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Baseline exposure–response assessment of metals from dried blood spots and personal household air pollution concentrations among pregnant women in Rwanda: household air pollution intervention network trial

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Abstract

Background Exposure to metals from the combustion of biomass via inhalation may result in negative health outcomes affecting a variety of organs and systems. Pregnant women cooking with biomass fuels may be exposed to metals, such as lead (Pb) and cadmium (Cd), and have unique risks for adverse health effects with potential impacts on the growing fetus. We assessed the associations between household air pollution and metals detected in dried blood spots from pregnant women at baseline in Rwanda.

Methods We analyzed data from 781 pregnant women aged 18–35 years who resided in rural households using biomass fuel and who were enrolled in the Household Air Pollution Intervention Network (HAPIN) Trial in Rwanda. We explored associations between 24-h average natural log-transformed personal exposures to fine particulate matter (PM_{2.5}), black carbon (BC), and carbon monoxide (CO) and K + standardized Pb and Cd concentrations using linear regression models adjusted for potential confounders (i.e., age, body mass index, bicycle ownership, fish consumption, and food insecurity).

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Results The adjusted models showed positive but non-significant associations between air pollutant concentrations and metals detected in blood: PM_{2.5} and Pb (β coefficient: 0.06; 95% CI – 0.03–0.15), BC and Pb (0.11; 95% CI – 0.01–0.24), PM_{2.5} and Cd (0.04; 95% CI – 0.02–0.09), and BC with Cd (0.02; 95% CI – 0.05–0.09).

Conclusions While associations were not statistically significant, the directionally consistent increases in blood Pb and Cd with increased PM_{2.5} and BC exposures align with existing evidence and underscore the need for continued research and policy action to reduce household air pollution exposures and protect maternal and fetal health.

Keywords Biomass cookstove, Lead, Cadmium, Dried blood spots, Indoor air pollution, Rwanda

Introduction

Household air pollution is a critical public health issue, particularly in low- and middle-income countries (LMICs) [1]. Approximately 3 billion people worldwide, primarily in LMICs, rely on solid fuels for their daily energy needs [2]. According to the Global Burden of Disease Study 2021, household air pollution from solid fuels affects about 2.67 billion people—roughly one-third of the global population [3]. In 2021, household air pollution was linked to 111 million disability-adjusted life years (DALYs), representing 3.9% of the total global disease burden. The highest impacts were seen in sub-Saharan Africa, where Rwanda is located and South Asia [4].

Lead (Pb) and Cadmium (Cd) are metals that occur naturally in the environment and are in biomass materials, such as wood, which is often burned for household energy needs, such as cooking. When biomass fuels are burned, they can release Pb and Cd into the air, leading to exposure through inhalation [5]. Studies on the associations between exposure to these two metals and health conditions suggest harmful impacts, including cardiovascular diseases [6], as both Pb and Cd have shown to be risk factors for hypertension, coronary artery disease, and other cardiovascular diseases [7]. Biomass burning releases particulate matter containing these metals, which accumulates in the human body and induces oxidative stress and inflammation, leading to endothelial dysfunction and arterial stiffness [8, 9]. Populations relying on biomass fuels for cooking and heating are particularly vulnerable to these health risks due to prolonged exposure to metal-containing smoke [10, 11].

Metal levels in the body change with age due to differences in exposure sources, absorption rates, and cumulative effects [12]. Pregnant women exhibit a heightened susceptibility to environmental exposures due to unique physiological and immunological adaptations during pregnancy. Increased respiratory ventilation [13], modulated immune responses [14], oxidative stress, and altered metabolism [15] can amplify the toxic effects of pollutants and toxicants, making maternal health itself a critical concern not only for fetal development. Emerging literature highlights associations between environmental exposures and maternal outcomes such as gestational diabetes, and systemic inflammation [16, 17].

For example, low levels of exposure to Pb and Cd have been associated with high blood pressure, changes in kidney function, and increased risk of preeclampsia for pregnant women [18–20].

Socioeconomic and demographic characteristics may impact exposure potentials in vulnerable populations in addition to acting conjointly with exposures, leading to increased effects on health and to the central nervous system, specifically [21]. Pb and Cd have no known beneficial roles in the human body, and both pose serious risks during pregnancy. As noted in the literature, Pb can pass through the placenta during pregnancy, leading to fetal exposure to toxic metals [22–24].

Several studies have also shown that certain foods can serve as sources of Pb and Cd exposure due to their capacity to accumulate these metals from contaminated soil, water, or fertilizers [25, 26]. In addition, exposure to secondhand tobacco smoke has been associated with elevated blood levels of Pb and Cd among exposed individuals compared to non-smokers [27]. Therefore, examining dietary items, overall dietary diversity, and secondhand smoke exposure is important for understanding potential pathways of Pb and Cd exposure in the study population.

We aimed to assess the associations between Pb and Cd from dried blood spots and 24-h personal exposure to household air pollution, specifically particulate matter (PM_{2.5}), black carbon (BC), and carbon monoxide (CO), among pregnant women in Rwanda from the baseline visit of the Household Air Pollution Intervention Network Trial (HAPIN), where solid biomass was the primary source of household fuel. According to national data, 80.4% of the population relied on wood or wood-based products for cooking, typically using traditional open stoves in poorly ventilated kitchens (71.9%); [28]. The most commonly used cooking types included traditional three-stone fires (62.6%) and clay brazier stoves (34.6%), fueled primarily by wood (89.9%) or charcoal (8.1%) [29].

