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Research Article

Hypertension in Preterm Neonates and Small-for-Gestational-Age Infants: A Silent Epidemic

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Abstract

Preterm newborns and small for gestational age (SGA) are particularly vulnerable to the development of hypertension (HTN) and chronic kidney disease (CKD). Fetal programming of HTN occurs in response to an insult during intrauterine life, which leads to adaptations by the fetus to allow fetal survival. But it also results in permanent structural and physiological changes with long-term consequences such as an increased risk for cardiovascular disease and HTN. The mechanisms involved are: renal alterations, vascular dysfunction, oxidative stress and epigenetic changes. Diagnosis and treatment of neonatal HTN remain challenging, with global incidence from 0.2%-3%, and there are a multitude of causes of neonatal hypertension. Most prematurity-related neonatal HTN resolves, but the compensation mechanisms responsible may leave them at risk of later cardiovascular and kidney disease in later childhood or adulthood, with a prevalence of HTN in children/adolescents born preterm up to 25%. Diagnosis is made with both health check and ambulatory blood pressure monitoring. In adulthood, gestational age is inversely associated with ischemic heart disease risk. They could present altered cardiac shape characterized by increased right and left ventricular mass, reduced right and left ventricle lengths, and smaller internal cavity diameters. Up to 10% of the population are preterm individuals, so we are facing a "silent epidemic" of CKD and HTN in these patients; preventive strategies should be implemented early to avoid the progression of these and CVD.

Key words: *preterm neonates, low birth weight, arterial hypertension, fetal programming, small for gestational age, cardiovascular disease.*

Introduction

Preterm birth (those born before 37 weeks gestational age) affects ~11% of births worldwide, similar with an annual prevalence of prematurity in Argentina between 8 and 9%. Infants born at 22 or 23 weeks weighing close to 500g survive thanks to the new therapeutics and the increasing complexity of neonatal intensive care units[1-3].

Preterm newborns and small for gestational age (SGA) (birth weight of less than 10th percentile for gestational age) are particularly vulnerable to the development of hypertension (HTN) and chronic kidney disease (CKD). In preterm newborns, there is premature exposure to the conditions of extrauterine life in organs that are not yet prepared for it. In these organs, the premature arrest of the development of the vascular tree results in stiffer and narrower arteries, which predisposes to glomerular and endothelial damage, structural alterations due to glomerular hyperfiltration, and increased systolic blood pressure (SBP) in children and adults[3;4]. SGA infants may be at increased risk of higher BP later in life, which may be in part due to a decreased nephron development as well as other factors, such as exposure to intrauterine stress that generates an altered fetal programming, placental insufficiency, or altered vascular system.

Although the morbidity and the complications of the appearance of arterial HTN in the neonatal period has not been completely established, it could be a predisposing factor for the appearance of cardiovascular and renal disease in the long term. Hence, this is an important disease that needs to be recognized and addressed prior to discharge.

We consider that we are facing a "silent epidemic" of CKD and HTN in these patients, so preventive strategies should be implemented early to avoid the progression of these and CVD.

Methods

This review was conducted to synthesize current evidence on the epidemiology, pathophysiology, diagnostic evaluation, and long-term outcomes of hypertension in preterm and small-for-gestational-age (SGA) infants. A comprehensive literature search was performed across major biomedical databases, including **PubMed, Scopus, Web of Science, and Google Scholar**, for studies published between **January 2000 and August 2025**. The search combined controlled vocabulary and free-text terms such as *"neonatal hypertension," "preterm neonate," "small for gestational age," "blood pressure," "chronic kidney disease," "fetal* *programming,"* and *"cardiovascular outcomes."*

All original research articles, systematic reviews, meta-analyses, and relevant case series reporting data on neonatal, pediatric, or adult hypertension following preterm birth or intrauterine growth restriction were considered. Publications not available in English, those without accessible full text, or studies lacking neonatal data were excluded. Reference lists of selected papers were also hand-searched to identify additional relevant studies.

