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Association between Personal Exposure to Household Air Pollution and Glycated Hemoglobin among Women in Rural Areas of Guatemala, India, Peru, and Rwanda: Household Air Pollution Intervention Network Trial

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Background: Household air pollution from biomass cookstoves is a major concern in low- and middle-income countries because it may be linked with increasing rates of metabolic disorders such as diabetes. We assessed cross-sectional associations between household air pollution concentrations and glycated hemoglobin (HbA1c) levels.

Methods: We analyzed data from 346 women 40 to <80 years of age who cooked with biomass fuel and were enrolled in the Household Air Pollution Intervention Network (HAPIN) Trial in Guatemala, India, Peru, and Rwanda. We explored associations of 24-h average personal exposure to fine particulate matter [PM ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$)], black carbon (BC), and carbon monoxide (CO) with HbA1c through individual pollutant linear models adjusted for potential confounders. We examined the effect modification of age, body mass index (BMI), and research site on the associations.

Results: We did not observe evidence of associations between HbA1c (percentage points) and 1-unit increases in log-transformed $PM_{2.5}$ [−0.07; 95% confidence interval (CI): −0.18, 0.05], BC (0.01; 95% CI: −0.15, 0.13), or CO (0.07; 95% CI: −0.24, 0.10). Effect modification of the BC associations with HbA1c was observed for BMI and research site. An association in the hypothesized direction was observed among women with high BMI (≥25 kg/m^2): 0.13 (95% CI: −0.06, 0.31) compared with low BMI (<25 kg/m^2): −0.17 (95% CI: −0.38, 0.04; $p_{interaction} = 0.04$). In the Guatemala research site, there was an association in the hypothesized direction with HbA1c and log-transformed BC (0.36; 95% CI: 0.03, 0.70) that was countered by an association in the opposite direction as that hypothesized for the India site (−0.21; 95% CI: −0.45, 0.02) and associations consistent with the null association in the Peru and Rwanda sites ($p_{interaction} = 0.05$). No other evidence of effect modification was observed.

Conclusions: Evidence suggests a need for further research to better understand household air pollution's influence on HbA1c, with particular attention on potential effect modifiers. https://doi.org/10.1289/JHP1053

Introduction

Exposure to household air pollution is one of the most important risk factors for morbidity and mortality worldwide and is a serious public health issue.[1,2] One of the primary sources of exposure to household air pollution in low- and middle-income countries (LMICs) is inefficient solid fuel burning for cooking and heating in poorly ventilated homes.[3] Approximately 2.4 billion people still cook over open flames and inefficient stoves using solid fuels and kerosene.[2] These energy sources burn inefficiently, releasing toxic smoke containing pollutants, including carbon monoxide (CO) and particulate matter, which is a mixture of organic and inorganic molecules.[4] The carbonaceous component of fine particulate matter [PM ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$)], black carbon (BC), is produced from the incomplete combustion of biomass and fossil fuels.[5] BC has received more attention given that it is now recognized as a major contributor to global warming in addition to its association with numerous adverse health impacts.[6–8]

In 2019, diabetes directly contributed to 1.6 million deaths worldwide, and it was the fifth greatest cause of mortality for women and the eighth leading cause of death overall.[9] Metabolic, behavioral, and environmental risk factors are widely acknowledged to be associated with an increased incidence of diabetes. Evidence supports an association between exposure to ambient air pollution and diabetes or prediabetes.[10–15] According to the 2020 Health Effects Institute report, exposure to $PM_{2.5}$ from any

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source was estimated to be responsible for ~5% of the global burden of type 2 diabetes, with an estimated 3.78 deaths per 100,000 people and 167 disability-adjusted life years (DALYs) per 100,000 people.[16]

In addition to ambient air pollution, household air pollution is increasingly suspected to be a risk factor for diabetes.[17] Household air pollution contributed to ~6.5% of type 2 diabetes-related fatalities and 5.9% of total DALYs.[16] Several studies have observed a correlation between household air pollution exposure and the prevalence of diabetes. For instance, a study conducted in China found that individuals exposed to household air pollution from solid fuel use had a higher risk of developing type 2 diabetes compared with those using cleaner fuels.[18] Other studies conducted in India and Bangladesh have shown that women exposed to household air pollution from cooking with biomass fuels have higher rates of obesity and metabolic syndrome, which are precursors to diabetes.[19] Furthermore, exposure to household air pollution has been linked to increased risk of cardiovascular diseases, which often coexist with metabolic disorders.[18]

Most investigations in populations depending on unclean fuels for domestic energy have assessed exposure to $PM_{2.5}$, which is a less specific marker of inefficient combustion than BC, or have concentrated on self-reported stove types and other cooking-related factors without directly measuring household air pollution concentrations. A growing body of evidence supports the linkage between BC and diabetes.[20] Mechanistic studies show that BC induces systemic inflammation, oxidative stress, and endothelial dysfunction, all of which contribute to insulin resistance and diabetes.[21–23] Epidemiologic studies further support these findings by demonstrating higher diabetes incidence and prevalence in populations exposed to high levels of BC.[24,25]

