High Blood Pressure at Early School Age Among Extreme Preterms

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abstract

BACKGROUND AND OBJECTIVES: Former preterm infants are at increased risk of hypertension with increasing age. Our objective was to identify rates of high blood pressure (BP) (≥90th percentile) and hypertension (BP ≥95th percentile) and associated risk factors among extreme preterm (EPT) infants at 6 to 7 years of age.

METHODS: Assessment included BP and anthropometrics. Comparisons were made by BP ≥90th versus <90th percentile. Regressions were run to identify relative risk (RR) of factors associated with BP ≥90th percentile.

RESULTS: Among 379 EPT infants, 20.6% had systolic high BP, 10.8% systolic hypertension, 21.4% diastolic high BP, and 11.4% diastolic hypertension. Children with systolic high BP had higher rates of BMI, triceps skinfolds >85th percentile, and waist circumference >90th percentile. In regression analyses, weight gain velocity from 18 months to school age (RR = 1.36), and maternal gestational diabetes (MGD) (RR = 2.04) predicted systolic and either systolic and/or diastolic high BP (RR = 1.27 and RR = 1.67). Among children with BMI <85th percentile, 17% had systolic and 19% had diastolic high BP. Regression analysis for normal weight children indicated public insurance (RR = 2.46) and MGD (RR = 2.16) predicted systolic high BP, and MGD (RR = 2.08) predicted either systolic or diastolic high BP.

CONCLUSIONS: Both overweight and normal weight EPT children are at risk for high BP and hypertension. Public insurance, MGD, and weight gain velocity are risk factors. Findings of high BP among EPT children at early school age are worrisome and indicate a need for close follow-up.

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Dr Vohr conceptualized and designed the study, drafted the initial manuscript, reviewed and revised the manuscript, and gave final approval of the version to be published; Dr Heyne provided substantial contributions to the study, including methodology, investigation, and review and editing of the manuscript; Drs Bann and Das provided substantial contributions to the study including data curation and formal analysis; Drs Higgins and Hintz provided substantial contributions to the study, including methodology and investigation and review and editing of the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Former preterm infants are at increased risk of high blood pressure and hypertension with increasing age.

WHAT THIS STUDY ADDS: Both normal weight and overweight former extreme preterm infants are at risk for high blood pressure at early school age. Risk factors include maternal diabetes, public insurance as a marker of poverty, and child postdischarge weight gain velocity.

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ARTICLE

Researchers have shown that former preterm (PT) infants are at increased risk of high blood pressure (BP) in adolescence and adulthood compared with control group members.[1–7] Factors that have been associated with increased risk of hypertension among former PT infants include intrauterine growth restriction,[8] maternal hypertension,[2,6,7] brain injury,[2,9] renal disorder,[10] and rapid weight gain.[2,11] Higher BP in adults born at term or near term has been attributed to growth restriction in utero.[12] Also, PT infants are known to have high rates of postnatal growth restriction.[13] Barker[14] first proposed the fetal origins of adult disease hypothesis, which states that alterations in fetal nutrition causing intrauterine growth restriction result in developmental adaptations in structure and physiology predisposing the child to subsequent cardiovascular disease. This concept has been expanded to concerns regarding rapid early catch-up growth of premature infants predisposing to subsequent increased cardiovascular risk.[15] Mhanna et al[11] identified a 7.3% hypertension rate among extreme preterm (EPT) infants at 3 to 10 years of age, which was highly associated with weight gain. In addition, 33% of the children with hypertension were obese.

In the Indomethacin prevention trial,[2] former PT infants were shorter, weighed less, and had higher rates of systolic and diastolic BP (≥90th percentile) than controls. Predictors of increased systolic BP were weight gain velocity between birth and 36 months, preeclampsia, being multiracial, and male sex. Predictors of diastolic BP were weight gain velocity between birth and 36 months, brain injury, and male sex. The authors of a recent review of an international cohort of adults born PT from 9 sites reported higher systolic and diastolic BP compared with matched control group members.[7] Although the association between higher BP and higher BMI has been reported among former PT adolescents and adults compared with control group members,[2,3,16,17] there have been limited evaluations of the rates of hypertension comparing normal or underweight with overweight and obese EPT infants at early school age.

