Developmental origins of cardiovascular risk in Jamaican children: The Vulnerable Windows Cohort Study

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Both intra-uterine and early childhood development contribute to the risk of developing CVD in adult life. We therefore evaluated the maternal, placental, fetal, birth, infant and childhood determinants of cardiovascular risk in a cohort of Afro-Jamaican children. The Vulnerable Windows Cohort is a longitudinal survey of 569 mothers and their offspring recruited from the first trimester. The offspring's anthropometry was measured at birth, at 6 weeks, every 3 months to 1 year and then every 6 months. At mean age 11·5 years, fasting blood was sampled for glucose, insulin and lipids. Analyses were confined to 296 women and their offspring who had complete data. Waist circumference (WC) was related to maternal weight and BMI, placental weight and to the size of the offspring *in utero*, at birth and the rate of growth in childhood ($P < 0.05$). Total cholesterol, TAG and glucose concentrations were unrelated to maternal, placental, fetal, neonatal and childhood measurements. Fasting insulin and homeostasis model assessment of insulin resistance were related to maternal weight and BMI ($P < 0.05$), but not after adjusting for WC. HDL-cholesterol was inversely related to placental and birth weight, and inversely related to weight and BMI throughout childhood ($P < 0.001$), but not after adjusting for WC. Systolic blood pressure was directly related to maternal weight, child's height, weight and BMI ($P < 0.05$), but not after adjustment for WC. Systolic blood pressure and fasting glucose concentration were inversely related to birth weight in boys but directly associated in girls. We concluded that maternal anthropometry during pregnancy, fetal size, and childhood growth rate contribute to cardiovascular risk factors in childhood.

Growth: Fetus: Body composition: Cardiovascular risk factors

Maternal anthropometry is positively related to fetal growth and weight at birth. Birth weight itself is associated with the risk of developing diabetes and CVD in adulthood[1,2]. Birth weight and anthropometry are markers for altered organ structure and function, and these structural and functional set points and capacities may underlie the increased susceptibility to disease[3,4]. Reduced infant growth and rapid weight gain through childhood are further independent risk factors for diabetes and CVD[5,6].

CVD patterns and rates vary widely among ethnic groups, in part due to exposure to classical risk factors, but also to susceptibility to these risk factors[7–9]. An example is the difference in the BMI associated with minimum risk of diabetes and CVD in different populations[9,10]. Very little information on markers and mechanisms of underlying susceptibility is available for African-origin populations. The 'Vulnerable Windows Cohort Study' was established in the Tropical Metabolism Research Unit, University of the West Indies in 1993 as an observational study to describe such susceptibility to cardiovascular risk in black Jamaicans[11].

We hypothesised that small maternal size, small birth size and increased growth rates during early childhood are associated with increased cardiovascular risk in later childhood. Thus, in this cohort of Jamaican children aged 12 years, we describe the maternal, placental, fetal, birth, infant and childhood determinants of cardiovascular risk, specifically waist circumference, blood glucose, serum insulin, serum lipids and blood pressure.

Experimental methods

Study design and subjects

As previously described[11], in 1992–3, 712 women attending the antenatal clinic at the University Hospital of the West Indies, Kingston, Jamaica, were invited to participate in the Vulnerable Windows Cohort Study. Women who were aged between 15 and 40 years, were 7–10 weeks pregnant, sure of their last menstrual period (which was confirmed by a 14-week ultrasound), and without systemic illnesses (for example, pre-eclampsia and diabetes), or genetic abnormality (for example, sickle cell disease) were included. After eighty-two pregnancy losses, fifty-six withdrawals for reasons such as work constraints and migration, and five sets of twins were

excluded, 569 babies were included in the study. All women were offered transport to and from the hospital to enhance participation. For the present report, data analysis was confined to 296 women and their offspring who were seen within 2 years of every scheduled visit between birth and age 12 years. Each mother gave written informed consent. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committee of the University of the West Indies.

