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Anthropometric measures at birth and early childhood are associated with neurodevelopmental outcomes among Bangladeshi children aged 2–3 years

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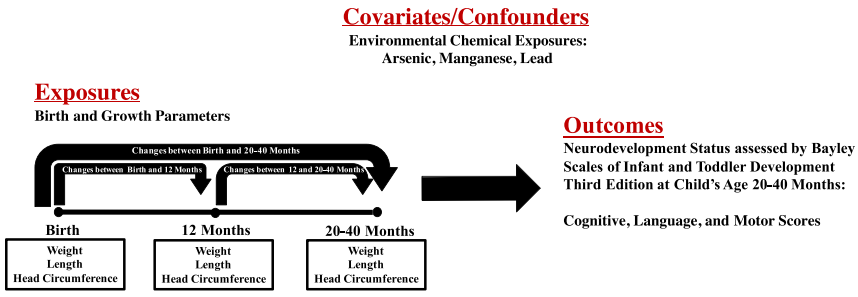
HIGHLIGHTS

- Children affected by high levels of exposure to environmental metals were included.
- Associations of anthropometric measures and neurodevelopmental status were assessed.
- Birth and growth parameters were associated with neurodevelopmental outcomes.
- These remained associated after accounting for metal exposures, such as arsenic.

GRAPHICAL ABSTRACT



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ABSTRACT

Among a cohort of children located in rural areas of Bangladesh affected by high levels of exposure to environmental metals, we investigated the associations between anthropometric measures, growth trajectory, and neurodevelopment at age 20–40 months. Our study population included mothers and their children who participated in a longitudinal birth cohort study that took in place in the Pabna and Sirajdikhan areas of Bangladesh. Anthropometric measures including weight, length, and head circumference were measured at birth, age 12 months, and age 20–40 months. Neurodevelopment was assessed using Bayley Scales of Infant and Toddler Development Third Edition (BSID-III) multi-scale at age 20–40 months. A total of 777 mother-child pairs were included. Higher anthropometric measures at 20–40 months were associated with higher cognitive, language, and motor scores on BSID-III. For example, a 1-kg increment in birthweight was associated with an increase of 2.11 for cognitive score ($p < 0.0001$), 1.63 for language score ($p = 0.006$), and 0.89 for motor scores ($p = 0.03$). Greater positive changes in growth parameters, or growth trajectory, between birth and 20–40 months were also associated with higher BSID-III scores. These associations remained significant after adjusting for potential confounders and prenatal exposure to environmental metals. These findings suggest that even when

Abbreviations: BSID-III, Bayley Scales of Infant and Toddler Development Third Edition; HOME, Home Observation for Measurement of the Environment.

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taking into account high environmental metal exposures, prenatal and early childhood growth have strong associations with neurodevelopmental test scores in early childhood.

1. Introduction

Anthropometric measures at birth and early in childhood are associated with health outcomes across infancy, childhood, adolescence, and adulthood (Kuh et al., 2003; Gamborg et al., 2009). Low birth weight is associated with increased risk of developing hypertension (de Jong et al., 2012; Curhan et al., 1996), diabetes mellitus (Curhan et al., 1996), and cardiovascular disease (Smith et al., 2016) in late childhood and adulthood. Similarly, early childhood stunting, defined as height-for-age more than two standard deviations below the median of World Health Organization Child Growth Standards (World Health Organization Department of Nutrition for Health and Development, 2006), is a strong predictor of many adverse health outcomes including obesity(Popkin et al., 1996) and metabolic disorders (Dewey & Begum, 2011). In addition to increasing risk of cardiovascular and metabolic diseases, low birthweight and stunting are associated with higher risk of long-term neurodevelopmental impairment (de Kieviet et al., 2009; Hediger et al., 2002; Vohr et al., 2000), and a growing body of literature suggests that the associations between physical growth and neurodevelopment are also found among infants within the normal ranges of anthropometric measures (Richards et al., 2001; Shenkin et al., 2004; Gale et al., 2006).

Early life exposure to chemicals in the environment may further increase the risk of neurodevelopmental impairment (Grantham-McGregor et al., 2007). In particular, metals such as arsenic, manganese, and lead have been found to be associated with poorer performance on neurodevelopmental assessments, and these associations have been found across a wide range of exposure levels (Sanders et al., 2015; Claus Henn et al., 2010; Rodrigues et al., 2016). Chemical exposures are more prevalent and are found at higher levels in low- and middle-income countries (Rahman et al., 2001; Smith et al., 2000; Sun, 2004; Rodríguez-Lado et al., 2013), many of which also have high rates of malnutrition and other risk factors that contribute to poor physical growth.