Materials and methods

Study site and population

The data from this paper were derived from the HAPIN trial, which has been described in detail elsewhere [30]. In brief, the HAPIN trial was a randomized controlled

trial of the effect of a liquefied petroleum gas cookstove and fuel intervention on exposure to air pollution and health in four rural LMICs. For this analysis, we assessed only the baseline visit as a cross-sectional study design before the intervention was introduced to participants. Personal exposures and Pb and Cd levels were obtained from 781 pregnant women enrolled in the HAPIN trial research site in Rwanda.

To participate in the study, a pregnant woman had to meet the following inclusion criteria: confirmed pregnancy (human chorionic gonadotropin positive blood or urine test); 18 to <35 years of age (confirmed by government-issued ID, whenever possible), cooked primarily with biomass stoves, planned to live in the study area for 12 months following recruitment, 9 to <20 weeks gestation with a viable singleton pregnancy with normal fetal heart rate confirmed by ultrasound, continued pregnancy at the time of randomization (via self-report), and agreed to participate with informed consent. Eligible pregnant women were excluded if they were smoking cigarettes or other tobacco products, planned to move permanently outside the study area in the next 12 months, used a clean fuel stove predominantly, or were likely to use liquefied petroleum gas or another clean fuel predominantly in the near future [30].

Exposure measurements

The HAPIN trial's exposure assessment has been previously described in detail [31]. To summarize, at baseline, PM_{2.5} was assessed over 24-h sampling periods using the Enhanced MicroPEM (ECM), a small integrated and real-time PM_{2.5} monitor. BC was measured on the PM_{2.5} filters collected via the ECM using a SootScan™ Model OT21 transmissometer (Magee Scientific) [32]. The EL-USB-300 CO monitors (Lascar Electronics) used an electrochemical sensor to measure real-time CO with 0.5 ppm resolution; personal real-time CO measurements were logged at 1-min intervals and data were averaged into daily exposures for each participant's sampling session [31].

Prior to data collection, ECMs were calibrated and set to run for 24 h at a flow rate of 0.3 L/minute. Three-point flow calibrations were performed before each deployment, as well as nephelometer, temperature, and humidity offsets. Flow calibration was done with National Institute of Standards and Technology traceable flow calibrators [31]. PM mass was collected on 15 mm polytetrafluoroethylene filters (Measurement Technology Laboratories). After 24 h, ECMs turned off automatically [31]. Before going to the field, the ECM was set up and placed into a clean sealed Ziploc bag to avoid contaminating the filter. Trained HAPIN team members took ECMs into the field on the first day, also known as deployment day.

Using a personal apron or vest, the woman wore the exposure devices for 24 h. On day two the HAPIN research team returned to the household to collect the exposure device and complete health measures. The ECM was put in a new Ziploc bag and sealed, then it was taken to the laboratory office for further processing. In the field laboratory office, ECMs were first cleaned with ethanol; flow rates were then evaluated using a primary flow meter. ECMs were taken to the clean room to remove the filters, then the filters were wrapped in Aluminum foil and stored in a refrigerator at below 23 degrees Celsius until transported to centralized weighing facilities (University of Georgia, Athens, GA), where the filters were weighed to estimate PM_{2.5} mass and assessed for BC concentrations. BC depositions were estimated per Garland et al. [33] using the BC attenuation cross-section values for similar Teflon filters ($\sigma_{\text{ATN}} = 13.7 \mu\text{g} = \text{cm}^2$) collected from similar source types. Limit of detection (LOD) was calculated as it was for gravimetric mass (three times the blank standard deviation). Values below the LOD were replaced with LOD/(2^{0.5}). We removed any values that were flagged as 'invalid.' The PM_{2.5}, CO, and BC samples were considered invalid due to being missing, equipment failure, damaged or misplaced filters, or failure to meet quality assurance criteria as described.

Clinical biomarkers from dried blood spots

Dried blood spots were collected in conjunction with other health measures immediately following the 24-h exposure measurements. We used dried blood spots as the biological matrix due to their minimally invasive collection, and integration within the HAPIN Trial protocol, which ensured methodological consistency across research sites; alternative matrices such as nails, hair, or urine were not collected in this study. Using a GE Whatman 10,534,612 903 Protein Saver Card as the filter paper, and a BD contact-activated 2.0 mm lancet, the field technicians labeled each card with the participant's ID before proceeding with collection. For the finger-stick puncture, the technicians selected the participant's non-dominant hand, choosing either the middle or ring finger. The technician cleaned the puncture site with 70% isopropanol and allowed it to dry completely. Participants were asked to hold their hands downward to improve blood flow, and the lancet was pressed firmly at a perpendicular angle to the puncture site. After triggering, the lancet was removed and discarded in a biohazard waste bin.

Following the puncture, the first blood drop was wiped away with a sterile gauze pad to remove excess tissue fluids, which could compromise sample accuracy. The technician then gently massaged the hand, keeping it below elbow level to promote blood flow, while avoiding "milk-ing" the finger to avoid squeezing out excess tissues. To collect the blood spots, the participant's hand was turned

palm down, allowing large drops of blood to fall naturally onto the filter paper without touching the fingertip to the paper directly. The technician aimed to fill all five circles completely, ensuring a sufficient sample.

At the study center, the technician left the blood spot cards to dry uncovered for 24–48 h at room temperature. After drying, each card was sealed in a biospecimen bag with two packets of desiccant and a humidity indicator card, with a sample ID label affixed to the bag. For storage, all samples were kept at -20°C , both at the field centers and before shipping to Emory University for storage in a -80°C freezer. Humidity indicator cards were checked regularly, and additional desiccant was added if needed. Samples were shipped on dry ice to maintain their frozen state and were sent within six months of collection.

