

Original

Central adiposity in children born small and large for gestational age

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Abstract

Objective: To evaluate body composition differences between children that were born small (SGA) or large for gestational age (LGA) compared with their counterparts born adequate for gestational age (AGA).

Methods: Body composition was assessed in 124 healthy Caucasian children (50% girls) aged 6-10, classified according to their birth weight for gestational age as AGA, SGA and LGA. Fat mass (FM), percentage of FM, lean mass (LM), bone mineral content (BMC) and bone mineral density were measured by dual-energy X-ray absorptiometry (DXA) in the whole body and at different body regions.

Results: LM (adjusted for age and sex) and total BMC (adjusted for age, sex and weight) were both significantly higher in LGA children and lower in SGA when compared with those born AGA. After adjustments for height, LM and BMC differences between groups were not significant. In SGA children, truncal ($P < 0.05$) and abdominal fatness ($P < 0.01$) were higher when compared with both AGA and LGA children, after adjustments for age, sex and height. There were no differences in the percentage of total and central FM between children born LGA and AGA.

Conclusions: During childhood, children born SGA had higher central adiposity regardless of their body size. Children born LGA seem to have a higher body size but with harmonic body composition and adequate body fat distribution. Small size for gestational age at birth could programme excess abdominal fat deposition in children, which is a major factor for the clustering of cardiovascular disease risk factors defining the metabolic syndrome.

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Key words: Birth weight. Body composition. Body fat. Bone mineral content.

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ADIPOSIDAD CENTRAL EN NIÑOS QUE NACIERON CON POCO O CON EXCESIVO PESO PARA SU EDAD GESTACIONAL

Resumen

Objetivo: Evaluar las diferencias que existen en la composición corporal de aquellos niños que nacieron pequeños (PEG) o grandes para su edad gestacional (GEG) en comparación con los que presentaban un peso adecuado al nacer (AEG).

Métodos: La composición corporal se valoró en 124 niños caucásicos (50% niñas) con edades entre 6 y 10 años, clasificados según su peso al nacer como AEG, PEG y GEG. La masa grasa (MG), el porcentaje de MG, la masa magra (MM), el contenido mineral óseo (CMO) y la densidad mineral ósea se midieron mediante absorciometría dual de rayos X (DXA) tanto globalmente como en las diferentes regiones corporales.

Resultados: La MM (ajustada por edad y sexo) y el CMO (ajustado por edad, sexo y peso) fueron mayores en los GEG y menores en los PEG al compararlos con los AEG; al ajustar la MM el CMO por la altura, dichas diferencias ya no fueron significativas. En los PEG, la grasa abdominal ($p < 0,01$) y en el tronco ($p < 0,05$) eran mayores que en los AEG y que en los GEG tras ajustar por edad, sexo y altura. No existían diferencias en el porcentaje de MG total corporal y en porcentaje de grasa central entre los niños nacidos GEG y AEG.

Conclusiones: Durante la infancia, los niños que nacieron PEG tenían mayor adiposidad central independientemente de su tamaño corporal. Los nacidos GEG seguían siendo grandes pero con una distribución armónica de la composición corporal y una adecuada distribución de la grasa corporal. Nacer con poco peso puede programar la grasa abdominal durante la infancia, cuyo aumento constituye uno de los factores de riesgo cardiovascular que definen el síndrome metabólico.

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Palabras clave: Peso al nacer. Composición corporal. Grasa corporal. Contenido mineral óseo.

Abbreviations

AGA: Adequate for gestational age.
BMC: Bone mineral content.
BMD: Bone mineral density.
BMI: Body mass index.
DXA: Dual-energy X-ray absorptiometry.
FM: Fat mass.
LGA: Large for gestational age.
LM: Lean mass.
SGA: Small for gestational age.

Introduction

Nutrition during both pregnancy and the first months of life seems to have an important role in later body size and composition, although the relative impact of the different periods has not been elucidated.¹ Intrauterine growth restriction or low birth weight has been associated with, among other things, the development of overweight issues, central adiposity, early puberty, postnatal hyperinsulinism, dyslipidemia, and increased risk of type 2 diabetes mellitus and cardiovascular disease later in life.²⁻⁴ The common element could be a hormonal reprogramming causing insulin resistance, metabolic adaptation and changes in body composition as long-term effects.^{5,6} Therefore, fetal growth restriction correlates with later disease implying that early nutritional deprivation is a strong programming stimulus.