Data extracted from each eligible article included study design, sample size, gestational age and birth-weight categories, blood-pressure measurement methods, diagnostic criteria used, comorbidities, and follow-up outcomes. Emphasis was placed on clinical correlations between gestational maturity, renal function, and cardiovascular remodeling in later life.

Given the heterogeneity of study designs and populations, findings were analyzed descriptively. Quantitative synthesis (meta-analysis) was not performed; instead, trends and consistent associations were highlighted. The review follows standard ethical principles for literature-based research and does not involve human or animal experimentation.

Pathophysiology

There are few mechanisms linking impaired fetal growth and the increased risk of CVD and HTN in adulthood. Fetal programming of HTN occurs in response to an insult during intrauterine life, which leads to adaptations by the fetus to allow fetal survival. But it also results in permanent structural and physiological changes with long-term consequences such as an increased risk for CVD and HTN[5;6]. The intensity, timing and nature of the fetal insult are critical to the phenotypic outcome.

The renal alterations that have been reported in fetal programming of HTN include small kidney size at birth (reduced nephron number), kidney disfunction, and alterations in sodium transport, renin-angiotensin aldosterone system (RAAS), and sympathetic renal nerves.

It has been demonstrated that subjects preterm or low birth weight have a lower nephron number with a smaller glomerular filtration area, causing compensatory glomerular hyperfiltration and hypertrophy, and eventually glomerulosclerosis with kidney injury favoring the development of HTN[3;5;7]. Alterations in the RAS appear to contribute to hypertension programmed in response to certain fetal insults, with different impact and with tissue-specific effects[6]. For example, in an animal model, late gestational exposure to glucocorticoids leads to an increase in fetal pulmonary angiotensin converting enzyme (ACE), an expression associated with an increase in blood pressure[8]. Conversely, another experimental study in sheep shows that placental insufficiency leads to suppression of the fetal renal RAS. This could alter the activity of the intrarenal RAS and so affect growth and development of the kidney[9].

Another mechanism involved in the fetal programming of hypertension is vascular dysfunction. Fetal stress may affect vasculogenesis and cause vascular remodeling. This process is characterized by changes such as an alteration in wall thickness and lumen diameter, which may develop or be precursors of HTN later in life. In the case of intrauterine growth restriction, elastin synthesis is altered during the fetal stage, reducing arterial elasticity[10;11]. Preterm birth results in a restricted vascular bed, impaired endothelial function, narrowed and stiffer arteries, predisposing to endothelial dysfunction and arterial hypertension[6].

On the other hand, it has been proposed that oxidative stress produced by vascular, immune, and enzyme systems may account for several organ system alterations such as endothelial dysfunction with increased vascular tone. Maternal deprivation, sodium overload during pregnancy, and placental dysfunction are associated with higher oxygen radicals being one of the plausible mediators between adverse fetal growth and higher risk for CVD and HTN[6;12-13].

In addition, studies suggest that epigenetic changes are one of the mechanisms responsible for fetal programming that may explain both organ system alterations and vascular dysfunction and HTN in the offspring. These epigenetic changes consist in modifications in genes related to the RAAS, angiotensin type 1 receptor, vascular tone, ion channels, epithelial sodium channels, Na+-K+-2Cl- cotransporter, an increased expression of micro-RNA that regulates the translation of angiotensin converting enzyme-1, micro-RNA associated with cardiac injury, angiogenesis and cell changes, modifications in endothelial nitric oxide synthase (eNOS), and DNA modifications in important genes in endocrine hypertension.[5;14]

Neonatal hypertension

Diagnosis and treatment of neonatal HTN remain challenging due to the scarcity of normative data on neonatal blood pressure values, the relative rarity of the condition, and exclusion of neonates from clinical trials of antihypertensive medications[15]. The global incidence ranges from 0.2%-3%, but these values may change according to population studies, being higher in preterm newborns who were in critical condition[16].

The gold standard for blood pressure measurement remains to be the invasive intra-arterial measurement; this is most commonly done in a NICU and measured with an umbilical artery catheter. However, the majority of umbilical arterial catheters are not placed to monitor for hypertension. In this population the method of choice is oscillometric devices, which have a good correlation between oscillometric and umbilical or radial artery BP, are easy to use and provide the ability to follow BP trends over time[17;18].