Possible mechanisms from human-based studies suggest that systemic inflammation and oxidative stress, caused by household air pollution, have been found to impair insulin signaling and glucose metabolism, contributing to insulin resistance and the development of type 2 diabetes.[26] Certain pollutants present in household air pollution, including polycyclic aromatic hydrocarbons and heavy metals, can function as endocrine disruptors. In humans, these chemicals have the potential to disrupt hormonal regulation of metabolism and have been linked to metabolic disorders.[27] Furthermore, mouse studies have shown that exposure to pollutants leads to damage in mitochondria, the organelles responsible for energy production within cells; such mitochondrial dysfunction disrupts cellular energy homeostasis and metabolism, establishing a connection between air pollution and the development of obesity and diabetes.[28]

To better describe the health impacts of $PM_{2.5}$, BC, and CO concentrations, we explored the baseline cross-sectional associations of these three air pollutants on hemoglobin A1c (glycated hemoglobin, HbA1c), the average plasma glucose level over the previous 8–12 wk, among women in Guatemala, India, Peru, and Rwanda from the Household Air Pollution Intervention Network (HAPIN) trial. We tested two hypotheses: *a*) Increased household air pollution concentrations ($PM_{2.5}$, CO, and BC, assessed separately) are positively associated with increased levels of HbA1c among women; and *b*) age, BMI, and research site potentially modify the effect of the association between household air pollution measures and HbA1c, as assessed in interaction analyses.

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.[29] In brief, the full 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 primarily rural LMIC settings. 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 health outcomes were obtained from 418 women 40 to <80 years of age who resided in the same households as an enrolled pregnant woman in the HAPIN trial across research sites (Guatemala, India, Peru, and Rwanda; one per household), provided they did not meet any of the following exclusion criteria: currently smoking cigarettes or other tobacco products, pregnant (via self-report), or planning to permanently move out of their current household within the next 12 months.[29]

The study was conducted in four LMICs where solid biomass was the primary source of fuel for a large proportion of the population. In India, 90% of the people who resided in rural areas preferred to cook indoors rather than outside, using traditional plastered clay or mud stoves with biomass as their primary fuel source.[30] In rural Guatemala, cooking was characterized by the use of chimney stoves and open fires; 97% used wood fuel and cooked mainly indoors.[29] In Peru, cooking was primarily done indoors, with 80% of rural households using solid fuels as their primary source of domestic energy.[30,31] In Rwanda, 80.4% of the population relied on wood or wood-based products for cooking, which was typically done on traditional open stoves in poorly ventilated kitchens (71.9%)[32]; most used traditional three-stone fires (62.6%) or clay brazier stoves (34.6%) fueled with wood (89.9%) or charcoal (8.1%).[33]

Informed consent was obtained from all study participants included in the study, and the study protocol was approved by institutional review boards 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), ABB 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). In addition, the study was registered with ClinicalTrials.gov (identifier NCT029446282). All data were collected by trained local researchers who were familiar with the cultural and linguistic context of the participants.

Exposure Measurements

The HAPIN trial's exposure assessment procedures have been previously published in greater detail.[29,34] At baseline, $PM_{2.5}$ was assessed over 24-h sampling periods using an Enhanced MicroPEM (ECM), a small integrated and real-time $PM_{2.5}$ monitor for participants' personal exposure measurements.[34] With EL-USB-300 CO monitors (Lascar Electronics) that use an electrochemical sensor to measure real-time CO with 0.5-ppm resolution, personal real-time CO concentration measurements were logged at 1-min intervals and averaged for all women. All household air pollution concentrations were calculated based on a 24-h average.[35]

Prior to data collection, ECMs were calibrated and set to run for 24 h with a pump flow rate of 0.3 L/min and using 15-mm polytetrafluoroethylene filters (Measurement Technology Laboratories); after that time, ECMs turned off automatically.[29] 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 device for 24 h. On day 2 (known as household air pollution collection day), the HAPIN research team returned to the household to collect the exposure device and complete health measures. They observed whether the participant was wearing the vest and recorded this information and asked the participant a series of questions about the participant's activities during the 24-h sampling period, including the amount of time spent not wearing the vest. Participants were instructed to wear the vest continuously for 24 h and were advised to keep the vest within 1 m when bathing, eating, or sleeping, ensuring the inlet remained unobstructed. 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 and checked for flow rates. ECMs were taken to a clean room to remove the filters, and the filters were wrapped and stored in a refrigerator at <23°C until analysis for $PM_{2.5}$ and BC. Real-time and gravimetric methods were used to characterize $PM_{2.5}$ concentrations, and SootScanTM Model OT21 Transmissometers were used to estimate BC from the $PM_{2.5}$ filters (Magee Scientific), with details provided previously.[34]

Field staff collected data on password-protected tablets, which they subsequently uploaded daily to a secure REDCap server managed by Emory that complied with the Health Insurance Portability and Accountability Act and the Federal Information Security Management Act. The tablets were updated each day after uploads, and all data were removed from the mobile device.[29]

HbA1c Measurement

HbA1c was measured among women using the A1CNow+ system, a point-of-care instrument from PTS Diagnostics. The monitor required 5 μL of capillary blood from a finger prick, inserted into the monitor's single-use cartridge, and results were available within 5 min. HbA1c was recorded in REDCap for each participant. The HAPIN research team also provided and explained the results to the woman. When explaining the results to the participants, we placed the measurement in the context of established cut points (i.e., normal HbA1c was defined as <5.7%, prediabetes was defined as 5.7%–6.4%, and diabetes was defined as having an HbA1c of ≥6.5%), noting the limitation of a one-time measurement to each participant.

