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Relationships between birthweight and biomarkers of chronic disease in childhood: Aboriginal Birth Cohort Study 1987–2001

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Summary

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Reports of relationships between lower birthweight and later chronic diseases are mainly from populations with low rates of low birthweight (LBW) and growth-restricted births. A prospective study of an Australian Aboriginal birth cohort with a mean birthweight of 3050 g (SD 630), 16% LBW and 28% fetal growth restriction was used to examine the relationships between birthweight and selected biomarkers of chronic adult disease.

At a mean age of 11.4 years (range 8.9–14), the mean weight was 35.7 kg (SD 11.8) and the mean height was 143.8 cm (SD 10.6). Using the Centers for Disease Control and Prevention (CDC) 2000 growth references, weight and height-for-age z-scores were –0.8 (SD 1.4) and –0.5 (SD 1.07) respectively and using World Health Organisation criteria, 19% of children were classified as underweight (weight for age Z-score <2.0). The relationships between birthweight and blood pressure ($n = 475$), total cholesterol ($n = 461$), Apolipoprotein A-1 ($n = 343$), Apolipoprotein B ($n = 390$), respiratory function tests ($n = 427$), kidney size determined by ultrasound ($n = 446$), urinary albumin/creatinine ratio ($n = 420$) and fasting triglycerides ($n = 281$), insulin ($n = 272$) and glucose ($n = 279$) were examined using regression models adjusted for sex, gestational age, current age and puberty status. In this population with high rates of fetal growth restriction at birth and an excess of under-nutrition at age 11 years we found that birthweight had a negative relationship with child blood pressure only, while current child weight was positively related to blood pressure, total cholesterol, Apolipoprotein B, respiratory function tests, kidney size, and fasting triglycerides, insulin and glucose.

Keywords: *birthweight*, *childhood weight*, *glucose*, *blood pressure*, *lipids*, *kidney size*, *lung function*, *birth cohort*.

Introduction

The chronic non-communicable diseases of ischaemic heart disease, cancer, chronic lung disease and diabetes are the leading causes of death in the world. Globally, these diseases are increasing, with the greatest increases occurring in developing populations.[1]

Over 90% of the world's low birthweight (LBW) babies are born in developing populations where LBW is mainly due to fetal growth restriction.[2] Observational evidence links LBW and growth-restricted births to chronic disease outcomes in adult life and plausible biological mechanisms have been postulated to link these proxies of fetal nutrition to later disease.[3,4] This has led to the Developmental Origins of Health and Disease hypothesis that under-nutrition *in utero* results in permanent changes that influence later disease development.

Currently, there is an expanding literature on the relationships between birthweight and later chronic diseases, but information from populations with high rates of LBW and growth-restricted births remains

limited despite the potential economic impact of improved birthweight on chronic disease outcomes in these populations.[5]

Although living within the highly developed nation of Australia, the Aboriginal peoples of the Northern Territory (NT) have LBW rates double those of the non-Aboriginal NT population,[6] and 25% of newborns are classified with fetal growth restriction,[7] which is associated with poor growth outcomes in childhood.[8] At the same time more than 25% of Aboriginal adults are obese[9] and 10–30% have type 2 diabetes with early age of onset.[10] End stage renal disease rates are the highest reported in the world[11] and Indigenous Australians are 1.3 times more likely than non-Indigenous people to report heart disease and/or circulatory problems.[9] As a result of these conditions, life expectancies of 59 years for Aboriginal males and 65 years for Aboriginal females[12] are 17 years less than for non-Aboriginal people in Australia and similar to the United Nations Children's Fund 2006 estimate of 65 years for developing countries.[13]

Using an Aboriginal birth cohort recruited in the NT, we examined the relationships between birthweight and a selection of childhood biomarkers of chronic adult diseases.