Measurements

Weight was measured to the nearest 0·01 kg using a Weylux beam balance (CMS Weighing Equipment Ltd, London, UK). Height was measured to the nearest 0·1 cm with a stadiometer (CMS Weighing Equipment Ltd)[11].

Abdominal ultrasound was performed at 14, 17, 20, 25, 30 and 35 weeks of gestation using a linear probe (ATL Ultra-mark IV; Philips Medical Systems North America, Bothell, WA, USA). Fetal measurements including abdominal circumference were estimated sonographically at all visits. The average of three measurements was used. Placental volume was measured sonographically at 14, 17 and 20 weeks[12].

Anthropometric measurements of the infant were obtained within 24 h of delivery. We measured birth weight with a Health o Meter® 459 scale (Pelstar LLC, Bridgeview, IL, USA), placental weight with an electronic balance (Digimail 800100; Soehnle, Murrhardt, Germany), crown–heel length with a length board (Holtain Ltd, Crymych, Dyfed, UK) and head circumference with a fibreglass tape. We measured offspring anthropometry at birth, at 6 weeks, every 3 months to 2 years and then every 6 months. BMI was calculated by dividing body mass (kg) by the square of height (m^2). Blood pressure was measured every 6 months from the age of 1 year using an oscillometric sphygmomanometer[11]. Inter- and intra-observer variability was measured every 3 months, followed by training and recertification for any observer whose scores were not acceptable. Staging of the pubic hair and breast development was done according to the method of Marshall & Tanner[13,14]. Testicular volume was measured with a Prader orchidometer with volumes ranging from 1 to 25 ml. At clinic at age 11·5 (SD 1·3) years we sampled fasting blood using EMLA® cream as a local anaesthetic. At that time, total body water was estimated by bioelectrical impedance analysis using a single frequency (50 kHz model 101Q; RJC Systems, Clinton Township, MI, USA) with the subjects wearing light clothing. The analysers were calibrated using a 500 Ω resistor before all measurements. Fat-free mass was determined using the manufacturer's equations and fat mass by difference from body weight.

Assays

Plasma glucose was measured by the glucose oxidase system. Total cholesterol, HDL-cholesterol and TAG were measured by enzymic techniques using a VP biochromatic analyser (Abbott, Irving, TX, USA). Plasma insulin was measured with an immunometric assay (Immulite Insulin; Diagnostic Products Corporation, Los Angeles, CA, USA). The assay had an analytical sensitivity of 2 μIU/ml and the intra-assay

CV was < 8·0 %. The homeostasis model assessment of insulin resistance (HOMA-IR) score was calculated as the product of insulin and glucose divided by 22·6[15].

Statistical analysis

Insulin, HOMA-IR and TAG had skewed distributions and were log transformed towards normality for analysis. Growth was measured in three time intervals: birth to 6 months; 6 months to 2 years; and 2 years to age 11 years.

Table 1. Maternal, placental, fetal, neonatal, infant and childhood measurements

(Mean values and standard deviations)