Because of the implications of long-term cardiovascular morbidity, the findings of high BP and hypertension among former EPT infants <28 weeks' gestation at early school age has important clinical significance. In addition, the relationships between early weight catch-up and hypertension and between brain injury and hypertension deserve replication and may contribute to new knowledge of risk factors that are amendable to changes in both NICU and postdischarge management.

The primary objective was to assess BP and determine rates of high BP and hypertension at ages 6 to 7 years within the Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT) Neuroimaging and Neurodevelopmental Outcomes School age cohort study. The secondary objective was to assess the relationship between maternal risk factors of hypertension and maternal gestational diabetes mellitus (GDM), neonatal risk factors of abnormal cranial ultrasound (CUS) and MRI findings, and child postnatal weight gain velocities on BP. It was hypothesized that a subgroup of EPT children would have high BP or hypertension at 6 to 7 years of age and that maternal hypertension in pregnancy; GDM; being multiracial; public insurance; and infant factors including small for gestation, neonatal brain injury, and early growth velocity would be associated with EPT high BP at 6 to 7 years.

METHODS

The BP study was a selective secondary to the *Eunice Kennedy Shriver* National Institutes of Child Health and Human Development Neonatal Research Network SUPPORT Neuroimaging Cohort with 15 sites participating.[18] The cohort includes 379 of 498 eligible survivors of the Neuroimaging Cohort (531 infants) with complete neonatal CUS and MRI data, and anthropometric and BP data at 6 years and 4 months to 7 years and 2 months (Fig 1). Eighteen children died postdischarge, 15 were excluded because of severe growth failure associated with either congenital syndromes and/or major malformations (12) or short bowel syndrome (3), 83 were lost to follow-up, and 36 had height or BP values missing. The 379 seen versus the 119 lost or with missing data were compared for multiple maternal and infant characteristics. Those seen were less likely to have public insurance (49% vs 61%, $P = .023$), cesarean delivery (65% vs 79%, $P = .004$), and diastolic BP (7% vs 13%, $P = .035$). Severe neonatal brain injury was defined as the presence on early or late CUS of either grade 3 to 4 intraventricular hemorrhage or cystic periventricular leukomalacia on 1 or both sides. Adverse findings on near term MRI were defined as moderate or severe white matter abnormality or significant cerebellar findings.

For the assessment at 6 to 7 years, techniques for obtaining BP recommended by the Fourth Task Force on Blood Pressure Control for Children were followed.[19,20] Children sat in a quiet room with the right arm fully exposed and resting on a supportive surface at the heart level. The American Diagnostic Corporation E Sphygmomanometer was used to accurately and automatically (oscillometric determination) measure BP and pulse rate. The girth of the right arm was measured in cm with a flexible tape at the midpoint to determine appropriate cuff size to cover ~75% of the upper arm between the top of the shoulder to the olecranon. The BP was

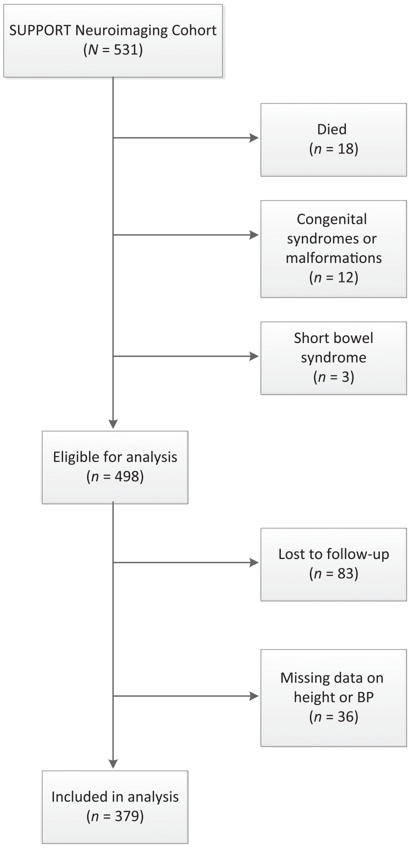

FIGURE 1
Study selection flowchart.

taken twice 2 minutes apart. If the systolic or diastolic BP was ≥90th percentile by the automatic method, it was repeated manually with auscultation. BP was interpreted by using standard definitions of normal (average systolic and diastolic BP <90th percentile for age and sex), high BP (average systolic and/or diastolic BP between the ≥90th and 94th percentile for age and sex), and hypertension (average systolic and/or diastolic BP ≥95th percentile for age and sex). Updated Fourth Task Force or Blood Pressure BP nomograms by age and sex for height were used.[20]

Child anthropometric measurements[21] included weight, height, head circumference, waist circumference, and tricep, subscapular, and abdominal skinfold measurements.[22] Weight and height were obtained twice by using a standard upright scale. Fenton[23] growth charts were used at birth and 36 weeks, and Centers for Disease Control and Prevention charts[24,25] were used at 18 months corrected age (CA) and 6 to 7 years.