HTN is defined as systolic and/or diastolic BPs persistently equal to or greater than the 95th percentile according to the tables for gestational age and postmenstrual or postconceptional age[15;16;19]. Dionne et al. created tables which provide derived systolic and diastolic BP percentiles based on post-menstrual age[18]. **(Table 1)**

Table 1. Blood Pressure Percentiles by Post-Menstrual Age

Post-menstrual Age (weeks)	Mean Systolic BP (mm Hg)	95th Percentile Systolic BP (mm Hg)	Mean Diastolic BP (mm Hg)	95th Percentile Diastolic (mm Hg)
24 – 26	45	60	30	40
27 – 29	50	65	32	42
30 – 32	55	70	35	45
33 – 35	60	75	37	47
36 – 38	65	80	40	50
39 – 41	70	85	42	52
> 42	75	90	45	55

In term and preterm infants, blood pressure (BP) increases with gestational age and postmenstrual age, along with birth weight[15-17]. In the former, the strongest predictor of BP appears to be postmenstrual age, with a rise in the first 3–7 days of age in both systolic and diastolic BPs that is considered normal[17].

In this sense, BP values change rapidly over the first days of life, especially in those born preterm[20]. In a prospective study, Pejovic et al. found that in infants born <28 weeks, the mean BP increases by 26% in the first week and >50% over the first month of life. It also showed the most premature and lowest weight neonates having the lowest blood pressures at birth. However, that same study demonstrated the most rapid rate of increase in BP in the most premature infants[6;21]. For most term infants, BP increases significantly from the first to second day of life but less so on subsequent days[19], with a less marked rise in BP (by >20% over the first month of life)[20].

It is not entirely defined at what level birth weight influences or determines blood pressure. In one study of preterm infants, BP inversely correlated with birth weight in those born with SGA, especially in the first week of life; on the other hand, the infants born with an appropriate weight for gestational age had a positive correlation[3;22].

While intrauterine growth restriction (IUGR) (a fetus not achieving the expected in utero growth potential due to genetic or environmental factors, estimated fetal weight <10th percentile) is considered as a possible risk factor for kidney damage and high BP in later life, one recent study did not observe any significant differences in BP values and urinary protein/creatinine ratios between IUGR and non-IUGR neonates and young infants[21]. The most common causes of neonatal hypertension are umbilical artery catheter-associated thromboembolism, kidney disease, and chronic lung disease[23]. However, numerous other causes and coexisting conditions have been identified in infants with HTN: antenatal steroid exposure, maternal HTN, acute kidney injury, extracorporeal membrane oxygenation (ECMO) therapy, congenital or acquired renal disease, parenteral nutrition (volume, calcium and salt excess), coarctation of the aorta and disorders of the endocrine system[15-17,24-26]. Historically, the leading causes of hypertension have been renal abnormalities (polycystic kidney diseases)[17]. Notwithstanding, in up to 50% of cases of neonatal HTN, no cause was detected[16-17;27]. **(Table 2)**

Table 2. Common Causes of Neonatal Hypertension

Category	**Specific Etiologies**	**Approximate Frequency / Comment**
Renal / Urologic	Polycystic kidney disease, renal vein thrombosis, renal artery stenosis, congenital obstructive uropathy, acute kidney injury (AKI)	40 – 50 % of cases
Iatrogenic / Mechanical	Umbilical arterial catheter–associated thromboembolism, prolonged mechanical ventilation, extracorporeal membrane oxygenation (ECMO), steroid or caffeine therapy	15 – 25 %
Cardiovascular / Anatomic	Coarctation of aorta, patent ductus arteriosus closure, congenital heart disease	10 – 15 %
Endocrine / Metabolic	Congenital adrenal hyperplasia, hyperthyroidism, mineralocorticoid excess, hypercalcemia	5 – 10 %
Medications / Fluids	Excess parenteral sodium or calcium, volume overload, adrenergic or steroid therapy	Variable
Idiopathic / Unknown	No identifiable cause despite evaluation	Up to 50 % in some series

