Published in final edited form as:

J Toxicol Environ Health A. 2014 ; 77(17): 993–1003. doi:10.1080/15287394.2014.897281.

Lead Levels in the Breast Milk of Nursing Andean Mothers Living in a Lead-Contaminated Environment

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Abstract

Concentrations of lead (Pb) in breast milk (PbM) and blood (PbB) were measured in a current cohort of lactating mothers living in Andean communities where women of child-bearing age engage in the occupational use of Pb, and compared to results obtained in earlier studies. Mean PbM concentration in the current group of breastfeeding mothers tested in 2012/2013 was 3.73 µg/l (SD: 7.3; range: 0.049 - 28.04), and significantly lower than the 9.83 µg/l (SD: 12.75; range: 0.2 - 49) previously observed in breastfeeding mothers in the study area from 1999 to 2007.

Breastfeeding women in the current cohort showed an average PbM/PbB ratio of 3.6%, which is in agreement with other studies. The mean PbB level obtained for the current cohort was 7.8 µg/dl (SD: 5.2; range: 1.4 - 21), and significantly lower than the mean PbB level of 20.8 µg/dl (SD: 16.4; range: 4-73) obtained for the comparison group of breastfeeding mothers tested between 1999-2007. A correlation of .687 between paired PbM and maternal PbB was found, indicating that maternal PbB level is a significant predictor of PbM. Current PbM levels remain higher than international averages, but indicate that maternal Pb exposure has declined over time in the environmentally Pb-contaminated study area. The current reduction in Pb in milk and blood of breastfeeding mothers may be due to adherence to a Pb-exposure education and prevention

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The authors declare no conflict of interest

program initiated by the authors in the study area years earlier, as well as recent improvements in local healthcare delivery.

Keywords

Lead; Human Breast Milk; Lactating; Blood; Nursing Mothers; Children; Andean; Environment

INTRODUCTION

Lead (Pb) is a naturally occurring toxic metal to which human populations are exposed globally. Pb has no known biological benefit, and a body of evidence has shown it to be immunotoxic, hematotoxic, nephrotoxic and neurotoxic in humans (Luebke et al. 2006; ATSDR, 2007; García-Lestón et al. 2012). Pb intoxication in adults and children derives mainly from environmental and occupational sources, but also from traditional medicines and cosmetics contaminated with Pb (Cohen and Roe, 1991; Maas et al. 2005; Chien et al. 2006). Children are most vulnerable to Pb toxicity, primarily because of the fragility of their developing central nervous (CNS) system and vulnerability of other physiological systems. Children typically are exposed to Pb from environmental sources through the ingestion of Pb-contaminated substances (ATSDR 2007). However, Pb exposure may occur *in utero* as a result of maternal Pb poisoning from the ingestion of Pb-contaminated foods, and environmental or occupational exposures. Maternal Pb from blood is stored in trabecular and cortical bone, from which it is mobilized during pregnancy. The developing fetus may be exposed to Pb during pregnancy as a result of Pb crossing the placenta from mobilization of maternal bone Pb stores (Li et al. 2000; Lamadrid-Figueroa et al. 2006; Ettinger et al. 2010). Further, Pb interferes with the development of the fetal blood brain barrier, and easily crosses the barrier in the developing fetal brain, as well as that of the neonate (Patrick, 2006; ATSDR 2007). Pb exposure during infancy and early childhood may lead to adverse neurocognitive outcomes (Lanphear, et al. 2005; ATSDR 2007).

Pb exposure among women of child-bearing age is higher in some populations, particularly in developing countries where Pb is widely used in unregulated occupational enterprises that involve females. In adults, more than 90% of absorbed Pb is stored in bones and teeth (Barbosa, et al. 2005; ATSDR, 2007). Absorbed Pb is concentrated in plasma and milk of lactating mothers, as well as in soft tissue and bone (Gulson et al. 2003). It has been recently reported that the milk-to-plasma ratio is higher than previously thought, and the transfer of Pb from plasma to milk appears to be higher at low plasma level (Ettinger et al. 2014). In the neonatal and infant stages, children may be exposed to Pb through the breast milk (PbM) of lactating, nursing mothers (ATSDR, 2007; Ettinger et al. 2010). This may cause Pb poisoning and its associated adverse physiological and neurodevelopmental sequelae.

