fixed dose combination
- Use of less costly regimen
- Acknowledge progress towards goals and the exclusion of other the drugs that can interfere with BP control.

4. Exclude secondary causes of hypertension

5. Adjust the pharmacological treatment:

- Studies suggest that change in diuretics therapy (adding a diuretic, increasing the dose, or changing the diuretics class based on kidney function) will help 60% of these patients achieve BP goals.
- The rationale behind the use of diuretics is that volume expansion seems to be the most frequent pathogenic finding in this group of patients

Fixed dose antihypertensive are very useful for patients with resistant hypertension, especially those with an adherence problem.

12 -Prevention of hypertension

Lifestyle modifications:

- Weight control,
- Increased physical activity
- Adopting the DASH eating plan

Target groups for primary prevention:

- Pre-hypertensive patients
- Individuals with family history of hypertension
- Diabetic patients
- Females with history of hypertension with pregnancy or toxemia of pregnancy
- Individual with risk factors (e.g. smokers, overweight, sedentary lifestyle, unhealthy diet).

The above approach should also be directed towards: communities, schools, work sites, and food industries.

Primary prevention of hypertension at Primary Health Care (PHC) settings

PHC providers should:

Measure the B.P. regularly in all persons above 18 years of age; even if they are asymptomatic, at least once a year.

Advise patients with pre-hypertension and hypertension on lifestyle modifications,

Community approach to hypertension prevention

The objectives of Sudan's Community Approach for hypertension prevention goes in line with the East Mediterranean Approach to Non-communicable diseases (EMAN) primary hypertension prevention which could be achieved through launching community based programs that target both prevention and control of hypertension in addition to development of standards of care and cost effective case managements

ANNEXES

Annex 1 : Anti hypertensive Drugs

Drug	Dose/ mg/day	Doses/ day	Mechanism of action	Special consideration
Diuretics				
Thiazides and related drugs			They initially lower BP by reducing plasma extracellular fluid volume and cardiac output. Within 6–8 weeks, these parameters return toward normal and the lower BP is related to fall in peripheral resistance	• Thiazides are more effective antihypertensive than loop diuretics, unless serum creatinine is 2.0 mg/ml or creatinine clearance 50 ml/min • Without concomitant diuretics, antihypertensive drugs which do not block the RAA mechanism may cause sodium retention • Week diuretics may cause hypekalaemia particularly when combined with ACE inhibitors, K supplements or NSAIDS
• Hydrochlorothiazid	12.5-25	1		
• Chlorothalidone	12.5-25	1		
• Indapamide	2.5	1		
Loop diuretics				
• Furosemide	20-320	2		
• Bumetanide	0.5-5	2		
• Ethacrynic acid	24-100	2		
• Torsemide	50-100	1		
K sparing diuretics				
• Spironolactone	25-100	2-3		
• Triamterene	50-100	2		
Calcium antagonists				• May cause initial

Nondihydropyridine			Block entry of calcium into smooth muscle cell Deltiazem and Verapamil blunt increases in exercise rate	natriuresis, resulting in vasodilatation. • Effect not blunted by NSAID • Short acting agents may increase risk of ischaemic heart disease
•Verapamil	80-480	2-3		
•Verapamil SR	120-480	1-2		
•Verapamil-covera HS	180-240	1 (bed time)		
•Diltiazem	90-360	3-4		• Liquid Nifidipine reduces BP quickly but may precipitate cerebral and myocardial ischaemia
•Diltiazem CD	180-360	1		
Dihydropyridines				
•Nifedipine	30-120	3		
•Nifedipine GTS	30-120	1		
•Amlodipine	2.5-10	1		
•Felodipine	43952	1		
•Isradipine	2.51	2		
ACE inhibitors			Block conversion of angiotensin I to angiotensin II, thus removing the effects of the latter as a vasoconstrictor and as a stimulant of aldosterone synthesis. They inhibit break down of bradykinin, incease levels of vasodilatory prostaglandins decrease level of endothelins, and inhibit RAA system within the heart and other tissues.	• First dose may precipitate dramatic fall in BP but full effect may not appear for up to 7 to 10 days. • Renal function test and K should be measured one week after starting the treatment to detect the presence of side effects • Effect is potentiated by diuretics. • May cause hyperkalaemia in patients with renal failure,hypoaldosteronism and those receiving K-sparing diuretics or NSAID. • Particularly effective in patients with diabetic vasculopathy, heart failure or systolic dysfunction after myocardial infarction.
•Captopril	12.5-100	2-3		
•Enalapril	2.5-4	1-2		
•Fusinopril	10-40	1		
•Lisinopril	5-40	1		
•Perindopril	1-16	1-2		
•Ramipri	1.25-20	1		
•Trandolapril	1-4	1		
Angiotensin II receptor blockers				
•Losartan	25-100	1-2	Block the angiotensin II receptors	• <u>Can be used interchangeably with ACE inhibitors, or as a primary renin angiotensin blockade agents in patients who develops cough on ACE inhibitors</u>" •
•Valsartan	80-320	1		
•Candesartan	8-32	1		
•Irbesartan	150-30	1		

