Childhood blood lead levels and environmental risk factors in Madagascar

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Abstract
One-third of children globally have blood lead levels (BLLs) exceeding the (former) US CDC reference value of 5 µg/dL; this value may be as high as one-half for children in low- and middle-income countries (LMICs). Lead exposure occurs through a variety of routes (e.g., water, dust, air), and in LMICs specifically, informal economies (e.g., battery recycling) can drive lead exposures due, in part, to absent regulation. Previous work by our team identified a ubiquitous source of lead (Pb), in the form of Pb-containing components used in manually operated pumps, in Toamasina, Madagascar. Characterization of BLLs of children exposed to this drinking water, and identification of additional exposure routes were needed. BLLs were measured for 362 children (aged 6 months to 6 years) in parallel with surveying to assess 14 risk factors related to demographics/socioeconomics, diet, use of pitcher pumps, and parental occupations. BLL data were also compared against a recent meta-review of BLLs for LMICs. Median childhood BLL (7.1 µg/dL) was consistent with those of other Sub-Saharan African LMICs (6.8 µg/dL) and generally higher than LMICs in other continents. Risk factors significantly associated \((p < 0.05,\) univariate logistic regression) with elevated BLL (at \(\geq 5 \mu g/dL\)) included male gender, living near a railway or major roadway (owing potentially to legacy lead pollution), having lower-cost flooring, daily consumption of foods (beans, vegetables, rice) commonly cooked in recycled aluminum pots (a previously identified lead source for this community), and a maternal occupation (laundry-person) associated with lower socioeconomic status (SES). Findings were similar at the \(\geq 10 \mu g/dL\) BLL status. Our methods and findings may be appropriate in identifying and reducing lead exposures for children in other urbanizing cities, particularly in Sub-Saharan Africa, where lead exposure routes are complex and varied owing to informal economics and substantial legacy pollution.

Keywords Childhood lead exposure · Risk assessment · Low- and middle-income countries (LMICs) · Global south

Introduction
An estimated 815 million children globally have blood lead levels (BLLs) exceeding the (former) U.S. Centers for Disease Control and Prevention (CDC) reference value of 5 µg/dL (Pure Earth 2020, U.S. Centers for Disease Control and Prevention 2020a). Elevated BLLs place children at risk of long-term effects including damage to the brain and nervous system, slowed development, and learning and behavior problems (U.S. Centers for Disease Control and Prevention 2020b, World Health Organization 2019). The majority of children globally with elevated BLLs reside in low- and middle-income countries (LMICs). A recent literature review of BLL data in LMICs determined “background” (i.e., non-exposed in terms of occupation or nearby
point sources) country-level mean childhood BLLs to range between 1.7 and 9.3 µg/dL globally, and that 49% of children in these countries have BLLs exceeding 5 µg/dL (Ericson et al. 2021). Therefore, childhood lead exposure is a leading concern threatening global progress.

Typical routes for lead exposure include leaded paint, plumbing, food, and medicine (Agency for Toxic Substances and Disease Registry 2020). The youngest populations are considered to be both the most vulnerable and susceptible to lead poisoning given their behavior (e.g., hand-to-mouth, outdoor play) and developing neurological system (World Health Organization 2010). Additional exposure routes specific to children in LMICs include the more recent phasing-out of leaded gasoline (as opposed to phaseouts occurring in the 1970s and 1980s, resulting in higher dust and soil lead concentrations) and poorly regulated, highly emitting informal industries (e.g., battery recycling) (Buerc et al. 2021; Street et al. 2020). Communities are thus often exposed, simultaneously, to multiple lead sources. Malnutrition (Mahaffey 1995; Kordas 2017), limited awareness of the deleterious effects of lead (Williams et al. 2021), and reduced access to health screening and treatment (Wagner et al. 2011) further compound the issue.

Madagascar, located off the coast of East Africa, is one of the world’s least developed countries, ranking 222 of 232 in terms of gross domestic product purchasing power parity (World Bank 2021a) and with more than 80% of its population living in extreme poverty (UNICEF 2017). The country ranks 164 out of 189 according to the 2020 Human Development Index (United Nations Development Programme 2022). Pollution of air, water, and soil are leading health risk factors in Madagascar, resulting in an estimated US$117–166 million in lost productivity annually (Global Alliance on Health and Pollution 2018). In coastal Madagascar, centrally treated or piped “utility” water is out of reach for many, and the use of locally manufactured tube wells and hand pumps (“pitcher pumps”) is common (MacCarthy et al. 2013). These pumps employ two valves using components typically manufactured with lead sourced from used lead-acid batteries (ULABs). Our previous work determined the self-supply market for pitcher pumps here to be a robust model for supply of water (MacCarthy et al. 2013), but that levels of lead in the pumped water exceed WHO drinking water guidelines in many circumstances (Akers et al. 2015, 2019).

Therefore, the objectives of the present study are to (i) characterize BLLs in Toamasina, Madagascar, (ii) identify potential environmental risk factors, (iii) relate the measured BLL data to existing LMIC datasets, and (iv) provide guidance for similar urbanizing areas with disperse lead sources. This study is unique in that it characterizes childhood BLLs in a “typical” community as opposed to a higher risk population (e.g., mining communities, neighborhoods next to battery recycling facilities) (Haefliger et al. 2009; Dooyema et al. 2012; Amin Chowdhury et al. 2021). Additionally, the location is a rapidly urbanizing city in Sub-Saharan Africa, representative of the urbanization occurring throughout other LMICs, especially within the African continent.