Methods

Subjects and procedures

The recruitment and follow-up of this birth cohort has been previously published in detail.[14] In brief, 686 out of 1238 Aboriginal babies born at the Royal Darwin Hospital between January 1987 and March 1990 were recruited into the study. Although the babies were not randomly selected there were no significant differences in the mean birthweight, birthweight frequencies or sex ratio between those recruited and not recruited. Midwives measured the birthweights and birth lengths within 2 h of delivery and a neonatal paediatrician measured the head circumference within 4 days. Birthweights were recorded to the nearest gram using a balance scale, crown-heel lengths were measured with a length board using standard anthropometric techniques. The same neonatal paediatrician performed gestational age assessment on study participants within 4 days of birth according to the Dubowitz Scoring System.[15] This system had previously been found to be a satisfactory method for postnatal clinical assessment of gestational age in this population.[16] Fetal growth restricted infants were identified as <10th percentile of birthweight for gestational age using an Australian reference standard contemporary with cohort recruitment.[17]

At follow-up between December 1998 and March 2001, children were examined in light clothing while barefoot, with researchers examining the children blind to their perinatal outcomes.

The following measurements were made: height to the nearest millimetre with a portable stadiometer; weight to the last complete 0.1 kg with a digital electronic scale (TBF-521, Tanita Corporation, Illinois, USA); sitting blood pressure using an automatic unit (Lifesigns BP Monitor, Welch Allyn, New York, USA); pubertal staging by a paediatrician according to Tanner staging.[18,19] Blood samples were taken and urine was collected. Children were defined as fasting if they stated they had fasted for 8 h or more prior to the sample collection.

Blood samples were separated as soon as possible after collection (for a minority of samples this was up to a maximum of 2–3 h) and transported in cold-boxes to Darwin. Plasma glucose concentration, cholesterol and triglycerides concentrations were measured enzymatically (Hitachi 917 autoanalyser, Roche, Switzerland). Low density lipoprotein-cholesterol (LDL-c) was calculated from the Friedewald equation (LDL-c = total cholesterol – [high density lipoprotein-cholesterol (HDL-c) – (triglyceride/2.2)]). Plasma insulin was measured using a two-site immunoenzymometric assay in the AIA-PACK performed by the TOSOH AIA-600 immunoanalyser with no cross-reactivity with proinsulin, and Apolipoprotein B (ApoB) and Apolipoprotein A–1 (ApoA) were measured by rate immunonephelometry (Dade Behring Nephelmeter 2, Dade Behring, Inc. Illinois, USA). Urinary albumin/creatinine ratio (ACR) analysis was measured by Beckman immunoassay.

The methodology of the respiratory function testing using spirometry has previously been described.[20] In brief, it was conducted by one paediatrician using a Vitalograph 2120 hand-held closed system with American Thoracic Society criteria used to determine reproducibility and acceptability of tests.[18] The highest forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were selected from all acceptable, but not necessarily the same, blows.[21]

Kidneys were measured using a portable ultrasound machine (Aloka SSD 500). A standardised technique was used to measure kidney length, depth

and width. Kidney volumes were then calculated using the formula (kidney volume = length*depth*width*0.523).[22]

Statistical analyses

Weight and height-for-age z-scores were calculated using the Centers for Disease Control and Prevention (CDC) 2000 growth references.[23] Underweight and stunting (shortness) were categorised according to World Health Organisation criteria (i.e. more than two SDs below the median for weight-for-age and height-for-age respectively).[24] Overweight was defined using age and sex-specific cut-offs for body mass index.[25]

The selected biomarkers of chronic disease were: cholesterol (mmol/L), HDL-c (mmol/L), LDL-c (mmol/L), ApoA (g/L), ApoB (g/L), fasting insulin (mU/L), fasting glucose (mmol/L), fasting triglyceride (mmol/L) concentrations, systolic and diastolic blood pressures (mm/Hg), ACR, kidney size and the lung function measures of FEV1 (L) and FVC (L).

