Neurocognitive and Health Correlates of Overweight and Obesity among Ten-Year-Old Children Born Extremely Preterm

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Objective To assess the relationship between overweight (body mass index [BMI] percentile ≥85 and <95) and obesity (BMI ≥95 percentile) and developmental and health outcomes at 10 years of age in a cohort of individuals born extremely preterm.

Study design This was an observational cohort study of children born extremely preterm and then assessed at age 10 years for neurocognitive function and parent-reported behavior and health outcomes. Participants included 871 children aged 10 years. To describe the strength of association between overweight or obesity and outcomes, we used logistic regression models adjusting for confounders. Neurocognitive function, academic achievement, parent-reported health outcome surveys, and height and weight were measured.

Results BMI category at 10 years of age was not associated with differences in intelligence, language, or academic achievement. Parents of children with obesity were more likely to report their child had asthma (OR 2.2; 95% CI 1.4-3.5), fair/poor general health (OR 3.2; 95% CI 1.4-7.5), and decreased physical function (OR 1.7; 95% CI 1.1-2.9) but less likely to have physician diagnosed attention-deficit/hyperactivity disorder (OR 0.5; 95% CI 0.3-0.97) or an individualized education plan (OR 0.6; 95% CI 0.4-0.99).

Conclusion Among children born extremely preterm, an elevated BMI, compared with normal or low BMI, is not associated with a difference in neurocognitive function. However, asthma, fair/poor general health, and decreased physical function were more prevalent among study participants with obesity, and attention-deficit/hyperactivity disorder and individualized education plan were less prevalent. *(J Pediatr 2018;■■:■■-■■).*

Infants born extremely preterm and infants with extremely low birth weight often exhibit growth delay during the first several postnatal months.[1,2] As a result of more rapid growth in infancy, children born extremely preterm often attain weights similar to those of full-term normal birth weight peers.[3,4] Children born extremely preterm who exhibit greater growth during infancy have better cognitive outcomes in childhood[5,6] but are also more likely to develop obesity.[5,7,8]

Childhood obesity is associated with worse school performance[7,9] and decreased cognitive functioning,[8,10,11] outcomes for which infants born preterm are already at high risk.[12,13] A potential mechanism for this association is suggested by the observation that in preclinical models, overfeeding is associated with brain inflammation[14] and neurocognitive impairment.[15,16] Another correlate of childhood obesity is asthma.[5,17,18] Potential explanations for this association include overlapping environmental, developmental, and behavioral risk factors as well as obesity-induced immune dysregulation contributing to asthma risk.[19]

Given the potential trade-offs associated with rapid infant weight gain after discharge from neonatal intensive care, it is important to know whether individuals born extremely preterm who become overweight or obese are more or less likely to have impaired cognitive functioning or other adverse outcomes. In this study, we evaluated the null hypothesis that in a cohort of children born extremely preterm, cognitive function does not differ for those children who are overweight or obese at 10 years of age compared with those who are healthy weight.

Methods

We evaluated a total of 1506 infants born before the 28th week of gestation and enrolled in the Extremely Low Gestational Age Newborn (ELGAN) study during the years 2002-2004. The ELGAN study is a multicenter, prospective,

ADHD	Attention-deficit/hyperactivity disorder
BMI	Body mass index
ELGAN	Extremely Low Gestational Age Newborn

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*Additional members of this study can be found at www.jpeds.com (**Appendix 1**).

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observational study of infants born extremely preterm.[20] From the original ELGAN cohort, 1198 (80%) children survived to 10 years of age. Because the primary aim of this second phase of the ELGAN study involved relationships between inflammation and outcomes during childhood, 966 surviving members of the EGLAN cohort from whom we had collected blood spots during the first postnatal month for measurement of inflammation-related proteins were recruited actively for a second follow-up evaluation at 10 years of age between February 2012 and April 2015. Height and weight were obtained on 90% (n = 871) of these children. These children are the subjects of this report. Anthropometric data were unable to be collected on some children with severe cerebral palsy (n = 6), when home visits were conducted and a scale was unavailable (n = 5), or when parents did not consent for measurements (n = 4). In 3 children, the reason for missing height and weight measurements was not recorded. Enrollment and consent procedures for this follow-up study were approved by the institutional review boards of all participating institutions.