Skinfolds were measured twice on the right with a Lange Skinfold Caliper (Cambridge Scientific Corporation, Watertown, MD) by using standard techniques. BMI was calculated, and overweight was defined as a BMI >85th percentile and obesity as a BMI >95th percentile. Also, weight gain velocities were calculated between birth and 36 weeks, 36 weeks and 18 to 22 months CA, and 18 to 22 months CA to 6 to 7 years.

A brief physical activity questionnaire derived from the *Eunice Kennedy Shriver* National Institutes of Child Health and Human Development study on growth and calcium intake were completed. The activity questionnaire includes questions from which sedentary activity (television and computer time) and physical activity (sports or dance) scores are derived. Site examiners were trained in reliability in all study procedures. Institutional review board's approval and informed consent were obtained.

Bivariate analyses including *t* tests for continuous and χ^2 for categorical variables were run to examine the characteristics of children with a BP ≥90th percentile and <90th percentile. Median tests were conducted for continuous variables with skewed distributions. Association of maternal and infant characteristics, growth velocities, and 6- to 7-year growth parameters and activity levels with BP were explored. Bivariate comparisons were exploratory. Multiple regression analyses adjusting for site were used to identify antenatal, neonatal, social, and demographic factors that predicted BP ≥90th percentile and BP ≥95th percentile on the basis of systolic BP, diastolic BP, and/or systolic or diastolic BP for the total cohort and for the subgroup of children of normal or low weight at 6 to 7 years. Independent variables associated with hypertension including male sex,[4] public insurance as a marker of poverty,[26–29] being multiracial,[30] maternal hypertension in pregnancy,[2,7] GDM,[31] and weight gain velocity[2,11] were selected on the basis of the literature. The same model was run for the subgroup of children who were normal weight or low weight at the visit. Finally, we also fit a multinomial logit model among the total cohort with a 3-level outcome variable: (1) systolic or diastolic hypertension, (2) systolic or diastolic high BP, and (3) normal systolic and diastolic BP.

RESULTS

Among 379 EPT children, 20.6% had systolic BP ≥90th percentile, 10.8% had systolic BP ≥95th percentile, 21.4% had diastolic BP ≥90th percentile, 11.4% had diastolic BP ≥95th percentile, and 22.6% BMI ≥85th percentile. For the entire cohort, the mean systolic BP was 101 ± 9 and the mean diastolic BP was 63 ± 8.

Table 1 shows the maternal and infant characteristics and growth velocities by systolic and diastolic BP <90th percentile and ≥90th percentile. In bivariate analyses, children of mothers with GDM were more likely to have BP ≥90th percentile. No additional characteristics including birth weight <10th percentile, CUS or MRI abnormalities, or weight gain velocities were associated with BP.

Table 2 shows the child characteristics at 6 to 7 years of age. Children with a systolic BP ≥90th percentile were more likely to be overweight (BMI ≥85th percentile), have a larger waist circumference, waist circumference >90th percentile, and triceps skinfold >85th percentile. Among children with BMI

TABLE 1 Maternal and Infant Characteristics and Weight Gain Velocities by BP Percentiles

