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Exposure to $PM_{2.5}$ and its constituents in relation to thyroid function of pregnant women: Separate and mixture analyses

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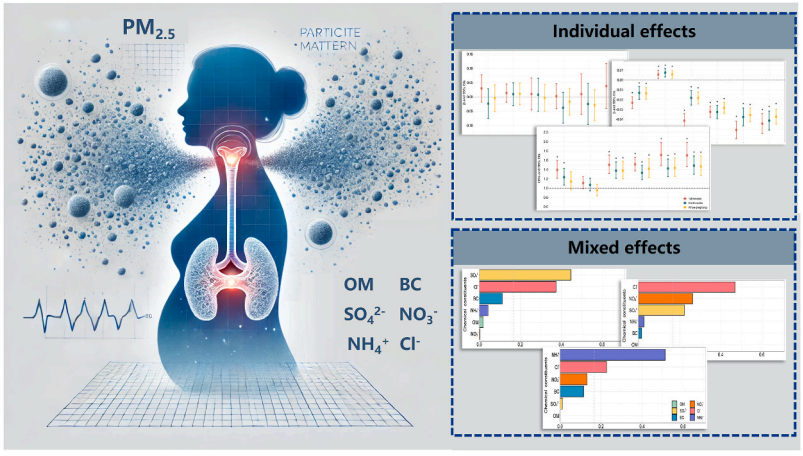
HIGHLIGHTS

- $PM_{2.5}$ and its components may individually disrupt thyroid function in pregnancy.
- $PM_{2.5}$ components have mixed effects on thyroid function of pregnant women.
- $PM_{2.5}$ and components exposure in 1st trimester of pregnancy has the greatest effect.

GRAPHICAL ABSTRACT



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ABSTRACT

The relationships between exposure to $PM_{2.5}$ and its constituents and thyroid hormone (TH) levels in pregnant women are still uncertain, particularly regarding the impact of mixed exposure to $PM_{2.5}$ constituents on thyroid function during pregnancy. This study aimed to investigate the individual and mixed effect of $PM_{2.5}$ and its

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Pregnant women
Mixture analysis

constituents on TH levels during pregnancy. Fluorescence and chemiluminescence immunoassays were utilized to measure serum concentrations of free thyroxine (FT4) and thyroid-stimulating hormone (TSH) in pregnant women participating in the Fujian Birth Cohort Study (FJBCS). $PM_{2.5}$ and its constituents were obtained from the ChinaHighAirPollutants dataset. Generalized linear regression model and mixture analysis were applied to explore the individual and mixed effect of $PM_{2.5}$ and its constituents on TH levels. 13711 participants from the FJBCS were taken into the final analysis. In the context of separate exposure, an increase of one interquartile range (IQR) in $PM_{2.5}$ exposure during the 1st trimester, 2nd trimester, and entire pregnancy was associated with a decrease of −0.042 (−0.050, −0.034), −0.017 (−0.026, −0.009), and −0.011 (−0.017, −0.004) in FT4 level, respectively. As well, significant negative associations were observed between FT4 level and $PM_{2.5}$ constituents. Additionally, $PM_{2.5}$ and its constituents were in relation to an increased risk of hypothyroxinemia in pregnant women. It is noteworthy that, in the context of mixed exposure, the weighted quantile sum regression (WQS) indices were significantly associated with both FT4 level (1st trimester: −0.031 (−0.036, −0.026); 2nd trimester: −0.026 (−0.030, −0.023); whole pregnancy: −0.024 (−0.028, −0.020)) and hypothyroxinemia risk (1st trimester: 1.552 (1.312, 1.821); 2nd trimester: 1.453 (1.194, 1.691); whole pregnancy: 1.402 (1.152, 1.713)). $PM_{2.5}$ and its chemical constituents may affect thyroid function in pregnant women individually and in combination, with the effect observed during early gestational exposure being most pronounced.

