Original Article

Growth patterns during the first 12 months of life: post-hoc analysis for South Australian Aboriginal and Caucasian infants in a randomised controlled trial of formula feeding

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Background and Objectives: To compare growth characteristics of Aboriginal and Caucasian formula-fed infants in the first 12 months of life. **Methods and Study Design:** We conducted post-hoc data analysis of infants who were part of a previous randomised controlled trial comparing infants randomly assigned to cow or goat milk-based infant formulae. Weight, height, and body composition were assessed at serial time points between study entry (~1-2 weeks of age) and 12 months. There was no growth difference between the randomised groups so the two groups were combined and the data were used to conduct a non-randomised comparison of the growth between Aboriginal (n=11) and Caucasian formula-fed (n=169) infants. **Results:** Aboriginal formula-fed infants had significantly higher mean z-scores for weight (0.65 difference, [95% CI 0.11, 1.18], *p*=0.018) and weight-for-length (0.82 difference [95% CI 0.20, 1.44], *p*=0.010) at 2 months, and all time points onward compared with Caucasian formula-fed infants. Mean length z-scores and the overall growth trajectory across time did not differ between Aboriginal and Caucasian formula-fed infants. Concordant with the weight and weight-for-length z-scores, Aboriginal infants had increased fat mass at 2 months (292 g difference [95% CI 56, 528], *p*=0.015), and all time points onward compared to Caucasian infants. There was no difference in fat free mass. **Conclusions:** Though there was only a small number of Aboriginal infants for comparison, our data indicate Aboriginal formula-fed infants were heavier and had a larger increase in fat mass over time compared with Caucasian formula-fed infants. Further studies using a larger cohort are needed to substantiate these findings.

Key Words: infants, growth, Aboriginal, body composition, fat mass.

INTRODUCTION

Failure to thrive and excessive weight gain have both been identified as important health issues for Aboriginal children and more recent studies have shown a tendency toward overweight and obesity.[1–4] An Australia-wide study found that Aboriginal children aged 5-9 years were heavier and shorter than the average Australian child, especially in capital cities.[5] Multivariate analysis of a national cohort of Australian children aged 4-5 years found Indigenous status was a clear predictor of higher body mass index (BMI), with 11.3% of indigenous children in the obese category compared with 5.3% of non-indigenous children.[6] A recent study of South Australian Aboriginal children aged 3-6 years revealed overweight and obesity rates of 17% and 11% compared to 14% and 4% in non-Aboriginal children.[2,6]

Only one study has investigated the growth of Aboriginal children between birth and 2 years. The Gudaga study team measured anthropometrics at study entry then six monthly until 24 months of age, and found rapid weight gain in the first year of life was associated with overweight and obesity by two years of age.[3]

Our aim was to compare serial growth measures and estimates of body composition (fat free mass and fat mass) between Aboriginal and Caucasian formula fed (FF) infants from birth to 12 months, by conducting a non-randomised post-hoc analyses using data from the chil-

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Manuscript received 21 December 2015. Initial review completed 15 February 2016. Revision accepted 04 March 2016.
doi: 10.6133/apjcn.042016.09

dren who were part of the Tolerance of Infant Goat Milk Formula and Growth Assessment (TIGGA) study, a randomised controlled trial (RCT) that compared growth and nutritional status of infants fed either goat milk or cow milk formula.[7] During the RCT, infants were fed study formula with equivalent energy composition for the first four months, and intake of solid foods and fluids, other than study formula, were measured over the course of 12 months.

METHODS

Population

The participants were recruited to the TIGGA trial between April 2008 and April 2009 from three tertiary hospitals in Adelaide according to a protocol approved by the Human Research Ethics Committees of the Women's and Children's Health Network (Ethics Number: 1980/08/10), and Flinders Medical Centre (Ethics Number: 25/07). Details of the initial RCT study design and methods have been previously published.[7] Briefly, 200 term infants with appropriate weight for gestational age at birth were randomly allocated to either a goat-milk infant formula or a typical whey-based cow-milk infant formula if they were exclusively fed formula prior to day 14. A cohort of 101 healthy, term breastfed infants was also included for comparison. All families provided written informed consent.

Infants were fed either a standard goat or cow milk infant formula with the same energy and nutrient composition, and results of the RCT showed no significant difference in growth between the two formula groups. For analyses, the two formula groups were combined and the original trial data was split into non-randomised groups for comparison of growth by infant race.

