Prenatal exposure to household air pollution and adverse birth outcomes among newborns in Sri Lanka

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ABSTRACT

Background.

Nearly 74% of the Sri Lankan population use biomass in the form of unprocessed wood as the primary cooking fuel. Growing evidence for meta-analyses and individual studies have reported increased risk of adverse birth outcomes associated with prenatal exposure to household air pollution (HAP) from cooking with biomass fuel. We thus established a birth-cohort study in Sri Lanka to evaluate the association between prenatal exposure to HAP and adverse birth outcomes including low birth weight (<2500 gms), small for gestational age (LBW in term births) and pre-term births.

Methods.

We followed 545 pregnant women from their 1st trimester until delivery and assessed outcomes at birth including weight, height and head circumference, and gestational age. HAP exposure was ascertained from questionnaires, and 2-hour area measurements were conducted in 56% of households (n=303). Data on covariates related to household characteristics, socio-demographic indicators, maternal health and lifestyle factors were collected from the baseline interviews. We performed multiple log binomial regression analysis to evaluate the association between HAP and birth outcome including LBW, SGA and preterm births.

Results.

The mean age of women among high and the low exposure groups was similar, 29 ± 5 years, and 28 ± 5 years, respectively. The proportion women using wood as primary or secondary fuel (n=425, 78%) was almost 4-times higher than women using only LPG or kerosene (n=122, 22%) as primary fuels. Households using wood had 4-fold higher $PM_{2.5}$ levels and CO concentrations

than those using LPG. A positive trend was observed in $PM_{2.5}$ and CO levels with increasing quantities of wood use. The prevalence of LBW and SGA was 2-3 times higher among wood users compared to clean fuel users ($p<0.05$). A 10-unit increase in $PM_{2.5}$ was associated with increased odds for LBW (OR=1.69; 95%CI=1.15-2.49; p=0.03) and SGA (OR=1.56; 95%CI=1.14-2.19, p=0.01), after adjusting for covariates. Positive associations were noted between categorical fuel use variables and LBW and SGA but the results were not significant. No remarkable differences were noted for stillbirths, miscarriages, preterm births, and gestational age between wood users and LPG users

Conclusions.

Analysis of the data indicated that HAP exposure was associated with LBW and SGA. The results of the study add to the increasing body of evidence linking HAP to adverse birth outcomes. The results of the study are important to most developing countries where the women in child bearing age are carry most of the burden of cooking and household tasks and the prevalence of HAP exposure is high.

Key words

Household air pollution, Low birth weight, Sri Lanka, Birth cohort

INTRODUCTION AND AIMS

Almost 40% of household worldwide, accounting for 2.8 billion people, rely on solid fuels (coal and biomass) for cooking and heating. In some developing countries, the use of biomass fuel is as high as 70 % to 90% (1,2). Household air pollution (HAP) from combustion of solid fuels used for cooking and heating, is ranked 10th as a contributor to the global burden of disease (3,4) and the third leading risk factor for global mortality and disability-adjusted life years (DALYs)(5). Long-term exposure to fine particulate matter ($PM_{2.5}$) of size 2.5 μm contributes to 4.2 million deaths and a loss of 103.1 million DALYs; majority of this burden is borne by developing countries (6). In 2004, HAP exposure resulted in nearly 2 million deaths globally with illnesses including 12% from pneumonia, 34% from stroke, 26% from ischemic heart disease, 22% from chronic obstructive pulmonary disease (COPD), and 6% from lung cancer(7).

Studies have found an association between air pollution and adverse pregnancy outcomes including stillbirths, low birth weight (LBW), small for gestational age (SGA), preterm births and birth defects.(8–10) Results from a meta-analysis found that birth weight in grams (g) was negatively associated with 10 $\mu g/m^3$ increase in ambient PM_{10} (-10.31 g; 95% confidence interval [CI], -13.57 to -3.13 g; I-squared=0%, p=0.947) and $PM_{2.5}$ (-22.17 g; 95% CI, -37.93 to -6.41 g; I-squared = 92.3%, p<0.001) exposure during entire pregnancy, adjusted for maternal smoking (11). Increasingly, studies have evaluated the role of HAP from solid fuel combustion and found a stronger association between HAP and adverse birth outcomes compared to the effect of ambient air pollution (12,13). A recent meta-analysis found that exposure to HAP from solid fuels resulted in an 86.4 g (95% CI: 55.49, 117.37) reduction in birth weight, and a 35% (EE=1.35, 95% CI: 1.23, 1.48) and 29% (EE=1.29, 95% CI: 1.18, 1.41) increased risk of LBW and stillbirth respectively (14). Smoke emissions from solid fuel combustion in inefficient

cookstoves and inadequate ventilation releases relatively high concentrations of $PM_{2.5}$, carbon monoxide (CO) and several other organic and inorganic compounds (15). Several of these compounds share similar toxic properties as those found in environmental tobacco smoke (ETS) (16). Evidence from ETS and animal studies have indicated that these pollutants may be absorbed by maternal blood and may cross the blood brain barrier to cause toxicity to the fetus (17,18). In many developing countries, women of child-bearing age typically spend a large portion of their time cooking daily. They are exposed to higher levels of HAP for longer duration and are thus more vulnerable to the adverse health effects of HAP exposure. Since almost one-third of world's population is exposed to HAP from solid fuel, even modest increase in the risk of adverse pregnancy outcomes has large scale implications on the overall health of the population.

Despite growing evidence on prenatal HAP exposure and adverse birth outcomes, certain questions remain. For example, most studies conducted to date studying HAP and birth outcomes have been conducted in developing countries such as India Guatemala, Pakistan, and Ghana, which have other competing risk factors for adverse birth outcomes such as malnutrition, poverty, infections and poor access to health care (14,19). In-home deliveries and limited access to prenatal care in rural regions may often result in gaps in information related to fetal growth and pregnancy-related complications making it difficult to control for residual confounding factors to estimate the true effect of HAP on the fetal health. The labor-intensive and high costs associated with conducting air quality monitoring in all households, further limit several HAP studies to qualitative exposure assessment. These assessment can lead to exposure misclassification , especially in households with mixed fuel usage (20). To address some of these challenges, we designed a birth-cohort study in Sri Lanka, to study the association between

prenatal exposure to HAP from biomass smoke emissions and adverse birth outcomes. We hypothesized that prenatal exposure to HAP from biomass cooking fuel in pregnant mothers is associated with increased risk of adverse birth outcomes including miscarriages, LBW, SGA, and preterm births. Sri Lanka, a middle-income country with a population of about 21 million people, has 92% literacy and maternal-child health indicators comparable to most developed nations (21). About 74% of the population in Sri Lanka continue to use biomass fuel (unprocessed wood) in urban, semi-urban and rural areas (22,23). The high prevalence of biomass fuel use and low prevalence of other competing factors such poor nutrition and 98% coverage of antenatal care, made Sri Lanka an ideal setting to study the effects of HAP on birth outcomes.

