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Lead, mercury, and cadmium in umbilical cord serum and birth outcomes in Chinese fish consumers

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HIGHLIGHTS

- Metals exposure levels in umbilical cord serum of fish consumers were determined.
- Multivariable regression analyses showed negative effects of Pb and Hg on birth outcomes.
- Middle tertile Pb and Hg exposure levels were found significantly negative effects.

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ABSTRACT

Heavy metals such as lead (Pb), mercury (Hg), and cadmium (Cd) were detected in the islands of Yangtze River estuary and Hangzhou bay and their exposure caused potential health risk for the residents. To assess the exposure levels of Pb, Hg, and Cd, the umbilical cord serum samples were collected from 103 mother-newborn pairs as the noninvasive specimens. The association of the concentration of Pb, Hg, and Cd with the birth outcomes was evaluated. Pb, Hg, and Cd had high exposure levels with the median concentrations at 76.20 μg L^{-1} [interquartile range (IQR): 44.71, 115.80], 21.94 μg L^{-1} (IQR: 15.10, 27.64), and 6.36 μg L^{-1} (IQR: 3.63, 13.34), respectively. A unit increase in the Pb umbilical cord serum concentration (μg L^{-1}) was significantly associated with a 0.29 cm (95% CI: −0.50, −0.09) decrease in birth height and a 0.22 cm (95%CI: -0.44, 0.00) decrease in head circumference. The middle tertile Pb and Hg exposure levels were found significantly negative effects on birth outcomes compared with low tertile exposure levels. Exposure to Cd showed no apparent effect on birth outcomes. Our results suggested that Pb and Hg exposure has potential adverse effects on birth outcomes in Chinese fish consumers from Yangtze River outlet and Hangzhou bay estuary regions.

1. Introduction

Small birth size and premature birth more frequently occur in infants whose mothers were exposed to heavy metals during pregnancy (Al-Saleh et al., 2014; Sanjose et al., 1991). Some heavy metals may pass through the placental barrier to reach the fetus and have lasting effects on fetal growth (Afeiche et al., 2011; Esteban-Vasallo et al., 2012). Umbilical cord blood is thought to be an adequate bioindicator for heavy metals exposure and have been frequently used to assess the prenatal exposure level and predict the mother-infant transfer of heavy metals.

Lead (Pb), mercury (Hg), and cadmium (Cd) are heavy metals and rank as top 10 most toxic substances as reported in the Priority List of Hazardous Substances (ATSDR, 2013). Pb and Hg were reported to easily cross the placenta and enter the fetal circulation of the blood (Iyengar and Rapp, 2001). Exposure to low levels of Pb may affect calcium transfer in human placental syncytiotrophoblasts (Lafond et al., 2004) and has the indirect effect of brain development strain (Vejrup et al., 2013). The interaction of Hg with

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glutathione S-transferase may reduce fetal growth (Schlawicke et al., 2008). Cd, a heavy metal associated with "Itai–Itai disease" in Japan, is one of 12 universal dangerous matters determined by UNEP (United Nations Environment Programme) in 1984 (UNEP, 2010), and classified as carcinogenic to humans by the IARC (International Agency for Research on Cancer) (IARC, 2014). Although the placental barrier may prevent some degree of Cd transfer, low-level exposure carries prenatal risk due to its long half-life and estrogen interference (Kippler et al., 2011). Impaired nutrient transport and endocrine disruption from Cd exposure are the main mechanisms that affect fetal growth (Barrett, 2012).

The exposure to Pb, Hg and Cd, based on samples of umbilical cord blood, has detrimental effects on fetal growth. Low-level Pb exposure in cord blood from Chinese mother-infant pairs ($n = 252$) was revealed to have a negative relationship with birth length (Xie et al., 2013). An epidemiological study that included 554 newborns revealed that decreased birth weight was associated with exposure to Hg in cord blood due to fish consumption (Ramon et al., 2009). For Cd exposure, decreases in birth weight (Galicia-Garcia et al., 1997), birth length (Al-Saleh et al., 2014), and birth head circumference (Lin et al., 2011) were observed in cord blood with higher levels of Cd. Despite these negative effects, most population-based studies have found inconsistent results. For instance, no relationship between Hg contaminants in cord blood and birth outcomes was noted in studies conducted in Greenland (Bjerregaard and Hansen, 2000) and China (Ding et al., 2013). Another study in a Chinese population detected 14 heavy metals and trace elements in cord blood, nevertheless neither Cd nor Pb was found to have adverse effects on pregnancy outcomes (Zheng et al., 2014).