Considering causes associated with renal abnormalities, the AWAKEN study has shown a significant association with acute kidney injury (AKI) and neonatal hypertension[28]. Between 10% and 20% of newborns with AKI have hypertension, usually associated with hypervolemia, so treatment focuses on correcting fluid overload with furosemide if needed[29]. The diagnosis of AKI is mostly based on imperfect parameters including serum creatinine levels and urine output. In neonates, obtaining accurate glomerular filtration rate (GFR) is challenging, as serum creatinine values have several drawbacks, for at the beginning neonates reflect maternal creatinine levels[30]. Other endogenous or exogenous markers for GFR exist, but are rarely used in daily clinical care[30]. The evaluation with complementary studies to reach an etiological diagnosis can be guided by the tests proposed in Table 3.

Table 3. Diagnostic Evaluation for Etiology of Neonatal Hypertension

Investigation Type	**Specific Tests / Modalities**	**Clinical Purpose / Interpretation**
Clinical Evaluation	Detailed maternal, perinatal, and medication history; physical exam for dysmorphic or cardiac findings	Establish baseline and identify secondary causes
Blood / Biochemical Tests	Serum creatinine, BUN, electrolytes, calcium, thyroid function tests, cortisol, aldosterone, renin activity	Evaluate renal, endocrine, and metabolic contributions
Urine Studies	Urinalysis, protein/creatinine ratio, urine culture, electrolytes	Detect renal injury, infection, or proteinuria
Imaging (Non-invasive)	Renal ultrasound with Doppler, echocardiogram	Assess renal size, perfusion, and cardiac structure
Imaging (Invasive / Advanced)	CT/MR angiography, radionuclide scan	Detect vascular abnormalities or renal perfusion defects
Monitoring and Follow-up	Serial oscillometric BP measurements, ambulatory BP monitoring, renal function tests	Evaluate response to therapy and detect persistence or relapse

In a retrospective study, showed that term infants were diagnosed with HTN significantly earlier, with higher incidence of resistant HTN. Some required more than 3 medications to control their blood pressure and underwent a shorter treatment compared to preterm infants. The major risk factors for preterm infants were bronchopulmonary dysplasia and iatrogenic factors (ex. chronic steroids), and in term infants they were cardiac and other systemic disease[26].

Treatment aimed at reducing the BP (objective below the 90th percentile) needs to be considered carefully, and guided by the pediatric nephrologist. There are wide options of pharmacological treatments. However, the literature on treatment of neonatal hypertension is limited[17,].

For most neonates diagnosed with HTN, the long-term outcomes should be good, and HTN will resolve over time. A study indicates that most infants will be off medication by 6 months of age. Infants with HTN associated with bronchopulmonary dysplasia almost universally resolve by 2 years of age. However, long-term outcome studies of infants with neonatal HTN are needed[15;25].

Long-term monitoring of infants with neonatal HTN is essential, with periodic monitoring of BPs and renal function, at least until the HTN has resolved, but it is unclear how long and what follow-up is required. Serial ultrasonography may be helpful to follow renal growth, or the evolution of renal parenchymal disease[15].

Hypertension in Children and adolescents born preterm

Most related neonatal hypertension resolves but the compensation mechanisms responsible for the improvement may leave them at risk of later cardiovascular and kidney disease[31].

Several publications highlight the relationship between fetal growth restriction, low birth weight, preterm delivery and elevated BP later in life[3;32].

One publication reported a prevalence of HTN in children and adolescents born preterm ranged from 6 to 25%[33;34].

Rodriguez et al. showed that in children aged 1–7 with a history of PTN and SGA, systolic BP (SBP) and diastolic BP (DBP) increased in 21% and 37% of patients respectively, with a mean SBP and DBP increase of between 10 and 15 mmHg above the mean of healthy term newborns. They have associated a decreased glomerular filtration rate (GFR) (78 ± 26.8 ml/min/1.73 m2) and Umicroalbuminuria/Ucreatininuria (85 ± 187 mg/gr)[35].

Along the same lines, Mhanna et al. evaluated 204 patients over 3 years of age, born weighing <1,000 g, and with gestational age of 26 weeks. They found a prevalence of HTN of 7.3%, associated with an increase in the body mass index (BMI) and with higher weight gain from birth[36].

