Title
Relationship Between Daily Exposure to Biomass Fuel Smoke and Blood Pressure in High-Altitude Peru

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Abstract—Household air pollution from biomass fuel use affects 3 billion people worldwide; however, few studies have examined the relationship between biomass fuel use and blood pressure. We sought to determine if daily biomass fuel use was associated with elevated blood pressure in high altitude Peru and if this relationship was affected by lung function. We analyzed baseline information from a population-based cohort study of adults aged ≥35 years in Puno, Peru. Daily biomass fuel use was self-reported. We used multivariable regression models to examine the relationship between daily exposure to biomass fuel smoke and blood pressure outcomes. Interactions with sex and quartiles of forced vital capacity were conducted to evaluate for effect modification. Data from 1004 individuals (mean age, 55.3 years; 51.7% women) were included. We found an association between biomass fuel use with both prehypertension (adjusted relative risk ratio, 5.0; 95% confidence interval, 2.6–9.9) and hypertension (adjusted relative risk ratio, 3.5; 95% confidence interval, 1.7–7.0). Biomass fuel users had a higher systolic blood pressure (7.0 mmHg; 95% confidence interval, 4.4–9.6) and a higher diastolic blood pressure (5.9 mmHg; 95% confidence interval, 4.2–7.6) when compared with nonusers. We did not find interaction effects between daily biomass fuel use and sex or percent predicted forced vital capacity for either systolic blood pressure or diastolic blood pressure. Biomass fuel use was associated with a higher likelihood of having hypertension and higher blood pressure in Peru. Reducing exposure to household air pollution from biomass fuel use represents an opportunity for cardiovascular prevention. (Hypertension. 2015;65:00-00. DOI: 10.1161/HYPERTENSIONAHA.114.04840.)

Key Words: air pollution ■ blood pressure ■ global health ■ health status disparities ■ indoor air pollution ■ Latin America ■ rural health

Household air pollution (HAP) has been identified as the third leading risk factor for death worldwide,¹ and it is estimated to affect 3 billion people each year. HAP results from the burning of wood, animal dung, and other organic debris for cooking and heating. The negative health effects disproportionately burden households in resource-poor settings, as cleaner, more efficient fuels, such as liquefied petroleum gas, are more commonly used in households in urban settings and with higher incomes.²

The relationship between exposure to HAP and respiratory conditions, including chronic obstructive pulmonary disease, lung cancer, and pneumonia has been well established.¹ However, given the evidence of the association between ambient air pollution exposure and cardiovascular outcomes, including heart failure, myocardial infarction, arrhythmia, and cardiovascular-related mortality, there has been increased interest in examining the cardiovascular effects of HAP exposure.²⁴–⁷ Conflicting data on the association between HAP exposure and adverse cardiovascular outcomes exist. Observational studies of HAP exposure and cardiovascular disease have shown that biomass fuel use is associated with increased systemic blood pressure and an increased prevalence of hypertension.⁸–¹⁰ On a cellular and biochemical level, biomass fuel use is associated with a prothrombotic, proinflammatory biological state, with increased platelet aggregation, reactive oxygen species, and anticoagulant IgG.¹¹

Although it is estimated that HAP from biomass fuel use is a considerable risk factor for cardiovascular disease in resource-poor settings worldwide, additional evidence on the specific ways by which HAP increases systemic blood pressure is needed. Moreover, both pulmonary disease and systemic blood pressure are associated with biomass fuel use, yet the interaction between pulmonary function and systemic blood pressure in the setting of biomass fuel use has not been adequately characterized. Although several large cohort studies have described an association between reduced lung function with blood pressure and arterial elasticity, it remains
unclear whether cardiovascular disease from HAP occurs with concomitant reduced lung function.12-15 We sought to determine the association between daily biomass fuel use with systemic blood pressure, prehypertension, and hypertension in a population-based cohort of adults in Puno, Peru and if lung function, as measured by spirometry, was an effect modifier of the relationship between daily biomass fuel use and systemic blood pressure.

Methods

Study Setting

We conducted a longitudinal cohort study designed to characterize the prevalence and risk factors of chronic disease in 3 geographically distinct settings in Peru.16 This study used the baseline round of questionnaire and clinical data in Puno, a city in southeastern Peru at 3825 m above sea level where biomass fuels are used almost exclusively in surrounding rural villages. Puno primarily consists of indigenous, Andean people with both Quechua- and Aymara-speaking populations.

