Birth Status, Child Growth, and Adult Outcomes in Low- and Middle-Income Countries

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Objective To assess the impact of being born preterm or small for gestational age (SGA) on several adult outcomes.

Study design We analyzed data for 4518 adult participants in 5 birth cohorts from Brazil, Guatemala, India, the Philippines, and South Africa.

Results In the study population, 12.8% of males and 11.9% of females were born preterm, and 26.8% of males and 22.4% of females were born term but SGA. Adults born preterm were 1.11 cm shorter (95% CI, 0.57-1.65 cm), and those born term but SGA were 2.35 cm shorter (95% CI, 1.93-2.77 cm) compared with those born at term and appropriate size for gestational age. Blood pressure and blood glucose level did not differ by birth category. Compared with those born term and at appropriate size for gestational age, schooling attainment was 0.44 years lower (95% CI, 0.17-0.71 years) in those born preterm and 0.41 years lower (95% CI, 0.20-0.62 years) in those born term but SGA.

Conclusion Being born preterm or term but SGA is associated with persistent deficits in adult height and schooling, but is not related to blood pressure or blood glucose level in low- and middle-income settings. Increased postnatal growth is associated with gains in height and schooling regardless of birth status, but not with increases in blood pressure or blood glucose level. *(J Pediatr 2013;163:1740-46)*.

Growth failure in childhood, usually measured as stunting (height for age <−2.0 SDs compared with the reference population), is associated with short stature in adulthood and with lower schooling attainment.[1] Multiple studies, primarily but not exclusively from high-income countries, have found inverse associations between size at birth and later blood pressure and blood glucose levels[2,3]; however, many of those studies did not pay adequate attention to the potential independent contributions of gestational age (GA) and birth size according to GA. Although both prematurity (ie, birth before 37 completed weeks gestation) and being born small for GA (SGA; typically defined as birth at <10th percentile of birth weight for GA) are associated with increased risk of neonatal mortality,[4] increased emphasis on the identification and care of such infants has led to a significant decrease in mortality, such that these infants are increasingly surviving to adulthood. Nevertheless, the prevalence of preterm births and SGA births remains high in many populations,[5] and although preterm birth and SGA status have been associated with undernutrition at age 2 years,[6] the later growth patterns of children born preterm have not been examined extensively, especially in low- and middle-income countries. Furthermore, whether any potential adverse impact of prematurity or SGA status on later outcomes might be mitigated or potentiated by the pattern of postnatal growth is unclear.

We previously reported that size at birth and growth patterns in childhood are related to attained adult height[7] and body composition,[8] schooling,[9] and blood

AGA	Appropriate for gestational age
BMI	Body mass index
GA	Gestational age
IFG	Impaired fasting glucose
LGA	Large for gestational age
LMP	Last menstrual period
SGA	Small for gestational age

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pressure[10] and glucose[11] levels in young adulthood in 5 lower and middle-income countries. Specifically, growth during the first 2 years of life is strongly associated with adult height, but not with elevated blood pressure or glucose levels, and growth later in childhood and through adolescence, especially gains in weight, is associated with increased risk for hypertension and impaired fasting glucose (IFG).[12] Those analyses did not systematically examine whether the association between child growth patterns and adult outcomes varied among individuals differing by preterm status or by size for GA at birth. Understanding whether postnatal growth patterns affect risk differentially for individuals born preterm or SGA has implications for the management of these infants. Thus, we conducted an analysis of child growth and adult health in 5 low- and middle-income countries to investigate the association of both preterm status and weight for GA with later growth, schooling attainment, and cardiometabolic outcomes.

