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Exposures to fine particulate matter ($PM_{2.5}$) and birthweight in a rural-urban, mother-child cohort in Tamil Nadu, India

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ABSTRACT

Background: Exposure to $PM_{2.5}$ (fine particulate matter < less than 2.5 μm in aerodynamic diameter) related to ambient and household air pollution has been associated with low birthweight. Few of these studies, however, have been conducted in high exposure settings that are commonly encountered in low and middle income countries (LMICs).

Objectives: We examined whether $PM_{2.5}$ exposures during pregnancy were associated with birthweight in an integrated rural-urban, mother-child cohort in the state of Tamil Nadu, India.

Methods: We recruited 1285 pregnant women in the first trimester of pregnancy from primary health care centers and urban health posts and followed them until birth to collect antenatal care data and birthweight. We estimated pregnancy period $PM_{2.5}$ exposures through direct serial measurements of 24-h household $PM_{2.5}$ concentrations, performed across each trimester. Mothers also completed detailed questionnaires to provide data on covariates related to household, socio-economic, demographic and maternal health characteristics. The association between $PM_{2.5}$ exposures and birth weight was assessed using linear and logistic regression models that controlled for potential confounders.

Results: A 10-μg/m^3 increase in pregnancy period $PM_{2.5}$ exposures was associated with a 4 g (95% CI: 1.08 g, 6.76 g) decrease in birthweight and 2% increase in prevalence of low birthweight [odds ratio(OR) = 1.02; 95%CI:1.005,1.041] after adjusting for gestational age, infant sex, maternal BMI, maternal age, history of a previous low birth weight child, birth order and season of conception.

Conclusions: The study provides some of the first quantitative effects estimates for linking rural-urban $PM_{2.5}$ exposures and birthweight in India, adding important evidence for this association from high exposure settings in LMICs, that also experience dual health burdens from ambient and household air pollution. Study results also point to the need for considering maternal $PM_{2.5}$ exposures alongside other risk factors for low birthweight in India

1. Introduction and purpose

Air pollution ranks among leading risk factors contributing to the burden of disease in India (Forouzanfar et al., 2015) with both urban and rural populations at risk from $PM_{2.5}$ (fine particulate matter < less than 2.5 μm in aerodynamic diameter) exposures related to ambient (AAP) and household air pollution (HAP)(Balakrishnan et al., 2014; Cohen et al., 2017; Smith et al., 2014). Preterm births (< 37 weeks

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gestation), reduced birthweight and low birthweight (LBW) have been associated with AAP (Dadvand et al., 2013; Sapkota et al., 2010; Shah et al., 2011; Stieb et al., 2012; Sun et al., 2016; Zhu et al., 2015) and HAP (Amegah et al., 2014; Pope et al., 2010) exposures. There is however considerable heterogeneity in the reported strength of association across studies included in these meta-analyses. Further, as with other adverse health outcomes contributing to the disease burden attributable to air pollution, there is limited representation from studies at the higher end of the exposure spectrum making it difficult to understand the nature of exposure –response relationships in this range, a situation commonly encountered in many low and middle income countries (LMICs).(Burnett et al., 2014; Fleischer et al., 2014). Due to these uncertainties, low birthweight related impacts are not included in current disease burden estimates for air pollution.

Nevertheless, reduced birthweight is an important public health concern and has been associated with increased infant mortality and morbidity (Lacasana et al., 2005), child cognitive development (Shenkin et al., 2004; Sorensen et al., 1997) as well as cardio-metabolic disorders that may persist into adult life (Barker, 2003; Johnson and Schoeni, 2011; Osmond and Barker, 2000; Rogers and Velten, 2011).

Nearly 50% of India's population resides in districts where annual average ambient $PM_{2.5}$ concentrations are in excess of the Indian national standard of 40 μg/m^3 and nearly 99% in districts that exceed the World Health Organization Air Quality Guideline (AQG) levels of 10 μg/m^3 (Brauer et al., 2016). Further, national average household (24-hr) $PM_{2.5}$ concentrations among solid cook-fuel users are estimated to range from 113 μg/m^3 to 450 μg/m^3 (Balakrishnan et al., 2013b). If such $PM_{2.5}$ exposures were convincingly linked to birthweight, it would have major implications for India, given the high prevalence(~ 18.5%) of low birthweight (NFHS, 2016) and the widespread prevalence of health damaging air pollution exposures within rural and urban communities (Balakrishnan et al., 2014).

