Overweight, Obesity, and Body Composition in 3.5- and 7-Year-Old Swedish Children Born with Marginally Low Birth Weight

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Objectives To assess the prevalence of overweight/obese children and to explore body composition in a Swedish cohort of preschool children born with marginally low birth weight (MLBW, ie, 2000-2500 g).

Study design We included 285 Swedish children with MLBW (44% small for gestational age), and 95 control children with normal birth weights. At 3.5 years and 7 years of age, we assessed anthropometrics, including the prevalence of overweight/obese children. At 7 years, dual-energy X-ray was used for body composition.

Results There were no significant differences between groups in the prevalence of overweight/obesity or in skinfold thickness; however, at 3.5 years, mean height, weight, and BMI in children with MLBW were 2.1 cm (95% CI 1.2-3.1), 1.2 kg (95% CI 0.7-1.6), and 0.47 kg/m^2 (95% CI 0.17-0.76) lower compared with controls. The corresponding mean differences also were lower in children with MLBW compared with control children at 7 years; 2.5 cm (95% CI 0.9-4.1), 1.6 kg (95% CI 0.6-2.8), and 0.48 kg/m^2 (95% CI 0.01-0.94). The differences were greater in those born small for gestational age. Dual-energy X-ray analyses showed lower fat-free mass index in MLBW infants and a similar trend in fat mass index. Within children with MLBW, BMI at 7 years correlated positively to growth velocity in infancy.

Conclusion Children with MLBW had lower BMI and did not show increased risk of overweight or obesity up to 7 years. Nevertheless, the BMI in MLBW children was positively correlated to growth-velocity in infancy. *(J Pediatr 2015;167:1246-52)*.

Trial registration Clinicaltrials.gov: NCT00558454.

The prevalence of overweight and obese adults as well as children and adolescents is increasing worldwide. This is a major public health problem, considering the well-documented adverse outcomes that accompany these conditions, such as sedentariness, cardiovascular diseases, noninsulin-dependent diabetes mellitus, sleep apnea, and other noncommunicable diseases. Of further concern is that these correlations to later morbidity also are observed in overweight and obese children. Thus, more knowledge of when and how to identify and prevent young children at risk of overweight and obesity should be prioritized.[1,2]

In 1989, Barker et al[3] correlated low birth weight (LBW) with coronary heart disease later in life. They suggested that the origins of metabolic syndrome (MS), which includes obesity, dyslipidemia, insulin resistance, glucose intolerance, and elevated blood pressure, could be found already in the intrauterine and immediate postnatal stages of life as a consequence of early malnutrition.[3-5] This concept of "early metabolic programming" has since generated substantial interest in epidemiologic and experimental research.[6-8] Particularly, the roles of LBW, preterm birth, and intrauterine growth restriction (IUGR) have been explored and discussed.[8-11] In common for many infants born too early or too small is an increased growth velocity at some point after birth. Mismatch in nutrition, resulting in poor prenatal growth followed by accelerated postnatal growth triggered by overnutrition, may be a particularly important link in the causal chain of metabolic programming.[8,12,13]

Overweight and obesity are frequently studied outcomes with regard to early metabolic programming after LBW. Several studies have confirmed an association between LBW and later increased body mass index (BMI)[14,15]; however, the mechanisms of this association are unclear, and there are several studies,

AGA	Appropriate for gestational age
BMI	Body mass index
FFMI	Fat-free mass index
FMI	Fat mass index
IOTF	International Obesity Task Force
IUGR	Intrauterine growth restriction
LBW	Low birth weight
MLBW	Marginally low birth weight
MS	Metabolic syndrome
SGA	Small for gestational age

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including a recent meta-analysis, which failed to show any correlation between LBW and BMI/obesity.[16,17] The reason for these previously diverging results is most likely because LBW occurs at different degrees and subgroups and because of different settings with regard to nutrition, time periods, and sociodemographic factors.[8,16] The majority of children with LBW are born only with marginally LBW (MLBW; 2000-2500 g), with or without IUGR, and the magnitude and emergence of overweight and obesity in these subjects are less known, especially in healthy and well-nourished populations. Furthermore, the proportions of lean and fat mass may be altered in children born with LBW. More knowledge regarding the association between birth weight and body composition is needed.[18,19]

The aim of this cohort study was to investigate the possible associations between MLBW and early childhood risk of overweight and obesity as well as other anthropometric signs of MS in a Swedish setting. We hypothesized that preschool children born MLBW would show early anthropometric signs of MS as a consequence of early metabolic programming.

