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The correlation between $PM_{2.5}$ exposure and hypertensive disorders in pregnancy: A Meta-analysis

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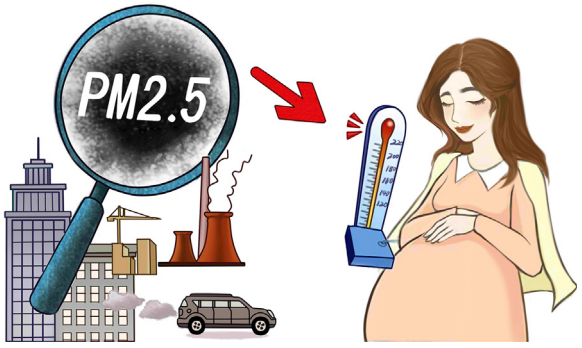
HIGHLIGHTS

- Meta-analysis of relation between $PM_{2.5}$ and hypertensive disorders in pregnancy.
- $PM_{2.5}$ (per 10 μg/m^3) increases the risk of hypertensive disorders in pregnancy.
- We advise to strengthen protective measures against air pollution during pregnancy.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective: To find the correlation between exposure to $PM_{2.5}$ (fine particulate matter) and hypertensive disorders in pregnancy (HDP), and provide medical evidence for decreasing the incidence of hypertensive disorders in pregnancy.
Method: A combination of computer and manual retrieval was used to search for keywords in PubMed (385 records), Cochrane Library (20 records), Web of Science (419 records) and Embase (325 records). Finally, ten epidemiological articles were considered in this meta-analysis. Stata 13.0 was used to examine the heterogeneity among the studies and to calculate the combined effect value (OR, odds ratio) by selecting the corresponding models. Sensitivity analysis and publication bias test were also performed.
Results: Meta-analysis indicated that there was an association between $PM_{2.5}$ exposure (per 10 μg/m^3 increase) and hypertensive disorders in pregnancy (OR = 1.52, 95% CI: 1.24–1.87). Exposure to $PM_{2.5}$ (per 10 μg/m^3 increase) enhanced the risk of pre-eclampsia (OR = 1.31, 95% CI: 1.07–1.61), but there was no evidence relating exposure to $PM_{2.5}$ to gestational hypertension (OR = 1.35, 95% CI: 0.98–1.87).
Conclusion: There is a significant link between exposure to $PM_{2.5}$ and hypertensive disorders in pregnancy. The first and the third trimester were more susceptible to $PM_{2.5}$ exposure. It is recommended to further strengthen protective measures against $PM_{2.5}$ during pregnancy.

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1. Introduction

Hypertensive disorders in pregnancy (HDP) have been classified into two categories by The International Society for the Study of Hypertension in Pregnancy (ISSHP). Pre-pregnancy diagnosis, or newly discovered hypertension before 20 weeks of pregnancy, includes chronic hypertension, white coat hypertension and occult hypertension; and hypertension after 20 weeks of pregnancy includes transient pregnancy hypertension, pregnancy hypertension and pre-eclampsia. Together, HDPs account for up to 10% of all complications during pregnancy (Chan et al., 2018). The most familiar forms are gestational hypertension and pre-eclampsia. HDP is highly related to increased neonatal and maternal morbidity and mortality (Conti-Ramsden et al., 2019). It can also lead to maternal edema, hypoproteinemia, and liver and kidney dysfunction during pregnancy, which can cause convulsions, coma and even death. The probability of placental abruption and postpartum hemorrhage in parturients also increases as a result of decreased placental blood flow and impaired function (Parker et al., 2015). In addition, having HDP increases the likelihood of developing cardiovascular disease and type 2 diabetes in later life (Bauer and Cleary, 2009; Mito et al., 2018). HDP also puts infants at higher risk. By affecting the growth and development of the intrauterine fetus, HDP can lead to premature birth, low birth weight, neonatal asphyxia and death, etc (Backes et al., 2011). Studies have suggested that many factors may be related to the incidence of hypertensive disorders in pregnancy, such as high maternal body mass index (BMI), low educational level and poor household economic status. In recent years, exposure to air contaminants during pregnancy has also been recognized as an important hazardous factor (Pedersen et al., 2017).

With rapid global economic development, the level of air pollution caused by motor vehicles and industrial emissions has risen sharply (Prunicki et al., 2018; Seeni et al., 2018). In the atmosphere, inhalable particulate matter with aerodynamic equivalent diameter ≤ 2.5 μg is called $PM_{2.5}$ (fine particulate matter). A type of atmospheric suspended particle, $PM_{2.5}$ has become the focus of air pollution research in recent years. Its composition is complex, and the common components are mainly various organic pollutants, heavy metals, water-soluble ionic salts, bacteria, viruses, etc (Mukherjee et al., 2018). With a small volume, large specific surface area and long residence time in the air, $PM_{2.5}$ easily carries poisonous and harmful substances, and can enter the body via respiration, even infiltrating alveoli and blood. Through oxidative stress, inflammatory reactions and other mechanisms, $PM_{2.5}$ causes damage to multiple organ systems and can greatly promote the occurrence of genetic variations such as teratogenicity, carcinogenicity and mutagenicity (Cakmak et al., 2018; Schwindt et al., 2018; Yang et al., 2018; Zhao et al., 2013).

