Maternal Exposure to biomass smoke and carbon monoxide in relation to adverse pregnancy outcome in two high altitude cities of Peru

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Abstract

Background—Exposure to pollution from biomass fuel has been associated with low birthweight in some studies. Few studies have included exposure-response analyses.

Methods—We conducted a case-control study of biomass fuel use and reproductive outcome at high altitude in Peru. Cases (n=101) were full term births who were SGA (birth weight <10th percentile for gestational age). Controls (n=101) had a birthweight $\geq 10^{th}$ percentile, and were matched to cases on birth week and residence. Biomass fuel use during pregnancy was determined by questionnaire. Carbon monoxide (CO) in the kitchen was measured in a subgroup (n=72). Logistic regression was used to estimate the effects of biofuel and CO on the risk of SGA, controlling for maternal education and parity.

Results—Among cases, 30%, 27% and 44% used gas, gas+biomass, and biomass, respectively, while the figures for controls were 39%, 33%, and 29%. The adjusted odds ratio (OR) for biomass fuel alone compared with gas alone was 4.5 (95%CI: 1.3, 15.5, p=0.02), while the OR for biomass +gas vs. gas alone was 2.1 (0.80-5.5)(p=0.13). Among the subgroup with measured CO, the mean 48-hour kitchen CO levels were 4.8, 2.2 and 0.4 ppm for biofuel only, biofuel+gas, and gas respectively. ORs by increasing tertile of CO level were 1.0, 1.16, and 3.53 (test for trend, p=0.02). The exposure-response trend corresponds well with one other study with analogous data.

Conclusion—Despite limited sample size, our data suggest that maternal exposure to biomass smoke and CO, at high altitude, is associated with SGA among term births.

Keywords

biomass; carbon monoxide; small for gestational age; low birthweight; indoor air; biofuel; altitude; Peru

INTRODUCTION

Traditional biomass fuels (wood, agricultural wastes and animal dung) are a major source of household energy in developing countries. About half of the world's population depends on biomass as the primary source of household energy, burning 2 billion kilograms of biomass every day in developing countries (Lakshimi et al. 2012). The daily exposures to high concentrations of smoke from cookstoves inside kitchens create large smoke exposures for women and their small children (Northcross et al. 2010, Elledge and Phillips 2012).

An estimated 3.5 million deaths are directly associated with household air pollution (HAP) each year, primarily infant deaths due to pneumonia (Lim et al. 2010). More recent data suggest biomass fuel has adverse impacts on reproductive outcomes, but these data are not conclusive.

Literature on HAP and birthweight remains relatively limited. A recent meta-analyses found that IAP was associated with increased risk of low birth weight (LBW) (odds ratio = 1.38, 95% confidence interval: 1.25, 1.52), of stillbirth (odds ratio = 1.51, 95% confidence interval: 1.23, 1.85), and of reduced mean birth weight (−95.6 g, 95% confidence interval: −68.5, −124.7 g) (Pope et al. 2010). Six studies were of birthweight were included in this meta-analysis ((Boy et al. 2002, Siddiqui et al. 2008, Mishra et al. 2004, Tielsch et al. 2009, Mavalankar et al. 1992, Thompson et al. 2005, updated by Thompson et al. 2011). Of particular note is the only interventional study among the six studies included (Thompson et al. 2011), where stoves were provided to pregnant women in the second and third trimester of pregnancy. These authors found an increase of 89 g in the birth weight of children of mothers using the intervention stoves (vs. open fires) (95% CI −27, 204), and reduced odds of a low birth weight child (OR 0.74, 95% CI 0.33-1.66)(Thompson et al.2011). Since the above-cited meta-analysis, three other observational studies have found reduction of birth weight among women who used biofuel for cooking (compared with gas users) of 78 gms (Epstein et al. 2013), 178 gms (Amegah et al. 2012), and 186 gms (Abusalah et al. 2012). Amegah et al. (2012) reported an odds ratio for low birth weight of 2.95 (1.10-7.92) among biofuel users. Only one of these studies (Thompson et al. 2011) provided data on the quantitative exposure-response between exposure to HAP and adverse reproductive outcomes.

