MANAGEMENT OF HYPERTENSION IN WOMEN: PAKISTAN HYPERTENSION CLINICAL PRACTICE GUIDELINES

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PREAMBLE

Hypertension has been recognized as a global health concern. In developing countries, it is not addressed and described to the extent that the actual prevalence of the disease makes it necessary. In these countries, control of blood pressure (BP) remains suboptimal. Worldwide BP reduction is a serious issue, and the situation is more alarming situation in our country. Pakistan is one of them, more than 46% of the Pakistani population are hypertensive. In 2010, hypertension was the leading cause of death and disability worldwide, and a greater contributor to events in women. South Asia contributes 24% of world population and is undergoing a rapid epidemiological transition with significant rates of hypertension in different countries. The prevalence of hypertension in low socioeconomic population in Pakistan is 39% in women vs. 37% in men.

There is no proper data regarding hypertension in women in Pakistan, except for a few populations based surveys conducted which showed the prevalence of hypertension. The pooled prevalence in Pakistani women is 24.76% vs. 24.9% for men for an age bracket of above 40 years. The occurrence is higher in urban compared to rural areas. General practitioners (GP) in Pakistan underdiagnose and undertreat high BP, especially in the elderly women. Only in 37% of patients, the treatment was initiated by a GP. 23% of this group received only sedatives alone or combination of sedatives and hypertension control medication. We lack published guidelines regarding hypertension.

Hypertension still remains the major preventable cause of cardiovascular disease. Hypertension is a leading cause of mortality globally, and especially in our continent. The purpose of these guidelines is to highlight the neglected population (i.e., Women) of Pakistan, who are physically and hormonally different from men. They have more complications as a result of hypertension. Early diagnosis and proper treatment and adherence to the treatment is therefore important.

The task of developing guideline on hypertension is by Go Red Chairperson and Scientific Council Pakistan in collaboration with Pakistan cardiac society. This is first clinical practice guidelines for management of hypertension which is a need of our time with the objective to control the epidemic of hypertension in women.

This scientific document on hypertension in women with local recommendation which are made local studies and randomized trials and south Asian studies. These educational tool help the health care providers GP and doctors because all see the women in theirs practice and using this guideline facilitate them for treatment because specially in elderly women usually received only sedative alone or in combination with antihypertensive medicines by GPS. Our efforts will encourage GPs and medical practitioners to practice these guidelines in their clinical judgment about risk and complications, as well as in the determination and implementation of preventive, diagnostic or therapeutic medical strategies for control of hypertension. What is new in this guideline is that we focused on treatment of hypertension according to our circumstance as women have limited access to health care and are undertreated. That is the reasons why more women develop complications of hypertension as delay in diagnosis, initiation of recommended treatment and the control is only in 50% in women.

These guidelines focused on risk factors and complication throughout the life cycle of women. Lifestyle management should be started in adolescent and more focus should be given to adherence to treatment. This is crucial for control of hypertension. New topics like management of hypertension in chronic kidney diseases is added. Recommendation-based treatment should be started in such cases. The initiation of widespread and intensive continuing medical education for all physicians involved in the management of women patients with hypertension will be the main benefit from this guideline.

1 Introduction and Prevalence of Hypertension in Women in Pakistan

1.1 Hypertension in South Asian Women: Hypertension is a key risk factor for cardiovascular disease (CVD) and adverse health conditions among women.[1] The gender difference in blood pressure levels appears during puberty.[2] In south Asia the prevalence of hypertension in Pakistani female 29.3% vs. 36.8% compare to men in 2016 which is highest in South Asian. The risk factor most common for hypertension in women are obesity, menopause, preeclampsia, polycystic ovary disease and use of oral contraceptives.[3]

Table 1: Prevalence of hypertension in South Asian countries according to most recent available data

Country	Gender	Prevalence (%)	Year of the latest survey data
Pakistan	Male	36.8	2016
	Female	29.3	
India	Male	27.4	2018
	Female	23.6	
Bangladesh	Male	28	2016
	Female	24.3	
Nepal	Male	16.9	2014
	Female	33.6	
Sri Lanka	Male	32	2014
	Female	6	
Afghanistan	Male	10.3	2015
	Female	51.1	
Maldives	Male	2	2017
	Female	4	

1.2 Pakistan Aspects: The age-standardized prevalence of hypertension is 34.4%.[4] The overall pooled prevalence of hypertension is 25% in males and 24.76% in females. Subgroup analysis showed higher urban prevalence of 26.6% than for the rural dwellers at 21.03%. The high prevalence is seen in Punjab 49%, followed by Sindh 46% Baluchistan 33% and in Peshawar 23% by Basit et al. The Increasing trend of Hypertension in women because of obesity, lack of awareness, lack of physical activity and low level of education.[5,6]

1.3 The Need for Guidelines for Women: The high prevalence of Hypertension in Pakistan specially women which is often underestimated in trials and remain undiagnosed and presented with complications of hypertension. It necessitates the need to write guidelines to recommend accurate measurement, evaluation and treatment of women according to recommendation in this guideline which are according to available data on women.

2 What is Hypertension?

- Primary hypertension 90%
- Secondary 10%

Hypertension is defined as blood pressure greater than 140/90 mmHg.[7]

Category	SBP (mmHg)		DBP (mmHg)
Optimal	<120	and	<80
Normal	120 – 129	and/or	80 – 84
High-Normal	130 139	and/or	85 89
Grade 1 hypertension	140 – 159	and/or	90 – 99
Grade 2 hypertension	160 – 179	and/or	100 – 109
Grade 3 hypertension	≥ 180	and/or	≥ 110
Isolated Systolic Hypertension	≥ 140	and	< 90

Figure 1: Categories for conventionally measured seated office blood pressure

3 Measurement of Blood Pressure

3.1 Steps in Accurate Measurement of Blood Pressure: The accurate measurement of blood pressure (BP) is an important diagnostic and monitoring tool. It is important to measure blood pressure in both arms. A study published in Lancet about the accuracy of BP readings in both arms, the researchers indicated a systolic number difference of 10-15 mm Hg or more could be an indication of a more serious problem, such as narrowing arteries, decreased blood flow to the brain, and a significantly increased chance of heart attack and stroke in women.[8]

3.2 Use of Validated Blood Pressure Apparatus: The devices need to be validated by the American Association of Medical Instrumentation (AAMI), British Hypertension Society (BHS) or the European Society of Hypertension (ESH).

Table 2: Advantages and disadvantages of use of various blood pressure apparatus

Type of apparatus	Advantages	Disadvantage
Mercury Sphygmomanometers	Simple, portal doesn't required calibrations	Bulky device
Aneroid Apparatuses	Cheaper more portable The aneroid gauge can be placed in any position for easy reading come with built in stethoscope	Needs frequent recalibration the device is giving faulty reading
Automated Digital Sphygmomanometer	The device is very compact and portable. Easy to use the preferred device of choice monitoring at home. Chances of human error are minimum.	The device is delicate. Repairing the device can be complicated serviced by the manufacturer. For accuracy.

Table 3: Cuff sizes

Small adult	22 - 26 cm
Adult	27 -34 cm
Large adult	35 - 44 cm
Adult thigh	45 - 52 cm

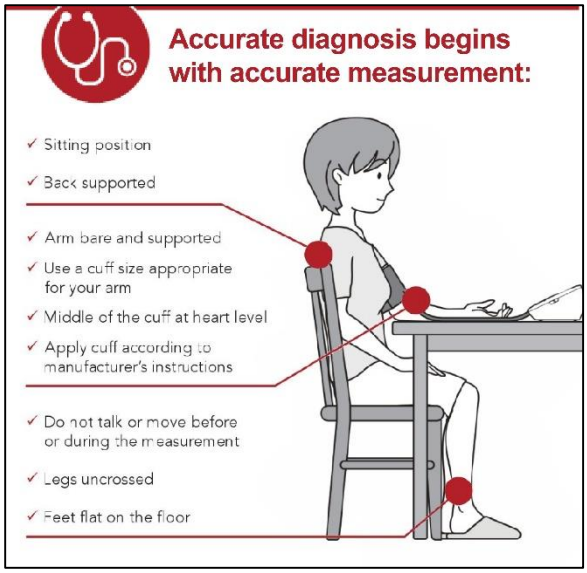


Figure 2: Steps of blood pressure measurement

4 Different Types of Blood Pressure Measurement

4.1.1 Office blood pressure monitoring: It is by nurses or physician readings are not properly correlated to actual readings because of inadequate cuff size, improper technique and non-fully deflated cuff and reading taken by physician are high in women because of white-coat effect.