Methods

The location of this study is Toamasina (Tamatave), the chief seaport of Madagascar. The city has undergone rapid urbanization in the past few decades, and faces issues common among other rapidly urbanizing areas including lack of reliable and affordable drinking water supply (MacCarthy et al. 2013) and informal/unregulated industries that can drive dispersed pollution that results in high exposures (Buerc et al. 2021). Socioeconomic data is limited for Toamasina, but an estimated 97% of households are classified as “poor”, and the International Wealth Index value (a metric representing material ownership that generally related to health outcomes) is 33 out of 100 (Global Data Lab 2020). Despite recent urbanization, poverty rates in the area have remained “nearly flat” for decades (International Monetary Fund 2017). Toamasina represents a typical urban/peri-urban setting in the nation of Madagascar.

Sample size calculation

The estimated sample size for the study (n = 367) was based on the 2009 population of Toamasina (the most recent available from the national statistics bureau) (N≈233,000) (INSTAT 2009), a confidence interval of 95%, and a hypothesized prevalence of BLL > 5 µg/dL of 34.4% in the region, based on previous BLL modeling efforts (National Institute of Standards and Technology 2012, Kadam and Bhalerao 2010).

Study recruitment

Study participants were recruited from nine local health clinics (consisting of public and private clinics and a biomedical center, and accounting for all health facilities in the target community) dispersed throughout the five city districts (or arrondissements) following a cluster sampling approach. Most families in Toamasina utilize these clinics, and recruitment was intended to capture a representative sample of the city population; the aim of this paper was not necessarily to reach families from lower SES, but rather to broadly characterize the emerging issue of lead exposure in this community. We relied upon the local organizational structure (e.g., annual identification of indigents for access to care) (Honda and Hanson 2013), as well as conversations with community partners, to determine that
use of these clinics provides an important avenue to reach the larger Toamasina population. While visiting a clinic, potential adult participants were referred to a trained team member if their child was between the age of 6 months and 6 years. Following a description of the research and signed consent, the participant and their child were enrolled in the study. Recruitment aimed to represent the population from each of the five districts.

Collection and determination of blood lead levels

Blood samples were collected and measured for lead level by local Malagasy public health officials using the LeadCare II instrument (Meridian Bioscience, Cincinnati, OH) at the local health clinics between September and December of 2020; note that our test kits were unaffected by the 2021 FDA recall (U.S. Food and Drug Administration 2021). Health officials were trained by the study team in the use of the instrument and followed manufacturer quality assurance/control (QA/QC) guidelines. In brief, the child’s finger was carefully cleaned with soap and water, wiped with alcohol, and lanced. The first drop of blood was wiped away, and 50 µL of blood was collected into a capillary tube. The blood was added to the reagent tube, and a sensor from the appropriate lot number (corresponding to a specific QA/QC batch) was inserted into the machine. Finally, a dropper was used to place the lysed blood from the treatment/reagent tube onto the sensor and the BLL reading recorded.

The operating range of the LeadCare II is 3.3–65 µg/dL. Values below the detection limit (DL) were imputed as the lower DL/√2 (i.e., 2.33 µg/dL), consistent with previous studies (Desai et al. 2020), while those above were assumed to be the upper DL itself (65 µg/dL). In total, 16% of our BLL data were at or below detection and imputed, while only one data point (<1%) required imputation for exceedance of the instrument’s upper DL. The LeadCare II instrument can be sensitive to operating temperature and relative humidity (Magellan Diagnostics 2021), with high temperatures (exceeding 27 °C) potentially resulting in readings biased high due to sample evaporation (Neri et al. 2014), and high relative humidity (exceeding 80%) resulting in lower (i.e., more conservative) readings (Personal communication, February 11, 2021); the relative effect of these conditions in relation to one another is unclear. Using historic daily weather data (Weather Underground 2021), 4.4% and 20% of sampling days, respectively, had average temperature and relative humidity readings with levels exceeding the manufacturer’s recommendations; a Wilcoxon test found no significant difference in BLLs (p = 0.88) between the “normal” and “high” relative humidity groups.

Environmental scan survey

An environmental scan survey was administered in the local language (Malagasy) by local health officials and project personnel to the consenting adult present with the child (typically a mother) in combination with the aforementioned BLL testing. The English version of this survey is presented in the Appendix Section A1 and was based on past efforts to relate risk factors to childhood BLLs (Sun et al. 2018) but modified for the local context. The survey included 14 questions pertaining to demographics, SES, diet, habits, and potential exposure routes. Environmental scan data were collected at the clinic, transported to the local project partner’s office, and then inputted into an online application for review.

Geospatial analyses

Geospatial analyses were conducted to relate pump location (as a proxy for home location) to railways and major roadways using ArcMap (v10.8.1); note that “community-scale” water pumps are uncommon here, and most households have a single pump within their property. A total of 197 BLL readings were associated to 175 pump locations; these pumps are located nearby the home. Railroads were identified using default base maps provided in the ArcMap database. Major roadways were identified by our study team living in Toamasina (in addition to national roads typically mapped). Based on previous studies of lead in air and soil (Smith 1976; Maxwell and Nelson 1978; Jian-Hua et al. 2009; Stojic et al. 2017), buffer zones of 400 m and 200 m were defined for railways and major roadways, respectively.

Data processing and statistics

Blood lead level and environmental scan data were entered and verified in Microsoft Excel. Survey data were post-processed and coded in R (R Core and TEAM 2020). BLL data were lognormally distributed (i.e., natural log transformations yielded normal distributions) (Shapiro–Wilk test, p < 0.001). Descriptive statistics were calculated for BLL data and included geometric mean and standard deviation (both considered to be more appropriate than their arithmetic counterparts for these lognormal data). Additionally, Wilcoxon rank-sum tests were conducted between response groups (e.g., “Child usually eats beans on daily basis” vs. counterfactual) to determine significant differences, here defined as p < 0.05. The Wilcoxon rank-sum test was employed here for two reasons: (1) non-normal distribution of BLL data, and (2) many survey questions were open-ended, allowing for multiple responses (e.g., numerous foods consumed daily, multiple maternal/paternal occupations owing to nature of informal economy).
Finally, adjusted ORs were determined using a multiple logistic regression model (Eq. (1)) that included significant factors (i.e., those with significant crude ORs, defined as \( p < 0.05 \), using univariate logistic regression). Note that categories of variables with fewer than 5 observations (i.e., at or below \( \leq 1\% \) of study population size) were excluded from discussions on statistical significance, including tabulation and reporting of odds ratios. Single-response questions/factors included all factor levels in the calculation of adjusted ORs, while multiple-response questions (i.e., those without a “reference” level) included only the significant levels as model terms.

