Growth outcomes for Australian Aboriginal children aged 11 years who were born with intrauterine growth retardation at term gestation

Susan Sayers, Dorothy Mackerras, Stephen Halpin and Gurmeet Singh
Menzies School of Health Research, Institute of Advanced Studies, Charles Darwin University, Northern Territory, Australia

Summary


Long-term poor growth outcomes are well documented for intrauterine growth retarded babies (IUGR) in developed populations but there is a paucity of IUGR studies from disadvantaged populations where the greatest burden of IUGR occurs. Using a Northern Territory, Aboriginal cohort recruited at birth and followed up at a mean age of 11.4 years, comparisons of body size were made between children born at term who had been IUGR (n = 121) and those non-IUGR (n = 341), and between those IUGR babies who had an appropriate ponderal index at birth (n = 72) and those with a low ponderal index (n = 49).

Compared with non-IUGR children, at follow-up the IUGR children were almost 2 cm shorter (P = 0.10), 4 kg lighter (P < 0.01) and their head circumferences were almost a 1 cm smaller (P < 0.01). For the 121 term IUGR children, there were no significant differences in growth outcomes according to ponderal index measures at birth. These findings from an Australian Aboriginal sample are consistent with other comparisons of IUGR and non-IUGR children in developed populations and suggest there may be no additional effects of IUGR on growth in childhood for disadvantaged populations similar to the Aboriginal population in the Northern Territory.

Keywords: child growth, IUGR, birthweight-for-gestation, birth ponderal index, childhood height, childhood weight.

Introduction

Intrauterine growth retardation (IUGR) is a major public health problem. It occurs mainly in underdeveloped populations and accounts for 24% or approximately 30 million births worldwide per year. Long-term poor growth problems are well recognised for IUGR babies with some studies reporting growth differences according to ponderal index at birth. Currently most prospective studies of IUGR babies are from developed populations where IUGR rates are considerably lower that those of disadvantaged populations and most do not extend beyond early childhood.

Prospective studies from developed populations indicate that despite partial catch-up growth during the first 1 to 2 years of life, IUGR babies continue to have a smaller body size relative to their non-IUGR peers in childhood. By age 17–19 years, IUGR subjects were about 5 cm less in height and 5 kg less in weight than those who were non-IUGR. Similar findings are reported for a disadvantaged Guatemalan population assessing growth outcomes of IUGR at 14 years of age.

Using the ponderal index ([weight(g)/length³ (cm)] × 100) as a measure of neonatal nutritional status or wasting, studies suggest IUGR newborns born thin or asymmetrical with a low ponderal index (IUGR-LPI) have more marked catch-up growth compared with those IUGR who are symmetrically small with an adequate ponderal index (IUGR-API). However, by
the age of 18 years a New Zealand study showed there were few differences between these groups.\textsuperscript{12} Although some studies suggest that poor fetal growth is associated with early puberty there remain limited and conflicting data concerning the timing of puberty in children born with IUGR.\textsuperscript{15–18}

There is a need for studies on IUGR from underdeveloped populations where the consequences of IUGR may be changed by settings of malnutrition and infection.\textsuperscript{2} However home births, unreliable gestational aging with failure to distinguish preterm births from IUGR, and difficulties in tracking mobile populations, all contribute to a paucity of IUGR studies from these disadvantaged populations.

In the Northern Territory of Australia (NT), the Aboriginal population is an example of a disadvantaged population living within a developed nation. The majority of the Aboriginal population continues to live in remote communities on traditional lands with poor social and physical infrastructures. In this NT population there are high rates of IUGR, and low birthweight rates are double those of the non-Aboriginal NT population.\textsuperscript{19,20} Childhood infections are common,\textsuperscript{21} with the main reasons for hospital admissions of Aboriginal children being respiratory and diarrhoeal diseases with rates up to a hundred times greater than for the non-Aboriginal NT population.\textsuperscript{22} Consistent with a population undergoing early transition the children living in remote areas show a large excess of underweight, while the urban dwellers include an excess of both underweight and overweight.\textsuperscript{23} The life expectancies at birth of 59 years for men and 65 years for women,\textsuperscript{24} are similar to the United Nations Children’s Fund (UNICEF) 2006 estimation of 65 years for developing countries.\textsuperscript{25}