The relationships between birthweight and biomarkers were analysed in a series of regression models recommended by Lucas *et al.*,[26] examining the associations of birthweight alone (early model), birthweight adjusted for current child weight (combined model), a model examining an interaction between birthweight and child weight and lastly a model with child weight alone (late model) using Stata 10.[27]

Birthweight (kg), the biomarkers of chronic disease and child weight (kg) were all studied as continuous variables. All non-normal continuous variables were transformed to natural logarithms to yield normal distributions. All models were adjusted for gestational age, gender, chronological age and puberty status. Adjustment for height was also made in those models relating to respiratory function and blood pressure. Pubertal status was dichotomised as pre-pubertal and commenced puberty. Using urban status as a crude measure of socio-economic status at the time of follow-up, models were also analysed with urban status dichotomised as 'urban' or 'other'.

For completeness, other variables of birth size examined were birth length (cm) head circumference (cm) and ponderal index (birthweight ÷ cube of birth length)/100, a measure of thinness at birth).

The numbers of children in the regression models varied because some children were seen by an incomplete study team, some had disabilities that prevented all measurements, others refused procedures and occasionally biochemical analyses were limited by only small blood samples being obtained.

Residual and influence analyses were used to verify the underlying assumptions and suitability of all models.

Ethics

The Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research, including the Aboriginal Ethical Subcommittee which has the power of veto, approved the study. Written consent was obtained from the caregivers of all children. Children were able to refuse any procedure.

Results

Of the 686 neonates recruited at birth, 603 had a clinical estimation of gestational age. At follow-up, of the original cohort, 32 children could not be found. Of the 654 children traced, 572 were individually examined of which 512 had a gestational age assessment recorded at birth (83% follow-up rate). Of those children not seen, 18 had died, one parent refused permission for her child to be examined and 63 were traced but could not be physically accessed.

The characteristics of the children seen are given in Table 1. At birth, mean birthweight was 3050 g (SD 630), 16% had been of low birthweight (<2.5 kg) and 28% were classified with fetal growth restriction. The mean age of the children at follow-up was 11.5 years (range 8.9–14), 53% were boys, 540 (95%) had had their pubertal staging recorded of which 49% had commenced puberty. The mean weight was 35.7 kg (SD 11.8) and mean height 143.8 cm (SD 10.6). Mean weight and height for age z-scores were –0.8 (SD 1.4) and –0.5 (SD 1.07) respectively. Compared with the CDC growth reference curves, instead of the expected 2.3% of children below 2 SD for both weight and height for age, the proportion of children with Z-scores for weight and height below –2 was 19% and 5% respectively. Consequently, in this cohort there was an excess of under-nutrition and to a lesser extent stunting.

Of the 306 children fasting >8 h, 281 children had gestational age data available. This sub-set was not significantly different from the non-fasting children in measures of birth size, gestational age, sex ratio and current age. Within the non-fasting subjects the

Table 1. Demographic and clinical characteristics of children seen at follow-up: Aboriginal Birth Cohort study 1987–2001