The field team marked any questionable or invalid spots on the blood spot cards to guide lab processing. If a spot was invalid due to “milking,” accidental finger contact onto the filter paper, or double spotting, an “X” was marked above the “tuck cover here” line. If a spot was potentially too small but otherwise valid, a “?” was marked. This labeling allowed the lab to assess and selectively use the valid spots during analysis.

Emory University’s Laboratory for Exposure Assessment and Development in Environmental Research (LEADER) analyzed dried blood spot samples collected from the field site in Rwanda. Dried blood spots were soaked in 200 μL phosphate-buffered saline overnight to recover the whole capillary blood from the spot. The extracted residues were heat digested with concentrated nitric acid before the addition of dilute nitric acid and a solution containing the internal standard (ISTD) iridium. The samples were then analyzed via inductively coupled plasma mass spectrometry (Agilent Technologies, Santa Clara, CA) alongside a six-point calibration curve, removing polyatomic spectral interferences with a dynamic collision reaction cell. Concentrations of Pb and Cd were derived from an equation defining the relative response of the element to the ISTD response across the calibrant concentration range. Multiple isotopes of each metal were monitored to ensure the reliability of results.

Each sample card served as its own individual blank sample by punching a spot the size of a blood spot from the card (in a blank area that did not contain blood) and it was subjected to preparation and analysis alongside the blood spot samples. Unknown samples were prepared concurrently with three additional laboratory blank samples, calibration samples, NIST reference material SRM 1643f, and two levels of quality control samples per analytic run. All samples were blank subtracted to provide the most accurate concentrations.

To help ensure consistency across samples, all samples were standardized to 4 mmol/mL potassium (K^{+}) to

correct for volume discrepancies in dried blood volume. For Pb, the limit of quantification, relative standard deviation (%), and NIST SRM recoveries (SD) were 0.001 $\mu\text{g}/\text{dL}$, 7%, and 101, respectively. For Cd, the limit of quantification, relative standard deviation (%), and NIST SRM recoveries (SD) were 0.1 ng/mL, 4%, and 99, respectively.

Other variables

We collected additional variables to explore as potential covariates in the analyses that may be linked to household air pollution exposure or metal concentrations, including the woman’s age at baseline and body mass index (BMI, kg/m^2 as a continuous variable) (34). Weight and height were measured in duplicate using Seca 876 electronic scales and Seca 213 stadiometer platforms (Seca GmbH & Co. KG., Hamburg, Germany), respectively. If the weight or height measurements differed by more than 0.5 kg or 1 cm, respectively, a third measurement was taken and the two closest readings were averaged. We also recorded other sociodemographic characteristics.

Educational status for women was defined in three levels: (1) no formal education or primary school incomplete, (2) primary school complete or secondary school incomplete, (3) secondary school complete or vocational or some college or university. Dietary diversity was determined by using the Minimum Dietary Diversity for Women (MDD-W) indicator, which is based on ten food groups [34]. Dietary diversity was considered low if the participant reported consuming less than four of the ten food groups over the previous 30 days ($\text{MDD-W} < 4$), medium if they reported consuming four or five food groups ($4 \leq \text{MDD-W} \leq 5$), and high if they reported consuming more than five ($\text{MDD-W} > 5$) [35]. In addition, 17 individual food items were assessed by never or < 1 time/month, monthly and weekly/daily intake of grains, tubers, legumes, nuts, flesh meat, organ meat, poultry, fish, dairy, eggs, dark green vegetables, vitamin A rich fruits and vegetables, snacks, soft drinks, insects, fruit juice, sugar in coffee or tea for each woman. Food insecurity was assessed using the Food Insecurity Experience Scale (FIES), developed by the Food and Agriculture Organization of the United Nations (FAO): <http://www.fao.org/3/as583e/as583e.pdf>.

We surveyed participants about their secondhand exposure to tobacco smoke by any household members (yes vs. no), personal alcohol consumption in the last 30 days (yes vs. no), and food insecurity (none, mild and moderate/severe). Household-level socioeconomic status was estimated by possession of 5 material assets: color TV, radio, mobile telephone, bicycle, and bank account (yes vs. no per asset).

Field staff collected data on password-protected tablets, which they subsequently uploaded daily to a secure REDCap™ server managed by Emory which complied

with the Health Insurance Portability and Accountability Act and Federal Information Security Management Act. The tablets were updated each day after uploads, and all data were removed from the mobile device [30].

Statistical analysis

Data were managed and analyzed using R version 4.2.2 (R Foundation for Statistical Computing) and RStudio (<https://www.R-project.org/>). Initially, 798 pregnant women enrolled at baseline in the Rwanda sites were included in the raw data. For data cleaning, we removed those who had missing K+ values for standardization (n=13) and missing Pb and Cd values (n=4). For all personal household air pollution measures, we removed any values that were flagged as invalid, as described previously (31), thus removing n=77 PM_{2.5}, n=223 BC, and n=81 CO observations. The final datasets for analysis included n=781 women with valid Pb and Cd concentrations, of whom were then analyzed for exposure–response associations with n=704 PM_{2.5} observations, n=558 BC observations, and n=700 CO observations.

For the K+standardization calculation for Pb and Cd, each metal value was multiplied by 4 mmol/mL and then divided by the individual's specific K+value:

(metal*4)/K+. For the natural log-transformation of CO, we added +1 to each CO value to account for zero values.