According to the Global Alliance for Clean Cookstoves, "while the link between exposure to cookstove smoke and a wide range of health problems such as pneumonia, chronic obstructive pulmonary disease, and lung cancer is well established, the current body of evidence linking cookstoves with other potentially important health effects, such as cataracts and adverse pregnancy outcomes is compelling but somewhat limited" (Global Alliance for Clean Cookstoves, 2013). The plausibility of an association of indoor air with adverse reproductive outcomes has been strengthened by a recent large meta-analyses showing that outdoor air PM2.5 and outdoor air C0 are significantly associated with low birth weight (Dadvand et al. 2013, Steib et al. 2012). Indoor air pollution due to biomass burning is generally higher than outdoor air pollution.

Biomass fuel is commonly used at high altitude in Peru. 1.2 million households of people living over 2000 meters in Peru use wood as fuel for cooking (INEI 2007). The type of biomass used at high altitude in Peru changes above the tree line, where use of dung replaces use of firewood.

In a prior case-control study conducted in two high altitude cities of Peru (Huancavelica and Abancay), we found that cooking with biomass increased significantly the risk of low birthweight (OR: 3.80; 95% CI 1.17-12.14), but was less strongly associated with preterm births (OR 1.59, 95% CI 0.41-6.18) (Yucra et al. 2011).

The present study aimed to investigate in a new population whether indoor air pollution at high altitude, due to the use of biomass fuel, contributes to the risk of full-term births which are small for gestational age (birth weight <10th percentile). Furthermore, we measured CO levels in kitchen areas among a sub-sample of women (n=72, 36 cases and 36 controls), and analysed the risk of small births by CO level. Carbon monoxide (CO) is one of the major constituents of biomass fuel (Naeher et al. 2007).

METHODS

Study population, definition of cases and controls

This study was conducted among adult females living in urban and rural areas of the provinces of Huancavelica at 3680 meters and Junin at 4105 meters in Peru from August 2011 to May 2012, within 3 hours travel time to public regional hospitals or public health centers (clinics offering primary health care). The hospitals included in the study were: Regional Hospital of Huancavelica (and its associated health centers), Junin hospital (and its associated Carhuamayo Health center). The population studied was chosen and recruited from the records of births in these public hospitals and health centers. Cases were selected if they were SGA (<10% percentile weight at a specific gestational age) at full term birth ($\geq$ 37 weeks of gestation). Controls were full term births who had birthweights greater than or equal to the 10th percentile for their gestational age, and were pair-matched with cases by hospital of birth, week of birth, and maternal district of residence. The percentile of birth weight specific to a gestational age was determined from standard curves (Williams et al. 1982).

We defined cases and control in this manner based on our prior work, and for theoretical and practical considerations. Our prior work found the strongest association with biofuel was found for low birth weight babies (<2500 gms) at full term, rather than pre-term births. We also felt that premature births might represent other pathologies rather than growth restriction, which we felt was the most likely consequence of exposure to biofuel (Zeitlin et al. 2000). As our sample size was limited due to budget restrictions, we wished to focus on the most likely strongest associations. Hence we focused on growth restriction in full term births. Furthermore, we wanted to restrict the eligible population to recent births (over the last two years), to maximize the chance that current fuel use was the same as fuel use during pregnancy – given that we wanted to measure current CO levels, which we hoped would represent past CO use. Given a finite number of births available in the two study areas, we chose to broaden our prior case definition of low birth weight (<2500 grams), which was

anticipated to be about 5% of births based on data in the area, to a slightly broader case definition of SGA at full term (lowest 10% of births).

Women giving birth in government hospitals and clinics represent the great majority of births in the study area. According to data from the Peruvian Ministry of health in 2011, home births represented 9.3% of all births in Huancavelica, and 8.4% of all births in Junin (www.minsa.gob.pe/estadisticas/estadisticas/nacimientos/NACMacros.asp?05, last accessed 9/16/2013). Virtually no births in these two departments occur in private clinics, which are very few.

Cases and controls were included only if they were using the same type of cooking fuel as they had used at the time of their pregnancy. Preterm births were not included in the case groups since our prior study showed that pre-term births were less associated with biofuel use (Yucra et al. 2011).