Characteristics[a]	Total	Boys	Girls	*P*
Age (years)	11.48 (1.1) 571	11.60 (1.13) 302	11.35 (1.15) 269	0.0076
Sex (M/F)	100.0% 571	52.9% 302	47.1% 269	
Commenced puberty	48.7% 540	34.3% 282	64.3% 258	<0.001
Birthweight (g)	3050 (630) 571	3126 (656) 302	2966 (590) 269	0.002
Birth length (cm)	48.84 (2.93) 561	49.25 (3.03) 297	48.39 (2.74) 264	<0.001
Ponderal index	2.60 (0.27) 561	2.59 (0.26) 297	2.60 (0.28) 264	0.716
Gestational age (weeks)	38.86 (1.78) 512	38.89 (1.80) 263	38.82 (1.76) 249	0.664
% Low birthweight	15.9% 571	14.6% 302	17.5% 269	0.344
% Fetal growth restricted	27.7% 512	29.3% 263	26.1% 249	0.423
Weight (kg)	35.87 (11.83) 571	35.44 (11.87) 302	36.32 (11.79) 269	0.375
Weight for age z-score	–0.79 (1.4) 571	–0.89 (1.39) 302	–0.68 (1.33) 269	0.066
% underweight (WAZ < –2)[24]	19.3% 571	21.5% 302	16.7% 269	0.147
Height (cm)	143.80 (10.54) 571	143.74 (10.41) 302	143.87 (10.71) 269	0.883
Height for age z-score	–0.46 (1.07) 571	–0.52 (1.04) 302	–0.39 (1.10) 269	0.168
% Stunted (HAZ < –2)[24]	4.9% 571	4.6% 302	5.2% 269	0.753
Body mass index (kg/m^2)	16.96 (3.51) 571	16.78 (3.51) 302	17.15 (3.51) 269	0.196
% overweight and obese[25]	10.5% 571	9.6% 302	11.5% 269	0.455
Systolic blood pressure (mmHg)	107.57 (10.29) 558	107.79 (10.02) 293	107.33 (10.58) 265	0.604
Diastolic blood pressure (mmHg)	68.06 (7.17) 558	67.51 (7.07) 293	68.66 (7.23) 265	0.057
Cholesterol (mmol/L)	4.04 (0.76) 540	4.10 (0.78) 285	3.97 (0.73) 255	0.043
HDL-c (mmol/L)	1.20 (0.31) 538	1.25 (0.33) 284	1.16 (0.28) 254	0.001
LDL-c (mmol/L)	2.29 (0.69) 537	2.33 (0.7) 284	2.25 (0.67) 253	0.169
ApoA-1 (g/L)	1.18 (0.22) 405	1.21 (0.23) 214	1.14 (0.21) 191	0.001
ApoB (g/L)	0.72 (0.18) 463	0.73 (0.20) 246	0.72 (0.16) 217	0.609
Fasting insulin (mU/L)	8.74 (10.9) 316	7.17 (6.83) 171	10.60 (14.02) 145	0.008
Fasting glucose (mmol/L)	4.50 (0.62) 325	4.50 (0.61) 178	4.50 (0.64) 147	0.921
Fasting triglycerides (mmol/L)	1.11 (0.61) 328	1.03 (0.60) 179	1.21.(0.62) 149	0.012
FEV1 (L)	1.93 (0.51) 538	2.00 (0.52) 283	1.90 (0.48) 255	0.115
FVC (L)	2.24 (0.60) 498	2.32 (0.65) 257	2.15 (0.54) 241	0.001
Kidney volume (cm^3)	94.3 (27.7) 466	95.8 (28.4) 234	94.3 (27.9) 232	0.968
Urinary ACR (gmean)[b]	0.83 (0.76, 0.9) 440	1.02 (0.89, 1.12) 219	0.67 (0.60, 0.74) 221	<0.001

[a]Data presented as mean (SD) and *n*, or per cent and *n*.

[b]Presented as geometric mean as data very skewed.

ApoA-1, Apolipoprotein A-1; ApoB, Apolipoprotein B; ACR, albumin/creatinine ratio; FEV1, forced expiratory volume at one second; FVC, forced vital capacity; HDL-c, high density lipoprotein-cholesterol; LDL-c, low density lipoprotein-cholesterol.

numbers with outcome measures in the regression models ranged from a maximum of 475 for the blood pressure outcome to a minimum of 343 for the ApoA outcome. However, there were no significant differences in birthweight, ($P = 0.6$), gestational age ($P = 0.5$) and current weight ($P = 0.9$) between these two groups with only chronological age significantly greater by 2 months in the ApoA model ($P = 0.03$).

Hence for each outcome variable studied the numbers of children with complete birthweight, gestational age, sex, puberty status and current weight data for analysis in the regression models varied (Table 1, Fig. 1).

Relationships between birthweight and biomarkers

Table 2 shows the relationships of birthweight with the selected biomarkers summarised by the regression coefficients.