1. Introduction

Air pollution poses a significant risk to public health, ranking as one of the most pressing environmental concerns. Extensive publications have established that exposure to ambient particle with aerodynamic diameter of 2.5 μm ($PM_{2.5}$) serves as one of the primary contributors to the global burden of disease (Ghosh et al., 2021; Yin et al., 2020; Yu et al., 2023). It should be emphasized that $PM_{2.5}$ is a complex mixture composed of various chemical constituents, with major components including sulfate (SO_4^{2-}), nitrate (NO_3^-), ammonium (NH_4^+), chloride (Cl^-), black carbon (BC), and organic matter (OM) etc. (Li et al., 2017; van Donkelaar et al., 2019). The components of $PM_{2.5}$ can detach from particulate matter deposited in the lungs, traverse the epithelial layer, enter the bloodstream, and ultimately exert diverse types and varying degrees of health threatens on the human body through different pathways (Liu et al., 2023a; Yang et al., 2019). Therefore, it is imperative to extensively identify the health effect of $PM_{2.5}$ components.

It is widely recognized that thyroid hormones (TH) during pregnancy play a crucial role in embryogenesis, as well as the normal growth, development, and maturation of the fetus during pregnancy (Burrow et al., 1994; Derakhshan et al., 2020). The inadequate levels of TH in pregnant women, even if they are subclinical, are linked to impaired neurological development in children (Modesto et al., 2015). The balance of thyroid function, regulated by the hypothalamic-pituitary-thyroid axis, is highly susceptible to environmental disruptors. Animal models have revealed that exposure to $PM_{2.5}$ leads to elevated oxidative stress in rats, which in turn disrupts the biosynthesis of TH (Dong et al., 2021). Epidemiological studies from both the general population and pregnant women have revealed associations between exposure to particulate matters and alterations in TH levels, along with the occurrence of abnormal hormone states such as hypothyroxinemia (Liu et al., 2023b; Zhang et al., 2022a; Zhao et al., 2019). However, at present, only two small-sample studies have explored the impact of $PM_{2.5}$ components during the 1st trimester on thyroid function in Chinese pregnant women, with one study primarily focusing on the effect of inorganic metal ions (Wang et al., 2019; Zhou et al., 2022). Further evidence is needed to ascertain whether exposure to specificity of $PM_{2.5}$ chemical constituents during different time windows of pregnancy disrupts thyroid function. More important, humans inhabit a complex exposure environment and are exposed to intricate mixtures comprising various particle constituents. To date, no study has been designed to figure out the underlying mixed effect among $PM_{2.5}$ constituents on thyroid function during pregnancy.

Thus, based on the Fujian Birth Cohort Study (FJBCS), the first objective of this study was to investigate the associations of $PM_{2.5}$ and its chemical components exposure with thyroid function in pregnancy. We used the status of serum-free thyroxine (FT4) and thyrotropin (TSH) to reflect the thyroid function in pregnant women, as they were widely utilized indicators for assessing thyroid homeostasis in population studies (Zhao et al., 2019; Wang et al., 2019). Furthermore, we also assessed the potential mixed effect of $PM_{2.5}$ components on thyroid function during pregnancy through mixture analysis. Considering that the majority of current studies have focused only on a single gestational exposure window, it is important to recognize that women in the early to mid-stages of pregnancy are regarded as being in a heightened state of susceptibility to toxic environmental pollutants (Ghassabian et al., 2019; Howe et al., 2018; Janssen et al., 2017). Therefore, this study conducted analyses during different exposure windows in pregnancy to fill the research gap.

2. Method

2.1. Study design and population

The FJBCS has been in progress since January 2019 at the Maternal and Child Health Hospital in Fujian Province, China. Its primary objective was to examine how prenatal exposure affects both maternal health and children's development. This program invited women aged 18 years or older, who were within 14 weeks of pregnancy, had a singleton pregnancy, and underwent their initial antenatal appointment at the Fujian Provincial Maternal and Child Health Hospital to participate. The FJBCS excluded women with severe medical conditions (i.e., cerebrovascular diseases, kidney disease, intellectual disability, mental illness, and other related conditions et al.). Throughout the study period, trained nurses communicated with each participant to gather information on their sociodemographic characteristics, physical measurements, and gynecological history. The postpartum charts provided clinical information for each participant. Additional detailed information can be found within the existing papers (Zhu et al., 2023; Li et al., 2022a, 2022b). This program was approved by the Research Ethics Committee of the Fujian Provincial Maternal and Child Health Hospital (approval number: 2017 KR-030).

