Birth Weight for Gestational Age, Anthropometric Measures, and Cardiovascular Disease Markers in Children

Stefan Kuhle, MD, PhD[1], Bryan Maguire, MSc[1,2], Nicole Ata, MD, MSc[3], Natasha MacInnis, BSc[1], and Linda Dodds, PhD[1]

Objective To examine the association of birth weight for gestational age with anthropometric measures and cardiometabolic markers in a population-based sample of Canadian children.

Study design The study used data from 2016 children aged 6-12 years from the first 2 cycles of the Canadian Health Measures Survey, a population-based survey of Canadian residents. The main exposure was birth weight for gestational age (small [SGA], large [LGA], and appropriate for gestational age [AGA]). The outcomes were anthropometric measures, blood pressure, and laboratory cardiovascular disease markers. The association between the exposure and the outcomes was examined using multiple regression. Analyses were weighted to account for the complex sampling design and for nonresponse.

Results SGA infants had lower and LGA infants had higher z scores for anthropometric measures compared with the AGA group but most differences were not statistically significant. There were no differences between the SGA or LGA infants and the AGA group in blood pressure or individual cardiometabolic markers but SGA infants were significantly less likely to have elevated levels of 3 or more components of the metabolic syndrome compared with their AGA peers.

Conclusions Former SGA and LGA infants have lower (SGA) and higher (LGA) body mass index and waist circumference, respectively, than their AGA peers. The known long-term increased cardiovascular disease risk among SGA or LGA infants was not reflected in the blood pressure and laboratory measurements at age 6-12 years. *(J Pediatr 2017;182:99-106).*

The intrauterine environment provides a foundation on which chronic disease may develop in offspring throughout their life. Barker[1] and others (eg, Curhan et al[2]) have shown that impaired fetal growth manifesting as small for gestational age (SGA) at birth is associated with cardiovascular disease (CVD) and type 2 diabetes in adulthood, but there is conflicting evidence on whether this association is mediated by adiposity. A number of studies have shown that SGA infants remain lighter and have less body fat than their appropriate for gestational age (AGA) counterparts,[3-7] and others found that SGA infants are more likely to be obese in childhood,[8-10] in particular when the infants exhibit catch-up growth.[11,12] Reasons for the discrepancies between studies may be the use of small, selected samples as opposed to population-based samples, the omission of gestational age in the assessement of fetal growth (ie, using birth weight and not birth weight for gestational age), and a limited ability to adjust for confounders, such as socioeconomic status.[5] Regardless of body weight status in childhood, it appears that decreased insulin sensitivity plays a key role in the pathway from SGA birth to increased CVD risk in adulthood.[13-15]

At the other end of the birth weight spectrum, infants born large for gestational age (LGA) are also at a higher risk of CVD in adulthood.[2] High birth weight is strongly associated with obesity in childhood,[3,16] which in turn is associated with obesity and increased CVD risk in adulthood.[17,18] However, it is unclear when the first metabolic changes predating the development of CVD can be observed in LGA infants. Some studies have reported higher adverse levels of cardiometabolic markers in childhood in infants with high birth weight,[19-21] and others did not find any differences.[22-24] Similar to the association between SGA and obesity, selected study samples and confounding may have contributed to the conflicting findings.

The objective of the present study was to compare anthropometric measures and cardiometabolic markers by birth weight for gestational age in a population-based sample of Canadian children aged 6-12 years.

AGA	Appropriate for gestational age	HDL	High-density lipoprotein
BMI	Body mass index	LGA	Large for gestational age
CHMS	Canadian Health Measures Survey	SGA	Small for gestational age
CRP	C-reactive protein	WC	Waist circumference
CVD	Cardiovascular disease	WHtR	Waist-to-height ratio
HbA1c	Hemoglobin A1c		

From the [1]Perinatal Epidemiology Research Unit, Departments of Obstetrics and Gynaecology and Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada; [2]Department of Mathematics and Statistics, Dalhousie University, Halifax, Nova Scotia, Canada; and [3]School of Health and Human Performance, Dalhousie University, Halifax, Nova Scotia, Canada

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Methods

The present study used data from children aged 6-12 years from the first 2 cycles of the Canadian Health Measures Survey (CHMS). The CHMS is a representative, cross-sectional survey assessing indicators of health and wellness in Canadians between aged 6 (3 years in cycle 2) and 79 years.[25,26] The survey consisted of a household interview to obtain sociodemographic and health information and a visit to a mobile examination center to perform a number of physical measure tests (including blood and urine samples and a fitness test). The sampling frame of the Canadian Labour Force Survey was used to identify 15 (cycle 1) and 18 (cycle 2) collection sites for the mobile examination centers, respectively. Within each collection site, households were selected using the 2006 Census as the sampling frame. Interviews and examinations for the CHMS were performed between 2007 and 2009 (cycle 1) and 2009 and 2011 (cycle 2) with a response rate of 51.7% and 55.5%, respectively. Information for the household interview for children aged 6-11 years was provided by an adult with assistance from the child; children aged 12 years answered the questions on their own where possible.