MATERIALS AND METHODS

Study cohort and recruitment

The study was conducted in Ragama Ministry of Health (MoH) in Sri Lanka. The Ragama MoH is divided into 16 Public Health Midwife (PHM) areas and is the designated field practice area of University of Kelaniya (UKe) in Sri Lanka. A total of 721 pregnant women (n = 721) were screened between July 2011 and June 2012 from the Ragama MoH antenatal clinics. Eligibility was limited to pregnant women with less than 12 weeks of gestation, between ages 18 and 40 years, who planned to continue antenatal care and deliver at the Colombo North Teaching Hospital, and permanently resided in the Ragama MoH area. A written informed consent in Sinhala was obtained from all women and the study procedures were explained prior to enrollment. Women were interviewed at enrollment (mean: 10.8 weeks' gestation, standard deviation (SD): 2.5) to collect baseline information on socio-demographics and determinants of HAP exposure. All interviews were conducted by bilingual study interviewers using structured

questionnaires. A total of 545 mother-infant pairs were retained in the study at the end of follow-up at birth. Of 721, 176 pregnant mothers were excluded for the following reasons: (i) being pregnant with twins (*n* = 5, 2.9%); (ii) stillbirths (n=9, 5.1%); (iii) delivered in different hospitals (n=13, 7.4%); (iv) lost contact (n=15, 8.2%); (v) changed residence (n=15; 8.5%); (vi) changed consent (n=59, 33%); (vii) miscarriages (n= 60, 35%).

Data collection

At enrollment, a structured baseline questionnaire was administered to all participants to elicit information on demographic factors, residential history, medical history, maternal and paternal occupational history, history of active and passive tobacco smoking; and household characteristics. A section of the questionnaire collected detailed information on factors related to HAP resulting from solid fuel use. Information was also collected on other sources of indoor and outdoor pollution, contributing to household pollution. Maternal pregnancy history and fetal measurements at birth, were obtained from antenatal clinics at birth.

(i) Exposure assessment

Exposure to HAP exposure during the pregnancy was assessed using information collected from baseline questionnaire (n=545) on routine cooking practices and two-hour real-time area measurements for $PM_{2.5}$ and CO during the cooking period in a subset of households (n=303 out of 545). The baseline questionnaire elicited detailed information on: (a) household characteristics such as dimensions and relative position of the kitchen and other rooms, number and size of door and windows, type of stove, availability of a chimney, condition of chimney (b) cooking practices such as types of fuels used for cooking including primary and secondary cooking fuels, percent use of each fuel used during cooking, daily average hours spent cooking, opening of door and windows of the kitchen during cooking; and (c) other sources of HAP such

as tobacco smoking habits of household members, burning of incense and mosquito coils, and proximity of sources of ambient air pollution such as vehicular traffic, industry or garbage disposal sites.

Based on the information collected in the baseline questionnaire, households were categorized into ‘high’ and ‘low’ exposure categories if the women used biomass fuel or clean fuel as primary cooking fuel, respectively. Using a stratified random sampling method, we selected 303 households (high exposure group, n=158; low exposure group, n=146) for conducting 2-hour air quality measurements in the kitchen. We scheduled at least one measurement per household during the pregnancy period. In 36% (n=106) of the households, two sets of measurements were conducted in two of the three trimesters and in 26 households, three measurements were conducted, once in each trimester during the pregnancy. All measurements were collected over a 2-hour cooking session during preparation of lunch. The $PM_{2.5}$ concentrations were measured using a TSI Dusttrak II Aerosol Monitor 8530 and the CO concentrations were measured using Q-Trak Indoor Air Quality Monitor 7565. Inlets of monitors were fixed at 145 cm above the floor, 100 cm from the cook stove and at least 150 cm away from an open window or door.

HAP exposure was modeled as both categorical and continuous variables.

Categorical HAP exposure. The majority of the households in the study used a second fuel to supplement their primary fuel use (n=423, 78%). We thus re-categorized ‘high’ and ‘low’ exposure groups in to ‘any wood use’ vs. ‘clean fuel use’. If any households used wood even in small quantities, they were categorized as ‘wood users’. Next we created a three-category fuel variable based on type of primary and secondary fuels and the percentage use of each fuel type during an average week, as reported on the questionnaire. The variable categorized households in

to three categories defined as (i) those using >50% to 100% of wood; (ii) households using 50-100% of LPG or kerosene and supplementing it with wood 25 to 45% of the time; and (iii) household using 100% LPG or kerosene and supplementing it with electric stoves.

Continuous $PM_{2.5}$. For households with 2-hour air quality monitoring (n=303), measured continuous $PM_{2.5}$ was used as main exposure.

Predictors of kitchen $PM_{2.5}$. We compared mean $PM_{2.5}$ concentrations across the two and three level fuel categories. We also examined the impact of other factors such as kitchen type (indoor, temporary hut or outdoor); type of cookstoves (traditional cookstove (TCS), improved cookstove (ICS), kerosene or LPG stove); number of doors and windows open at the time of cooking as a surrogate for ventilation; total sum of area of doors and windows open to outside during cooking; and average daily cooking time, on kitchen $PM_{2.5}$ concentrations (Table 1). $PM_{2.5}$ was log-transformed as the variable was skewed. Factors significantly associated with log-transformed $PM_{2.5}$ at $\alpha < 0.1$ were then included in a multivariable linear regression model to develop a predictive equation to estimate kitchen $PM_{2.5}$ levels.