A prospective observational case–control study showed that children born preterm at <30 weeks GA had higher systolic and diastolic BPs and higher prevalence of elevated BP beyond the 90th, especially in those with lower GA and younger age at last follow- up. Albumin and calcium excretion in the urine were similar in preterm-born children and term-born controls[33].

Andrea Solís et al. carried out a descriptive study to evaluate the prevalence of HTN by ambulatory blood pressure monitoring (ABPM) in patients aged 5-7 years who were premature < 32 weeks gestational age and less than 1,500g birth weight[37]. Although the sample size is small (19 patients) and no diagnosis of HTN was made, there are noteworthy pathological findings such as the absence of systolic and/or diastolic nocturnal dipping[37].

Similarly,. assessed BP patterns with ABPM and found preterm children and adolescents with similar 24-hour and daytime blood pressure, but with higher nighttime blood pressure and less nocturnal dipping than term controls[38].

There are no pediatric studies showing a direct relationship between the absence of nocturnal dipping and target organ damage, but it has been proposed that the presence of an alteration in the normal variation of pressure during the day would be a risk factor for progression to HTA[39].

Another analysis made in adolescents of median 14-year-olds that were born PTN (mean 27.8 weeks) with very low birth weight (mean 1,048g) compared to term peers, showed that the former had higher SBP and DBP (3.5 mmHg, 95% CI − 0.1 to 7.2 and 3.6 mmHg, 95% CI 0.1 to 7.0). The preterm birth cohort also had a significantly greater rate of high blood pressure. The differences in DBP was greater in individuals without overweight/obesity. The PTN group had significantly higher rates of maternal hypertensive pregnancy, maternal smoking and cesarean section. There were no differences in weight, BMI, or rates of overweight[40].

In adolescents born PTN, albumin-to-creatinine ratio was modestly greater in subjects with overweight. This suggests that the development of obesity during adolescence may compound the risk of developing renal disease in these individuals[40].

Being born intrauterine growth-restricted or SGA has been associated with higher rates of HTN later in life[31].

A prospective study compared children aged 6-10 years, born at term *and* SGA, with children born with adequate GA (AGA) by ABPM measurements. Of the SGA group, 18% had HTN, while none of the AGA children had HTN. Also, elevated BP was found in 50% of the SGA children, compared to only 16% in those born AGA. In addition, a significantly higher blood pressure load (systolic and diastolic) was found in the SGA patients[41]. In part, these differences could be attributed to vascular alterations in those born SGA, showing more arterial stiffness and endothelial dysfunction[31]. However, other studies suggest that SGA children had significantly lower BP values than AGA, so it is difficult to clearly assess the impact of IUGR in preterm babies on BP values in future life[34].

The most frequently targeted organs damaged in childhood due to hypertension are the heart (left ventricular hypertrophy) and blood vessels such as the coronary, the cerebral and the kidney vessels.

In another study, one-third of children who had AKI during the neonatal period had at least one sign of long-term kidney dysfunction (hypertension, proteinuria or hyperfiltration). The ones who had a worse stage of AKI tended to have a higher rate of ABPM hypertension, non-dipper patron or other abnormal ABPM results, although the differences did not reach statistical significance[42]. In this group, ABPM hypertension was more frequent in patients with a gestational age<32 weeks and birth weight <1,500 g.

As a consequence of low nephron endowment, prematurity is associated with chronic kidney disease. Emerging evidence suggests that perinatal characteristics could be indicators of future risk of transplant[43]. One Canadian cohort investigated the degree to which maternal and neonatal complications of pregnancy were associated with the likelihood of requiring an organ or tissue transplant before 14 years of age. Preterm birth was associated with 6.30 times the risk of kidney transplant (95% CI, 3.23-12.31), compared with term birth, especially in children with urinary anomalies[43]. Other perinatal factors associated were neonatal sepsis, intubation, blood transfusion, oligohydramnios, and congenital anomalies.