In the early models with the biomarkers regressed on birthweight adjusted for sex, current age, puberty and gestational age, birthweight was only significantly and negatively related to height-adjusted systolic blood pressure and significantly positively related to height-adjusted FEV1 and FVC and kidney volume.

After adjustment for current child weight, the negative relationship of birthweight with systolic blood

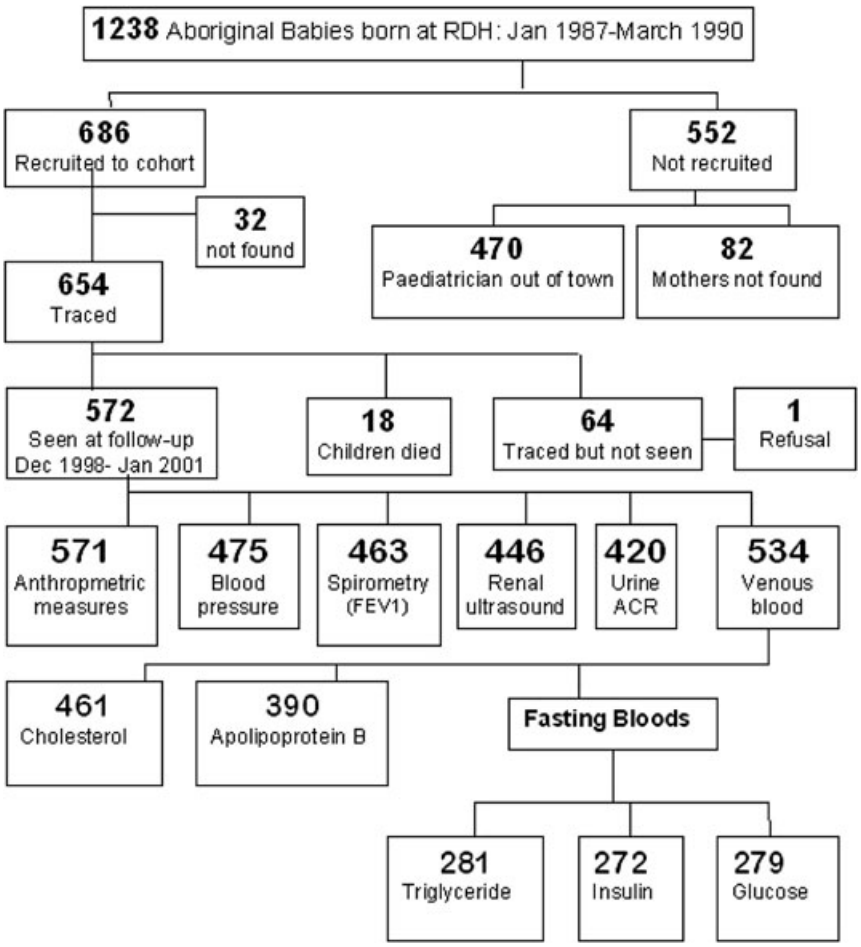

Figure 1. Flow chart showing details of Aboriginal Birth Cohort participants 1987–2001.

pressure was strengthened and a negative relationship with diastolic pressure became statistically significant but birthweight was no longer significantly related to FVC and kidney volume.

Further analysis by gender and puberty showed that the negative relationship between birthweight and systolic pressure was confined to boys who had commenced puberty ($n = 80$), with no gender or pubertal effects for the negative relationship with diastolic pressure.

Apart from these main effects in the early and combined models, a significant interaction between birthweight and child weight was found in the FEV1, FVC and ApoB models (not shown). This allows for an extra increment in FEV1, FVC and ApoB values for children who have moved from low birthweight to higher child weight. Figures 2 and 3 show the magnitude of these changes to FVC (FEV1 similar) and ApoB for birthweights of 1.5, 2.5 and 3.5 kg. Hence for a fixed current child weight those children with lower birthweights had higher respiratory function and ApoB values. Repeat analysis of all models with the inclusion of the urban status variable showed no changes in the direction or significance of the birthweight relationships.