Methods

The Consortium of Health-Orientated Research in Transitioning Societies is a collaborative endeavor pooling data from birth cohorts in 5 low- and middle-income countries: Brazil, Guatemala, India, the Philippines, and South Africa.[13] Descriptions of these cohorts are available elsewhere.[14-18] All 5 cohorts were established during gestation or at delivery, included at least 1000 individuals under study since birth, had multiple anthropometric measures obtained during childhood, and at the time of establishment of the collaboration had reached at least age 15 years (**Table I**; available at www.jpeds.com). The youngest cohort (South Africa) has completed data collection at age 18 years; we used those more recent data in the present analysis. All field work was conducted under protocols approved by the respective Ethical Review Committees, and all subjects (or their parents, as appropriate) gave informed consent.

Measures at Delivery

In India and Guatemala, birth weight was measured by research teams. In the Philippines, birth weight was measured by birth attendants using hanging scales for home births and was obtained from hospital records for hospital births. In Brazil and South Africa, birth weight was measured by birth attendants in hospitals and was extracted from the hospital birth records. In Guatemala, India, and the Philippines, birth length was measured by the research teams using portable length boards within 15 days of delivery. Birth length was not measured in Brazil or South Africa.

GA was calculated based on the reported date of the last menstrual period (LMP) and the date of delivery. In Guatemala and India, ongoing surveillance was used to identify incident pregnancies. In Brazil and South Africa, the date of LMP was extracted from the medical records. In the Philippines, the date of LMP was reported by the mother at the time of recruitment; the Ballard score, based on clinical assessment of the newborn's neuromuscular and physical characteristics,[19] was used for infants with low birth weight. The Ballard score was used in the Philippines because in 1982, it was considered more accurate than LMP, especially in populations in which a significant proportion of women did not experience a menstrual period between pregnancies. The Ballard score was used to define GA whenever available.

We classified subjects born at <259 days post-LMP (37 completed weeks of gestation) as preterm, and those born at ≥294 or more days post-LMP (42 completed weeks) as postterm. We classified term and postterm infants as SGA if they were below the 10th percentile of the sex-specific birth weight for GA distribution,[20] as large for GA (LGA) if they were above the 90th percentile, or as appropriate for GA (AGA). There were insufficient sample sizes within individual cohorts to permit classification of preterm infants by SGA status.

Measures in Childhood

Each of the 5 study cohorts collected anthropometric measures (height and weight) at study-specific intervals.[14-18] Across the 5 cohorts, common ages at measurement included 12 months for subsamples in Brazil and South Africa, 24 months, and an age that for convenience we designate as mid-childhood (48 months for the cohorts from Brazil, Guatemala, and India; 60 months for the South African cohort; and 102 months for the Philippine cohort). We computed height-for-age *z*-scores using the current World Health Organization reference population data.[21]

Measures in Adulthood

In all 5 cohorts, standing height was measured using a fixed stadiometer and weight was measured with a portable scale. Blood pressure was measured using mercury sphygmomanometers in the Philippines and digital devices in the other cohorts (Omron HEM-629 in Brazil [Omron Healthcare Inc, Lake Forest, Illinois], A&D Medical UA-767 in Guatemala [A&D Medical, Milpitas, California]; Omron M6 in South Africa; Omron 711 in India). Appropriate cuff sizes were used, and measurements were made with the subjects seated after a 5- to 10-minute rest. Field protocols differed across the cohorts; for Brazil, India, and South Africa, the mean of 2 measurements (for South Africa, 3 measurements were taken, but the first was discarded) was used; for the Philippines and Guatemala, 3 measures were averaged. In all cohorts but Brazil, the research team collected fasting blood samples to determine glucose levels; in Brazil, random blood samples were obtained, and values were adjusted for the time since the last meal.[22] In the Philippines, glucose levels were assayed from whole venous blood samples. Because glucometers overestimate glucose concentrations in whole venous blood compared with standard laboratory methods,[23] we subtracted 0.97 mmol/L from the values in the Philippines cohort to estimate the best equivalent to venous plasma as analyzed by a laboratory autoanalyzer.[24] The highest grade of schooling completed was ascertained by questionnaire.

Body mass index (BMI) was calculated as weight in kilograms divided by height squared in meters. Prehypertension or hypertension was defined as systolic blood pressure ≥120

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