The efficiency of Pb transferred from maternal blood and bone to breast milk, referred to as the PbM/PbB ratio, has been the subject of numerous investigations. Some studies reported a low (less than 3%) PbM/PbB ratio, or relative transfer efficiency of Pb from maternal blood to breast milk, suggesting that the mammary gland barrier is efficient in maintaining a low

transfer rate between maternal PbB and PbM (Gulson, et al. 1998, 2003; Choi et al. 2008; Ettinger et al. 2010; Koyashiki et al. 2010).

In previous investigations of maternal Pb exposure, Counter et al. (2000, 2004, 2007) measured concentrations of Pb in milk and blood of lactating mothers living in Pb-glazing communities in the Andes Mountains of Ecuador. These investigations showed PbM and PbB levels of some mother-infant pairs in the study area to be markedly elevated. However, recent studies by Ortega et al. (2013a, 2013b) found declining PbB levels in children and adults in the same study area. It is important to know whether a similar declining trend exists in the levels of Pb in the breast milk of nursing mothers in the study area. Therefore, the aim of the present study was to investigate the current Pb levels in breast milk and blood of lactating Andean Ecuadorian mothers currently living in the same Pb-contaminated study area.

METHODS

Participants and Location

The participants in the current study (tested in 2012 and 2013) consisted of 22 nursing mothers who ranged in age from 17–40 years (mean: 25.3; SD: 5.6; median: 24.5). The ages of the breastfed infants tested in this study ranged from 1 month to 2 years. All participants in the current study reside in the ceramic production and Pb-glazing Ecuadorian neighboring communities of La Victoria, El Tejar, and Mulinliví, collectively referred to as the study area. The PbM and PbB concentrations for the 22 lactating, breastfeeding mothers in the current study were compared to previously unpublished and published Pb data obtained between 1999 and 2007 (Counter et al. 2000, 2004, 2007) on 29 nursing mothers (mean age: 26.3 years; SD: 6.2; median: 25) tested in the same study area. The study area is located in Cotopaxi Province at an altitude of approximately 2,850 m (Counter et al. 2009; Buchanan et al. 2011). Most women of childbearing age in the study area have traditionally engaged in several aspect of the Pb glazing cottage industry, including manual extraction of Pb from Pb-acid automotive storage batteries, mixing of the Pb-glazing slurry, application of the Pb mixture onto handmade ceramic roof tiles, vases, urns and other objects, and the baking of Pb-coated ceramics in family-owned kilns located adjacent to their dwellings. Current reports from local medical personnel, however, suggest that women in the study area are not as actively engaged in the Pb-glazing process as previously observed, and are adhering to a considerable extent to the principles of a Pb-exposure education and prevention program initiated by Counter et al. (1997, 2000) more than a decade earlier. Nevertheless, women in the study area, including those who are pregnant and are breastfeeding, live in close proximity to active Pb-glazing kilns, and are thus exposed to Pb in their milieu, whether or not they currently participate directly in the Pb-glazing process.

Informed consent was obtained from each participant in this study prior to testing. This study was approved by the Human Studies Committee (Comité de Bioética) of Universidad San Francisco de Quito. The study was conducted under the auspices of Universidad San Francisco de Quito Colegio Ciencias de la Salud, Escuela de Medicina in Quito, Ecuador. The results of this investigation were provided to the participants in the study, who were

counseled regarding their Pb exposure levels, and referred to local health officials for medical intervention and counseling as needed.