Many studies indicate that people who have been exposed to air pollution are more likely to suffer from hypertension (Hassanvand et al., 2018; Honda et al., 2018). Air pollution mainly affects high blood pressure via the following three mechanisms (Van den Eeden et al., 2018): (1) contaminants interact with the sympathetic nervous system, and then increase blood pressure by transmitting signals to regulate blood volume and vascular tension; (2) contaminants generate markers of circulating oxidative stress, and affect blood pressure by changing endothelial cells and hemodynamic functions; (3) pollutants cause vasoconstriction dysfunction, which directly affects blood pressure. Pregnancy consists of a period when women are especially vulnerable to hazards and sensitive to toxic pollutants in the air (Shih et al., 2017), so contaminant exposure during this time may play a crucial role in the development of HDP (Madsen et al., 2018; Xie et al., 2018).

There is still a lack of systematic reviews exploring the correlation between $PM_{2.5}$ and HDP. We conducted a meta-analysis to evaluate the relationship of $PM_{2.5}$ exposure during pregnancy to HDP.

2. Materials and methods

2.1. Search methods

Articles were identified through four electronic bibliographic databases: PubMed, Cochrane Library, Web of Science and Embase, up until March 28, 2019. We used terms such as maternal, pregnancy or pregnant women to enhance the veracity. The following search terms were used to retrieve relevant articles:

#1: (maternal) or (pregnancy) or (pregnant women)
#2: (air pollution) or (traffic pollution) or (fine particulate matter) or ($PM_{2.5}$) or (particulate matter) or (outdoor pollution) or (indoor pollution)
#3: (eclampsia) or (cardiovascular) or (pre-eclampsia) or (hypertension) or (blood pressure)
#4: #1 AND #2 AND #3

In addition, we manually traced back all references to avoid omission. We were thus able to comprehensively identify relevant information. We followed published quality standards for conducting and reporting *meta*-analyses (Stroup et al., 2000).

2.2. Inclusion criteria

We selected studies that:

(1) Included the full text of the literature;
(2) Were designed to be epidemiological studies based on observation, including descriptive study, cohort study and case-control study;
(3) Had pregnant women as subjects;
(4) Had $PM_{2.5}$ as the air pollutant exposure factor;
(5) Explicitly specified at least one hypertensive disorder as an outcome of the investigation;
(6) Were most recent or had the largest sample size, if multiple studies used the same population
(7) Provided data, such as OR (odds ratio) and 95% CI (95% confidence interval) or relevant statistical data that could be converted, on the correlation between $PM_{2.5}$ and outcome variables.

We excluded studies that:

(1) Did not conform to the research topic;
(2) Had defects in research design and poor literature quality;
(3) Did not subdivide types of air pollution, or include relevant data on $PM_{2.5}$;
(4) Were reviews, systematic reviews meta-analyses, lecture literature, conference reports, animal studies, etc;
(5) Did not have extractable statistical data.

2.3. Study selection and data extraction

Based on the inclusion and exclusion criteria, we initially reviewed the title and abstract of all identified publications in order to screen for eligibility. Then, by reviewing the full paper, we evaluated the remaining references. Studies were exported in Endnote, and duplicates were automatically removed. A predefined

template was used to extract the following information: author name, publication time, study design, location, sample size, outcome, exposure distribution, effect size and covariate adjustment (Bai et al., 2018). When necessary information was missing from the main manuscripts, supplementary materials and associated publications were considered.

2.4. Quality assessment

We independently evaluated the quality of each study by referring to the Newcastle Ottawa Scale (NOS) standard (Margulis et al., 2014). The four items in this standard include the selection of subjects, exposure assessment methods, outcomes and comparability. Each item received at most one score, and the score of seven was considered as high quality literature.

2.5. Statistical methods

Software Stata 13.0 was used for data processing. Relevant information was abstracted from the selected studies to establish a database, and the meta-analysis module was used for statistical analysis. The adjusted OR value in pregnancy outcome was taken as the effect value. There were two types of independent variables, including continuous exposure (the interquartile range of $PM_{2.5}$ concentration rise) and classified exposure (the lowest quartile).