4.1.2 Post clinic measured blood pressure: It is by nurses or by physician and in women reading taken by physician are higher. Shahab et al. showed that post clinic blood pressure after 15 minutes was significantly lower and more accurate.[9]

4.1.3 Orthostatic hypotension: Defined as taking BP in quiet setting than standing for 2 minutes rechecked BP if difference is 20/10 mm HG than it is orthostatic hypotension

Recommendation for office BP

- Use proper technique, validated apparatus and proper cuff size because tight cuff size gives falsely high readings and loose cuff gives false low BP readings
- Check after 5 minutes of rest and take three readings with 2 minutes apart average of last 2 readings
- Check for orthostatic hypertension

4.2 Home measured blood pressure monitoring (HBPM): Home blood pressure monitoring (HBPM) can be used in the diagnosis of hypertension in following conditions.[10]

- Inadequately controlled hypertension
- Diabetes mellitus
- Chronic kidney disease
- Suspected non-adherence
- Demonstrated or suspected white coat effect
- BP controlled in the office but not at home (masked hypertension)
- White coat or masked hypertension is suggested by HBPM, then ABPM

Recommendation:

- Home blood pressure is class I recommendation in women in our population but can be used as alternative to ABMP if not available.
- Home blood pressure recording wrist monitors are not recommended used Omron arm monitor

4.3 Ambulatory blood pressures: Systolic blood pressures (SBP) and pulse pressures (PP) were higher in males than in females among adults less than 45 years old. After age 45, SBP and PP were higher in females. The predictors of CVD risk in women are non and reverse dippers and high hyperbaric index in pregnancy.[11,12]

- Hypotension
- White coat hypertension
- Nocturnal hypertension
- Pregnancy with hypertension
- Resistant hypertension
- Chronic kidney Disease
- Obstructive sleep Apnea

Table 4: Corresponding Values of Systolic BP/ Diastolic BP for Clinic, Home (HPBM), Daytime, Nighttime, and 24 -Hour Ambulatory (APBM) Measurements

Clinic	HPBM	Daytime ABPM	Nighttime ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

Recommendation:

- Ambulatory is class I recommendation for diagnosis of hypertension and drug monitoring of antihypertensive medicines
- Accurate recording of 24 hours of ambulatory blood pressure monitoring training of staff and patient consoling is mandatory.

5 White coat/masked hypertension

Women were more likely to be diagnosed with white coat hypertension. Prevalence is 10-15% mostly associated hypertension in young females especially pregnancy females and it is not benign entity it is associated with CVD risk in women.[13]

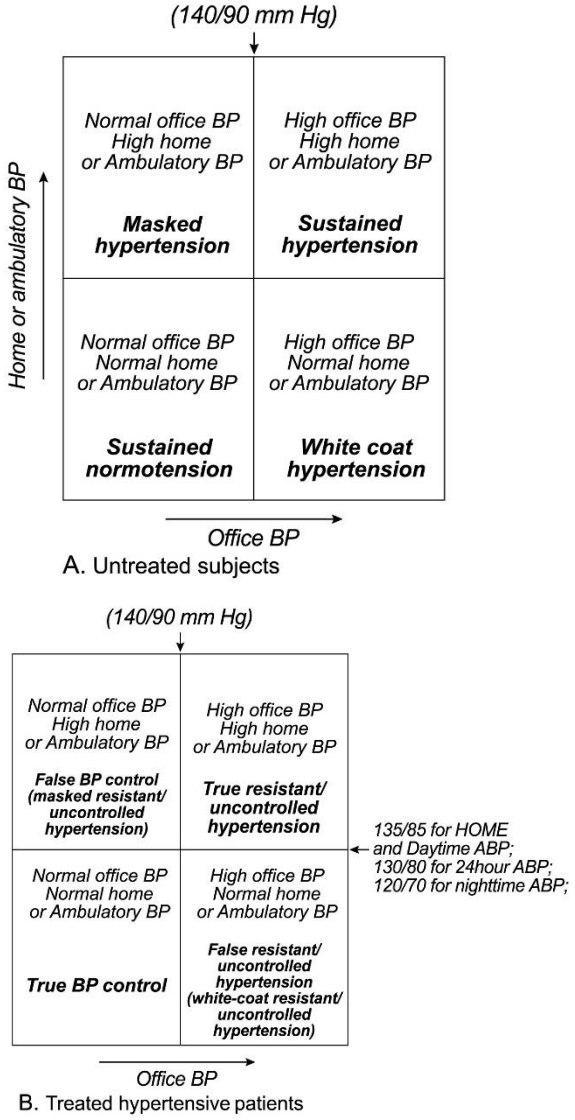


Figure 3: White coat/masked hypertension[13]

Recommendation:

- White coat hypertension and masked hypertension is not benign in women should be evaluated with Ambulatory blood monitoring device.

6 Risk factors of Hypertension

Factor	Females	Males
Age	++	+
Obesity	++	+
Visceral obesity	++	+
Metabolic syndrome	+ (++ after menopause)	++
Type 2 diabetes	+	+ (+)
Dyslipidaemia	++	+
Smoking	+	++
Obstructive sleep apnoea	+	++
Autoimmune disorders	+++	+
Reduced eGFR	++	+
Albuminuria	+	++
Gout	+	+++

+Common; ++more common; +++much more common vs. other sex.

Figure 4: Sex differences in conventional CV risk factors and co-morbidities in hypertension[14]

Recommendation:

- Hypertension in women should also be evaluated for other risk factors like diabetes, dyslipidemia and Metabolic Syndrome in our population.

7 Evaluation of Hypertension

In Evaluation of hypertension recommended blood investigations and examination for target organ damage.

7.1 Baseline investigation

- Complete blood count
- Fasting blood sugar
- Serum creatinine with eGFR
- Sodium, potassium
- Urine detailed report
- Electrocardiogram (ECG)

7.2 Addition test if BP is difficult to control

- Thyroid stimulating hormone
- echocardiogram
- Urine albumin creatinine ratio
- Uric acid
- HbAIC

8 Symptoms of Hypertension

Majority of women presents with symptoms of hypertension[15]

- Tightness, nagging and often continuous chest pain at rest
- Pain may radiate to the jaws, left arm, shoulder blades
- Stress-related chest pain, with/without radiation
- Tiredness, loss of energy, sleeping disturbances
- Hot flushes, severe sweating day/night
- Palpitations, tachycardias, paroxysmal atrial fibrillation
- Intermittent fluid retention, ankles, hands, eyes
- Repeated admissions with chest pain like angina
- Repeated admissions in Hospital chest pain and underwent coronary angiography without any indication.

Recommendation:

- The symptoms related to hypertension most like related to vascular spasm. Endothelial dysfunction and hormone effects.
- Symptoms should be evaluated because microvascular angina is one of the complications of hypertension.
- The symptoms should not be ignored and labelling as anxiety and discharge on sedatives not recommended.

