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Distribution and predictors of 20 toxic and essential metals in the umbilical cord blood of Chinese newborns

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HIGHLIGHTS

- Exposure to heavy metals or trace metal deficiencies/excesses can impact health.
- We measured 20 toxic and essential metals in the cord blood of Chinese infants.
- 10 metals (Sb,Co,Cs,Cu,Pb,Mo,Rb,Se,Sr,Ti,Zn) were detected in all blood samples.
- Birth season and parent occupation were associated with infant cord blood metals.

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ABSTRACT

Early-life exposure to heavy metals and/or trace metal imbalances can have negative developmental effects. Here we sought to characterize exposure profiles for 20 heavy metals and trace elements in umbilical cord blood plasma and identify demographic predictors of exposure. Twenty metals were measured in cord plasma from 357 Chinese infants using ICP-MS. Relationships between demographic variables and metals were analyzed using generalized linear models and logistic regression. Ten metals (antimony [Sb], cobalt [Co], cesium [Cs], copper [Cu], lead [Pb], molybdenum [Mo], rubidium [Rb], selenium [Se], strontium [Sr], titanium [Ti], zinc [Zn]) were detected in all samples. Season of birth was the strongest predictor of metals in cord blood across analyses. Infants born in the spring had 0.1–0.2 μg L-1 higher logAs and logCo in their cord blood (β [95%CI] = 0.22 [0.01,0.42], p = 0.04; 0.11 [0.01,0.22], p = 0.04), while infants born in the summer had higher Sb, logB, logHg, and logZn (β [95%CI] = 0.74 [0.24,1.24], p = 0.004; 0.11 [0.00,0.21], p = 0.04; 0.29 [0.08,0.49], p = 0.007; 0.18 [0.06,0.31], p = 0.005), compared to those born in fall/winter. Prenatal heavy metal exposure and/or trace metal deficiencies are global concerns because of increasing awareness of downstream developmental effects.

1. Introduction

Metals have a wide variety of applications in the telecommunications, electronics, agriculture, mining, construction, health care, information technology, and other industries (Mamtani et al., 2011). In the past few decades, China has experienced a technological boom and rapid industrialization, leading to ever-increasing levels of heavy metals in the environment (Chen et al., 2016; Liu et al., 2014). There are reports of heavy metal contamination of soil (Chen et al., 2015; Ye et al., 2015), food (Huang et al., 2013; Pan et al., 2016; Tang et al., 2014; Zhang et al., 2015), air (Zhang et al., 2017), and surface water (Liu et al., 2009; Zhen et al., 2016) in China. The improper handling of "E-waste" is also a growing concern in China, where they produce more than 2 million tons per year (Mamtani et al., 2011). Due to this ubiquitous environmental contamination, humans are exposed to metals via a number of pathways: consumption of food grown in contaminated soil, inhalation of polluted air, drinking or cooking with contaminated water (Mamtani et al., 2011).

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The widespread presence of metals in the environment presents important health risks (Mamtani et al., 2011). Heavy metals are persistent in the human body and have been associated with negative health effects on a diverse range of systems, including neurological, cardiovascular, respiratory, reproductive, renal, skeletal, and gastrointestinal systems (Jaishankar et al., 2014; Jarup, 2003; Zeng et al., 2016).

Exposure to heavy metals, in particular, is a concern during gestation and early infancy when rapid development is occurring. Exposure during these sensitive periods could result in permanent structural or functional changes (Caserta et al., 2013). While regarded as a protective barrier for the embryo and fetus, the placenta does not provide protection against heavy metals, such as lead (Pb), cadmium (Cd), and mercury (Hg) (Al-Saleh et al., 2011; Iyengar and Rapp, 2001).

Epidemiological studies have found that prenatal and childhood heavy metal exposures are associated with downstream neurological and cognitive deficits in childhood. For example, prenatal exposure to Pb has been associated with decreases in motor (Parajuli et al., 2013) and sensory (Silver et al., 2016a) function in infants, while childhood Pb exposure has been associated with lower IQ and cognitive abilities, behavioral abnormalities, inattention, and other neurological deficits (Bellinger, 2008; Wigg, 2001). Prenatal exposure to Cd, Hg and other heavy metals have also been found to be associated neurodevelopmental deficits, such as decreased social skills and delayed behavioral development (Gao et al., 2007; Wang et al., 2016).

While heavy metals, such as Pb, arsenic (As), Cd, and Hg can be toxic, even at low levels of exposure, other metals, such as iron (Fe), copper (Cu), zinc (Zn), and selenium (Se), are essential for a host of physiological and metabolic functions (Mamtani et al., 2011). Deficiencies or excesses of these essential trace metals can similarly have negative health effects.