Specific steps: (1) standardization : normalized the correlation effect values that extracted from the study, considered 10 μg/m^3as the increase unit. (2) heterogeneity test: If $p < 0.05$, it indicates that there is a greater heterogeneity among these articles, and the random-effect model was chosen to calculate the combined effect value (Doi et al., 2015). Otherwise, fixed-effect model is selected (Mantel and Haenszel, 1959). Forest map shows OR values of each study and summary. (3) Subgroup analysis: glance over the characteristics of the original studies and analyze hierarchically according to the possible confounding factors in the research process, the OR values and 95% CI of each subgroup are calculated respectively. (4) Test and correction of publication bias: Begg's funnel chart and Egger's method were adopted to carry out qualitative and quantitative examination and evaluation of publication bias on literature data. If necessary, recombine the effect values and analyze the reasons for the large publication bias of test results. The funnel plot should be similar to a symmetrical inverted funnel, and the studies are evenly distributed around the central axis. The Egger's method is used to assess whether there is an asymmetry related to the standard error in the findings. (5) Sensitivity analysis: potential unstable factors in the meta-analysis are analyzed to appraise the impact of publication bias on the overall results.

3. Results

3.1. Study search and characteristics overview

As a result, a total of 1149 studies were initially included, with 616 studies remaining after eliminating duplicates. After reading titles and abstracts, we excluded 486 studies that had irrelevant exposures or outcomes. In addition, 39 studies were excluded for being non-epidemiological studies. We reviewed the full papers of the remaining 91 studies. Six studies were lecture or conference reports, and were further excluded; 74 studies were not considered because they did not obtain OR values and 95% CIs, or other related factors. There were two studies conducted at different times with the same population, so only one of them was selected for inclusion. The final ten articles were included in our study (Choe et al., 2018; Dadvand et al., 2013; Dadvand et al., 2014; Lee et al., 2013; Mobasher et al., 2013; Rudra et al., 2011; Savitz et al., 2015; Vinikoor-Imler et al., 2012; Wu et al., 2009; Xu et al., 2014) (Fig. 1).

The characteristics of these studies are displayed in Table 1. With the exception of one case-control study, all were retrospective cohort studies. The sample sizes ranged from 305 to 348,585, comprising a total sample size of 788,768. In terms of research area, most of the studies were conducted in the United States and two studies were in Spain. For exposure assessment, Mobasher (Mobasher et al., 2013) allocated exposure based on data from the center's site monitoring; Dadvand (Dadvand et al., 2013) and Savitz (Savitz et al., 2015) used the land use regression model (LUR), which took into account the situation of air monitors and factors such as traffic conditions, population density and geographical characteristics. Rudra (Rudra et al., 2011) used exposure models to assess exposure. The OR and 95% CI of each study were the correction values after adjusting for the mother's age, weight, BMI, smoking, education level, fetal birth time and other factors. Of the ten studies, which received scores ranging from 5 to 8, six studies (60%) were high-quality documents and had scores ≥ 7 based on the NOS standard.

By systematically evaluating the included articles, we found that most of the results suggested an association between exposure to $PM_{2.5}$ and HDP. Wu (Wu et al., 2009) and Dadvand (Dadvand et al., 2013) indicated that effective exposure was com-

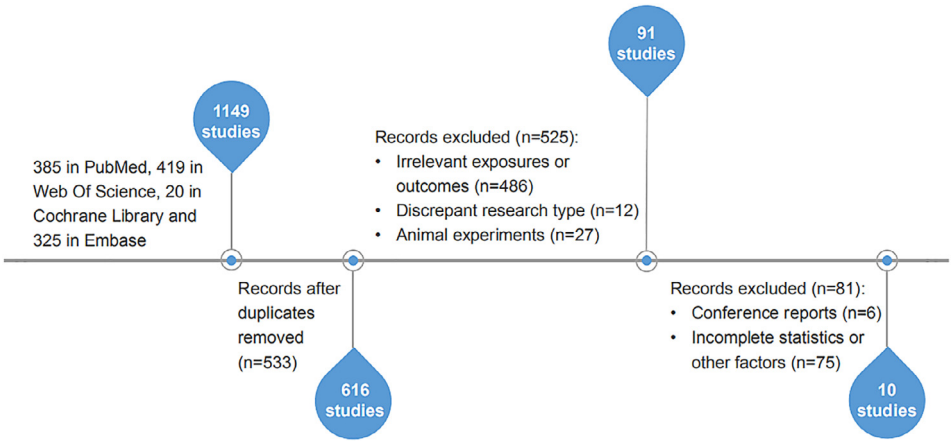

Fig. 1. The flow chart of literature retrieval.

Table 1
Main characteristics of studies included in the meta-analysis.