Infant race was documented as Aboriginal if one of the biological parents identified as Aboriginal, and Caucasian if both biological parents identified as Caucasian. Of the formula fed infants 169 were Caucasian (Caucasian FF), and 11 were Aboriginal (Aboriginal FF). Caucasian breastfed (Caucasian BF) infants were included for comparison (n=87). All other infants (n=34) were excluded from these secondary analyses, including, infants from African/Asian parentage, mixed race parentage (not including Aboriginal children), or infants who had one parent with unlisted race.

Anthropometric Measures

Infant weight, length and body composition measures were taken at study entry (~2 weeks of age), then monthly between 1 and 4 months of age, and at 6 and 12 months. Infants were weighed naked to the nearest 5 g using digital baby scales (In clinic, Seca, Germany; Home visit, Wedderburn, Australia), and length was measured in the Frankfort plane to the nearest 0.5cm using a recumbent length board (Ellard Instruments, America).[8] All anthropometric growth data were converted to z-scores using WHO Child Growth Standards (http://www.who.int/childgrowth/en/), to standardise age at assessment and infant sex.[7] Fat free mass and fat mass were estimated by bioelectrical impedance spectroscopy. Measurements were performed using the Imp SFB7 (ImpediMed, Brisbane, QLD, Australia), a single channel, tetra-polar bioelectrical impedance spectroscopy device that measures resistance and reactance at 256 logarithmically spaced frequencies between 4 and 1000 kHz. The protocol followed has been described previously.[9] Fat free mass was calculated using resistance at 0 kHz (R_0) using the following formulae from Lingwood, Storm van Leeuwen, Carberry, Fitzgerald, Callaway, Colditz & Ward: $1.169 + 0.568W - 0.128S + 0.032L^2/R_0$ (1) for 1 and 2 month measures, $1.315 + 0.449W - 0.169S + 0.153L^2/R_0$ (2) for 3 month measures, and $1.909 + 0.280W - 0.279S + 0.305L^2/R_0$ (3) for 4, 6 and 12 month measures, where W is weight in kg, S is sex (1=Male, 2=Female) and L is length in cm.[10]

Other assessments

Demographic and baseline characteristics, including infant sex, weight and length at birth, parity, history of smoking during pregnancy, maternal age at birth, maternal/paternal BMI (kg/m^2) and education were recorded at trial entry. Average study formula consumed per day between 2 weeks and 4 months of age (mL) was also reported.

Statistical analyses

Data were analysed using Stata v11.2 and v13 (Texas, USA) and SAS v9.3 (North Carolina, USA). Differences in baseline and feeding characteristics between the Caucasian FF and Aboriginal FF groups were assessed using Fishers Exact test or t-tests for categorical and continuous variables, respectively.

To test whether Aboriginal FF infants differed from Caucasian FF infants in z-score or body composition outcomes, linear regression models were fitted, including a generalised estimating equation to account for repeated measures. An interaction term was included in the model to test whether the trajectory of z-scores or body composition measures over time differed between Aboriginal FF and Caucasian FF groups, and estimates of the group differences were derived separately for each group and time point. Both unadjusted and adjusted analyses were performed, with the adjusted analyses including study centre and TIGGA treatment group (formula type) as covariates.

In order to address the concern that Caucasian FF infants may not be representative of the population of Caucasian infants (hence limiting the interpretability and generalisability of the comparisons between Caucasian FF and Aboriginal FF infants), the same analyses were also performed to compare z-score and body composition outcomes between Caucasian FF and Caucasian BF infants.

RESULTS

Sociodemographic and feeding characteristics

The Aboriginal and Caucasian FF groups were similar overall, with the exception of maternal pre-pregnancy BMI and father's education level, which were both significantly lower in the Aboriginal group than the Caucasian group, Table 1.