	Boys (n 134)		Girls (n 162)	
	Mean	SD	Mean	SD
Maternal measurements at first antenatal visit				
Age (years)	26·9	5·4	26·4	4·9
Weight (kg)	67·4	13·2	66·6	14·0
Height (cm)	163·8	5·8	162·8	6·1
Pregnancy weight gain (kg per 4 weeks)	1·4	0·6	1·3	0·7
Placental measurements				
14-week volume (ml)	126	61	121	58
17-week volume (ml)	250	78	238	75
20-week volume (ml)	361	81	351	90
Weight at delivery (g)	592	136	563	124
Fetal abdominal circumference (mm)				
14 weeks	89	14	86	14
25 weeks	210	14	204	16
35 weeks	317	17	312	20
Newborn measurements				
Birth weight (g)	3280	503	3087	458
Crown–heel length (cm)	50·2	2·7	49·1	2·7
Head circumference (cm)	32·9	2·2	32·2	2·0
Gestation at delivery (d)	276	11	276	11
Size at age 6 months				
Weight (kg)	8·2	0·9	7·7	1·0
Height (cm)	67·9	1·9	66·3	2·0
Size at age 2 years				
Weight (kg)	12·2	1·4	11·8	1·6
Height (cm)	87·5	2·8	86·9	2·9
Size at age 11 years				
Weight (kg)	38·7	8·7	42·2	9·9
Height (cm)	146·7	6·1	149·7	6·3
Age and body composition at examination				
Age (years)	11·5	1·3	11·6	1·3
Weight (kg)	43·7	12·9	47·6	14·2
Height (cm)	150·6	10·4	152·9	9·9
Waist circumference (cm)	67·9	9·3	69·5	10·5
Fat mass (kg)	12·2	8·5	16·9	9·5
Outcome variables				
Fasting insulin (pmol/l)*	29·4	1·9	43·2	2·1
Fasting glucose (mmol/l)	4·9	0·4	4·8	0·4
HOMA-IR*	6·3	2·0	9·1	2·1
Total cholesterol (mmol/l)	4·4	0·8	4·4	0·8
HDL-cholesterol (mmol/l)	1·3	0·3	1·3	0·3
TAG (mmol/l)*	0·5	1·6	0·6	1·7
Systolic blood pressure (mmHg)	100·1	6·1	99·6	5·5

HOMA-IR, homeostasis model assessment of insulin resistance.
* Values for fasting insulin, HOMA-IR and TAG are geometric mean and standard deviation.

It was defined as the amount by which the size at the end of a time interval exceeded that which would have been predicted by linear regression using the measurements available at the beginning of the interval[16]. This approach ensures that the growth indices are uncorrelated. Multiple regression analyses including age and sex were used to measure the associations of cardiovascular risk factors with maternal factors, placental, fetal and neonatal size, and infant and childhood growth. We used outcomes and predictors in standardised form (i.e. for a standardised score, a value of 0 corresponds to the mean and a value of 1 corresponds to 1 SD above the mean and so on). To test for similarity of effects between boys and girls we used product terms of sex with anthropometric variables. We always adjusted risk factors for age at the clinic visit. $P < 0.05$ was considered statistically significant. SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used for the statistical analyses.

Results

The 296 subjects studied were similar to the other members of the cohort in maternal age, height, weight, BMI and socio-economic status. They were not different in birth length, head circumference or placental weight, but were 129 g heavier in weight ($P = 0.004$) and 3.2 d older in gestational age at birth ($P = 0.006$).

Mean values for maternal, placental, fetal, newborn and postnatal measurements and anthropometric and biochemical measurements are shown in Table 1. As expected, males tended to be larger until age 11 years, at which stage more girls had started their pubertal growth spurt and had a higher BMI, fat mass and percentage body fat. Including measurements made subsequent to venepuncture, the median

age at reaching Tanner stage 3 for pubic hair development was 11.1 years in girls and 12.8 years in boys.

Tables 2 and 3 show the associations of the eight outcomes measured with maternal, placental, fetal and newborn size. Table 4 extends this to include infant and childhood growth. We describe the outcomes in sequence.

Waist circumference

Waist circumference in the children was positively correlated with maternal size in the first trimester, placental weight, size of the fetus in the third trimester and with the length and weight of the infant at birth (Table 2). Faster rate of growth of children also predicted waist circumference (Table 4; Fig. 1(a)). Thus, waist size in children was positively related to maternal size, placental size, fetal size and birth size, as well as growth rate in infancy and childhood.

Fasting plasma insulin and homeostasis model assessment of insulin resistance

Fasting insulin was directly related to maternal weight and BMI in the first trimester (Table 2). However, these associations were no longer statistically significant following adjustment for waist circumference measured at clinic (Table 3). Fasting insulin was positively related to rate of postnatal growth in height, weight and BMI (Table 4). Thus, fasting insulin was directly related to maternal size in early pregnancy and growth in childhood.