The list of births was obtained in public hospitals from the database of the Perinatal Informatic System (PIS), database based on reports from each Peruvian hospital. Records of mothers that had had their babies over a two-year period prior to study initiation were used.

For this study, gestational age was determined for all births by last menstrual period. Gestational age for all births was also assessed according to Capurro method , which is a method relying on clinical examination of the fetus in the first two days of life, and which has been shown to have a 95% confidence limit of 11 days (Williams et al. 1982, Narayanan et al. 1982). When these two estimates differed by more than 2 weeks (n=4), subjects were excluded from the study.

Population recruitment and questionnaire

Cases and controls were selected from medical records in the order in which they were encountered, beginning with the most recent births. The addresses of mothers were available. Mothers were contacted by study investigators and asked to voluntarily participate in the study. An informed consent form was signed by mothers who accepted to voluntary participate in the study. The houses were re-visited if nobody was home. When the address was wrong, we chose the next subject in the records belonging to the same group: case or control.

After recruitment, mothers completed an in-person pre-tested questionnaire. The questionnaire was administered by trained nurses. The questionnaire included questions regarding to: the type of stove and fuel used for cooking, socio-demographic data, reproductive history, social habits, the type of fuel used for heating, time spent cooking or using biofuel, and household characteristics. The time required to administer the questionnaire was approximately 20 minutes.

If the mother changed type or quantity of fuel used since pregnancy, she was not included in the study, given that we planned to measure current CO levels which were to serve as a proxy for past exposure during pregnancy. Data regarding to the households' characteristics, ventilation, house type (straw/mix of straw and bricks/bricks only) and number of rooms,

and source of water was gathered in the questionnaire. If the case was not located, their control was automatically eliminated.

The study was conducted after approval from the ethical committees of Emory University, the University of Georgia, and the Peruvian Cayetano Heredia University. Participants had the freedom to continue or retire from the study at any time. Data were maintained in strict confidentiality.

Exposure assessment

Area Indoor CO-Area Sampling—We collected indoor area CO measurements for a randomly chosen sub-sample of 36 cases and 36 controls. Budget restrictions prohibited CO collection on the whole population. These cases and controls were not matched as in the overall study, due to logistical difficulties in carrying out the sampling only in matched pairs. The CO measurements were collected using a passive Drager Safety diffusion tubes (Drager Safety AG & Co. KGaA, Germany) with nominal cumulative exposure ranges of 50-600 ppm/hour for sampling time of 48 hours in the kitchen. This diffusion tube is sensitive to typical ranges of CO found in households using biomass for cooking and is sufficiently small, light, non-obtrusive and safe for use on infants (Smith et al. 2010). The passive diffusion tubes operate by changing color as CO diffused through the tube. The length of the color stain and the amount of time the tube is exposed to the air are used to determine the both cumulative and the time weighted average CO concentration over 48 hours (Northcross et al. 2010).

CO measurements were taken at relative breathing height (approximately 1.5 m) in the kitchen where the mothers spend more time. The sample in the kitchen was taken at approximately one meter distance from the stove or fire pit. The women were told to live and act as usual, doing whatever they would normally do. At the end of each sampling period an air tight plastic cap was placed over the open end of the tube. The tubes were stored in airtight containers and moved to a special box in a field station where they were read. and then returned to the box for storage.

A consistent and unbiased reading of each tube was essential for an accurate CO concentration. Tubes were read by three independent readers who read each tube under standard conditions using a sunlight spectra lamp; this lamp illuminated the tube reading area, which consisted of a standardized seating arrangement at a table covered with white paper. The time-weighted average exposure was determined on site by measuring the length of the discoloration, and the corresponding exposure in ppm-hours averaging this estimate across the three readers, and then and dividing the total CO exposure in ppm-hours by the length of the measurement period (48 hours). Seven samples had readings above the maximum limit of 600 ppm-hours and were assigned 600 ppm-hours.

Data analysis—The data was filled in a excel database and statistical analysis was performed with a statistical package STATA 10v.

