Prenatal exposure to particulate matter ($PM_{2.5}$) and low birth weight in a Sri Lankan birth cohort

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ABSTRACT

Background.

About 74% of the Sri Lankan population use biomass in the form of unprocessed wood as the primary cooking fuel. A growing body of evidence from meta-analyses and individual studies although limited by few prospective studies, report that prenatal exposure to particulate matter of size 2.5 µm ($PM_{2.5}$) emissions from biomass fuel burning may be associated with low birth weight (LBW) (<2500 grams). We present results examining the association between $PM_{2.5}$ and LBW in context of a birth cohort study in Sri Lanka. **Methods.**

We followed 545 pregnant women from their first trimester until delivery and assessed outcomes at birth. Exposure to household air pollution (HAP) from biomass smoke was assessed using detailed questionnaire about fuel type, kitchen characteristics and cooking practices; two-hour measurements of kitchen $PM_{2.5}$ were collected in a subset of households (n=304, 56%). Data from questionnaires and measured $PM_{2.5}$ were used to estimate two-hour kitchen $PM_{2.5}$ concentrations in unmeasured households. Data on covariates related to household characteristics, socio-demographic, maternal health and lifestyle factors were collected from baseline interviews. We performed linear and logistic regression analysis to evaluate the association between HAP exposure, and birth weight and LBW.

Results.

Of the total, 78% of the households used wood as primary or secondary fuel (n=425); households using wood had four-fold higher $PM_{2.5}$ levels compared to those using LPG. In linear regression models, we found an inverse association between a 10-unit increase in $PM_{2.5}$ and birth weight (β, -0.03; SE, 0.02; p, 0.06) adjusted for covariates. Similarly, categorical HAP exposure (>50% wood use) was significantly associated with birth weight as compared to LPG users (β, -0.13;

SE, 0.06; p, 0.0331). In logistic regression models, a 10-unit increase in $PM_{2.5}$ was associated with increased odds for LBW (OR, 1.26; 95%CI, 1.02-1.55; p, 0.0355), while the prevalence of LBW was highest among >50% wood users (OR, 2.82; 95%CI, 1.18-6.73; p, 0.0124), as compared to those using >50% LPG with wood and only LPG users. The association between HAP exposure and birth weight/LBW were consistent among term births (n=486).

Conclusions.

The finding of a significant association between prenatal $PM_{2.5}$ exposure and LBW in a low-middle income country (LMIC) setting where competing risk factors are minimal fills a gap in the body of evidence linking HAP from biomass smoke to LBW. These results underscore the crucial need to implement prevention and reduction of HAP exposure in LMICs where the HAP burden is high.

Key words

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

INTRODUCTION AND AIMS

Household air pollution (HAP) from combustion of solid fuels such as wood, dung and coal, used for cooking and heating, is ranked 10th as a contributor to the global burden of disease (1,2) and the third leading risk factor for global mortality and disability-adjusted life years (DALYs)(3). 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 (4). 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 low middle income countries (LMICs) (5)(6). More than three billion people accounting for 43% of the world's population use solid fuels (coal and biomass) for cooking and heating; about 80% of these people live in LMICs (7,8). In most LMICs, women of child-bearing age typically spend several hours a day in cooking chores. Consequently, they are exposed to high levels of HAP for long periods and are at high risk for adverse health effects from HAP. In Sri Lanka, a LMIC in South Asia with a population of 20 million, about 74% of the population uses some form of solid fuel (unprocessed wood) for cooking.(8,9) Recent reports from the Sri Lankan National Demographic Surveys indicate that the prevalence of solid fuel use remains mostly unchanged with only slight decrease from 78% to 74% in the last 15 years.(10) (11,12)