2.2. Exposure assessments

The daily ambient $PM_{2.5}$ and its chemical constituents data were collected from the ChinaHighAirPollutants (CHAP) dataset, which can be accessed at https://weijing-rs.github.io/product.html. The CHAP dataset utilized a combination of satellite remote sensing, ground-based measurements, atmospheric reanalysis, and model simulations to access high-resolution data (1-km spatial resolution) of ground-level $PM_{2.5}$ concentration in China. A more powerful spatiotemporal deep forest model was used to apportion the chemical constituents from total $PM_{2.5}$ (Wei et al., 2022). These constituents include SO_4^{2-}, NO_3^-, NH_4^+, Cl^-, BC, and OM. More detailed information can be found in previous literature (Wei et al., 2021, 2023). The validation of each constituent was carried

out using a 10-fold cross-validation coefficient of determination (CV-R). The analysis demonstrated excellent model performance and a strong predictive ability. The CV-R values, indicating the correlation between estimated and measured $PM_{2.5}$ constituents, were determined to be 0.86, 0.84, 0.87, 0.81, and 0.88 for SO_4^{2-}, NO_3^-, NH_4^+, Cl^-, and BC, respectively (Wei et al., 2023). In this study, we estimated the daily exposure to air pollution for each participant according to their residential address and summed these daily exposures to produce an average exposure for three exposure windows: 1st trimester, 2nd trimester, and entire pregnancy (Ma et al., 2024; Zhu et al., 2024). The trimesters of pregnant women were determined by their last menstrual period.

2.3. Thyroid function assessment

Peripheral venous blood of pregnant women was collected during the follow-up and centrifuged at 3500 rpm for 15 min to obtain serum. Serum concentrations of TH (FT4, TSH, and thyroid peroxidase antibody (TPOAb)) were quantified using chemiluminescence immunoassays using ADVIA CentaurXP instruments and kits (Siemens, Munich, Germany) to assess thyroid homeostasis. The laboratory reference ranges of FT4, TSH, and TPOAb for the pregnant women were 0.89–1.76 ng/dL, 0.550–4.780 mIU/L, and 0.00–60.00 IU/mL, respectively. Pregnant women were categorized as TPOAb negative (≤60 IU/mL) or positive (>60 IU/mL). The diagnostic standards for hypothyroxinemia in pregnancy were FT4 below the reference level (<0.89 ng/dL) with normal TSH levels.

2.4. Covariates ascertainment

We incorporated a series of covariates into our study: age (years), employment (current employment or non-current employment), education (university level or non-university level), alcohol consumption status (never drinking, former drinking, or current drinking), smoking status (never smoking, former smoking, or current smoking), passive smoking (yes or no, a proxy of indoor air pollution (Cheng et al., 2022; Siegel et al., 2023)), folic acid intake during pregnancy (yes or no), BMI (underweight (<18.5 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (24–28 kg/m^2), or obese (≥28 kg/m^2)), living areas (urban, town, or rural; living areas of participants were defined according to the urban/rural division codes that issued by the Chinese Bureau of Statistics, https://www.stats.gov.cn/sj/tjbz/qhdm/), gestational age (weeks), season of conception (spring, summer, fall, and winter), maternal TPOAb status (positive or negative), and ambient temperature (°C). Temperature data for Fujian, China over the study period were derived from the China Meteorological Data Sharing Service System (http://data.cma.gov.cn/). We calculated the temperature corresponding to the exposure windows.

2.5. Analytical cohort

Of 17047 participants enrolled in the FJBCS from the beginning of 2019 until 2021, we excluded participants with following conditions: (1) Participants with missing residential address (n = 683); (2) Participants with missing air pollutants exposure (n = 76); (3) Participants with missing outcome (n = 2577). After the exclusion process, a total of 13711 participants were incorporated in the final analyses.