Relationships between other measures of birth size and biomarkers

Length, head circumference and ponderal index at birth were all positively related to the lung function measures and there was a positive relationship between ApoA and birth length. These other measures of birth size were correlated with birthweight ($r = 0.88$, 0.82 and 0.55 respectively).

Relationships between current child weight and biomarkers

In the later models examining the relationships between current weight (adjusted for sex, current age, puberty and gestational age) and the biomarkers, there were no significant relationships with LDL-c, HDL-c

Table 2. Summary outcome measures of biomarkers in 11-year-old children, each modelled by birth and or child weight: Aboriginal Birth Cohort study 1987–2001

Model	Independent variable(s)		Biomarker[a]													
			Chol	HDL	LDL	SBP	DBP	Ins	Gluc	Trig	ApoB	ApoA1	FVC	FEV1	ACR	KidV
Early model[b]	Birthweight (kg)	*n*	461	459	458	475	475	272	279	281	390	343	427	463	420	446
		Coefficient	0.013	0.0062	−0.023	−0.020	−1.26	0.16	0.027	0.070	0.0083	0.010	0.11	0.12	−0.000019	0.013
		95% CI	−0.021, 0.047	−0.038, 0.050	−0.15, 0.10	−0.037, −0.0037	−2.58, 0.067	−0.050, 0.37	−0.12, 0.17	−0.046, 0.19	−0.023, 0.044	−0.034, 0.055	0.071, 0.15	0.080, 0.15	−0.00019, 0.00016	0.0082, 0.017
		P-value	0.44	0.78	0.72	0.02	0.063	0.14	0.72	0.24	0.65	0.65	<0.001	<0.001	0.83	<0.001
Combined model[b]		*n*	460	458	457	475	475	271	278	280	390	343	426	462	419	445
	Birthweight (kg)	Coefficient	−0.0011	0.015	−0.033	−0.030	−1.70	−0.16	−0.064	0.017	−0.012	0.0027	0.02	0.030	0.000032	0.0016
		95% CI	−0.037, 0.035	−0.032, 0.062	−0.17, 0.10	−0.046, −0.013	−3.01, −0.38	−0.37, 0.043	−0.22, 0.094	−0.11, 0.14	−0.053, 0.021	−0.045, 0.050	−0.012, 0.048	0.0013, 0.058	−0.00022, 0.00015	−0.0019, 0.0050
		P-value	0.951	0.53	0.63	<0.001	0.012	0.12	0.43	0.8	0.39	0.91	0.23	0.041	0.74	0.37
	Child weight (kg)	Coefficient	0.0021	−0.0012	0.0015	0.0042	0.20	0.037	0.011	0.0065	0.0034	0.0012	0.014	0.013	0.0020	1.64
		95% CI	0.00033, 0.0039	−0.005, 0.0012	−0.0051, 0.0082	0.0030, 0.0054	0.11, 0.30	0.028, 0.046	0.0036, 0.019	0.00046, 0.012	0.0016, 0.0052	−0.0012, 0.0037	0.012, 0.015	0.012, 0.014	−0.0069, 0.011	1.47, 1.81
		P-value	0.02	0.332	0.65	<0.001	<0.001	<0.001	0.004	0.035	<0.001	0.33	<0.001	<0.001	0.67	<0.001
Late model[b]	Child weight (kg)	*n*	460	458	457	475	475	271	278	280	390	343	426	462	419	445
		Coefficient	0.0021	−0.00089	0.00096	0.0039	0.18	0.034	0.0010	0.0068	0.0031	0.0013	0.014	0.013	0.0015	1.66
		95% CI	0.00043, 0.0038	−0.0031, 0.0013	−0.0052, 0.0072	0.0027, 0.0050	0.087, 0.29	0.026, 0.043	0.0030, 0.017	0.0013, 0.013	0.0014, 0.0048	−0.0012, 0.0036	0.013, 0.015	0.012, 0.015	−0.0070, 0.01	1.50, 1.82
		P-value	0.014	0.42	0.76	<0.001	<0.001	<0.001	0.005	0.012	<0.001	0.29	<0.001	<0.001	0.73	<0.001