Studies on exposure to $PM_{2.5}$ from either ambient or indoor sources have found positive associations with adverse pregnancy outcomes including stillbirths, low birth weight (LBW), small for gestational age (SGA), preterm births and birth defects.(13–15). Results from a meta-analysis of ambient air pollution and birth weight found that birth weight in grams (g) was negatively associated with 10 $\mu g/m^3$ increase in ambient PM_{10} and $PM_{2.5}$ exposure during the prenatal period, adjusted for maternal smoking (16). Studies that have evaluated the role of HAP from solid fuel combustion and LBW indicate a stronger association, than ambient air exposure studies (17–20). A meta-analysis found that exposure to HAP from solid fuels based mostly on self-reports, resulted in an 86.4 g reduction in birth weight, and a 35% and 29% increased risk of LBW and stillbirth, respectively (21). Several of the pollutants found in ambient and indoor air share similar toxic properties as those found in environmental tobacco smoke (ETS) (22). Evidence from ETS and animal studies indicate that these air pollutants are absorbed by maternal blood, and then may cross the blood brain barrier and cause adverse effects on the fetus (23,24).

Previous studies of HAP and adverse birth outcomes including birth weight and LBW have several limitations. Most studies are either cross-sectional or case-control. Many of these studies are also subject to exposure misclassification. The labor-intensive and high costs associated with conducting air quality monitoring in all households, limit several HAP studies to qualitative exposure assessment resulting in exposure misclassification, especially in households with stacking of fuel (25). 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.

Most studies to date have been conducted in LMICs including India, Guatemala, Pakistan, and Ghana, countries where other competing risk factors for adverse birth outcomes such as malnutrition, poverty, infections and poor access to health care, are highly prevalent (21,26). Further, 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 fetal health. Only a few were birth cohort or experimental in design but except for a study conducted by Balakrishna et. al., (2017), most had smaller sample size.

To address some of these challenges, we designed a prospective birth-cohort study in Sri Lanka. The goal of the study was to evaluate the association between prenatal exposure to HAP from biomass smoke emissions and adverse birth outcomes. Our choice of the study setting is unique and offered several advantages. Sri Lanka has a literacy rate of 92% and maternal-child health indicators comparable to most high-income countries (27); thus, confounding/competing risk factors are minimized. Next, Sri Lanka's primary care infrastructure includes routine follow-up of almost all (> 95%) pregnant women and their children until five years of age facilitating assembling a cohort of women early in their pregnancy, following them through childbirth, and to subsequently follow their children until five years of age.

MATERIALS AND METHODS

Study setting

Sri Lanka is divided into approximately 270 MoH areas under the management of a Ministry of Health; each MoH serves a population of 60,000 to 100,000 (28,29). The MoH area is further divided into several Public Health Inspector (PHI) areas and, within each PHI areas are Public Health Midwife (PHM) areas, the smallest administrative unit of the government health system in Sri Lanka. Typically, a PHI area serves a population of 10,000-15,000 which is subdivided into 3-4 PHM areas. The PHM is the female grass roots level family health worker primarily responsible for maternal-child health services and serving a population of 3000-5000 people.

The PHM registers newly pregnant women, typically before 10 weeks of gestation. Thereafter, women are followed at the field clinic and in their homes every four weeks until the

28th week of gestation, every two weeks from the 28th to the 36th week of gestation and weekly thereafter until delivery. The PHM is also responsible for mothers' immunizations and health education. Almost 99% of births in Sri Lanka occur in hospitals. After delivery, the PHM visits the mother at home (a minimum of three visits within the first 10 days) to follow-up and identify early post-partum complications of the mother, if any and newborn problems including feeding complications.

Study area and recruitment

The study was conducted in the Ragama, Medical Officer of Health (MoH) and comprises of 16 PHMs. Two research assistants (RAs) worked with the PHMs to identify eligible study participants. A total of 721 pregnant women (n = 721) were screened between July 2011 and June 2012 from Ragama MoH antenatal field clinics. Eligibility criteria included: pregnant women in their first trimester; between 18 and 40 years of age; who planned to continue prenatal care and deliver at the Colombo North Teaching Hospital, Ragama; 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. Of the 721 women, 545 were followed until delivery. Loss of participants were due to: miscarriages (n=60); twin births (n=5); stillbirth (n=9); delivered in different hospitals (n=13); lost to contact due to changed residence (n=15) or changed consent (n=74).