Other Variables

We collected additional variables, including the woman's age at baseline (in years; as a continuous variable) and body mass index (BMI; in kilograms per meter squared; as a continuous variable) as the ratio between weight and height squared.[36] Weight and height were measured in duplicate using Seca 876 electronic scales and Seca 213 stadiometer platforms (Seca GmbH & Co.), respectively. If the weight or height measurements differed by >0.5 kg or >1 cm, respectively, a third measurement was taken, and the two closest readings were averaged. Physical activity was assessed by asking the woman how many hours per day and how many days per week they performed vigorous or moderate levels of physical activity (≥10 min/day; yes/no). Educational status for women was defined in two levels: *a*) no formal education or primary school incomplete, and *b*) primary school complete, secondary school incomplete, secondary school complete, or vocational or some college or university. Dietary diversity was determined using the Minimum Dietary Diversity for Women (MDD-W) indicator, which is based on 10 food groups.[37] Diet diversity was considered low if the participant reported consuming food from <4 of the 10 food groups over the previous 30 d (MDD-W <4), medium if they reported consuming food from 4 or 5 food groups (4 ≤ MDD-W ≤5), and high if they reported consuming food from >5 food groups (MDD-W >5).[36] Dietary diversity was assessed by monthly or less vs. weekly or daily intake of grains, tubers, legumes, nuts, flesh meat, organ meat, poultry, fish, dairy, eggs, dark green vegetables, vitamin A–rich fruits and vegetables, other fruits, sweets, snacks, soft drinks, fruit juice, and sugar in coffee or tea.[37] Secondhand smoke exposure inside the household (yes/no) was collected. Socioeconomic status (SES) was calculated from a combined index variable provided by the HAPIN Data Management Core by using principal component analysis (PCA) to construct a SES index based on ownership of selected household assets ($n = 24$), water and sanitation quality, access to electricity, number of people in the household, food insecurity, the participant's education level, and floor, wall, and roofing material.[36]

Statistical Analysis

Data were managed and analyzed using R (version 4.2.2; R Development Core Team). Initially, 418 women enrolled at baseline were included; these were nonpregnant "other adult" women who were living with a pregnant woman originally recruited in the HAPIN trial. We removed those with missing HbA1c values ($n = 29$), "888" data entry HbA1c values indicating monitor errors ($n = 36$), a data entry error of 0.5 HbA1c ($n = 1$), and any woman with self-reported use of high blood glucose medications ($n = 5$) or missing information for high blood glucose medications ($n = 1$). Our final dataset included 346 women with valid HbA1c measures.

For all personal household air pollution measures, we removed any values that were flagged as "invalid"; with the large number of samples collected, some sample loss was inevitable. The $PM_{2.5}$, CO, and BC samples were invalid due to being missing, equipment failure, damaged or misplaced filters, or failure to meet quality assurance criteria as described by Johnson et al.,[34,35] yielding a remaining total of 313 women with HbA1c and valid $PM_{2.5}$, $n = 271$ for BC, and $n = 286$ for CO. We conducted natural log transformations of the continuous values of $PM_{2.5}$, BC, and CO and assessed distributions as raw vs. transformed variables, with the decision to use the transformed versions to better meet the assumptions of linear regression modeling. We also assessed Spearman correlation coefficients between all household air pollutants.

We calculated descriptive statistics for exposure, demographics, SES, health characteristics, research site, and other potential confounders. Exploratory data analysis assessed distributions, frequencies, means and standard deviations (SDs), percentiles, outliers, and correlations between exposures, outcomes, and covariates.

The final multivariable linear models evaluated the mean difference in HbA1c levels per unit increase in natural log-transformed personal $PM_{2.5}$, BC, or CO levels as separate models, adjusted for the following covariates that were selected *a priori* as potential confounders, to improve validity, or those with evidence of an association with the outcome, to improve precision, from the literature: age, BMI, SES as a combined index, secondhand smoke exposure, vigorous and moderate physical activity, and dietary diversity.

We also considered final models without BMI owing to its potential impact as a mediator. We assessed diagnostic plots of the full combined models to evaluate the model assumptions.

Last, we considered several potential effect modifiers on the associations between household air pollution and HbA1c. Previous studies have shown that older adults might be more susceptible to the adverse effects of air pollution due to the decline in respiratory and cardiovascular functions with aging, which can exacerbate the impact on metabolic processes, including glucose metabolism and HbA1c levels,[38] and individuals with higher

BMI are more vulnerable to the effects of air pollution on glucose metabolism. Overweight and obese individuals already experience a state of chronic low-grade inflammation and insulin resistance, which can be further aggravated by exposure to pollutants. The higher BMI is linked to adipose tissue inflammation, which enhances systemic inflammation and oxidative stress. These conditions disrupt insulin signaling and glucose uptake, leading to elevated HbA1c levels.[39] Therefore, we assessed effect modification by age (median cut point of <51 vs. ≥51), BMI (median cut point of <25 vs. ≥25),[40,41] and research site (Guatemala, India, Peru, Rwanda) on the association between household air pollutants and HbA1c by including a product term for the potential effect modifier and the air pollutant in the model, adjusted for the same covariates in the full models. Furthermore, we added a sensitivity analysis to explore possible nonlinearity in the exposure–response relationship between household air pollution concentrations and HbA1c. To do this, we calculated quartiles for each household air pollution measure ($PM_{2.5}$, BC, and CO) and reran the multivariable linear regression models with these exposures as quartiles instead of continuous log-transformed variables.