Significant differences were found between the Caucasian FF and Caucasian BF groups. On average, mothers in the Caucasian FF group were younger, had given birth to more children, and had a higher pre-pregnancy BMI. A larger proportion of mothers reported smoking during

Table 1. Maternal, paternal and infant characteristics by race and type of feeding

Characteristic	Caucasian FF group (n=169)	Aboriginal FF group (n=11)	Caucasian BF group (n=87)	*p*-value* Caucasian vs Aboriginal FF	*p*-value* Caucasian FF vs BF
Maternal characteristics					
Parity, mean (SD)	2.31 (1.2)	2.64 (2.1)	1.91 (0.9)	0.405	0.005
Maternal age (years), mean (SD)	28.2 (6.1)	24.5 (5.4)	30.7 (5.4)	0.056	<0.001
BMI pre-pregnancy, mean (SD)	27.8 (7.3)	22.7 (3.3)	25.1 (4.5)	0.021	0.001
Smoked during pregnancy, n (%)	65/169 (38.5)	5/11 (45.5)	8/87 (9.2)	0.753	<0.001
Completed secondary/further education, n (%)	114/169 (67.4)	6/11 (54.5)	78/87 (89.7)	0.510	<0.001
Paternal characteristics					
Paternal BMI, mean (SD)	28.0 (6.1)	26.4 (4.9)	27.3 (4.0)	0.437	0.390
Completed secondary/further education, n (%)	117/165 (70.9)	4/11 (36.4)	76/87 (87.4)	0.037	0.003
Infant characteristics					
Female, n (%)	87/169 (51.5)	9/11 (81.8)	47/87 (54.0)	0.064	0.792
Birth weight (g), mean (SD)	3387 (443)	3531 (582)	3599 (408)	0.306	<0.001
Birth length (cm), mean (SD)	49.4 (2.0)	49.6 (3.2)	50.3 (2.0)	0.812	0.002
Feeding information					
Study compliant infants†, n (%)	113/169 (66.9)	7/11 (63.6)	68/87 (78.2)	1.000	0.081
Average SF p/day (mL) between 2 wks-4 mths‡, mean (SD)	992 (171)	1026 (148)	N/A	0.577	N/A

FF: formula fed; SF: study formula; NSF: non-study formula.
†Study compliant infants: those that completed the trial and did not consume any other liquids or solids including non-study formula, for >12 days between 2 wks-4 mths of age.
‡Average SF per day was calculated as follows: Infants were included if they had at least one recorded value in the first 2 mths, and at least one recorded value in 3 mths and 4 mths. Average formula per day at 2 wks, 1 mth, 2 mths, 3 mths and 4 mths calculated by (number bottles per/day×mL p/bottle) – mL discarded p/day. Average formula mL/per day in month 1 was calculated by averaging average formula mL/per day at 2 wks, and average formula mL/per day at 1 mths. Average formula mL/per day from 2 wks to 4 mths was calculated by averaging average formula mL/per day at 1 mth, 2 mths, 3 mths and 4 mths.
*Continuous and categorical variables between Caucasian formula fed and Aboriginal formula fed infants, and between Caucasian formula fed and Caucasian breast fed infants, were compared using independent-samples *t* tests and Fishers Exact tests respectively.

pregnancy in the FF group, and fewer fathers or mothers had completed secondary or further education. Mean birth weight and length in the Caucasian FF group was also significantly lower, Table 1.

Weight, length, and weight-for-length z-scores

Figure 1 shows mean weight, length, and weight-for-length z-scores plotted by time for Caucasian FF, Aboriginal FF, and Caucasian BF infants.

The Aboriginal FF group had significantly higher mean z-scores for weight at all time points from 2 months onward compared with the Caucasian FF group. At 2 months, the difference between the two groups was 0.65 (CI 0.11, 1.18, p=0.018), with the Aboriginal FF group 397 g heavier on average. By 12 months the difference had increased to 0.75 (CI 0.21, 1.28, p=0.006), or 428 g, Figure 1.

There was no difference between groups for length z-scores, and by 12 months due to the large increase in weight z-score, the Aboriginal FF group had a mean weight-for-length z-score of 1.61, which was 0.91 higher than the Caucasian FF group (CI 0.29, 1.52, p=0.004).

The overall growth trajectory (interaction effect) across time did not differ between the Aboriginal FF and Caucasian FF groups.

A comparison between the two Caucasian groups (FF v BF) showed that Caucasian FF infants were significantly smaller at birth both for weight and length (212 g weight difference, p<0.001; 0.9 cm length difference, p=0.002), Table 1. A comparison of z-scores also showed Caucasian FF infants had significantly lower weight (0.33 difference, CI 0.09, 0.57, p=0.006) and length (0.53 difference, CI 0.28, 0.79, p<0.001) z-scores at study entry, although weight-for-length z-scores were not significantly different, Figure 1. There was a statistically significant interaction effect between group and time for both weight z-score and length z-score, with the Caucasian FF infants having a steeper growth trajectory than Caucasian BF infants, Figure 1. As a consequence, the difference in weight z-scores was no longer statistically significant from 2 months onwards, and the difference in length z-scores was no longer statistically significant after 4 months. This suggests that the Caucasian FF infants caught up to the Caucasian BF infants and afterwards followed a similar growth trajectory.