Data collection

Women were interviewed at enrollment (mean, 11±2.5 weeks of gestation) to collect baseline 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 exposure information on factors related to HAP including fuel use, kitchen characteristics and cooking practices. Information was also collected on other sources of indoor and outdoor pollution, contributing to HAP. Maternal pregnancy history and infant anthropometric measurement record at birth, were obtained from hospital records. All interviews were conducted by bilingual study interviewers using structured questionnaires.

Prenatal exposure assessment

Qualitative exposure to HAP exposure was obtained from the baseline questionnaire administered to all study participants. The baseline questionnaire elicited detailed information on: 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, type of stove, presence of a chimney and its condition, ventilation in the kitchen during cooking including number and size of open doors and windows, type of kitchen, its dimensions and relative position of the kitchen and other rooms, number and size of door and windows. Information was also collected on 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.

Quantitative exposure to HAP was ascertained from two-hour $PM_{2.5}$ and carbon monoxide (CO) measurements in the kitchen during the cooking period in a subset of households (n=304 out of 545). Based on fuel use, 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 304 households (high exposure group, n=158; low exposure group, n=145) for conducting two-hour air quality measurements in the kitchen. At least one measurement per household was scheduled during the pregnancy period; in 106 households (36%), two sets of measurements were conducted in two of the three trimesters and in 26 households, three measurements were conducted, once every trimester; all others had one measurement (n=197, 65%). All measurements were conducted during a two-hour cooking session while preparing a typical lunch. Using this data, $PM_{2.5}$ concentrations were estimated for unmeasured household (described below). $PM_{2.5}$ 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.

Birth outcome assessment

All births occurred in the North Colombo Teaching Hospital. RAs collected data on birth outcomes from hospital records. Information abstracted included: birth weight, length and head circumference measured within 24 hours of birth; prenatal and delivery medical history. Gestational age was estimated based on the date of the last menstrual period and substantiated with ultrasound in the first trimester to classify infants as preterm vs. term births; pre-term births were defined as <37 weeks of gestation. LBW was defined as birth weight <2500 grams at birth. Term LBW were defined as full-term babies weighing <2500 grams at birth, as per standard definitions by the World Health Organization(30,31) .

Covariates and confounding variables

Data on covariates obtained from baseline questionnaire included: (i) demographic and SES factors such as maternal age, education, occupations, household income, type of housing, toilets, drinking water supply, ownership of house; (ii) maternal lifestyle factors such as use of alcohol and tobacco; (iii) maternal exposure to toxic chemicals such as ETS, pesticides and lead; (iv) parity; (v) past and present obstetric history of pregnancy induced hypertension, gestational diabetes, other pregnancy-related complications, miscarriages and still births, iron deficiency, and calcium intake; (vi) and child's gender.

Ethical review

All study protocols were approved by the Institutional Review Boards at the University of Kelaniya and the University of Alabama at Birmingham (UAB).

Statistical analysis

(i) Exposure estimation.

Categorical HAP exposure. In the baseline questionnaire, we collected information on the primary fuel and supplementary fuels used in the households. A Likert scale was used to quantify fuels used typically during an average week. The scale ranged from 1 to 4, 1 being 0 to 25% of fuel use and 4 being 75% to 100% of fuel used. Most of the households (n=423, 78%) in the study used a second fuel in varying quantities to supplement their primary fuel use. Combining the above information, we created two exposure variables. The first was a dichotomous variable classifying household into two categories: 'only LPG' and 'any wood use'. The second variable classified the households into three categories with gradients of wood use: (i) those using >50% to 100% of wood; (ii) those using >50-100% of LPG or kerosene and supplementing it with wood; and (iii) those using 100% LPG. Since, only three households used 100% kerosene supplemented occasionally by LPG, these households were included in the third fuel category of 100% LPG.