Study Design

Individuals aged ≥35 years, full-time residents in the area, who provided informed consent were invited to participate in the study. We identified a sex, age-stratified (35–44, 45–54, 55–64, and ≥65 years), and location-stratified (urban versus rural) sample, and only 1 participant per household was enrolled. The study was approved by the Institutional Review Boards at Universidad Peruana Cayetano Heredia and A.B. PRISMA, in Lima, Peru, and at the Bloomberg School of Public Health, Johns Hopkins University, in Baltimore, MD.

Study Procedures

Participants responded to a questionnaire on sociodemographics, cardiopulmonary risk factors, and history of cardiopulmonary symptoms. Fieldworkers measured weight, height, blood pressure, and spirometry. Spirometry was conducted using the Easy-On-PC spirometer (ndd, Zurich, Switzerland) before and after 200 μg of inhaled salbutamol via a spacer following standard guidelines.17 Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in triplicate using a digital sphygmomanometer (OMRON HEM-780; Osaka, Japan) that was previously validated for an adult population.18 We used the right arm for all measurements using an appropriately fitted cuff size. Participants were asked to sit comfortably for 5 minutes before the first measurement was taken, and the set interval of time between measurements was 5 minutes. The right forearm was supported on a table for all measurements. Final SBP and DBP were calculated as the average of the second and third measurements.

Definitions

The following variables were determined by self-report in a structured questionnaire: daily biomass fuel use, hypertension diagnosis, use of antihypertensive medications, and pack-years of tobacco smoking. Daily biomass fuel use was defined as self-reported daily burning of wood or dung for cooking or heating for >6 months at any time during the participant’s lifetime. Prehypertension was defined as SBP of 120 to 139 mm Hg or DBP of 80 to 89 mm Hg in the absence of antihypertensive medication use18; and, hypertension as SBP of ≥140 mm Hg or DBP of ≥90 mm Hg or self-reported diagnosis by a physician with concomitant use of antihypertensive medications. Forced vital capacity (FVC) was defined as the total volume of air (in liters) expired during forced expiration. Percent predicted values were determined using the predictions derived from a healthy Mexican-American population.19 Physical activity was determined based on leisure time and transport time domains of International Physical Activity Questionnaire as recommended for Latin American populations.20 Alcohol abuse was measured using the Alcohol Use Disorders Identification Test.21 Depressive symptoms were defined as a score of ≥23 in the Spanish-validated version of the Center for Epidemiological Studies Depression Scale.22 Education was categorized by schooling years (<6, 7–11, and ≥12 years). Socioeconomic status was defined as wealth index based on household income, assets, and household facilities as previously described.24

Biostatistical Methods

Our primary aim was to compare blood pressure outcomes in participants with and without daily exposure to biomass fuel smoke. We used multivariable linear and multinomial logistic regressions to model continuous blood pressure outcomes and categories of hypertension, respectively. In a minimally adjusted model, we controlled for differences in age, sex, and body mass index. In the fully adjusted model, we controlled for age, sex, body mass index, height, tertiles of wealth index, categories of education years, presence or absence of depressive symptoms, pack-years of smoking, alcohol abuse, and low physical activity. Antihypertensive medication use was included in the model for continuous blood pressure outcomes only. We examined for interaction effects between biomass fuel use and either sex or postbronchodilator percent-predicted FVC on blood pressure, and used the likelihood ratio test to evaluate for effect modification. Statistical analyses were conducted in STATA 12 (STATA Corp, College Station, TX) and R (www.r-project.org).

Results

Participant Characteristics

A total of 1004 participants were included in this analysis (Table 1). Participants with daily exposure to biomass fuel smoke were more likely to be women and live in a rural setting; had a lower prevalence of obesity, lower values of lung function, lower prevalence of tobacco smoking, increased physical activity, fewer years of education, and a lower wealth index than did participants who did not have daily exposure to biomass fuel smoke. Overall, the prevalence of daily tobacco smoking was low in both the groups.