City,country	Reference (year, author)	Study design	Maternal age	Participants	Exposure assessment method	Pregnancy phase	Outcome	Adjustment variables	Quality assessment score
California, USA	Wu et al. (2009)	Cohort	30.0 ± 6.2	81,186	Dispersion model	Gestational period	Pre-eclampsia	Maternal age, maternal race/ethnicity, parity, prenatal care insurance type, poverty, diabetes and season of conception	7
Washington, USA	Rudra et al. (2011)	Cohort	≤20 21–34 35–39 ≥40	3509	Dispersion model	Gestational period	Pre-eclampsia	Age, race/ethnicity, BMI, smoking history and season of conception	7
North Carolina, USA	Vinikoor-Imler LC et al. (2012)	Cohort	< 15 15–44 ≥45	222,775	Personal monitor	Gestational period	Gestational hypertension	Maternal age, maternal education, previous birth ,race, marital status and smoking history	6
Barcelona, Spain	Dadvand et al. (2013)	Cohort	< 35 ≥35	8398	LUR	Gestational period	Pre-eclampsia	Neighborhood socioeconomic status, ethnic origin, education level, marital status, age, smoking, alcohol consumption, BMI, diabetes, parity, multiple pregnancy, season of conception and year of conception	8
Pittsburgh, USA	Lee et al.(2013)	Cohort	29.1 ± 6.1	34,705	Personal monitor	First trimester	Pre-eclampsia and gestational hypertension	Maternal age, race, parity, number of cigarettes smoked during pregnancy, season of birth, and year of conception	7
California, USA	Mobasher et al. (2013)	case-control	cases: 27.7 ± 7.4 controls: 27.0 ± 7.0	cases:136 controls: 169	Personal monitor	Three trimesters	HDP	Maternal age, parity, maternal smoking history, exposure to second hand smoke during pregnancy and year of conception	6
Florida, USA	Xu et al. (2014)	Cohort	<20 20–24 25–29 30–34 35–39 ≥40	24,483	Personal monitor	Gestational period	HDP	Maternal age, race, education, marital status, smoking during pregnancy, season of conception, year of conception, prenatal care began and tract median household income	8
Barcelona, Spain	Dadvand et al. (2014)	Cohort	<35 ≥35	3182	Personal monitor	Duration of pregnancy	Pre-eclampsia	Ethnic origin, education level, age, smoking, alcohol consumption, BMI, diabetes, parity, multiple pregnancy, season of conception and year of conception	8
New York, USA	Savitz et al. (2015)	Cohort	<20 20–24 25–29 30–34 35–39 ≥40	348,585	LUR	First and second trimester	Pre-eclampsia, gestational hypertension and HDP	Maternal age, maternal ethnicity, maternal education, medicaid status, parity, conception year, deprivation index and BMI	8
Rhode Island, USA	Choe et al. (2018)	Cohort	29.0 ± 5.9	61,640	Spatio-temporal model	Three trimesters	Pre-eclampsia and gestational hypertension	Maternal age, tobacco use, parity, education, race, insurance, marital status, NSES z-score, year of last menstrual period, and conditional on town of residence	6

pactly related to pre-eclampsia; However, Vinikour (Vinikoor-Imler et al., 2012) and Savitz (Savitz et al., 2015) found that $PM_{2.5}$ would increase the risk of gestational hypertension as well. It is worth noting that some studies not only paid attention to the whole pregnancy, but also divided the pregnancy into three trimesters to explore whether there were differences in the impact of $PM_{2.5}$ during different periods. We found that all of these studies excluded chronic hypertension during pregnancy, so we used the restrictive definition of HDP that only involves gestational hypertension (GH) and pre-eclampsia. Due to the controversy about whether GH and pre-eclampsia are degrees of the same disease or different diseases, we did three meta-analyses: (1) the correlation between $PM_{2.5}$ exposure and pre-eclampsia; (2) the correlation between $PM_{2.5}$ exposure and GH; (3) and the correlation between $PM_{2.5}$ exposure and HDP (including pre-eclampsia and GH). Subsequently, subgroup analysis was further conducted. To detect sources of heterogeneity, the sources were stratified by their characteristics and confounding factors.

3.2. Relationship between $PM_{2.5}$ exposure and related diseases

A total of 10 articles were combined to analyze the effects between $PM_{2.5}$ exposure and HDP. The results were as follows: $I^2 = [(Q\text{-}df)/Q] * 100\% = 90.9\%$ (Degrees of freedom, df), $p < 0.001$. The forest plot (Fig. 2) showed that there was little overlap in the confidence intervals of these studies, indicating a large amount of heterogeneity among these studies. As a result, the random-effect model was adopted, the increase ($10\ \mu g/m^3$) in $PM_{2.5}$ was associated with a change in HDP, yielding an OR of 1.52 (95% CI: 1.24–1.87), $p < 0.05$, which illustrated an association between $PM_{2.5}$ and HDP.

Among the ten included articles, seven involved the effect of $PM_{2.5}$ exposure on pre-eclampsia, and the results indicated heterogeneity ($I^2 = 83.8\%$, $p < 0.001$). The random-effect model was used, with $10\ \mu g/m^3$ increase in concentration, the risk of pre-eclampsia changed, OR = 1.31 (95% CI: 1.07–1.61), $p < 0.05$, indicating that exposure to $PM_{2.5}$ was correlated with pre-eclampsia. The meta-analysis forest plot is shown in Fig. 3.

Four of the included articles referred to the relationship between $PM_{2.5}$ and gestational hypertension. Statistical analysis showed that $I^2 = 97.6\%$, $p < 0.001$, using a random-effect model, and the combined OR = 1.35 (95% CI: 0.98–1.87), $p > 0.05$, which was not statistically significant. The meta-analysis forest plot is shown in Fig. 4.