9 Gender Difference in Target Organ Damage

Table 5: Gender Difference in Target Organ Damage[16]

Complications	Men	Women
Cerebrovascular diseases Stroke Transient ischemic attack Hypertensive encephalopathy	Young men have more ischemic stroke 12% vs. 9.8%	Stroke and hypertensive encephalopathy more in elderly women
Eyes Retinopathy	Higher prevalence of retinopathy compared with women (15.9% vs. 14.0%)	Significant associations between retinopathy and microalbuminuria
Coronary artery disease Myocardial infarction Angina Heart failure Atrial fibrillation Left ventricular hypertrophy (LVH)	CAD are more common in men	CAD increased from 30% to 45.7% Heart failure with preserved ejection fraction in women LVH more common Atrial fibrillation
Kidney Hypertensive nephropathy (EGFR<60ml/mi/1.732 Albuminuria	Progression end stage is faster in men Microalbuminuria is poorly tolerated	CKD is more common but progression to end stage is low Microalbuminuria is more common
Arteries (peripheral artery disease		In hypertensive women because arterial stiffness

- Approximately 40% of stroke cases, 39% of myocardial infarction cases and 28% of end-stage renal diseases are attributable to hypertension in women
- Left ventricular hypertrophy (LVH) is independent cardiovascular risk factor in women for CVD and it developed at lower blood pressure level in young women.[17]
- Hypertensive women have stronger association between microalbuminuria, a marker of endothelial dysfunction, and total mortality in hypertensive women.[18]

Recommendation:

- Every hypertension woman should be evaluated for target organ damage
- Complications related to hypertension can be managed at early stage according to disease based guidelines

10 Treatment of hypertension

10.1 Risk stratification

Hypertension disease staging	Other risk factors, HMOD, or disease	BP (mmHg) grading			
		High normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP 160-179 DBP 100-109	Grade 3 SBP ≥180 or DBP ≥110
Stage 1 (uncomplicated)	No other risk factors	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to Moderate risk	Moderate to high risk	High Risk	High risk
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk
Stage 3 (established disease)	Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk

Figure 5: Risk stratification calculator in women to treat the hypertension according to the risk

10.2 Threshold of blood pressure treatment:

The threshold of blood pressure treatment is 140/80 mmHG in women without risk factors if they risk factors the target should be less than 130/80 mmHG.

10.3 Hurdles in treatment of hypertension[19]

Diagnosis

- BP threshold for diagnosis.
- Staging of blood pressure.
- No validated CVD risk calculator.

Treatment

- Threshold for initiating pharmacological treatment.
- Difference in initiating treatment in stage I, II or III.
- Recommendation vs. single pill or combination pil.

Recommendation:

- Follow the guideline for diagnose and management of hypertension
- It is made for our population but treatment can be individualized according to need of the patient.

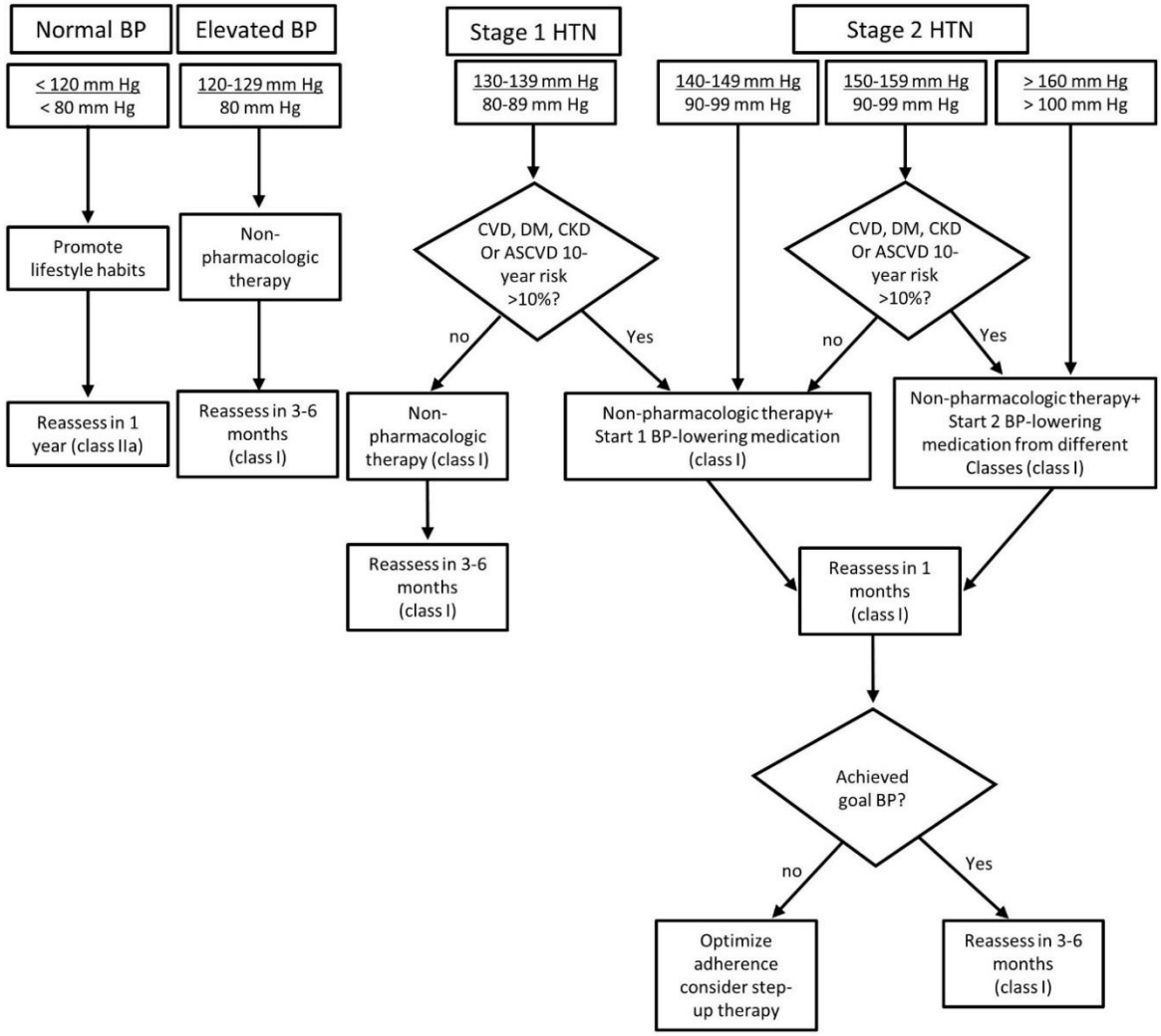


Figure 6: Recommendation is to follow the guideline to diagnose and management of hypertension

Recommendation:

- Follow-up visit is according to the Guidelines unnecessary follow-up should be avoided until there is compiling indication.

11 Lifestyle Modification

Table 6: Lifestyle modification

Modification	Recommendation	Approximate Reduction (mmHg)
Physical activity	Engage in regular aerobic physical activity (e.g., brisk walking) 150min/week	4 – 9
DASH eating plan	Consume diet rich in fruits, vegetables, and dairy products and low-fat avoid reduced saturated like beef animal fats and junk foods and avoid soda and fruits juices	8 – 14
Dietary sodium restriction	Reduced dietary sodium intake to max of 100 mmol/day (2.4 g sodium or 6 g sodium chloride	2 – 8
Moderate alcohol consumption	Limit daily consumption to max of 1 drink for women or 2 drinks for men	2 – 4
Weight loss	Maintain normal body weight (BMI 18.5 – 24.9 kg/m^2	5 – 20 per 10-kg weight loss
Stress reduction	Practice a stress-reduction modality such as Transcendental meditation	5

Recommendation:

- Lifestyle modification should begin from childhood to whole life span.
- Adherences to Life-style modification should be convey to patient in native language or use of simple template of healthy lifestyle habits.