HOMA-IR followed closely the associations seen with fasting insulin (Tables 2 and 4). The association of HOMA-IR with height, weight and BMI through childhood is illustrated in Fig. 1(b).

Table 2. Regression coefficients between maternal, placental, fetal and neonatal measurements of 296 Afro-Jamaican children and their measurements made at clinic†

	Waist circumference	Fasting insulin	Fasting glucose	HOMA-IR	Total cholesterol	HDL-cholesterol	TAG	Systolic blood pressure
Maternal measurements								
Age at booking (years)	0.054	0.028	0.009	0.006	−0.018	−0.024	−0.019	0.041
Height (cm)	0.144*	0.008	−0.053	−0.010	0.043	−0.104	0.056	0.063
Weight at booking (kg)	0.239*	0.134*	−0.036	0.106	−0.016	−0.071	0.031	0.119*
BMI at booking (kg/m²)	0.203*	0.128*	−0.022	0.106	−0.030	−0.043	0.015	0.104
Pregnancy weight gain (kg per 4 weeks)	0.065	−0.082	−0.011	−0.076	0.042	0.041	−0.006	0.018
Placental measurements								
14-week volume (ml)	0.010	−0.096	−0.042	−0.094	−0.107	0.021	−0.119	−0.039
17-week volume (ml)	−0.087	−0.116	−0.048	−0.126*	0.004	0.005	−0.097	−0.090
20-week volume (ml)	0.060	0.001	−0.039	−0.014	0.001	−0.054	−0.036	−0.005
Weight at delivery (g)	0.140*	0.076	0.008	0.062	−0.068	−0.129*	−0.006	0.056
Fetal abdominal circumference (mm)								
14 weeks	0.064	−0.021	0.051	0.008	0.026	−0.065	0.064	0.072
25 weeks	0.036	−0.031	0.077	−0.012	0.000	−0.078	0.063	0.018
35 weeks	0.144*	−0.022	−0.010	−0.031	0.019	−0.113	0.002	0.067
Newborn measurements								
Weight (kg)	0.189*	0.008	0.036	0.011	0.057	−0.127*	0.033	0.022
Length (cm)	0.093	0.015	0.012	0.020	0.092	−0.049	−0.002	−0.040
Head circumference (cm)	0.130*	0.029	0.042	0.025	0.040	−0.075	0.012	−0.044
Gestation at delivery (d)	0.091	0.078	0.068	0.085	0.090	0.010	−0.052	−0.054

HOMA-IR, homeostasis model assessment of insulin resistance.

* $P < 0.05$.

† Analyses are adjusted for sex and age at clinic visit. All measurements are in standardised form, i.e. for a standardised score, a value of 0 corresponds to the mean and a value of 1 corresponds to 1 SD above the mean and so on.

Table 3. Regression coefficients of maternal, placental, fetal and neonatal measurements of 296 Afro-Jamaican children and their measurements made at clinic*

	Fasting insulin	Fasting glucose	HOMA-IR	Total cholesterol	HDL-cholesterol	TAG	Systolic blood pressure
Maternal measurements							
Age at booking (years)	0·000	0·004	−0·004	−0·019	−0·006	−0·029	0·014
Height (cm)	0·048	−0·040	0·036	0·019	−0·069	0·017	0·041
Weight at booking (kg)	0·097	−0·048	0·088	−0·030	0·006	−0·017	0·021
BMI at booking (kg/m²)	0·075	−0·039	0·069	−0·037	0·026	−0·022	0·008
Pregnancy weight gain (kg per 4 weeks)	−0·106	−0·008	−0·105	0·034	0·064	−0·023	0·001
Placental measurements							
14-week volume (ml)	−0·049	−0·049	−0·050	−0·103	0·027	−0·121	−0·058
17-week volume (ml)	0·051	−0·045	0·061	0·009	−0·024	−0·082	−0·061
20-week volume (ml)	0·025	−0·040	0·031	−0·004	−0·037	−0·051	−0·030
Weight at delivery (g)	0·038	0·007	0·040	−0·081	−0·091	−0·038	0·007
Fetal abdominal circumference (mm)							
14 weeks	−0·022	0·043	−0·011	0·028	−0·045	0·057	0·038
25 weeks	−0·019	0·071	−0·016	0·002	−0·069	0·061	−0·005
35 weeks	−0·013	−0·016	−0·011	0·010	−0·072	−0·028	0·009
Neonatal measurements							
Weight (kg)	0·030	0·038	0·040	0·040	−0·075	−0·010	−0·046
Length (cm)	0·064	0·028	0·079	0·074	−0·027	−0·032	−0·054
Head circumference (cm)	0·069	0·050	0·073	0·023	−0·040	−0·022	−0·085
Gestation at delivery (d)	0·100	0·074	0·111	0·078	0·039	−0·077	−0·085