\[
\ln \left( \frac{\hat{p}}{1-\hat{p}} \right) = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_4X_4 + b_5X_5 + b_6X_6 + b_7X_7 + b_8X_8 + b_9X_9
\]

(1)

Where:

- \( \hat{p} \) expected probability that outcome is present (i.e., elevated BLL status at 5 µg/dL)
- \( b_0 \) model intercept
- \( b_1 \) through \( b_9 \) estimated regression coefficients for model terms defined below
- \( X_1 \) through \( X_9 \) predictor variables (i.e., model terms), in order: (1) gender, (2) living within 400 m of a railway, (3) living within 200 m of a major roadway, (4) home flooring type, daily diet term of (5) beans, (6) vegetables, (7) rice, or (8) baby food, and (9) maternal occupation of laundry-person.

**IRB approval**

The study was approved by the Ministry of Public Health General Secretariat of the Medicines Agency of Madagascar (#051-MSANP/SG/AGMED/CERBM) and the University of South Florida Institutional Review Board (IRB #000143) prior to field sampling.

**Results**

**Study demographics**

A total of 362 children aged 6 months to 6 years took part in the study. Clinic and household water pump locations are illustrated in Figure A1 of the Appendix. Mean (SD) age was 2.6 (1.7) years; 50.3% were male and 49.7% female. Regarding household flooring, 68% of children lived in homes with cement, 21% wood, 9.1% tile, and 5.0% bamboo. For household fuel, 90% used charcoal, 17% used wood, 3.0% used induction (i.e., electric and requiring specialized cooking.
pot), and 1.9% used bottled propane (or liquified petroleum gas, LPG). Every home in this study used an aluminum pot to cook. There has been a ban on export of aluminum pots from Madagascar to Réunion Island since 2019 due to high lead content (ranging between 3 and 4600 times the guideline) from the recycled metals used in production and repair of the pots (Imax Press Réunion 2019); recycled aluminum pots are an established lead exposure route in the global south (Weidenhamer et al. 2017). Only one child (0.3%) lived in a home also using glazed ceramics to cook. Tables 1 and 2 present descriptive statistics and results of the Wilcoxon test for those risk factors identified by the survey (for single and open-ended responses, respectively).

Blood lead levels in a global context

The geometric mean BLL (geo-SD) in our study was 6.9 (2.0) µg/dL. The median BLL was 7.1 µg/dL, exceeding that of both Sub-Saharan Africa LMICs (6.8 µg/dL, n = 6 countries) and global LMICs (5.5 µg/dL, n = 10 countries) for the same age range (≤6 years; Table A1). Specific to Sub-Saharan LMICs, median and geomean values for the present study exceeded “pooled” mean values (i.e., those estimated to be representative of each country’s population, and typically approximating a geomean) for half of the countries with available data (i.e., 3 of 6, or the 50th percentile), and was lower than Cameroon (8.7 µg/dL), Democratic Republic of Congo (8.2 µg/dL), and Nigeria (7.7 µg/dL).

Compared to global LMICs, our data ranked higher than most, but lower than Pakistan (11.4 µg/dL) and Palestine (10.4 µg/dL). Median country-wise pooled means for other World Bank-defined regions were 10.4 (n = 2) (Middle East & North Africa), 6.6 (n = 4) (South Asia), 4.9 (n = 2) (East Asia & Pacific), 3.3 (n = 2) (Latin America & Caribbean), and 2.3 µg/dL (n = 2) (Europe & Central Asia). Regarding income groups, low-income countries had the highest median BLL at the 0–6-year age range (7.1 µg/dL, n = 2), matching that of the present study for the same age group (7.1 µg/dL). Lower-middle and upper-middle income countries had lower median BLLs of 6.7 (n = 7) and 3.6 µg/dL (n = 7), respectively.

Environmental risk factors and elevated BLL status

Tables 3 and 4 report crude odds ratios using the dichotomous BLL status at ≥5 µg/dL. Responses with statistically significant (p < 0.05) crude ORs related to elevated BLL status at ≥5 µg/dL were: male gender (OR: 1.57), living within 400 m of a railway (OR: 2.80), living within 200 m of a major roadway (OR: 3.25), having bamboo flooring (OR:

| Exposure variable                              | Category           | n a | Geomean (µg/dL) | Geo SD (µg/dL) | p-value Wilcoxon |
|-----------------------------------------------|--------------------|-----|----------------|---------------|------------------|
| Gender                                        | Male               | 182 | 7.3            | 2.0           | 0.12             |
|                                               | Female             | 180 | 6.6            | 2.0           |                  |
| BMI                                           | > 85th percentile  | 53  | 6.1            | 2.2           | 0.16             |
|                                               | < 85th percentile  | 296 | 7.2            | 2.0           |                  |
| Does child have the habit of washing hands?   | Yes                | 11  | 6.9            | 1.7           | 0.96             |
|                                               | No                 | 350 | 6.9            | 2.0           |                  |
| Do you live near the railway?                 | Within 400 m       | 33  | 8.1            | 1.7           | 0.13             |
|                                               | Not within 400 m   | 164 | 6.7            | 2.0           |                  |
| Do you live near a major road?                | Within 200 m       | 29  | 8.7            | 1.8           | 0.05             |
|                                               | Not within 200 m   | 168 | 6.6            | 2.0           |                  |
| Are you breastfeeding?                        | Yes                | 152 | 6.6            | 2.1           | 0.36             |
|                                               | No                 | 210 | 7.2            | 1.9           |                  |
| Do you use the pitcher pump for drinking/cooking? | Water only       | 10  | 8.1            | 2.2           | 0.70             |
|                                               | Neither            | 89  | 7.1            | 2.0           | 0.88             |
|                                               | Water and food     | 211 | 7.0            | 1.9           | 0.46             |
|                                               | Food Only          | 44  | 6.2            | 2.3           | 0.27             |
| What type of floor does your house have?     | Wood               | 74  | 7.4            | 1.9           | 0.25             |
|                                               | Cement             | 237 | 7.1            | 2.0           | 0.52             |
|                                               | Bamboo             | 18  | 6.9            | 1.7           | 0.85             |
|                                               | Tile               | 33  | 5.3            | 2.0           | 0.01             |