To identify potential confounders for multivariable modeling, we conducted crude analyses between each covariate and the exposure variables, as well as between each covariate and the outcome. Covariates that showed evidence of association with the exposure and the outcome were considered for inclusion as potential confounders. Final models were adjusted for key confounders, including maternal age, BMI, bicycle ownership, fish consumption, and food insecurity.

We calculated descriptive statistics for exposure, demographic, socioeconomic status and other potential confounders. We assessed Spearman correlation coefficients (rho) between Pb, Cd, and the three exposure concentrations. We assessed diagnostic plots of simple linear regression models for Pb and Cd measures and exposure concentrations to see if these measures needed to be natural log-transformed to meet the assumptions of linear regression by calculating the natural logarithm (log base e) of each concentration. Finally, we built multivariable linear regression models with natural log-transformed household air pollution measures and natural log-transformed Pb and Cd as separate exposures and outcomes, respectively.

Results

Baseline characteristics

Table 1 presents the baseline characteristics of pregnant women in Rwanda who had valid Pb and Cd measures (n=781). The average age of participants was 27 years (SD=4.4), while the mean BMI was 23.4 kg/m² (SD=3.4). In terms of educational attainment, levels were generally low; 331 (42.3%) of women had no formal education or had not completed primary school. In contrast, 312 (40.0%) had completed primary or some secondary education, and only 138 (17.7%) had completed secondary school or had higher education. With respect to household assets, the majority of households 616 (78.9%) reported owning mobile phones, 440 (56.3%) having radios, and 241 (30.8%) owning bicycles. However, fewer households owned a color TV 99 (12.7%) or had a bank account 228 (29.2%). The average Minimum Dietary Diversity score was 2.9 out of 10 (SD=1.5). Furthermore, food insecurity was also prevalent: 216 (28.4%) of households experienced mild food insecurity, while 253 (33.2%) experienced moderate to severe food insecurity. A small proportion of women 28 (3.6%) reported secondhand smoke exposure. Regarding fish consumption, 287 (36.8%) of women consumed fish rarely (never or less than once a month), 227 (29.1%) consumed fish monthly, and only 266 (34.1%) reported weekly or daily fish intake.

Supplemental materials include a table comparing baseline characteristics between the original full sample

Table 1 Baseline characteristics among pregnant women with valid Pb and Cd measures (K+standardized) in Rwanda at baseline for the HAPIN Trial (n=781)

Variable	Mean (SD); or n (%)
Age (years)	27 (4.4)
BMI (continuous, kg/m ²)	23.4 (3.4)
Education level	
1. No formal education or Primary school incomplete	331 (42.4%)
2. Primary school complete or Secondary school incomplete	312 (39.9%)
3. Secondary school complete or Vocational or Some college or university	138 (17.7%)
Households have color TV	99 (12.7%)
Households have radio	440 (56.3%)
Households have mobile telephone	616 (78.9%)
Households have bicycle	241 (30.9%)
Households have bank account	228 (29.2%)
Dietary diversity (Mother: Minimum Diet Diversity (0–10)	2.9 (1.5)
Food insecurity (household-level)	
0. None	292 8.4%)
1. Mild	216 8.4%)
2. Moderate/Severe	253 (33.2%)
Secondhand smoke exposure (yes)	28 (3.6%)
Fish consumption	
0. Never or < 1 time/month	287 6.8%)
1. Monthly	227 9.1%)
2. Weekly/daily	266 (34.1%)

Table 2 Descriptive of valid Pb, Cd (K+ standardized) and HAP measures in Rwanda at baseline for the HAPIN Trial

Variable	N	Min	Q1	Median	Q3	Max
Metals (K+ standardized)						
Pb µg/dL	781	0.02	0.85	1.35	2.39	16.89
Cd ng/mL	781	0.05	0.60	0.88	1.25	3.56
24-h personal exposures						
PM _{2.5} µg/m ³	704	14.2	54.2	90.2	139.4	1089.8
BC µg/m ³	558	2.7	7.3	11.0	15.0	76.9
CO ppm	700	0	0.5	1.1	2.4	44.4

Table 3 Adjusted associations between 24-h average personal log-transformed household air pollution concentrations and Lead (Pb, K+ standardized and natural log-transformed)¹

24-h average personal exposures (natural log-transformed)	N	Adjusted Estimate	95% CI
PM _{2.5} µg/m ³	683	0.06	−0.03, 0.15
BC µg/m ³	540	0.11	−0.01, 0.24
CO ppm	676	−0.03	−0.12, 0.07

Table 4 Adjusted associations between 24-h average personal log-transformed household air pollution concentrations and Cadmium (Cd, K+ standardized and natural log-transformed)¹

24-h average personal exposures (natural log-transformed)	N	Adjusted Estimate	95% CI
PM _{2.5} µg/m ³	683	0.04	−0.02, 0.09
BC µg/m ³	540	0.02	−0.05, 0.09
CO ppm	676	0.0002	−0.06, 0.06

(n=798), the reduced valid Pb and Cd sample (n=781), and each individual pollutant sample (PM_{2.5} n=704, BC n=558, CO n=700) (Supp. Table S1). Overall, it shows that none of the key characteristics were changed with different sample sizes, eliminating the concern of potential bias with missing data (Supp. Table S1).