2.6. Statistical analysis

For the included participants, continuous variables were expressed as means (± standard deviation) and categorical variables as frequencies (percentages). Covariates with missing data (<5%) were handled as a separate category. Levels of FT4 and TSH were transformed using the natural logarithm function to approximate a normal distribution.

Multivariate linear regression model was fitted to explore the relationships between FT4 and TSH levels and the $PM_{2.5}$ and its components (in continuous format or categorized by tertiles) during different exposure windows. As well, multivariate logistic regression model was built to examine the associations between the risk of hypothyroxinemia and exposures of interest across different exposure windows. The weighted quantile regression (WQS) model was performed to evaluate the mixed effect of components of $PM_{2.5}$ on the outcomes of interest by constructing weighted combinatorial quantiles and accounting for covariates in the analysis (Ma et al., 2022; Keil et al., 2020). Depending on the characteristics of the outcomes, both linear and logit links were utilized in the process of model fitting. The analyzing dataset was randomly divided into a training set, which comprised 40% of the samples, while the remaining 60% were allocated to a validation set. Mixture variables in the WQS model were ranked in quartiles (q = 4). To maximize the likelihood function of the model, the training set underwent 1000 bootstrap iterations. The WQS cutoff value (1/number of exposures) was used to determine which exposure require more attention in the context of mixture exposure (Carrico et al., 2015). Models incorporated several potential confounders: maternal age, employment, education, alcohol consumption status, smoking status, passive smoking, folic acid intake during pregnancy, BMI, living areas, season of conception, gestational age, maternal TPOAb status, and ambient temperature. Results were presented as β or odds ratios (ORs) accompanied by their respective 95% confidence intervals (CIs).

To examine the possible influence of autoimmune damage, we stratified the study population based on TPOAb status and evaluated the relationships between $PM_{2.5}$ exposure and thyroid function separately in women who tested positive and negative for TPOAb. For the effect modification of TPOAb status, we calculated the *P* for interaction by including an interaction term in the model.

We conducted multiple sensitivity tests to assess the robustness of the results: (1) A constituent-$PM_{2.5}$ joint model was built to control the confounding effect of the total $PM_{2.5}$ mass; (2) A single-constituent residual model was fitted to control the potential collinearity between $PM_{2.5}$ and each constituent; (3) To mitigate the confounding effect of other constituents, we replaced the constituent with its residual. This was achieved by establishing a simple linear regression between $PM_{2.5}$ and the component, and utilizing the residuals in the model (Shen et al., 2022; Yu et al., 2020); (4) We further adjusted pre-existing hypertension and diabetes in the model; (5) We further incorporated pregnancy complications, such as gestational diabetes and gestational hypertension (defined as women over 20 weeks of gestational age with a systolic blood pressure of 140 mm Hg or higher, or a diastolic blood pressure of 90 mm Hg or higher), into the model. (6) We estimated the inhalation concentrations of $PM_{2.5}$ and its chemical components based on a prior study and re-conducted the analysis (Xue et al., 2016). All statistical analyses were carried out using the R programming language (version: 4.2.2).

3. Results

This study comprised 13711 pregnant women from the FJBCS (Table 1). The average age of participants was 30.38 (±3.99) years, with 78.76% holding a university degree and 72.37% currently employed. Moreover, approximately 85.47% of women reported no alcohol consumption, while 97.64% and 59.60% reported no smoking or passive smoking. More than half of pregnant women (62.06%) had regular intake of folic acid. Thyroid function screening was conducted for all participants during the follow-up period. The average (SD) levels of TSH and FT4 were 0.98 (0.74) mIU/L and 1.19 (0.21) ng/dL, individually. Based on the laboratory's reference range and diagnostic criteria, 1791 (13.06%) participants were found to have tested positive for TPOAb, while 562 (4.10%) participants were identified to have hypothyroxinemia.