*aNote that sums of responses for a given factor may not equal the study sample size (n = 362) due to either missing survey data, or for the geospatial analyses, lack of associated pump (and therefore location) information
Table 2 Descriptive statistics of environmental risk factors identified by survey (open-ended response). Bold values are those identified as significant ($p<0.05$) by the Wilcoxon rank-sum test.

| Exposure variable | Category                      | $n$ | Geomean (µg/dL) | Geo SD (µg/dL) | $p$-value Wilcoxon |
|-------------------|-------------------------------|-----|-----------------|---------------|--------------------|
| Where does the child spend most of their time? | Shop                          | 7   | 10.8            | 2.4           | 0.09               |
|                   | **Family**                    | **129** | **7.6**       | **1.9**      | **0.02**          |
|                   | Outside                       | 269 | 7.0             | 2.0           | 0.55               |
|                   | School                         | 128 | 7.0             | 2.0           | 0.93               |
|                   | House                          | 347 | 6.9             | 2.0           | 0.82               |
| What does your child usually eat on a daily basis? | **Beans**                     | **40** | **9.3**       | **1.7**      | **0.00**          |
|                   | Fruit                          | 104 | 7.8             | 2.1           | **0.01**          |
|                   | Pasta                          | 27  | 7.8             | 1.9           | 0.28               |
|                   | **Vegetables**                 | **186** | **7.7**       | **2.0**      | **0.00**          |
|                   | Meat/fish                      | 124 | 7.5             | 2.0           | 0.08               |
|                   | **Rice**                       | **297** | **7.3**       | **2.0**      | **0.00**          |
|                   | Bread                          | 67  | 7.0             | 2.2           | 0.98               |
|                   | Soup                           | 17  | 6.4             | 2.4           | 0.38               |
|                   | Dairy/eggs                     | 59  | 6.1             | 1.9           | 0.14               |
|                   | **Baby food**                  | **22** | **5.3**       | **2.0**      | **0.01**          |
| What does your child usually drink on a daily basis? | Tap water                     | 108 | 7.4             | 2.2           | 0.41               |
|                   | Tea                            | 220 | 7.1             | 1.9           | 0.19               |
|                   | Bottled water                  | 14  | 7.1             | 1.9           | 0.97               |
|                   | Milk                           | 9   | 6.4             | 2.2           | 0.64               |
|                   | Pitcher pump                   | 11  | 6.0             | 1.9           | 0.29               |
|                   | Boiled water                   | 19  | 5.7             | 2.4           | 0.23               |
| Household fuel?   | Charcoal                       | 325 | 7.0             | 2.0           | 0.94               |
|                   | Wood                           | 63  | 6.1             | 1.9           | 0.20               |
|                   | Induction                      | 11  | 5.9             | 1.4           | 0.41               |
|                   | Natural gas                    | 7   | 5.1             | 1.9           | 0.25               |
| Have there been infrastructural changes in your home surroundings within last 6 months? | Furniture/sawmill | 23  | 7.5             | 1.8           | 0.69               |
|                   | Smelter/welding/aluminum pot   | 16  | 7.5             | 1.9           | 0.57               |
|                   | Car/posy/moto/bicycle repair   | 21  | 5.8             | 2.1           | 0.28               |
|                   | House built                    | 10  | 4.9             | 1.8           | 0.15               |
| Father’s occupation? | **Metal seeker/worker**       | **8** | **15.5**      | **2.1**      | **0.00**          |
|                   | **Plumber/pump technician**    | **6** | **12.7**      | **2.5**      | **0.03**          |
|                   | Gardener/fertilizer/farmer     | 7   | 10.0            | 2.3           | 0.28               |
|                   | Gas pump attendant             | 5   | 7.3             | 2.0           | 0.88               |
|                   | Tour guide/driver              | 56  | 7.2             | 2.0           | 0.68               |
|                   | Port worker/fisherman          | 18  | 7.2             | 2.2           | 0.66               |
|                   | Manager/secretary/accountant/office | 15  | 6.8             | 2.6           | 0.74               |
|                   | Mechanic                       | 13  | 6.8             | 2.3           | 0.67               |
|                   | Police                         | 42  | 6.8             | 2.1           | 0.77               |
|                   | Painter                        | 5   | 6.8             | 1.2           | 0.87               |
|                   | Builder/mason                  | 32  | 6.5             | 2.0           | 0.62               |
|                   | Seller                         | 38  | 6.4             | 1.9           | 0.71               |
|                   | Welder                         | 11  | 6.4             | 1.8           | 0.65               |
|                   | Teacher/student                | 11  | 4.8             | 1.5           | 0.05               |
4.71), daily consumption of beans (OR: 6.58), vegetables (OR: 1.59), and rice (OR: 2.14), and maternal occupation of laundry-person (OR: 4.71). The only protective response identified (i.e., significant crude OR < 1.0) at the BLL status of ≥ 5 µg/dL was daily consumption of baby food (here, a fortified porridge distributed by a local NGO) (OR: 0.24).