Results

Baseline Characteristics

Table 1 presents baseline characteristics of the women included in the analysis with valid HbA1c measures ($N = 346$). Our study population had an average ± SD age of 52 ± 7.9 y, a BMI of 25.1 ± 5.0 kg/m^2, and an HbA1c of 5.3% ± 1.0%. A significant proportion ($n = 242$, 70%) of women was engaged in moderate physical activity for at least 10 min continuously per day, whereas a small proportion ($n = 109$, 31.5%) of women was engaged in vigorous physical activity for at least 10 min continuously per day. In addition, a majority ($n = 227$, 65.6%) of women fell within the lowest category of dietary diversity. Most of the women did not have secondhand tobacco smoke exposure ($n = 297$, 86.1%), and sugar intake was approximately equally distributed between monthly or less ($n = 141$, 40.8%) vs. weekly or daily ($n = 205$, 59.2%) (Table 1).

Personal Exposure Results for $PM_{2.5}$, BC, and CO

Table 2 presents the 24-h personal exposure concentrations as raw (not transformed) values for $PM_{2.5}$, BC, and CO among women at the baseline visit with valid HbA1c values for all four research sites. Raw personal $PM_{2.5}$ ($n = 313$) had the following distribution parameters: mean ± SD of 120.1 ± 116.5 $\mu g/m^3$, median = 87.6 $\mu g/m^3$ (25th, 75th percentile: 44.5, 143.7), minimum value of 10.0, and maximum value of 803.4 $\mu g/m^3$. Raw personal BC ($n = 271$) had the following distribution parameters: mean ± SD of 13.0 ± 9.6 $\mu g/m^3$, median = 11.1 $\mu g/m^3$ (25th, 75th percentile: 6.9, 16.3), minimum value of 1.1, and maximum value of 69.2 $\mu g/m^3$. Raw personal CO ($n = 286$) had the following distribution parameters: mean ± SD of 2.2 ± 3.4 ppm, median = 1.3 ppm (25th, 75th percentile: 0.4, 2.8), minimum value of 0, and maximum value of 38.7 ppm. The Spearman correlation coefficient between $PM_{2.5}$ and BC was 0.73, and between $PM_{2.5}$ and CO, it was 0.48, and between BC and CO, 0.39, suggesting moderate positive correlations between all pairs of exposures, with the strongest observed between the $PM_{2.5}$ and BC concentrations.

HbA1c by Research Site

Distributions of HbA1c results among women at baseline for all four research sites are displayed in Figure 1. The highest average HbA1c levels were observed in India (5.5% ± 1.3%) and Guatemala (5.5% ± 0.8%), followed by Peru (5.1% ± 0.8%) and Rwanda (4.7% ± 0.6%). The red dashed line in Figure 1 shows the cutoff for diabetes at 6.5%, and the gray shaded region shows the prediabetes range from 5.7% to 6.4%. Table 3 summarizes the HbA1c values into diabetes categories, showing 6.4% ($n = 22$) of women at baseline were over the threshold for diabetes, and 16.7% ($n = 58$) of women fell into the prediabetes category, with an HbA1c from 5.7% to 6.4% (Table 3).

Results from Adjusted Linear Regression Models

The adjusted estimates for the associations of $PM_{2.5}$, BC, and CO exposure on HbA1c are displayed in Tables 4 and 5, with BMI included and excluded as a covariate, respectively. After adjusting for covariates in the full model, including BMI, we did not observe evidence of any exposure–response associations between 24-h personal exposures and HbA1c, given that all estimates were small in magnitude. There was a decrease in HbA1c by 0.06 [95% confidence interval (CI): −0.17, 0.06] percentage points for every 1-unit increase in log-transformed $PM_{2.5}$, a decrease in HbA1c by 0.01 (95% CI: −1.48, 0.13) percentage points for every 1-unit increase in log-transformed BC, and a decrease in HbA1c by 0.04 (95% CI: −0.21, 0.14) percentage points for every 1-unit increase in log-transformed CO. Overall, higher concentrations of personal $PM_{2.5}$, BC, and CO were not associated with higher HbA1c levels as hypothesized. In the full model excluding BMI, results were not meaningfully changed.

From the sensitivity analysis exploring household air pollution measures as quartiles, we did not find exposure–response associations between quartile levels of $PM_{2.5}$, BC, and CO and HbA1c (Table 6). These results are consistent with our primary models (Tables 4 and 5), which found evidence of a null association between household air pollution measures and HbA1c at baseline among our study population.

Results from Effect Modification of Exposures on HbA1c by Age, BMI, and Research Site

Overall, there was no consistent evidence of age, BMI, or research site modifying the effect between HbA1c and the three personal household air pollution exposures (Table 7). However, there was potential effect modification of the association between BC and HbA1c modified by BMI and research site. For example, women with higher BMI showed a stronger exposure–response association with HbA1c per unit increase in BC compared with women with lower BMI [e.g., −0.17 (95% CI: −0.38, 0.04) for BMI <25 vs. 0.13 (95% CI: −0.06, 0.31) for BMI ≥25, $p_{interaction} = 0.04$]. For the Guatemala research site, there was an exposure–response association in the hypothesized direction with HbA1c per unit increase in BC (0.36; 95% CI: 0.03, 0.70) that was countered by an association in the opposite direction as that hypothesized for the India research site [−0.21 (−0.45, 0.02)] and the effect estimates showed associations consistent with the null in the Peru and Rwanda sites, with the interaction term suggesting potential effect modification (Table 7). All other effect modification models suggested no interactions, as illustrated in Table 7.