Exposure model and validation. Data from 275 out 303 households with air quality measurements were used to develop the exposure model to estimate kitchen $PM_{2.5}$. We excluded 26 samples as the comparison between fuel use and $PM_{2.5}$ values suggested potential misclassification of fuel use or possible outliers. For example, a household using >75% of LPG had measured value of $PM_{2.5}$ as high as 1000μg/m^3. We partitioned the data (n=275) randomly into training (n=192) and test (n=83) datasets using a 7:3 ratio respectively. The training dataset was then used to identify factors significantly associated with log-transformed $PM_{2.5}$ and fit a multivariable linear regression to model log-transformed $PM_{2.5}$ as a function of significant risk factors. Adjusted R^2 was used to evaluate the model fit. We identified three independent risk

factors associated with log-transformed $PM_{2.5}$ including multilevel fuel categories, kitchen type, and daily cooking time at $p < 0.05$ (Table 1). The model R^2 was 0.57 (Table 2).

In the test dataset, the beta (β) coefficients from training model were used to predict $PM_{2.5}$ values. We calculated the difference between the observed and the fitted $PM_{2.5}$ values and plotted the residuals to evaluate the robustness of the predictive model. The regression model is given below:

$$Ln\ (Y) = \alpha + \beta_{wood} + \beta_{LPG+Wood} + \beta_{LPG} + \beta_{K_ind} + \beta_{K_temphut} + \beta_{K_outdoor} + \beta_{cookingtime} \quad \text{..... equation.(1)}$$

where: α, intercept =4.31; β_{wood} = 2.10, estimate for wood use >50%; $\beta_{LPG+Wood}$ = 0.42, estimate for LPG use 50% to 100% supplemented by wood; β_{LPG} = 0, estimate for 100% LPG; β_{K_ind} = -0.18, estimate for indoor kitchen; $\beta_{K_temphut}$ = 1.17, estimate for temporary outdoor hut kitchen; $\beta_{K_outdoor}$ = 0, estimate for outdoor open kitchen; and $\beta_{cookingtime}$= 0.006, total daily cooking time.

Estimated $PM_{2.5}$ measurements. The validated exposure model (equation 1) was then used to predict kitchen $PM_{2.5}$ levels for households that did not undergo air quality measurements (n=242). Exposure to HAP exposure was then modeled as continuous variable combining measured and estimated values of $PM_{2.5}$ for all subjects in the study (n=545).

(ii) ***Birth outcome assessment***

In our study, 100% of the births occurred in the hospitals and measurements for fetal growth were recorded within 24 hours of delivery. Prenatal and delivery medical records were abstracted by the research assistants from the hospital records, including prenatal medical history, delivery complications, infant birth weight, length, head circumference, and gestational age at birth. Gestational age was estimated based on the date of onset of the last menstrual period and ultrasound in the first trimester. LBW was defined as birth weight <2500 grams at birth. Small

for gestational age was defined as full-term babies weighing <2500 grams at birth. Pre-term births were defined as <37 weeks of gestation.

(iii) Covariates and potential confounders

The baseline questionnaire collected detailed information on socio-demographics, general household information, occupational history for pregnant mothers and their spouse, past medical history for mothers, and parity. The body mass index (BMI) at 1st and 3rd trimester was calculated from measured weight and height. We also examined smoking, alcohol and drug use during pregnancy and exposure to environmental tobacco smoke (ETS) and other toxic chemicals such as pesticides and lead.

Ethical review

All study protocols were approved by the Ethical Review Board at the UKe and at the University of Alabama at Birmingham (UAB).

Statistical analysis

We computed mean, standard deviation and median for continuous variables; and frequencies and percentages for categorical variables. All variables were using the student's t-test, Analysis of Variance (ANOVA), Wilcoxon's and Kruskal Walli's for parametric and non-parametric continuous variables; and the chi-square (χ^2) test or Fisher's Exact test for categorical variables as appropriate. The outcomes including LBW, SGA and pre-term births were coded as binary variables (had the outcome = 1; no outcome = 0). In bivariate analysis, we examined the relationship between HAP exposure and LBW, pre-term births and SGA. We also examined the prevalence of outcomes across all the categories of covariates to identify potential risk factors.

We used logistic regression to compute crude odds ratio and their 95% confidence intervals of LBW, pre-term births and SGA across HAP exposure. Covariates were included in multiple

regression models if they were associated in bivariate analyses with HAP (categorical or continuous) and outcomes for a p-value < 0.1. Several factors were identified as *a priori* covariates including maternal age, education, parity, body mass index in the 1st and 3rd trimester, family income, and maternal risk factors associated with poor birth outcomes such gestational diabetes and pregnancy induced hypertension, and child's gender, to be included in the final model. Models for LBW were adjusted for pre-term births. We used a multivariable logistic regression to compute odds ratio as a measure of association between HAP exposure and birth outcomes, adjusting for potential confounding factors. We constructed separate models for different types HAP exposure. Use of 100% LPG was the referent group for both dichotomous and three-category HAP exposure. All analyses were conducted using SAS 9.4.

RESULTS

Table 3 summarizes the socio-demographic characteristics of the pregnant women. The average age of mothers was 29 years (SD = 4.9; median = 29), were all married. About 34% of the women were primiparaous (n=184). Most women had completed their secondary education (86%) and majority were of Sinhalese ethnicity. None of the women smoked cigarettes, drank alcohol or used drugs during pregnancy. Almost 80% of the participants owned the house that they lived in (n= 439, 80%) while 16% (n=87) rented their homes. Based on the use of materials for building floors, walls and roofs, the homes were categorized as either permanent (n=350, 66%) or semi-permanent (n= 179, 33%). About 53% of the subjects' households had piped water supply, 24% had tube-well water, and 18% had well water-supply. The main source of drinking-water in majority of household was located inside the yard (48%, n=261); in 26% of households, it was located inside the house (n=143) and in 17% of homes it was located outside the house (n=92). Almost 82% of the households had private flushed toilets (n=450); remaining households

had either shared flushed toilets (n=14) or private pit latrine, composting or bucket latrines (11%, n=62).