12 Pharmacological Treatment

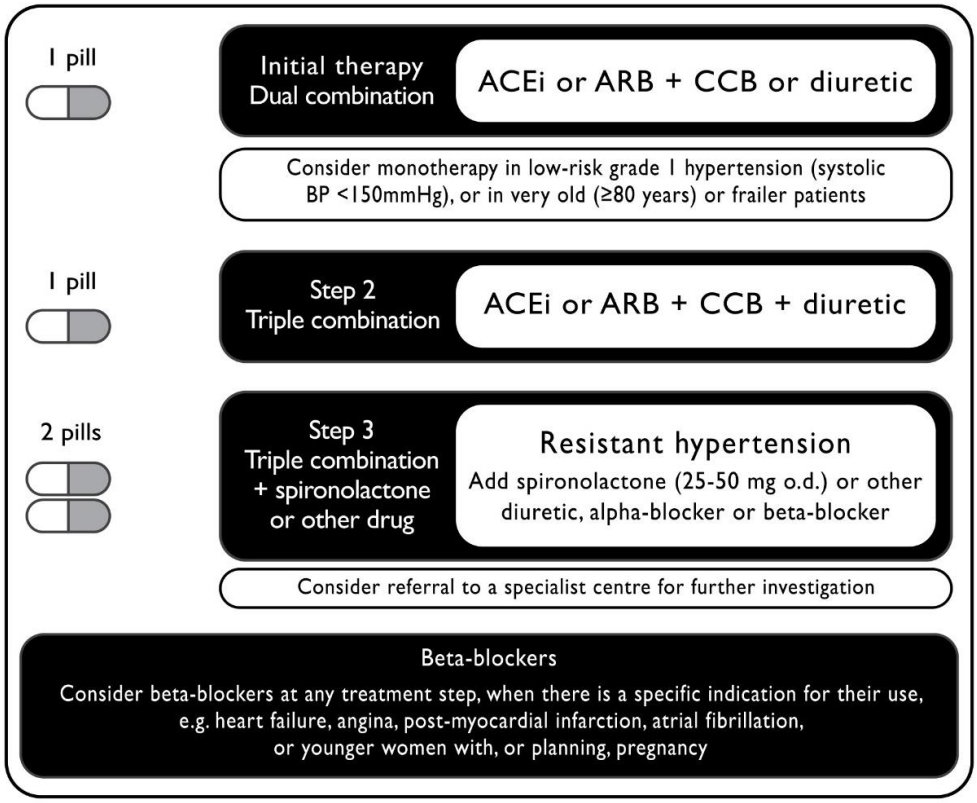


Figure 7: Pharmacological treatment[20]

13 Gender Difference in Side Effects of Antihypertensive Medicines

Women have different pharmacodynamics effects of drugs because of decrease absorption and metabolism by P450 enzymes.[21, 22]

Diuretics

- Reduced urinary calcium excretion, may have a positive effect on the prevention of bone loss and osteoporosis in postmenopausal women.
- Thiazides are not tolerated in South Asian women as they develop polyuria and resulting in self-withdrawal should be given cautiously in small doses.

Calcium channel blockers

- Calcium channel blockers are more beneficial than ACE inhibitors for stroke prevention.

Angiotensin-inhibitor or Angiotensin Receptor blockers

- Women are more prone d ACE-inhibitor induced cough three times more often than men. And cautiously used in women with childbearing age because of its adverse effects in pregnancy.

Recommendation:

- Whenever choosing medicines for hypertension consider the side effects of medicines in our population to avoid self-withdrawal of medicine.
- The choice of medicine can be modified to compelling indication like other concomitant diseases.

14 Adherence to Antihypertensive[23]

Improve patient adherence using a multi-disciplinary approach.

- Consider tailoring or simplifying pill taking to fit your patient's daily habits.
- Use single pill combinations when second can be modified.
- Have your patient get involved in his /her treatment by providing adherence feedback, self-monitoring BP at home and reporting the results.
- Patient at each follow-up take HBP medications physician aware of doses of the medications and how to take them.
- Make sure you refill your medications before they run out. Take your medications exactly as prescribed—don't skip days or cut tablets in half.
- In patients with hypertension who are not on target, review adherence to all health behaviors, including the use of prescription medications, before considering therapy adjustments.
- Beyond the office adherence by telemedicine, WhatsApp messages, electronic monitoring devices and biomedical detection of medicines in urine of blood.

Recommendation:

- Gives single combination pill which is cost effective, evidence based and properly tolerated by patients
- Adherence consoling and involving patients in her care and identify some support member which can monitor regular provision of medicine and report self with drawl.

15 Use of aspirin in hypertension in women[24]

The Aspirin is indicated in Women aged 40 and 59 at high risk (10% or greater) of having a heart attack or stroke and 23% hypertensive women are taking Aspirin without any indication.

16 Use of statins in women[25]

In adults at increased CVD risk but without prior CVD events, statin therapy for primary prevention of CVD was associated with reduced risk of all-cause mortality and CVD events statin are poorly tolerated by women with myalgias, abdominal pain especially elderly Asian women.

17 Algorithm of Pharmacological Treatment

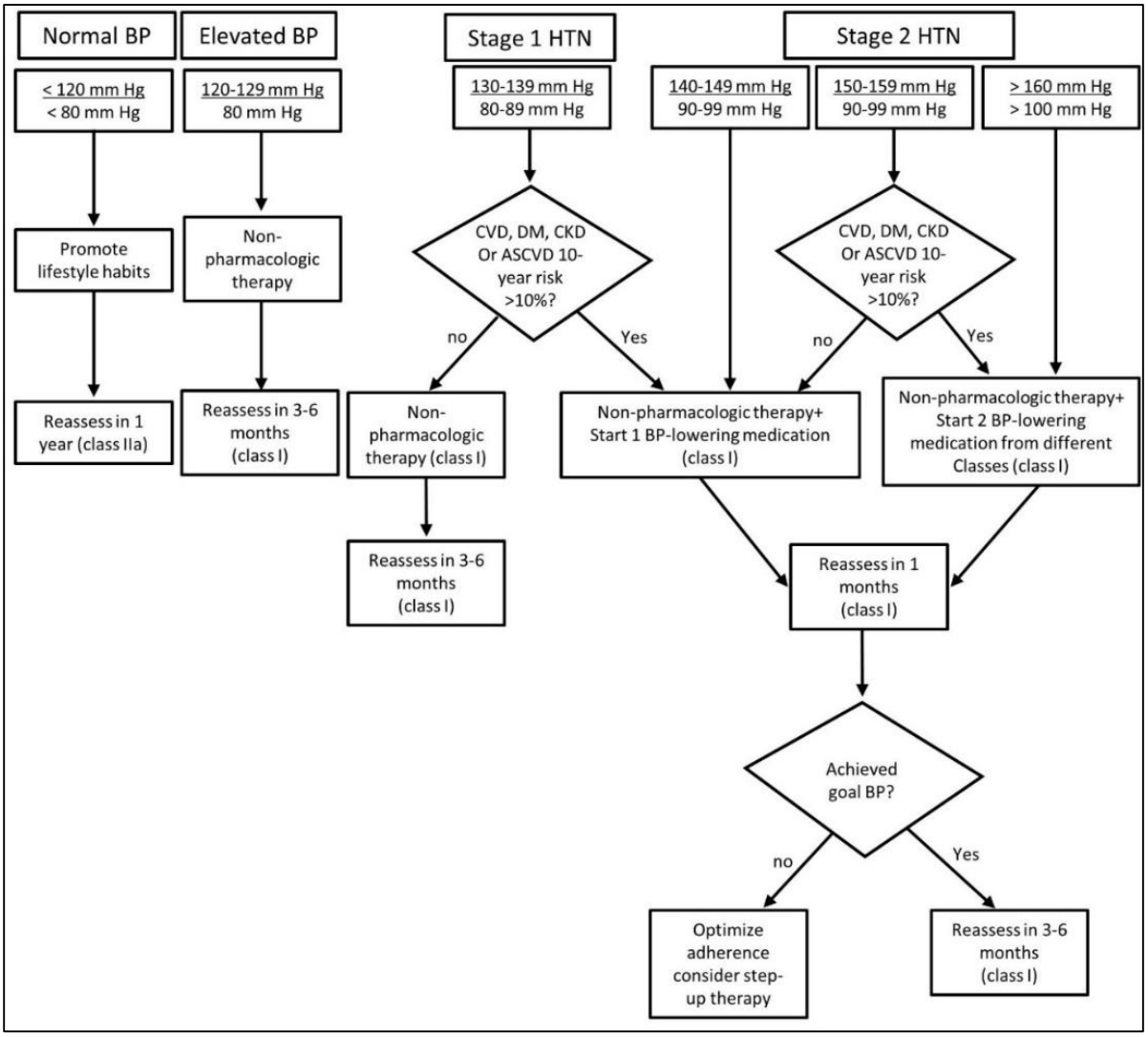


Figure 8: Algorithm of pharmacological treatment

18 Hypertension in Special Consideration

18.1 Hypertension in Adolescent[26]

Hypertension also an important problem in adolescent and female has higher blood pressure till age of 7 to 12 after than male. Adolescent mostly have primary hypertension about 85% of cases obesity, renal parenchymal disease and family history and in female psychological stress is one of the risk factors. Alarming left ventricular hypertrophy, kidney failure and cognitive disorders are commonly seen microvascular dysfunction is other cause of hypertension because narrow retinal arteries are seen