3.3. Subgroup analysis

According to whether the original study excluded women with a history of hypertension, genetically related diseases, chronic metabolic diseases and kidney diseases, the 10 included studies were divided into two groups. The results (Fig. 5) showed that after excluding women with these related diseases, exposure to $PM_{2.5}$ (per $10\ \mu g/m^3$higher) reduced the risk of HDP (OR = 1.41, 95% CI: 1.13–1.75). Pregnant women were also distributed into three groups according to their stages of pregnancy. The results (Fig. 6) showed that exposure to $PM_{2.5}$ (per $10\ \mu g/m^3$higher) was strongly connected to HDP especially in the first (OR = 1.26, 95% CI: 1.03–1.52) and third (OR = 2.69, 95% CI: 1.07–6.72) trimesters. According to whether the sample size was>10,000, studies were divided into two groups. The results (Fig. S1) showed that exposure to $PM_{2.5}$ was strongly correlated to HDP when the sample size was small (OR = 2.08, 95% CI: 1.45–2.98).

3.4. Sensitivity analyses

In this meta-analysis, we used a one-by-one elimination method for sensitivity analysis. Random-effect model was selected due to the obvious heterogeneity among these studies. The results showed that the pooled OR value and 95% CI before and after excluding a certain study were not significantly changed, suggesting that the original meta-analysis was reliable (Fig. S2).

3.5. Publication bias

This study adopted Begg's funnel plot and Egger's linear regression method to check publication bias. Quantitative analysis showed the results of Begg test ($p = 0.592$), and funnel plots did not exhibit a notable asymmetry (Fig. 7). At the same time, Egger test had no statistical significance ($p > 0.05$), indicating that there was no virtual publication bias among the included articles (Table S1).

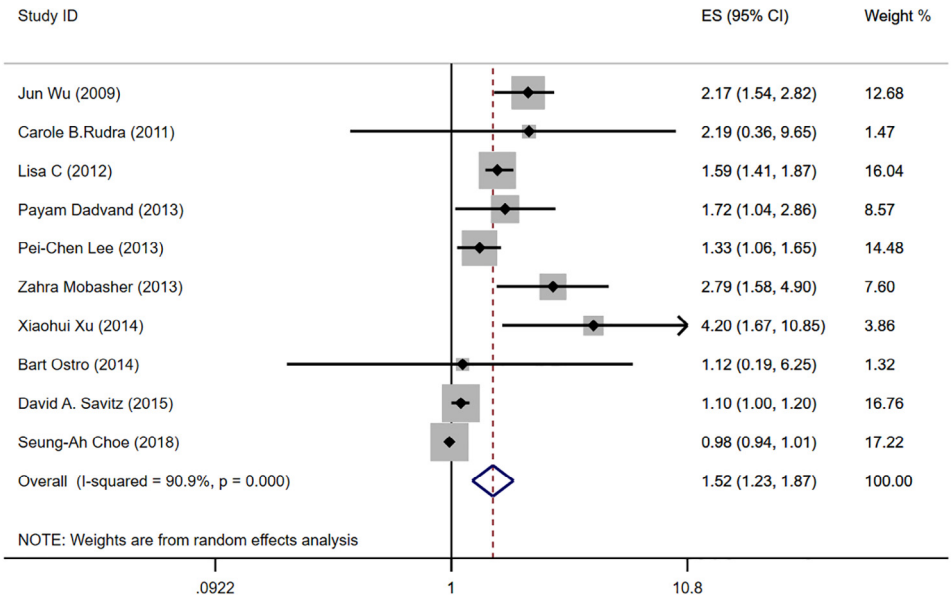

Fig. 2. Forest plot of $PM_{2.5}$ exposure (per $10\ \mu g/m^3$ increase) and hypertensive disorders in pregnancy.