Conditional logistic regression appropriate for matched data was used to estimate the effects of biofuel used on adverse outcomes. We explored the potential confounding effects of

maternal education, parity, mother's age at child's births, residence type (urban, rural), and post-pregnancy BMI (body mass index). Variables were retained in the final model only where significantly (p<=0.05) associated with outcome and exposure, or if they changed the exposure coefficient by greater than 10%. Marital status was categorized as: with partner/ without partner. Parity was defined as the number of prior live births. Urban area was defined as a residence in a groups of buildings and structures in continuous blocks, bounded by streets and avenues, with services such piped water, electricity, hospitals, and nearby schools. Rural was defined by dispersed housing, without general services. Low education was defined as no or only primary education, and high education level was defined as secondary school or greater.

Biofuel exposure was defined as biofuel use, biofuel use plus gas, and gas only, used for cooking. Houses in the study area generally did not have any separate system for heating other than the kitchen. The fuels included gas, kerosene, firewood, dung, and champa (the mix between a high altitude plant named "ichu" and dung of the llama or sheep). Information on cooking fuel types was used to categorize mothers into two groups: exposed from homes using biomass fuels (firewood, dung, champa and charcoal) and not exposed to biomass (use gas, electricity or kerosene).

We also analysed risk of SGA among the subsample with CO levels. We grouped CO values in three tertiles (33%): < 1.05 ppm; 1.05 – 3.81 ppm; 3.82 ppm, with approximately equal numbers of subjects. For this analysis we used unconditional logistic regression, appropriate for unmatched data. Only variables that changed the effect estimate for biofuel by 10% or more were included in final models as confounders.

RESULTS

We identified from hospital and clinic records 440 women (220 cases and 220 controls) who fulfilled study eligibility, with birth dates between July 2009 and July 2011 . Of these, we were able to obtain good current addresses and contact 327, of whom all but 5 (3 cases, 2 controls, 1.5%) agreed to participate. Of these 322 women, 120 (37%, 61 cases, 59 controls) were subsequently excluded because they either moved before they could participate, or because they changed either the type or quantity of fuel they used since the pregnancy. This left us with a study population of 202 women, 101 cases and 101 controls.

Table 1 summarizes baseline characteristics of participants in the control and case groups. The average age was 28.7 and 27.3 years respectively (p = 0.17). Most women using biofuels used them with an open fire (73%), although some had stoves with chimneys. Significant differences between cases and controls were found in alcohol use (p = 0.001), and post-pregnancy BMI (p=0.01), but neither of these variables acted as confounders in regression models. It is worth noting that alcohol use was only occasional, ie, 1 or 2 times per year. The proportions using different types of fuel did not differ significantly between cases and controls in Table 1 (p=0.24), but this result does not take in account either the pair matching nor control for confounders, as does the logistic regression analysis.

Data obtained from the hospitals and clinics for non-participants showed they were similar to participants. Among non-participating cases, the average age, gestational age, and child's birthweight (grams) were 26.4, 39.5, and 2572. Among non-participating controls the corresponding figures were 27.3, 39.3, and 3197. As seen in Table 1, the corresponding figures for participating cases were 27.3 years, 38.9 weeks, and 2570 grams, while for participating controls they were 28.7 years, 39.1 weeks, and 3186 grams.

Table 2 shows results for the association between maternal exposure to biofuels for cooking during pregnancy from the logistic regression. We found that cooking with biofuel was associated with higher risk of SGA compared with gas (adjusted OR 4.53; 95%CI: 1.34, 15.49; p=0.02).

Table 3 contains the 48 hour average indoor (kitchen) concentration of CO according the type of fuel used; kitchen levels were markedly higher in mothers that used biofuel than the mothers that used gas as fuel (4.79 ± 4.32 ppm vs. 0.40 ± 0.27 ppm; p = 0.03). CO levels were markedly higher in mothers that belonging in the case group than the control group (5.29 ± 0.30 ppm vs. 2.32 ± 0.55 ppm; p = 0.001).

Tables 2 and 3 suggest that the higher risk of SGA for those using bio-fuels may be due to the higher levels of CO among those using biofuels. To analyse this further, we analysed the risk of SGA in relation to CO levels in the sub-sample where we measured CO.