Continuous $PM_{2.5}$. Next, using regression models, we examined the influence of several physical characteristics on concentration of $PM_{2.5}$ levels in the kitchen fuel types (>50% wood, >50% LPG + <50% wood, 100% LPG), kitchen type (indoor, temporary hut or outdoor);

cookstoves (traditional cookstove (TCS), improved cookstove (ICS), kerosene or LPG stove); presence or absence of functional chimney, number of doors and windows open at the time of cooking as a surrogate for kitchen ventilation, and average daily cooking time categorized into three groups (0 to 60 minutes; 60 to 90 minutes and >90 minutes).

Prediction model. Data from 275 out of 303 households with air quality measurements were used to develop the exposure model to estimate kitchen $PM_{2.5}$ airborne concentrations. We excluded 26 samples as the comparison between fuel use and $PM_{2.5}$ values suggested potential misclassification of fuel use or were identified as possible outliers. For example, a household using >75% of LPG had measured value of $PM_{2.5}$ as high as 1000μg/m^3 significantly greater than the concentration that would be expected. The final regression model was then used to quantify kitchen concentrations for $PM_{2.5}$ levels for households without air quality measurements (n=270, 49.5%); data on percentage of fuel use was missing for one subject and thus, had missing value for $PM_{2.5}$.

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 used to identify factors significantly associated with log-transformed $PM_{2.5}$. Linear regression was used to model log-transformed $PM_{2.5}$ as a function of significant risk factors. We computed arithmetic and geometric means for $PM_{2.5}$ and compared them across the physical variables. In bivariate analysis, factors significantly associated with log-transformed $PM_{2.5}$ at $\alpha < 0.05$ were included in a multivariable linear regression model to derive the final model. 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 functional chimney at $p < 0.05$ (supplementary table

1). The model R^2 was 0.57 (supplementary table 2). The regression model equation is described below.

$$Ln\ (Y) = \alpha + \beta_{fuel\_category} + \beta_{kitchen} + \beta_{functional\_chimney} + \beta_{cooking\_time} + \varepsilon \text{ …… equation.(1)}$$

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 $\beta_{chimney}$ =0.06, estimate for functional chimney (equation 1)

Validation of the model. 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 predicted $PM_{2.5}$ values and plotted the residuals to evaluate the robustness of the predictive model.

(ii) HAP exposure and outcomes

Initial analyses compared the mean distribution of birth weight and prevalence of LBW with exposure variables and covariates using t-test, ANOVA, and the chi-square test (supplementary table 1). We restricted the latter comparisons and further analyses to those potential risk factors, to which at least 10 subjects were exposed.

HAP exposure was analyzed as continuous (log-transformed $PM_{2.5}$) and categorical variables (dichotomous and three-level fuel categories). We used linear regression to evaluate the association between HAP exposure and birth weight. Covariates significantly associated with exposure and/or birth weight in univariate statistics at $p<0.05$ were included in the multivariable linear regression to compute adjusted beta-estimate and standard error, and adjusted means for birth weight.

We used logistic regression to evaluate the association between HAP exposure and LBW. Covariates significantly associated with exposure and/or LBW in bivariate analysis at $p<0.05$ were included in the multivariable model. We computed the odds of LBW in relation to HAP exposure modeled as continuous or categorical variable, adjusting for other risk factors.

We further stratified the analysis by term and preterm births and examined the association between HAP exposure and birth weight and LBW. All analyses were conducted using SAS version 9.4.

RESULTS

Of the total mothers (n=545) followed-up from 1st trimester until delivery, 423 (78%) used wood in varying quantities, while 122 (22%) women used only LPG for cooking. The average age of mothers enrolled was 29 years (SD = 4.9; median = 29); all women were married. We found significant differences between wood users and LPG users for maternal education, spouse's education, main household water source, ownership of the household, type of house (semi-permanent vs. permanent), income, kitchen type, functional chimney, average daily cooking time, and sources of HAP other than biomass fuel including ETS, burning of candles or incense ($p<0.05$). No remarkable differences were noted for mother's age at the time of enrollment, past and current obstetric history, parity or child's gender (supplemental table 1).