Body composition measures (fat free mass, fat mass)

Figure 2 shows mean fat free mass and fat mass plotted by time for Caucasian FF, Aboriginal FF and Caucasian BF infants.

The results of analyses for fat mass are consistent with those for weight and weight-for-length z-scores reported above; the Aboriginal FF group had a significantly higher mean fat mass at all time points except study entry and 1 month, with a difference in fat mass of 292 g (CI 56, 528, p=0.015) at 2 months compared with the Caucasian FF group, to a 383 g difference (CI 133, 632, p=0.003) at 12 months, Figure 2. There was no significant interaction effect between race group and time.

At 6 months the Aboriginal FF group had the highest estimated fat free mass, but the lowest by 12 months (Figure 2). This resulted in a direction reversal interaction

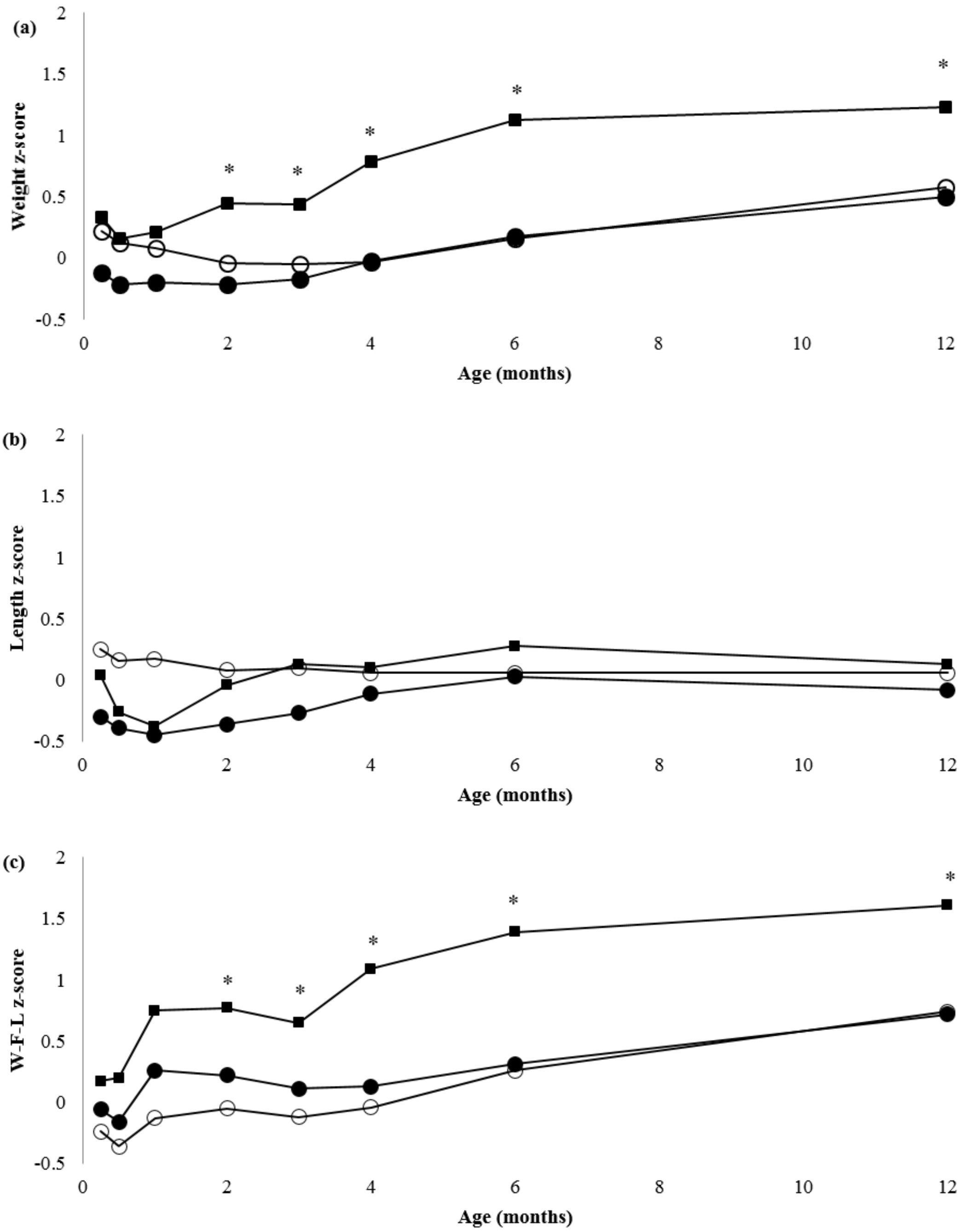

Figure 1. Weight (a), length (b), and weight-for-length (c) mean z-scores of Aboriginal formula fed infants (■), Caucasian formula fed infants (●), and Caucasian breast fed infants (○). Z-score data were based on WHO reference data. Comparisons between Aboriginal FF and Caucasian FF groups: interaction p value and mean differences (Aboriginal FF – Caucasian FF). *p value <0.05.

Weight z-score: interaction p=0.070. Mean difference at study entry 0.48 (-0.05, 1.02), p=0.076; 2 wks 0.43 (-0.11, 0.97), p=0.116; 1 mth 0.42 (-0.11, 0.96), p=0.123; 2 mths 0.65 (0.11, 1.18), p=0.018; 3 mths 0.70 (0.17, 1.24), p=0.010; 4 mths 0.78 (0.24, 1.32), p=0.005; 6 mths 0.97 (0.44, 1.51), p<0.001; 12 mths 0.75 (0.21, 1.28), p=0.006.