Table 4 shows the logistic regression results for SGA and CO values grouped as: < 1.05 ppm; 1.05 – 3.81 ppm;   3.82 ppm. The risk of SGA among women with CO levels   3.82 ppm. was three times higher than the bottom tertile (adjusted OR 3.53, 95% CI 0.95-13.23, p 0.06). An exposure-response trend test using continuous levels of CO was significant (p=0.02, coefficient 0.19 for increase in log odds with each unit of CO). The odds of a SGA birth increased approximately 20 % for each increase of 1 ppm of CO.

DISCUSSION

In our data biofuel users had significantly higher levels of kitchen C0 than gas users, Kitchen CO level in homes of subjects using both gas and biomass fuel was intermediate between the two.

CO levels for biofuel users in our study were similar or slightly lower than those recently reported in two studies in Guatemala among open fire users. Our mean CO level for biofuel users (only) was 4.8 ppm (std. dev. 4.3)(median 3.5), with a range of 0.3-12.4. Smith et al. obtained a mean of 8.6 ppm (std. dev. 4.6)(n=150) in kitchens among biofuel users using open fires (48 hours samples)(Smith et al. 2010). Northcross et al. found a mean of 7.2 mg/m3 (std. dev. 6.2) CO among 130 open fire users, which converts to a mean of approximately 4.1 ppm (Northcross et al. 2010).

In this study cooking with biofuel alone, versus gas, was associated with SGA (OR adjusted 4.53; 95%CI: 1.33, 15.49, p=0.02). There findings are similar to our earlier findings, where the OR was 3.04 (CI 95% 1.2 – 7.77) (Yucra et al. 2011). These results suggest higher risks than those found previously for biofuel use (Boy et al. 2002, Siddiqui et al. 2008), although

our finding is based on small numbers and has a wide confidence interval. It is possible that there is a synergism between biofuel use and high altitude in increasing the risk for adverse pregnancy outcome.

Maternal lifestyle, such smoking cigarettes, and use of alcohol, plays an important role in determining fetal growth. Among women enrolled in this study we found no significant difference to the use of cigarettes; most women the Peruvian Andes are non-smokers. Although differences were found between cases and controls in alcohol consumption, it should be noted that consumption was only occasional (celebrations, in baptisms) 1 or 2 times a year.

In our sub-sample of the population (n=72) where we measured CO, we found a significant positive exposure-response trend (p=0.02), and the top tertile of CO exposure, in comparison with the lowest, had an OR of 3.5 (p=0.06). These results are concordant with other air pollution studies indicating that ambient CO exposure is associated with lower birthweight. Stieb et al.(2012) found that the majority of studies reported reduced birth weight and increased odds of low birth weight in relation to exposure to carbon monoxide (CO), nitrogen dioxide (NO_2) and PM10 and PM2.5. The pooled estimate of a decrease in birthweight was 11.4 g per 1 ppm CO. More analogously to our study, Thompson et al. (2011) found that a mean increase of 1.6 ppm in CO was associated with an increase of 0.30 in the log odds of a low birthweight (<2500gms) child; assuming a linear relationship, this would be an increase of 0.19 in the log odds for a one ppm increase in CO. Our data indicated the same relationship; in our sub-sample with CO measurements, we found that a one ppm increase in CO was associated with an identical increase of 0.19 in the log odds of having a full-term birth in the lowest 10% of weight; the mean birthweight of our SGA births was 2570 grams. While the outcomes in these two studies differ (LBW vs. SGA for full term births), and the design (intervention study vs. a case-control study) differ, these results are remarkably similar.

A number of potential mechanisms for CO have been suggested. The fetus in the uterus may be particularly susceptible to hypoxia from CO exposure even if the maternal blood level of CO is nontoxic (Gabrielli and Lavon 1995). Therefore, exposure to low levels of ambient CO during pregnancy could result in tissue hypoxia by increasing maternal and fetal carboxyhemoglobin concentrations and decreasing fetal O_2 tensions or O_2 carrying capacity (Longo 1977). Furthermore, maternal CO inhalation can affect the fetus more severely than the mother in terms of oxygenation of tissues (Longo 1977). We believe that the altitude and CO pollution are factors that could both result in adverse effects in pregnancy.