Pb Concentrations in Blood and Milk

All whole blood and breast milk samples were stored in a refrigerated container, and later analyzed. For assessment of PbB concentration, 2-4 ml of whole blood were drawn (using Liheparin Vacutainer sets) from the antecubital vein of volunteer nursing mothers following a thorough cleaning of the skin with swabs containing isopropanol. The blood samples were analyzed for Pb levels by graphite furnace atomic absorption spectroscopy with Zeeman background correction at the Department of Laboratory Medicine, Boston Children's Hospital. In addition, zinc protoporphyrin levels (ZPP) were measured on a subsample of the current participants in the study to obtain information on long-term Pb exposure. ZPP/heme was measured directly using a hematofluorometer (ProtoFluor-z, Helena Laboratories, Inc., Beaumont, TX), which presents results in $\mu\text{mol/mol}$ heme. Control samples (Kaulson Laboratories, West Caldwell, NJ) were run at low, medium and high levels. All instrumentation was checked regularly for quality control and calibrated accordingly.

Breast milk samples of 4 ml were collected from volunteer lactating mothers in sterile glass tubes after a thorough cleaning of the mammary area with water and alcohol swabs. In addition to measuring Pb concentration in milk samples of the nursing mothers, the levels of arsenic (As), cadmium (Cd) and mercury (Hg) were measured in the milk samples of a subset of the nursing mothers. Breast milk samples were analyzed by inductively coupled plasma-mass spectrometry (ICP-MS) at the Mayo Medical Laboratories in Rochester, Minnesota. The breast milk samples were checked for analytical drift and for overall quality control every 10 samples. If the sample values were outside the validated acceptable deviation of the quality control material, the sample was not used, and the instrumentation was recalibrated.

Statistical Analysis

The mean, standard deviation, range, median, and percentiles were calculated for PbB and PbM concentrations obtained from the participants in the study. Because some of the PbM and PbB data were skewed (> 2 standard errors of skewness), nonparametric statistics were used in the data analysis. Differences between groups were analyzed by the Mann-Whitney U test. The associations between PbM and maternal PbB levels, PbM concentration and age, and PbB level and age were analyzed by Spearman ρ correlation analyses. All Z and p values reported for the Mann-Whitney U test and the Spearman correlation coefficient are tied values. An alpha level of < 0.05 was accepted as an indication of statistical significance.

RESULTS

Pb Concentration in the Blood of Lactating Andean Mothers

The box plots of Figure 1A illustrate the comparative analysis of the PbB concentrations in 22 nursing Andean mothers in the current cohort (2012-2013) and 21 nursing mothers who were tested between 1999-2007 (previous cohort). The mean PbB level obtained for the current cohort of nursing mothers was $7.8 \mu\text{g/dl}$ (SD: 5.2; range: 1.4 - 21; median: 6;

geometric mean: 6.3), which was significantly lower than the mean PbB level of 20.8 µg/dl (SD: 16.4; range: 4-73; median: 19.4; geometric mean: 15) obtained for the comparison group of nursing mothers who were tested between 1999-2007.

Pb Concentration in the Breast Milk of Lactating Andean Mothers

The mean level of PbM in the current group of lactating mothers tested in 2012 and 2013 (Figure 1B) was 3.73 µg/l (SD: 7.3; range: 0.05-28.04 µg/l; median: 0.8; geometric mean: 1.14), which was significantly lower than the 9.83 µg/l (SD: 12.75; range: 0.2 - 49; median: 4.2; geometric mean: 4.5) previously observed in nursing mothers living in the same study area from 1999 to 2007. The bar graph of Figure 2 compares current and previous mean PbM concentrations of the Ecuadorian Andean mothers with the mean PbM levels observed in nursing mothers in other nations. The current Ecuadorian cohort tended to be higher than the background PbM levels of nursing mothers in other countries, except for China.

To evaluate the relationship between the concentrations of Pb in milk and blood, the previous group's (1999-2007) maternal PbB and PbM levels, and the current cohort's (2012-2013) maternal PbB and PbM levels were pooled, and a correlation analysis was performed on the paired PbB and PbM data. The results of this analysis are presented in Figure 3, which shows a high correlation coefficient (Spearman $\rho = .687$), indicating that maternal PbB level is a significant predictor of PbM concentration. The correlation remained high at 0.662 when the outlier (the mother with a PbM of 49 µg/l) was temporarily removed for data analysis. To further assess the relationship of PbB and PbM, the PbM-to-maternal-PbB ratio was examined. For the mothers in the current study, the mean PbM/PbB ratio was 0.048 (SD: 0.07) or 4.8%, with a range of 0.002-0.25. When the one outlier (the participant with a PbM of 28.04 µg/l, which was more than 3 SD greater than the mean) was temporarily removed from the dataset, the PbM/PbB ratio was 0.036 (SD: 0.05) or 3.6%. When the outlier was removed from the ratio analysis for milk to blood for the current group of participating mothers, the correlation coefficient was .513. A Spearman rho correlation analysis was performed to investigate a possible association of PbM with age. The results of this analysis indicated that, although the younger mothers tended to have greater PbM levels than the older mothers, this relationship did not reach statistical significance. A correlation analysis was also performed to ascertain any association between maternal PbB and maternal age in the current cohort. The results showed no significant correlation of maternal age with maternal PbB.