Discussion

This cross-sectional study conducted among women 40–74 years of age aimed to assess the association between household air pollution exposure ($PM_{2.5}$, CO, and BC) and HbA1c in Guatemala, India, Peru, and Rwanda. The primary results were consistent with the null associations between 24-h personal household air pollution measures and HbA1c.

In effect modification analyses, we observed a positive exposure–response association between BC and HbA1c among women within the overweight/obese category (BMI ≥25),

Table 1. Baseline characteristics of the adult women participants included in the study of air pollution and HbA1c in the HAPIN trial (Guatemala, India, Peru, Rwanda) ($n = 346$).

Variable	All research sites (Guatemala, India, Peru, Rwanda) ($n = 346$) [mean ± SD; min–max or n (%)]	Guatemala ($n = 126$) [mean ± SD; min–max or n (%)]	India ($n = 87$) [mean ± SD; min–max or n (%)]	Peru ($n = 95$) [mean ± SD; min–max or n (%)]	Rwanda ($n = 38$) [mean ± SD; min–max or n (%)]
Age at baseline (y)	52.0 ± 7.9; 40.1–74.3	53.0 ± 8; 40.4–74.2	49 ± 6.7; 40–72	52.2 ± 7.6; 40.1–73.6	53.3 ± 8.8; 40.5–74.3
BMI (kg/m^2)	25.1 ± 5.0; 15.4–39.2	25.9 ± 4; 17.9–38.8	20.8 ± 3.3; 15.9–30.5	28.8 ± 4.5; 18.5–39.2	23.5 ± 4.4; 15.4–34.5
HbA1c (%)	5.3 ± 1.0; 4–11.5	5.5 ± 0.8; 4.2–10.5	5.5 ± 1.3; 4–11.5	5.1 ± 0.7; 4–8.6	4.7 ± 0.6; 4–7
Moderate physical activity (≥10 mins continuously per day)					
No	104 (30)	53 (42)	41 (30)	5 (5.3)	5 (13.2)
Yes	242 (70)	73 (58)	46 (70)	90 (94.7)	33 (86.8)
Vigorous physical activity (≥10 mins continuously per day)					
No	237 (68.5)	76 (60.3)	56 (64.4)	77 (81.1)	28 (73.7)
Yes	109 (31.5)	50 (39.7)	31 (35.6)	18 (18.9)	10 (26.3)
Dietary diversity					
Low	227 (65.6)	95 (75.4)	83 (95.4)	20 (21.1)	29 (76.3)
Medium or high	119 (34.4)	31 (24.6)	4 (4.6)	75 (78.9)	9 (23.7)
Secondhand tobacco smoke exposure					
No	297 (86.1)	112 (88.9)	56 (64.4)	0 (0)	34 (91.9)
Yes	48 (13.9)	14 (11.1)	31 (35.6)	95 (100)	3 (8.1)
Sugar intake added to coffee/tea					
Monthly or less	141 (40.8)	5 (4)	22 (25.3)	80 (84.2)	34 (89.5)
Weekly or daily	205 (59.2)	121 (96)	65 (74.7)	15 (15.8)	4 (10.5)
SES combined index[a]	0.19 ± 0.97; −2.1 to 2.1	−0.21 ± 0.8; −1.9 to 2.0	1 ± 0.72; −0.7 to 2.1	0.6 ± 0.53; −1.3 to 1.7	−1.2 ± 0.7; −2.1 to 0.4
Education level					
No formal schooling or primary incomplete	282 (82.9)	115 (95.8)	81 (95.4)	58 (61.1)	26 (68.4)
Primary complete or secondary incomplete; secondary complete, vocational, or some college	58 (17.1)	5 (4.2)	4 (4.6)	37 (38.9)	12 (31.6)
Mud floor					
No	91 (26.3)	9 (7.1)	51 (58.6)	21 (22.1)	10 (26.3)
Yes	255 (73.7)	117 (92.9)	36 (41.4)	74 (77.9)	28 (73.7)
Food insecurity					
None	195 (56.4)	69 (56.1)	68 (78.2)	43 (46.2)	10 (26.3)
Mild, moderate, severe	151 (43.6)	54 (43.9)	19 (21.8)	50 (53.8)	28 (73.7)
Household size (number of persons)	6 (2.6), 2–18	8 (2.9), 3–18	4 (1.4), 2–9	7 (1.9), 2–12	6 (2.1), 2–10
Households have color TV					
Yes	187 (54.1)	60 (47.6)	23 (26.4)	41 (43.2)	35 (92.1)
No	159 (45.9)	66 (52.4)	64 (73.6)	54 (56.8)	3 (7.9)
Households have radio					
Yes	164 (47.4)	68 (54)	72 (82.8)	21 (22.1)	21 (55.3)
No	182 (52.6)	58 (46)	15 (17.2)	74 (77.9)	17 (44.7)
Households have mobile phone					
Yes	316 (91.3)	4 (3.2)	14 (91.3)	2 (2.1)	10 (26.3)
No	30 (8.7)	122 (96.8)	73 (8.7)	93 (97.9)	28 (73.7)
Households have bank account					
Yes	152 (43.9)	85 (67.5)	9 (10.3)	71 (74.7)	29 (76.3)
No	194 (56.1)	41 (32.5)	78 (89.7)	24 (25.3)	9 (23.7)
Households have bicycle					
Yes	85 (24.6)	110 (87.3)	78 (89.7)	45 (47.4)	28 (73.7)
No	261 (75.4)	16 (12.7)	9 (10.3)	50 (52.6)	10 (26.3)

Note: BMI, body mass index; HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; max, maximum; min, minimum; SD, standard deviation; SES, socioeconomic status.
[a]SES combined index calculated from principal component analysis based on the following variables: roof type, floor type, wall type, color TV, 24 household assets, electricity, toilet, water source, food insecurity, education, and household size.

