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Relation of Birth Weight and the Double Product in Childhood, Adolescence and Adulthood (from the Bogalusa Heart Study)

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Abstract

Low birth weight is associated with cardiovascular disease and its risk factors, including heart rate and blood pressure. Therefore, we examined the hypothesis that birth weight is related to blood pressure-heart rate product (double product, DP), an index of oxygen consumption and workload of the heart, at different ages. Resting heart rate, blood pressure, and birth weight data were available in 2,340 children (4–11 years), 1,621 adolescents (12–19 years), and 2,315 adults (20–52 years) from the Bogalusa Heart Study (total n=6,276). After adjustment for age, sex, race, and body mass index, gestational age-adjusted birth weight was inversely associated with DP, with per 100 gram decrease in birth weight associated with an increase of 12.8, 22.9, and 23.2 beats/min×mmHg in DP in children (p=0.016), adolescents (p=0.0007), and adults (p=0.0006), respectively. An amplifying trend of the association with age was observed in the total sample (P=0.002). In conclusion, birth weight is associated with increased DP beginning in childhood, which may partly mediate the association between low birth weight and increased cardiovascular risk later in life.

Keywords

birth weight; pressure-rate product; longitudinal analysis

Blood pressure-heart rate product or double product (DP) is a reliable surrogate measure of myocardial oxygen consumption and an important indicator of the workload of the heart^{1–4}.

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As both resting heart rate (HR) and blood pressure (BP) are risk factors for cardiovascular morbidity and mortality^{5–8}, it is not surprising that DP is also a predictor of future cardiovascular risk^{9,10}. We previously reported that low birth weight is associated with high BP¹¹, high BP variability¹², and HR¹³, which may partly explain the low birth weight-cardiovascular disease association. However, no studies have examined the association of birth weight with DP at different ages. Such an association, if it exists, would be informative in understanding how low birth weight leads to increased cardiovascular disease in adult life. The present study aimed to examine the association between birth weight and DP in children, adolescents and adults in a community-based, black-white cohort.

Methods

The Bogalusa Heart Study, established in 1973 by Dr. Gerald Berenson, is based on a series of long-term studies in a semi-rural community (65% white and 35% black) in Bogalusa, Louisiana, United States to explore the natural history of cardiovascular disease from childhood¹⁴. Between 1973 and 2010, 9 BHS cross-sectional surveys were conducted in children and adolescents aged 4–19 years, and 10 BHS surveys were conducted in adults aged 20–52 years. Information on birth weight, gestational age, year of birth and parents' age at birth was retrieved from birth certificates. Exclusion criteria included gestational age <37 weeks or >42 weeks of pregnancy, birth weight >4.5 kg or resting HR >150 beats/min. We excluded those with a missing value for body mass index (BMI), HR or systolic BP and those taking antihypertensive medication. In total, 2,340 children aged 4–11 years (59% white, and 49% male), 1,621 adolescents aged 12–19 years (57% white, and 55% male) and 2,315 adults aged 20–52 years (67% white, and 45% male) formed the study sample. All subjects or their legal guardians in this study gave informed consent at each examination. Study protocols were approved by the Institutional Review Board of the Tulane University Health Sciences Center.

A standardized operations protocol was followed by trained observers during all examinations. Height and weight were measured twice to the nearest 0.1 cm and 0.1 kg, respectively, and the mean values of these measurements were used to calculate BMI. Three sitting BP measurements were obtained on the right arm of each participant using the correct size cuff following at least 5 minutes of quiet rest by each of 2 randomly assigned trained staff members. Systolic and diastolic BP levels were recorded as the first, fourth (in children), and fifth (in adults) Korotkoff phases using a mercury sphygmomanometer. Heart rate was measured by counting the radial pulse at the blood pressure station following each BP measurement. BP levels and HR were reported as the mean of 6 replicate readings, respectively. DP was calculated as systolic BP (mm Hg) multiplied by HR (beats/min).

All statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC). General linear models were used to test the race and gender differences in risk factor variables separately. All *P* values were 2-tailed and adjusted for covariates when appropriate. The adjusted birth weight (birth weight × mean gestational age of the total sample/gestational age) was calculated for each individual to better represent the rate of pre-birth growth and used in all subsequent analyses. For individuals who had been examined multiple times, only the first measurement in childhood and the last record in adolescence

and adulthood were selected for analysis to minimize the bias due to correlations between repeated measurements. The relationship between birth weight and DP was examined in multiple linear regression models with adjustment for age, sex, and BMI in blacks and whites separately and in the total sample (with additional adjustment for race). The interaction effect between age and birth weight on DP was further examined in a sample that only included unique individuals (n=5196) using a general linear model by including the product of race and birth weight in the model.

Results

Characteristics of the study participants are presented by race and sex in Table 1. Birth weight was inversely associated with DP across race-age groups (Table 2). There was no race difference in the regression coefficients of DP on birth weight ($p=0.58$ in children, $p=0.44$ in adolescents, and $p=0.69$ in adults, for interaction between race and birth weight). In the total sample, the significant inverse association between birth weight and PD was observed in all age groups ($p=0.016$ in children, $p=0.0007$ in adolescents and $p=0.0006$ in adults) (Table 2); DP by birth weight quartile showed a linear association for the 3 growth periods. In the sample that included only unique individuals, there was a significant interaction effect between age and birth weight on DP ($P=0.002$) with the regression coefficient of DP on birth weight being -11.2 ± 7.4 , -22.9 ± 6.7 , and -23.2 ± 6.8 beats*mmHg per 100-gram birth weight increase in childhood, adolescence, and adulthood, respective (Figure 1).

Discussion

The current analysis supports our hypothesis that low birth weight is associated with DP in blacks and whites in different growth periods. The association tended to strengthen with increasing age. Together with our previous observations that birth weight is inversely associated with SBP¹¹ and HR¹³, the findings of the current study provide additional evidence for the well-established association between low birthweight and increased cardiovascular risk in adult life.

Our findings that birth weight was associated with DP beginning in childhood are consistent with earlier observations that lower birth weight is linked to higher BP and HR in the same cohort^{11,13}. However, the associations of birth weight with BP and HR begin only in or after adolescence^{11,13}. While the association between DP and birth weight may largely reflect the birth weight-BP¹¹ and birth weight-HR¹³ associations, the significant association between birth weight and DP began in childhood and persisted across the life span in the current study. This suggests that the adverse effects of non-ideal intrauterine development may emerge early after birth and underscores the power of using DP to detect subtle changes in hemodynamic parameters.

It seems that the association between birth weight and DP strengthened over time, which is consistent with our previous findings that the associations between birth weight and BP and between birth weight and HR are amplified with age^{11,13}. This strengthening association with age may indicate the cumulative effects of growth and development, the aging process

after birth, and the increasing mismatch between the anticipated after-birth environment by the fetus, who had adapted to the intrauterine environment, and the real environment after birth^{15,16}. Nevertheless, whether the association continues to strengthen over time after middle age is yet to be examined. Of note, we did not observe race difference in the associations between birth weight and DP, although blacks display a different hemodynamic trajectory from childhood to adulthood compared with whites living in the same community¹⁷.

Since both BP and HR are established risk factors for cardiovascular events, one would expect that DP, a strong indicator of myocardial oxygen consumption and an important index of workload of the heart^{1,3,18}, would be a marker for cardiovascular risk. Studies have shown that DP is an independent predictor of future events, with most suggesting that DP is a better predictor of risk than either BP or HR on their own^{10,19}, although some conflicting results have been reported^{20,21}. Uen et al. reported that an increase in DP preceded ST segment depression in patients with hypertension and ischemic heart disease²². Our findings in the current study provide new evidence supporting the link between intrauterine growth and cardiovascular risk.