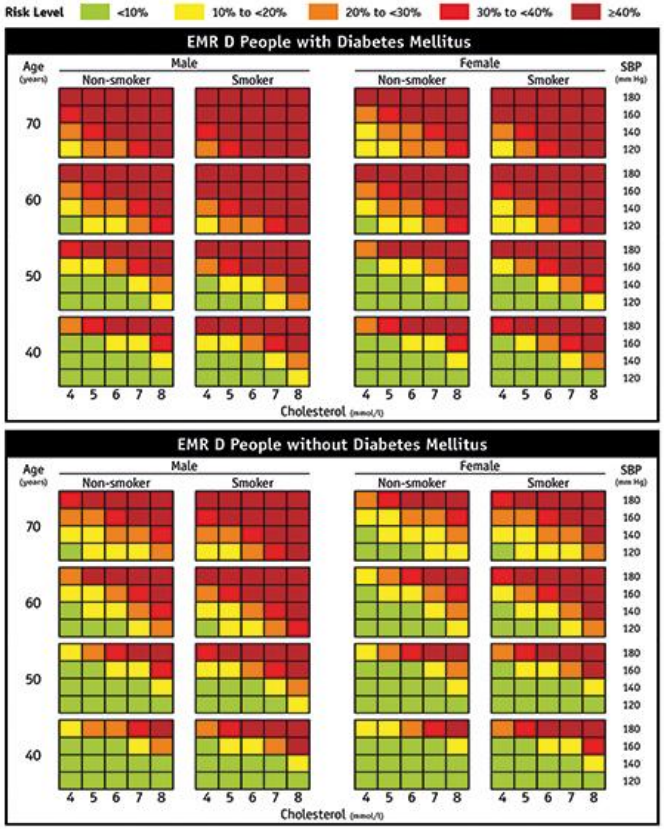
•A-Adrenergic receptors antagonists			Selective antagonists of postsynaptic α-1 receptors because presynaptic α – adrenergic receptors is left unblocked, the feedback inhibiton of NE release is intact	• Inhibition of NE release may lead to first- dose hypotension • Useful for prostatic hypertrophy • In older patients, doxazocin may increase the risk of stroke and heart failure
•Prazocin	2-20	1-2		
•Doxazocin	2-16	1		
•Terazocin	1-20	1		
B- adrenergic receptor antagonists			These cause decrease in cardiac output, rennin release and sympathetic discharge. Intially, vasoconstriction develops by overtime, vascular resistance is normalized	• The three most important differences in clinical use are cardio-selectivity. ISA and lipid solubility • Cardio-selectivity disappears when higher doses are given. • Cardio-selectivity results in less metabolic side effects. • ISA causes less decrease in heart rate, renin release and cardiac output and less metabolic side effects. • Less Lipid soluble agents do not enter brain readily and thus cause less nervous side effects.
Cardioselctive				
•Atenolol	25-100	1		
•Metoprolol	50-200	1-2		
Non-cardioselective				
•Propranolol	40-240	1-2		
•Nadolol	20-240	1		
With intrinsic sympathetic activity				
•Acebutolol	200-1200	2		
•Pindolol	22190	2		
A-/B- blocker			Fall in blood pressure results mainly from decrease in peripheral resistance. α-/B-blocker is 10-1 for Labetalol and 4:1 for Carvedilol	• B-blockers are well suited for younger and middle-aged hypertensive particularly in patients with myocardial ischaemia and high level of stress. They may interfere with athletic performance.
•Labetalol	200-800	2-3		
•Carvedilol	3.75-25	2		
Acting within neurons				• Frequently cause orthostatic hypotension and sexual dysfunction
•Reserpine	0.05-.25	1	Depletes postganglionic adrenergic neurons of NE by inhibiting its reuptake in storage vesicles	
•Guenfancine	0.5-2.0	1	Inhibits release of NE from adrenergic neurons	
Central α-agonists				• May cause inflammatory disorders in various organs commonly the liver. • Haemolytic anemia rarely occurs
•Methyle dopa	250-1500	2	A methyl NE, derived from methyldopa stimulates central α- adrenergic receptors reducing sympathetic outflow.	
•Clonidine	0.1-0.6	2	Same action as Methyldopa but also inhibits NE release from pre-synaptic α – neurons	• Central α – agonists have short half life, so when discontinued, the inhibition of NE release disappears and rebound hypertension occurs.
•Clonidine TTS	0.1-0.3	once/week		
Direct vasodilatation				