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 four times higher than 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)].

HAP exposure and birth weight

Of the total 545 newborns, 52% were boys. The mean birthweight of infants in the cohort was 2.95 (±0.47) kg. 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 term LBW births were 46 (10%) out of 486 live births. About 65% of the mothers had vaginal delivery including forceps (n=6) and vacuum deliveries (n=5).

Table 1 presents distribution of mean birth weight across all covariates. Birth weight was significantly associated with continuous $PM_{2.5}$, three-level fuel categories, type of house, pregnancy induced hypertension and preterm births at $p <0.05$. In multivariable linear regression models (Table 2), continuous log-transformed $PM_{2.5}$ was inversely associated with birth weight (β, -0.06; SE, 0.02; p, 0.06), adjusted for covariates. All multivariable models were adjusted for mother's education, father's education, income, permanent or semi-permanent house, ownership of the house, type of toilet, average daily cooking time, other sources of indoor pollution, and pregnancy induced hypertension. In addition, models with categorical HAP exposure were also adjusted for type of kitchen and functional chimney.

Use of wood fuel as compared to LPG use was associated with lower birth weight but the association was non-significant (β,-0.07; SE, 0.05; p, 0.20). In model with three-level HAP exposure, birth weight was significantly inversely associated with >50% wood use (β, -0.13; SE, 0.06; p, 0.03) as compared to 100% LPG use (as referent). No difference was observed between >50% LPG with wood use as compared to 100% LPG use (β, 0.002; SE, 0.06; p, 0.5309).

HAP exposure and LBW

The prevalence of LBW was significantly associated with continuous $PM_{2.5}$; a 10 unit (in $\mu g/m^3$) increase in $PM_{2.5}$ was associated with 1.26 times increased odds of LBW (95% CI, 1.01-1.57; $p = 0.04$). No association was observed between dichotomous fuel use variable and LBW

(OR, 1.78; 95% CI, 0.78-4.09, p, 0.17). For three-level HAP exposure variable, the odds of LBW were significantly higher for >50% wood users (OR, 2.27; 95% CI=0.94-5.12; p=0.04) compared to 100% LPG users; no difference was noted between >50% LPG with wood users and 100% LPG users (Table 3).

Term births.

In stratified models by term birth, the relationship between exposure variables and birth weight and LBW were consistent as observed in the full models but effect estimates were lower. A moderately significant association was found between 10-unit increase in $PM_{2.5}$ and decrements in birth weight (β, -0.04; SE, 0.02; p, 0.03) and LBW (OR = 1.27; 95% CI, 0.98-1.65, p, 0.07). Similarly, >50% wood use was associated with decrease in birth weight (β, -0.12; SE, 0.06; p, 0.05) and prevalence of LBW (OR, 1.76; 95% CI, 0.61-5.03; p= 0.08), but the associations were not significant. We did not run models on preterm birth due to small number of observations (n= 55).

Discussion

In the present study, we investigated the relationship between prenatal exposure to HAP from biomass fuel use for cooking and birth weight, in a birth cohort study of 545 mother-child pairs in the Western Province of Sri Lanka. Our study modeled exposure to HAP as continuous and categorical variables. We found a significant association between two-hour kitchen concentrations of $PM_{2.5}$ and birth weight and prevalence of LBW, after adjusting for significant confounding factors. Similarly, households using most wood were associated with decrease in birth weight and increased prevalence of LBW as compared to households using clean fuels. The results are consistent with previous air pollution studies including ambient and HAP and LBW (15,16,32). In our study, we used a combination of self-reported information on sources of HAP exposure and measured kitchen concentrations of $PM_{2.5}$ during cooking in subset of households to quantify kitchen concentrations of $PM_{2.5}$ in unmeasured households. To our knowledge, our study is the first to use both measured and estimated $PM_{2.5}$ measurements to evaluate the association between $PM_{2.5}$ and birth weight. We discuss the exposure estimation methods, effect exposure estimates for birth weight and LBW in context of previous literature and highlight the strengths and limitations of our study.

