12 Hypertension

Neonatal hypertension (HTN) has been reported in 0.2% of healthy term neonates compared to 0.8 to 3% in NICU-admitted neonates.[1-3] However, its incidence in very low birth weight (VLBW) neonates with bronchopulmonary dysplasia (BPD) varies from 12% to 40%. HTN may be detected during NICU stay or may appear after discharge. In high risk neonates with BPD, HTN can appear from 15 days to 15 months of postnatal age.[4]

Definition

In newborns, normal blood pressure (BP) varies with gender, birth weight and gestational age. After initial decrease in BP in 1st three hours, it increases rapidly during 1st two weeks. The systolic blood pressure (SBP) increases by 2.2 to 2.7 mm Hg/day and diastolic blood pressure (DBP) increases by 1.6 to 2.0 mmHg per day during initial five days, thereafter they increase by 0.2 to 0.3 and 0 to 0.2 mmHg/day, respectively.[5] Rate of rise of BP in preterm neonates is more than term neonates.

In neonates, HTN is defined as per PCA (GA at birth + postnatal age in weeks).

- **Stage 1**: BP 95th to 99th percentile + 5 mmHg
- **Stage 2**: Blood pressure >99th percentile + 5mm Hg

Measurement of BP[6,7]

Intra-arterial BP monitoring is the gold standard method and is recommended in sick neonates. However, in relatively stable neonates oscillometric method is commonly used.[5] This method has good correlation with intra-arterial BP. The 4th task force on HTN recommended a BP cuff size of 4x8 cm^2 size for neonates.[6] Neonatal BP cuffs come in different sizes (# cuff size number 1: 3 to 6 cm; #2: 4 to 8 cm; #3; 6 to 11 cm; #4: 7 to 13 cm; #5: 8 to 14 cm)

but one has to use appropriate BP cuff whose bladder length should cover 75% to 80% of arm circumference and whose width to arm circumference ratio is 0.44 to 0.55.

Method of non-invasive BP measurment[7]

- Measure BP one and half hour after feeding or medical intervention/procedure
- Tie appropriate size BP cuff on right upper arm. Wait for 15 minutes.
- Baby should be asleep or quietly awake.
- Take mean of three readings taken at two minute intervals.

Risk factors

Antenatal risk factors: Small for gestational age, LBW, infants born to mothers with preeclampsia and cocaine intake.

Postnatal risk factors: History of umbilical arterial or venous catheterization, intake of drugs e.g. steroids, caffeine, theophylline, phenyephrine. Around 2.6% of neonates with history of NICU stay developed HTN within 3 years of discharge.[2]

In neonates with risk factors, BP should be checked at discharge from NICU and at 1st visit. If infant is normotensive then monitor BP six monthly.

The causes of HTN are listed in Table 12.1.

Table 12.1: Causes of neonatal HTN[2-4,8-10]

Renovascular	Renal artery stenosis, renal venous thrombosis, thromboembolism, renal artery compression, acute kidney injury, acute tubular necrosis, interstitial nephritis, hemolytic-uremic syndrome, nephrolithiasis, congenital nephritic syndrome, CAKUT (congenital anomalies of kidney and urinary tract e.g. polycystic kidney diseases, ureteropelvic junction obstruction, renal hypoplasia)
Pulmonary	Bronchopulmonary dysplasia
Cardiovascular	Coarctation of aorta, interrupted aortic arch, patent ductus arteriosus (PDA), fibromuscular dysplasia, post PDA ligation
Endocrine	Congenital adrenal hyperplasia, hyperaldosteronism, hyperthyroidism
CNS	Intraventricular hemorrhage, subdural hematoma, raised intracranial pressure
Tumors	Wilms tumor, neuroblastoma
Iatrogenic	Pain, umbilical artery and vein catheterization, total parenteral nutrition
Drugs	Dexamethasone, phenylephrine, caffeine /theophylline, vasopressors, indomethacin, hypervitaminosis D
Miscellaneous	Hypercalcemia, closure of anterior abdominal wall defects, ECMO, birth asphyxia, adrenal hemorrhage
Idiopathic	

Which reference chart to use?

Defining HTN is a cumbersome task as there is lack of comprehensive normative data. Zubrow et al developed reference curves defining mean BP (± 95% confidence limits) for different gestational ages (22 to 42 weeks), PCA (24 to 46 weeks), birth weights (750 to 4000 g) during first 99 days of age and found significant correlation of BP with PCA.[5] Similarly Pejovic et al had given reference values for BP in neonates i.e. mean (±95% confidence limits) for neonates with GA from 24 to 44 weeks and birth weight from 500 to 5000gm.[7]

As there is scarcity of data for defining and staging persistent hypertension, Dioene et al did pooling of available data and generated BP values after two weeks of age in neonates of 26 to 44 weeks of PCA.[8]

We use Zubrow's charts for first two weeks of age and Dioene's BP percentiles thereafter for management of HTN.

