

*Short Report***Fetal Growth Restriction and 18-Year Growth and Nutritional Status: Aboriginal Birth Cohort 1987–2007**SUSAN SAYERS,<sup>1\*</sup> SUSAN MOTT,<sup>2</sup> AND GURMEET SINGH<sup>1,3</sup><sup>1</sup>*Menzies School of Health Research, Institute of Advanced Studies, Charles Darwin University, Northern Territory, Australia*<sup>2</sup>*Centre for Chronic Disease, University of Queensland, Herston, Queensland*<sup>3</sup>*Northern Territory Clinical School, Flinders University, Adelaide, South Australia*

**ABSTRACT** The main objective of the work is to compare the growth and nutritional status of Australian Aboriginal term infants born with ( $n = 81$ ) and without fetal growth restriction ( $n = 260$ ). A prospective birth cohort study of 341 Aboriginal babies from the Top End of the Northern Territory of Australia was recruited at birth (1987–1990) and re-examined at a mean age of 18.3 years (2006–2008) for outcome measures of growth and nutrition status. Those with growth restriction at birth were 3 cm shorter ( $P = 0.0026$ ) and 9 kg lighter ( $P = 0.0001$ ) with head circumferences 0.95 cm smaller ( $P = 0.0008$ ) than those without growth restriction. The proportions of growth restricted participants with body mass index  $<18.5$  kg/m<sup>2</sup> were significantly greater ( $P = 0.028$ ), and those with BMI  $> 25$  kg/m<sup>2</sup> and with fat percentage  $>85$ th percentile were significantly smaller ( $P = 0.012$  and  $0.004$ , respectively). In this cohort, those Aboriginal babies born smaller and lighter have remained smaller and lighter at 18 years of age. However, the highest risk of later chronic noncommunicable disease has been reported in subjects who were born small and become relatively larger in later life. The continued study of this Aboriginal birth cohort will give us an opportunity to determine if and when in later life the effects of birth weight are modified by environmental nutritional factors. *Am. J. Hum. Biol.* 23:417–419, 2011. © 2010 Wiley-Liss, Inc.

The Indigenous people of Australia have high rates of low-birth weight (LBW) (Leeds et al., 2007) and chronic noncommunicable adult diseases leading to premature adult mortality with current life expectancies 17 years less than for other Australians (Fearnley et al., 2009).

The Developmental Origins of Health and Disease (DOHaD) hypothesis postulates the relationship between early life events and later health and disease (Barker, 2004).

Recently, described associations of LBW with deaths due to pulmonary, renal, and cardiovascular causes in an Australian Aboriginal population (Hoy et al., 2010) suggest that improved survival of babies with LBW and fetal growth restriction (FGR; Australian Institute of Health and Welfare, 2008) may be contributing to the current epidemic of chronic disease in the Australian Aboriginal population.

Past reports suggest that the highest risk of later nutritionally related chronic noncommunicable diseases is in subjects who were born small and become relatively larger in later life (Bavdekar et al., 2000; Yajnik, 2000).

To examine if small Aboriginal babies become larger Aboriginal adults, the growth and nutritional status of young Aboriginal adults who were born at term, with and without FGR, was compared.

**METHODS***Participants*

The participants are in a prospective Aboriginal Birth Cohort study, which has been previously described in detail (Sayers et al., 2003, 2009). In brief, 686 Aboriginal babies born at the Royal Darwin Hospital in the Northern Territory of Australia (NT) between January 1987 and March 1990 were recruited into the study. Between December 2006 and January 2008, they were followed up in

over 40 different NT locations. Of the 686 participants recruited at birth, 469 participants were re-examined: 27 participants were known to have died, 68 could not be traced, and 121 traced participants could not be examined. Of those 121, 11 were refusals, and the remainders were not seen due to logistic reasons such as aircraft cancellations due to poor weather conditions, local flooding preventing access to remote communities, absence of a participant from a community at the time of the only scheduled research visit or because they were single participants living in very remote localities (Sayers et al., 2009).

*Procedures*

Standardized weight, length, and head circumference measures and gestational age estimations taken at birth have previously been described in detail (Sayers et al., 2007). At recruitment nonurban residence was defined as maternal residence outside Darwin city and its satellite town of Palmerston.

At follow-up, participants were measured while wearing light clothing and no shoes. Weight was measured to the nearest 0.1 kg using a digital electronic scale (model TBF-521; Tanita Corp, Arlington Heights, IL). Body composition (fat % and free fat mass) was measured using a bioelectric impedance analyzer (model TBF-521; Tanita Corp).