Variable	Statistic	Systolic High BP and/or Hypertension			Diastolic High BP and/or Hypertension		
		<90% (*N* = 301)	≥90% (*N* = 78)	*P*	<90% (*N* = 298)	≥90% (*N* = 81)	*P*
Birth wt, g	Mean (SD)	862 (198)	882 (161)	.41	868 (195)	856 (178)	.61
Birth wt <10th%	*N* (%)	22 (7)	3 (4)	.27	20 (7)	5 (6)	.86
Birth wt *z* score	Mean (SD)	−0.02 (0.89)	0.02 (0.75)	.73	−0.01 (0.87)	0.01 (0.84)	.87
36-wk wt *z* score	Mean (SD)	−1.67 (0.99)	−1.47 (0.77)	.13	−1.66 (0.95)	−1.55 (0.96)	.40
Male sex	*N* (%)	162 (54)	46 (59)	.42	162 (54)	46 (57)	.70
Female sex	*N* (%)	139 (46)	32 (41)	.42	136 (46)	36 (43)	.70
Maternal hypertension in pregnancy	*N* (%)	74 (25)	23 (29)	.38	77 (26)	20 (25)	.83
Maternal gestational diabetes	*N* (%)	14 (5)	9 (12)	.02	18 (6)	5 (6)	.97
Multiracial	*N* (%)	176 (58)	44 (56)	.74	172 (58)	48 (59)	.80
Public insurance	*N* (%)	142 (47)	42 (54)	.29	144 (48)	40 (49)	.87
Antenatal steroids	*N* (%)	288 (96)	72 (92)	.22	284 (95)	76 (94)	.59
Cesarean delivery	*N* (%)	197 (65)	49 (63)	.67	198 (66)	48 (59)	.23
Bronchopulmonary dysplasia	*N* (%)	111 (37)	24 (31)	.32	106 (36)	29 (36)	.97
No. d of oxygen	Median (IQR)	52 (24–86)	49 (17–66)	.19	52 (22–82)	49 (24–75)	.25
Postnatal steroids	*N* (%)	19 (6)	6 (8)	.68	20 (7)	5 (6)	.87
Late-onset sepsis	*N* (%)	92 (31)	24 (31)	.97	95 (32)	21 (26)	.30
Early CUS abnormality	*N* (%)	25 (8)	6 (8)	.85	27 (9)	4 (5)	.23
Late CUS abnormality	*N* (%)	19 (6)	4 (5)	.69	18 (6)	5 (6)	.97
Moderate-to-severe white matter injury	*N* (%)	55 (18)	15 (19)	.85	53 (18)	17 (21)	.51
No. d in the NICU	Median (IQR)	95 (78–116)	85 (70–108)	.08	92 (76–114)	93 (78–114)	.69
Wt gain velocity birth to 36 wk, g per wk	Mean (SD)	134 (33)	142 (30)	.09	135 (33)	138 (30)	.49
Wt gain velocity 36 wk to 18–22 mo, kg per mo	Mean (SD)	0.44 (0.08)	0.46 (0.09)	.08	0.44 (0.08)	0.45 (0.09)	.24
Wt gain velocity 18 mo to 6–7 y, kg per mo	Median (IQR)	0.18 (0.15–0.22)	0.20 (0.16–0.26)	.28	0.19 (0.15–0.23)	0.19 (0.16–0.24)	.99

IQR, interquartile range.

<85th percentile, 17% had systolic and 19% had diastolic BP ≥90th percentile compared with 29% and 26% of children with a BMI ≥85th percentile. Waist circumference >90th percentile and increased physical activity measures were associated with elevated diastolic BP. The mean heart rate was higher for children with either systolic or diastolic BP ≥90th percentile. Among the children with BP ≥90th percentile, boys were more likely than girls to have high systolic (59% versus 41%) and diastolic (43% versus 25%) BP. Children in the high versus low systolic BP groups had similar sedentary activity and physical activity levels. Children in the high versus low diastolic BP groups had similar sedentary activity levels but higher reported levels of physical activity.

As shown in Table 3, regression analyses of the total cohort revealed that maternal GDM predicted systolic BP ≥90th percentile (relative risk [RR] = 2.04) and either systolic or diastolic BP ≥90th percentile (RR = 1.67). For child characteristics,

TABLE 2 Anthropometric Outcomes and Activity Levels at 6–7 Years by BP Percentiles