Maternal ZPP Levels

ZPP levels were measured on a subsample of the current participants in the study to obtain information on long-term Pb exposure. The results of this analysis are presented in Figure 4, which compares the maternal PbB levels (Figure 4A), maternal ZPP levels (Figure 4B), and PbM concentrations (Figure 4C). The comparative analysis illustrates trends showing an overall decline in maternal PbB, ZPP and PbM from 2006 to 2013.

As, Cd, and Hg concentrations in Breast Milk of Lactating Andean Mothers

Table 1 shows the means and percentiles for the concentrations of 4 toxic metals, Pb, As, Cd and Hg, in the breast milk of a subset of nursing mothers living in the study area. The toxic

metal concentrations in the breast milk of the Ecuadorian nursing mothers were compared to median PbM levels obtained in 6 countries (Guatemala, Hungary, Nigeria, Philippines, Sweden, and Zaire) by the World Health Organization (WHO)/International Atomic Energy Agency (IAEA) (WHO, 1989; Parr, et al. 1991), and a more recent study of PbM concentration in breastfeeding mothers in Sweden (Björklund et al. 2012). In the present study, Spearman *rho* correlation analyses showed no significant associations with Pb concentrations and levels of As, Cd and Hg in the breast milk samples.

DISCUSSION

Pb exposure in neonates and infants may induce damage to the developing CNS that leads to neurocognitive impairment. One important source of early Pb exposure in children is from the milk of breastfeeding mothers who are Pb-exposed. The present study investigated the concentrations of Pb in the breast milk and blood of nursing mothers living in Andean communities with a history of environmental Pb contamination from a local Pb-glazing cottage industry. Previous investigations (Counter, et al. 2004, 2007) in the study area found high levels of Pb in the milk of lactating mothers that correlated with maternal PbB levels, as well as elevated PbB levels in their infants. The present study also revealed a significantly high association between PbM and PbB concentrations in the current group of nursing mothers. These findings suggest that for the current group, maternal PbB level is a reasonably good predictor of PbM. Some studies showed an association between maternal age and PbM, suggesting that age may be a useful predictor of PbM (Silbergeld, 1991). However, the results of the present study found that there was no significant age effect on the PbM levels, indicating that Pb exposure was similar for younger and older nursing mothers in the Pb-contaminated study area. Also, there was no significant correlation of maternal age with PbB level.

The results of the present study showed that the current concentrations of Pb in the milk, as well as blood, of Andean nursing mothers living in the Pb-contaminated study area have declined significantly over the years. There was also a declining trend in ZPP concentration, indicating that not only has acute Pb exposure declined in the study area, but longer term Pb exposure has as well. The wide range of Pb levels observed in the milk of the breastfeeding mothers may be the result of several variables. These include the degree and frequency of the mothers' involvement in the occupational Pb-glazing process, proximity to Pb-glazing kilns that produce large volumes of Pb-contaminated smoke, varying exposure to Pb-contaminated dust within the household, and variable consumption of Pb-contaminated foods. Individual susceptibility to Pb toxicity should also be considered as a factor in the wide range of PbM levels.