Clinical features[2,3,8]

In most neonates, HTN is an incidental finding detected during routine BP measurement. The signs and symptoms of HTN overlap with other neonatal illnesses. Clinical features include feeding difficulties, unexplained tachypnea, apnea, lethargy, irritability and seizures. Features of severe hypertension include hypertensive retinopathy, left ventricular hypertrophy, congestive cardiac failure, seizures, stroke and renal dysfunction. Neonates with risk factors need meticulous BP monitoring. In case of persistent hypertension, pediatric nephrology and cardiology consultation must be taken.

Diagnostic work up[2,3,8,9]

It involves detailed history taking, examination and laboratory investigations (Table 12.2).

Table 12.2: Evaluation of neonate with HTN

History	Antenatal risk factors, perinatal insult, NICU procedures and neonatal morbidities
Examination	Peripheral pulses, radio-radial and radio-femoral delay, 4 limb BP, heart murmur (cardiac causes), any lump in abdomen (palpable kidney), bruit in lumbar area (renal causes), genital hyperpigmentation (congenital adrenal hyperplasia), dysmorphic features
Laboratory investigations	Serum sodium, potassium, calcium, urine RBC, urine routine (albumin/RBC), protein/creatinine, renal function test, fundus, ECG, CXR, USG kidney, renal and aortic Doppler study, echocardiography.
Investigations depending on the cause	

Treatment[8,9]

Management of HTN includes correction of iatrogenic causes, control of BP with antihypertensive drugs (Table 12.3) and treatment of underlying aetiology (Figure 12.1).

Treatment is indicated if:

1. Stage 2 HTN or
2. Stage 1 HTN with presence of underlying secondary cause or symptoms or

Table 12.3: Commonly used anti-hypertensive drugs[8,9]

Drug	Class	Route	Dose	Interval	Comment
ACE inhibitors	Enalapril	Oral	0.08-0.6 mg/kg/day	BD	May cause rapid drop in BP, especially if receiving diuretics. Monitor serum creatinine and Na,K. Avoid use in preterm infants, aortic arch anomalies, renal artery stenosis. Do not use in neonates with GFR<30mg/min/1.73m^2
+ antagonist	Labetalol	Oral	0.5-1.0 mg/kg/dosemax 10 mg/kg/day	BD-TDS	
		IV	infusion 0.25-3.0 mg/kg/hr	Infusion	
	Propranolol	Oral	0.5 -1.0 mg/kg/dosemax 6 mg/kg/day	BD-TDS	Monitor heart rate. Avoid in BPD
Calcium channel blocker	Amlodipine	Oral	0.05 to 0.3 mg/kg /dose (max 0.6 mg/kg/d)	OD	May cause tachycardia
	Nicardipine	IV	1–4 mcg/kg/min infusion	Infusion	
Central agonist	Clonidine	IV	3-10 mcg/kg/day	BD-TDS	CNS depression & bradycardia
Diuretic	Chlorothiazide	Oral	10–30 mg/kg/day	BID	Monitor electrolytes
	Hydrocholrthiazide	Oral	1-3 mg/kg/day	BID	
	Spirolactone	Oral	1-3 mg/kg/day	OD	
Vasodilators	Hydralazine	IV	0.1-0.6 mg/kg/dose	4 hourly	Occasional tachycardia
		Oral	0.25 to 7 mg/kg/day	QID	
	Sodium nitroprusside	IV	0.3-8 µg/kg/min (in 5% dextrose)	Infusion	Renal failure, monitor for cyanide toxicity