In the cohort, 52% (n= 284) of the women reported using wood, 3.5% used kerosene (n=19) and 45% used LPG (n = 245), as the main primary fuel on the baseline questionnaire (table 1). The households were further classified into three fuel use categories based on the type of primary and secondary fuels used and the percentage of the fuels used on a weekly basis. Majority of the household either used to >50% of wood (n=157, 50%). The second largest group was households using >50% of LPG or kerosene supplemented with wood (n=134, 25%). The third group used only LPG supplemented occasionally by kerosene or electric stoves (n=122, 22%). Households using wood either used a traditional (29%, n=157) or improved cookstove (21%, n=114). Majority of kitchens were indoor kitchen (85%, n=466). Other kitchen types included temporary hut separate from the main house (8.8%, n=48) and outdoor kitchen with a wall on one side and open to outdoors on three sides (2.7%, n = 15). A functional chimney was present in 56% of the indoor kitchens (n=262). In baseline questionnaire, subjects were questioned on number of windows and doors kept open during the cooking period. About 34% of the kitchen had no windows or doors open during the cooking of meals (n= 187). The remaining households either had a window, door or both windows and doors open during kitchen.

Among households with 2-hour air quality measurements (n=303), the geometric mean (GM) for $PM_{2.5}$ among wood users [n = 157, 52%; geometric mean (GM) = 737 $\mu g/m^3$, standard error (SE) = 80] was almost 4 times higher that the levels measured in households using >50% of LPG with wood and almost 7 times higher than households using 100% LPG [n=68, 22%; GM (SE) =100 $\mu g/m^3$ (10)].

The proportion of LBW children in the cohort was 13% (n= 70 of 545) and the preterm births were 10% (n=57). The total number of SGA births were 46 (10%) out 486 term births. About 65% of the mothers had vaginal delivery including forceps (n=6) and vacuum deliveries (n=5). Of the total 545 newborns, 52% were boys.

LBW

In bivariate analyses (tables 3), HAP exposure was significantly associated with LBW but not with preterm births. Other factors significantly associated with prevalence of LBW included history of pregnancy induced hypertension (p=<.0001), maternal weight gain in the 3rd trimester (p=0.0281), number of doors and windows open during cooking (p=0.0625). There were no remarkable differences between normal birth and LBW children in terms of socio-demographic factors, household characteristics or lifestyle related factors.

Table 4 provides results for adjusted models for HAP exposure and LBW. In model (a) dichotomous HAP exposure was positively associated with increased LBW; however, the association was not significant (OR = 2.0; 95% CI =0.9-4.92, p = 0.0878). In model (b), HAP exposure was modeled as an ordinal variable with three categories for fuel use. Compared to >75% LPG use, all other categories were positively associated with increased odds or LBW; but the association was non-significant. No trend was observed with increasing percentage of wood use and LBW. In model (c), continuous $PM_{2.5}$ was used to characterize HAP exposure. The model was limited to subjects with air quality monitoring data. The effective sample size was 238 subjects after excluding those with missing values for some of the covariates. A 10-fold increase (i.e., one log-unit increase) in $PM_{2.5}$ was significantly associated with 50% increased odds of LBW (OR = 1.54, 95% CI = 1.12-2.12). The association was consistent in the model (d) using combination of estimated and measured $PM_{2.5}$ and included all subjects. An increase in

$PM_{2.5}$ was significantly associated with increased odds of LBW (OR = 1.32; 95% CI = 1.03-1.68).

SGA and preterm births.

We found significant positive association the two and three level categorical HAP exposure and SGA but the results were not significant in the adjusted models (Table 5). A moderately significant association was found between 10-unit increase in $PM_{2.5}$ and SGA (OR = 1.69; 95% CI = 1.03-2.02), after adjusting for significant covariates (Table 5). No association were noted between HAP exposures and pre-term birth (not displayed in tables)

Discussion

In our study, we found significant positive associations between continuous $PM_{2.5}$ and LBW and SGA. Association between categorical HAP exposure and LBW and SGA were positive but not significant. The results are consistent with previous air pollution studies including ambient and household air pollution.(10,11,24) To our knowledge, our study is the first to quantify kitchen $PM_{2.5}$ using a exposure model, in households without monitored data and evaluating the association between estimated $PM_{2.5}$ and birth outcomes. We discuss the exposure estimation methods and effect estimates for LBW and SGA in context of previous literature and highlight the strengths and limitations of our study.

Exposure estimation

In our study, we used information on stacking of fuel during an average week, to characterize gradient in HAP exposure. Stacking of fuel is where the household supplements the main fuel with secondary fuel for cooking certain dishes such as rice or beans or for special occasion such as festivals or holidays. We then used the gradient exposure categories and other drivers of exposure to $PM_{2.5}$ including kitchen characteristics and average daily cooking time to

predict total kitchen $PM_{2.5}$. This novel approach was used to evaluate the feasibility of using questionnaire responses to predict $PM_{2.5}$ concentration in kitchen during cooking period, for households that did not have monitoring data. Cross-validation approach evaluated the robustness of the model and found it 57% to predict $PM_{2.5}$. In ideal circumstances, accurate measurement of HAP exposure would require continuous personal monitoring using portable monitors for a period of 24-48 hours period in all subjects. But conducting air quality monitoring in all subjects significantly increases study costs and respondent burden. Previous HAP studies have mostly relied on questionnaire responses as surrogate for exposure. In more recent studies, questionnaire data is supplemented with area measurements for short time periods (snapshots) at multiple time points to generate time-integrated exposure metric to characterize chronic exposure. In these studies, households using solid fuel as primary cooking fuel are classified into at most three fuel type categories including wood, kerosene and those using LPG or electricity. However, simply relying on the type of main fuel use may not allow for evaluation of exposure-response effects of HAP.

Balakrishnan et al.(2013), conducted one of the first studies which involved 24-hour $PM_{2.5}$ measurements in all study households (n=474) and fitted a regression analysis to model 24-hour data to create a predictive household $PM_{2.5}$ concentrations.(25) They identified fuel type, kitchen type, ventilation, geographical location and cooking duration, to be significant predictors of $PM_{2.5}$ concentrations (R^2= 0.33) with a fair degree of correlation (r=0.56) between modeled and measured values.(26) Another study conducted by Baxter et al. (2007), used questionnaire information combined with ambient air quality measurements to predict indoor concentrations of nitrogen dioxide, $PM_{2.5}$, and elemental carbon in lower socio-economic status homes in urban Boston, Massachusetts (27). Their study found that outdoor concentrations, cooking time and

occupant density were significant predictors of indoor $PM_{2.5}$ concentration (adjusted R^2 =0.36). The inclusion of open windows as an effect modifier for ambient air increased the R^2 to 0.40. A recent study conducted by Zhou et al. (2018) in Shanghai, China, used outdoor air measurements and household characteristics to predict outdoor $PM_{2.5}$ infiltration of indoor air (28). The models stratified by seasons and including information on air conditioning use, meteorological factors, floor of residence and building age, predicted 60.0%-68.4% of the variance in 7-day averages of indoor $PM_{2.5}$ infiltration by outdoor air.