Length z-score: interaction p=0.394. Mean difference at study entry 0.34 (-0.26, 0.95), p=0.267; 2 wks 0.26 (-0.35, 0.87), p=0.401; 1 mth 0.06 (-0.55, 0.67), p=0.842; 2 mths 0.06 (-0.55, 0.68), p=0.838; 3 mths 0.42 (-0.20, 1.03), p=0.183; 4 mths 0.33 (-0.28, 0.94), p=0.292; 6 mths 0.24 (-0.36, 0.85), p=0.432; 12 mths 0.22 (-0.39, 0.83), p=0.485.

Weight-for-length z-score: interaction p=0.204; mean difference at study entry 0.27 (-0.34, 0.89), p=0.382; 2 wks 0.27 (-0.35, 0.89), p=0.395; 1 mth 0.50 (-0.11, 1.12), p=0.109; 2 mths 0.82 (0.20, 1.44), p=0.010; 3 mths 0.64 (0.02, 1.26), p=0.045; 4 mths 0.80 (0.18, 1.43), p=0.011; 6 mths 1.11 (0.49, 1.72), p<0.001; 12 mths 0.91 (0.29, 1.52), p=0.004.

effect between race and time. However there was no significant difference of fat free mass between the groups at any individual time point, it's likely that the interaction effect was due to high variation within the small sample of Aboriginal infants.

Comparisons between the two Caucasian groups (FF v BF) in relation to fat free mass and fat mass showed that there were few significant differences between the groups, including no statistically significant difference in relation to fat mass.

The Caucasian FF group had a lower mean fat free mass from study entry until 3 months (non-statistically significant), then had a somewhat higher fat free mass at 4 months (93 grams, CI 44, 230, p=0.18) and a signifi-