HOMA-IR, homeostasis model assessment of insulin resistance.

* Analyses are adjusted for sex, age at clinic visit and subject's waist circumference. All measurements are in standardised form, i.e. for a standardised score, a value of 0 corresponds to the mean and a value of 1 corresponds to 1 SD above the mean and so on. No coefficient corresponded to a P value < 0·05.

Fasting plasma glucose

The highest observed fasting glucose concentration was 6·0 mmol/l, which occurred in one subject only. Fasting glucose was unrelated to maternal, placental, fetal and childhood measurements (Table 2). Growth in children was not associated with any influence on fasting glucose (Table 4).

Serum lipids

Total cholesterol concentration was unrelated to maternal, placental, fetal, newborn and childhood measurements (Table 2), or rate of growth during infancy and childhood (Table 4).

HDL-cholesterol concentration was inversely related to placental and birth weight (Table 2), but these associations were no longer statistically significant following adjustment for waist circumference measured at clinic (Table 3). It was also inversely related to weight and BMI in childhood (Table 4). The relationships of HDL-cholesterol and childhood height, weight and BMI are illustrated in Fig. 1(c).

Serum TAG concentrations were not predicted by any maternal, placental, fetal, newborn or childhood variables (Tables 2 and 4).

Table 4. Regression coefficients of size at birth and childhood growth of 296 Afro-Jamaican children and their measurements made at clinic†

Measurement of size and growth	Waist circumference	Fasting insulin	Fasting glucose	HOMA-IR	Total cholesterol	HDL-cholesterol	TAG	Systolic blood pressure
Height								
Size at birth	0·092	0·009	0·007	0·014	0·093	−0·049	0·000	−0·041
Growth: from 0 to 6 months	0·224***	0·062	0·014	0·064	0·051	−0·020	0·092	0·201***
Growth: from 6 months to 2 years	0·169	0·093	0·095	0·095	−0·105	0·034	−0·010	0·209***
Growth: from 2 years to 11 years	0·241***	0·271***	0·082	0·266***	−0·156	−0·132	−0·023	0·161
Weight								
Size at birth	0·187***	0·005	0·033	0·008	0·056	−0·126	0·032	0·022
Growth: from 0 to 6 months	0·215***	0·064	0·000	0·056	0·008	−0·015	0·114	0·195***
Growth: from 6 months to 2 years	0·363***	0·202***	0·042	0·207***	−0·159	−0·144	−0·004	0·317***
Growth: from 2 years to 11 years	0·689***	0·469***	0·071	0·459***	0·049	−0·227***	0·140	0·250***
BMI								
Size at birth	0·180***	0·018	0·038	0·019	0·013	−0·105	0·041	0·066
Growth: from 0 to 6 months	0·170***	0·048	0·021	0·039	−0·061	−0·044	0·080	0·140
Growth: from 6 months to 2 years	0·375***	0·200***	−0·012	0·209***	−0·095	−0·237***	0·044	0·256***
Growth: from 2 years to 11 years	0·696***	0·433***	0·057	0·421***	0·083	−0·175	0·119	0·265***

HOMA-IR, homeostasis model assessment of insulin resistance.