Management is lifestyle for obese children because obesity is independent predictor of LVH in children and regarding pharmacological treatment is first line treatment in children with stage two hypertension or stage I hypertension with LVH. No sufficient evidence for choice of specific antihypertensive

18.2 Hypertension in young women - 30 to 40 years

- Family history of hypertension in a young age x3 higher risk.
- Premenstrual syndrome and migraine in 15% of teens and adolescents
- Recurrent miscarriages PCOs, and infertility.
- Low seriocomic status
- Low level of ferritin

- Autoimmune disease
- Stress
- Lack of sleep

In young females working in district of Punjab[27] aged 20-40 years the risk factors associated hypertension educational level, socioeconomic factors level, obesity and tractional risk factors along with sodium, potassium and ferritin in this study they found low in prehypertensive and hypertensive.

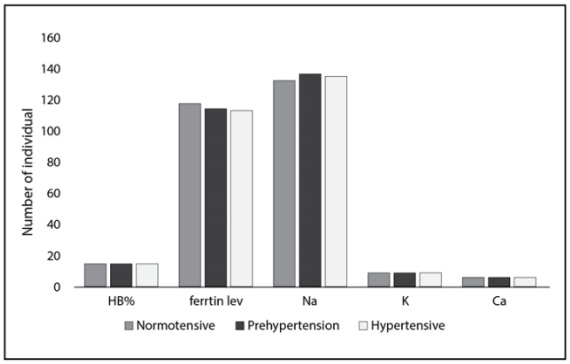


Figure 9: Level of HB, Ferritin, Sodium, Potassium, and Calcium in Normotensive, Prep-hypertensive and hypertensive

19 Hypertension in Pregnancy[28,29]

The Blood Pressure in Pregnancy should be measure in left lateral decubitus in right arm. Supine reading are falsely low.

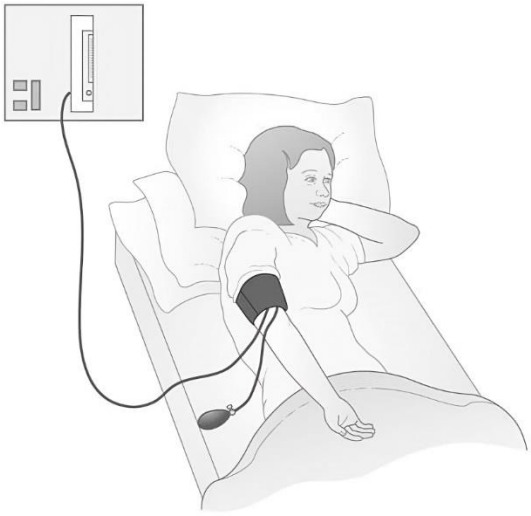


Figure 10: Measurement of blood pressure in pregnancy

The risk factors contributing to Hypertension

- Family history of hypertension
- Previous history of hypertensive disorders of pregnancy
- Multipara women,
- Personal/family history of chronic hypertension/diabetes mellitus, high energy diet,
- Gestational diabetes,
- Mental stress during pregnancy,
- Long inter-pregnancy interval,
- Lower socioeconomic status and
- Inadequate antenatal supervision

19.1 Classification of Hypertension in Pregnancy:

Table 7: Classification of hypertension in pregnancy

Pre-Eclampsia to Eclampsia	Hypertension in proteinuria >300mg per 24 hours after 20 weeks gestation. Eclampsia is the convulsive form of pre-eclampsia.
Gestational Hypertension	Hypertension induced in pregnancy after 20 weeks gestation without proteinuria
Chronic Hypertension	BP >140/90 mm Hg pre-pregnancy or before 20 weeks gestation
Pre-Eclampsia Super imposed on chronic hypertension	Chronic hypertension, developing pre-eclampsia with proteinuria, sudden increase in BP, elevated or abnormal liver function tests, thrombocytopenia or sudden increase in BP in a patient with previously controlled BP

19.2 Antenatal care

- Weekly appointments if hypertension is poorly controlled.
- Appointments every 2 to 4 weeks if hypertension is well-controlled.
- Offer pregnant women with chronic hypertension aspirin 75–150 mg once daily from 12 weeks.

19.3 Follow-up

- Medical review should be done at 2 weeks after transfer to community care if antihypertensive treatment is to be continued.
- Patient should be reviewed at 6–8 week postnatal with their Physician.