Some studies have reported a PbM/PbB ratio, or relative transfer rate, of approximately 3% or less, suggesting a low transfer rate between maternal blood and breast milk (Gulson, et al. 1998, 2003; Choi et al. 2008; Koyashiki et al. 2010). The breastfeeding women in the current cohort displayed an average PbM/PbB ratio of 3.6% when one outlier was removed from the data calculation, which is in general agreement with some previous studies (Ettinger et al. 2010). These data further suggest that the PbM/PbB transfer capacity in the current group of nursing mothers living at high altitude in the Ecuadorian Andes Mountains

is similar to those residing at sea level in some other countries. It should be noted however, that the PbM levels obtained in the current group of Ecuadorian breastfeeding mothers are higher than the background PbM levels obtained from nursing mothers in other countries, except for China, indicating that Pb exposure in these Andean pregnant women and breastfeeding mothers, and their infants needs to be continually monitored. Pb exposure monitoring is also indicated by the fact that the women reside in a Pb-contaminated environment, and some continue to engage in Pb-glazing activities as a means of livelihood.

Breastfeeding is a recognized source of postnatal Pb exposure, and may contribute to pediatric Pb poisoning during a critical or vulnerable period of development that can lead to adverse neurodevelopmental outcomes (Lanphear, et al. 2005; ATSDR 2007; Ettinger et al. 2010). Breastfeeding may also be a pathway for maternal and infant exposure to other toxic metals such as As, Cd and Hg, particularly in the study area where discarded utility and automotive batteries containing these metals are used in the ceramic Pb-glazing process. However, the concentrations of these toxic metals in the breast milk of lactating mothers in the present study were found to be similar to the background levels obtained recently in a study of Swedish mothers (Björklund et al. 2012).

Breastfeeding is important for the infant's nutritional status, and for mother-infant bonding. Further, breastfeeding provides protection against some infectious diseases, such as acute respiratory infections or diarrhea, and reduces neonatal mortality (WHO, 2000). Thus, a clinical decision to recommend that a mother ceases breastfeeding based on PbB or PbM concentrations should be considered carefully. The U.S. CDC guidelines indicate that if the mother's PbB level is $> 40 \mu\text{g/dl}$, it is recommended that the mother pump and discard her milk (Ettinger et al. 2010). However, the U.S. CDC guidelines also indicate that this recommendation may not be appropriate for breastfeeding mothers in some developing countries where there is a high prevalence of infectious diseases.

The decline in PbM levels observed for the current group of Ecuadorian nursing mothers is consistent with an overall decline in Pb exposure of children and adults in the study area (Ortega et al. 2013a, 2013b) and may be attributed to a Pb-exposure education and prevention program that was initiated years earlier in the study area (Counter et al. 1997, 2000), as well as improvements in healthcare delivery in the study area. During the past 5 years, the Ministry of Public Health in Ecuador developed a series of health initiatives, including the construction of a new infirmary in La Victoria, and an increase in the medical staff and auxiliary healthcare personnel. Since 1995, the healthcare personnel in the La Victoria study area has increased from one auxiliary (practical) nurse to two registered nurses, two physicians and one dentist. In addition to providing medical care in the clinic, the new medical personnel also visit households of the villagers periodically to deliver healthcare and engage in health education, including Pb exposure prevention.

In conclusion, the current study showed a significant reduction in PbM in Ecuadorian Andean breastfeeding mothers compared to nursing mothers examined in the same environmentally Pb-contaminated villages in earlier years. The decrease in PbM corresponds to a decline in maternal PbB levels in the study group. The overall reduction in the concentration of Pb in the breast milk and blood of the lactating Andean mothers may be

attributable in part to a Pb-exposure education and prevention program initiated years earlier, and to recent improvements in healthcare delivery in the study area. The decline in PbM levels of breastfeeding mothers in the current cohort notwithstanding, the observations of elevated PbM concentrations in some of the lactating mothers in the study group indicate that pregnant and breastfeeding women and their infants residing in the environmentally Pb-contaminated study area are still at risk, and need to be examined periodically for Pb exposure.