Metal concentrations and 24-h personal household air pollution exposures among pregnant women

Table 2 summarizes valid Pb and Cd concentrations and 24-h personal household air pollution exposures among pregnant women in Rwanda who participated in the HAPIN Trial. Blood Pb concentrations, standardized for K+, showed a median value of 1.35 µg/dL with 1st and 3rd quartiles (Q1, Q3) of 0.85 and 2.39 (range: 0.02, 16.89). Cd concentrations had a median of 0.88 ng/mL (Q1, Q3: 0.60, 1.25; range: 0.05, 3.56) (Table 2).

For the 24-h personal exposure to household air pollutants, the median level of PM_{2.5} was 90.2 µg/m³ (Q1, Q3: 54.2–139.4, range: 14.2, 1089.8 µg/m³). BC had a median concentration of 11.0 µg/m³ (Q1, Q3: 7.3–15.0, range: 2.7, 76.9 µg/m³). CO concentrations had a median of 1.1 ppm (Q1, Q3: 0.5–2.4, range: 0, 44.4) (Table 2).

Supplemental Figure S1 displays the Spearman correlation coefficients between Pb, Cd, and each air pollution concentration. There was a strong correlation between 24-h PM_{2.5} and BC (rho=0.84), weak correlations between PM_{2.5} and CO (rho=0.23) and Pb and Cd (rho=0.22), and no correlations between any of the pollutants and the metals (e.g., PM_{2.5} and Pb rho=0.08) (Supp. Figure S1).

Results from adjusted linear regression models

Tables 3 and 4 present the results of multivariable linear regression models examining the associations between 24-h average personal exposure to household air pollution and Pb and Cd concentrations among pregnant women in Rwanda.

In all models, the exposures (PM_{2.5}, BC, and CO) and outcomes of Pb and Cd concentrations were natural log-transformed, with adjustment for key potential confounders, including maternal age, BMI, bicycle ownership, fish consumption, and food insecurity. For blood Pb levels, PM_{2.5} exposure showed a suggestive positive association (adjusted estimate: 0.06; 95% CI −0.03–0.15), although the 95% CI included the null value (Table 3). BC exposure also showed a trend of a positive association with blood Pb (estimate: 0.11; 95% CI −0.01–0.24), with the confidence interval narrowly including the null value. Figures 1 and 2 display forest plots of the associations between PM_{2.5} and BC on Pb, showing the estimated impacts of personal exposures on Pb concentrations after adjusting for other variables. In contrast, CO exposure demonstrated a negative association with blood Pb (estimate: −0.03; 95% CI −0.12–0.07), although not statistically significant (Table 3).

Table 4 shows that the associations between household air pollution exposures and blood Cd levels were uniformly weak and not statistically significant. PM_{2.5} exposure had a suggestive association with an increase in Cd (estimate: 0.04; 95% CI −0.02–0.09), while BC exposure showed a small increase, although the 95% CI included the null value: 0.02; (95% CI −0.05–0.09) (Table 4). CO exposure showed no association with blood Cd levels