Recent studies indicate that birth weight is also a predictor of later lean mass, and has a much weaker relation with fatness.^{7,8} To be born small for gestational age (SGA) is associated with lower lean mass in adult life and thus contributes to the relative risk of sarcopenia and functional inability at the end of the lifespan.⁹

Pre- and postnatal excessive nutrition have been also related with later adiposity and metabolic syndrome development,^{10,11} but controversial results have been reported. In studies which attempted to address potential confounding factors such as gestational age, parental fatness, or social group, the relationship was less consistent and it seems that children born large for gestational age (LGA) did not have an increased risk of later disease.¹² There is not enough scientific evidence explaining long term body composition differences between children born LGA and those born adequate or SGA up to 6 years and previous studies comparing growth, muscularity and fatness in young children born LGA, mainly used anthropometric measurements.¹³

Not only birth weight, but also postnatal growth, has been positively related to body composition in adolescence.¹⁴ It has been proposed that increased weight gain during the first year of life had a stronger effect than prenatal growth, suggesting that infancy is a more critical period in relation to early body composition programming.¹⁵ Early rapid weight gain, or catch-up growth, has shown to increase the risk of later obesity and diabetes in adult life.¹⁶⁻²⁰ Therefore, individuals

who were born small and grow fast due to a postnatal catch-up are at the highest risk. In fact, prevention of early catch-up growth reversed the development of glucose intolerance and obesity in a mouse model of low birth weight associated diabetes.²¹ A period of perinatal undernutrition, followed by catch-up growth and renutrition, may induce important modifications in adipose tissue, high risk of early development of insulin resistance and a disproportionate preferential higher rate in recovering body fat than lean body mass.^{22,23}

The aim of this study was to assess, in prepubertal children, body composition differences (lean body mass, bone mineral content, body fat mass, fat mass percentage) and regional adiposity between those that were born small and large for gestational age, when compared with their peers born with adequate weight by using dual-energy X-ray absorptiometry (DXA).

Methods

We selected a sample of 124 healthy Caucasian children (50% girls) born at term aged 6 to 10 years according to their birth weight for gestational age in the Hospital Clínico Universitario "Lozano Blesa" (Zaragoza, Spain) from 1998 to 2000. Children were classified according to their birth weight for gestational age as follows: 1) adequate for gestational age (AGA), with a birth weight between 10th and 90th percentile from Lubtechecko et al. charts;²⁴ 2) SGA, with a birth weight less than 10th percentile; and 3) LGA, with a birth weight higher than 90th percentile. The sample was selected pairing every SGA child with an AGA and a LGA one. Children with conditions that could modify body composition were excluded: maternal gestational diabetes, malformations, celiac disease, diabetes, chromosomal diseases, etc. All selected children were singleton newborns, there were no parental obesity and familiar socio-economic conditions were similar.

The study was approved by the Clinic Research Ethics Committee of Aragon. Subjects that agreed to participate attended the first meeting. Further information was given then and informed written consent was obtained from parents.

Analysis of body composition included measurements of fat mass (FM), lean mass (LM), bone mineral content (BMC) and bone mineral density (BMD); and it was performed with DXA using an extended research model and a paediatric version of the software QDR-Explorer (Hologic Corp., Software version 12.4, Waltham, MA). All scans were performed by the same investigator using the standard methodology recommended in the manufacturer's guide. Abdominal adiposity was assessed at three different regions, R1, R2, and R3. A rectangle was drawn on the digital scan image to establish every region. All regions had the lower horizontal border on the top of the iliac crest and the upper border was established parallel to the end of the lowest rib for R1, to the junction of the T12 and L1 vertebrae for