Table 2. Baseline 24-h personal exposures to $PM_{2.5}$, BC, and CO concentrations (raw values) among women using biomass cookstoves, based on valid samples only among the HbA1c dataset, HAPIN trial (Guatemala, India, Peru, Rwanda).

24-h average personal exposures	*n*	Mean ± SD	Median (25th, 75th percentiles)	Min–max
$PM_{2.5}$ ($\mu g/m^3$)				
All research sites	313	120.1 ± 116.5	87.6 (44.5, 143.7)	10.0–803.4
Guatemala	122	145.9 ± 131	113.0 (70.1, 170.8)	13.7–803.4
India	76	110.2 ± 114	72.3 (43.8, 128.7)	10–531.4
Peru	79	105.4 ± 109	72.7 (29.8, 124)	14–477.8
Rwanda	36	85.4 ± 61.4	60.2 (46.1, 110.9)	14.7–297.1
BC ($\mu g/m^3$)				
All research sites	271	13.0 ± 9.6	11.1 (6.9, 16.3)	1.1–69.2
Guatemala	109	12.9 ± 6.5	12.3 (9.1, 15.3)	1.1–46.8
India	73	14.5 ± 12.0	12.1 (6.1, 20.7)	1.4–69.2
Peru	64	12.9 ± 12.1	9.8 (3.5, 16.6)	1.3–52.7
Rwanda	25	9.4 ± 4.3	9.6 (6.2, 12.3)	2.8–16.5
CO (ppm)				
All research sites	286	2.2 ± 3.4	1.3 (0.4, 2.8)	0–38.7
Guatemala	114	1.9 ± 1.8	1.4 (0.6, 2.7)	0–9.5
India	73	1.5 ± 2.9	0.6 (0.2, 2.1)	0–21.4
Peru	66	3.9 ± 5.4	2.4 (1.3, 5.2)	0–38.7
Rwanda	33	1.3 ± 1.9	0.6 (0.2, 1.3)	0–8.9

Note: BC, black carbon; CO, carbon monoxide; HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; max, maximum; min, minimum; $PM_{2.5}$, fine particulate matter; SD, standard deviation.

whereas the effect was in the opposite direction as that hypothesized among women with lower BMI levels ($p_{interaction} = 0.04$). There were also apparent differences by research site. For example, a hypothesized exposure–response effect for the association with BC and HbA1c was observed among participants in Guatemala; however, among participants in India, the opposite was observed ($p_{interaction} = 0.05$).

Our main effect results tend to be inconsistent with previous studies on air pollution and chronic diseases, including prediabetes or diabetes. Results from a study conducted on household air pollution exposure from biomass burning cookstoves and HbA1c and diabetic status among Honduran women revealed a higher prevalence of prediabetes in women with higher exposure to household air pollution.[42] The average HbA1c levels in that study population were 5.5%, and there was suggestive evidence of a larger effect in women ≥40 years of age; the mean difference in HbA1c per unit increase in log-transformed kitchen $PM_{2.5}$ mass was 0.028% (95% CI: −0.029, 0.086). Increasingly, research has linked a number of air pollutants to the chronic development of cardiometabolic illness.[21]

According to experimental research on the pathways linking air pollution exposure to diabetes, $PM_{2.5}$ mediates the relationship between endothelial dysfunction and insulin resistance. Air pollutants such as $PM_{2.5}$ generate reactive oxygen species that can damage endothelial cells directly by inducing oxidative stress.[21] This mechanism explains how exposure to air pollution in humans changes endothelial function. In addition, increases in insulin resistance frequently precede changes in endothelial function and reduce peripheral glucose uptake.[43]

The reported small changes in HbA1c associated with household air pollution exposure indicate that air pollutants may not have strong clinical effects on metabolic health. However, considering