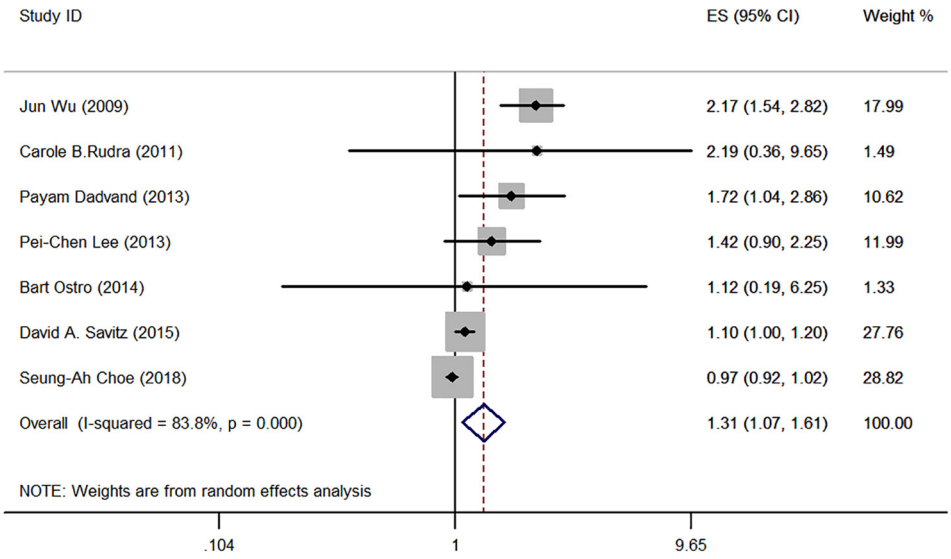

Fig. 3. Forest plot of $PM_{2.5}$ exposure (per 10 $\mu g/m^3$ increase) and pre-eclampsia.

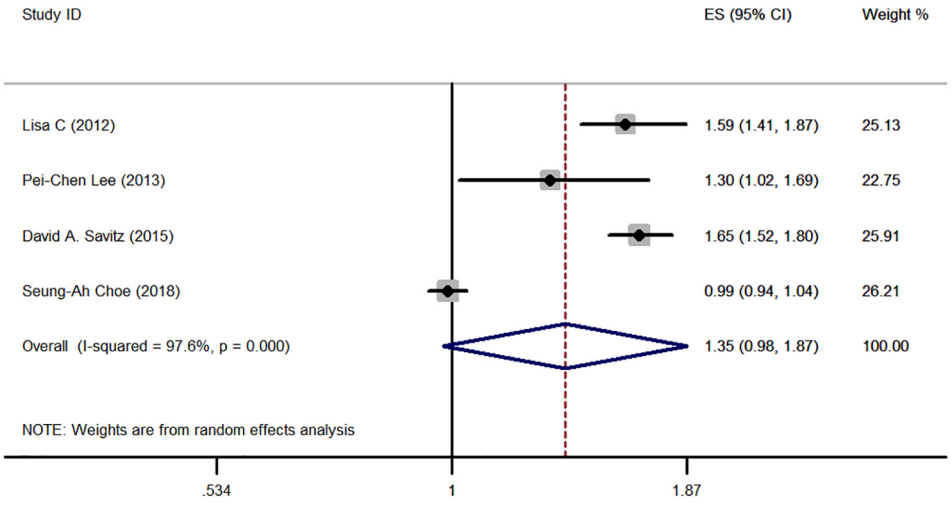

Fig. 4. Forest plot of $PM_{2.5}$ exposure (per 10 $\mu g/m^3$ increase) and gestational hypertension.

4. Discussion

With social and economic progress, atmospheric $PM_{2.5}$ has become one of the most important factors menacing human health. It is generally believed that atmospheric pollution can accelerate the progression of atherosclerosis and thus lead to hypertension (Campen et al., 2012). There are many similarities between HDP and atherosclerotic cardiovascular disease, which suggest that many mechanisms resulting in cardiovascular disease, such as oxidative stress, inflammation and endothelial dysfunction, may also lend itself to HDP (Choi et al., 2018; Lee et al., 2018). For example, the occurrence of pre-eclampsia may be due to placental abnormalities caused by endothelial dysfunction and failure of vascular remodeling (Valencia-Ortega et al., 2019). In addition, the damage to placental function indirectly caused by air pollution will lead to the production of free radicals, which makes pregnant women susceptible to HDP. $PM_{2.5}$ exposure also affects the release of cytokines (interleukin-6), which has been implicated in the pathogenesis of pre-eclampsia (Lu et al., 2018).

Our study is the first systematic review analyzing existing evidence to show a correlation between $PM_{2.5}$ and HDP. We searched four major databases and ultimately included 10 studies with different characteristics. Although the number of studies was small, the total number of observation objects reached 788,768. Most studies excluded women with genetic diseases, chronic metabolic diseases, kidney diseases, and a history of hypertension, which to some extent strengthened the relationship between factors and results. In addition, subgroup analysis can provide more accurate results than the individual studies and increase the statistical power. The final results showed a relationship between exposure to $PM_{2.5}$ (per 10 $\mu g/m^3$increase) and increased risk of pre-eclampsia, as well as a weaker connection to gestational hypertension. After excluding women with malignant diseases, chronic metabolic diseases and related medical history, OR values showed inconsistency, and the difference was statistically significant, suggesting that these diseases may be potential confounding factors. The more sensitive periods of exposure are the first and third trimesters of pregnancy. The possible reason is that mother is imperfect for the adjustment of various tissues and organs in the early pregnancy, and it is sensitive to external pollutants. With prolonged pregnancies, the compensatory increase of maternal circulating blood volume makes women in the third trimester more