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\*Correspondence to: Susan Sayers, Menzies School of Health Research, P.O. Box 41096, Casuarina, Northern Territory, Australia 0811. E-mail: sue.sayers@menzies.edu.au

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TABLE 1. Comparison of key characteristics between excluded and analyzed subsets of term ( $\geq 37$ – $< 42$  weeks) gestation Aboriginal Birth Cohort study participants, 1987–2007

Characteristics	Excluded subset ( <i>n</i> = 197)	Analysed subset ( <i>n</i> = 341)	<i>P</i> -value
Birth weight (kg), mean (SD)	3.14 (0.56)	3.15 (0.50)	0.93
Gestation (weeks), mean (SD)	39.12 (1.00)	39.43 (0.93)	0.0065
Male sex (%)	53.3	49.27	0.37
Non Urban (%)	72.73	80.94	0.20

Height was measured to the nearest millimeter with a portable wall-mounted stadiometer. Mid-upper arm circumference, waist circumference, and hip and head circumference were measured to the nearest millimeter using a nonflexible tape and standardized procedures.

### Analysis

Birth weight-for-gestation was dichotomized at the 10th percentile using an Australian-based sex-specific reference curve comparable in time to the cohort recruitment (Guaran et al., 1994). FGR was defined as those with birth weight for gestational age  $< 10$ th percentile and non-FGR as those with birth weight for gestational age  $\geq 10$ th percentile and  $< 90$ th percentile.

Body mass index (BMI) of  $< 18.5$  kg/m<sup>2</sup> was used to define underweight and  $> 25$  kg/m<sup>2</sup> defined overweight. Body fat percentages were dichotomized using the internal reference of the 85th percentile.

Differences between participants were tested using *t* tests for continuous variables and  $\chi^2$  or Fisher's exact tests for categorical variables using Stata 11 software (StataCorp, 2009).

Analyses were restricted to 341 participants of term gestation with complete data for all measures at follow-up. Apart from a gestational age difference of 0.31 weeks ( $\sim 2$  days), there were no significant differences between this subset and the term babies recruited at birth but excluded from the follow-up analysis (197) for mean birth weight, the proportion that were male and the proportion with maternal nonurban residence (Table 1).

The study was approved by Human Research Ethics Committee of NT Department of Health and Families and Menzies School of Health Research, which included an Aboriginal Ethical Subcommittee with absolute power of veto.

### RESULTS

At follow-up, 341 (FGR = 81) of the original 538 term babies had complete data for all measures. The mean age was  $18.2 \pm 1.1$  years (range, 16.0–20.5), 46.9% were men, and the mean weight, height, and BMI were  $60.7 \pm 18.5$  kg,  $167.6 \pm 8.3$  cm, and  $21.3 \pm 5.5$  kg/m<sup>2</sup>, respectively.

For the term babies, there were no significant differences between those originally recruited and those seen at follow-up for mean birth weight (3.12 kg vs. 3.15 kg, *P* = 0.4), male percentage (50.7 vs. 49.3, *P* = 0.81), and the proportion who were FGR (25.8% vs. 23.8%, *P* = 0.59). At follow-up, there were also no significant differences between the FGR and non-FGR for mean age in years (18.4 vs. 18.2, *P* = 0.159) and the percentage male (46.9% vs. 50%, *P* = 0.63).

TABLE 2. Characteristics, growth and nutritional status of Aboriginal participants at 18 years by FGR at term gestation: Aboriginal Birth Cohort study, 1987–2007

Characteristics	FGR <sup>a</sup>	Non-FGR <sup>b</sup>	<i>P</i> -value <sup>c</sup>
Number of participants	260	81	
Age (years), mean (SD)	18.39 (1.13)	18.20 (1.07)	0.159
Male sex (%)	46.91	50.00	0.628
Outcomes			
Height (cm), mean (SD)	165.18 (8.14)	168.35 (8.27)	0.0026
Weight (kg), mean (SD)	53.56 (9.89)	62.88 (19.97)	0.0001
HC (cm), mean (SD)	54.60 (2.05)	55.55 (2.25)	0.0008
MUAC (cm), mean (SD)	24.94 (2.93)	27.25 (4.86)	0.0001
Waist (cm), mean (SD)	74.86 (9.02)	80.78 (15.06)	0.0009
Hip circumference (cm), mean (SD)	88.42 (7.65)	94.36 (12.82)	0.0001
Waist/height ratio, mean (SD)	0.45 (0.061)	0.48 (0.086)	0.013
Waist/hip ratio, mean (SD)	0.85 (0.064)	0.85 (0.069)	0.422
BMI (kg/m <sup>2</sup> ), mean (SD)	19.63 (3.36)	22.02 (5.91)	0.0006
BMI $< 18.5$ (kg/m <sup>2</sup> ) (%)	46.91	33.46	0.028
BMI $> 25$ (kg/m <sup>2</sup> ) (%)	8.64	22.31	0.006
Fat percentage, mean (SD)	17.43 (9.86)	21.60 (11.84)	0.0043
Fat $> 85$ th percentile (%)	6.17	17.69	0.012