[a]**Chol**, total cholesterol (mmol/L)*; **HDL**, high density lipoprotein-cholesterol (mmol/L)*; **LDL**, low density lipoprotein-cholesterol (mmol/L); **SBP**, systolic blood pressure (mmHg)#*; **DBP**, diastolic blood pressure (mmHg)#; **Ins**, fasting insulin (mU/L)*; **Gluc**, fasting glucose (mmol/L); **Trig**, fasting triglyceride (mmol/L)*; **ApoB**, Apolipoprotein B (g/L); **ApoA1**, Apolipoprotein A1 (g/L); **FVC**, forced vital capacity (Litres)#; **FEV1**, forced expiratory volume at one second (Litres)#*; **ACR**, urinary albumin/creatinine ratio (mg/mmol)*; **KidV**, kidney volume (cm^3). (#Model additionally adjusted for current child height. *Natural log transformed.)

[b]Adjusted for sex, puberty status, gestational age and chronological age.

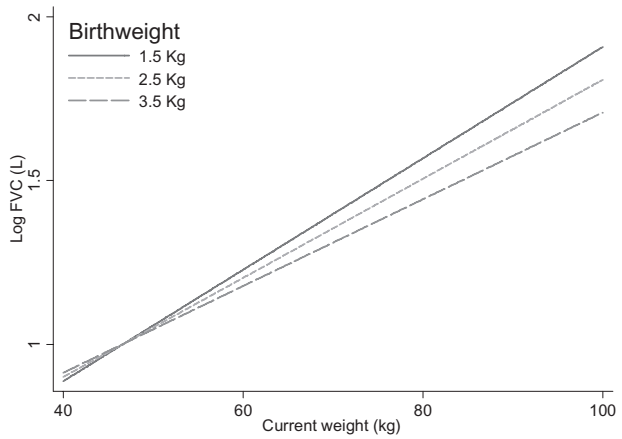

Figure 2. Interaction between current weight and birthweight in the regression on log forced vital capacity (FVC).

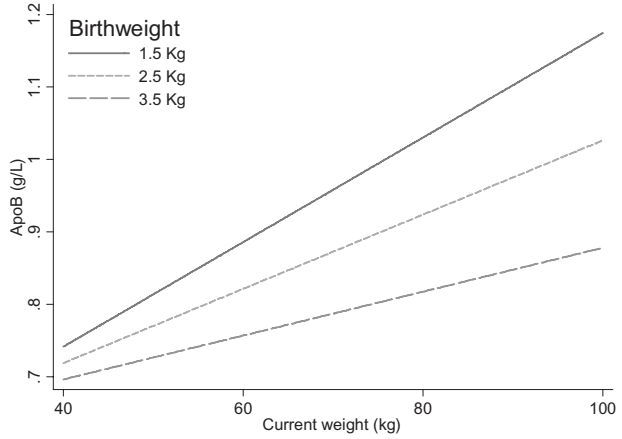

Figure 3. Interaction between current weight and birthweight in the regression on Apolipoprotein B (ApoB).

(not shown), ApoA and urinary albumin/creatinine ratio. However, Table 2 shows that child weight was significantly and positively related to the lung function measures, total cholesterol, ApoB, diastolic and systolic pressures, kidney volume and the fasting measures of insulin, glucose and triglyceride concentrations.