Maternal characteristics for this infant sample, including prepregnancy height and weight (converted to body mass index [BMI]), were self-reported within a few days of the delivery. Perinatal characteristics, including reason for preterm delivery, were obtained by maternal chart review shortly after the mother's discharge.

The birth weight z score is the number of SDs the infant's birth weight is above or below the median weight of infants at the same gestational age.[21,22] Data reported by Yudkin et al were used for reference because this data set excluded infants born after pregnancies with growth-restricting conditions.[21] Chronic lung disease (bronchopulmonary dysplasia) was defined as supplemental oxygen use at 36 weeks of postmenstrual age. Patients discharged home on oxygen before 36 weeks of postmenstrual age were included as having chronic lung disease.

Families willing to participate were scheduled for 1 visit, during which all the measures reported here were administered. Although the child was tested, the parent or caregiver completed questionnaires regarding the child's medical status and behavior.

Anthropometric Data

Weight and height were obtained by study personnel. To obtain these measurements, all outer garments such as coats and shoes were removed. If children were unable to stand unsupported, either a wheelchair scale or the difference of the parent's weight plus child's weight and the parent's weight alone was used for weight measurements. As a substitute for height in these patients, the child's length was measured while lying down. BMI was then calculated using the following formula: BMI = weight (in kilograms)/height (in meters).[2] BMI z scores and percentiles for age and sex were then determined centrally by the study statistician, using the Statistical Analysis Software program (Stata version 15.0, StataCorp, College Station, Texas) based on current Centers for Disease Control and Prevention growth charts.[23,24]

Neurocognitive Measures

Neurocognitive ability was assessed with the School-Age Differential Ability Scales-II, Oral and Written Language Scales, Developmental NEuroPSYchological Assessment-II, and the Wechsler Individual Achievement Test-III. The Pediatric Quality of Life Inventory Measurement Model is a modular approach that was used to measure health-related quality of life. Details on the specific subsets of these tests can be found in **Appendix 2** (available at www.jpeds.com).

Statistical Analyses

We evaluated the null hypothesis that at age 10 years, neither a BMI percentile between 85 and just less than 95 (overweight) nor a 10-year BMI percentile of 95 or above (obese) is associated with any cognitive, executive, communication or social dysfunction, achievement limitation, or unfavorable parent-reported health outcome. The reference group used was children in this cohort with BMI percentile at 10 years <85. We began by assessing correlates of these BMI percentile groups, including the maternal demographics, pregnancy and newborn characteristics, and educational history at age 10 years.

To allow for the differences in age at the time of the assessment and to facilitate a comparison of our findings to those reported for children presumably born very near term, we used z scores based on distributions of values reported for the historical normative samples that are described by the authors of the assessments we used.[25-27] We created logistic regression models of the risk of a score ≥1 SDs below the normative mean of each assessment. These models, which included potential confounders (including infant's sex and birth weight z score <−1, as well as maternal characteristics of Hispanic ethnicity, education ≤12 years, single marital status, and prepregnancy BMI <25 and 25 to <30), allowed us to calculate ORs (and 95% CIs) of each 10-year characteristic associated with a BMI percentile between 85 and <95 or ≥95. Similar data analysis also was performed excluding children with BMI percentile <5 (underweight).

Results

The children not seen at 10-year follow-up were more likely than those assessed to have a mother who had less formal education, was not married, and was eligible for government-provided (public) healthcare insurance. The children who returned for the assessment were similar in the frequency of neonatal complications to those not evaluated at age 10 years, except that those who were assessed at age 10 years were more likely to have had chronic lung disease than those not assessed (**Table I**; available at www.jpeds.com). There were few notable differences between those with BMI available at 10 years and those without measurements (**Table II**; available at www.jpeds.com).

Sample Characteristics

A greater percentage of women who identified as Hispanic and, who at the time of delivery, were <21 years of age had a child who was overweight or obese at 10 years (**Table III**; available

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