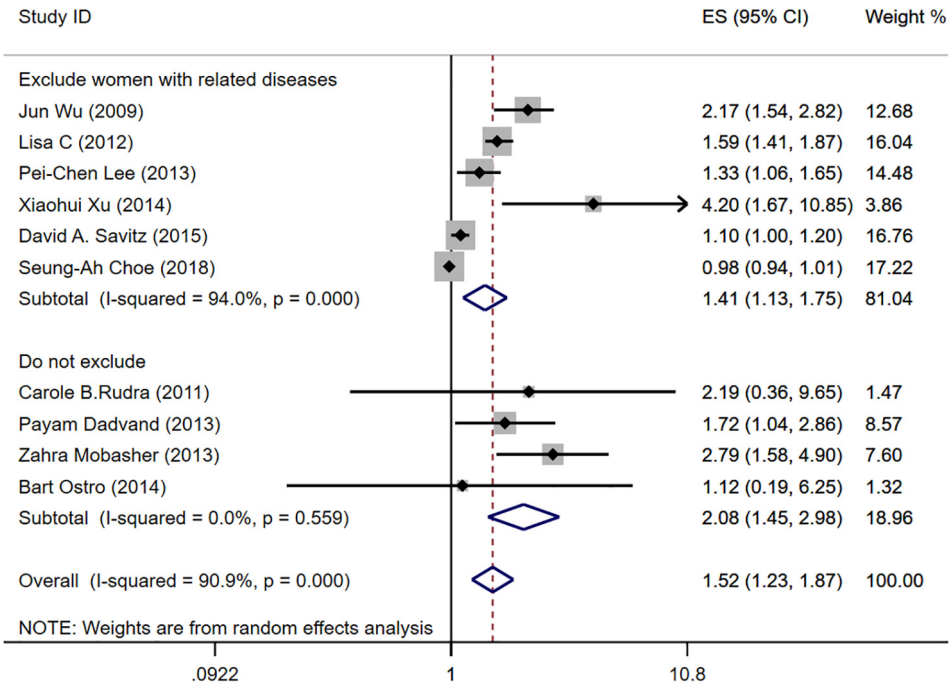

Fig. 5. Forest plot of subgroup analysis on whether study excluded women with related diseases or not.

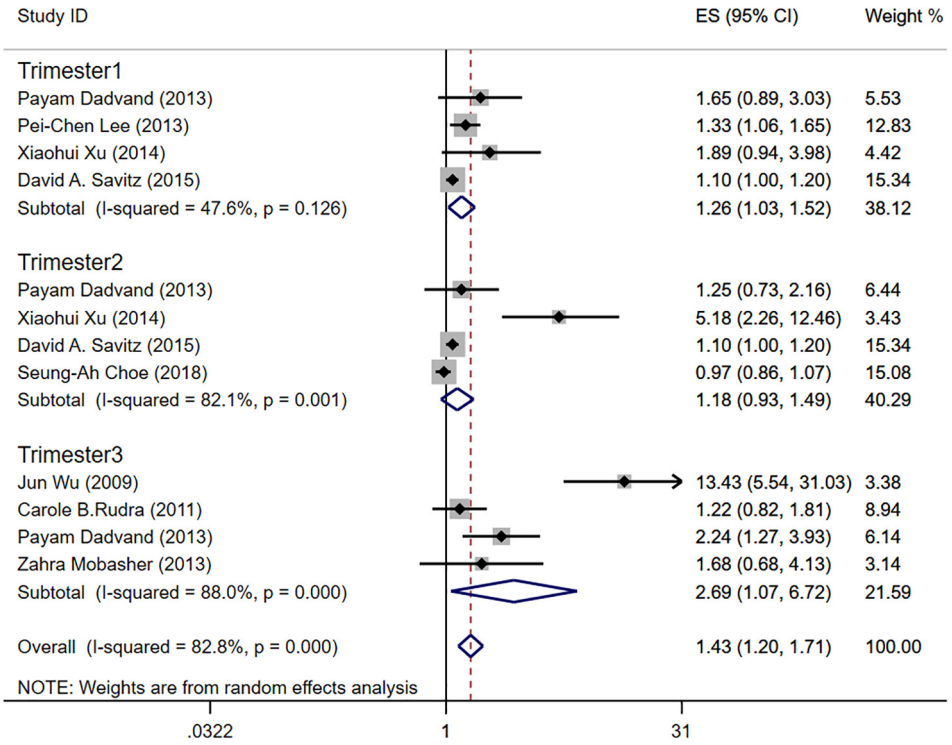

Fig. 6. Forest plot of subgroup analysis on different pregnancy stages.

vulnerable to the influence of exposures and aggravates blood pressure load. In the subgroup analysis based on sample size, both of the two group were statistically significant, studies with a smaller sample size showed a stronger correlation between $PM_{2.5}$ and HDP. From a statistical perspective, the small sample size is sensitive to extreme values, which could cause the results to deviate from the real situation. However, as the sample size increases, the sampling error decreases, and the survey results become closer to the actual situation.