HAP, birth weight, 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. (2017) reported a decrease of 4 grams (95% CI:1.08 g, 6.76 g) decrease in birthweight and 2% increase in prevalence of low birthweight (OR, 1.02; 95% CI, 1.01-1.04) with a 10-$\mu g/m^3$ increase in $PM_{2.5}$. Results from other meta-analyses also found increased prevalence of LBW between 10% to 45%, associated with HAP exposure (17,19,21,33–37). Similarly, a recent meta-analysis conducted by Sun et al. (2016), found significant association between 10$\mu g/m^3$ increment of ambient $PM_{2.5}$ and increased odds of LBW (OR,1.09; 95% CI, 1.03-1.15) (32). 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 average two-hour kitchen $PM_{2.5}$ in kitchens using wood 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 $\mu g/m^3$ vs. 1649±166 $\mu g/m^3$; LPG/electricity: 59.3±45.7 $\mu g/m^3$ vs. 143±12 $\mu g/m^3$]. 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 drawn.

The increased odds for term LBW (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)(38) and Mavalankar et al., (1992) (OR=1.23; 95% CI : 1.01, 1.49) (39).

Exposure estimation

In our study, we used information on stacking of fuel during an average week, to categorize HAP exposure into three categories. We developed a predicted model using information on fuel stacking, type of kitchen, and stove ventilation to predict kitchen $PM_{2.5}$ concentrations. 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 air pollution measurement data. Cross-validation approach evaluated the robustness of the model with a R^2 of 57%. Personal monitoring of exposure to HAP by wearing portable devices for a period of 24 to 48 hours can substantially reduce exposure misclassification and improve the power of the study to detect relationships between exposure to HAP and adverse health outcomes (40). However, conducting area or personal air quality monitoring in all study 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 (25). In these studies, households are categorized based on their primary fuel use as households using wood, kerosene or LPG and electricity. Few studies have considered multiple types of fuel use or the proportion of fuels used, resulting in uncertainty in nature and magnitude of exposure variability and misclassification of exposure in epidemiologic studies (25).

Balakrishnan et al.(2013), conducted one of the first studies to conduct 24-hour $PM_{2.5}$ measurements in all study households (n=474) and fit a regression analysis to model 24-hour data to predict household $PM_{2.5}$ concentrations (41). 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.(42) 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 (43). 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 (44). 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 lower than the R^2 (66%) reported by Zhou et al (44); and 1.6 times greater than the R^2 (0.36) as reported by Balakrishnan et al (2013) (42). The correlation between estimated and measured $PM_{2.5}$ (r = 0.74 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 kitchen $PM_{2.5}$ concentrations. Several other factors can affect personal exposure including the high degree of variability from stacking of fuels, different stove types and kitchen designs, and time-activity pattern of the subjects i.e., the amount of time spent in the kitchen and inside the homes as compared to outside. Furthermore, changes in patterns of fuel use over the course of pregnancy could change personal exposure. Increased frequency, longer duration of air quality monitoring and time activity diary of time spent indoor can improve the accuracy of our predictive model.

Our study has several strengths. We modeled exposure HAP in several different ways and found internal consistency in the overall results. 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 antenatal 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. 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 antenatal 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 ETS 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 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 was the 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 and was used to quantify indoor air quality for remaining 40%, which could have resulted in some exposure misclassification. However, internal consistency in results suggest minimum bias.

Conclusion.

Our study evaluating HAP and birth outcomes in Sri Lanka adds to the growing evidence linking HAP to LBW and term LBW. 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. 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.

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Conflict of Interest

The authors declare that they have no competing financial interests.