Table S1 provides a summary of the distribution of $PM_{2.5}$ and its components in the different time windows during pregnancy. The mean (standard deviation) $PM_{2.5}$ exposure for the 1st, 2nd trimester, and the

Table 1
Characteristics of the included participants.

Characteristics	Total participants (n = 13711)
Maternal age (years)	30.38 (3.99)
Educational levels (%)	
Non-university level	2893 (21.10)
University level	10799 (78.76)
Missing	19 (0.14)
Employment status (%)	
Current employment	9922 (72.37)
Non-current employment	3770 (27.50)
Missing	19 (0.14)
Alcohol status (%)	
Never drinking	11719 (85.47)
Former drinking	1451 (10.58)
Current drinking	514 (3.75)
Missing	27 (0.20)
Smoking status (%)	
Never smoking	13388 (97.64)
Former smoking	292 (2.13)
Current smoking	14 (0.10)
Missing	17 (0.12)
Maternal folic acid status (%)	
No	5172 (37.72)
Yes	8509 (62.06)
Missing	30 (0.22)
Season of conception (%)	
Spring	4571 (33.34)
Summer	2829 (20.63)
Fall	2292 (16.72)
Winter	4019 (29.31)
Passive smoking (%)	
No	8175 (59.60)
Yes	5536 (40.40)
Living area (%)	
Urban	8450 (61.63)
Town	2535 (18.49)
Rural	2726 (19.88)
BMI (%)	
Underweight (<18.5 kg/m^2)	2696 (19.66)
Normal weight (18.5–24 kg/m^2)	8256 (60.21)
Overweight (24–28 kg/m^2)	2548 (18.58)
Obese (≥28 kg/m^2)	87 (0.63)
Missing	124 (0.90)
Gestational age (weeks)	39.18 (1.44)
Ambient temperature (°C)	21.16 (0.71)
Thyroid-stimulating hormone (uIU/mL)	0.98 (0.74)
Free thyroxine (ng/dL)	1.19 (0.21)
Maternal TPOAb status (%)	
Positive	1791 (13.06)
Negative	11920 (86.94)
Prevalence of hypothyroxinemia (%)	562 (4.10)

whole pregnancy were 22.051 (4.458) μg/m^3, 20.533 (4.880) μg/m^3, and 21.074 (1.941) μg/m^3, respectively. The Pairwise correlations between $PM_{2.5}$ and its constituents are presented in Fig. S1.

Table 2 displays an overview of the relationships between maternal $PM_{2.5}$ exposure and the thyroid function of pregnant women. An IQR increase in $PM_{2.5}$ exposure in the 1st, 2nd trimester, and the whole pregnancy was associated with a −0.042 (−0.050, −0.034), −0.017 (−0.026, −0.009), and −0.011 (−0.017, −0.004) change in FT4 level, respectively. Similarly, when $PM_{2.5}$ categories were defined by tertiles, we found that $PM_{2.5}$ exposure, both in intermediate and high levels, was linked to a decreased FT4 level in the 1st trimester, with a trend showing statistical significance ($P < 0.05$). Notably, we also found that $PM_{2.5}$ exposure (per IQR increase) increased the risk of hypothyroidism in pregnant women by 45.3% (24.9%, 69.3%), 48.0% (28.8%, 70.1%), and 40.9% (21.6%, 63.4%), respectively, in the different exposure windows. The results regarding the relationship between high level of $PM_{2.5}$ exposure and the risk of hypothyroidism in pregnancy remained significant, with P for trend <0.05. However, we failed to observe a statistically significant association between $PM_{2.5}$ exposure and TSH concentration. Associations between chemical constituents of $PM_{2.5}$ and thyroid functions of pregnant women during different exposure windows are shown in Fig. 1. The majority of $PM_{2.5}$ constituents (SO_4^{2-}, NO_3^-, NH_4^+, Cl^-, and BC) exhibited negative associations with FT4 levels. Likewise, exposure to SO_4^{2-}, NO_3^-, NH_4^+, Cl^-, and BC was found to elevate the risk of hypothyroidism, with the highest ORs observed in the 1st trimester. Similar results were discovered when categorizing $PM_{2.5}$ constituents into tertiles (Tables S2–S7). In the stratified analyses (Table S8), the adverse effect of $PM_{2.5}$ exposure on the risk of hypothyroxinemia during pregnancy appeared to be stronger in TPOAb positive women across different exposure windows. However, a significant interaction between $PM_{2.5}$ exposure and TPOAb status was only observed in the 1st trimester (P for interaction = 0.018).