Using an Aboriginal birth cohort recruited in the NT during 1987–1990 the aims of our study were:

1. to compare the body sizes at 11 years of age of children who were term IUGR and term non-IUGR at birth;
2. to compare the body sizes of children at 11 years of age who were term IUGR-LPI with term IUGR-API at birth.

**Methods**

**Subjects**

The subjects were 462 children who were born between 37 and 42 weeks and were able to be located and examined in childhood. The subjects were nested within the Aboriginal birth cohort study which has been previously published in detail.\textsuperscript{26} In brief, 686 out of 1238 Aboriginal children born at the Royal Darwin Hospital between January 1987 and March 1990 were recruited into the study. Births in this hospital include all routine deliveries of babies from the immediate Darwin Health Region and high-risk deliveries referred from a larger area in northern Australia. Although the babies were not randomly selected there were no significant differences in the mean birthweight, mean gestational age, birthweight frequencies or sex ratio between those recruited and not recruited.\textsuperscript{26}

The children were followed up between December 1998 and March 2001 in over 70 locations in northern Australia. Of the 686 participants recruited at birth, 572 were examined at follow-up (86% follow-up of living children); 18 had died, 64 were traced but could not be accessed for examination due to weather and access difficulties on the assessment day, one child refused examination and 31 children could not be found. The comparisons between participants seen and not seen have been previously described in detail.\textsuperscript{26} In brief, at follow-up there were no significant differences between those children seen and those not seen in regard to mean birthweight, sex ratio and proportions of low birthweight, preterm and small-for-gestational-age (SGA) births. Only the mean gestational ages were slightly but significantly different between those children seen and those not seen (38.9 vs. 38.4 weeks). For the term babies, there were no significant differences between 539 babies seen at birth and the 462 seen at follow-up for mean birthweight, sex ratios and the proportion who were IUGR; only the mean gestational ages were slightly and significantly different (39.0 vs. 39.3 weeks).

**Procedures**

At recruitment, midwives measured the birthweights and crown-heel lengths within 2 h of delivery. The one neonatal paediatrician measured the head circumference of all participants within 4 days. Birthweights were recorded to the nearest gram using a balance scale. The crown-heel lengths were measured with a length board by the standard anthropometric technique. The gestational age was estimated within 4 days of birth by the same neonatal paediatrician using the Dubowitz scoring system,\textsuperscript{27} previously evaluated for Aboriginal babies.\textsuperscript{28}
At follow-up, children were measured while wearing light clothing and no shoes. Weight was measured to the last complete 0.1 kg with a digital scale (Tanita model 5810) and height to the nearest millimetre with a portable wall mounted stadiometer. Mid-upper arm and waist circumferences were measured to the nearest millimetre directly on the skin using a non-flexible tape. Triceps and subscapular skin folds were measured three times to the nearest millimetre using a Harpenden calliper by a trained researcher. A paediatrician examined the children and assessed pubertal development according to Tanner staging.32,33

**Analysis**

Birthweight-for-gestation was dichotomised at the 10th percentile using an Australian-based sex-specific reference curve comparable in time to the cohort recruitment.31 IUGR was defined as those <10th percentile and non-IUGR as those ≥10th percentile and <90th percentile. Using an Australian ponderal index reference standard,31 IUGR-API was defined as those IUGR with a ponderal index ≥10th percentile and IUGR-LPI as those IUGR with ponderal index <10th percentile for gestational age.

In order to compare the height and weight outcomes with the Guatemalan study two birthweight groups were defined as consistent with that study: a surrogate IUGR group and upper birthweight group with birthweights at term <2500 g and ≥3001 g, respectively.