The R^2 for the exposure model developed in our study (57%) was comparable with the R^2 (66%) reported by Zhou et al (28); and 1.6 times greater than the R^2 (0.36) as reported by Balakrishnan et al (2013) (26). The correlation between estimated and measured $PM_{2.5}$ (r = 0.71 vs. r= 0.56) was also higher in our study compared to that reported by Balakrishnan (2013) study.

Our results indicate moderate feasibility of using detailed questionnaire information to quantify HAP exposure. Increased frequency and longer duration of air quality monitoring can improve the accuracy of the predictive model. The high degree of variability resulting due to stacking of fuels and kitchen characteristics, and time-activity pattern among the subjects could have resulted in exposure misclassification. Furthermore, changes in patterns of fuel use over the course of pregnancy could also result in exposure misclassification. However, we evaluated the consistency in fuel use reported at baseline and at the time of air quality measurement in 2nd and 3rd trimester and found limited change.

HAP, LBW and previous studies

The results of our birth-cohort evaluating the relationship between HAP and LBW were consistent with the largest birth-cohort study to-date as well as several meta-analyses published

in the last decade. Balakrishnan et al., reported an OR of 1.01–1.18 for LBW per 10-μg/m^3 increase in $PM_{2.5}$. The most recent meta-analysis conducted by Sun et al. (2016), found significant association between 10μg/m^3 increment of HAP and LBW with an odds ratio of 1.09 (95% CI: 1.032, 1.150) (24). Results from other meta-analyses also found increased prevalence of LBW between 10% to 45%, associated with HAP exposure (12,14,29–34). The effect estimates in our study are closer to the higher end of central estimates reported by individual studies and meta-analyses. In our study, the mean 2-hour kitchen $PM_{2.5}$ in kitchens using any biomass fuel was almost 12 times higher than households using LPG (1649 vs. 143). Balakrishnan et al., (2018) reported 24-h average kitchen concentrations in households which were much lower than those reported in our study (wood use: 228.5±232.8 μg/m^3 vs. 1649±166 μg/m^3; LPG/electricity: 59.3±45.7 μg/m^3 vs. 143±12 μg/m^3]. The higher concentration of kitchen $PM_{2.5}$ found in our study may account for the higher effect estimate reported in our study as compared to the results reported by Balakrishnan et.al. (2016). However, without additional data on 24-hour average kitchen concentration from our study, no firm conclusions can be made.

The increased odds for SGA ((OR = 1.69; 95% CI = 1.03-2.02) associated with 10-unit increase in $PM_{2.5}$ were similar to those reported by Tielsch et al., (2009) (OR = 1.21, 95% CI= 1.11, 1.31) and Mavalankar et al., (1992) (OR=1.23; 95% CI : 1.01, 1.49). We did not find significant association between HAP and pre-term births and still births. Given the small numbers for still births (n=9), the study lacked sufficient power to make any notable findings.

Our study had several strengths. We modeled exposure HAP in several different ways and found consistent results across all various regression models. The retention rate in the study was almost 84% (545/656) after accounting for miscarriages, still births and twin pregnancies. The study participants were identified through routine prenatal check-ups at the ante-natal clinics

and were representative of the study population. All births occurred in hospitals and birth weight was recorded within 24-hours. Gestational age was determined by ultrasound examination in 1st trimester if there was doubt about the last menstrual period. Consequently, reducing information bias for LBW and SGA. In Sri Lanka, government-funded public health system provides prenatal and antenatal care to almost 99% of the pregnant mothers. Thus, we were able to verify self-report of maternal medical history with maternal pregnancy records obtained from the ante-natal clinics. Maternal lifestyle, such as smoking cigarettes, and use of alcohol, are known confounding factors for adverse birth outcomes. However, none of the mothers in our study smoked or consumed alcohol. Information on environmental tobacco smoke was self-reported but no significant differences were noted for LBW and normal children. We were able to collect and adjust for known confounding factors associated with LBW and SGA including pregnancy induced hypertension, gestational diabetes, and other complications during pregnancy such as essential hypertension, high head, hyperemesis, hyperthyroidism, hypothyroidism, and threatened miscarriage.

The major limitation of our study lack of 24-hour air quality measurements for indoor and ambient air quality. Data on indoor air quality was available for 60% of total household in the study, thus decreasing the accuracy of exposure estimation as a result of some exposure misclassification. However, internal consistency in results suggest minimum information bias. HAP exposure and outcome in several different ways and assessing the consistency between the results. Secondly, data was missing maternal weight 1st and 3rd trimester, as well as information on open doors and windows, thus reducing the effective sample size for analysis. However, the missing data was distributed equally across all fuel categories. Thus, the effect estimates were most likely biased towards null.

Conclusion.

Our study evaluating HAP and birth outcomes in Sri Lanka adds to the growing evidence linking HAP to LBW and SGA. Although, air quality measurements were conducted in a subset of households, we maximized the use of information gathered from interviews to quantify HAP exposure in household without measured data. Results of this study are important as almost 74% of the population in Sri Lanka continue to use wood for cooking.

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Conflict of Interest

The authors declare that they no competing financial interests.