Methods

This prospective cohort study included 285 children with MLBW and 95 control children born between March 2004 and November 2007. The MLBW participants originally took part in an iron supplementation trial and were identified by the use of delivery records for inclusion at 6 weeks of age.[20] Inclusion criteria were birth weight 2000-2500 g, no signs of disease at inclusion, no chronic disease, no previous blood transfusion, and never having received iron supplements. The participants were collected at 2 tertiary hospitals in Sweden—Umeå University Hospital, Umeå, and Karolinska University Hospital, Stockholm. This trial was approved by the Ethical Review Boards at Umea University and the Karolinska Institute and registered with Clinicaltrials.gov, number NCT00558454.

The MLBW infants were randomized into 3 intervention groups receiving different doses of iron supplementation from 6 weeks to 6 months of age (0 mg/kg/day [placebo], 1 mg/kg/day, or 2 mg/kg/day). The children were assessed for iron status and growth as described previously.[20] Because iron supplements did not have any effect on growth in our previous analyses, we analyzed all 3 intervention groups as 1 cohort in the present analyses.

Before the 3.5-year control, every third MLBW child was chosen as an index case for recruitment of controls (matched for age, sex, and study center). For each index child, a list of 10 possible control children was made. These were the children born closest in time at the same study center and with the same sex as the index child as well as fitting into the following criteria: born in gestational weeks 37-42, born with birth weight between 2501 and 4500 g, and not being admitted to neonatal unit. The parents of the child born closest in time were contacted and offered to participate with their child as a control and if the parents declined, the next one was contacted until each index child had a corresponding control child, or the list of eligible controls was exhausted.

At inclusion of MLBW and control children, background data were collected from parents and from delivery records, including gestational age at birth, sex, anthropometric data, neonatal diagnoses, maternal birth country, smoking habits, income, and family situation. Using a Swedish gestational age–corrected growth standard,[21] we calculated the weight for age SDS (SDS for weight) and defined small for gestational age (SGA) at birth as a birth weight SDS for gestational age less than −2 and appropriate for gestational age (AGA) in all other cases. As a part of the original iron supplementation trial, the children with MLBW were examined at 6, 12, and 19 weeks and at 6 and 12 months regarding anthropometric data such as weight, height, and waist and head circumference. At each visit, we calculated the SDS for weight and height and its change (ΔSDS) since last visit.

The present follow-up trial included visits at 3.5 and 7 years of age. At each visit, skinfold thickness (triceps and subscapular) was assessed with the use of a skinfold measuring instrument (Harpenden Skinfold Caliper; Baty International, West Sussex, United Kingdom), waist and head circumference with a measuring tape (Seca 212; seca, Hamburg, Germany), weight with an electronic scale (Seca 701; seca), and height with a wall stadiometer (Hyssna Measuring Equipment AB, Hyssna, Sweden). On one occasion, we also measured the weight and length of the parents and, if any parent was not present at the 3.5- or 7-year follow-up, we used the reported values (18.5% of mothers and 58.2% of fathers).

BMI values of children and mothers were calculated according to the International Obesity Task Force (IOTF), and obesity and overweight were determined using the age- and sex-specific SD by Cole at al.[22]

At the 7-year visit, the children were examined with dual-energy X-ray absorptiometry. These dual-energy X-ray absorptiometry measurements were performed at both study centers by use of the Lunar Prodigy Advance (GE Medical Systems Lunar, Madison, Wisconsin) with enCORE software version 13.31016 (GE Medical Systems Lunar). The X-ray spectrum was produced with a cerium filter resulting in 2 energy peaks at approximately 38 and 70 keV, and the 2 machines were cross-calibrated by the use of an aluminum and acrylic lumbar spine phantom showing a less than 1% difference in measured bone mineral density values. Fat-free mass was calculated as bone mineral content + lean mass, and fat mass index (FMI) and fat-free mass index (FFMI) were calculated as fat mass/height^2 (kg/m^2) and fat free mass/height^2 (kg/m^2), respectively.[23]

Statistical Analyses

Statistical analyses were performed using SPSS 22.0 for Windows (SPSS Inc, Chicago, Illinois). Differences between the groups were analyzed using the independent *t* test for continuous variables and the χ^2 test for categorical variables. The main outcomes of the present article were compared between all MLBW and control subjects. To further explore the