This study has limitations, the most important of which is small sample size. We were also unable to measure CO on all women in the study, resulting in an especially small sample size for analyses of SGA births by CO level; furthermore, we were able to measure only area and not personal CO. We also were not able to measure CO at the time of pregnancy because our study was retrospective, although we did restrict the population to mothers who had not changed their manner of cooking or their biofuel use since pregnancy. On the other hand, this study had some strengths. Our study population is one of the few in which the effect of biofuel use on reproductive outcome was assessed among people living at high

altitude. Despite the limited sample size, this is also one of the few studies to provide quantitative exposure-response data on adverse reproductive outcome in relation to measured CO level.

CONCLUSION

Outcomes from the present study suggest an association between SGA births and maternal exposure to biofuel and CO, among women who live at high altitude.

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Highlights

- Data on biofuel use and adverse reproductive outcomes are not conclusive

- Half the world's population depends on biofuel for household energy

- We did a study of biofuel use and small for gestational age (SGA) births in Peru

- Those using only biofuel had a 4-5 fold risk of SGA births vs. gas users (p=0.02)

- We found a positive exposure-response trend (p=0.02) between CO and SGA

Table 1

Characteristics of mothers enrolled in the study according to case and control group.

Characteristic	Case (n= 101)	Control (n=101)	P-value*, case vs control
Mean Age (years) ± s.e.*	27.3 ± 0.54	28.7 ± 0.48	0.17
Child's birthweight (g) ± s.e.	2570 ± 21.00	3186 ± 30.19	0.001
Post- pregnancy maternal BMI ± s.e.	22.3 ± 0.17	23.6 ± 0.39	0.01
Gestational age (weeks) ± s.e.	38.9 ± 0.11	39.1 ± 0.10	0.31
% Parity: >=3 children	25	19	0.32
%Low education	47	38	0.36
% prior Miscarriage	19	14	0.62
% Current Smoker	3	6	0.15
%Drink alcohol	36	60	0.001
% Without partner	15	13	0.68
% With chimney	32	26	0.35
% with windows	66	62	0.58
Residence area			
%Urban	70	65	
%Rural	30	35	0.55
Biofuel Use in the last pregnancy			
%Gas	30	39	
%Biofuel	43	32	
%Gas+Biofuel	27	29	0.24
Method to revive the fire			
%Not applicable (gas)	31	37	
%Tube	32	35	
%Directly	38	28	0.32
Form of cooking:			
%Standing up	54	55	0.90
%Sitting/squatting	46	45	0.90

*
MacNemar Test for categorical variables with two categories, chi-square test for categorical variables with three categories, and t-Test for continuous variables

Table 2

Odds ratios (ORs) for association between maternal exposure to biofuels for cooking during pregnancy and SGA in Peruvian Andean women. Case and controls (n=202)

Exposure Measure	OR crude Estimates	p-value	OR adjusted*	p-value	CI 95%	
Gas	1.0					
Gas + Biofuel	1.86	0.18	2.10	0.13	0.80	5.55
Biomass	4.58	0.01	4.53	0.02	1.33	15.49

*
adjusted for education level, and parity, 101 cases and 100 controls, conditional logistic regression

Table 3

Indoor 48-hr CO exposure in parts per million (ppm) according to fuel type used (subsample n=72).

Biofuel in pregnancy:	CO ppm ± Std Dev (n)	Median	Range
Gas only	0.40 ± 0.27 (6)	0.31	0.14 - 0.87
Gas+Biofuel	2.18 ± 2.93 (16)	1.16	0.45 - 12.00
Biofuel	4.79 ± 4.32 (50) [*]	3.47	0.28 - 12.50

[*] ANOVA test (Scheffe), gas vs biofuel, p=0.03

Table 4

Levels of indoor CO higher associated with SGA in Peruvians Andean women. (subsample n=72, 36 cases, 36 controls)

Indoor CO (ppm) (tertiles)	OR crude	p-value	OR adjusted*	p-value	95% Conf. Int.
0.03 to < 1.05	1.0		1.0		
1.05 – 3.81	1.83	0.31	1.16	0.82	0.32 - 4.26
3.82	4.25	0.02	3.53	0.06	0.94 - 13.23

*Logistic regression adjusted for education level and parity. Test for trend (continuous CO) was 0.02