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None declared.

Prenatal exposure to particulate matter and term low birth weight: systematic review and meta-analysis

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Review question / Objective: **To assess the effects of particulate matter exposure during various periods of pregnancy on low birth weight and term low birth weight. Population:pregnant women and their singleton live-births; Exposure: maternal exposure to ambient PM2.5 and PM10 during the entire pregnancy or each trimesters were estimated based on ground-level atmospheric pollution monitoring stations or validated exposure models (μg/m3); Comparator(s): risk estimates were presented as hazard ratios (HRs) or odds ratios (ORs) and their 95% confidence intervals (95% CI) with per specific increment in PM2.5; Outcomes: term LBW(≥37weeks and<2500g) or LBW(<2500g)were defined as a dichotomous variables.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 August 2022 and was last updated on 17 August 2022 (registration number INPLASY202280064).

INTRODUCTION

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term LBW(≥37weeks and<2500g) or LBW(<2500g)were defined as a dichotomous variables.

Rationale: Despite the establishment of pathways and biological processes, causality determinations for PM exposure and birth outcomes were classified as "suggestive, but not sufficient to infer or inadequate to infer" by the United States Environmental Protection Agency (EPA) based on current research. Large birth cohort studies seems to document consistent positive association between PM exposure and term low birth weight. However, some analyses were limited to pregnant women living near air monitoring stations, which may limit applicability of the study findings to broader populations. It is not determined whether the inclusion of macrosomia (defined as birthweight>4000 g) and post-term birth (≥42weeks gestation) attenuate the main association. In addition, the lack of standardized assessment methods may increase maternal exposure assessment error and differences in health effect estimates. Whether relying on fixed-site monitoring data or exposure prediction models including land use regression (LUR) model, inverse distance weighting (IDW) spatial interpolation algorithm, dispersion model, and bayesian model, such methods ignore spatial heterogeneity and the individual difference of time-activity patterns, which may be a source of between-study heterogeneity. Furthermore, we were unable to obtain risk estimates for the effects of particulate matter exposure on low birth weight from current systematic reviews and meta-analyses that have not extensively adjust for potential confounders such as maternal age, gestational age, infant sex, passive smoking, diabetes, hypertension during pregnancy, etc.

Condition being studied: Air pollution contributes to the global burden of disease, with the largest increase in risk exposure for ambient particulate matter(PM) pollution. PM is a mixture of solid particles and liquid droplets found in the ambient air, mainly produced by industrial activities, motor vehicles, cooking, fuel combustion, and biomass burning. Increasing epidemiologic evidence is indicating ambient PM pollution is associated with adverse health effects including total (nonaccidental) mortality, increased hospital admissions for major cardiovascular disease, contributor to deaths from chronic obstructive pulmonary disease, and adverse birth outcomes. Birth weight is an important marker of maternal and fetal health and nutrition. Nearly 15% of all infants worldwide are born with low birth weight (LBW) in 2015, jeopardizing their survival, health and development. Triggers of fetal growth restriction, especially in susceptible populations, which remain a significant public health problem, is linked to progress towards the global nutrition target of a 30% reduction in low birthweight prevalence between 2012 and 2025.

METHODS

Search strategy: We conducted a comprehensive search of PubMed and Web of science from database inception until 7 April 2022. Both subject headings and free text terms were searched for two themes of "air pollution" and "low birth weight" separately (Supplemental Table S1) to increase sensitivity to potentially appropriate studies. Synonymous terms were first combined with the Boolean operator "OR." These 2 themes were then combined with the Boolean operator "AND." No restrictions were applied for PubMed. Filters were applied to exclude reviews article, meeting, and non-English publication in Web of science. Reference lists of all included studies were also screened for additional records.

Participant or population: pregnant women and their singleton live-births.

Intervention: NA.

Comparator: Risk estimates were presented as hazard ratios (HRs) or odds ratios (ORs) and their 95% confidence intervals (95% CI) with per specific increment in PM2.5.

Study designs to be included: Birth cohort studies; observational studies.