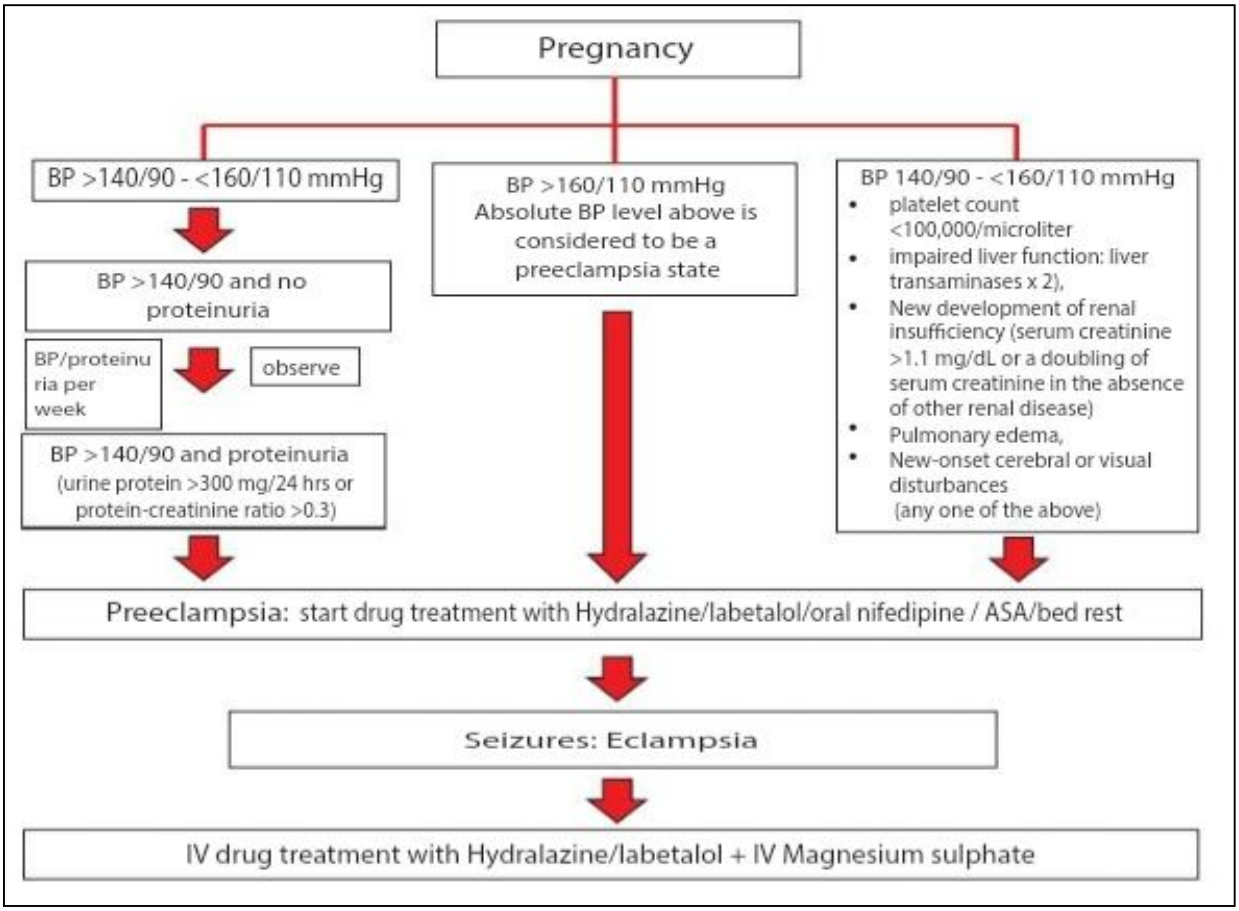


Figure 11: Hypertension in pregnancy

19.4 Drug Treatment in Pregnancy – first line drugs

Pregnancy: First line drugs for BP Control					
Drug	**Dose**	**FDA Class**	**Safety**	**Side Effects**	**Breast Feeding**
First Line drug					
Methyldopa	0.5 to 3g/day in 2 divided doses	B	Proven safety and efficacy	Some concern with depression Hepatic disturbances, hemolytic anemia-may not lower BP adequately	Compatible with Breast milk
Labetalol	200 to 1200mg/day per oral in 2-3 divided doses 20-40mg intravenous (max 220mg total)	C	Safety similar to methyldopa may be more efficacious than methyldopa	May be associated with fetal growth restriction. Neonatal hypoglycemic with larger doses	Usually compatible with breast milk

Figure 12: Drug treatment in pregnancy – first line drugs

19.5 Drug Treatment in Pregnancy – Second line drugs

Pregnancy : Second line drugs for BP Control						
Drug	Dose		FDA Clsaa	Safety	Side Effects	Breast Feeding
Nifedipine Long-acting	10-30 mg Per oral	C	Widely used	May inhibit labor; Rarely, profound hypotension if short-acting agent is used with magnesium	May inhibit labor; Rarely, profound hypotension if short-acting agent is used with magnesium	Usually Compatible with breast milk
Verapamil	80mg three times a day per oral	C	Similar efficacy to other agents	Risk of interaction with magnesium-bradycardia	Risk of interaction with magnesium-bradycardia	Usually Compatible with breast milk
Clonidine Alternative option	0.1-0.6mg/day in 2	C	Efficacy similar to methyldopa	Safety similar to methyldopa limited data regarding fetal safety	Efficacy similar to methyldopa	Possible breast milk effects
Hydrochlorothiazide useful in chronic hypertension		B	Volume contraction, electrolyte abnormalities – rare with small doses	Volume contraction, electrolyte abnormalities – rare with small doses	Volume contraction, electrolyte abnormalities – rare with small doses	May reduce breast milk production
Hydralazine Not recommended by ESC	50-300 mg/dl in 2-4 divided doses Efficacious IV agent	D	Possible maternal polyneuropathy drug-induced lupus, neonatal lupus and thrombocytopenia; Tachyphylaxis	Possible maternal polyneuropathy drug-induced lupus, neonatal lupus and thrombocytopenia; Tachyphylaxis	Possible maternal polyneuropathy drug-induced lupus, neonatal lupus and thrombocytopenia; Tachyphylaxis	Usually compatible with breast milk

Figure 13: Drug treatment in pregnancy – Second line drugs

18.6 Postnatal management:

One third women with pre-eclampsia will sustain hypertension in post-natal period and should remain in hospital until asymptomatic, there blood pressure stable within safe limits and biochemical indices are resolving.

Women in community should check her blood pressure once between day 3 and 5.

Recommendations:

- Every pregnant woman should be screen for hypertension
- Blood should be managed according to guidelines to avoid complications like ecamplasia / preclampsia
- Chronic hypertension is associated with adverse maternal and fetal outcomes so should be managed with guidelines-based medicines until patients have concomitant diseases
- Post-natal care and follow-up screening for essential hypertension is strongly recommended

20 Hypertension in postmenopausal[29]

Postmenopausal women loss the effect of estrogen increased salt sensitivity decreases nitic oxide resulted increased prevalence of hypertension around 60%.The systolic blood pressure is considered a more sensitive predictor of future cardiovascular events than diastolic blood pressure. The high prevalence of obesity, the lack of regular physical exercise, and dietary salt are important factors contributing to and aggravating postmenopausal hypertension. The risk of stroke and kidney injury doubled after menopause so frequent medical evaluation are needed. The role hormone replacement therapy not recommended despite sexual dysfunction.

21 Hypertension in elderly

Old and frail women new target 130/80 but many women develop hypotension, fractures so target so target >140 SBP as diastolic is lower should be treated with lifestyle modification and if required medicine low dose combination and gradual reduction of blood.

Pharmacologic therapy may also be considered in fit individuals >80 years with an initial SBP ≥160. Treatment side effects must be closely monitored, particularly for those who are frail Hypotension and

may have Risk of fractures. Blood pressure should be gradually lower even in hypertensive urgencies normalization over month.

Table 8: Hypertension in elderly

	ACC/AHA 2017	ACP/AAFP 2017	ESC/ESH 2018
Definition of older patients	≥ 65 years	≥60 years	Older 65-79 years
			Very old ≥80 years
BP threshold for initiation of pharmacotherapy	≥ 130/80 mmHg	SBP ≥150 mmHg	Older ≥140/90 mmHg
			Very old ≥ 160/90mmHg
Blood pressure target	< 130/80 mmHg	SBP < 150 mmHg	SBP 130-139 mmHg
			DBP 70-79mmHg

22 Resistant Hypertension

As defined, resistant hypertension includes patients whose blood pressure is controlled with use of 3 or more than 3 medications and more common in women (25.1% vs. 24.2%).[30] Pseudo resistant hypertension is defined high blood pressure that seems to be resistant to treatment, but other factors are actually interfering with proper treatment or measurement. The most common causes of pseudo-resistance are inaccurate BP measurement technique, medication non-adherence, under-treatment, and white coat HTN.[31]

- Older women
- Women have higher systolic pressures
- High systolic glomerular filtration rate (eGFR)
- Cerebra-vascular diseases (16.9% vs. 14.3%; p = 0.062)
- Abdominal obesity, and metabolic syndrome
- Obstructive sleep apnea

Recommendations:

- The diagnosis of resistant hypertension is made after excluding the causes of pseudo hypertension.
- Management of resistant hypertension is according to guidelines-based treatment to avoid complications.