The emergence of the adverse effects of reduced birth weight on DP in early childhood suggests that the time window for interventions to mitigate the adverse cardiometabolic effects associated with low birth weight may be narrower than originally thought¹⁶. When and how to intervene to avoid cardiometabolic diseases in later life in those born small is a daunting challenge and yet to be fully investigated. Promoting women's health before and during pregnancy may be the only fail-safe approach to reducing cardiometabolic risk in their offspring.

In summary, our study demonstrates that birth weight is associated with DP in children, adolescents and adults, and the association strengthens with age beginning in adolescence. These observations are consistent with earlier reports that low birth weight is a risk factor for the development of cardiovascular disease later in life by increasing hemodynamic burden.

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Figure 1.

Regression coefficient of the double product on birth weight in children, adolescents, and adults (n=5196). Error bars show standard error.

Table 1Mean levels ($\pm$ SD) of study variables by race, sex and age groups

Variable	White		Black		Race difference	
	Males	Females	Males	Females	Males	Females
Childhood (4–11 years)						
	n=675	n=696	n=472	n=497		
Age (years)	9.0 $\pm$ 1.7	8.9 $\pm$ 1.7	8.8 $\pm$ 1.9	8.8 $\pm$ 1.9	0.02	0.13
BMI (kg/m ²)	18.0 $\pm$ 3.4	17.9 $\pm$ 3.6	17.7 $\pm$ 3.6	17.8 $\pm$ 3.6	0.37	0.75
HR (beats/min)	86.3 $\pm$ 10.3	89.3 $\pm$ 10.3 [§]	82.0 $\pm$ 10.1	85.7 $\pm$ 10.5 [§]	<0.001	<0.001
Systolic BP (mm Hg)	98.0 $\pm$ 8.4	97.8 $\pm$ 9.0	97.2 $\pm$ 8.6	97.0 $\pm$ 9.6	0.69	0.92
Diastolic BP (mm Hg)	57.4 $\pm$ 8.4	58.3 $\pm$ 9.0 [*]	56.8 $\pm$ 8.3	56.9 $\pm$ 9.7	0.63	0.04
DP/100 (mm Hg [*] beats)	84.7 $\pm$ 13.2	87.4 $\pm$ 13.5 [§]	79.7 $\pm$ 12.0	83.1 $\pm$ 13.5 [§]	<0.001	<0.001
Adolescence (12–19 years)						
	n=511	n=418	n=382	n=310		
Age (year)	14.7 $\pm$ 2.0	14.8 $\pm$ 2.0	15.7 $\pm$ 2.2	15.2 $\pm$ 2.1 ^{**}	<0.001	0.010
BMI (kg/m ²)	22.5 $\pm$ 5.0	22.2 $\pm$ 4.8	22.6 $\pm$ 5.0	23.1 $\pm$ 5.4	0.26	0.05
HR (beats/min)	78.0 $\pm$ 10.7	81.7 $\pm$ 11.2 [§]	71.8 $\pm$ 9.7	78.9 $\pm$ 10.4 [§]	<0.001	0.004
Systolic BP (mm Hg)	108.0 $\pm$ 9.2	105.4 $\pm$ 8.9 [§]	111.3 $\pm$ 9.8	108.1 $\pm$ 9.0 [§]	0.004	<0.001
Diastolic BP (mm Hg)	65.7 $\pm$ 7.8	66.6 $\pm$ 7.3	66.8 $\pm$ 8.9	67.7 $\pm$ 7.7 [*]	0.90	0.17
DP/100 (mm Hg [*] beats)	84.3 $\pm$ 13.9	86.2 $\pm$ 14.0 [*]	79.8 $\pm$ 12.5	85.3 $\pm$ 13.7 [§]	<0.001	0.57
Adulthood (20–52 years)						
	n=713	n=831	n=322	n=449		
Age (year)	34.0 $\pm$ 9.1	33.3 $\pm$ 9.0	32.3 $\pm$ 9.4	32.4 $\pm$ 9.3	0.01	0.08
BMI (kg/m ²)	28.3 $\pm$ 6.1	27.2 $\pm$ 7.6 ^{**}	27.2 $\pm$ 6.7	29.8 $\pm$ 8.3 [§]	0.06	<0.001
HR (beats/min)	69.0 $\pm$ 9.1	73.5 $\pm$ 9.8 [§]	68.0 $\pm$ 9.6	73.0 $\pm$ 9.6 [§]	0.15	0.25
Systolic BP (mm Hg)	116.9 $\pm$ 11.6	109.4 $\pm$ 10.1 [§]	121.8 $\pm$ 16.0	115.6 $\pm$ 16.2 [§]	<0.001	<0.001
Diastolic BP (mm Hg)	78.2 $\pm$ 9.4	73.6 $\pm$ 8.2 [§]	79.6 $\pm$ 13.0	75.8 $\pm$ 11.5 [§]	<0.001	<0.001
DP/100 (mm Hg [*] beats)	80.9 $\pm$ 14.7	80.4 $\pm$ 12.9	83.2 $\pm$ 19.0	84.3 $\pm$ 15.4	0.004	<0.001