Variable	Statistic	Systolic BP			Diastolic BP		
		<90% (*N* = 301)	≥90% (*N* = 78)	*P*	<90% (*N* = 298)	≥90% (*N* = 81)	*P*
Mean BP (SBP or DBP)	Mean (SD)	98 (6)	114 (6)	<.001	60 (6)	74 (5)	<.001
Mean heart rate	Mean (SD)	81 (12)	85 (14)	.002	81 (11)	84 (15)	.03
Wt, kg	Median (IQR)	21 (19–25)	23 (20–28)	.09	21 (19–25)	22 (19–25)	.31
Height, cm	Mean (SD)	119 (6)	120 (8)	.03	119 (7)	119 (7)	.60
BMI ≥85%	*N* (%)	59 (20)	25 (34)	.008	62 (21)	22 (28)	.18
BMI <85th%	*N* (%)	240 (80)	48 (66)	.008	232 (79)	56 (72)	.18
Waist circumference, cm	Median (IQR)	54 (52–59)	58 (53–66)	.01	55 (52–60)	55 (53–64)	.92
Waist circumference >90%	*N* (%)	14 (5)	14 (19)	<.001	18 (6)	10 (13)	.05
Abdominal skinfold, mm	Median (IQR)	7 (5–10)	8 (5–14)	.05	7 (5–11)	7 (5–12)	.61
Triceps skinfold, mm	Median (IQR)	9 (7–11)	10 (8–15)	.06	9 (7–11)	9 (7–13)	.69
Triceps skinfold >85%	*N* (%)	47 (16)	25 (34)	<.001	53 (18)	19 (25)	.19
Subscapular skinfold, mm	Median (IQR)	5 (4–7)	6 (4–9)	.11	5 (4–7)	6 (4–8)	.43
Weekend sedentary activity, h	Mean (SD)	5.7 (3.4)	6.3 (3.3)	.15	5.8 (3.4)	5.9 (3.3)	.78
Total sedentary activity, h	Mean (SD)	17.0 (10.2)	17.9 (9.6)	.29	17.0 (10.2)	17.7 (9.7)	.60
Total physical activity, h	Median (IQR)	0.00 (0.00–0.91)	0.00 (0.00–0.88)	.93	0.00 (0.00–0.88)	0.00 (0.00–0.93)	.02

DBP, diastolic blood pressure; IQR, interquartile range; SBP, systolic blood pressure.

only weight gain velocity between 18 months and 6 to 7 years (RR = 1.36) predicted systolic BP ≥90th percentile and either systolic or diastolic BP ≥90th percentile (RR = 1.27).

The results of the multinomial logit model allowed us to identify significant predictors of high BP (BP ≥90th percentile) and systolic or diastolic hypertension (BP ≥95th percentile) separately. The full model is not shown. Only weight gain velocity from 18 months to 6 to 7 years (RR = 1.80; confidence interval [CI]: 1.18–2.74) was associated with either systolic or diastolic hypertension (versus normal BP).

Table 4 reveals the regression for the children with a BMI <85th percentile. Only public insurance (RR = 2.46) and GDM (RR = 2.16) was associated with child systolic hypertension, and only maternal GDM (RR = 2.08) was associated with either systolic or diastolic BP ≥90th percentile.

TABLE 3 Regression Models for Total Cohort to Predict High BP ≥90th Percentile

Variable	BP ≥90th Percentile		
	Systolic BP	Diastolic BP	Systolic or Diastolic BP
	RR (95% CI)	RR (95% CI)	RR (95% CI)
Male sex	1.10 (0.68–1.78)	1.04 (0.65–1.67)	0.91 (0.65–1.31)
Public insurance	1.48 (0.93–2.34)	1.24 (0.78–1.99)	1.18 (0.83–1.68)
Multiracial	0.75 (0.47–1.20)	0.86 (0.54–1.39)	0.82 (0.58–1.17)
Birth wt, kg	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
High BP during pregnancy	1.19 (0.69–2.05)	0.72 (0.40–1.31)	0.98 (0.65–1.48)
Gestational diabetes	2.04 (1.15–3.64)	0.99 (0.40–2.45)	1.67 (1.04–2.67)
Wt gain velocity birth to 36 wk, g per wk	1.00 (1.00–1.01)	1.00 (0.99–1.01)	1.00 (1.00–1.01)
Wt gain velocity 36 wk to 18–22 mo, kg per mo	1.13 (0.05–28.54)	1.28 (0.07–22.39)	1.12 (0.11–11.24)
Wt gain velocity 18 mo to 6–7 y, kg per y	1.36 (1.09–1.71)	1.23 (0.95–1.59)	1.27 (1.06–1.53)

DISCUSSION

Consistent with our hypothesis, among the EPT children, 20.5% had systolic BP ≥90th percentile, 10.8% had systolic BP ≥95th percentile, 21% had diastolic BP ≥90th percentile, and 11.4% had diastolic BP ≥95th percentile. The finding of high BP and hypertension within an EPT cohort at 6 to 7 years is consistent with the literature.[2,8,11,32] The rates of hypertension identified in our cohort (10.8% systolic and 11.4% diastolic) are similar to that of Mhanna et al,[11] who reported that 7.3% had hypertension at 3 years of age.