• Hydralazine combined	50-200	2-4	Direct relaxation of smooth muscle cells	• Limited efficacy if given alone due to fluid retention and reflex sympathetic activation, so they should be given with a diuretics and B-blockers
• Minoxidil	2.5-80	1		• Hydralazine may cause lupus – like syndrome if dose >200 mg/day and in slow acetylators of the drug

WHO/ISH Risk prediction charts

for 14 WHO epidemiological sub-regions

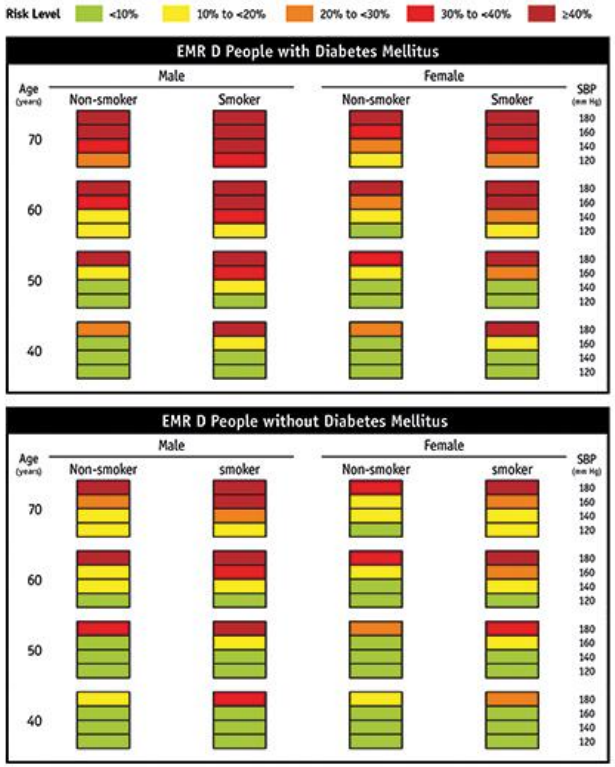
Figure 12. WHO/ISH risk prediction chart for EMR D. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus.



This chart can only be used for countries of the WHO Region of Eastern Mediterranean, sub-region D, in settings where blood cholesterol can be measured (see Table 1).

WHO/ISH Risk prediction charts
for 14 WHO epidemiological sub-regions

Figure 14. WHO/ISH risk prediction chart for EMR D. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus.



This chart can only be used for countries of the WHO Region of Eastern Mediterranean, sub-region D, in settings where blood cholesterol CANNOT be measured (see Table 1).