Weight-for-age Z-scores (WAZ) and height-for-age Z-scores (HAZ) were calculated using the WHO/NCHS reference population.32 Malnutrition was categorised as underweight or stunting (shortness) according to the WHO criteria (i.e. more than two SDs below the median weight-for-age or height-for-age, respectively).33 Body mass index (BMI) (kg/m²) Z-scores were also calculated from sex-specific reference curves using the WHO/NCHS reference population.32 Overweight was defined using the age and sex-specific cut-offs for BMI in children according to Cole et al.34 The three skin folds at each site were averaged and the triceps/subscapular ratio was calculated using the means. Pubertal status was dichotomised as pre-pubertal and commenced puberty. Children were classified as ‘urban’ if they were living in a suburban setting within the city of Darwin and its satellite city Palmerston, and ‘rural’ if they were living in rural communities with Aboriginal councils, small rural towns and non-suburban situations within Darwin-Palmerton (town camps and Aboriginal communities). The numbers of children in analyses varied as some had disabilities that prevented some measures and others refused some procedures.

Outcome differences between IUGR and non-IUGR babies, and between babies <2500 g and babies ≥3001 g were tested using t-tests for continuous variables and χ²-tests for categorical variables. Multiple linear and logistic regressions were used to test differences in continuous and categorical outcomes, respectively, after adjusting for sex, pubertal status and urban living, and their interaction with IUGR status. All analyses were performed using stata 8.2 statistical software.35

The study was approved by the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research. The Aboriginal Subcommittee of this Committee had veto power. The parents or carers gave written informed consent. Children were able to refuse any procedure.

**Results**

At recruitment there were 539 term births of whom 139 were IUGR. At follow-up 462 of the original term babies (121 IUGR) were assessed at a mean age of 11.4 years, 51% were boys, 49% had commenced puberty, 26% were urban dwellers, 5% had HAZ scores <−2 and 21% had WAZ scores <−2. There were no significant differences between the IUGR and non-IUGR children for mean age, sex ratio or the percentage that had commenced puberty.

Compared with non-IUGR children, at follow-up the IUGR children were almost 2 cm shorter (P = 0.10), 4 kg lighter (P < 0.001) and their head circumferences were almost 1 cm smaller (P < 0.01). After adjusting for age and sex there were statistically significant differences in mean HAZ and WAZ scores (Table 1). The proportion of children with a WAZ < −2 was significantly greater for the IUGR children than for the non-IUGR children but there was no significant difference in the proportion with HAZ < −2 (Table 1). There were no differences between the sexes in the relationships between non-IUGR and IUGR for HAZ, WAZ and the proportions with Z-scores < −2 for height and weight.

Consistent with these findings the other nutritional measures of median BMI, mid-arm and waist
circumference and triceps and subscapular skin folds were significantly lower and the proportion of overweight children (using the Coles international standard for overweight) was significantly less for the IUGR children than for the non-IUGR children (Table 1). However, there were no significant differences between the subscapular/triceps ratio by IUGR classification.

Table 1. Characteristics and growth outcomes for Aboriginal children at 11 years by IUGR at term, Aboriginal Birth Cohort Study, 1987–2001