Table I
Sample characteristics

	SGA*	AGA*	LGA*	P ^{a,b}
Sex, males/females (n)	20/25	25/26	17/11	0.101 ^a
Age (y)	7.70 (0.9)	8.07 (0.9)	8.60 (0.9)	0.008^a
Weight (kg)	26.4 (6.7)	28.2 (7.4)	33.1 (7.5)	<0.001^a
Weight Z score	-0.307 (1.2)	-0.188 (1.2)	0.274 (1.2)	<0.001^a
Height (cm)	123.8 (6.8)	128.2 (8.8)	135.3 (6.6)	0.158 ^a
Height Z score	-0.589 (1.0)	-0.158 (1.1)	0.404 (1.0)	<0.001^a
BMI (kg/m ²)	17.0 (2.9)	16.9 (2.9)	17.9 (2.9)	0.639 ^b
BMI Z score	-0.076 (1.2)	-0.190 (1.1)	0.062 (1.2)	<0.001^a
Birth weight (gr)	2013 (337)	3077 (385)	4190 (254)	<0.001^a
Birth length (cm)	43.9 (3.3)	48.8 (1.9)	53.0 (1.1)	<0.001^a
Mother age at delivery (y)	30.1 (4.7)	31.4 (4.5)	31.3 (5.9)	0.203 ^a
Mother's BMI (kg/m ²)	23.8 (5.2)	22.7 (3.8)	23.9 (4.1)	0.331 ^a
Father's BMI (kg/m ²)	26.3 (3.3)	25.4 (2.9)	25.9 (2.8)	0.124 ^a

*Mean (Standard deviation).

^aBy using ANOVA between three groups.

^bBy using ANCOVA between three groups adjusted for age and sex.

SGA: Children born small for gestational age. AGA: Children born adequate for gestational age. LGA: Children born large for gestational age.

R2, and parallel to the middle of the T12 vertebrae for the R3. The lateral sides of these regions were adjusted to include the maximum amount of abdominal tissue. Trunk FM and abdominal FM R1, R2 and R3 were used as surrogates of abdominal adiposity.^{25,26}

Statistical analyses were performed with SPSS (v16.0 Chicago, IL). The distributions of quantitative variables were tested for normality using the Kolmogorov-Smirnov test. Data are presented as mean and standard deviations unless otherwise stated. Differences in body composition variables among different groups (SGA, AGA, LGA) were analysed by using analysis of the covariance (ANCOVA) after adjustments for current age, gender, height and weight; the

latest in case of BMC and BMD. A P value of ≤ 0.05 was defined as statistically significant.

Results

Sample characteristics are summarised in table I. As there were statistically significant differences in mean age ($P < 0.001$) and gender percentages varied between groups, comparisons of mean body composition and fat distribution results were adjusted for these variables (tables II-IV). Maternal age at delivery and parent's body mass index did not show statistical significant differences between the groups.

Table II
Fat and lean mass measurements by DXA in the whole boy, and the trunk and extremities regions

	SGA*	AGA*	LGA*	P ^a	P ^b
Left arm lean (g)	847 (194)	932 (248)	1,113 (287)	0.065	0.743
Left arm fat (g)	517 (296)	503 (298)	628 (365)	0.451	0.144
Left arm fat (%)	35.6 (9.8)	33.3 (9.8)	34.2 (8.7)	0.369	0.166
Trunk lean (g)	8,132 (1485)	8,833 (1968)	10,679 (2147)	0.003	0.419
Trunk fat (g)	2,913 (1726)	2,805 (1838)	3,404 (2161)	0.573	0.077
Trunk fat (%)	24.5 (7.9)	22.4 (7.5)	22.6 (7.1)	0.209	0.027
Left leg lean (g)	2,778 (642)	3,099 (796)	3,689 (664)	0.015	0.950
Left leg fat (g)	1,597 (773)	1,725 (905)	1,942 (869)	0.764	0.207
Left leg fat (%)	34.8 (7.5)	34.0 (8.3)	33.4 (7.0)	0.836	0.177
Total body lean (g)	18,045 (3145)	19,676 (3961)	23,392 (3694)	0.001	0.550
Total body fat (g)	7,859 (3790)	8,019 (4096)	9,325 (4325)	0.707	0.108
Total body fat (%)	28.9 (7.0)	27.6 (7.1)	27.4 (6.4)	0.465	0.045

*Mean (Standard deviation).

^aBy using ANCOVA between three groups adjusted for age and sex.

^bBy using ANCOVA between three groups adjusted for age, sex and height.

SGA: Children born small for gestational age. AGA: Children born adequate for gestational age. LGA: Children born large for gestational age.