Till now the data on heavy metal exposure risk in Chinese pregnant women, particularly fish consumers are still very limited. According to Chinese Offshore Environmental Quality Bulletin in 2013, poor water quality in offshore waters of the East China Sea was observed; and the exceeding standard rates of Hg and Cd in the sediments of important fishery marine were 14.3% and 2.9%, respectively (Ministry of Environmental Protection of the People's Republic of China, 2014). Dietary intake, especially from seafood, is considered a substantial way to accumulate heavy metals in human tissues (Kippler et al., 2012; MacIntosh et al., 1996). Particularly for Hg, the US Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) issued a warning for pregnant women to eat recommended amounts and types of fish to prevent Hg dietary intake (FDA, 2014). Therefore, we conducted a Chinese population-based cross-sectional study on an island in the East China Sea, with umbilical cord serum samples collected from these fish consumers, (1) to determine the contaminant levels of Pb, Hg, and Cd in umbilical cord serum samples and (2) to investigate the effects of prenatal exposure to Pb, Hg, and Cd on birth outcomes.

2. Materials and methods

2.1. Study area and population

Shengsi islands face the Yangtze River estuary and Hangzhou Bay in China (Fig. 1). The Yangtze valley is the main agricultural region in China, and most agricultural non-point source pollution discharges into the sea through the Yangtze River estuary. Additionally, heavy metal emissions in the Yangtze River Delta, especially in the economically developed Hangzhou Bay, also threaten the health of the islanders. Shengsi Island is also located in the center of the East China Sea Fisheries, and variable seafood fishing in this region constitutes the main diet of the islanders.

120 pregnant Chinese women living on Shengsi Island agreed to participate in this cross-sectional study from July 2011 to May 2012. Approximately 240 pregnant women who delivered at the only hospital with obstetrics and gynecology on this island (Shengsi People's Hospital) were asked to participate, and the overall participation rate was 50%. Specific inclusion and exclusion criteria were applied in the baseline cohorts. Eligible pregnant women included those planning to deliver at the only hospital, without apparent clinical symptoms, without any maternal history of illness, and no poor habits such as drug use. Eligible infants were singleton births and had no congenital diseases. The pairs without qualified umbilical cord serum samples were excluded. Finally, a total of 103 mother-newborn pairs were included in the statistical analysis. All procedures were performed in compliance with relevant laws and institutional guidelines and informed consent was obtained for all participants.

2.2. Pb, Hg, Cd measurements

Umbilical cord serum ($n = 103$) was collected via a common aseptic procedure during delivery. Samples were collected by trained midwives or obstetricians using standard protocols. The samples of umbilical cord blood were centrifuged for stratification at 3000 r/min for 10 min, and the serum was extracted immediately after delivery at the hospital on Shengsi Island. All collected serum samples were collected in sterile centrifuge tubes and immediately frozen and stored at −20 °C until shipment to the laboratory for further analysis. In the laboratory, we measured Pb, Hg and Cd concentrations in all 103 umbilical cord serum samples using inductively coupled plasma-mass spectrometry (ICP-MS, Agilent 7500a, Agilent, Santa Clara, California, USA) at the Institute of Environmental Science of Zhejiang University, Hangzhou, China.

The Pb, Hg, and Cd levels in serum were determined using the same analysis method. We applied the sample preparation and analytical method described elsewhere (Okamoto and Fuwa, 1984), and we modified the digestion process (Appendix A). The limit of detection (LOD) for this method was 0.01 μg L^{-1} for Pb (all samples detected), 5.19 μg L^{-1} for Hg (2% < LOD in serum samples), and 0.03 μg L^{-1} for Cd (10% < LOD in serum samples). All the values below the LOD were estimated as metal-specific LOD divided by $\sqrt{2}$ according to the Fourth National Report on Human Exposure to Environmental Chemicals published by US Centers for Disease Control and Prevention (CDC) (CDC, 2009). The detected Hg concentrations represent all relevant forms, including inorganic and methyl Hg. The Teflon crucibles and all glassware were soaked in 10% HNO_3 overnight before use. The procedural blank samples were analyzed for quality control.

2.3. Birth outcomes and covariates

All of these infant anthropometric measurements, including birth weight, length, and head circumference, were collected at birth by professional health-care workers. Newborn weight, length, and head circumference data were abstracted from hospital birth records by registered nurses. Gestational age was obtained using the reported date of the last menstrual period and delivery date. If they did not know the exact last menstrual date, an ultrasound-based measurement for crown-rump length (Robinson et al., 1979) and bi-parietal diameter of gestational age at 12 weeks was used to estimate gestational age (Snijder et al., 2013).

Informed consent was received from all subjects. The commonly used covariates to adjust the association between exposure to Pb, Hg and Cd and birth outcomes were collected when conducting the questionnaire survey. General demographic characteristics, including residence, maternal age, educational level, smoking status, alcohol use, dietary habits, disease history, and prepregnancy weight and height, were recorded. For dietary habits, we focused on