The heterogeneity in this meta-analysis may be attributed to disparities in study design, exposure estimate, and definition of results. First, most articles were retrospective studies, which may have recall bias. Some studies used classified exposure as the independent variable, but we only extracted the OR value and 95% CI of

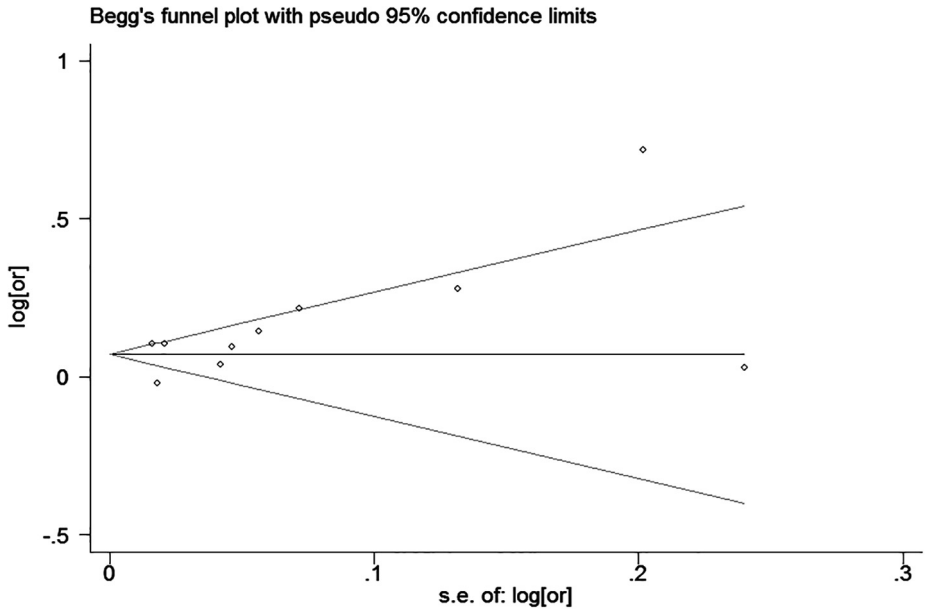

Fig. 7. Funnel plot of the effects of $PM_{2.5}$ exposure and hypertensive disorders in pregnancy.

continuous exposure in the statistical analysis. Therefore, we encourage future studies to analyze these two different independent variables as much as possible. Second, the methods and instruments for measuring $PM_{2.5}$ exposure were not the same for each study. Most studies used data from central air pollution monitoring stations, which have some limitations. As a result of small spatial coverage, the monitored data mostly reflect changes in pollutant levels over time, which will lead to selection bias. Other studies used models to evaluate air pollution. Although models provide higher spatial coverage, they still lean upon environmental particle monitors and ignore the influence of the atmosphere on the diffusion of pollutants. By contrast, using a personal monitor to measure an individual's exposure over a pre-selected window of time is both practical and economically feasible. Therefore, we suggest that future researchers use this method to more accurately assess individual exposure. Third, different studies used different outcomes. Although gestational hypertension and pre-eclampsia are both hypertensive diseases induced by pregnancy, different outcomes of individual studies may have contributed to the overall heterogeneity. Another source of heterogeneity is the difference in extent of controlling potential confounders, because these factors are unevenly distributed in various regions and populations. If they are not fully considered, insufficient adjustment will lead to deviation. Although the statistical data included in each study were adjusted for maternal age, BMI, education, race, smoking and other factors, there were differences in the adjustment factors in different studies that might lead to information bias. Some studies have ignored important covariates, such as the socio-economic status of pregnant women, which has been proved to affect the correlation between environmental pollutant exposure and HDP (Silva et al., 2008).

Our results illustrated that exposure to $PM_{2.5}$ has a strong relation to HDP. However, considering the limited number of existing studies and the inadequacy of the methodology, the results still need to be viewed with caution and objectivity. We hope that further studies continue to optimize design methods, improve the accuracy of exposure measurements by using the most biologically relevant sites and time windows, and explore further links. Since air pollution in developing countries is much more severe than that in developed countries, more cohort studies are suggested in developing countries to explore further associations.

5. Conclusions

This meta-analysis expounded that exposure to $PM_{2.5}$ was associated with hypertensive disorders in pregnancy, and the relationship with pre-eclampsia was much stronger. Subgroup analysis showed that a series of related diseases were confounding factors affecting the association between exposure and HDP. The first and third trimesters of pregnancy were more susceptible to $PM_{2.5}$ exposure. Studies with a smaller sample size showed a stronger correlation. In view of the adverse impact upon mothers and infants, we suggest that relevant departments introduce corresponding policies to strengthen the prevention and monitoring of $PM_{2.5}$, control traffic pollution and expand urban greening construction. During antenatal care, clinicians can provide some guidance for pregnant women regarding nutrition, exercise and daily living, reminding them that it is crucial to take protective measures when doing outdoor activities and to keep indoor air fresh. This study intends to reduce the occurrence of hypertensive disorders in pregnancy and protect the health of women and children.

Declaration of Competing Interest

The authors declare no competing interests.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.134985.

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