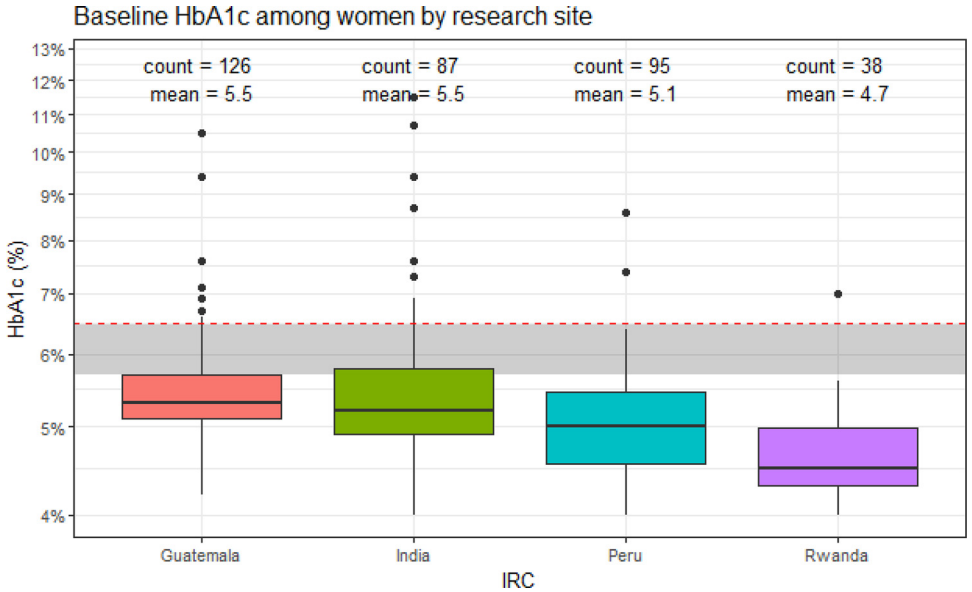

Figure 1. Box-and-whisker plot of HbA1c levels (%) among women at baseline by HAPIN research site. The central line in each box represents the median, the boxes represent the interquartile range (IQR), and the whiskers extend to 1.5 times the IQR. Outliers beyond the whiskers are shown as individual points. The red dashed line represents the standard cutoff for diabetes diagnosis at 6.5%, and the gray shaded region is the prediabetes range of 5.7%–6.4%. Summary statistics are displayed above each box, including counts and mean HbA1c values. Numeric values can be found in Tables 1 and 3. Note: HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; IRC, international research center.

Table 3. HbA1c levels with diabetes categories among women at baseline in the HAPIN trial (Guatemala, India, Peru, Rwanda) ($n = 346$).

Variable	n (%)
HbA1c (%) categories	
Normal (<5.7%)	266 (76.8)
Prediabetes (5.7%–6.4%)	58 (16.7)
Diabetes (≥6.5%)	22 (6.4)
Women with prediabetes by research site (n)	
Guatemala	24 (41)
India	17 (29)
Peru	17 (29)
Rwanda	0

Note: HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin.

the enormous number of persons exposed to household air pollution every day, even small changes in HbA1c at the population level might result in major health consequences globally.

This study had some limitations, including a limited sample size and some missing data for HbA1c and valid exposures. Exposure measurement error may have occurred if participants did not wear the instruments as advised during the 24-h monitoring period; this source of error may have resulted in a bias toward the null. The cross-sectional design of this study is another limitation because burning biomass is a long-term practice and increases in HbA1c brought on by air pollution exposure may require longer-term evaluation.[44] Although our measurements are meant to represent longer-term estimates of both exposure and health, a single HbA1c measurement and a 24-h household air pollution exposure measurement may not accurately reflect genuine average exposures or HbA1c levels, and the length of time of air pollution impacts on HbA1c cannot be determined by our analysis. It will be valuable to evaluate long-term changes in household air pollution exposure and HbA1c in the future among participants included in a longitudinal, repeat-measurements exposure–response association analysis over a certain time period. Future publications from the HAPIN trial will assess exposure–response associations over the entire study period with multiple time points.

This study has several important strengths, such as the use of high-quality instruments for the outcome evaluation and direct 24-h personal exposure monitoring. In addition, this study adds to the few studies that have quantified personal exposure and HbA1c among women to examine the relationship between household air pollution exposure and HbA1c in rural settings in LMICs. Furthermore, we evaluated $PM_{2.5}$, CO, and BC because they are important pollutants from burning biomass.

Overall, our results did not reveal a consistent association between 24-h personal household air pollution exposure and HbA1c despite our hypothesis that household air pollution would increase HbA1c levels based on evidence from existing ambient air pollution studies. Our study adds to the scant knowledge regarding the association between household air pollution and HbA1c in women and suggests the importance of considering BMI as an effect modifier on the impact of household air pollution on HbA1c. Moreover, other unmeasured factors impact household air pollution, such as cultural cooking practices and stove stacking. In many cultures, especially in rural areas of developing countries, cooking is done using biomass fuels. These fuels produce high levels of particulate matter, CO, and other harmful pollutants when burned.[45] Many traditional cooking methods involve open fires or rudimentary stoves that are not well ventilated. These methods allow smoke and pollutants to accumulate indoors, leading to high levels of household air pollution.[46] In addition, in many cultures, cooking is done indoors, without proper ventilation, trapping pollutants inside the home and increasing exposure to harmful smoke.[47] Understanding these practices will be essential for designing effective interventions to reduce household air pollution and its associated health risks. Further, it will be worth exploring potential contextual differences across the HAPIN research sites that may help explain our observation of different exposure–response effects (e.g., as in Guatemala and India).

Table 4. Adjusted associations between 24-h average personal log-transformed $PM_{2.5}$, BC, and CO and HbA1c measured in women participating in the HAPIN trial (Guatemala, India, Peru, Rwanda).

24-h average personal exposures	n	Adjusted HbA1c estimate	95% CI
$PM_{2.5}$	309	−0.06	−0.17, 0.06
BC	267	−0.01	−1.48, 0.13
CO	282	−0.04	−0.21, 0.14

Note: BMI was included as a covariate. Adjusted for age, SES (combined index), diet diversity, secondhand smoke exposure, moderate and vigorous physical activity, sugar intake, research site, and BMI. SES combined index calculated from principal component analysis based on the following variables: roof type, floor type, wall type, color TV, 24 household assets, electricity, toilet, water source, food insecurity, education, and household size. BC, black carbon; BMI, body mass index; CI, confidence interval; CO, carbon monoxide; HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; $PM_{2.5}$, fine particulate matter; SES, socioeconomic status.