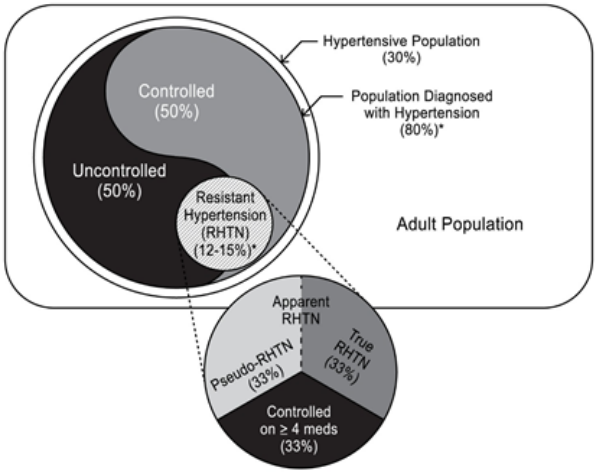
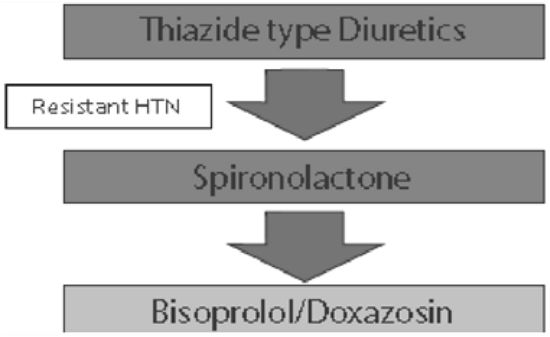


Figure 14: Resistant hypertension



23 Hypertensive Crisis

Severe and abrupt rise in blood pressure with impendeng or progressive acute target organ demagethe starting BP 180/120 it is more common 50% women have hypertensive emergencys.[32]

- Severe hypertension
- Hypertensive urgency
- Hypertensive emergency

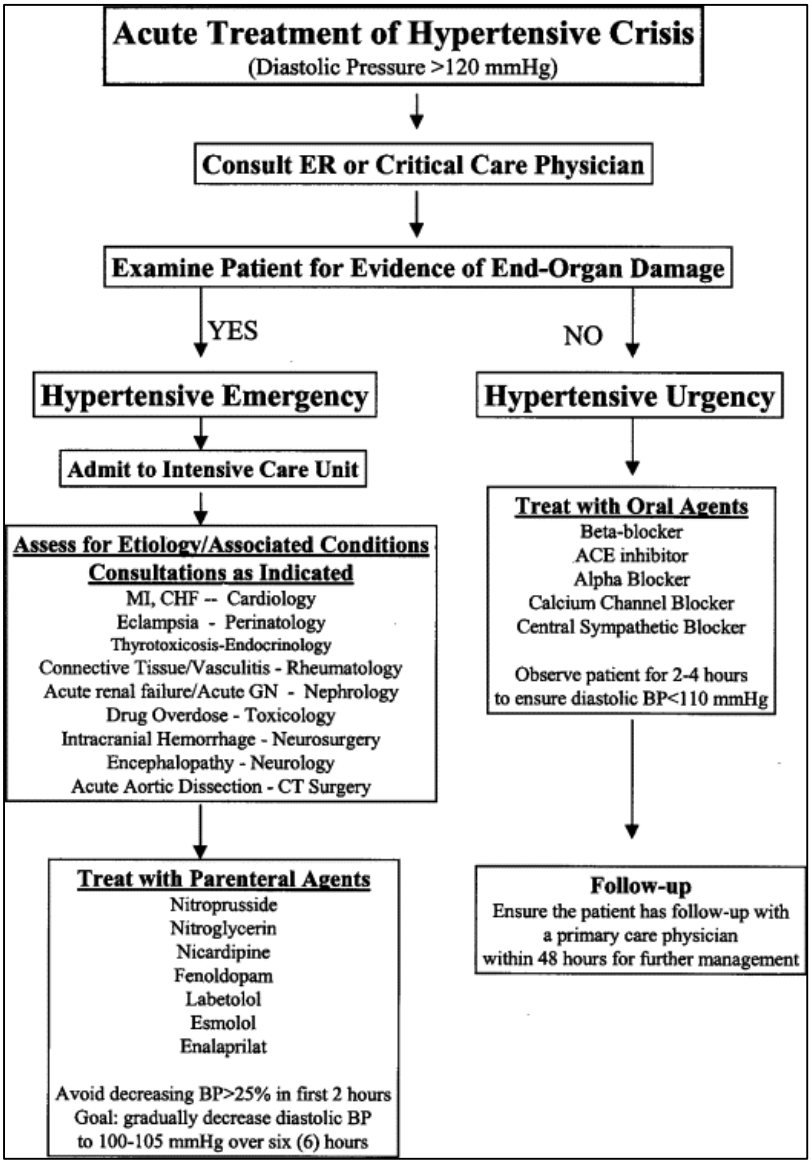


Figure 15: Acute treatment of hypertensive crisis

Recommendation:

- No use of sublingual captopril and oral nicardipine because of sudden reduction in the blood pressure causes hypotension to brain and kidney.
- Gradual reduction of blood pressure of 25% in first 2 hour is recommended

24 Secondary Hypertension

Secondary HTN is a type of HTN with an underline, potentially correctable cause the prevalence 10% to 10 percent of adults with hypertension have a secondary cause Renal artery stenosis caused by fibromuscular dysplasia and primary aldosteronism are two most cause in women with secondary hypertension.[33]

Table 9: Secondary hypertension

S. No	Disease	Sign & Symptoms	Investigations
1	Renal Artery Stenosis	Renal bruit Worsening in serum creatinine level > 30% after use of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker	• Ultrasonography (US) of the kidneys • Magnetic resonance/computed tomographic renal angiography • Percutaneous renal arteriogram
2	Renal Parenchymal disease	Mostly asymptomatic	• Serum creatinine test (elevated level) • Urinalysis
3	Primary Aldosteronism	Mostly asymptomatic	Aldosterone and renin levels (with ratio) • Hypokalemia (in a minority)
4	Pheochromocytoma	Episodic headaches, sweating, palpitations and flushing • Labile blood pressure (BP) / hypertensive episodes	24-hr urinary fractionated metanephros's
5	Cushing's syndrome	• Moon facies, central obesity, thin skin, easy bruising • Exogenous steroid use	24-hr urinary free cortisol
6	Hypothyroidism/Hyperthyroidism	• Symptoms of hypothyroidism or hyperthyroidism	Thyroid function tests
7	Coarctation of the aorta	• Radio-femoral delay • Differential BP in arms and legs (systolic BP > 20mmHg)	Transthoracic echocardiogram (Less accurate in adults)
8	Obstructive sleep apnea	• Obesity • Daytime somnolence, fatigue	Polysomnography
9	Medications	• Oral contraceptives, nonsteroidal anti-inflammatory drugs • Illicit drugs (cocaine, amphetamines, Ecstasy etc.	N. A

25 Management of Hypertension in Chronic Kidney Disease

Chronic kidney disease prevalence is higher in women than men.[34] The hypertension is a cause of CKD which in turn is a cause of resistant hypertension. The anti-hypertensive management described in flow chart but the use of hydralazine as antihypertensive can be used with caution because of side effects and tolerance is developed in three months recommended.[35]