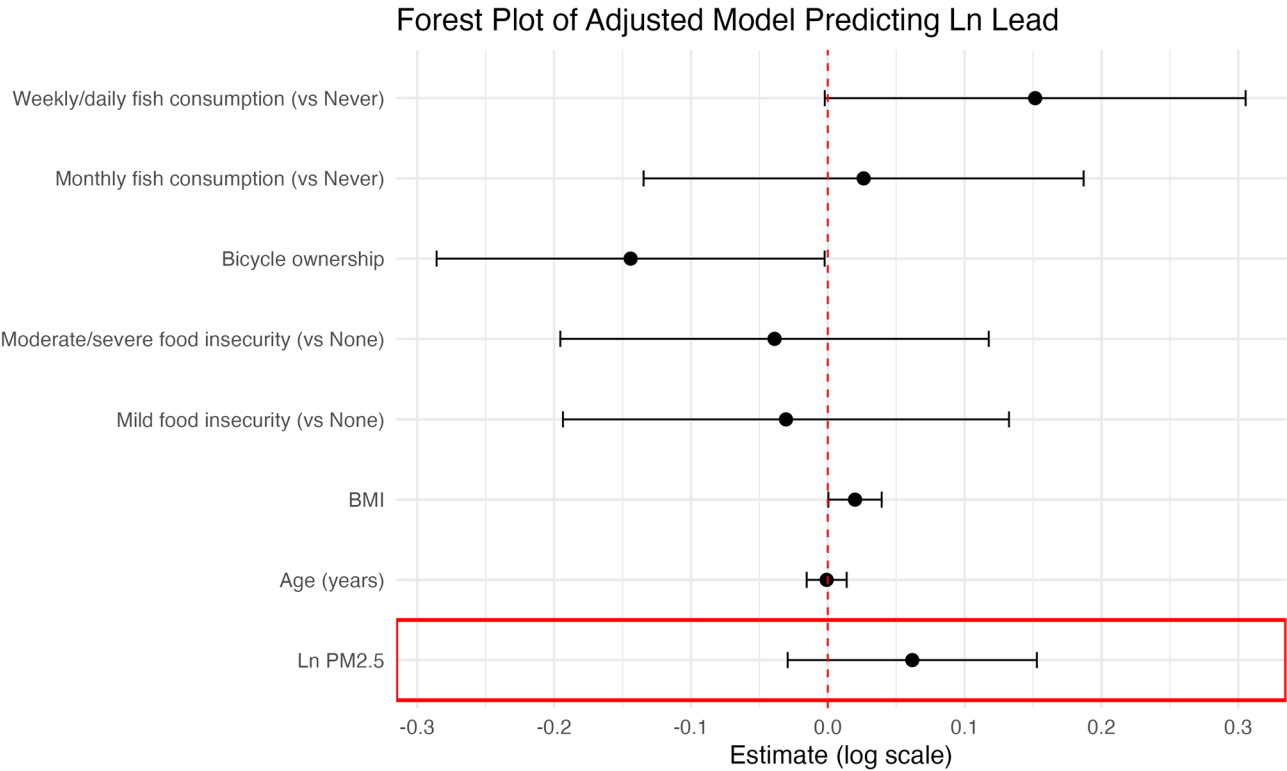


Fig. 1 Forest plot of adjusted model results for estimated associations between natural log-transformed (Ln) PM_{2.5} and other covariates on Ln Pb concentrations (n = 683). The red box highlights PM_{2.5}'s estimated impact on Pb

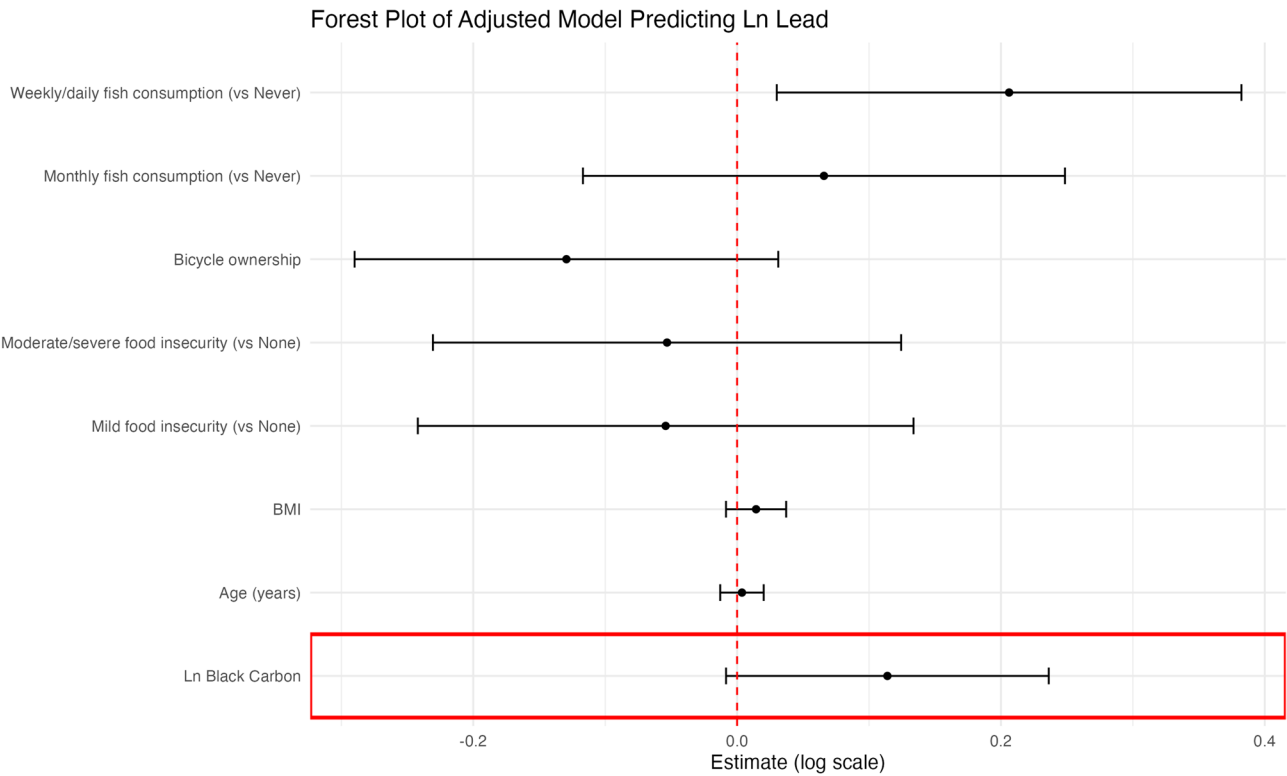


Fig. 2 Forest plot of adjusted model results for estimated associations between natural log-transformed (Ln) black carbon (BC) and other covariates on Ln Pb concentrations (n = 540). The red box highlights BC's estimated impact on Pb

(estimate: 0.0002; 95% CI – 0.06–0.06) (Table 4). Overall, these findings indicated that while there were suggestive positive trends between $PM_{2.5}$ and BC and Pb and Cd, none of the associations were statistically significant in this study.

Discussion

In LMICs, biomass fuel remains a primary energy source for cooking, resulting in household air pollution exposures, particularly among women who are primarily responsible for domestic cooking activities [36, 37]. Biomass smoke contains toxic metals such as Pb and Cd, which can be systemically absorbed and quantified through biomarkers like dried blood spots [37]. The concentrations of these metals in biomass smoke vary widely depending on factors such as fuel type, combustion conditions, and geographic context [38–40]. Prenatal exposure to Pb and Cd has been associated with adverse health outcomes, including hypertensive disorders of pregnancy, impaired fetal growth, and long-term neurodevelopmental impairments in offspring [41, 42]. Given these risks, it is important to consider how exposure occurs. Adults, including pregnant women, inhale approximately 15–20 m³ of air per day during light activity, which contributes to metal exposure through inhalation of particulate-bound pollutants. The inhalation pathway is critical as fine and ultrafine particles can penetrate deep into the lungs, allowing metals to be absorbed systemically with relatively high bioavailability compared to other exposure routes such as ingestion. While ingestion and dermal exposure can also contribute to overall metal burden, inhalation of household air pollution is a dominant exposure pathway in settings reliant on biomass fuels [43, 44]. Mechanistically, household air pollutants, serve as carriers of toxic metals such as Pb and Cd. When inhaled, these particles penetrate the alveolar region of the lungs, where soluble metal fractions undergo dissolution and absorption across the alveolar capillary barrier into systemic circulation [45–47]. Once in the bloodstream, Pb distributes to soft tissues such as the liver, kidneys, and brain, and eventually accumulates in bone, which acts as a long-term endogenous reservoir that can be mobilized during pregnancy due to increased bone turnover [48–50]. Cd, in contrast, has a high affinity for metallothionein and accumulates in the liver and kidneys, where its slow clearance results in decades-long biological retention [51–53].