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Table 1. Distribution of mean birth weight and prevalence of LBW across demographic, maternal and household characteristics

	Total	***Birth weight***	***LBW***
		Mean (SD)	***n(%)***
Demographic factors			
Mother's age			
N	529		68
Mean (SD)	29(4.9)		28(4.9)
Median (IQR)	29(7)		28(5.5)
Missing	18		
Mother's education			
0-5 years	74	2.9(0.5)	9(13)
5-10 years	316	2.9(0.5)	41(60)
>10 years	137	3(0.5)	18(26)
Missing	17		2 (2.9)
Father's education			
0-5 years	68	2.9(0.5)	12(18)
>5-10 years	333	2.9(0.5)	45(66)
>10 years	126	3(0.5)	11(16)
Missing	19		2 (2.9)
Water source			
Piped water	133	3(0.5)	41(60)
Well water	100	2.9(0.5)	12(18)
Tube well water	293	3(0.5)	15(22)
Missing	21		2 (2.9)
Drinking water supply			
In home	143	2.9(0.5)	19(29)
In yard	261	3(0.5)	32(48)
Outside home	92	2.9(0.5)	15(23)
Missing	51		4 (5.7)
Toilet			
Private flushed toilet	450	2.9(0.5)	60(88)
Shared flushed toilet	62	3(0.5)	2(3)
Private pit latrine, composting, bucket	14	3.1(0.3)	6(9)
Missing	21		2 (2.9)
Owning a house			
Yes	439	3(0.5)	58(85)
No	85	2.9(0.4)	10(15)
Missing	23		2 (2.9)
Type of house			
Semi-permanent or improvised	350	**2.9(0.5)****	51(75)

Table 1. Distribution of mean birth weight and prevalence of LBW across demographic, maternal and household characteristics

	Total	***Birth weight***	***LBW***
		Mean (SD)	***n(%)***
Permanent	179	**3(0.4)**	17(25)
Missing	18		2 (2.9)
Income			
LE 15000	96	2.9(0.4)	16(24)
15000-20000	93	3(0.5)	30(45)
20001 - 25000	93	2.9(0.5)	11(16)
>25000	243	3(0.5)	10(15)
Missing	22		6 (4.9)
Parity			
0	185(34)	2.9(0.4)	23(33)
1	220(40)	3(0.5)	29(41)
2	128(23)	2.9(0.5)	18(26)
Missing	14(2.7)		0
Past miscarriage			
Yes	28(5.3)	2.9(0.6)	4(6)
No	517(94)	3(0.5)	66(94)
Past pregnancy risk			
Yes	35 (6.4)	2.8(0.6)	4(6)
No	5.13 (94)	3(0.5)	66(94)
Pregnancy hypertension			
Yes	26(4.7)	**2.4(0.7)****	**13(19)****
No	522(95)	**3(0.4)**	**57(81)**
Gestational diabetes			
Yes	19(3.5)	2.9(0.5)	4(6)
No	529(96.5)	3(0.5)	66(94)
Kitchen characteristics			
Dichotomous fuel use			
Wood	423 (78)	2.9 (0.4)	58 (14)
LPG	122 (22)	3.0 (0.5)	12 (9.8)
Fuel percentage			
50%-100% Wood	275(50)	**2.9(0.5)****	**43(64)****
>50% LPG + wood	44(8)	**2.9(0.5)**	**7(10)**
100% LPG	205(38)	**3(0.5)**	**17(25)**
Missing	1		**1**
Continuous $PM_{2.5}$ (in µg/m^3)			
0-35	10 (1.8)	2.9 (0.4)	1 (1.4)
35-75	36 (6.6)	3.0 (0.5)	6 (8.6)

Table 1. Distribution of mean birth weight and prevalence of LBW across demographic, maternal and household characteristics