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Table 1. Descriptive statistics of exposure-related variables by data source, distribution of $PM_{2.5}$ across covariate categories

	All subjects	Households with AQM			Households with AQM (excluded extreme values)		
Exposure characteristics	**N (%)**	**N (%)**	**Arithmetic (SE)†**	**Geometric (SE)†**	**N (%)**	**Arithmetic (SE)†**	**Geometric (SE)†**
Total N	544	303*			276*		
Fuel use							
Any wood use	315(57.8)	177	1668(214)	689 (73)	235(78)	1667 (169)	839 (84)
Only clean fuel use	211(38.7)	116	250(53)	120 (11)	60(22)	144 (12)	105 (7.8)
Primary fuel use							
LPG	243(44.6)	135(45)	507(212)**	143(14)	124(45)	155(12.1)**	111.9(8.1)**
Kerosene	19(3.5)	10(3)	445(332)	130(53)	10(4)	445.4(332.4)	130.3(53)
Wood	283(51.9)	158(52)	1620(167)	740(80)	141(51)	1795(179.9)	970.5(94)
Fuel use by type and percentage							
>50-75% wood	274 (50)	157 (52)	1622 (167)**	737 (80)	141	1799 (181)**	969 (95)**
>50-100% LPG or Kerosene and <50% wood	134 (25)	76 (25)	792 (377)	189 (28)	68	234 (51)	137 (15)
100% LPG, Kerosene or Electricity	122 (22)	68(22)	179 (48)	100 (10)	66	115 (10)	91 (7.7)
Missing	15						
Primary stove type							
Traditional	156(28.7)	79(26)	1717(246)**	793(123)	71(26)	1902.6(265.2)**	1048.3(142.9)**
Improved cookstove	114(20.8)	74(24)	1364(228)	564(94)	66(24)	1463.4(250.4)	656.1(109.9)
Kerosene	25(4.6)	13(4)	137(33)	97(24)	13(5)	136.8(32.9)	96.9(23.6)
LPG/Electricity	250(46)	137(45)	660(217)	174(19)	125(46)	356.5(74.8)	147(14.3)
Kitchen							
Indoor	444(81)	275(86)	956(132)**	293(27)**	249(86)	870(93)**	298(27)**
Temporary hut	22(4)	16(5)	3263(2929)	1894(510)	15(5)	3290(993)	1843(527)
Outdoor	63(11.5)	11(9)	1179(288)	712(252)	10 (9)	1085(301)	638(238)
Missing	19(3.5)	1(0)			1		
Functional chimney[b]							
Yes	264(48.5)	135(44)	902(158)	412(47)	147(53)	1108.9(135)	256(42)
No	281(51.5)	168(56)	1229(202)	259(34)	128(47)	886.7(164)	433(69)**
Number of open windows during cooking							
Missing							
0	256(47)	116(38)	1226(189)	412(59)**	105(38)	1244.4(206)	415(61)

Table 1. Descriptive statistics of exposure-related variables by data source, distribution of $PM_{2.5}$ across covariate categories

	All subjects	Households with AQM			Households with AQM (excluded extreme values)		
Exposure characteristics	**N (%)**	**N (%)**	**Arithmetic (SE)†**	**Geometric (SE)†**	**N (%)**	**Arithmetic (SE)†**	**Geometric (SE)†**
1	261(48)	170(56)	992(191)	300(34)	153(56)	841(108)	308(35)
2	28(5.1)	17(6)	1020(574)	247(95)	17(6.1)	1020(574)	246(95)
Number of doors open while cooking							
Missing	200(36)	79(26)			74(27)		
1	78(14)	55(18)	657(132)	243(47)	49(18)	729(146)	284(58)
2	241(44)	148(49)	1148(224)	329(42)	135(49)	960(135)	322(41)
3	26(4.8)	21(6.9)	600(240)	206(61)	19(7)	658(262)	239(73)
Total kitchen space open to outside (in sq.cms)[d]			R^2 = -0.13 ; α= 0.0239			R^2 = -0.12 α= 0.05	
N	545		n=303			n=275	
Mean (SD)	22549 (20432)						
Std Dev	20424.8						
Median (IQR)	25950 (128700)						
Indoor smoking							
Yes	38(6.97)	26(9)	1961(1118) **	323(109)	20(7)	1043(486.3)	328.2(108.8)
No	507(93)	277(91)	1002(101)	336(30)	255(93)	1003.3(107)	341.6(31.6)
Other indoor pollutant sources[e]							
Yes	60(11)	31(10)	1874(879)	530(135)	29(11)	1309(314)	560(176)
No	485(89)	272(90)	991(106)	318(29)	246(89)	1112(142)	338(39)
Immediate outdoor pollution[f] sources							
Yes	40(7.3)	22(7)	1138(326	506(143)	18(10)	1018.4(242.7)	441.3(106.5)
No	505(93)	281(93)	1079(141)	325(30)	257(90)	1004.8(113.9)	330.4(31.5)
Cooking time (in minutes)							
N	520		N=299			n=272	
Mean (SD)	83 (29)[g]		R2= 0.14			R2= 0.17	
Median (IQR)	78 (342)		**α= 0.0138**			**α= 0.005**	

[a]Missing values are present in the R01 study
[b]Not available separately for checklist data
[c]Doors open to outside
[d]Calculated for open windows and doors

Table 1. Descriptive statistics of exposure-related variables by data source, distribution of $PM_{2.5}$ across covariate categories

	All subjects	Households with AQM			Households with AQM (excluded extreme values)		
Exposure characteristics	**N (%)**	**N (%)**	**Arithmetic (SE)†**	**Geometric (SE)†**	**N (%)**	**Arithmetic (SE)†**	**Geometric (SE)†**

[e]Including burning of incense, mosquito coil, and candles inside the homes
[f] Includes industry near the homes
[g]Average daily cooking time across 2-3 meals per day
*Subsetted for households with air quality measurements;
†Includes all subjects with at least one 2-hour air quality monitoring (n= 304)
‡Excludes subjects with extreme values and/or inconsistencies between primary fuel type and primary stove type. Total subjects retained (n=277)
**p<0.05

Table 2. Regression model to predict log-transformed $PM_{2.5}$ kitchen concentrations during cooking periods

Parameter	DF	Estimate	Standard Error	t Value	Cross Validation Estimates 1	2	3	4	5
Intercept	1	4.31	0.47	9.13	4.37	4.29	4.29	4.39	4.31
Fuel category 2 (50-100% LPG use)	1	0.42	0.20	2.12	0.30	0.45	0.51	0.39	0.47
Fuel category 3 (50-100% wood use)	1	2.10	0.17	12.06	2.04	2.07	2.22	2.10	2.06
Fuel category 1 (100% LPG use)	0	0.00	.	.	0.00	0.00	0.00	0.00	0.00
Indoor kitchen	1	-0.18	0.41	-0.45	-0.16	-0.24	-0.32	0.01	-0.24
Temporary hut kitchen	1	1.17	0.48	2.43	1.28	1.34	0.99	1.20	1.04
Outdoor kitchen	0	0.00	.	.	0.00	0.00	0.00	0.00	0.00
Daily cooking time	1	0.01	0.00	1.93	0.01	0.01	0.01	0.00	0.01