*** P < 0·001.

† Analyses are adjusted for sex and age at clinic visit. All measurements are in standardised form, i.e. for a standardised score, a value of 0 corresponds to the mean and a value of 1 corresponds to 1 SD above the mean and so on.
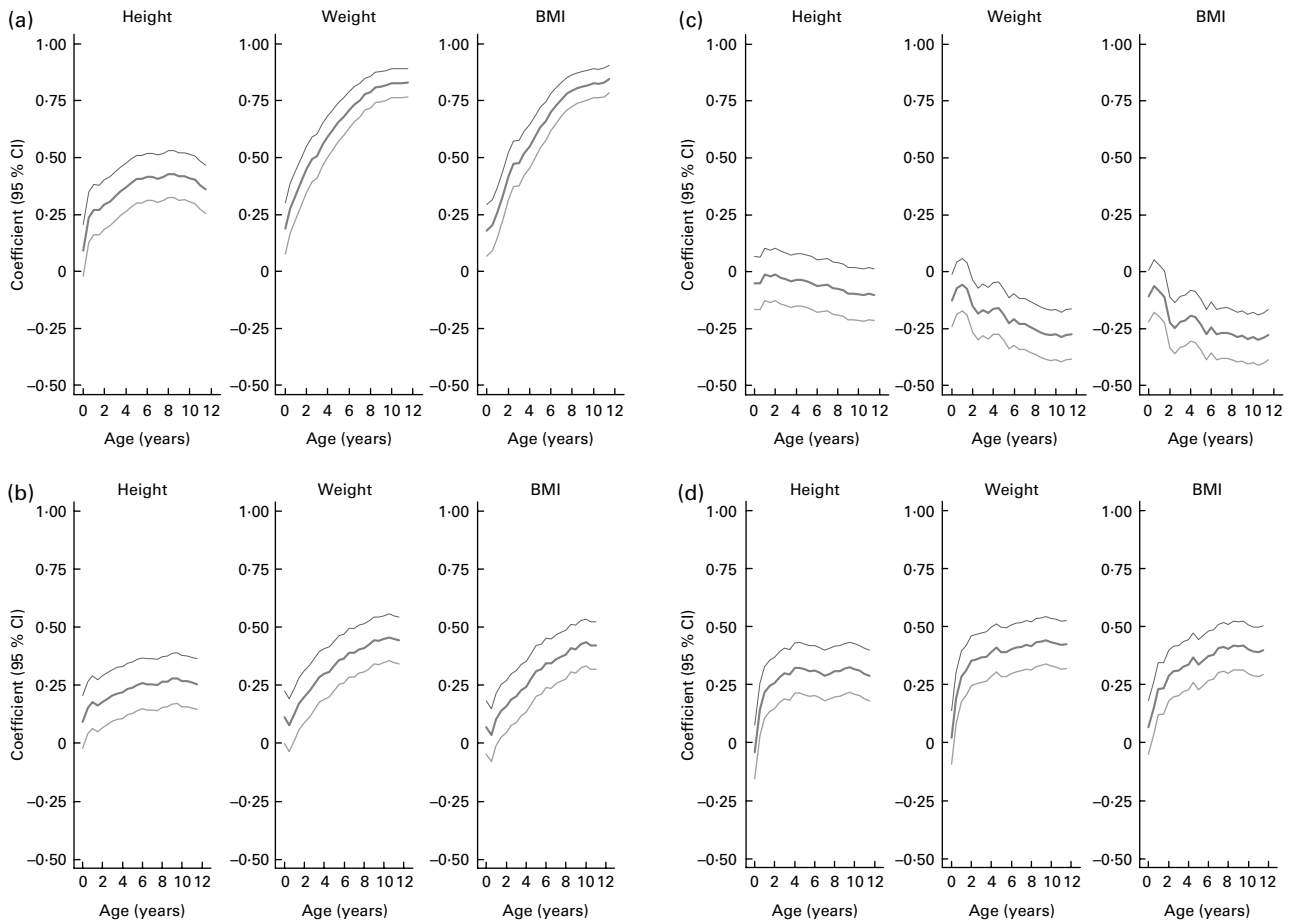
Fig. 1. Regression coefficients (—) and their 95 % CI (—) of (a) waist circumference, (b) homeostasis model assessment of insulin resistance (HOMA-IR), (c) HDL-cholesterol and (d) systolic blood pressure with height, weight and BMI of 296 Afro-Jamaican children from birth to age 11·5 years. Analyses are adjusted for sex.