Hypertension in adults

Impaired fetal growth is associated with CVD in adulthood[44]. IUGR and preterm birth are both risk factors for the development of adult HTN. IUGR or SGA are considered more associated with higher rates of HTN than prematurity alone[31;45], secondary to previously described renal and vascular compromise. This association both with prematurity and IUGR starts in early childhood and could become augmented in adulthood, at which stage blood pressures typically reach hypertensive ranges[46].

A meta-analysis including preterm-born adults concluded that the mean difference between preterm-born adults and controls was 4.2 mmHg for SBP and 2.6 mmHg for DBP. In another meta-analysis of 1,571 adults born with very low birth weight (defined according birth weight < 1,500 g) vs. 777 full-term controls, mean blood pressure averages were higher for subjects <1,500 g; they had 3.4 mmHg higher SBP and 2.1 mmHg higher DBP than controls. The only perinatal event associated with higher BP was maternal preeclampsia[3;47]. Along the same lines, in another study that included subjects born < 35 weeks and/or a birth weight below 2,000 g, birth weight was negatively associated with HTN, with the incidence being higher with smaller fetal size[48].

Evaluated a group of women aged 50 to 79 years, self-reported being born preterm. Preterm status was statistically significant associated with prevalent HTN (37% vs 33.1%), early-onset HTN (<50 years), and taking more antihypertensive medications. Women born preterm without actual HTN had elevated coronary heart disease compared with women born full-term[49].

A Swedish study cohort with median age 22.5 years showed that across all attained ages (0–43 years), gestational age at birth was inversely associated with HTN risk and each additional week of gestation was associated with a 4% lower risk of HTN. Persons born extremely premature had a 1.8-fold risk of HTN, and also have a major risk of ischemic heart disease, heart failure, and cerebrovascular disease. The highest risk of HTN was observed among those exposed to both preterm birth and preeclampsia[50].

Different studies consistently show a dose-response relationship between degree of prematurity and increase in BP, with higher resting systolic BP in the range of 3.8– 4.6 mmHg in individuals born preterm and an increase in diastolic BP of 2.6 mmHg. These are clinically important differences in cardiovascular risk (stroke mortality and mortality from other vascular diseases)[51].

These findings suggest that infants who are born preterm have modestly elevated BP at young adulthood, but are susceptible to develop HTN with associated other cardiovascular and renal complications[52]. Several studies have demonstrated a link between low birth weight and Chronic Kidney Disease (CKD)[52]. In a meta-analysis low birth weight was associated with CKD with overall odds ratio (OR) of 1.73[52;53]. Superimposed SGA seems to increase the risk of cardiovascular and renal diseases[52].

ABPM also reveals higher 24-h BP in 114 preterm- and compared to 103 term-born young adults, showing higher 24-hour and awake systolic and diastolic BP, and higher sleep systolic BP in preterm birth below 34 weeks[54].

Impact of preterm heart

Preterm-born individuals are at greater risk of all-cause mortality in young adulthood as well as cardiometabolic diseases, including type 1 and 2 diabetes mellitus, ischemic heart disease, HTN, pulmonary vascular disease and increased risk of heart failure[10].

A Published study with the incidence rates of heart failure that were inversely related to gestational age at birth, with a 17-fold increased risk in those born extremely preterm compared with those born at term[55].

In a Swedish cohort, Crump et al. studied the association between prematurity and increased risk of ischemic heart disease in adulthood. Gestational age was inversely associated with ischemic heart disease risk. Both preterm birth and early-term birth were associated with increased relative risks of ischemic heart disease (53% and 19%, respectively)[56].

An explanation for this is that the most premature individuals (<28 weeks' gestation) may have the lowest cardiac endowment and thus the fewest overall number of cardiomyocytes and lower cardiac mass[10]. This individual could have impairments in both left and right ventricular myocardial functional reserve, which is likely to increase susceptibility to heart failure later in life, particularly with additional insults such as hypertension or myocardial infarction[10]. Preterm-born young adults present altered cardiac shape characterized by increased right and left ventricular mass, reduced right and left ventricle lengths, and smaller internal cavity diameters for both ventricles. These alterations were independent of elevations in BP and were proportional to the degree of prematurity[51].