Tables A2 and A3 of the Appendix report crude odds ratios using the dichotomous BLL status at 10 µg/dL. Responses with statistically significant (p < 0.05) crude ORs related to elevated BLL status at ≥ 10 µg/dL included: living within 200 m of a major roadway (OR: 2.30), daily consumption of fruit (OR: 1.64), meat/fish (OR: 1.63), or rice (OR: 2.71), paternal occupation of metal worker/seeker (OR: 8.42), and maternal occupation of laundry-person (OR: 3.16). Therefore, living within 200 m of a major roadway, daily consumption of rice, and maternal occupation of laundry-person were the factors significantly associated with elevated BLL status at both ≥ 5 and ≥ 10 µg/dL. Differences in risk factors identified between the two BLL statuses occur due to variation in BLL distributions at said statuses.

Table 5 summarizes adjusted ORs as estimated by the multiple logistic regression analysis, controlling for gender, living near either the railway or a major roadway, home flooring type, daily diet terms, and maternal occupation. The only factor identified as having a significant adjusted OR at the ≥ 5 µg/dL threshold was daily consumption of vegetables (OR: 2.66). Table A4 reports adjusted ORs at the ≥ 10 µg/dL threshold and using the model described by Eq. (A1) (section A3 of the Appendix). Four factors were identified as having significant adjusted ORs at the ≥ 10 µg/dL status: living near a major roadway (OR: 4.06), daily consumption of meat/fish (OR: 2.25), paternal occupation of metal seeker/worker (OR: 24.74) and maternal occupation of laundry-person (OR: 11.39). Note that the relatively high adjusted ORs as related to occupational terms were also associated with large confidence intervals about the point estimates,
owing in part to limited sample size and high variability of BLL data associated with those factors.

**Discussion**

Observed BLLs in the present study are slightly higher than those of other "non-exposed" children in Sub-Saharan LMICs, and generally higher than global LMICs and LMICs in other regions. Our BLL data agree closely with literature data for similar non-exposed/background childhood (0–6 years) populations in low-income countries, and are higher than those groups in more wealthy nations. Therefore, the population studied here may be considered to be representative of that in other urbanizing, low-income areas, especially in Sub-Saharan Africa (e.g., median and geomean data from the present study lie in the 50th percentile of pooled mean data for Sub-Saharan Africa as compiled by Ericson et al. 2021). Additionally, our methods were largely based on childhood lead exposure assessments in other LMICs, and we expect our approach and findings to be representative of numerous other communities with similar socioeconomic and cultural constraints.

Several risk factors were identified by the survey and significantly related to elevated BLL status using crude ORs (here with discussion focusing on ≥ 5 µg/dL unless otherwise noted). Male gender (OR: 1.57) was associated with elevated BLLs as previously observed (Filigrana and Mendez 2012; Morales et al. 2005), owing potentially to distinct behavior patterns that increase exposure (e.g., playing outside more often, pica/geophagy). Living near a railway (OR: 2.80) or major roadway (OR: 3.25) was significantly associated with risk of elevated BLL status; proximity to major roadway was also significantly associated at the 10 µg/dL threshold (OR: 2.30). The more recent (ca. 2005) phase-out of leaded fuel, and an estimated ~15-year half-life of lead in soil (Mielke et al. 2019), suggests that lead contamination of soil is a likely ongoing source of exposure as observed in other LMICs (Pan et al. 2018; Shabanda et al. 2019). Children are especially prone to lead exposure from contaminated soil given their propensity for hand-to-mouth activities. Presence of bamboo flooring (OR: 4.71), as opposed to tile, a metric previously used to identify homes with higher SES (Arias and De Vos 1996), was identified as a significant factor for elevated BLL status. Less expensive flooring (e.g., bamboo here) has been previously related to higher BLLs in Indonesian children (Albalak et al. 2003).

Daily consumption of beans was significantly associated with elevated BLL (OR: 6.58), owing potentially to the ubiquitous use of aluminum pots in this community. The extended cooking time required for this staple compared to foods requiring different preparation (e.g., grilled foods) may result in leaching of lead into solution, especially in acidic solution (e.g., with vinegar) (Weidenhamer et al. 2017); fresh beans (vs. dried) require reduced cooking times, but are more expensive, and so lower SES may in part drive

| Exposure variable | Category | ≥ 5 µg/dL | Crude OR (95% CI) | p-value |
|-------------------|----------|-----------|-------------------|---------|
| Gender            | Male     | 1.57 (1.01–2.46) | 0.05              |
|                   | Female   | 1.00 (ref)     | na                |
| BMI               | > = 85th percentile | 0.57 (0.31–1.05) | 0.07              |
|                   | < 85th percentile | 1.00 (ref)     | na                |
| Does child have the habit of washing hands? | Yes | 0.47 (0.07–1.85) | 0.33              |
|                   | No       | 1.00 (ref)     | na                |
| Do you live near the railway?  | Within 400 m | 2.80 (1.11–8.58) | 0.04              |
|                   | Not within 400 m | 1.00 (ref) | na                |
| Do you live near a major road? | Within 200 m | 3.25 (1.20–11.4) | 0.04              |
|                   | Not within 200 m | 1.00 (ref) | na                |
| Are you breastfeeding? | Yes | 0.71 (0.45–1.10) | 0.13              |
|                   | No       | 1.00 (ref)     | na                |
| Do you use the pitcher pump for drinking/cooking? | Water only | 0.45 (0.12–1.72) | 0.23              |
|                   | Food only | 0.87 (0.41–1.87) | 0.71              |
|                   | Water and food | 1.01 (0.59–1.68) | 0.98              |
|                   | Neither  | 1.00 (ref)     | na                |
| What type of floor does your house have? | Bamboo | 4.71 (1.26–23.15) | 0.03              |
|                   | Cement   | 2.06 (0.98–4.32) | 0.05              |
|                   | Wood     | 2.27 (0.97–5.32) | 0.06              |
|                   | Tile     | 1.00 (ref)     | na                |
Table 4 Summary of crude odds ratios (open-ended response) at ≥ 5 μg/dL status. Bold values are those identified as significant ($p < 0.05$) using univariate logistic regression