	Total	***Birth weight***	***LBW***
		Mean (SD)	***n(%)***
75-28245	498 (92)	2.97 (0.5)	32 (46)
Kitchen type			
Indoor	466	3(0.5)	58(85)
Temporary hut	48	2.9(0.5)	8(12)
Outdoor	15	2.9(0.6)	2(3)
Missing	18		2 (2.9)
Primary stove			
Traditional	157(29)	2.9(0.5)	25(36)
Improved cookstove	114(21)	2.9(0.5)	17(24)
Kerosene	25(4.6)	2.9(0.5)	4(5.7)
LPG/Electricity	252(46)	3(0.5)	24(34)
Functional chimney			
Yes	282(51.5)	3(0.5)	35(50)
No	266(48.5)	2.9(0.5)	35(50)
Daily cooking time (in minutes)			
≤ 60	148 (27)	3.0)0.5)	18 (26)
>60 - ≤ 90	218 (40)	2.94 (0.5)	28 (40)
>90	154 (28)	2.9 (0.5)	21 (30)
Missing	25 (4.6)	3.0 (0.5)	3 (0.6)
Open windows			
0	258(47.1)	3(0.5)	32(46)
1	262(47.8)	3(0.5)	36(51)
2	28(5.1)	2.9(0.4)	2(3)
Open doors			
1	78(14)	3(0.5)	7(10)
2	242(44)	2.9(0.5)	40(57)
3	26(5)	3.1(0.5)	1(1.4)
Missing	200 (37)		22 (31)
Other source of indoor pollution			
1	61(11.1)	**2.8(0.5)****	12(17)
0	487(88.9)	**3(0.5)**	58(83)
Outdoor sources of pollution			
1	40(7.3)	2.9(0.5)	5(7)
0	508(92.7)	3(0.5)	65(93)
Smoking			
Yes	38(6.9)	3(0.6)	6(9)
No	510(93.1)	3(0.5)	64(91)

Table 1. Distribution of mean birth weight and prevalence of LBW across demographic, maternal and household characteristics

	Total	***Birth weight***	***LBW***
		Mean (SD)	***n(%)***
Environmental risk			
Yes	260	2.9(0.5)	28(40)
No	288	3(0.5)	42(60)
Birth outcomes			
Child's gender			
Male	285 (52)	2.97 (0.5)	38 (13)
Female	261 (48)	2.9 (0.4)	32 (12)
Missing	1		0

** significant at $p < 0.05$

Table 2. Relationship between HAP exposure and birth weight (in kgs)

	Exposure	Crude β (Standard error (SE))	Adjusted β(SE)	P-value	Adjusted R^2, sample size
Model[1]	Continuous $PM_{2.5}$	-0.06(-3.17)	**-0.03(0.02)**	**0.0553**	0.10, n=501
Model[2]	Wood	-0.07(0.05)	-0.07(0.05)	0.2008	0.09 (n=501)
	LPG	0			
Model[2]	>50% wood	-0.10 (0.05)	**-0.13(0.06)**	**0.0331**	0.11 (n=501)
	>50% LPG + wood	0.02 (0.06)	0.002(0.06)	0.9724	
	100% LPG	0			

[1]Adjusted for mother's education, father's education, type of house, ownership of the house, toilet, income, average daily cooking time, other sources of indoor pollution, pregnancy induced hypertension

[2]Adjusted for mother's education, father's education, type of house, ownership of the house, toilet, income, kitchen type, presence of functional chimney, average daily cooking time, other sources of indoor pollution, pregnancy induced hypertension

Table 3. Relationship between HAP exposure and LBW

	Exposure	Crude OR (95% CI)	Adjusted OR (95% CI)	P-value	c-statistic
Model[1]	Continuous $PM_{2.5}$	1.14(0.94-1.38)	**1.26(1.01-1.57)**	**0.0387**	0.72
Model[2]	Wood	1.46(0.76-2.81)	1.78 (0.78-4.09)	0.1727	0.76
	LPG	1.00	1.00		
Model[3]	>50% wood	1.64 (0.83-3.24)	**2.27(0.94-5.52)**	**0.0370**	0.72
	>50% LPG + wood	1.11 (0.50-2.47)	1.27(0.49-3.29)	0.6377	
	100% LPG	1.00	1.00		

[1]Adjusted for mother's education, father's education, type of house, ownership of the house, toilet, income, average daily cooking time, other sources of indoor pollution, pregnancy induced hypertension

[2]Adjusted for mother's education, father's education, type of house, ownership of the house, toilet, income, kitchen type, presence of functional chimney, average daily cooking time, other sources of indoor pollution, pregnancy induced hypertension