Adjusted $R^2 = 0.57$; P-value for F-statistics <0.0001

Table 3. Comparison sociodemographic and pregnancy risk factors with low birth weight (LBW = 1) and normal children (LBW = 0)

Variables	N (%)	LBW	Normal	P-value
Total	545	70(13)	475(87)	
Primary fuel use				0.1777
LPG	243(44.6)	24(34.3)	219(46.1)	
Kerosene	19(3.5)	3(4.3)	16(3.4)	
Wood	283(51.9)	43(61.4)	240(50.5)	
Fuel use*				0.2597
Any wood use	315(57.8)	58 (14)	365(86)	
Only clean fuel use	211(38.7)	18(9.8)	110 (90)	
Fuel use by type and percentage				**0.0762**
>50-75% wood	274 (50)	43 (62)	231 (50)	
>50-100% LPG or Kerosene and <50% wood	134 (25)	14 (20)	120 (26)	
100% LPG, Kerosene or Electricity	122 (22)	12 (17)	110 (24)	
Missing	15 (2.5)			
Primary stove type				0.2196
Traditional	156(28.6)	25(36)	131(28)	
Improved cookstove	114(20.9)	17(24.3)	97(20.4)	
†Kerosene	25(4.6)	2(3)	19(4.2)	
†LPG/Electricity	250(45.9)	17(24.3)	97(20.4)	
Kitchen				0.6743
Indoor	465(85.3)	58(85.3)	407(88.7)	
Indoor but separate building	47(8.6)	8(11.8)	39(8.5)	
Outdoor	15(2.8)	2(2.9)	13(2.8)	
Missing	18(3.3)			
Functional chimney				0.7870
No	264(48)	35(50)	229(48)	
Yes	281(52)	37(50)	246(52)	
Number of open windows during cooking				0.5915
Missing				
0	256(47)	36(51.4)	225(47.4)	
1	261(47.9)	32(45.7)	224(47.2)	
2	28(5.1)	2(2.9)	26(5.5)	
Number of doors open while cooking				**0.0729**
1	78(14.3)	7(14.6)	71(23.9)	
2	241(44.2)	40(83.3)	201(67.7)	
3	26(4.8)	1(2.1)	25(8.4)	
Missing	200(36.7)			
Total kitchen space open to outside (in cms) ‡				0.7268
N	545	70	475	
Mean (SD)	22,617 (20432)	22413(17478)	22648(20848)	
Median (range)	26000(35700)	27886(34600)	25630(36000)	
Indoor smoking				0.5737
Yes	38(6.97)	6(8.6)	32(6.7)	
No	507(93.1)	64(91)	443(93)	
Other indoor pollutant sources¶				**0.0791**

Yes	60(11)	12(17)	48(10)	
No	485(89)	58(83)	427(90)	
Immediate outdoor pollution sources[¥]				0.9461
Yes	40(7.3)	5(7.1)	35(7.4)	
No	505(93)	65(93)	440(93)	
Cooking time[§]				0.4725
N	520	67	453	
Mean (SD)	84(29)	86.8(32)	83.3(28)	
Median (range)	78(39)	80(39)	78(39)	
$PM_{2.5}$ (in μg/m^3)				0.5284
N	303	39	264	
Mean (SD)	1085(2317)	1371(2057)	1042(2353)	
Median (range)	265(1091)	273(1683)	259(1030)	
Maternal characteristics				
Age (mean (sd))		28 (4.9)	29 (4.9)	0.2592
N	527			
Mean (SD)	29(4.9)			
Median (IQR)	29(7)			
Missing	18			
Maternal education				0.9960
0-5 years	74 (14)	9(13)	65(14)	
5-10 years	314 (58)	41(59)	273(57)	
>10 years	137 (26)	18(26)	122(26)	
Missing	18	2(2.9)	15(3.2)	
Husband's education				0.3147
>0-5 years	68(13)	12(17.7)	56(12.2)	
>5-10 years	332(61)	45(66.2)	287(62.7)	
>10 years	126(23)	11(16.2)	115(25.1)	
Missing	19	2 (2.9)	17(3.6)	
Father's occupation				0.3039
Plant and Machine operators and Assemblers	6(1.1)	0(0)	6(1.3)	
Skilled Agricultural, Forestry and Fishery workers	8(1.5)	1(1.4)	7(1.5)	
Technical & Associate Professionals	13(2.4)	0(0)	13(2.7)	
Armed Forces Occupations	20(3.7)	6(8.6)	14(3)	
Managers, Senior Officials and Legislators	23(4.2)	3(4.3)	20(4.2)	
Clerks and Clerical support workers	28(5.1)	6(8.6)	22(4.6)	
Craft and Related Trades workers	63(12)	10(14)	53(11)	
Services and Sales workers	93(17)	10(14)	83(18)	
Professionals	93(17)	9(13)	84(18)	
Elementary occupations	105(19)	14(20)	91(19)	
Missing	93 (17)	11(15.7)	82(17)	
Environmental risk factors[€]				0.1770
Yes	259(48)	28(40)	230(49)	
No	286(52)	42(60)	244(51)	
Housing characteristics				
Water supply				0.2832
Piped water	133(24)	12(17.7)	121(26.5)	
Well water	291(53)	41(60.3)	250(54.8)	