BMI=body mass index; HR=heart rate

Sex difference within racial groups:

1000>d_g
'100>d_g
**
'50>d_g
*

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Table 2

Regression of rate-pressure product/100 on birth weight, adjusted for age, sex, BMI, and race (in the total sample only) in children, adolescents and adults.

	White			Black			Total		
	β	95% CI	P	β	95% CI	P	β	95% CI	P
<i>Childhood</i>									
Black Race							-4.70	(-5.77, -3.62)	<0.001
Age	-0.48	(-0.90, -0.06)	0.025	0.10	(-0.35, 0.54)	0.67	-0.22	(-0.53, 0.08)	0.154
Female Sex	2.57	(1.21, 3.94)	0.0002	3.24	(1.66, 4.83)	<0.001	2.85	(1.81, 3.88)	<0.001
BMI	1.13	(0.93, 1.33)	<0.001	0.86	(0.63, 1.09)	<0.001	1.02	(0.86, 1.17)	<0.001
Birth weight ^a	-1.66	(-3.04, -0.28)	0.019	-0.70	(-2.29, 0.89)	0.39	-1.28	(-2.33, -0.24)	0.016
<i>Adolescence</i>									
Black Race							-2.94	(-4.32, -1.56)	<0.001
Age	-1.01	(-1.46, -0.56)	<0.001	-0.55	(-1.02, -0.09)	0.019	-0.83	(-1.16, -0.51)	<0.001
Female Sex	1.63	(-0.17, 3.43)	0.077	4.81	(2.83, 6.79)	<0.001	2.89	(1.56, 4.22)	<0.001
BMI	0.33	(0.14, 0.51)	0.001	0.16	(-0.03, 0.35)	0.108	0.26	(0.13, 0.39)	0.0001
Birth weight ^a	-2.14	(-3.91, -0.36)	0.018	-2.55	(-4.54, -0.56)	0.012	-2.29	(-3.61, -0.96)	0.0007
<i>Adulthood</i>									
Black Race							2.53	(1.22, 3.83)	<0.001
Age	0.02	(-0.06, 0.09)	0.674	0.38	(0.25, 0.51)	<0.001	0.14	(0.07, 0.21)	<0.001
Female Sex	-0.37	(-1.73, 0.99)	0.593	-0.05	(-2.43, 2.33)	0.968	-0.22	(-1.42, 0.98)	0.719
BMI	0.49	(0.26, 0.47)	<0.001	0.36	(0.20, 0.52)	<0.001	0.37	(0.28, 0.45)	<0.001
Birth weight ^a	-2.89	(-3.92, -0.89)	0.002	-1.67	(-4.24, 0.91)	0.204	-2.32	(-3.65, -0.98)	0.0006

^a Gestational age-adjusted birth weight

CI: confidence interval