AAP studies concerning adverse birth outcomes conducted in USA, Canada and a few high income countries in Europe, usually relied on facility-based birth records to retrieve information on birthweight and reported limited abilities to adjust for residual confounding from covariates related to socio-economic status, maternal health and smoking. (Brauer et al., 2008; Estarlich et al., 2011; Gehring et al., 2011; Hannam et al., 2014; Jędrychowski et al., 2003; Lakshmanan et al., 2015; Morello-Frosch et al., 2010; Parker et al., 2005; Pedersen et al., 2013). Exposure assessment approaches in these (AAP) studies have relied on central site monitors and proximity based methods to estimate individual or community level exposures (Dadvand et al., 2013) as well as land use-regression (LUR) (Gehring et al., 2011; Ghosh et al., 2012; Pedersen et al., 2013) and hybrid LUR - satellite based methods (Hyder et al., 2014). The recent availability of high resolution (10 km × 10 km) globally gridded estimates for $PM_{2.5}$ concentrations have enabled the inclusion of LMIC sites that lack extensive ground based air pollution monitoring networks (Fleischer et al., 2014) in multi-centric AAP studies concerning birthweight. Only one AAP study (Jedrychowski et al., 2009) reported using personal exposure measurements and direct measurements of birthweight to examine the association.

HAP studies examining adverse pregnancy outcomes have nearly all been conducted in LMIC countries. Although data on birth outcomes and a range of confounding variables have been collected through a combination direct field assessments and birth records in these studies, virtually all HAP studies relied on qualitative indicators of exposure such as reported use of solid vs. gaseous fuels (Amegah et al., 2014; Pope et al., 2010) for cooking and/or heating. HAP studies to date, have thus not been able to characterize quantitative continuous exposure-response relationships for birthweight as done in AAP studies.

Use of study methods developed in previous AAP or HAP studies concerning birthweight (described above) are not readily applicable in India. Ambient air quality in major cities in India is monitored through the network of monitors under the National ambient air quality program(NAMP) of the Ministry of Environment (CPCB, 2011), Government of India, but the density of coverage for continuous $PM_{2.5}$ monitoring is low and rural areas are not currently included under the NAMP. This has also limited the abilities to validate recent modeling efforts based on satellite and chemical transport models to estimate population exposures (Brauer et al., 2016). Further, with limited information on time-activity profiles across urban and rural populations, relying on a limited number of central site monitors, using modeling approaches without adequate validation or using only qualitative indicators (such as reported cook-fuel use) could produce considerable exposure misclassification for exposure settings typically prevalent in India. Finally, facility based birth records are not readily accessible in India and often do not provide information on many co-variates. Establishing quantitative exposure-response relationships between air pollution exposures and birthweight in India have thus been challenging, both on account of the limitations of routinely collected health and exposure data and the complexity of the exposure setting.

We report results from the Tamil Nadu Air Pollution and Health Effects -Birthweight (TAPHE-BW) study that examined the relationship between $PM_{2.5}$ exposures and birthweight in a prospective rural-urban mother-child cohort in the state of Tamil Nadu, India. We hypothesized that increased maternal $PM_{2.5}$ exposures would be associated with lower birthweight. The primary objectives of the study were to estimate continuous exposure-response relationships between pregnancy period $PM_{2.5}$ exposures (through direct serial measures of household $PM_{2.5}$ concentrations performed across each trimester) and birthweight as well as examine the association with the increased risk of low birthweight.

2. Methods

The study was executed with the financial and technical support provided by the Indian Council of Medical Research (ICMR), Government of India between 2010 and 2015, as part of a larger effort to examine health effects of air pollution in Tamil Nadu and build exposure models relevant for adult, maternal and child outcomes in rural-urban cohorts (Balakrishnan et al., 2015b).

All study protocols were approved by the Institutional Ethics Committee of Sri Ramachandra University (that follows Guidelines for Human Subject Research issued by the Indian Council of Medical Research in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans). Permissions to conduct the study were also provided by the Offices of the Secretary of Health and Directorate of Public Health, Government of Tamil Nadu.

A detailed description of data collection methods has been published previously (Balakrishnan et al., 2015b). Select details of relevant protocols are briefly summarized below.

2.1. Subject recruitment

11 primary health care centers i.e. PHCs (serving ~110 villages in Thiruvallur and Kancheepuram districts of Tamil Nadu) and 17 urban health posts i.e. UHPs (serving the ten municipal zones of Chennai, the capital city of Tamil Nadu) were randomly selected to recruit pregnant women from rural and urban areas (defined as per Census of India, 2011) respectively (Supplemental material Fig. S1). 1822 pregnant women presenting at PHCs/UHPs between September 2010 and December 2013, were approached for screening at the time of their first ante-natal care visit (~8–10 weeks of gestation). 1537 (84%) were found eligible and 1416(94% of those eligible) provided an informed consent. Eligibility was based on (i) singleton pregnancy (ii) no use of assisted reproductive technologies (iii) no involvement in dusty occupations and (iv) no known plans, to be away from their current residence during the study period (including delivery of the child). No financial incentives were offered at any time to the participants. Project