In Bangladesh, where the current study takes place, an estimated 70 million people have been chronically exposed to high levels of arsenic via contaminated drinking water following the installation of approximately 19 million hand-pumped wells in the beginning of the 1980s (Rahman et al., 2001; Smith et al., 2000; Hasan & Ali, 2010). The wells were intended to provide pathogen-free groundwater for the prevention of waterborne diseases, but have since raised concerns regarding high levels of environmental arsenic found in the water. Studies of children exposed to arsenic in utero demonstrate that prenatal exposure to arsenic is associated with poorer performance on neurodevelopmental assessments in children (Calderon et al., 2001; Hamadani et al., 2011; Parvez et al., 2011; von Ehrenstein et al., 2007; Wasserman et al., 2007; Wasserman et al., 2004; Hamadani et al., 2010). Our previous study reported the associations between exposure to environmental arsenic with decreased cognitive scores among Bangladeshi children (Rodrigues et al., 2016), and our observations are consistent with other studies conducted in this country (Wasserman et al., 2007). Recent studies have also shown that children in areas of Bangladesh have high exposures to other environmental metals, including high levels of manganese and lead (Rahman et al., 2001; Gleason et al., 2016), both of which are recognized to be associated with adverse neurodevelopmental outcomes.

Growing evidence has described associations between environmental metal exposures and adverse birth and growth outcomes (Gleason et al., 2016; Rahman et al., 2009a; Kile et al., 2015; Rahman et al., 2009b). We have shown that the arsenic concentration in wells used by mothers during pregnancy is associated with decreased birth weight in infants (Kile et al., 2015). In addition, our group demonstrated that environmental lead exposure was associated with stunting among 2- to 3-year-old Bangladeshi children (Gleason et al., 2016). Despite the growing recognition that environmental chemicals influence prenatal and early childhood growth, most studies in Bangladesh and other countries with high levels of chemical exposures do not incorporate important exposure to environmental chemicals when evaluating the associations between growth and neurodevelopment; this omission may lead to significant issues with confounding (Khan et al., 2006; Ballot et al., 2012; Gladstone et al., 2015; Khan et al., 2012).

The primary purpose of this study was to investigate anthropometric measures at birth and in early childhood to identify which physical measures, and at which particular time points are associated with neurodevelopment at age 2–3 years. We further examined whether these associations changed after adjustment for exposure to environmental arsenic, manganese, and lead. Because our study population was exposed to high concentrations of environmental toxicants, secondary aims included assessing whether there was an independent effect of anthropometric measures on neurodevelopmental measures as well as identifying critical windows for growth on neurodevelopment.

2. Materials and methods

2.1. Study sample

The children in this study were participants in a prospective birth cohort study recruited in the Sirajdikhan and Pabna regions of Bangladesh between 2008 and 2011. The design, inclusion criteria, and recruitment strategy have been described previously (Rodrigues et al., 2016). Briefly, pregnant women (≤16 weeks of gestational age) were recruited between 2008 and 2011 from clinics associated with Dhaka Community Hospital in the Sirajdikhan and Pabna Sadar Upazilas of Bangladesh. Gestational age was determined by first trimester ultrasound. When children were aged 12–40 months, families were re-contacted and invited to participate in this current study. This study included two visits for mothers and their children, one at approximately 12 months of age, and one at 20 to 40 months of age. Anthropometric measures of the children, including weight, height (length) and head circumference, were assessed at three time points, which were at birth, at 12 months of age, and at 20–40 months of age.

The Human Research Committees at the Harvard T.H. Chan School of Public Health and Dhaka Community Hospital approved this study. Parents provided written informed consent for their children. The Institutional Review Board at Boston Children's Hospital formally ceded review of this study to the Harvard T.H. Chan School of Public Health.

2.2. Measurement of growth parameters

Weight, length, and head circumference of newborns were assessed at the time of delivery by trained field staff from the Dhaka Community Hospital clinics. Birthweight was recorded to the nearest 0.1 kg using a calibrated digital infant scale. Birth length was measured to the nearest 0.1 cm with extended legs and heels against the measuring board using an infantometer. Head circumference was measured to the closest 0.1 cm at the maximal occipital-frontal circumference using a standard measuring tape. Weight, length, and head circumference were also measured at the 12 month and 20–40 month visits.