The identification of different risk factors as predictors of BP ≥90th percentile between our total cohort of children and the subgroup of normal or low weight children is of interest. Consistent with the more recent interpretation of the Barker[14] hypothesis studies have reported as association between early weight gain velocity in the first 2 years of life and subsequent hypertension.[2] For our total cohort, an association of weight gain velocity between 18 months and 6 to 7 years with systolic BP at 6 to 7 years was identified. This is particularly important as there is increasing evidence of the association of early accelerated weight gain with emerging obesity among former PT infants, and obesity is known to be associated with systolic hypertension.[2,11,15,33] This was confirmed in our cohort because systolic BP ≥90th percentile was associated with a BMI ≥85th percentile, triceps skinfold >85th percentile, and a waist circumference >90th percentile, a marker of central adiposity. Central adiposity is of concern because it has been shown to be associated with subsequent metabolic disorders, cardiovascular disease, and hypertension.[34–36] The finding of an increased heart rate in children with a systolic or diastolic BP ≥90th percentile is consistent with the findings of Edstedt Bonamy et al,[37] who showed that higher heart rate was independently associated with higher BP at 6 years among PT infants.

The association between maternal GDM and subsequent child BP suggests a possible genetic contribution, as has been shown in twin studies,[38] or an environmental contribution as maternal diabetes affecting the intrauterine environment.[39–41] In addition, maternal GDM is associated with both maternal obesity and offspring obesity, which is also associated with offspring hypertension.[36,42]

TABLE 4 Regression Models for BP ≥90th Percentile Among Children With BMI <85th Percentile

Variable	BP ≥90th Percentile		
	Systolic BP	Diastolic BP	Systolic or Diastolic BP
	RR (95% CI)	RR (95% CI)	RR (95% CI)
Male sex	1.40 (0.76–2.59)	1.29 (0.74–2.28)	1.00 (0.65–1.54)
Public insurance	2.46 (1.26–4.78)	1.31 (0.72–2.37)	1.36 (0.85–2.17)
Multiracial	0.58 (0.31–1.09)	0.91 (0.50–1.65)	0.75 (0.47–1.19)
Birth wt, kg	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
High BP during pregnancy	1.64 (0.83–3.26)	0.79 (0.40–1.56)	1.11 (0.68–1.81)
Gestational diabetes	2.16 (1.01–4.60)	1.33 (0.46–3.87)	2.08 (1.18–3.65)
Wt gain velocity birth to 36 wk, g per wk	1.00 (0.99–1.01)	1.00 (0.99–1.01)	1.00 (0.99–1.01)
Wt gain velocity 36 wk to 18–22 mo, kg per mo	0.92 (0.01–60.25)	1.15 (0.03–49.95)	2.47 (0.11–53.55)
Wt gain velocity 18 mo to 6–7 y, kg per y	1.17 (0.69–2.00)	1.07 (0.64–1.82)	1.10 (0.73–1.65)

The authors of previous studies of PT patients have identified an association of brain injury or changes with hypertension in adolescence and young adult age.[2,43] Proposed mechanisms include alterations in the hypothalamic pituitary-adrenal axis, sympathetic nervous system activity and angiotensin production.[43–46] There was, however, no association identified in this contemporary cohort at 6 to 7 years between BP and CUS or MRI findings.

Because of the known relationship between growth restriction at birth and hypertension in term infants, we had speculated that there would be an association between early growth restriction among EPT infants and hypertension. However, an association of BP with birth weight <10th percentile or *z* score at birth or at 36 weeks was not identified. This is similar to the findings of others.[3,4]

Factors associated with BP for the normal- or low-weight children included public insurance and maternal GDM. Both public insurance as indicator of low socioeconomic status and being multiracial were queried in our regression models. The association of public insurance with systolic BP ≥90th percentile (RR = 2.46) in the normal or low weight subgroup and borderline association with systolic BP ≥90th percentile (RR = 1.48) in the total cohort is consistent with longitudinal studies showing increased risk of hypertension among children living in poverty.[27,28,38] Kivimäki et al[27] examined the association between parental socioeconomic status and child BP in a cohort of children seen between 3 and 18 years of age and again at 24 to 39 years of age. They found that low parent socioeconomic status was associated with higher systolic BP in childhood, adolescence, and adulthood. Their data suggest that early socioeconomic disadvantage influences later BP in part through effects in early life. There is increasing data that factors associated with poverty including poor diet, toxic stress, less opportunity for physical activity, and recurrent infections contribute to increased cardiovascular risk.[29] The 2016 American Academy of Pediatrics policy paper clearly describes the importance of short- and long-term effects of poverty and social determinants on child health.[47]

Similar to the findings in the total cohort, maternal GDM was associated with both systolic BP ≥90th percentile (RR = 2.16) and either systole or diastolic BP ≥90th percentile (RR = 2.08) in the children who were normal or low weight at 6 to 7 years.