Acknowledgments

The authors thank Universidad San Francisco de Quito Colegio Ciencias de la Salud, Escuela de Medicina in Quito, Ecuador for continued support of the Ecuadorian Lead and Mercury Exposure Project. We thank Dr. Gonzalo Mantilla, Dean of Colegio Ciencias de la Salud, Escuela de Medicina, Universidad San Francisco de Quito for ongoing support and advice. We thank nurse Gladys Pacheco of the Subcentro de Salud, La Victoria, Ecuador for assistance. We also thank Rosa Mercedes Cruz, auxiliary nurse; Fabiola Herrera, Erika Herrera and Jenny Bonifaz, healthcare providers at La Victoria Subcentro de Salud. We are grateful to Anthony B. Jacobs for excellent technical assistance. The authors thank the David Rockefeller Center for Latin American Studies at Harvard University for support of this project. We are thankful for the support of Dr. Jeremy Bloxham, Dean of Science at Harvard University; Boston Children's Hospital, Department of Laboratory Medicine; Mr. John Butz and associates at Mayo Medical Laboratories in Rochester MN; Harvard Biological Laboratories/MCB; Harvard University Health Services; and the Eunice Kennedy Shriver Center/University of Massachusetts Medical School. LHB is supported in part by NIH grant P30 HD04147.

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Figure 1.

Box plots comparing previous maternal blood lead (PbB) levels (obtained between 1999-2007) with current PbB levels (obtained in 2012 and 2013) (Figure 1A), and previous breast milk lead (PbM) with current PbM (Figure 1B). The boxes contain individual PbB levels between the 25th and 75th percentiles. The horizontal lines inside the boxes represent the 50th percentile (median). The small horizontal lines above the boxes represent the 90th percentile, and the small horizontal lines below the boxes represent the 10th percentile. The individual data points represent cases above the 90th percentile and below the 10th percentile.

Figure 2.

Comparison of mean lead (Pb) levels in breast milk (PbM) of nursing mothers living in the Pb-contaminated Ecuadorian Andean study area and mean PbM values reported for other countries. Ecu-1: Ecuador Previous PbM data obtained between 1999-2007; Ecu-2: Ecuador Current PbM data obtained in 2012 and 2013; Aus: Austria (Gundacker et al. 2002); Bra: Brazil (Koyashiki et al. 2010); Can: Canada (Dabeka et al. 1986); Chi: China (Li et al. 2000); Mex: Mexico (Ettinger et al. 2006); Swe: Sweden (Björklund et al. 2012); USA: United States (Rockway et al. 1984).

Figure 3. Correlation analysis showing the relation between lead in maternal breast milk (PbM) and lead in maternal blood (PbB). Spearman *rho* correlation coefficient shows a correlation of 0.687.

Figure 4.

Bar graphs comparing trends in maternal blood lead levels (PbB) (Figure 4A), zinc protoporphyrin levels (ZPP) (Figure 4B), and lead concentrations in breast milk (PbM) (Figure 4C). The trends show an overall decline in maternal PbB, ZPP and PbM from 2006 to 2013 in the study area.

Table 1

Means (standard deviations in parentheses) and Percentiles for Lead (Pb), Arsenic (As), Cadmium (Cd) and Mercury (Hg) in Breast Milk of Nursing Andean Mothers.

	Pb (µg/l) (n = 22)	As (µg/l) (n = 18)	Cd (µg/l) (n = 18)	Hg (µg/l) (n = 22)
Mean	3.73 (7.29)	.896 (1.04)	.025 (0.020)	.208 (0.240)
10th Percentile	0.240	0.0	0.0	0.012
25th Percentile	0.401	0.0	0.004	0.064
50th Percentile	0.804	0.311	0.022	0.125
75th Percentile	3.25	1.88	0.043	0.333
90th Percentile	11.11	2.43	0.050	0.432
WHO/IAEA (WHO, 1989; Parr et al., 1991) <i>Median Levels</i>	2-5	0.2-0.6	<1	1.4-1.7
Björklund et al. (2012) <i>Median Levels</i>	1.2	0.33	0.075	0.14 [*]

WHO/IAEA (World Health Organization/International Atomic Energy Agency) results from a multinational study of minor and trace elements in breast milk from women, which was initiated in 1973 and published in 1989 and 1991. Björklund et al. (2012) data represent recent background toxic metal concentrations in the breast milk of Swedish women.

* From Björnberg et al. (2005).