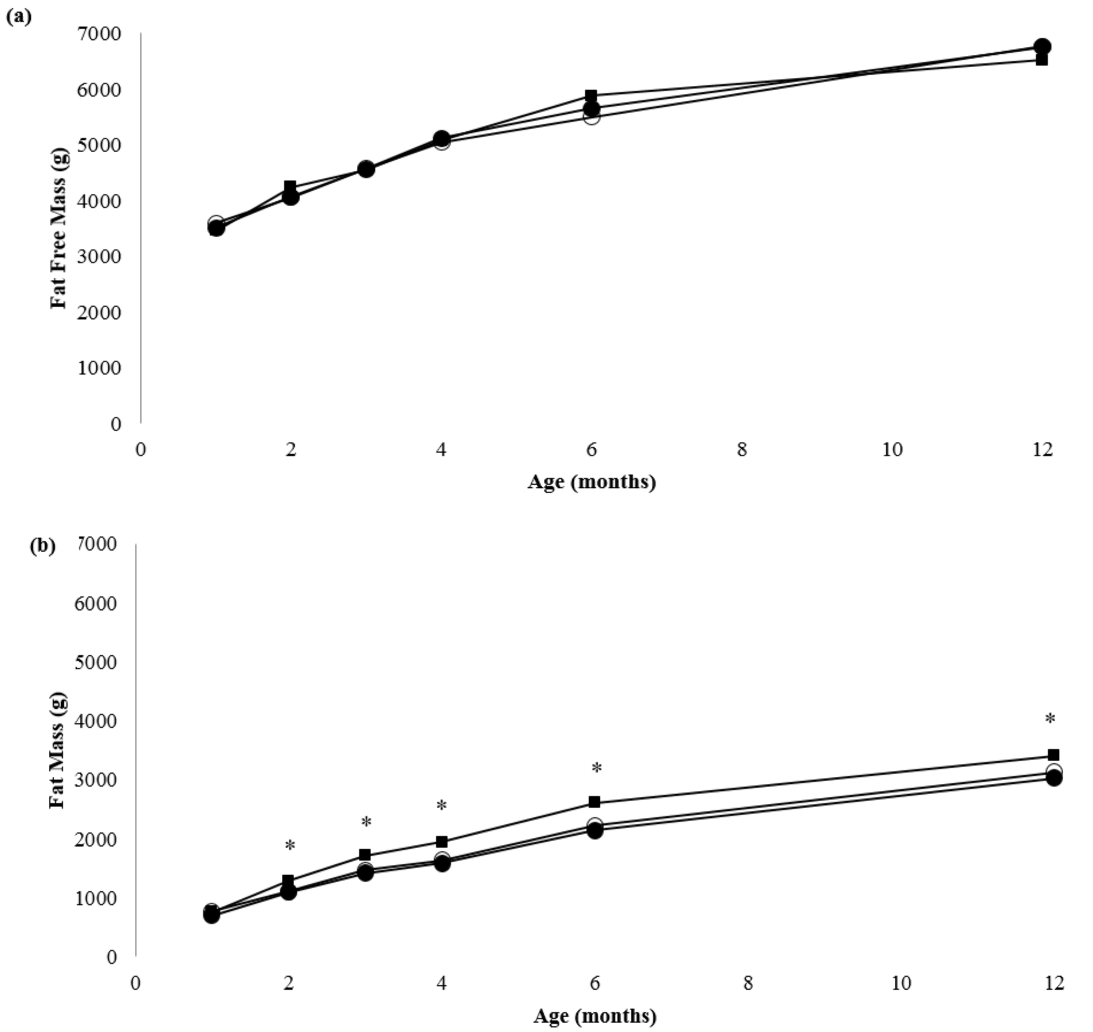

Figure 2. Fat free mass grams (a), Fat mass grams (b) of Aboriginal formula fed infants (■), Caucasian formula fed infants (●), and Caucasian breast fed infants (○). Comparisons between Aboriginal FF and Caucasian FF groups: interaction *p* value and mean differences. **p* value <0.05.

Fat free mass: interaction p=0.008. Mean difference at 1 mth: 188.42 (-113.30, 490.14), p=0.220; 2 mths: 101.95 (-187.97, 391.87), p=0.490; 3 mths: 106.71 (-214.03, 427.46), p=0.514; 4 mths: 84.29 (-228.42, 396.99), p=0.597; 6 mths: 278.64 (-20.67, 577.95), p=0.068; 12 mths: -226.01 (-529.09, 77.06), p=0.144.

Fat mass: interaction p=0.195. Mean difference at 1 mth: 139.47 (-108.61, 387.55), p=0.270; 2 mths: 292.22 (56.33, 528.12), p=0.015; 3 mths: 273.88 (0.09, 547.68), p=0.050; 4 mths: 407.90 (144.83, 670.96), p=0.002; 6 mths: 460.70 (215.04, 706.36), p<0.001; 12 mths: 382.59 (133.17, 632.01), p=0.003.

cantly higher fat free mass at 6 months (149 grams, CI 8, 289, p=0.04). This direction reversal resulted in a statistically significant interaction between group and time, but by 12 months there was no statistically significant difference between the groups, Figure 2.