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>IUGR</th>
<th>n</th>
<th>Non-IUGR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean, SD)</td>
<td>121</td>
<td>11.6 (1.1)</td>
<td>341</td>
<td>11.4 (1.2)</td>
<td>0.059</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>121</td>
<td>52.1</td>
<td>341</td>
<td>51.0</td>
<td>0.844</td>
</tr>
<tr>
<td>Commenced puberty (%)</td>
<td>113</td>
<td>54.0</td>
<td>321</td>
<td>48.0</td>
<td>0.248</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm) (mean, SD)</td>
<td>121</td>
<td>142 (10.1)</td>
<td>341</td>
<td>143.8 (10.6)</td>
<td>0.103</td>
</tr>
<tr>
<td>Weight (kg) (mean, SD)</td>
<td>121</td>
<td>32.3 (9.1)</td>
<td>341</td>
<td>36.6 (12.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Head circumference (cm) (mean, SD)</td>
<td>113</td>
<td>51.6 (1.8)</td>
<td>320</td>
<td>52.5 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height for age Z-score (mean, SD)</td>
<td>121</td>
<td>–0.8 (1.0)</td>
<td>341</td>
<td>–0.4 (1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight for age Z-score (mean, SD)</td>
<td>121</td>
<td>–1.4 (1.2)</td>
<td>341</td>
<td>–0.6 (1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stunted (%HAZ score &lt;−2)</td>
<td>121</td>
<td>8.3</td>
<td>341</td>
<td>4.1</td>
<td>0.077</td>
</tr>
<tr>
<td>Underweight (%WAZ score &lt;−2)</td>
<td>121</td>
<td>33.8</td>
<td>341</td>
<td>15.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²) (mean, SD)</td>
<td>121</td>
<td>15.7 (2.6)</td>
<td>341</td>
<td>17.3 (3.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MUAC (cm) (mean, SD)</td>
<td>112</td>
<td>20.1 (3.1)</td>
<td>320</td>
<td>21.7 (3.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist (cm) (mean, SD)</td>
<td>113</td>
<td>61.6 (7.2)</td>
<td>324</td>
<td>65.3 (10.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subscap skin fold (mm) (mean, SD)</td>
<td>119</td>
<td>28.2 (16.3)</td>
<td>333</td>
<td>37.7 (28.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triceps skin fold (mm) (mean, SD)</td>
<td>119</td>
<td>8.6 (3.1)</td>
<td>334</td>
<td>11.1 (6.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subscap/triceps ratio (mean, SD)</td>
<td>118</td>
<td>1.06 (0.3)</td>
<td>333</td>
<td>1.09 (0.3)</td>
<td>0.543</td>
</tr>
<tr>
<td>% Overweight²</td>
<td>121</td>
<td>3.3</td>
<td>341</td>
<td>12.9</td>
<td>&lt;0.008</td>
</tr>
</tbody>
</table>

²≤10th percentile of birthweight for gestational age.
³birthweight ≥ 10th < 90th percentile for gestational age.

BMI, body mass index; HAZ, height-for-age Z-scores; IUGR, intrauterine growth retarded; MUAC, mid upper arm circumference; Subscap, subscapular skin fold; Subscap/triceps ratio, subscapular/triceps ratio; Waist, waist circumference; WAZ, weight-for-age Z-scores.

Table 2. Growth outcomes for Aboriginal children at 11 years, by ponderal index for IUGR at term, Aboriginal Birth Cohort Study, 1987–2001

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>IUGR-API²</th>
<th>IUGR-LPI³</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight (g) (mean, SD)</td>
<td>2636 (235)</td>
<td>2505 (317)</td>
<td>0.011</td>
</tr>
<tr>
<td>Birth length (cm) (mean, SD)</td>
<td>46.4 (1.8)</td>
<td>48.1 (317)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years) (mean, SD)</td>
<td>11.6 (1.1)</td>
<td>11.7 (1.1)</td>
<td>0.681</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>50.0</td>
<td>55.0</td>
<td>0.581</td>
</tr>
<tr>
<td>Commenced puberty (%)</td>
<td>50.0</td>
<td>60.5</td>
<td>0.279</td>
</tr>
<tr>
<td>Anthropometric characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm) (mean, SD)</td>
<td>141.4 (10.6)</td>
<td>142.9 (9.5)</td>
<td>0.429</td>
</tr>
<tr>
<td>Weight (kg) (mean, SD)</td>
<td>31.9 (8.5)</td>
<td>33 (10.1)</td>
<td>0.515</td>
</tr>
<tr>
<td>Head circumference (cm) (mean, SD)</td>
<td>51.9 (1.8)</td>
<td>51.2 (1.7)</td>
<td>0.548</td>
</tr>
<tr>
<td>Height-for-age Z-score (mean, SD)</td>
<td>–0.9 (1.0)</td>
<td>–0.7 (0.9)</td>
<td>0.115</td>
</tr>
<tr>
<td>Weight-for-age Z-score (mean, SD)</td>
<td>–1.5 (1.2)</td>
<td>–1.2 (1.1)</td>
<td>0.246</td>
</tr>
<tr>
<td>Body mass index (kg/m²) (mean, SD)</td>
<td>15.7 (2.4)</td>
<td>15.8 (2.7)</td>
<td>0.739</td>
</tr>
</tbody>
</table>

