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Impact of organic mercury exposure and home delivery on neurodevelopment of Amazonian children

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ABSTRACT

In the transitioning Amazon, we addressed birth environment (home *vs* hospital) and associated perinatal organic-Hg exposures: methylmercury (MeHg) from maternal fish consumption and ethylmercury (EtHg) from pediatric Thimerosal-containing vaccines (TCVs) taken systematically during hospital delivery. We studied 365 children in relation to linear growth at 60 months and neurodevelopment (milestone achievements, Bayley Scale of Infant Development/BSID at 24 months, and Stanford-Binet intelligence tests at 60 months). Mothers delivered in hospitals *vs* those gave birth at home had significantly ($p < 0.0001$) lower hair-Hg (HHg) concentrations (12.2 *vs* 23.9 μg/g respectively) and shorter length of breastfeeding (8.5 *vs* 9.7 months respectively). Home-born children had significantly ($p < 0.0001$) higher HHg (7.1 μg/g) than hospital-born children (4.6 μg/g). Hospital-born children also had significantly earlier ($p < 0.0001$) hepatitis B vaccine than home-born children (1.5 *vs* 24.1 days respectively) and higher ($p < 0.0001$) exposures to total TCV-EtHg (75.8 *vs* 49.3 μg respectively). Neither anthropometric indices nor neurodevelopment (except for fluid reasoning) were directly affected by birth environment. The percentage of hospital-born children with BSID (MDI or PDI) scores <80 was not significantly different from those born at home. In spite of the differences in HHg and EtHg levels between hospital-born and home-born children, no impact on neurodevelopment was observed.

1. Introduction

Recent urbanization and socio-economic development in the Western Amazon (Brazil) have brought noticeable lifestyle changes to populations living in the Madeira River Basin. Such development has impacts on market integration, subsistence lifestyle, diet, maternal-infant health outcomes, demography, and formalized education. Shop-bought foods (*i.e.* less dependence on fish) and modern medicine (such as hospital and health outposts) have become increasingly common place (Veile et al., 2014).

Traditional lifestyles are usually related to subsistence fish-based diets, home birthing, and extended breastfeeding (Marques et al., 2016; Vieira et al., 2013). Communities such Western Amazonian live usually in rural and remote areas with limited health access and they have relatively elevated hair Hg (HHg) levels (Alves et al., 2006; Tschirhart et al., 2012; Hacon et al., 2014). In remote areas with little access to medical care facilities, home birth practices also delay newborn immunization to hepatitis B vaccine (HBV) unlike those in hospitals. Infant immunization occurs irregularly and less intensely as shown in the wide variation of ethylmercury (EtHg) exposure reported for this studied population (Marques et al., 2016).

As a result of high fish consumption, methylmercury (MeHg) exposure increases in both mothers and breastfed children (Marques et al., 2013a; Vieira et al., 2013). At least the first vaccine of the Brazilian immunization scheme, HBV, a TCV, never happens on the day of birth when the child is born at home (Marques et al., 2007a; Dórea et al., 2009). The afore-mentioned practices suggest that child exposure to Hg from maternal fish consumption is higher than immunization. However, while maternal transfer of Hg is chronic and attenuated by biological barriers (placenta and mammary gland), the exposure to ethylmercury in TCV is acute as a bolus (Dórea, 2007).

It should be noted at this juncture that health advisories regarding exposure to low doses of organic Hg compounds (MeHg and EtHg) are currently disproportional, especially in regard to vulner-

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able individuals. On the one hand, the World Health Organization (WHO) (Poulin and Gibb, 2008) advises reducing the consumption of fish containing MeHg, especially for pregnant women to protect the unborn child from neurological damage. On the other hand, there are no requirements to establish limits of Thimerosal in pediatric vaccines while in the laudable pursuit of full pediatric immunization. Despite a wealth of studies on the comparative neurotoxicity of EtHg and MeHg (Dórea et al., 2013), the WHO recommends unrestricted use of TCVs in newborns, neonates, infants, and young children (WHO, 2012). There are health implications of Hg exposure in children (Al-Saleh, 2009), and MeHg and EtHg are both neurotoxins (Dórea et al., 2013).

The objective of this study is to examine the association between birth practices and Hg exposure and whether both might impact Amazonian child growth and neurodevelopment taking into consideration urbanization and socioeconomic changes.

2. Materials and methods

2.1. The studied population

A cohort was organized to study the health, nutrition, and development of children in relation to maternal fish consumption and associated environmental issues in periurban and rural populations of Amazonian children (Marques et al., 2013b). There were preliminary surveys to identify potential participants and form this cohort (Dórea et al., 2014). The total cohort was formed after contacting 1668 pregnant mothers (with an expected delivery between 2006 and 2007) living in an area along approximately 733 km of the Madeira River Basin. Only 1433 pregnant women were enrolled. A comprehensive evaluation of health, growth and neurodevelopment of these children was conducted during regular visits.