SBP and DBP by Daily Biomass Fuel Use

In unadjusted analysis, SBP and DBP were higher by 3.0 and 2.5 mm Hg between participants with and without daily biomass fuel use, respectively (Table 2). In the minimally adjusted model, SBP and DBP were higher by 6.1 and 4.7 mm Hg between participants with and without daily biomass fuel use, respectively. The fully adjusted model further strengthened this relationship: SBP and DBP were higher by 7.0 and 5.9 mm Hg between participants with and without daily biomass fuel use, respectively. After stratification by sex, the association between daily biomass fuel use with SBP and DBP remained statistically significant in both men and women; however, there was no interaction effect between sex and daily biomass fuel use on either SBP (P=0.10) or DBP (P=0.56).

Prevalence of Prehypertension and Hypertension by Daily Biomass Fuel Use

In unadjusted analysis, daily biomass fuel use was associated with having prehypertension (Table 2). Both the minimally adjusted and the fully adjusted model increased the strength of the association between daily biomass fuel use
and having prehypertension. In unadjusted analysis, we did not find a relationship between biomass fuel use and having hypertension (Table 2); however, after minimal adjustment, an association between daily biomass fuel use and having hypertension became apparent. This suggests that age, sex, and body mass index were important confounders of the relationship between biomass fuels and having hypertension. The fully adjusted model further strengthened the relationship between biomass fuel use and having hypertension. Because of the low prevalence of prehypertension and hypertension, we were unable to adequately stratify these analyses by sex.

**Effect Modification of Blood Pressure by FVC**

In unadjusted analyses, the difference in SBP and DBP between participants with and without daily exposure to biomass fuel seemed to be greater in participants in the 2 highest quartiles of postbronchodilator percent-predicted FVC (Figure). Despite this trend, after multivariable analyses, we did not find interaction effects between daily exposure to biomass fuels smoke and percent predicted FVC for either SBP ($P=0.47$) or DBP ($P=0.57$).

**Discussion**

In a high altitude region of Peru, participants who reported daily use of biomass fuel had higher blood pressures and an increased risk of having prehypertension or hypertension than did those without daily biomass fuel use. Both men and women seemed to be equally affected. The relationship between biomass fuel use and blood pressure was not modified by lung function.

Our study adds to the growing body of literature on the cardiovascular effects of HAP from biomass fuel use, suggesting that although daily biomass fuel use is associated with increased blood pressure in multiple settings, the magnitude of the association varies. Baumgartner et al. studied PM$_{2.5}$ personal exposure in rural Chinese women and found a 2.2 mm Hg increase in SBP and 0.5 mm Hg increase in DBP for each 1-log-μg/m$^3$ increase in 24-hour mean PM$_{10}$ exposure. Lee et al. examined the cardiovascular effects of biomass fuel use in Chinese adults and found that self-reported biomass fuel use was associated with a 1.7 increased odds of hypertension, which is substantially less than the adjusted relative risk ratio of 6 from the analysis of our cohort. In addition, Lee et al. reported that women were more likely to have a doubling in the odds hypertension attributed to biomass fuel use than did men. In contrast, the results from our study show that daily exposure to biomass fuel smoke was associated with higher blood pressures and an increased risk of having prehypertension or hypertension.

There are no previous large studies of hypertension or any other cardiovascular disease in relation to biomass fuel use in Latin America, other than 2 small improved cookstove interventions in Guatemala and Nicaragua.

Differences in the magnitude of association and the effect of sex across the various studies are probably influenced by several factors, including gene by environment interactions, cultural practices, altitude, and other environmental variables. Aspects of the cooking environment, including ventilation of the cooking space and the types of biomass fuels used, influence the intensity of the exposure as well as the relative concentration of noxious gases and particulate matter released during combustion. In addition, our study was conducted in a population living at high altitude, and thus it is unclear to what extent the relationship between biomass fuel use and systemic blood pressure was affected by this environmental exposure. Although individuals who ascend to high altitude from sea level experience an increase in blood pressure, epidemiological studies of the blood pressure effect of chronic exposure to high altitude have had mixed results. The combined effect of altitude and exposure to HAP on blood pressure has not been well described and deserves further study, potentially increasing our understanding of blood pressure regulation.