Tube well water	100(18)	15(22.1)	85(18.6)	
Missing	21(4)			
Drinking water supply				0.6327
In home	143(26.2)	19(28.8)	124(29)	
In yard	92(16.9)	15(22.7)	77(18)	
Outside home	259(47.5)	32(48.5)	227(53)	
Missing	51(9)			
Toilet				0.7091
Private Flushed toilet	448(82.2)	60(88.2)	388(85.1)	
Shared Flushed toilet	62(11.4)	6(8.8)	56(12.3)	
Private pit latrine, composting, bucket	14(2.6)	2(2.9)	12(2.6)	
Missing	21 (3.9)			
Type of house				0.1011
Permanent	178(32.7)	17(25)	161(35.1)	
Semi-permanent or improvised	349(64)	51(75)	298(64.9)	
Missing	18(3.3)			
Own a house				0.7056
Own	437(80.2)	58(85.3)	379(83.5)	
Rent	85(15.6)	10(14.7)	75(16.5)	
Missing	23(4.2)			
Income				0.5173
LE 15000	96(17.6)	11(16)	85(19)	
15000-20000	93(17.1)	10(15)	83(18)	
20001 - 25000	92(16.9)	16(24)	76(17)	
>25000	242(44.4)	30(45)	212(47)	
Missing	22(4)			
Pregnancy risk factors				
Child's sex				0.6332
Male	285(52)	40(55)	245(52)	
Female	261(48)	33(45)	228(48)	
Missing	2			
Parity				0.9221
Primipara	184(34)	23(33)	161(35)	
1	219(40)	29(41)	190(41)	
2	128(24)	18(26)	110(24)	
Missing	14(2.6)			
Past pregnancy miscarriage				0.8149
Yes	28(5.1)	4(5.7)	24(5.1)	
No	517(94.9)	66(94)	451(95)	
Past or current pregnancy hypertension				**<.0001**
Yes	26(4.8)	13(18.6)	13(2.7)	
No	519(95.2)	57(81.4)	462(97.3)	
H/o of heart disease in mothers				0.2742
Yes	8(1.5)	2(2.9)	6(1.3)	
No	537(98.5)	68(97)	469(99)	
Gestational Diabetes				0.2763
Yes	19(3.5)	4(5.7)	15(3.2)	
No	526(96.5)	66(94.3)	460(96.8)	

Anemia				1.0000
Yes	5(0.9)	0(0)	5(1.1)	
No	540(99.1)	70(100)	470(99)	
Other pregnancy risk factors‡				0.9766
Yes	8(1.5)	1(1.4)	7(1.5)	
No	537(98.5)	69(98.6)	468(98.5)	
Pre-term births				**<.0001**
Yes	57(10)	24(32)	33(6.9)	
No	486(89)	46(66)	439(93)	
Missing	2(0.4)			
Maternal weight in first trimester				**0.0607**
N	435	52	381	
Mean (SD)	54.3(11.2)	52(11.9)	55(11.1)	
Median	54(17)	50(21)	54(16)	
Maternal weight in first trimester				**0.0020**
N	439	54	383	
Mean (SD)	63.6(11.2)	59(12.6)	64(10.8)	
Median	63(15)	56(19)	64(15)	
Maternal weight gain difference between 1st and 3rd trimester				**0.0052**
N	435	50	377	
Mean (SD)	9.3(6.3)	8(3.7)	10(4.4)	
Median	9(6)	8(6)	10(6)	

*Includes households using any amount of wood vs. households using only LPG and electricity
† Refer to households using Kerosene/ PG 100% of the time for daily cooking but using wood occasionally for special occasions
‡Calculated for open windows and doors
¶Including burning of incense, mosquito coil, and candles inside the homes
¥Includes industry near the homes
§Average daily cooking time across 2-3 meals per day based on questionnaire information
€Exposure to pesticides, fertilizers, possible poisons;
₱Essential hypertension, High head, hyperemesis, hyperthyroidism, hypothyroidism, threatened miscarriage;

Table 4. Results of logistic regression model for HAP exposure and birth weight, adjusted for covariates

Models	Total N	Crude OR (95% CI)	Adjusted OR (95% CI)	P-value	C-statistic
Model*[a]					
Wood	396	1.46 (0.76-2.81)	1.57(0.67-3.63)	0.40	0.80
Clean fuel (LPG+Kerosene)		1.00	1.00		
Model*[b]	394				0.81
>50-75% wood		1.71(0.87-3.37)	1.94(0.81-4.68)	**0.0604**	
>50-100% LPG or Kerosene and <50% wood		1.07(0.47-2.41)	1.03(0.35-3)	0.5061	
100% LPG, Kerosene or Electricity		1.00	1.00		
Model*[c]	234	1.09(0.88-1.36)	**1.69(1.15-2.49)**	**0.0055**	0.88
Model*[d]	395	1.12(0.93-1.35)	**1.34(1.02-1.75)**	**0.0342**	0.79

*Models adjusted for maternal age, maternal hypertension, parity, pregnancy risk factor, maternal weight gain between 1st and 3rd trimester, pre-term births, permanent or semi-permanent households (surrogate for SES), functional chimney, kitchen type, other sources of indoor pollution, and total open ventilation area.
[a]HAP exposure defined as categorical variable with 2 categories based on fuel use: Any wood users vs. LPG users; excluded subjects using kerosene as primary fuel >75%;
[b]HAP exposure defined as a multi-level gradient variable with five categories;
[c]HAP exposure defined as log-transformed continuous $PM_{2.5}$ levels;
[d]HAP exposure defined as estimated log-transformed continuous $PM_{2.5}$ levels;

Table 5. Results of logistic regression model for HAP exposure and SGA, adjusted for covariates

Models*	Total N	Crude OR (95% CI)	Adjusted OR (95% CI)	P-value	C-statistic
Model[g]	354	1.62(0.7-3.73)	**1.72 (0.68-4.37)**	0.2491	0.73
Model[h]	361			0.4117	0.77
>50 wood		1.97 (0.84-4.65)	1.47(0.55-3.92)	0.1778	
>50-100% LPG and <50% wood		1.001 (0.35-2.86)	0.70 (0.21-2.38)	0.2998	
100% LPG, Kerosene or Electricity		1.00	1.00		
Model[i]	208	1.28 (0.99-1.65)	**1.68 (1.18-2.42)**	0.0045	0.79

*Models adjusted for maternal age, maternal hypertension, parity, pregnancy risk factor, maternal weight gain between 1st and 3rd trimester, pre-term births, permanent or semi-permanent households (surrogate for SES), functional chimney, kitchen type, other sources of indoor pollution, and total open ventilation area.
[g]HAP defined as dichotomous variable (any wood users vs. clean fuel users);
[h]HAP defined as ordinal variable with five categories;
[i]HAP exposure defined as log-transformed continuous $PM_{2.5}$.