The third factor previously reported to be associated with child hypertension is maternal pregnancy hypertension. An association between maternal hypertension and systolic BP in former PT young adults has previously been reported.[2,7,48] Data from the Norwegian Nord-Trøndelag Health Study[48] of 15 778 participants reported that offspring whose mothers had either gestational hypertension or term preeclampsia had higher systolic and diastolic BP compared with offspring of normotensive pregnancies at 29 years of age. Additional studies have revealed that maternal pre-eclampsia among PT cohorts is associated with higher adolescent[2] and young adult BP[7] compared with term control group members. In our cohort, however, maternal hypertension in pregnancy did not meet statistical significance.

We examined parent report of both physical and sedentary activity levels, and in bivariate analyses only, high BP was associated with increased physical activity levels. However, no relationship was identified between sedentary activity and BP levels. Consistent with the findings of others, former PT infants in all study groups engaged in limited physical activity.[49] Finally, caloric intake in children in excess of caloric expenditure is associated with increased weight gain.[50,51] Although caloric intake in the NICU and postdischarge was not collected, this information would add to our understanding of the risk for hypertension among former PT and may be of particular relevance due to low levels of physical activity.

The method of obtaining BP in our study included a well-described protocol of duplicate measurements during a single visit with trained examiners. Ambulatory 24-hour BP measurement is more reliable than single or multiple office measurements to identify hypertension and as a predictor of cardiovascular outcomes.[52,53] It is currently the diagnostic tool recommended to confirm a diagnosis of hypertension. The Longitudinal Victorian Infant Collaborative Study of EPT and/or extremely low birth weight (ELBW) survivors performed a single reading of office BP at 8 years and revealed no differences compared with term control group members. However, by 18 years, the EPT and ELBW children were found to have higher BP compared with control group members by using both a single office measurement and 24 hours ambulatory BP. The researchers also identified a significant portion of masked hypertension in both the EPT and ELBW and control groups and recommended follow-up screening with referral as needed. Chiolero et al[54] reported the prevalence of hypertension with BP ≥95th percentile in sixth grade children on 3 separate visits obtaining BP at least 2 times during the visit by using the oscillometric device. The prevalence of BP ≥95th percentile was 11.4%, 3.8%, and 2.3% on the first, second, and third visit, respectively. Their data suggest the proportion of children with elevated BP is 5 times higher in children with 1 compared with 5 visits.

Strengths of this study are the availability of comprehensive perinatal, neonatal, maternal, infant, and early childhood data; serial anthropometric data; and comprehensive assessment including BP at 6 to 7 years of age. Limitations include the lack of a term control population; no data on maternal prepregnancy weight, weight gain in pregnancy, dietary intake, renal findings, or BP at earlier ages[55,56]; those lost to follow-up had higher rates of public insurance, cesarean delivery, and bronchopulmonary dysplasia, creating a possible bias; and a single visit with duplicate measurements of BP.

CONCLUSIONS

There is evidence that there are multiple competing factors that contribute to the development of high BP and hypertension with increasing age in former PT infants, including EPT birth, weight gain velocity, childhood poverty, maternal and infant medical risk factors, and probable genetic factors.[38] These findings sound the alarm for long-term surveillance and management of BP of former PT infants by both pediatricians and internists. Studies in which researchers examine the long-term cardiovascular, anthropometric, and metabolic outcomes of former PT infants are warranted.

ABBREVIATIONS

BP: blood pressure
CA: corrected age
CI: confidence interval
CUS: cranial ultrasound
ELBW: extremely low birth weight
EPT: extreme preterm
GDM: gestational diabetes mellitus
PT: preterm
RR: relative risk
SUPPORT: Surfactant Positive Airway Pressure and Pulse Oximetry Trial

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