2.2. Inclusion and exclusion criteria

The main criteria for inclusion and exclusion were (a) residence in the study area for at least five years, (b) being healthy at time of pregnancy (c) and absence of congenital malformations (Marques et al., 2013b). Eleven were excluded due to miscarriage (unknown origin), and nine were excluded due to congenital anomalies.

This sub-sample is restricted to the area where we found the greatest number of pregnant mothers that delivered at home. These rural families are mostly traditional riverines, sharing a fish-based diet, starchy cassava-based products, and foods provided by the forest. Among these communities, we identified a subsample of 365 children that differed in birth environment. Of these, 132 children were delivered by mid-wives in the home environment, according to the traditional local custom; 233 were delivered at hospitals served by modern medicine. In these facilities, expectant mothers receive anesthesia and a large proportion of them were subjected to cesarean birthing.

2.3. Ethical considerations

The study was approved by the Ethics Committee of the Federal University of Rondonia (Of. 001-07/CEP/NUSAU). The mothers participated on a voluntary basis after signing an informed consent.

2.4. Questionnaire

During visits, questionnaires (to obtain information on breastfeeding practices, age of walking and age of talking, as well as socioeconomic data) were applied (Marques et al., 2013b). Dietary information was obtained only in relation to frequency of fish consumption. Information on gestational age, birth weight and delivery conditions (home or hospitals) were obtained from hospital records or midwives. The total EtHg taken by infants during the first postnatal 6 months was evaluated from vaccination cards.

2.5. Anthropometric measurements

Anthropometric measurements (height/length and weight) were taken by experienced nurses. Measurements were taken with the infant or child dressed in light clothing. Length of babies and infants was measured with a stadiometer (0.1 cm) and weight with an electronic scale (to the nearest 0.1 kg), both in recumbent position; older children were measured in standing position dressed in underwear and barefoot. Weight and height results were transformed by Z-scores for weight-for-age (W/A-Z) and height-for-age (H/A-Z) using WHO Anthro (version 3.2.2., January 2011) (WHO Anthro, 2007).

2.6. Hair collection and analysis

Hair was sampled from the occipital area using a stainless steel scissors. Hair processing and analysis were done at the Radioisotopes Laboratory of the Federal University of Rio de Janeiro according to our routine laboratory protocol. This involves sample digestion followed by reduction to elemental Hg vapor (Marques et al., 2007b). The hair samples were washed with EDTA 0.01% and dried in an oven at 50 °C. A weighed portion was digested with 5 mL of HNO3:H_2SO_4 (1:1) and 4 mL of 5% $KMnO_4$ in a digestion block (80 °C for 40 min). Total Hg determination in these samples was done by cold vapor atomic absorption spectrometry with a flow injection system/FIMS (CV-AAS; Perkin-Elmer-FIMS 400, Ueberlingen, Germany).

2.7. Neurodevelopment tests and milestones

The outcomes of childhood neurodevelopment were assessed through milestone achievement (for the ages of talking and walking), at the age of 24 months using the Bayley Scales for Infant Development/BSIDII (Bayley, 1993), and at the age of 60 months the intelligence quotient (IQ) by using the Stanford-Binet Intelligence Scale (Roid and Barram, 2004). Both tests (BSIDII as well as IQ) were administered by experienced and qualified psychologists in the quiet and home environment of the children. The psychologists administering these tests were blinded to the levels of ante- and post-natal Hg exposures. The BSIDII is a standardized assessment technique adjusted for age that measures the developmental/cognitive level of young children. The BSIDII includes the Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) that measure cognitive, language, motor, social, emotional, and adaptive behavior. The MDI provides an index score for general cognitive development (measuring cognitive development, including items that tap memory, habituation, problem solving, early number concepts, generalization, classification, vocalizations, language, and social skills). The PDI provides an index score for overall motor development which includes items of fine and gross motor skills (e.g, rolling, crawling, creeping, sitting, standing, walking, running, jumping, prehension, use of writing implements, imitation of hand movements). The test results are integrated in scores indicating severe (score <69) and mild (scores 70–84) delays, normal limits (scores 85–114), and accelerated performance (score >115).

The Stanford-Binet Intelligence Scale (SB5) was used to assess abilities and aptitudes; it does not have Brazilian norms. This is an internationally standardized tool that covers five factors of cognitive ability: Fluid reasoning; knowledge; quantitative reasoning; visual-spatial processing; and working memory. There are 2 subtests for each of five factors, and within each factor there is one verbal subtest and one nonverbal subtest. A combined composite