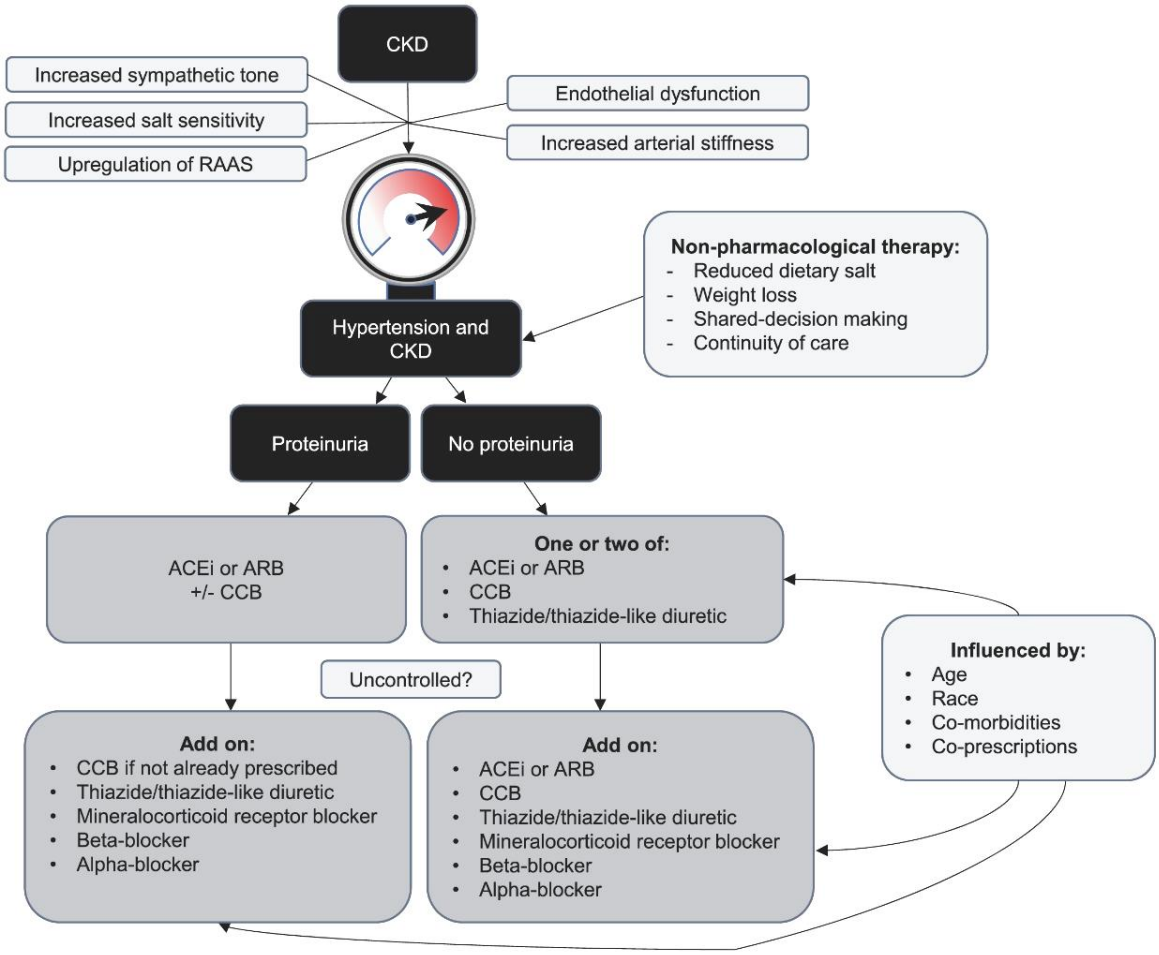


Figure 16: Management of hypertension in chronic kidney disease

25.1 Threshold for blood pressure

- <140/90mmHg in lower-risk patients;
- <130/80mmHg in higher-risk patients (those with diabetes, co-existing non-renal target organ damage, such as heart failure, stroke, etc.); and
- <125/75mmHg in those with significant proteinuria.

25.2 Lifestyle modification

25.2.1 Salt reduction

- Reducing dietary sodium intake to a target of < 50 mmol/day (~ 3 g/day of salt) decreased systolic BP by ~ 10 mmHg.
- Weight loss is effective in reducing BP and proteinuria and may slow CKD progression. In overweight patients (BMI > 27 kg/m2) with CKD and proteinuria (> 1 g/24 h), a mean weight loss of ~ 4% can reduce proteinuria by ~ 30%.

25.2.2 Pharmacological treatment

- CKD with proteinuria >1 gm AC/ARB decrease progression of CKD and mortality advantage
- CKD without proteinuria calcium Chanel blocker/ thiazides can be given if blood pressure not controlled spironolactone, alpha blocker or beta blocker can be added
- Patient on hemodialysis required MAP of 107mmHg, beta blocker can be used because due to sympathetic denervation they are prone to arrhythmia.

26 Management of Hypertension in Different Comorbidities

Management of Hypertension in different sceneries follow the latest recommendations by ESC.[35,36]

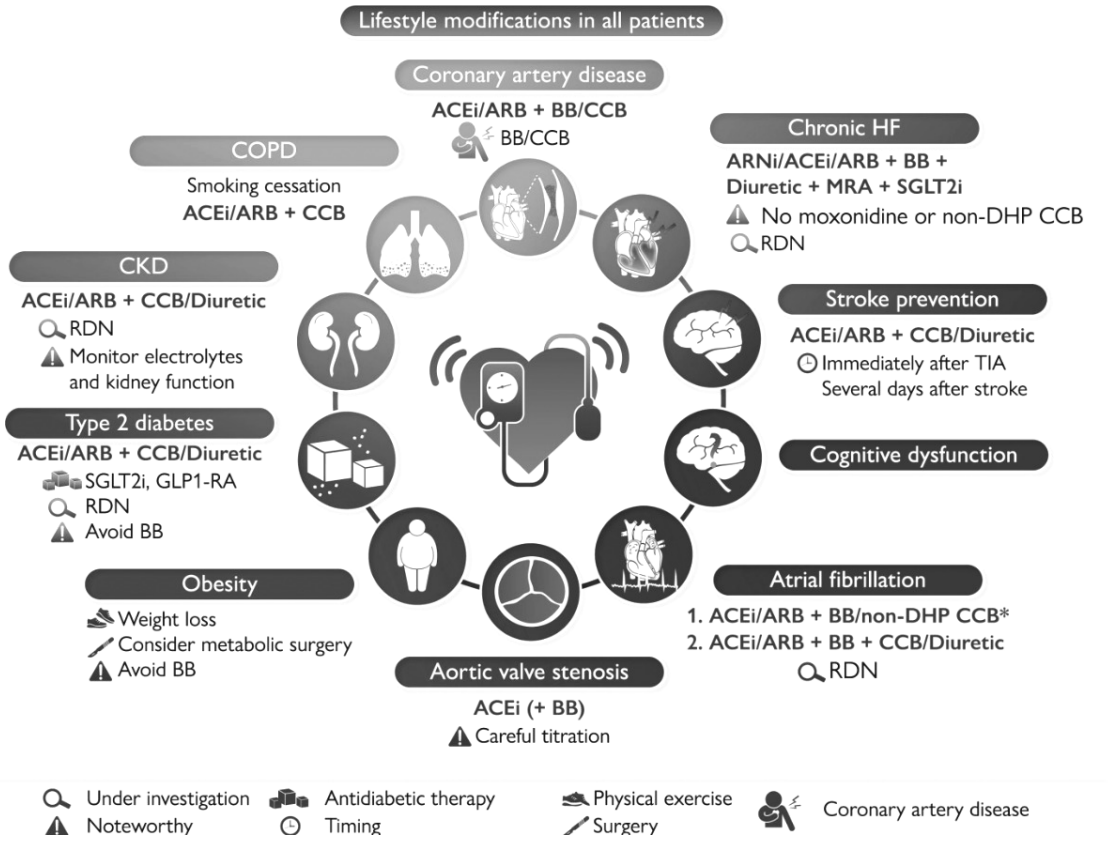


Figure 17: Management of hypertension in different comorbidities

Recommendation:

- Follow the management of hypertension in different diseases with emphasis on life-style modification.

CONCLUSION

Hypertension is increasing specially in adolescent and young women which is alarming and there is need of time for scientific guidelines for women which are not properly treated and have more complication of hypertension. These scientific practice guidelines facilitate all health care provider dealing in women with hypertension the correct diagnosis to treatment in whole life span of women and early identification of complications will reduce the mortality in our young. Pregnancy and hypertension should be managed according to this practice based guidelines for reducing the maternal and fetal mortality.

Using these practice guidelines will help in evaluation and treatment in standardized pattern and cost-effective according to our local population. Lifestyle modification should be started at all level of hypertension and emphasis should be given to obesity, increased salt intake and physical activity which can prevent from coronary artery disease, diabetes and metabolic syndrome which are commonly found in hypertensive women

Awareness and education about adherence to prescription is the key for control of hypertension. Education of general practinor, physician and cardiologist involved in women care of hypertension is important because women present differently for men in every aspect of hypertension from risk factors to complications. The management of hypertension in chronic kidney disease is evidence based so choice of medications can be tailored for the benefit of patients

These scientific practice guidelines from platform of Go Red and Pakistan cardiac society will provide a ground for more research in women so we will make evidence-based guidelines which can be cited internationally.

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Disclaimer: *These recommendations are written in best of shared professional knowledge and experience of the "Task Force - Go Red for Women-Pakistan" members and all members agree to be accountable for all aspects of work ensuring integrity and accuracy.*

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