<sup>a</sup> $< 10$ th percentile of birth weight for gestational age.

<sup>b</sup>Birth weight  $\geq 10$ th and  $< 90$ th percentile for gestational age.

<sup>c</sup>Unadjusted.

MUAC, mid upper arm circumference; waist, waist circumference; HC, head circumference; BMI, body mass index.

Compared to non-FGR participants, the FGR participants were 3 cm shorter (*P* = 0.0026) and 9 kg lighter (*P* = 0.0001), and their head circumferences were 0.95-cm smaller (*P* = 0.0008). Similarly, the nutritional measures of BMI, mid arm, waist, and hip circumferences, and fat percentages were all significantly lower for the FGR participants (Table 2). Consequently, for the FGR participants, the proportions of participants with BMI  $< 18.5$  kg/m<sup>2</sup> were significantly greater, and the proportions with BMI  $> 25$  kg/m<sup>2</sup> and with fat percentage  $> 85$ th percentile were significantly smaller. There were no significant differences between FGR and non-FGR participants for the waist/hip or waist/height ratios (Table 2).

### DISCUSSION

In this cohort of Aboriginal babies from the Top End of the Northern Territory, at 18 years of age, those that were FGR at birth are smaller, lighter, and have smaller head circumferences than those of appropriate birth weight for gestational age. For the waist/hip and waist/height ratios, there were no significant differentials suggesting that the fat distribution was the same for FGR and non-FGR participants. This is a continuation of the growth and nutritional status outcomes at 11 years of age (Sayers et al., 2007).

About 25% of the original cohort was not included in this follow-up analysis. However, there were no significant differences in the mean birth weight, sex ratio, or maternal residence at birth between the term babies originally recruited and the subset followed up. The basic characteristics of the subset of term babies that was excluded from the analysis were only significantly different in gestational age by 0.31 weeks from those included in the analysis. As a two-day difference in gestational age is unlikely to have an impact at 18 years of age, it is likely that this analyzed subset of term babies is a representative sample of the original term babies recruited.

The DOHaD hypothesis postulates the relationship between early life events and later health and disease. Adaptive fetal responses to an intrauterine environment

with poor nutrition are thought to improve immediate fetal survival but may contribute to the development of chronic noncommunicable diseases in a later nutritionally enriched and therefore mismatched environment. At birth, evidence of a poor intrauterine environment affecting fetal growth adversely is through the surrogate measures of FGR and LBW. LBW babies who become overweight or obese adults are reported to have the highest risk of later chronic disease (Bavdekar et al., 2000, Yajnik, 2000).

There are concurrently high rates of LBW (12.7%) (Leeds et al., 2007), overweight and obesity (60%) (Australian Institute of Health and Welfare, 2008), and chronic noncommunicable adult diseases (Fearnley et al., 2009) in the Australian Aboriginal population. Recently, associations of LBW with Aboriginal adult deaths due to pulmonary, renal, and cardiovascular causes have been described (Hoy et al., 2010), and, in a cross-sectional study, associations of LBW with higher blood pressure have been shown, with the highest mean pressures occurring in those adults with high BMI who were LBW (Singh and Hoy, 2003). These reports imply that, consistent with the DOHaD hypothesis, there may be relationships between LBW/FGR, adult obesity, and chronic disease development in the Australian Aboriginal population.

Nevertheless, in this cohort, those Aboriginal babies born smaller and lighter have remained smaller and lighter at 18 years of age. This suggests that the combination of poor fetal growth and excess adult weight is rare in this young adult population. The continued study of this Aboriginal birth cohort will give us an opportunity to determine if and when in later life the effects of birth weight are modified by environmental nutritional factors.

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