Discussion

Children in this cohort had high rates of fetal growth restriction at birth and an excess of under nutrition (and to a lesser extent of stunting) at mean age 11.4 years. There are limited data available for comparisons with non-Aboriginal Australians; however, the Australian National Nutritional Survey conducted in 1995 on a sample of Australian children showed a prevalence of overweight and obesity of 20% for boys and 21.5% for girls[28] for the age range 7–15 years, which is considerably higher than the 9.6% for boys and 11.5% for girls in this cohort. For our Aboriginal children, our results show that at a mean age of 11.4 years, birthweight was not associated with chronic disease biomarkers apart from a negative relationship between birthweight and blood pressure. This finding is consistent with other studies that have shown a small negative relationship between blood pressure and birthweight.[29] The association with systolic blood pressure was confined to post-pubertal boys and that for diastolic blood pressure only became apparent after adjustment for child weight. There were no other independent negative relationships for the birth size measures of length, head circumference or ponderal index with the biological markers analysed.

The advantages of this study are that it relates to a contemporary Indigenous population with high rates of LBW and fetal growth restriction.[7] At the time of recruitment less than 10% of mothers had home deliveries.[7] The single point tertiary hospital recruitment meant birth measures were reliable and gestational age estimations were all carried out by the one neonatal paediatrician within 4 days of birth. At follow-up, although 80% of children were rural or remote dwellers living in a vast area of the NT, the follow-up rate was high. Puberty staging, frequently not present in retrospective and developing population studies, was done by paediatricians and a range of dependent variables beyond the more common cardiovascular and metabolic outcomes were examined.

However, there are practical and statistical issues related to this study. Birthweight, used because of its ease of measurement and availability, has the disadvantage of not only being a crude measure of fetal nutrition (the focus of the hypothesis), but it is also a surrogate for other intrauterine exposures, apart from nutrition, such as genetic factors and congenital infections. Additionally, as the cohort subjects were still young it was necessary to use intermediary biomarkers of chronic disease instead of specific disease endpoints. Biological markers have been shown to track in varying degrees into adult life,[30,31] but this phenomenon has not yet been shown in the Aboriginal population and it is yet to be determined at what stage over the life course, potential risk factors may be important.

Social factors are important determinants of health and Aboriginal Australians are generally disadvantaged compared with the non-Aboriginal Australians.

A weakness in this study related to the children being the medical historians, so it was difficult to reliably collect factors such as family income and housing and maternal education. However, including the urban residence variable as a crude surrogate of social factors made no difference to the direction or significance of the relationships.

The biological mechanisms through which lower birthweight may influence chronic disease outcomes are not yet clearly defined. In studies of cardiovascular and metabolic outcomes, similar to our study, the effect of birthweight is often only apparent after inclusion of current weight variables in the regression models. This has been interpreted as an effect of postnatal growth (positive centile crossing) and has led to a focus on the role of postnatal growth particularly in early infancy when the greatest changes in growth rates occur. The likely mismatch of pre- and postnatal nutritional environments is postulated as the combination of exposures most likely to support the Developmental Origins of Health and Disease hypothesis.[32] Contemporary Indian studies where smaller babies became bigger children with higher insulin resistances[33] are consistent with this nutritional postulate.

However, others argue that including current weight variables in the regression models is problematic. Current weight influences biological measures during childhood, but if current weight is considered a causal variable that is one of the factors leading in sequence to an outcome, its inclusion in the models may be inappropriate.[34,35] In a series of simulations with blood pressure as the outcome, depending on the relative strengths of the associations between birthweight and current weight and of current weight with the outcome, it has been shown that inclusion of the current weight variable may produce a relationship which is an artefact.[35]

In our study, the only unadjusted relationship of birthweight with a biomarker was confined to a small negative effect on systolic blood in post-pubertal boys, but current child weight was positively related to blood pressure, cholesterol, Apo B, respiratory function, kidney size, and fasting triglycerides, insulin and glucose.

Hence, from our study of an Aboriginal birth cohort, birthweight appears to have a relationship only with systolic blood pressure in childhood. However, birthweight relationships may change if these children grow to be like their parents with 25% classified as obese over the age of 18 years.[9] The continued study of this cohort will give us an opportunity to determine if and when in later life the effects of birthweight are modified by environmental factors.

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