Physiologically, the mobilization of Pb during pregnancy is of particular concern because increased calcium demand enhances bone resorption, thereby releasing Pb into maternal blood and facilitating placental transfer to the fetus [54]. Similarly, Cd competes with essential micronutrients such as zinc and iron for intestinal and placental transporters, disrupting maternal–fetal nutrient

transfer [55]. Inhalation exposure may therefore amplify systemic burdens beyond dietary or other sources, especially in settings where women are chronically exposed to biomass smoke during daily cooking. These mechanisms strengthen the biological plausibility of our findings and underscore the potential for even small observed exposure–response associations to have cumulative implications for maternal and fetal health. Characterizing the exposure–response relationship between household air pollution and metal concentrations is therefore essential to inform targeted interventions that protect maternal and fetal health in rural areas.

This cross-sectional study conducted among pregnant women aged 18–35 years enrolled in the HAPIN trial aimed to assess the exposure–response relationships between 24-h personal household air pollution exposures to $PM_{2.5}$, BC, and CO and K+-standardized blood levels of Pb and Cd among pregnant women in Rwanda. We hypothesized that increased household air pollution exposure would be associated with elevated levels of these metals, adjusting for potential confounders.

In this study, the estimated associations between household air pollution exposures and blood metal concentrations were small in magnitude and did not reach statistical significance. While these effect sizes may appear to have limited practical implications in isolation, their potential relevance should be interpreted in the context of toxicokinetic profile of Pb and Cd. Pb, although its blood half-life is shorter (1–2 months), has extensive retention in bone and soft tissues, with bones serving as long-term endogenous source especially during pregnancy [56, 57]. Cd's retention half-life in human kidneys and liver extends from 6 to 38 years, with a potential cumulative burden over time [56].

Although the associations did not reach statistical significance, we observed consistent positive trends between $PM_{2.5}$ and BC exposures and blood concentrations of both Pb and Cd, whereas no associations were observed with CO and Pb and Cd. These findings aligned with previous studies conducted in LMICs, where biomass-related air pollution was implicated in elevated blood Pb levels. For example, [58] found significant positive associations between personal $PM_{2.5}$ and BC exposure and blood Pb among pregnant women in India, more than 80% of pregnant women reported blood lead levels ≥ 5 $\mu\text{g/dL}$. In addition to the study conducted among Taiwanese women reported high significant concentrations of Cd in nonpregnant women than in pregnant women (Cd: 2.41 $\mu\text{g/L}$ vs. 2.12 $\mu\text{g/L}$; Pb: 0.83 $\mu\text{g/dL}$ vs. 0.73 $\mu\text{g/dL}$) [59]. The lack of statistical significance in our results may reflect the differences in fuel types and cooking behaviors compared to those in other LMICs. Nevertheless, the direction and magnitude of effect estimates in our study were consistent with prior findings

and supported the biological plausibility of Pb uptake via inhalation of polluted indoor air.

For Cd, the observed associations were relatively weak. These findings were consistent with previous studies, which indicated that Cd exposure may be attributed to dietary sources and tobacco use. For instance, Nawrot et al. reported that dietary intake and smoking were the dominant Cd exposure routes among women in Bangladesh [60]. Moreover, Cd's toxicokinetic properties characterized by slow accumulation and a long biological half-life (10–30 years in the kidneys and liver) suggested that short-term household air pollution measurements might not strongly correlate with blood Cd levels [48].

This study was subject to several limitations. Our study was a baseline assessment conducted to inform the HAPIN randomized controlled trial. As such, it involved a single 24-h personal household air pollution measurement to characterize exposure among pregnant women prior to intervention. Although directly monitoring an individual's personal exposure to air pollution minimizes exposure measurement error and provides the most accurate measure of exposure as compared to the use of surrogates (e.g., stove type) or modeled exposures [61], we acknowledge that using this single short-term measurement to assess associations with blood metal concentrations particularly Cd, which has a biological half-life of 10–30 years, introduced a potential temporal mismatch between the exposure metric and the biomarker of long-term accumulation. Blood Cd levels reflect chronic exposure due to their slow biological clearance, whereas the 24-h household air pollution measurement captured only a snapshot of exposure. That said, when household air pollution from cooking is the primary source of air pollution exposure, it is common in our field to use 24–48 h measurements to represent “typical” exposures given the nature of daily cooking patterns. However, although correlation across repeated measures has been observed, the daily variability in cooking likely leads to exposure measurement error when only one daily measurement is used to estimate long-term exposure to air pollution [62]. This limitation was unavoidable given the baseline design and logistical constraints of a 24-h sampling window for real-life field conditions, rather than a preferred extended monitoring period. However, our models adjusted for relevant confounders potentially linked to cumulative exposures, and we interpreted the exposure–response findings with appropriate caution, recognizing that our results may be an underestimate of the true strength of air pollution exposure-metal associations. Therefore, the baseline data provided critical context for understanding exposure patterns before the intervention, and ongoing longitudinal measurements within the HAPIN trial will allow for more comprehensive characterization of temporal exposure variability and its relationship to

