High Body Mass Index in Infancy May Predict Severe Obesity in Early Childhood

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Objective To characterize growth trajectories of children who develop severe obesity by age 6 years and identify clinical thresholds for detection of high-risk children before the onset of obesity.

Study design Two lean (body mass index [BMI] 5th to ≤75th percentile) and 2 severely obese (BMI ≥99th percentile) groups were selected from populations treated at pediatric referral and primary care clinics. A population-based cohort was used to validate the utility of identified risk thresholds. Repeated-measures mixed modeling and logistic regression were used for analysis.

Results A total of 783 participants of normal weight and 480 participants with severe obesity were included in the initial study. BMI differed significantly between the severely obese and normal-weight cohorts by age 4 months ($P < .001$), at 1 year before the median age at onset of obesity. A cutoff of the World Health Organization (WHO) 85th percentile for BMI at 6, 12, and 18 months was a strong predictor of severe obesity by age 6 years (sensitivity, 51%-95%; specificity, 95%). This BMI threshold was validated in a second independent cohort (n = 2649), with a sensitivity of 33%-77% and a specificity of 74%-87%. A BMI ≥85th percentile in infancy increases the risk of severe obesity by age 6 years by 2.5-fold and the risk of clinical obesity by age 6 years by 3-fold.

Conclusions BMI trajectories in children who develop severe obesity by age 6 years differ from those in children who remain at normal weight by age 4-6 months, before the onset of obesity. Infants with a WHO BMI ≥85th percentile are at increased risk for developing severe obesity by age 6 years. *(J Pediatr 2017;183:87-93).*

Pediatric obesity is a major health concern in the US, even for young children. Once obesity is established, it is often persistent,[1,2] and increases the likelihood of lifelong health issues. Children who were overweight by kindergarten have been found to have a 4-fold greater risk of progressing to obesity by adolescence.[3] In the Bogalusa Heart Study, in all children with a body mass index (BMI) ≥99th percentile, obesity persisted into adulthood.[4] Furthermore, obesity can lead to metabolic abnormalities before age 5 years,[5] and severe obesity in childhood carries short-, medium-, and longer-term cardiovascular risks that exceed those of their less-obese peers.[6] All of these factors suggest an elevated lifetime risk of cardiometabolic disease in children with severe obesity, with a proportion of these children at risk for requiring bariatric surgery as early as adolescence.[7] Therefore, proper early identification and intervention for young children with obesity is critical.

Despite these compelling concerns about early childhood obesity, pediatricians have no clinical guidance for identifying young children at risk, given the lack of accepted standards for identifying clinically significant weight gain,[8] or even clinical obesity,[9] in children aged <2 years. In addition, there has been little study of growth trajectories in children who ultimately develop severe obesity to facilitate early identification and intervention. In the present study, we used a nested case-control design with prospectively collected growth data to characterize growth patterns of children with severe obesity (BMI ≥99th percentile) by age 6 years to identify whether these children experience a critical period of deviation from normal growth, characterize that growth relative to growth in

BMI	Body mass index
CCHMC	Cincinnati Children's Hospital Medical Center
CDC	Centers for Disease Control
CHC	Children's Health Clinic at Children's Hospital Colorado
EHR	Electronic health record
EPI-NW	Epidemiologic cohort study, normal weight
PPCC	Pediatric Primary Care Center
PPCC-NW	Pediatric Primary Care Center, normal weight
PPCC-OB	Pediatric Primary Care Center, obese
WFL	Weight-for-length
WHO	World Health Organization
YCC	Young Child Clinic
YCC-OB	Young Child Clinic, obese

normally developing children, and detect thresholds for identifying children at elevated risk of developing severe obesity in early childhood. We then validated these thresholds for clinical utility using an independent cohort from another institution.

Methods

We selected 4 initial study populations, including 2 groups with severe obesity and 2 groups of normal weight status, described below. We adopted this extreme phenotype approach to ensure maximal discriminatory value with minimal noise when identifying thresholds for severe obesity risk. We tested these thresholds in an independent validation cohort with children of any weight status, also described below. We obtained data on date of birth, birth weight, date of visit, sex, and self-reported race and ethnicity from the electronic health record (EHR) and/or pediatrician records. Insurance status was obtained for all cohorts except the cohort from the Young Child Clinic (YCC). The initial study was conducted with approval from the Cincinnati Children's Hospital Medical Center (CCHMC) Institutional Review Board. The validation study was approved by the Colorado Multiple Institution Review Board, and a Health Insurance Portability and Accountability Act and consent waiver was granted.