Another study investigated the cardiac impact of being born preterm in young adulthood using cardiovascular magnetic resonance in 234 individuals, of whom 102 were born preterm with an average gestational age of 30 weeks had smaller left ventricular (LV) end-diastolic volumes, smaller internal LV cavity dimensions and lengths, as well as greater LV wall thickness and mass[57].

In the perinatal period, some interventions and complications including infection, accelerated postnatal weight gain, parenteral nutrition, and antenatal and postnatal steroids have been shown to relate to increased vascular stiffness, and may contribute to long term cardiovascular remodeling. However, further research is needed to determine the long-term effects of these early life interventions[10].

Along the same lines, a systematic review[58] indicates that premature birth during the past 50 years is associated with modestly increased mortality in early to mid-adulthood. Gestational age at birth was inversely associated with all major causes of death including respiratory, cardiovascular, endocrine (mostly diabetes), neurological, cancer, and external causes, and across ages 0–45. In late adulthood there is a strong association with endocrine and respiratory mortality[58;59]. A study with the longest follow-up (maximum age of 86 but born in earlier years, 1915–1929) reported that gestational age at birth was inversely associated with risk of death from cerebrovascular disease and occlusive stroke, but not with ischemic heart disease or all-cause mortality[60].

There are limited data to suggest specific pharmacological therapeutic strategies in adults born preterm to treat HTN or modify heart failure risk. Considering that these diseases could be generated by elevated plasma levels of angiotensin I, low glomerular endowment with glomerular hyperfiltration, autonomic dysfunction and impaired heart rate recovery, there could exist a potential role for angiotensin or adrenergic blockade. However, these two blockades have not been specifically evaluated in preterm subjects.

Impact of maternal disorder

Maternal hypertensive disorders of pregnancy (preeclampsia or eclampsia, gestational hypertension, and pregestational hypertension) are associated with an increased risk of congenital heart disease and a number of risk factors of CVD in offspring. A Danish study reported individuals born to mothers with these disorders having a 23% increased risk of early onset CVD, especially mothers with a history of CVD or diabetes[61]. In individuals born at term also severe preeclampsia was found to be an independent risk factor for cardiovascular morbidity[62]. A systematic review evidenced that in utero exposure to preeclampsia was associated with higher systolic and diastolic blood pressure and higher BMI during childhood and young adulthood. There was no evidence of variation in lipid profile or glucose metabolism[63].

Conclusions

Preterm birth and being small for gestational age should be considered as new risk factors for the development of arterial hypertension and cardiovascular morbidities both in childhood (sometimes reversible) and in adulthood. These disorders are associated with modestly increased mortality risks in early to mid-adulthood, considering that fortunately most people who were born preterm survive into adulthood without major comorbidities.

For this, preterm birth should be recognized as a chronic condition and assessed as a CVD risk factor that requires long-term follow-up for preventive actions, monitoring, and treatment of potential health sequelae across the life course.

Preventive strategies involve efforts to improve global maternal gestational health and nutrition, prevent preterm birth and SGA, avoid repeated courses of antenatal steroids, promote maternal milk as first-line nutrition, avoid extra uterine growth restriction and avoid overgrowth after hospital discharge, limit exposure to nephrotoxic drugs from neonatal to adulthood, and to promote a healthy lifestyle including regular physical activity, avoid smoking, and overweight.

Limitations

This review has several limitations. Although every effort was made to include relevant and high-quality publications, data on neonatal hypertension remain limited due to the rarity of the condition and heterogeneous diagnostic criteria across studies. Most available evidence derives from single-center retrospective studies, small prospective cohorts, or animal models, which restricts the generalizability of findings. Additionally, there is a scarcity of long-term follow-up data linking neonatal blood pressure patterns with adult cardiovascular outcomes, and the influence of confounding factors such as perinatal interventions or socioeconomic determinants cannot be fully excluded. Future multicenter, prospective studies and standardized neonatal blood pressure monitoring protocols are required to validate the associations discussed.

Conflict of Interest

The author declares no conflict of interest related to the preparation or publication of this manuscript.

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