Table III
Abdominal body composition assessed by DXA

	SGA*	AGA*	LGA*	<i>p</i> ^a	<i>p</i> ^b
Region 1, lean (g)	1,455 (407)	1,489 (382)	1,731 (449)	0.299	0.301
Region 1, fat (g)	595 (455)	498 (392)	573 (414)	0.183	0.012
Region 1, fat (%)	26.2 (9.4)	22.8 (8.5)	22.8 (8.0)	0.044	0.004
Region 2, lean (g)	2,491 (543)	2,674 (687)	3,053 (727)	0.420	0.215
Region 2, fat (g)	773 (550)	658 (481)	757 (512)	0.174	0.008
Region 2, fat (%)	21.6 (8.3)	18.2 (7.0)	18.6 (6.7)	0.026	0.004
Region 3, lean (g)	2,861 (582)	3,137 (816)	3,538 (777)	0.357	0.340
Region 3, fat (g)	834 (580)	728 (540)	828 (563)	0.239	0.014
Region 3, fat (%)	20.7 (8.0)	17.3 (6.5)	17.7 (6.3)	0.022	0.003

*Mean (Standard deviation).

Region 1: the upper border parallel to the end of the lowest rib.

Region 2: the upper border parallel to the junction of the T12 and L1 vertebrae.

Region 3: the upper border was parallel to the middle of the T12 vertebrae.

Region 1-3: lower horizontal border on the top of iliac crest.

^aBy using ANCOVA between three groups adjusted for age and sex.

^bBy using ANCOVA between three groups adjusted for age, sex and height.

SGA: Children born small for gestational age. AGA: Children born adequate for gestational age. LGA: Children born large for gestational age.

LM measurements are detailed in tables II and III. LGA children had more and SGA less absolute LM in all the considered body areas (left arm, left leg, trunk, abdominal regions and total body) than the AGA group. LM differences between groups were statistically significant in the left leg, the trunk and the whole body measurements after adjustments for age and sex, but they did not persist when height was added into the model (table II). Total body bone mineral content was also significantly higher in LGA children and lower in the SGA group, when comparing with the AGA group (using age, sex and weight as confounders), but these differences were no longer significant after further adjustment for height (table IV).

SGA children had a significant higher FM percentage in whole body ($P < 0.05$), trunk ($P < 0.05$) and in the three abdominal regions ($P < 0.01$) regardless of

current age, sex and height (table II and III and fig. 1). There were no differences in the percentage of body FM between children born LGA and their peers born AGA.

Discussion

In the present study, we describe children's multiple body composition differences in three compartments (fat, lean and bone) and in their percentage of body fatness in several body regions (limbs, trunk and abdomen; accounting for total and central adiposity) according to their birth weight (adequate, small and large birth weight for their gestational age). DXA is a reliable method for measuring body composition and its distribution at several body locations.^{25,26} Until now,

Table IV
Bone mineral content (BMC) and bone mineral density (BMD) by DXA in whole body and in the extremities

	SGA*	AGA*	LGA*	<i>p</i> ^a	<i>p</i> ^b
Left arm area (cm ²)	1,132 (74)	1,197 (105)	1,286 (91)	<0.001	0.839
Left arm BMC (g)	821 (103)	897 (148)	1,012 (139)	0.003	0.834
Left arm BMD (g/cm ²)	0.722 (0.05)	0.745 (0.07)	0.784 (0.06)	0.832	0.260
Left leg area (cm ²)	934 (75)	991 (102)	1,069 (87)	0.455	0.789
Left leg BMC (g)	546 (89)	605 (119)	699 (118)	0.540	0.832
Left leg BMD (g/cm ²)	0.580 (0.05)	0.605 (0.06)	0.649 (0.06)	0.891	0.771
Total body area (cm ²)	190 (21)	207 (33)	222 (30)	0.004	0.255
Total body BMC (g)	131 (27)	151 (38)	173 (30)	0.009	0.380
Total body BMD (g/cm ²)	0.687 (0.08)	0.722 (0.10)	0.781 (0.10)	0.671	0.548

*Mean (Standard deviation).

^aBy using ANCOVA between three groups adjusted for age, sex and weight.

^bBy using ANCOVA between three groups adjusted for age, sex, weight and height.

SGA: Children born small for gestational age. AGA: Children born adequate for gestational age. LGA: Children born large for gestational age.