biomarker levels. The cross-sectional design could not establish causality or assess prolonged exposure impacts. Given that the study population consisted primarily of pregnant women from rural areas with relatively homogeneous occupational profiles, the potential for occupational exposure variability was limited. Nonetheless, we acknowledge that potential environmental sources of metal exposure were not directly measured, representing a limitation that may lead to residual confounding. Additionally, regardless of our exploration of specific food items and combined dietary diversity, residual confounding is still a possibility if certain food items were not measured or poorly surveyed. Future longitudinal data collection will allow for more comprehensive assessment and control of these and other potential confounders.

Another limitation of this study is the proportion of missing black carbon (BC) data (28.6%), which resulted from invalid gravimetric PM_{2.5} samples due to damaged filters, flow or pressure faults, or insufficient sampling durations. While approximately 14% of invalid PM_{2.5} samples were recoverable using nephelometer-based ECM estimates [63], BC concentrations could only be derived from valid gravimetric filters, leading to lower completeness. These data losses were driven by equipment malfunctions and filter handling rather than participant characteristics or exposure levels, suggesting that missingness was non-systematic and unlikely to introduce bias. Supporting this assumption for PM_{2.5}, imputation analyses demonstrated that observed and imputed values were closely aligned [63]. Although this reduces the likelihood of biased estimates, the reduced sample size limits the statistical power of our analyses, particularly in detecting small but meaningful associations. While the study may not be powered to detect very small associations between BC and metals, the sample size of over 500 pregnant women with BC data offered a unique dataset given this type of intensive fieldwork in Rwanda. The BC-metal association estimates are still informative in terms of direction and magnitude, are valuable in this setting where such data have not been previously collected and explored and set a point of reference for future studies.

The study's statistical power to detect very small associations was limited by the sample size. Therefore, the absence of statistically significant findings should not be interpreted as definitive evidence of no effect but rather as an indication that larger, longitudinal studies are needed to confirm or refute these associations and determine their clinical significance. Future studies would also benefit from choosing other biomarkers with shorter half-lives. Furthermore, the level of missingness in BC measurements was relatively higher compared to other pollutants, but since there were no systematic differences

in which participants did or did not have BC data, the potential for selection bias is unfounded.

Despite these limitations, this study also had several important strengths. Our findings contributed to the scarce literature on household air pollution related to metal concentrations in LMICs, focused on pregnant women, and highlighted the importance of further research incorporating repeated exposure and biomarker assessments. Additional strengths were the use of in-field collection of dried blood spots for analysis of Pb and Cd measurements and direct 24-h personal exposure monitoring. This study adds to the few studies that have quantified personal exposure and metals among pregnant women to examine the relationship between household air pollution exposure from biomass burning and metals in LMICs rural settings.

Conclusion

Although associations between household air pollution and blood levels of Pb and Cd did not reach statistical significance, the observed exposure–response relationship of Pb with increased PM_{2.5} and BC exposures were directionally consistent with our hypothesis and supported by mechanistic and epidemiological evidence from other LMICs. These findings highlighted the need for continued research on the health effects of household air pollution, particularly among pregnant women, and support public health and policy efforts aimed at reducing household air pollution from biomass burning to protect maternal and fetal well-being.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s41043-025-01178-6>.

Additional file 1.

Additional file 2.

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Concept and design (TC, WC, J-LP); data collection (BG, ED, FN, S-SG, C-LC); data analysis and interpretation (AN, B-NY, M-LC, PK, L-AW, YC, AP, JW, J-DDN, SJ); drafting of the manuscript (AN, B-NY), critical revision for intellectual content (M-LC, AP, A-DA, L-DLF, MJ, MK, J-PMC, V-GDR, LT, and GR); administrative, technical, or logistic support (A-EL), supervision (TN, EK, J-LP, B-NY and M-LC).

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Data availability

Deidentified data associated with the paper will be deposited in Emory's Dataverse data repository. A DOI for the data will be created, to allow citation with publication of the paper. Dataverse is widely accessible and provides long-term access to the public and to related research communities.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki (<https://www.wma.net/policies-post/wma-declaration-of-helsinki/>). The study protocol has been reviewed and approved by institutional review boards (IRBs) or Ethics Committees at Emory University (00089799), Johns Hopkins University (00007403), Sri Ramachandra Institute of Higher Education and Research (IEC-N1/16/JUL/54/49) and the Indian Council of Medical Research–Health Ministry Screening Committee (5/8/4-30/(Env)/Indo-US/2016-NCD-I), Universidad del Valle de Guatemala (146-08-2016/11-2016) and Guatemalan Ministry of Health National Ethics Committee (11-2016), A.B. PRISMA, the London School of Hygiene and Tropical Medicine (11664-5) and the Rwandan National Ethics Committee (No.357/RNEC/2018), and Washington University of St. Louis (201611159). The HAPIN trial has been registered with ClinicalTrials.gov (Identifier NCT029446282) on October 26, 2016. However, it is a randomized control trial (RCT) not a clinical trial. And all participants provided informed consent prior to participation in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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