Eligibility criteria: Inclusion criteria consisted of: (a) study design : birth cohort studies; observational studies; (b) study population (pregnant women and their singleton live-births); (c) maternal exposure to ambient PM2.5 and PM10 during the entire pregnancy or each trimesters were estimated based on ground-level atmospheric pollution monitoring stations or validated exposure models (μg/m3); (d) PM2.5 and PM10 were treated as linear terms or quartile; (e) the outcome of pregnancy: term LBW(≥37weeks and<2500g) or LBW(<2500g)were defined as a dichotomous variables; (f) risk estimates were presented as hazard ratios (HRs) or odds ratios (ORs) and their 95% confidence intervals (95% CI) with per specific increment in PM2.5; (g) If multiple articles reported results drawn from the same source dataset or cohort, we only included the most comprehensive study. Exclusion criteria were: (a)irrelevant studies; (b) time-series study, ecological study, trial; (c) non-English studies; (d)studies with no standard diagnostic criteria for LBW(not <2500g); (e)studies with a rate of LBW<1%, because we postulated that these studies findings may not be representative or underestimating effects; (f) studies published in the form of an abstract, review, letter, guidelines; or case report and animal or in vitro studies.

Information sources: Electronic databases.

Main outcome(s): Term LBW(≥37weeks and<2500g) or LBW(<2500g)were defined as a dichotomous variables.

Quality assessment / Risk of bias analysis: We developed a tailored version of the Risk of bias tool(Modified-OHAT) according to the Office of Health Assessment and Translation (OHAT) risk-of-bias questions and the Agency for Healthcare Research checklist, focusing on the bias questions applicable to the environmental health study designs. Two independent reviewers (JL, YMC) applied the tool to perform quality assessment, and discrepancies were resolved through discussion with a third reviewer (QZ). Specifically, we focused on four aspects that constitute major risk for bias in air pollution and perinatal outcomes studies: (1) selection of study population: birth cohort and reproductive data were obtained from National birth certificates or birth registry database. Extreme gestational age and birth weight values, such as 44weeks, or>5000g) were excluded to reduce their influence to effect. (2) exposure assessment: studies used the geocoded maternal pregnancy residential address rather than infant birth addresses to determine daily prenatal exposure to PM and accounted for residential mobility during pregnancy; No restriction on living within 5 or 10 km of a ground monitoring site. (3) confounding (models adjusted for five variables were considered as high?maternal age, infant sex, parity, maternal education, and gestational age); Studies tested whether there was a difference in birth weight and other parameters between excluded children due to missing covariates and non-excluded children. (4) PM exposure or meteorological data are assigned to the entire pregnancy or every trimester using a unified calculation formula; questionnaires or medical records were used to collect information about demographics, smoking, medical history, and other covariates. (5) More detailed analyses and complete data are provided in the main text or Appendix; outcome reporting is not selective. Each item is classified as of low, medium, high, or unclear risk of bias. Overall, bias potential in a study was considered to be high if any three or more of the five above-stated domain were present, medium if two was present, and low if one or less was present.

Strategy of data synthesis: We log transformed ORs and pooled them across studies using random-effects meta-analysis with inverse variance weighting and then exponentiated these values to obtain the pooled ORs. the increments were not transformed commonly for the

pooled RRs: We grouped effect estimates by gestational period (first trimester, second trimester, third trimester or entire pregnancy).χ2 test-based Q statistic and I2 were used to estimate the heterogeneity among studies. Random-effect model (DerSimonia-Laird method) was used to estimate the pooled RRs and 95% CIs.We used forest plots to assess overall effect.

Subgroup analysis: Subgroup analyses were conducted based on the economic status of the country, region of study, exposure assessment, risk of bias in component studies and adjustment for maternal age, infant sex, and parity (yes versus no).

Sensitivity analysis: Sensitivity analysis was performed for each excluded study.

Language restriction: English only.

Country(ies) involved: China.

Keywords: particulate matter; low birth weight; Term low birth weight; LBW; TLBW.

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