Some trace metals, such as Zn, Cu, manganese (Mn), and Se are essential for proper embryonal and fetal growth and development (Gernand et al., 2016). These elements are necessary for a number of important developmental processes, such as embryogenesis and fetal growth, myelin development, skeletal formation, and maintenance of cell membrane integrity (Chan et al., 1998; Hurley, 1981; Linder, 1991; Pieczynska and Grajeta, 2015; Shah and Sachdev, 2001; Srivastava et al., 2002). Other trace metals such as boron (B), rubidium (Rb), and strontium (Sr) may also play a role in fetal growth, though their roles are not well-established (Maynar et al., 2017). Additionally, deficiencies in essential elements such as Cu (Shen et al., 2015), Zn (Jeswani and Vani, 1991; Shen et al., 2015; Tamura et al., 2000; Terrin et al., 2015) and Se (Pieczynska and Grajeta, 2015) during the prenatal and early postnatal periods have been associated with an increased risk of pregnancy complications such as, miscarriage, low birth weight, and intrauterine growth restriction, as well as immune deficiencies.

Deficiencies or excesses in essential metals during pregnancy or childhood can also have negative downstream neurodevelopmental effects. For example, infants with Fe deficiency are more likely to perform worse on cognitive tests and to experience long-term developmental deficiencies, compared to infants with normal Fe (Lozoff et al., 1991). Prenatal Zn deficiency has been found to be associated with defects of the central nervous system (Shah and Sachdev, 2001; Uriu-Adams and Keen, 2010) and increased risk of autism spectrum disorder (ASD) (Arora et al., 2017), while Zn deficiency during infancy has been associated with deficits in memory (Fuglestad et al., 2016). Studies of prenatal Mn have revealed that both deficits and excesses during pregnancy can negatively impact cognitive and motor functions (Chung et al., 2015; Sanders et al., 2015; Zoni and Lucchini, 2013), while pre- and postnatal deficits have been associated with increased risk of ASD (Arora et al., 2017).

Furthermore, deficiencies of essential elements may potentially lead to increased absorption of toxic metals. For example, children with low blood calcium (Ca), Fe, and Zn are at increased risk of high blood Pb levels (Ahamed et al., 2007; Talpur et al., 2017). Similarly, iron deficient children and those with iron deficiency anemia are reported to have elevated blood levels of Cu (Turgut et al., 2007), Cd (Silver et al., 2013; Turgut et al., 2007) and Pb (Ahamed et al., 2007; Bradman et al., 2001; Rondo et al., 2011; Turgut et al., 2007).

Previous studies have investigated cord blood metals in China (Hu et al., 2015; Liang et al., 2017; Tang et al., 2016a, 2016b; Wang et al., 2016; Yang et al., 2013; Yu et al., 2011, 2014; Zheng et al., 2014). With a couple of exceptions (Tang et al., 2016b; Yang et al., 2013), these studies were largely focused solely on toxic metals. Additionally, only one included a robust analysis of predictors of prenatal metal exposure (Yu et al., 2011). Each of these studies focused on a particular geographical region, and their results indicate the presence of regional variation of metals exposure in China. None of the previous studies included Zhejiang province, the site of this study. Reports indicate that agricultural soil in Zhejiang has Pb and Hg levels that exceed the maximum allowable levels set by the Chinese Soil Quality Criterion (Ye et al., 2015) and that rice and other vegetables grown there may contain high levels of Pb, Hg, and Cd (Huang et al., 2013; Pan et al., 2016).

Given the potential for high exposure in Zhejiang and the important developmental implications for prenatal exposure to heavy metals, we sought to determine the concentrations of 20 heavy metals and trace elements in umbilical cord blood plasma and to identify demographic predictors of prenatal exposure to those metals. The consideration of both toxic and essential metals allows us to begin to consider the interplay of both environmental toxicants and nutritional exposures. This study will inform future work examining prenatal metals exposure and infant neurodevelopment in this cohort.

2. Methods

2.1. Ethics statement

Institutional review board approval was obtained from ethics committees at the University of Michigan (HUM00010107) and Zhejiang University Children's Hospital. Signed, informed consent was obtained from parents prior to commencing the study.

2.2. Study population

Blood metals analysis was performed for 357 infants. Pregnant women with healthy, uncomplicated, single pregnancies were recruited between 2008 and 2011 from Fuyang Maternal and Children's Hospital in rural Fuyang county, Zhejiang province, China. Women ($n = 1187$) consented to a cord blood screening at the time of recruitment. Of the infants born at term (37–42 weeks gestation), a subset ($n = 359$) was then enrolled in a study of infant neurodevelopment. This subset was selected based on cord blood iron status and parental consent for the developmental study. Of those, 229 had a sufficient volume of cord blood available for metals analysis. The remaining metals analysis samples ($n = 128$) were randomly selected from those with sufficient cord blood volume from the original cord blood screening cohort.

2.3. Determination of metals in umbilical cord blood

Following delivery, 10 mL of cord blood was collected in two royal blue top metals free EDTA tubes. Both tubes were immediately frozen and stored at −20 °C (°C). Frozen whole blood samples