²IUGR with ponderal index ≥ 10th percentile for gestational age.
³IUGR with ponderal index < 10th percentile for gestational age.

IUGR-API, IUGR babies who had an appropriate ponderal index at birth; IUGR-LPI, IUGR babies who had a low ponderal index.

Paediatric and Perinatal Epidemiology, 21, 411–417. ©2007 The Authors, Journal Compilation ©2007 Blackwell Publishing Ltd.
For those variables not based on Z-scores in Table 1 the significant differences remained between IUGR and non-IUGR children after further adjustment for age, sex, puberty status and urban location. Children that had commenced puberty or who lived in urban areas were heavier and taller but the interaction between puberty and IUGR status was not significant.

The proportion who had commenced puberty did not differ between IUGR and non-IUGR children ($P = 0.3$). As expected at this age, of those who had commenced puberty the majority were girls, 72% for IUGR children and 61% for non-IUGR children. For the IUGR and non-IUGR girls, 13% and 15% ($P = 0.7$), respectively, had commenced menstruation.

For the 121 term IUGR children, there were no significant differences in growth outcomes according to ponderal index at birth (Table 2).

The surrogate IUGR children ($n = 41$) were 6.1 kg lighter ($P = 0.002$) and 4.6 cm shorter ($P = 0.008$) than the children in the upper birthweight group ($n = 274$) and these differences remained after adjustment for gestational age and current age. For boys, the differences between the surrogate IUGR ($n = 19$) and upper birthweight group ($n = 152$) were $-3.8$ cm ($P = 0.1$) and $-5.5$ kg ($P = 0.05$) for height and weight, respectively; for girls the differences for height and weight between the surrogate IUGR ($n = 22$) and upper birthweight group ($n = 122$) were $-5.3$ cm ($P = 0.04$) and $-6.6$ kg ($P = 0.02$), respectively.

**Discussion**

There is a need for studies on IUGR outcomes in disadvantaged populations where the burden of IUGR births is the greatest and the long-term growth consequences of IUGR may be magnified by poor postnatal environments. Although living within a westernised country, rural Aboriginal children are more likely to live in extreme social disadvantage with overcrowded living conditions, inadequate water and washing facilities, and poor sanitation and sewage disposal. In the NT, high rates of IUGR and poor life expectancies reflect these social circumstances.

To our knowledge this is the first prospective study describing the growth outcomes of Australian Aboriginal children who were classified as IUGR at birth. In part, due to the difficulty of obtaining reliable gestational age estimations, the few growth outcome studies that have been carried out have been restricted to low-birthweight infants. Roberts et al. had a similar finding in a 5-year prospective study of 74 Aboriginal children in the Kimberley. However, for both these studies the low-birthweight group included both IUGR and preterm births with known different outcomes, and excluded those IUGR $>2500$ g.

Like other traditional populations, in this study few Aboriginal mothers knew their last menstrual period reliably or had had an early dating ultrasound. However, importantly, unlike other disadvantaged populations where home births are more common, the single point hospital recruitment of this cohort meant that birth anthropometric measurements were reliably recorded and the gestational age estimations were all done within 4 days of birth by the one neonatal paediatrician, using a method shown to be satisfactory for this population.