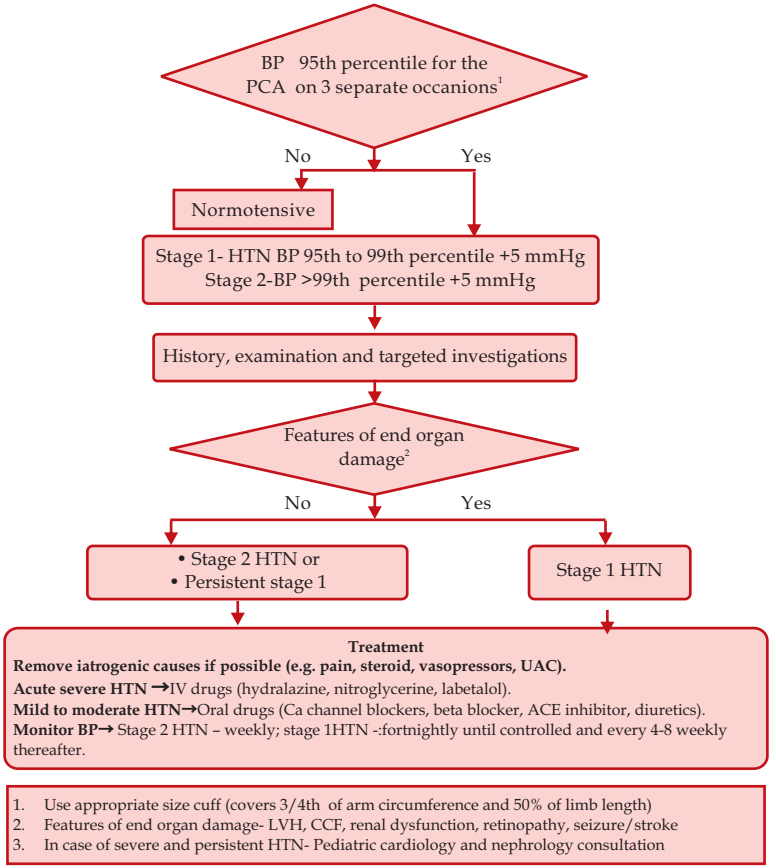

Figure 12.1: Algorithmic approach to neonatal hypertension (HTN). PCA-post conceptional age, LVH- left ventricular hypertension, CCF-congestive cardiac failure, UAC- umbilical artery catheter.

3. Persistence of BP 95th percentile (asymptomatic) more than 4 to 6 weeks

Goal of treatment

1. To reduce BP to <95th percentile for age
2. To reduce BP <90th percentile, if evidence of end organ damage or if a comorbid conditions (e.g. renal cystic disease) are present.

Hypertension with severe symptoms i.e. hypertensive emergency has to be treated with IV drugs like sodium nitroprusside, labetalol or hydralazine. The goal of treatment is to reduce MAP to 95th percentile gradually over 36 to 48 hours i.e. 25% reduction in increased MAP (difference between observed MAP and 95th percentile) is to be done over first 8 hours and rest 75 % reduction over next 36 to 48 hours. After initial control of hypertensive crisis, an oral antihypertensive drug is instituted within 12 hours of parenteral therapy and later is gradually withdrawn over next 12-48 hours.

Daily monitoring of BP is warranted in admitted neonates until BP is controlled while in others neonates, BP is checked every 1-2 weeks until it is controlled, and monitor BP every 4 to 8 weeks after that. During treatment with antihypertensive drugs, their side effects need to be monitored. After treatment of secondary causes and achieving adequate BP control, antihypertensive drugs may be de-escalated. During de-escalation, strict BP monitoring is required as HTN may recur after discontinuation of antihypertensive drug.

Follow up

Six monthly BP monitoring is required among prehypertensives. Steroid induced hypertension tends to resolve as early as 2 weeks after stopping therapy. However, patients with renovascular hypertension need to be followed upto 5 years of age. Most of the cases of neonatal hypertension get resolved by six months of age. Small for gestational age and IUGR neotates are at risk of developing hypertension in adolescence and adult life, hence six monthly follow up monitoring is required.[2,3,8-10]

References

1. American Academy of Pediatrics Committee on Fetus and Newborn: Routine evaluation of blood pressure, hematocrit,and glucose in newborns. Pediatrics 1993; 92:474.
2. Friedman AL, Hustead VA. Hypertension in babies following discharge from a neonatal intensive care unit. A 3-year follow-up. Pediatr Nephrol. 1987 ;1:30–34.
3. Seliem WA, Falk MC, Shadbolt B et al. Antenatal and postnatal risk

factors for neonatal hypertension and infant follow-up. Pediatr Nephrol 2007; 22:2081.
4. Abman SH, Warady BA, Lum GM et al. Systemic hypertension in infants with bronchopulmonary dysplasia. J Pediatr. 1984 ;104:928-31.
5. Zubrow AB, Hulman S, Kushner H et al. Determinants of blood pressure in infants admitted to neonatal intensive care units: a prospective multicenter study. Philadelphia Neonatal Blood Pressure Study Group. J Perinatol 1995; 15:470.
6. Nwankwo M, Lorenz J, Gardiner J. A standard protocol for blood pressure measurement in the newborn. Pediatrics 99:E10.
7. Pejovic B, Peco-Antic A, Marinkovic-Eric J .Blood pressure in non-critically ill preterm and full-term neonates. Pediatr Nephrol 2007; 22:249–257.
8. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome.Pediatr Nephrol 2012:27;17-32.
9. Mistry K , Gupta C. Neonatal Hypertension. Neo Reviews 2017;6 e357-e371.