Blood pressure

Systolic and diastolic blood pressure analyses revealed similar findings, but relationships were stronger with systolic blood pressure which is presented here. Systolic blood pressure in children was directly related to first trimester maternal weight (Table 2). This association of systolic blood pressure with maternal weight was no longer statistically significant following adjustment for waist circumference measured at clinic (Table 3). It was strongly associated with height, weight and BMI during childhood (Table 4, Fig. 1(d)).

Comparison of effects in boys and girls

The results for birth weight on blood glucose and systolic blood pressure are shown in Table 5. Systolic blood pressure was inversely related to birth weight in boys, but directly

Table 5. Multivariate regression analyses showing the systolic blood pressure and fasting blood glucose of 296 Afro-Jamaican children according to birth weight and sex

(Mean values and standard deviations)

	Systolic blood pressure (mmHg)						Fasting plasma glucose (mmol/l)					
	Boys			Girls			Boys			Girls		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*
Birth weight (kg)												
< 3·00	101·1	6·3	32	98·5	5·7	70	4·97	0·4	32	4·70	0·4	70
3·00−3·49	100·3	6·2	57	100·0	5·0	64	4·86	0·4	57	4·80	0·3	62
≥ 3·50	99·1	5·8	45	101·2	5·6	28	4·77	0·4	45	4·90	0·4	28
P for trend*	0·07			0·03			0·08			0·05		
P for trend†	0·009			0·18			0·07			0·01		
P for difference in trend			0·005						0·003			

* Adjusted for age at clinic visit.
† Adjusted for age at clinic visit and waist circumference.

associated in girls. Similar directions of association occurred for glucose concentration.

Discussion

These data suggest that there is a developmental contribution to cardiovascular risk factors in these peri-pubertal children. They add new detail about the influence of maternal anthropometry in pregnancy and fetal and childhood growth on risk factors for CVD. Our data are unique in having multiple sequential measures of maternal anthropometry and blood pressure, placental and fetal growth, and infant and child growth through to adolescence. Most published data come from cross-sectional studies or from cohorts that cover a subset of these phases[17–19].

The girls were larger than the boys as they had progressed further through puberty at the clinic visit. These differential rates of sexual maturation may explain some of the differences in anatomy and physiology, as puberty is associated with insulin resistance due to increases in growth hormone, cortisol and insulin-like growth factor-I levels[20–23]. The metabolic syndrome is associated with greater waist circumference, higher blood pressure, lower HDL-cholesterol and reduced insulin sensitivity[10].

We used waist circumference as the measure of current size because it is the most consistent anthropometric marker of insulin resistance even in children[24,25]. Waist circumference in children was positively correlated with the size of the mother, fetus and newborn. This might simply be a consequence of the size of the child. On the other hand, more rapid growth in childhood could be associated with central adiposity. Unfortunately, we do not have measurements of segmental body composition using either MRI or dual-energy X-ray absorptiometry, so this question remains unresolved.

Glucose tolerance was maintained. There was an inverse association of glucose concentration with birth weight in boys, but a positive association in girls (Table 5). Because more of the girls had advanced into puberty, the expected fetal programming effect, present in the boys, may have been obscured in the girls. Fasting plasma insulin was higher in girls, even allowing for their BMI and body composition. This might also be explained on the basis of earlier puberty (an insulin-resistant state), or conversely that girls may be intrinsically more insulin resistant[26].