Table 5. Adjusted associations between 24-h average personal log-transformed $PM_{2.5}$, BC, and CO and HbA1c measured in women participating in the HAPIN trial (Guatemala, India, Peru, Rwanda).

24-h average personal exposures	n	Adjusted HbA1c estimate	95% CI
$PM_{2.5}$	312	−0.07	−1.81, 0.05
BC	270	−0.02	−0.16, 0.12
CO	285	−0.04	−0.21, 0.13

Note: BMI was excluded as a covariate. Adjusted for age, SES (combined index), diet diversity, secondhand smoke exposure, moderate and vigorous physical activity, and sugar intake. SES combined index calculated from principal component analysis based on the following variables: roof type, floor type, wall type, color TV, 24 household assets, electricity, toilet, water source, food insecurity, education, and household size. BC, black carbon; BMI, body mass index; CI, confidence interval; CO, carbon monoxide; HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; $PM_{2.5}$, fine particulate matter; SES, socioeconomic status.

Table 6. Sensitivity analysis showing adjusted associations between 24-h average personal quartiles of $PM_{2.5}$, BC, and CO and HbA1c among women in the HAPIN trial (Guatemala, India, Peru, Rwanda).

24-h average personal exposures	N	Adjusted HbA1c estimate	95% CI
$PM_{2.5}$	309	—	—
Q1 (Ref)	78	Ref	Ref
Q2	78	−0.35	−0.63, −0.06
Q3	76	−0.18	−0.48, 0.11
Q4	77	−0.13	−0.42, 0.15
BC	267	—	—
Q1 (Ref)	67	Ref	Ref
Q2	67	−0.003	−0.33, 0.33
Q3	66	−0.13	−0.46, 0.20
Q4	67	−0.001	−0.32, 0.32
CO	282	—	—
Q1 (Ref)	71	Ref	Ref
Q2	71	−0.11	−0.42, 0.19
Q3	70	−0.13	−0.45, 0.19
Q4	70	−0.09	−0.41, 0.23

Note: BMI included as a covariate. Adjusted for age, SES (combined index), diet diversity, secondhand smoke exposure, moderate and vigorous physical activity, sugar intake, research site, and BMI. SES combined index calculated from principal component analysis based on the following variables: roof type, floor type, wall type, color TV, 24 household assets, electricity, toilet, water source, food insecurity, education, and household size. —, Not applicable; BC, black carbon; BMI, body mass index; CI, confidence interval; CO, carbon monoxide; HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; $PM_{2.5}$, fine particulate matter; Q, quartile; Ref, reference; SES, socioeconomic status.

Table 7. Assessing effect modification of the association between personal log-transformed household air pollution exposures and HbA1c by age, BMI, and research site within the HAPIN trial (Guatemala, India, Peru, Rwanda).

24-h average personal exposures	N	Adjusted mean difference in HbA1c (95% CI)	$p_{interaction}$
$PM_{2.5}$ per natural log unit increase ($\mu g/m^3$)			
Age (y)			
<51	162	−0.01 (−0.17, 0.15)	0.36
≥51	147	−0.12 (−0.28, 0.04)	
BMI ($\mu g/m^3$)			
<25 (normal weight)	156	−0.14 (−0.30, −0.03)	0.23
≥25 (overweight/obese)	153	0.001 (−0.16, 0.16)	
International research center			
Guatemala	120	0.08 (−0.12, 0.28)	0.34
India	76	−0.16 (−0.38, −0.05)	
Peru	78	−0.13 (−0.33, 0.08)	
Rwanda	35	0.06 (−0.38, 0.50)	
BC per natural log unit increase ($\mu g/m^3$)			
Age (y)			
<51	141	−0.03 (−0.21, 0.15)	0.75
≥51	126	0.02 (−0.20, 0.23)	
BMI ($\mu g/m^3$)			
<25 (normal weight)	131	−0.17 (−0.38, 0.04)	0.04
≥25 (overweight/obese)	136	0.13 (−0.06, 0.31)	
International research center			
Guatemala	107	0.36 (0.03, 0.70)	0.05
India	73	−0.21 (−0.45, 0.02)	
Peru	63	0.01 (−0.21, 0.22)	
Rwanda	24	0.09 (−0.57, 0.75)	
CO per natural log unit increase (ppm)			
Age (y)			
<51	140	−0.20 (−0.45, 0.05)	0.17
≥51	142	0.04 (−0.19, 0.27)	
BMI ($\mu g/m^3$)			
<25 (normal weight)	143	−0.04 (−0.28, 0.21)	0.73
≥25 (overweight/obese)	139	−0.09 (−0.33, 0.14)	
International research center			
Guatemala	112	0.14 (−0.17, 0.44)	0.41
India	73	−0.26 (−0.60, 0.09)	
Peru	65	−0.05 (−0.36, 0.25)	
Rwanda	32	0.04 (−0.51, 0.60)	

Note: Adjusted for age, BMI, SES (combined index), diet diversity, secondhand smoke exposure, moderate and vigorous physical activity, sugar intake. SES combined index calculated from principal component analysis based on the following variables: roof type, floor type, wall type, color TV, 24 household assets, electricity, toilet, water source, food insecurity, education, and household size. BC, black carbon; BMI, body mass index; CI, confidence interval; CO, carbon monoxide; HAPIN, Household Air Pollution Intervention Network; HbA1c, glycated hemoglobin; $PM_{2.5}$, fine particulate matter; SES, socioeconomic status.

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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.

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