The advantages of this study were the accurate identification of IUGR within the term gestational age interval so that preterm births were reliably excluded and the remarkable follow-up of 86% of the original IUGR babies – an exceptional achievement 11 years later considering the mobility, name changes and cultural challenges associated with tracing an indigenous population.

As serial fetal ultrasound measurements needed to reliably document IUGR are not possible in this population, for practical reasons the classification of IUGR was determined within 4 days of birth and was based on the SGA cut-off of $<10$th percentile of birthweight for gestational age using an Australian based reference standard. Using this SGA definition to identify IUGR had the two disadvantages of including ‘normal’ babies at the lower end of the weight-for-age distribution curve who are not growth retarded and excluding those who may have had significant growth retardation during gestation but who happen to have an appropriate weight-for-age at delivery.

In this study, at a mean age of 11.4 years the IUGR children were almost 2 cm shorter, 4 kg lighter and had head circumferences almost 1 cm smaller than the non-IUGR. The BMI was lower in the IUGR children as were the other fat measures except the subscapular/triceps skin fold ratios, suggesting the distribution of body fat was the same for non-IUGR and IUGR.

These height and weight differences of 2 cm and 3 kg for the 11-year-old Aboriginal children in this
study were not as great as those reported for the Guatemalan study of disadvantaged children at a mean age of 14.5 years which found IUGR children compared with non-IUGR children were 6.3 cm and 3.6 cm shorter and 3.8 and 5.6 kg lighter for boys and girls, respectively. However, these discrepancies are likely to be methodological as, when the analysis was repeated using the birthweight groupings of the Guatemalan study, the differences were similar with the surrogate IUGR group 6.1 kg lighter and 3.6 cm shorter than those in the upper birthweight grouping. These differences from Australian Aboriginal and Guatemalan populations are consistent with the −5 cm and the −5 kg differences found between IUGR and non-IUGR subjects at 17–18 years of age in studies from developed populations.

As previously reported, Aboriginal children living in the urban setting were heavier and taller than their rural peers.27 However, the lack of interaction between IUGR status and urban and rural dwellers in this study suggests childhood growth outcomes of IUGR are not magnified by the relatively impoverished environment of the rural setting.

Although there were no significant differences between the growth outcomes of the Aboriginal IUGR babies according to ponderal index, there was a trend for the IUGR children who were API at birth (72) to be shorter and lighter than those children who had been LPI (49). Two studies from Guatemala (59 and 39 subjects) with follow-up at 3 and 14 years show that children who had been IUGR-API at birth were shorter and lighter,25 suggesting symmetrical growth retardation may be a surrogate for an intrauterine insult of early onset persisting throughout pregnancy.40 However, a New Zealand study of 71 IUGR subjects showed few differences in height and weight according to ponderal index by age 18 years.12 As the differences according to the ponderal index have been shown mainly in younger disadvantaged populations it is possible that ponderal index is a measure of the severity rather than the timing of an intrauterine insult and, by 18 years of age in a nutritionally appropriate environment, these growth differences are no longer present.

In this study at 11 years of age the proportion of children who had commenced puberty was similar for IUGR and non-IUGR children, which suggests, for this sample, that puberty was not delayed in those children born IUGR.

Although direct comparisons with other studies are difficult due to different methodologies, these findings from an Australian Aboriginal sample are consistent with other comparisons of IUGR and non-IUGR children in developed populations and suggest there may be no additional effects of IUGR on growth in childhood for disadvantaged populations similar to the Aboriginal population in the NT.

Acknowledgements

This work was supported by the National Health and Medical Research Council of Australia, the Colonial Foundation and the Channel 7 Children’s Research Foundation of South Australia. Initially Jenny Powers helped with data management and analysis, Aleeta Dawes helped with recruitment at birth, Kathryn Flynn traced the children at follow-up and Dr Ingrid Bucens assisted with data collection at follow-up. Thanks go to the Aboriginal mothers who agreed for their babies and later their children to be part of this study.

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35 *Stata Statistical Software*: Release 8 0. College Station, TX: Stata Corporation, 2003.