We had expected HDL-cholesterol concentration to be directly related to placental and birth weight. However, the association was inverse (Table 2). This seems to be explained by their common link with high child waist circumference.

The major determinant of systolic blood pressure was size in childhood, which was itself linked to maternal size. Again, girls and boys behaved differently (Table 5). There were positive associations in girls with maternal, placental and birth size, counterbalanced by negative associations in boys. These differences in the directions of associations might also be explained on the basis of earlier puberty in girls.

Our data are consistent with the concept that the nutritional status of mothers (as reflected by their anthropometry during pregnancy) influences the risk in their offspring of increased visceral fat (as reflected by the waist circumference). This increased visceral adiposity might directly result in insulin

resistance and higher blood pressure, since the associations disappear when the data are adjusted for waist circumference. Visceral adipocytes secrete many inflammatory cytokines (for example, TNF, IL-6), NEFA, as well as induce hypoadiponectinaemia, and all these factors can increase insulin resistance[27]. It is not clear how visceral adiposity can increase systolic blood pressure, but increased production of leptin, angiotensinogen, NEFA, reactive oxygen species and adipocytokines could be causes[28].

Maternal size and body composition could influence the offspring's visceral adiposity in two ways. First, maternal size may be related to the maternal hypothalamic–pituitary–adrenal axis activity[29–31]. In a thin, undernourished woman, the relatively hypercortisolaemic intra-uterine environment that the fetus is exposed to results in a resetting of the fetal hypothalamic–pituitary–adrenal axis, leading to increased ambient cortisol levels *ex utero*. Second, larger mothers may have increased nutrient flux, as they are known to have higher insulin-like growth factor-I levels in late pregnancy[32]. Insulin-like growth factor-I can induce greater trans-placental NEFA, glucose and lactate transfer and thus increase the number of adipocyte cells in the offspring. Subsequent exposure to a high-fat energy-dense diet would increase the risk of adiposity, insulin resistance and systolic blood pressure[33]. Alternatively, our data cannot exclude the possibility that genetic factors influencing attainment of body size and cardiovascular risk factors may also be contributing to the variance of the observed associations[34,35]. At present, these risk alleles are thought to only contribute a small amount to the variance.

It is well recognised that the major determinant of newborn size is maternal nutritional status, as measured by height, weight, weight gain, BMI and dietary intake[36,37]. We therefore infer that maternal anthropometry contributes not only to fetal and newborn size but also to childhood size, and thus to the physiological correlates of insulin sensitivity, lipids and blood pressure. Thus, the maternal nutritional influence on fetal, neonatal and childhood growth, as well as the sexual maturation difference in boys and girls, are the major determinants of size, body composition and the physiological correlates. While it is not clear if traditional cardiovascular risk factors in children have the same weight or effect size as one would expect in adults, it is clear that these risk factors can track throughout life and may therefore have some impact in later life. Our data provide evidence for this biologically plausible possibility, although we cannot quantify the magnitude of the effect.

The fundamental mechanism underlying the developmental determination of risk is thought to be epigenetic modification of the fetal genome, due mainly to the effects of the maternal environment during pregnancy[4,38,39]. Such modifications are induced by maternal nutritional and hormonal environments during peri-conception and gestation. Modification may also occur during infancy when the baby remains developmentally plastic[4]. These functional epigenomic changes have the capacity to modify cellular, organ and whole-body metabolism, whole-body physiology and, ultimately, anatomy[3]. Individuals whose phenotype fits them to their environments have greater likelihood of reproductive fitness, longevity and good health[40]. In the event of a mismatch between the individual and his environment, the risk of adiposity and CVD

would be the product of epigenetically induced susceptibility and exposure.

In summary, in this cohort of Afro-Caribbean children, maternal anthropometry during pregnancy, fetal size, and childhood growth rate, contribute independently to cardiovascular risk factors in childhood.

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