Ethics approval for the conduct of the CHMS was obtained from the Health Canada Research Ethics Board. Children aged 6-12 years provided assent to participate, and their parents or guardians consented on their behalf.[25,26] The current study was approved by the IWK Health Centre Research Ethics Board, Halifax, Nova Scotia, Canada (1014413).

Outcomes

The primary outcomes were the age- and sex-standardized z scores of anthropometric measures, CVD risk markers, and blood pressure; secondary outcomes were the presence of elevated levels (see below for definition) of these markers.

All anthropometric measurements were performed by trained health professionals at the mobile examination centers. Weight was taken on a calibrated digital scale, and standing height was measured with a fixed stadiometer with a vertical backboard and moveable headboard. Body mass index (BMI) was calculated from weight and height using the formula weight/height^2 (kg/m^2). The measurement of waist circumference (WC) was based on the Canadian Physical Activity, Fitness and Lifestyle Approach protocol.[27] A Gulick tape measure (North Coast Medical, Inc, Gilroy, California) of 150 or 200 cm was used and WC was measured at the midpoint between the bottom of the rib cage and the top of the iliac crest at the end of a normal expiration. Waist-to-height ratio (WHtR) was calculated as WC over standing height. Skinfold thickness was measured 3 times using a Harpenden skinfold caliper to the nearest 0.2 mm, and the average of the 3 measurements was used. Triceps skinfold thickness was measured on the midline of the back of the arm at the midpoint level between the acromium process and the tip of the olecranon process. Subscapular skinfold thickness was measured below the inferior angle of the scapula at an angle of 45 degrees to the spine. Within-sample z scores for BMI, WC, WHtR, and skinfold thickness were calculated using the LMS method[28] as described previously.[29]

Blood pressure was measured using a new protocol created for the CHMS based on the work by Campbell et al.[30] Blood pressure was measured on the right arm using an automated blood pressure oscillometric blood pressure device (BP-300; BpTRU Medical Devices Ltd, Coquitlam, British Columbia, Cananda) after a 5-minute resting period. A total of 6 readings were performed, of which the average was based on the last 5 readings. Mixed effects linear regression models as per Appendix B of the *Fourth Report on Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Youth* were used to compute age-, height- and sex-specific expected blood pressures for boys and girls.[31] Each respondent's average systolic and diastolic blood pressure were converted to z scores using the formula:

$$(\text{Systolic blood pressure} - \text{Expected systolic blood pressure})/\text{SD}$$

Blood samples were collected in the mobile examination center via standard venipuncture. In a random subsample, blood was taken after overnight fasting for triglycerides and insulin measurement. The blood samples were centrifuged within 2 hours and aliquotted within 4 hours of collection. Samples were stored in the refrigerator or freezer before weekly shipment to the Health Canada reference laboratory in Ottawa. Total cholesterol, high-density lipoprotein (HDL), and triglycerides were tested using a colorimetric test. C-reactive protein (CRP) was tested using a high sensitivity 2-point rate test. Hemoglobin A1c (HbA1c) was tested using an end-point test and fasting insulin was tested using a solid-phase, 2-site chemiluminescent immunometric assay. Within-sample z scores for total cholesterol, HDL, triglycerides, and HbA1c were calculated using the LMS method.[28] Because of a large proportion of values below the limit of detection (>15%), no z scores could be calculated for fasting insulin and CRP.

Because there are no generally accepted definitions of what constitutes elevated CVD risk in children for many of the outcomes used in the present study and because the use of clinical cut-offs often yields numbers too small for release under the Statistics Canada confidentiality guidelines, we used thresholds similar to those used in the Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study.[32,33] A value ≥75th within-sample percentile (corresponding to a z score of 0.6745) for age and sex was used to define high levels of anthropometric measures, total cholesterol, triglycerides, and HbA1c; low levels of HDL were defined as values ≤ 25th within-sample percentile for age and sex.[34] High levels of fasting insulin were defined as ≥ 75th percentile for age and sex based on European children aged 6-10 years in the IDEFICS study.[35] High levels of CRP were defined as a CRP ≥ 3 mg/L based on the recommendations of the American Heart Association.[36] We also calculated an indicator of CVD risk defined as having ≥3 components of WC, systolic blood pressure, triglycerides, and fasting insulin ≥75th percentile or HDL ≤ 25th percentile for age and sex.