There are several potential mechanisms by which biomass fuel use might affect blood pressure. Biomass fuel combustion...
releases gases and fine particulate matter. Fine particulate matter exposure in controlled studies has been shown to increase blood pressure, affecting vasomotor tone through nitric oxide pathways.\textsuperscript{29–35} Acute exposure to air pollution also exerts autonomic effects, resulting in increased heart rate and decreased heart rate variability.\textsuperscript{35,36} Moreover, exposure to fine particulate matter (2.5 μm in size) has been associated with systemic inflammation, increased oxidative stress, and decreased endothelial function, including increased plasma fibrinogen, serum C-reactive protein, and changes in leukocyte adhesion molecule expression.\textsuperscript{37–40} One hypothesis is that the presence of fine particulate matter in the lung interstitium causes systemic inflammation that, in turn, increases blood pressure.\textsuperscript{41,42}

In looking at the role of lung function as measured by FVC as a potential mediator in the relationship of daily biomass fuel use with SBP and DBP, our study found no effect modification by quartiles of lung function. However, the trend toward increased difference in SBP and DBP between daily biomass fuel users and nonusers in the higher 2 quartiles of FVC suggests that increased lung function might be associated with increased SBP and DBP in setting of HAP exposure from biomass fuel use. The biological mechanism by which HAP from biomass fuel increases blood pressure might involve translocation of ultrafine particulate matter (0.1 μm in size) via the alveolar capillaries, although studies of ultrafine particle translocation via the lungs in healthy human volunteers

\begin{table}
\centering
\caption{Single Variable and Multivariable Analysis of the Association Between Daily Biomass Fuel Use and Blood Pressure Outcomes*}
\begin{tabular}{|l|c|c|c|c|}
\hline
Blood Pressure Variable & Single Variable & P Value & Minimally Adjusted Model & P Value \tabularnewline
\hline
Increase in SBP, mm Hg (95% CI) & & & & \tabularnewline
Overall & 3.0 (1.0 to 5.1) & 0.004 & 6.1 (4.2 to 8.0) & <0.001 \tabularnewline
Men & 5.8 (3.3 to 8.4) & <0.001 & 8.9 (6.3 to 11.4) & <0.001 \tabularnewline
Women & 1.4 (–1.6 to 4.4) & 0.37 & 3.8 (1.0 to 6.6) & 0.007 \tabularnewline
Increase in DBP, mm Hg (95% CI) & & & & \tabularnewline
Overall & 2.5 (1.3 to 3.8) & <0.001 & 4.7 (3.5 to 6.0) & <0.001 \tabularnewline
Men & 3.4 (1.7 to 5.1) & <0.001 & 5.5 (3.7 to 7.3) & <0.001 \tabularnewline
Women & 2.1 (0.4 to 3.9) & 0.02 & 4.1 (2.4 to 5.8) & <0.001 \tabularnewline
Prehypertension, RRR (95% CI) & 1.8 (1.0 to 2.8) & 0.005 & 3.5 (1.7 to 7.0) & <0.001 \tabularnewline
Hypertension, RRR (95% CI) & 1.0 (0.7 to 1.5) & 0.91 & 2.0 (1.2 to 3.3) & 0.005 \tabularnewline
\hline
\end{tabular}
\end{table}

CI indicates confidence interval; DBP, diastolic blood pressure; RRR, relative risk ratio; and SBP, systolic blood pressure.

*Multivariable models were either minimally adjusted (for age, sex, and BMI) or fully adjusted (for age, sex, BMI, height, tertiles of wealth index, categories of education years, presence or absence of depressive symptoms, pack-years of smoking, alcohol abuse, and low physical activity).
have had conflicting results.\textsuperscript{43,44} Particulate matter other than PM\textsubscript{2.5} may also account for the association between air pollution exposure and increased in blood pressure. One study in rural China found that exposure to black carbon among women was more greatly associated with increased blood pressure than PM\textsubscript{2.5} exposure.\textsuperscript{45} Additional studies of the interaction between individual components of air pollution, lung function, and systemic blood pressure are needed.

The results of our study support the need for additional research on the effect of HAP from biomass fuel use on cardiovascular disease. Globally, there are initiatives to reduce HAP exposure by replacing traditional cookstoves with cleaner technology that either replaces biomass fuel use with liquefied petroleum gas or electricity, or effectively vents the smoke from biomass fuel combustion out of the home. However, as these initiatives are evaluated, evidence on both the cardiovascular and the pulmonary health benefits of each cookstove initiative is needed to better direct investment. Cultural acceptance and economic sustainability are key components of clean cookstove technology initiatives, however, the precise understanding of potential health benefits is needed to encourage public and private investment and avoid wasting resources on ineffective cookstove technologies. Given the widespread use of biomass fuels globally, reducing exposure to HAP presents a potential opportunity to reduce morbidity and mortality from cardiovascular disease in resource-poor settings.