| Exposure variable | Category                  | ≥ 5 µg/dL | Crude OR (95% CI) | p-value |
|-------------------|---------------------------|-----------|-------------------|---------|
| Where does the child spend most of their time? | Shop | 2.84 (0.48–53.93) | 0.34 |
|                   | Family | 1.33 (0.83–2.14) | 0.24 |
|                   | Outside | 1.18 (0.71–1.93) | 0.53 |
|                   | School | 1.04 (0.65–1.66) | 0.88 |
|                   | House | 0.52 (0.12–1.69) | 0.33 |
| What does your child usually eat on a daily basis? | Beans | **6.58 (2.31–27.67)** | **0.00** |
|                   | Fruit | 1.58 (0.96–2.67) | 0.08 |
|                   | Pasta | 1.69 (0.70–4.71) | 0.27 |
|                   | **Vegetables** | **1.59 (1.02–2.50)** | **0.04** |
|                   | Meat/fish | 1.45 (0.90–2.36) | 0.13 |
|                   | **Rice** | **2.14 (1.23–3.70)** | **0.01** |
|                   | Bread | 0.87 (0.50–1.54) | 0.62 |
|                   | Soup | 0.65 (0.24–1.84) | 0.40 |
|                   | Dairy/eggs | 0.63 (0.35–1.12) | 0.11 |
|                   | Baby food | **0.24 (0.09–0.58)** | **0.00** |
| What does your child usually drink on a daily basis? | Tap water | 1.23 (0.76–2.03) | 0.41 |
|                   | Tea | 1.17 (0.74–1.83) | 0.50 |
|                   | Bottled water | 1.74 (0.53–7.80) | 0.40 |
|                   | Milk | 0.57 (0.15–2.35) | 0.41 |
|                   | Pitcher pump | 0.55 (0.16–1.94) | 0.33 |
|                   | Boiled water | 0.50 (0.19–1.28) | 0.14 |
| Household fuel? | Charcoal | 0.66 (0.29–1.41) | 0.31 |
|                   | Wood | 1.10 (0.61–2.01) | 0.76 |
|                   | Induction | 2.14 (0.54–14.16) | 0.34 |
|                   | Natural gas | 0.61 (0.13–3.16) | 0.53 |
| Have there been infrastructural changes in your home surroundings within last 6 months? | Furniture/sawmill | 1.34 (0.54–3.81) | 0.55 |
|                   | Smelter/welding/aluminum pot | 2.07 (0.65–9.18) | 0.26 |
|                   | Car/posy/moto/bicycle repair | 0.74 (0.30–1.93) | 0.52 |
|                   | House built | 0.45 (0.12–1.66) | 0.22 |
| Father’s occupation? | Metal seeker/worker | 3.32 (0.58–62.53) | 0.26 |
|                   | Plumber/pump technician | 2.36 (0.37–45.40) | 0.44 |
|                   | Gardener/fertilizer/farmer | 2.84 (0.48–53.93) | 0.34 |
|                   | Gas pump attendant | 0.69 (0.11–5.33) | 0.69 |
|                   | Tour guide/driver | 0.98 (0.54–1.84) | 0.95 |
|                   | Port worker/fisherman | 0.93 (0.35–2.72) | 0.88 |
|                   | Manager/secretary/accountant/office | 0.39 (0.13–1.11) | 0.08 |
|                   | Mechanic | 0.53 (0.17–1.68) | 0.26 |
|                   | Police | 0.92 (0.47–1.87) | 0.82 |
|                   | Painter | 1.88 (0.27–36.93) | 0.58 |
|                   | Builder/mason | 1.03 (0.48–2.34) | 0.95 |
|                   | Seller | 1.34 (0.65–3.00) | 0.45 |
|                   | Welder | 0.55 (0.16–1.94) | 0.33 |
|                   | Teacher/student | 0.55 (0.16–1.94) | 0.33 |
### Table 4 (continued)

| Exposure variable | Category            | Crude OR (95% CI) | p-value |
|-------------------|---------------------|-------------------|---------|
| Father’s job/hobby exposure routes | Valves/fittings | 1.34 (0.54–3.81) | 0.55 |
|                   | Furniture           | 1.41 (0.70–3.02) | 0.36 |
|                   | Welding/smelting    | 0.68 (0.37–1.27) | 0.22 |
|                   | Fishing             | 0.93 (0.32–3.04) | 0.89 |
|                   | Electrical          | 0.82 (0.42–1.64) | 0.56 |
|                   | Building houses     | 0.76 (0.42–1.40) | 0.37 |
|                   | Painting            | 0.74 (0.41–1.35) | 0.32 |
|                   | Radiators           | 0.50 (0.19–1.28) | 0.14 |
|                   | Mechanic            | 0.52 (0.25–1.06) | 0.07 |
|                   | Battery/lead recycling | 0.54 (0.27–1.07) | 0.07 |
|                   | Chemicals           | 0.45 (0.15–1.34) | 0.14 |
|                   | Pipeline            | 0.39 (0.14–1.06) | 0.06 |

| Mother’s occupation | Category            | Adjusted OR (95% CI) | p-value |
|---------------------|---------------------|----------------------|---------|
| Laundry-person      | 4.71 (1.34–29.88)    | 0.04                 |
| Businessperson/manager | 1.17 (0.69–2.05) | 0.57 |
| Housekeeper         | 0.72 (0.46–1.13)    | 0.15                 |
| Dress/matting maker | 2.36 (0.37–45.40)   | 0.44                 |
| Chef/baker          | 2.36 (0.37–45.40)   | 0.44                 |
| Teacher/student/university/worker | 0.65 (0.24–1.84) | 0.40 |
| Health worker/midwife/caregiver | 0.64 (0.20–2.21) | 0.46 |
| Agent/real estate   | 0.23 (0.03–1.18)    | 0.09                 |

| Do you take herbal remedies? | Category | Crude OR (95% CI) | p-value |
|-------------------------------|----------|-------------------|---------|
| Fruit                         | 0.64 (0.10–5.02) | 0.64 |
| Leaves                        | 2.30 (0.98–6.08) | 0.07 |
| Roots                         | 0.75 (0.35–1.54) | 0.44 |
| Bark                          | 0.75 (0.21–2.97) | 0.66 |
| Other                         | 0.67 (0.21–2.34) | 0.51 |