Pediatric Primary Care Center

Two of the 4 initial study populations were drawn from the same clinical population. The Pediatric Primary Care Center (PPCC) at CCHMC offers primary care to a low-income, predominantly Medicaid-covered population of children from birth through adolescence. For the case group, designated PPCC, obese (PPCC-OB), children with a Centers for Disease Control (CDC) BMI ≥99th percentile at any time between age 2 and 5.99 years seen in the PPCC between January 2008 and January 2014 were identified from the EHR. The EHR automatically calculates and records the CDC BMI percentiles for all encounters in which height and weight are measured. The 99th percentile was chosen to define those with severe obesity, because there was no way to identify the 120th percentile of the 95th percentile using EHR data.

For the control group, designated PPCC, normal weight (PPCC-NW), children seen in the PPCC during the same years with a BMI consistently between the 5th and the 75th percentiles from age 2 to 5.99 years were also identified by EHR data.

Young Child Clinic

A second population with severe obesity was drawn from CCHMC's Young Child Clinic (YCC), a tertiary referral clinic for the evaluation and treatment of early-onset severe obesity, among other disorders. Patients seen in the YCC for obesity with an initial visit at age 1-6 years between August 2008 and March 2013 were identified from EHR data and designated the YCC, obese (YCC-OB) group. Patients with a known endocrine abnormality or a genetic cause for obesity, or who were taking a medication that causes weight gain (eg, corticosteroids), were excluded.

Epidemiologic Cohort Study Group

A second normal-weight control group, designated the epidemiologic cohort, normal weight (EPI-NW), was chosen from a longitudinal epidemiologic study of growth and body composition consisting of 372 healthy Cincinnati children enrolled at age 3 years between March 2001 and August 2002. These children were assessed every 4 months up to age 7 years (a total of up to 13 study visits). Length/height and weight data were requested from the child's pediatrician for 9 ages: 2-4 weeks and 2, 4, 6, 9, 12, 15, 18, and 24 months. Children with available infant/toddler growth data whose BMI was consistently between the 5th and 75th percentiles from age 3 to 6 years were included in this analysis.

Validation Cohort

A validation cohort from the Child Health Clinic (CHC) at Children's Hospital Colorado was included to assess the clinical validity of the BMI thresholds identified from our initial study. The CHC is a metropolitan, hospital-based clinic offering primary care primarily to low-income families. Patients with weight and length or height measurements obtained during at least 1 visit to the CHC at age 6, 12, or 18 months and at least 1 visit between age 3 and 5.99 years were identified from EHR data. The visit closest to the 6-, 12-, or 18-month milestone was selected for patients with multiple visits near a given milestone visit, and 1 visit was selected at random for patients with multiple visits between age 3 and 5.99 years.

Calculated Variables/Measurements

For measurements obtained at age ≤2 years, recumbent length measurements were assumed, with anthropometric percentiles calculated using 2005 WHO growth standards, as recommended by the CDC.[10] For measurements obtained at age >2 years, standing height was assumed, with percentiles calculated using 2000 CDC growth standards.

Obesity was defined as WHO BMI ≥97.7th percentile in children aged ≤2 years[10] and as CDC BMI ≥95th percentile in children aged >2 years. In the 2 obese cohorts (PPCC-OB and YCC-OB), the onset of obesity was identified as the exact age at the first visit at which criteria for obesity were met (for those aged ≤2 years) or at the first visit at which the criteria for obesity were met following at least 1 visit at which these criteria were not met (for those aged >2 years). Children aged >2 years without a visit at which the criteria for obesity were not met excluded from the analysis.

Statistical Analyses

All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, North Carolina). EHR data outliers were identified and removed from the analysis when length/height was flagged as biologically implausible (<-5 or >+5 SD; <1% observations were excluded). Owing to the large sample sizes, we believed that additional data cleaning (eg, identifying large changes from visit to visit, aberrant but not biologically implausible values) would have a minimal impact on estimates of means and SDs. Moreover, most such errors would result in misclassification of truly normal-weight individuals as having