Recommended response when Hypertension is suspected (diagnosis of Hypertension)

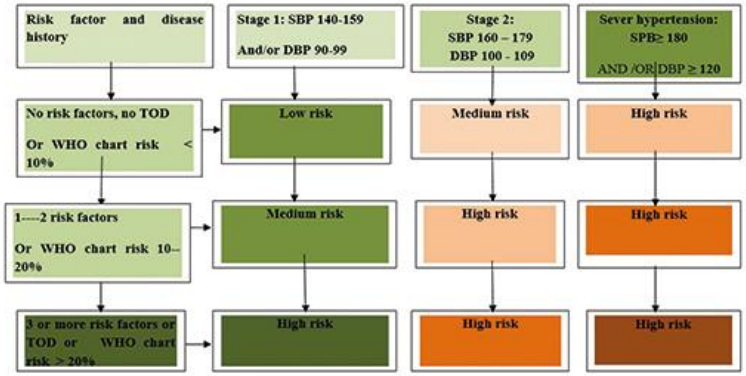
Normal BP: <130/80:	Recheck every year if the age is more than 40
Prehypertension: SBP130---139 and /or /DBP 80---89	Recheck every 6 months
STAGE 1 : :SBP140---159 and /or /DBP /90—99	Check every week for one month
STAGE 2 : :SBP160--179 and /or / DBP/100—119	Confirm with two readings every week for two weeks
Sever hypertension: SPB≥ 180 AND /OR DBP ≥ 120	CONFIRM. IF URGENCY OR EMERGENCY. TREAT ACCORDINGLY

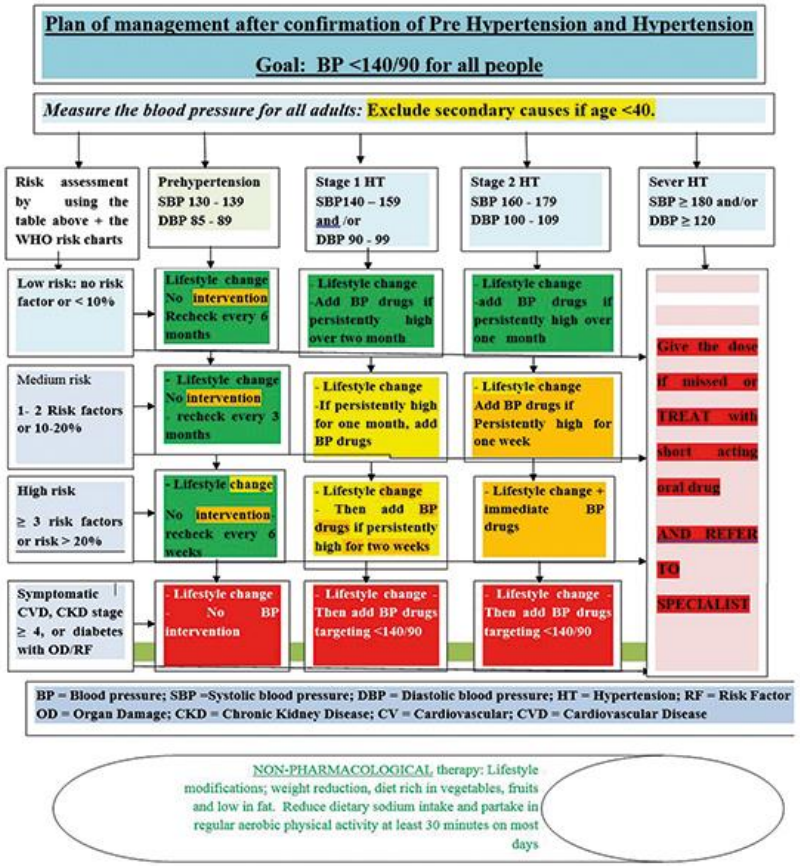
• IF 24 HOUR B.P. MONITOR IS USED HYPERTENSION IS DIAGNOSED WHEN : daytime ambulatory measurements of ≥135/85 m Hg Or nocturnal measurements of ≥120/70 mm Hg

Assess the risk the risk of developing CVD in the coming 10 years {fatal or nonfatal major cardiovascular event (myocardial infarction or stroke) according to

A- Age > 55years 2-level of B.P 3-smoking 4-DM 5-Abdominal obesity (Waist circumference >102 cm (Male), >88 cm (Female) 6-Family history of premature CVD7-Hypercholesterolaemia (if cholesterol level measurement is available) or