The primary limitation of this study is that it is observational in design at a single site and thus cannot determine causation. Although we have adjusted for many confounding variables in our analysis, there may be potentially unmeasured confounders. Specifically, biomass fuel use was closely associated with rural residence, which may be associated with unmeasured environmental variables that might affect blood pressure. Moreover, we measured neither individual exposure to HAP nor the gaseous or particulate matter composition of the biomass fuel smoke but rather used self-reported daily biomass fuel use as a proxy for exposure. However, in previous studies in a subgroup of the same cohort, we have determined that 24-hour mean PM\textsubscript{2.5} exposure in individuals living in rural Puno, where 95% of the population used biomass fuels daily, was substantially greater than in individuals living in urban Puno, where biomass fuel use was low or nonexistent.\textsuperscript{46} In addition, unpublished data from our group of ambient PM\textsubscript{2.5}, monitoring in rural Puno suggest that ambient PM\textsubscript{2.5} levels are low and do not significantly contribute to the air pollution exposure of rural Puno residents (W. Checkley, unpublished data, 2014). Another limitation of our study is that we measured blood pressure in a single examination rather than in multiple visits. We are also unable to account for recent acute environmental exposures that might have transiently affected blood pressure measurement during the day of examination. Given the numerous potentially blood pressure raising exposures found in the urban environment in which most biomass fuel nonusers reside, and the heterogeneity of the biomass fuel smoke exposure captured in our liberal definition of biomass fuel use, our study probably underestimates the true association of biomass fuel smoke exposure and blood pressure in this population. Rural biomass fuel users generally have less access to medical care than urban participants and thus might be less likely to receive a diagnosis of hypertension. The underdiagnosis of hypertension in the rural population may have resulted in further underestimation of the association of biomass fuel use with hypertension.

Perspectives
This study expands on the growing body of literature that examines the cardiovascular risk associated with HAP from biomass fuel use. We have demonstrated an association between biomass fuel use with blood pressure and hypertension prevalence, but additional research is needed to understand the degree to which exposure to HAP affects hard cardiovascular outcomes, including heart failure, myocardial infarction, and cardiovascular-related mortality. In addition, further studies are needed to determine whether improved biomass fuel cookstove technology improves cardiovascular outcomes, or if it is necessary to replace biomass fuels with cleaner fuels, such as liquefied petroleum gas, to effectively reduce cardiovascular risk. This area of future research has broad implications for not only public health policy but also energy policy on a national and regional level. Uncovering the totality of cardiovascular and pulmonary disease associated with HAP from biomass fuel use is necessary to influence policymakers to enact effective public policy to improve the health of the rural poor.

Conclusions
In a high-altitude region of Peru, biomass fuel use was associated with elevated blood pressure and a higher prevalence of hypertension. The association between daily biomass fuel use with SBP and DBP was present and consistent for both men and women. Lung function as measured by FVC was not an effect modifier in the relationship between biomass fuel use with SBP and DBP. Additional studies of the effect of HAP and cookstove interventions on cardiovascular risk and outcomes are needed.

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Although it is estimated that exposure to household air pollution is one of the largest contributors to poor health worldwide, there are few studies that closely examine how household air pollution exposure from biomass fuel use might negatively affect cardiovascular disease outcomes. The results of this study have implications for cardiovascular disease prevention, particularly in resource-poor settings.

Summary

In a high-altitude region of Peru, biomass fuel use was associated with higher blood pressure and a higher likelihood of having hypertension.

Novelty and Significance

What Is New?

- This study is one of the few studies that investigate the systemic blood pressure outcomes associated with household air pollution exposure from biomass fuel use. Moreover, there are no other published studies that consider lung function as a potential effect modifier in the relationship between biomass fuel use and systolic blood pressure.

What Is Relevant?

- Although it is estimated that exposure to household air pollution is one of the largest contributors to poor health worldwide, there are few studies that closely examine how household air pollution exposure from biomass fuel use might negatively affect cardiovascular disease outcomes. The results of this study have implications for cardiovascular disease prevention, particularly in resource-poor settings.
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