DISCUSSION

We observed that healthy full-term Aboriginal infants were heavier at study entry than Caucasian infants and remained significantly heavier from 2 months of age. At 12 months all groups had a similar mean length (near the 50th percentile), but Aboriginal infants had a much larger mean weight (near the 95th percentile), and this was associated with fat mass gain. Excessive weight gain that leads to overweight and obesity is one of the most prevalent child health concerns globally.[6,11] In the Australian Aboriginal population, approximately 20% and 10% of children are estimated to be overweight and obese, respectively, compared with 18% and 7%, respectively, for the overall Australian child population.[12] To our knowledge there is only one previously published study reporting Australian Aboriginal growth patterns in the first two years of life,[3] and our study is the first to report infant growth patterns using both anthropometric and body composition data where a Caucasian cohort was available for comparison.

Our findings are consistent with data reported from other Aboriginal early childhood studies; Aboriginal children are heavy for their height,[5,6] and those that rapidly gain weight in early childhood are at risk of being overweight or obese.[3] Our data suggests that this growth disparity starts early in infancy, however we interpret this with caution due to the small number of Aboriginal infants.

We were in a unique position to access feeding behaveiour, which may be an important contributor to the overgrowth of Aboriginal infants. Participant reporting of food and liquid intake is notoriously variable and although the average difference between the groups was not significant, Aboriginal infants were reported to consume 34mL more study formula per day compared with the Caucasian infants up until 4 months of age, which theoretically would account for approximately 360 g of the weight disparity.

A number of other genetic, clinical and environmental factors may contribute to overgrowth. The small sample size limited our ability to further explore the nature of this weight and fat mass disparity, however our findings of growth in both the Aboriginal cohort and the two Caucasian cohorts were consistent with other published data, and these factors are worthy of further investigation in a larger cohort.

There were a number of strengths in this study. We were able to utilise serial anthropometric and body composition measures taken between birth and 12 months, so we obtained a clear picture of the growth trajectory, fat free mass and fat mass gain, and when differences between Aboriginal and Caucasian infants started to occur. A Caucasian BF comparator group was included to determine whether Caucasian FF infants were representative of the larger Caucasian study population, and to assess the likelihood of any chance differences between Caucasian and Aboriginal FF infants. There were significant differences between the BF and FF Caucasian groups in relation to maternal characteristics and birth anthropometric measures, but the weight and length gap between the two groups closed and all Caucasian infants followed the same growth trajectory from four months onward, with no statistical difference between the two Caucasian groups. This supports findings that FF infants are often smaller at birth due to a range of reasons such as maternal smoking and intrauterine growth restriction, and experience postnatal catch up growth over the first 12 months.[13]

There were some limitations. Aboriginal infants in the trial were predominantly female term babies of normal weight; all were formula fed, and we were therefore unable to explore the impact of formula compared with breast feeding on the growth of Aboriginal infants, and compare the growth trajectories of breastfed Aboriginal and Caucasian infants.

This, along with the small number of infants, limited the representativeness and generalisability of all Aboriginal infants in the wider population.[14] Though we did not adjust for potential confounders such as maternal pre-pregnancy BMI, parent education, and birth weight, due to the small number of infants, we did descriptively assess differences in relation to all characteristics other than complications during pregnancy. These findings showed that there was unlikely to be substantial confounding. It is important to separate the effects of potential confounders from the effects of ethnicity, which should be assessed through further adequately powered prospective studies.

With these limitations in mind, the larger weight and fat mass gain in Aboriginal infants is still cause for concern. Collecting accurate and comprehensive longitudinal data in a large cohort of Aboriginal infants is crucial to better understand growth patterns, not just for healthy, full term infants, but also the known ‘at risk’ populations; those born small for gestational age (SGA), preterm infants, low and high birth weight infants, and infants experiencing catch up growth and rapid weight gain.

Our data suggest that disparity in overgrowth previously described for Aboriginal children aged two and over may start in infancy. There are well documented links between rapid or excess weight gain in early infancy and childhood/adolescent overweight and obesity.[11,15] A larger cohort study is needed to substantiate these findings, allowing us to explore Aboriginal growth patterns in more detail including contributing factors such as feeding practices and epigenetics, and to potentially identify specific intervention points in early infancy.

AUTHOR DISCLOSURES

None of the authors have a conflict of interest. Dairy Goat Co-operative (N.Z.) Limited, New Zealand, provided the funding to conduct the original trial. M. M. and R. A. G. are supported by the National Health and Medical Research Council Senior Research Fellowships (ID: 565000 for M. M. and ID: 519324 for R. A. G.).

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