B- Use the WHO risk prediction chart





NON-PHARMACOLOGICAL therapy: Lifestyle modifications; weight reduction, diet rich in vegetables, fruits and low in fat. Reduce dietary sodium intake and partake in regular aerobic physical activity at least 30 minutes on most days

Pharmacological therapy: ***initiate the*** **treatment with Thiazide diuretics or long acting calcium channel blockers, Choice of other drugs according to compelling indications**

Class of drug	Alpha-blockers	ACE inhibitors	Beta-blockers	CCBs (rate limiting)	ARBs
compelling indication	Benign prostatic Hypertrophy	Heart failure, LV dysfunction, post-MI, Established HD, type I diabetic nephropathy. C/I in pregnancy.	Post MI, Angina. Aortic dissection	Angina, arrhythmias	ACE inhibitor intolerance, Type II diabetic Nephropathy, LVH, Heart failure, post MI. C/I in pregnancy

Start **with low dose of a single drug aiming for a reduction of 5 to 10 mm Hg in blood pressure at each step In order to avoid symptoms related to overly aggressive blood pressure reduction. Patients with resistant HTN or type 2 diabetes mellitus should be monitored with Ambulatory BPM if they are at high risk for cardiovascular complications**

Decide **whether to continue the same management plan or to modify it. If adequate response is not achieved as follows: -- Thiazide Diuretics: after one month**
-- ACEIs, CCBs, ARBs: 2 weeks to 1 month

Better to choose **long acting preparations**

Start combination therapy: ***when blood pressure is >20/10 mmHg above the target goal***
Steps of combining the drugs are:
1-Use of two drugs at low dose 2-Use of the two drugs at full dose 3-Use previous combination at full dose in addition to a third drug (low – max.) dose 4-Use of the three drug combination at full dose.

FIRST STEP: THIAZIDE DIURETIC OR CCBS + ACEI/ARB (low dose of 2nd drug)	*SECOND STEP*: THIAZIDE OR CCBS + ACEI / ARB (max. dose of 2nd drug)
THIRD STEP: THIAZIDE + CCBS + ACEI / ARB (low-max. dose of 3rd drug)	FOURTH STEP: THIAZIDE + CCBS + ACEI / ARB (max. doses) + {B- BLOCKER OR α – Blockers OR SPIRONOLACTONE OR OTHER DIURETICS OR CENTRALY ACTING DRUGS}. Screen for secondary causes if still not controlled. Consider ambulatory BP monitoring.
OTHER DRUGS: Aspirin: Unless contraindicated, low-dose aspirin (75 -150mg/ day) is recommended for all people needing secondary prevention of ischemic CVD, and primary prevention in people with hypertension over the age of 50 years who have a high CVD risk > 30%(AFTER THE BP IS CONTROLLED)	Statin: therapy is recommended for all people with high BP complicated by CVD and for primary prevention in people with high BP who have a moderate CVD risk >20%

Frequency of the follow-up visits at PHC level	What to do during the follow-up visit;
All patients with hypertension should be provided with regular follow-up, the follow up intervals can vary from one week to one year according to patient's condition. Arrange follow- up visits as follows: ➢ STAGE 1: Monthly until goal blood pressure is achieved, then every 3 to 6 months. ➢ STAGE 2: every 2 weeks until goal blood pressure achieved then every 3 months. ➢ SEVERE HYPERTENSION: refer and then F.U. weekly until the goal blood pressure achieved then every 3 months ➢ In the presence of co-morbidity as DM or heart disease; follow up frequency may be increased.	1-Check the blood pressure 2-Check adherence to medication 3-Advice and educate on life style modification 4-Inquire about symptoms that indicate the presence of target organ damage (complication) e.g. breathlessness, chest pain 5-Investigate as required: One week after initiating ACEIs: Serum creatinine and electrolytes Annual routine investigations: Lipid profile. renal function test and electrolytes resistant hypertension {(Office blood pressure >140/90 or> 130/90 in patients with diabetes or chronic kidney disease And Patient prescribed 3 or more antihypertensive in full doses including diuretics if possible }

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