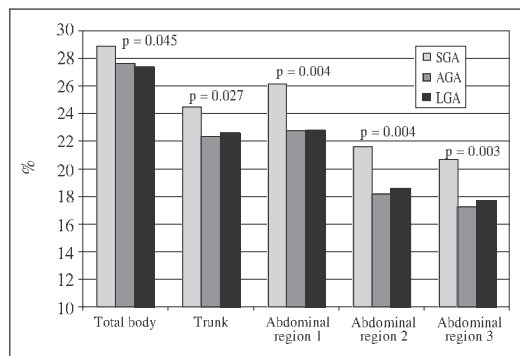


Fig. 1.—Percentage of body fat (%) by DXA in whole body, trunk and in the three abdominal group.

there has been no data about the three-compartmental body composition analysis comparing groups of children with both large and low birth weight for their gestational age with a control group (AGA). All children in our sample were healthy when the study began and they only had a previous history of common paediatric processes.

It has been suggested that the prenatal period is a “critical” period for the development of adiposity, but it is unclear how far associations between birth weight and subsequent body composition are genetic in origin and how far they result from intrauterine “programming”. Studies of monozygotic twins found environmentally determined differences in birth weight which were unrelated to subsequent BMI; and it is also observed that the association between birth weight and BMI was substantially reduced after adjustments for parental BMI.²⁷

Studies linking low birth weight with a more central adipose tissue distribution in later life remain controversial, mainly in healthy children and adolescents,²⁸⁻³¹ or require confirmation using more sophisticated methods.^{28,28,32} Two studies have used precise measures of body composition to show associations between later central adipose tissue distribution and birth weight.^{30,31} Dolan et al.³⁰ in 101 children aged 12.9 (± 2.4), found a negative association between birth weight and truncal fat mass. Nevertheless, using a 4-compartment body composition model in 391 healthy children aged 17.7 (± 4.2), Chomtho et al.³¹ did not find evidence for fetal programming of later central adiposity. Our sample is small but results and comparisons between groups are reliable (after age, gender and body size adjustments) and results are statistically significant, because initial group classification defines a clear risk characteristic (birth weight) that is associated later with central adiposity.

The strengths of our study include the use of an accurate body composition technique such as DXA. One important finding from our study is that, after statistical adjustments, the percentage of central adiposity (fat mass in the three abdominal regions and the trunk) was

significantly higher in the SGA group, compared with the other two groups in spite of their higher whole body mass. Some studies have supported the hypothesis that children born small seem to have more visceral adiposity,²⁸⁻³³ even when overweight indicators do not exist, and there is evidence that abdominal obesity is correlated with metabolic syndrome in this at-risk population.^{2,3} Consistent techniques of body-composition measurement support the suggestion that percentage fat in children is programmed from the intrauterine period (regardless of body build and BMI).³⁴ Recent advances in the ability to measure body composition during postnatal and early infant periods offer a major opportunity to improve understanding of the nutritional programming of body composition and its evolutionary changes from birth to preadolescence, in infants born SGA.³³ For this aim, future longitudinal studies must be designed to control their different growth trajectories.

Another important finding from our study is that, at an average age of 8 years, children born LGA remain larger than those children born AGA, whereas their percentage of body fat and adiposity distribution were similar. Thus, LGA have no signs of excess body fat deposition or impaired metabolic adaptation. It seems that body composition in children born LGA is similar to those born with AGA, but with a higher physiological harmonic size. Likewise, both BMC and BMD were also higher in children born LGA composing a harmonic bone-LM unit.

Body weight control during infancy is advocated as a preventive tool for those children born SGA, but it is unknown whether such control is sufficient to prevent later visceral fat accumulation. Dietetic interventions avoiding caloric and protein overnutrition in children born small should be considered. Findings in some studies support an adverse effect of relative “overnutrition” during infancy on long-term cardiovascular disease risk, having this “catch up” period implications for the early origins of cardiovascular disease hypothesis in infants born small for gestational age.³⁵

In conclusion, our findings further support the idea that fetal nutrition, as reflected by birth weight, may have a programming effect on abdominal adiposity later in life and a subsequent cardio-metabolic risk. A low birth weight is associated with central adiposity regardless of body size and with low lean body mass and low bone mineral content. A high birth weight without any other perinatal abnormality did not show a positive association with later central adiposity and LGA birth weight children seem to have a higher size later in life, but with harmonic body composition and adequate body fat distribution.

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