### Table 5 Summary of adjusted odds ratios for exposure variables (factors) included in model with elevated BLL status at ≥ 5 µg/dL

| Exposure variable | Category            | ≥5 µg/dL | Adjusted OR (95% CI) | p-value |
|-------------------|---------------------|---------|----------------------|---------|
| Gender            | Male                | 1.26 (0.66–2.44) | 0.48 |
|                   | Female              | 1.00 (ref)     | na                   |
| Do you live near the railway? | Yes | 1.98 (0.75–5.82) | 0.19 |
|                   | No                  | 1.00 (ref)     | na                   |
| Do you live near a major road? | Yes | 1.74 (0.63–5.27) | 0.30 |
|                   | No                  | 1.00 (ref)     | na                   |
| What type of floor does your house have? | Bamboo | 6.66 (0.76–152.51) | 0.13 |
|                   | Cement              | 1.60 (0.60–4.27) | 0.34 |
|                   | Wood                | 1.76 (0.49–6.51) | 0.39 |
|                   | Tile                | 1.00 (ref)     | na                   |
| What does your child usually eat on a daily basis? | Beans | 4.62 (0.76–90.06) | 0.17 |
|                   | Vegetables          | 2.66 (1.41–5.13) | 0.00 |
|                   | Rice                | 1.59 (0.70–3.63) | 0.27 |
|                   | Baby food           | 0.41 (0.07–2.12) | 0.29 |

| Mother’s occupation | Laundry-person | 0.54 (0.27–1.07) | 0.07 |

*aBold entries signify statistically significant (p<0.05) exposure variables

*bCalculation of odds ratio not possible due to low sample size and high variability in data
exposure through this route. Rice was significantly associated with elevated BLL (OR: 2.14), potentially for this same reason; rice was also significantly associated at the ≥10 µg/dL threshold (OR: 2.71). Though lead may be found in uncooked rice (Ok et al. 2011), no studies have identified this as a source of lead exposure in Madagascar. Lead sorbs to starches such as rice (Sharma et al. 2021), and as the concentration of lead in water increases, the contribution of overall lead exposure owing to consumption of starches increases (Akers et al. 2019). Anecdotally, it is common for there to be a grey/silver residue observed on top of the cooked rice, potentially from the cooking vessel, or from hardness of the water. Export of these cooking pots has been banned from Madagascar to Réunion Island owing to analyses confirming high lead content.

Consumption of vegetables was also significantly associated with elevated BLL status (OR: 1.59). Unwashed vegetables may serve as an ingestion source for lead, especially if sold near highly trafficked areas where lead-contaminated soil and dust may serve as exposure routes, as previously observed in Tanzania (Magoha et al. 2008); vendors in this community typically reside near major roadways. Legacy lead contamination of soil here is plausible as the half-life of lead in soil is on the order of ~15 years (Mielke et al. 2019). Additionally, vegetables may be cooked in a similar manner to beans and rice, therefore likely resulting in lead leaching into the cooked product. Additional diet terms identified as significant at the ≥10 µg/dL threshold included fruit (OR: 1.64) and meat/fish (OR: 1.63). If unwashed, fruit may serve as a similar exposure route as vegetables. Aforementioned results of the geospatial analyses (e.g., distances from railways and major roadways) support the importance of legacy soil contamination from leaded fuel use. Interestingly, consumption of baby food was a protective factor against elevated BLL status (OR: 0.24). Baby food (here, a fortified porridge) is used to supplement breastfeeding for malnourished infants in this community. Additionally, breastfeeding can be a key lead exposure route for infants in LMICs (Lozoff et al. 2009) due to mobilization of bone-stored lead in nursing mothers (Téllez-Rojo et al. 2002); however, our survey data included a question specific to breastfeeding, and found no relationship to elevated BLLs.

Regarding potential occupational or “take-home” exposures (i.e., those associated with occupational exposures but affecting a home environment, an important contributor to lead exposures in LMICs) (Williams et al. 2021), the maternal occupation of laundry-person was significantly related to elevated BLL status (OR: 4.71); the same association was observed at the ≥10 µg/dL threshold as well. This finding may be related to the typically lower SES of this occupation, or potentially to exposures owing to use of local river water for washing; these rivers (e.g., the Pangalan) may contain mining tailing from nearby cobalt–nickel operations.

Lead-laden clothing (associated with some activities within the informal economy) may also drive exposures for these laundry-persons. Additionally, the paternal occupation of metal/seeker (i.e., either someone who finds scrap metal at disposal/construction sites, or who works with metal soldering) was significantly related to elevated BLL status at ≥10 µg/dL (OR: 8.42), owing potentially to exposures to co-produced/recycled materials/metals containing lead (Obeng-Gyasi 2019, Pure Earth 2020) including paint dust (Nduka et al. 2016).

In terms of adjusted ORs (Table 5), only the diet consumption of vegetables (OR: 2.66) was associated with elevated BLL at the ≥5 µg/dL threshold. This finding further supports the hypotheses of cooking vessels (i.e., aluminum pots in this community), and contamination of foods sold by roadside vendors owing to legacy soil contamination by leaded fuel use. At the ≥10 µg/dL threshold (Table A4), living near a major roadway (OR: 4.06), daily consumption of meat/fish (OR: 2.25), paternal occupation of metal/seeker/worker (OR: 24.74), and maternal occupation of laundry-person (OR: 11.39) were associated with elevated BLL. The risk associated with living near a major roadway aligns with legacy soil contamination. The relationship between elevated BLL and the diet term associated with meat/fish is unclear, though previous work has associated higher BLLs with frequent consumption of fish (Birgisdottir et al. 2013). Finally, the occupational terms of metal/seeker/worker and laundry-person may be related to direct exposures and overall lower SES, respectively. Despite the prevalence of lead-containing pitcher pumps in this community, the consumption of pumped drinking water for drinking or cooking (as assessed through survey questions 3–5; Appendix Section A1) was not associated (or “correlated”) with elevated BLL status. The lack of statistical significance here may be due to the lack of power, potential confounding by other risk factors, or due to the open-ended nature of questioning (Q3). This potential source is currently being examined in greater detail by our team, in part through the analysis of paired (pre- and post-intervention) BLL data.

Strengths of the present study include novel measurement of BLLs in Madagascar, one of the world’s least developed nations, as well as use of established statistical approaches to relate BLL data to results of an environmental risk factor survey. Additionally, comparison against recently compiled and published global BLL data allowed for an understanding of BLLs in the target community in the context of other Sub-Saharan African and low-income nations. Finally, we expect our approach and findings to be appropriate for other communities in LMICs, and especially for those under-going rapid urbanization. Limitations of the study included a relatively limited sample size, and the use of a point-of-care vs. reference-grade instrument. We computed the sample size to estimate the prevalence of BLL > 5 µg/dL and not for the
purpose of hypothesis testing. Future work with larger sample sizes is required and may also explore interaction terms (e.g., in terms of daily diet combinations).

In summary, more than two-thirds (68%) of the children in our study were at or above the CDC threshold of 5 µg/dL, higher than the 49% estimated by Ericson and colleagues for children in LMICs with published BLL data. More than one-quarter (27%) were above 10 µg/dL, compared to 32% as estimated by Ericson and colleagues. In addition to the lead-containing hand pumps in the community (which are the focus of another manuscript in preparation by our study team), there likely exist multiple exposure routes including air, soil, food, and those associated with parental occupations and infrastructure near the home. Air quality data are limited in the country, but sampling in Antananarivo in 2007–2008 (the capital city, located 350 km west of Toamasina) determined lead concentrations in PM$_{2.5}$ to be well below the WHO guideline (0.5 µg/m$^3$) following the phase-out of leaded gasoline (Rasoazanany et al. 2012); therefore exposures to lead in the air may be minimal unless there is a source not accounted for in Toamasina (a port-city, and location of a mine tailing storage site).

However, the legacy of leaded fuel in the country likely results in continuous daily exposures via contaminated dust and soil (with relatively long lead contamination half-life), as confirmed by our geospatial analyses. Studies in Sub-Saharan Africa have shown generally lower BLLs (of women) associated with earlier phase-out of leaded gasoline (Bede-Ojimadu et al. 2018). The practice of pica and geophagy observed in some Sub-Saharan African communities, and especially among children (girls in particular), may contribute to elevated lead exposures in these younger populations (Msoffe et al. 2019; Nchito et al. 2004). Regarding ingestion however, the use of recycled aluminum pots for cooking is a likely contributor to lead exposure in this community, where staple foods requiring extended cooking times (e.g., rice) are common (82% of respondents consume rice daily); previous modeling efforts by our team have highlighted the importance of rice consumption in Madagascar as a potential lead exposure route (especially at elevated pump water lead levels) (Akers et al. 2019), and additional work should be conducted to assess contributions of the dietary exposure route in this community.

Finally, nearly half (47%) of Madagascar’s children suffer from chronic malnutrition (US Aid 2018), and more than one-third of adults are anemic. Iron deficiency has been extensively linked to elevated BLLs (Kwong et al. 2004), owing to similar biological pathways of iron and lead. Therefore, nutritional interventions may serve as secondary prevention in this community. However, sources of lead linked to exposed children must be the priority of any intervention here. Proposed lead exposure interventions must occur over extended time periods and involve multiple sectors/approaches (e.g., regulatory, environmental, educational) (Pfadenhauer et al. 2014).

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Author contribution Wyatt M. Champion: Writing – Original Draft, Writing – Review & Editing, Data Curation, Formal Analysis, Validation, Software, Methodology. Adaline M. Buerck: Writing – Review & Editing, Project Administration, Validation. Christopher Nenninger: Writing – Review & Editing, Formal Analysis, Methodology. Korede Yusuf: Writing – Original Draft, Writing – Review & Editing, Supervision, Data Curation, Formal Analysis, Validation, Methodology, Conceptualization. Luke J.P. Barrett: Funding Acquisition, Project Administration, Supervision, Data Curation, Resources, Investigation, Validation, Conceptualization. Lova Rakotaraisoa: Funding Acquisition, Project Administration, Supervision, Data Curation, Investigation, Validation. Rinah Rakotondrazaka: Project Administration, Data Curation, Investigation, Validation. Katherine Alfredo: Writing – Review & Editing, Conceptualization. Jeffrey Cunningham: Funding Acquisition, Writing – Review & Editing, Conceptualization. Mahmooda Khaliq: Writing – Original Draft, Writing – Review & Editing, Funding Acquisition, Project Administration, Supervision, Methodology, Conceptualization. James R. Mihelcic: Writing – Original Draft, Writing – Review & Editing, Funding Acquisition, Project Administration, Supervision, Methodology, Conceptualization.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate The study was approved by the Ministry of Public Health General Secretariat of the Medicines Agency of Madagascar (#051-MSANP/SG/AGMED/CERBM) and the University of South Florida Institutional Review Board (IRB #000143) prior to field sampling. Informed consent was obtained from all individual participants included in the study.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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