Table 3 presents the results of WQS model adjusting for various covariates. There was a negative relationship between the WQS indices and FT4 level (1st trimester: −0.031 (−0.036, −0.026); 2nd trimester: −0.026 (−0.030, −0.023); whole pregnancy: −0.024 (−0.028, −0.020)). Additionally, a positive relationship between the WQS indices and hypothyroidism was also discovered. The respective effect estimates were 1.552 (1.312, 1.821) in the 1st trimester, 1.453 (1.194, 1.691) in the 2nd trimester, and 1.402 (1.152, 1.713) during the whole pregnancy. For the mixed effect of components of $PM_{2.5}$ on the thyroid function of pregnant women, the weights of the various chemical constituents in the WQS indices are displayed in Figs. S2–S4. Furthermore, the mixed effect of $PM_{2.5}$ chemical constituents on the FT4 level (SO_4^{2-}, NO_3^-, NH_4^+, and Cl^-) and hypothyroidism risk (OM, NO_3^-, Cl^-, and BC)

Table 2
Associations between $PM_{2.5}$ and thyroid functions of pregnant women during different exposure windows.

$PM_{2.5}$	TSH during pregnancy		FT4 during pregnancy		Hypothyroxinemia during pregnancy	
	β and 95% CIs	*P* for trend	β and 95% CIs	*P* for trend	ORs and 95% CIs	*P* for trend
1st trimester						
Low tertile	0 (Ref.)	0.410	0 (Ref.)	**<0.001**	1 (Ref.)	**<0.001**
Intermediate tertile	−0.000 (−0.071, 0.070)		**−0.024 (-0.033, -0.015)**		0.998 (0.798, 1.248)	
High tertile	0.036 (−0.050, 0.121)		**−0.047 (-0.057, -0.036)**		**1.475 (1.200, 1.816)**	
$PM_{2.5}$, per IQR increase	0.031 (−0.033, 0.094)	–	**−0.042 (-0.050, -0.034)**	–	**1.453 (1.249, 1.693)**	–
2nd trimester						
Low tertile	0 (Ref.)	0.936	0 (Ref.)	**<0.001**	1 (Ref.)	**<0.001**
Intermediate tertile	**0.074 (0.014, 0.134)**		−0.002 (−0.010, 0.005)		**1.499 (1.190, 1.892)**	
High tertile	0.015 (−0.073, 0.104)		**−0.033 (-0.044, -0.022)**		**1.969 (1.584, 2.457)**	
$PM_{2.5}$, per IQR increase	−0.013 (−0.082, 0.055)	–	**−0.017 (-0.026, -0.009)**	–	**1.480 (1.288, 1.701)**	–
Whole pregnancy						
Low tertile	0 (Ref.)	0.637	0 (Ref.)	**0.002**	1 (Ref.)	**<0.001**
Intermediate tertile	0.032 (−0.029, 0.093)		−0.006 (−0.013, 0.002)		**1.494 (1.196, 1.870)**	
High tertile	−0.020 (−0.091, 0.051)		**−0.014 (-0.023, -0.005)**		**1.679 (1.351, 2.094)**	
$PM_{2.5}$, per IQR increase	−0.004 (−0.054, 0.047)	–	**−0.011 (-0.017, -0.004)**	–	**1.409 (1.216, 1.634)**	–

Models adjusted for age, educational level, employment status, alcohol status, smoking status, passive smoking, maternal folic acid status, living areas, BMI, gestational age, maternal TPOAb status, season of conception, and ambient temperature.

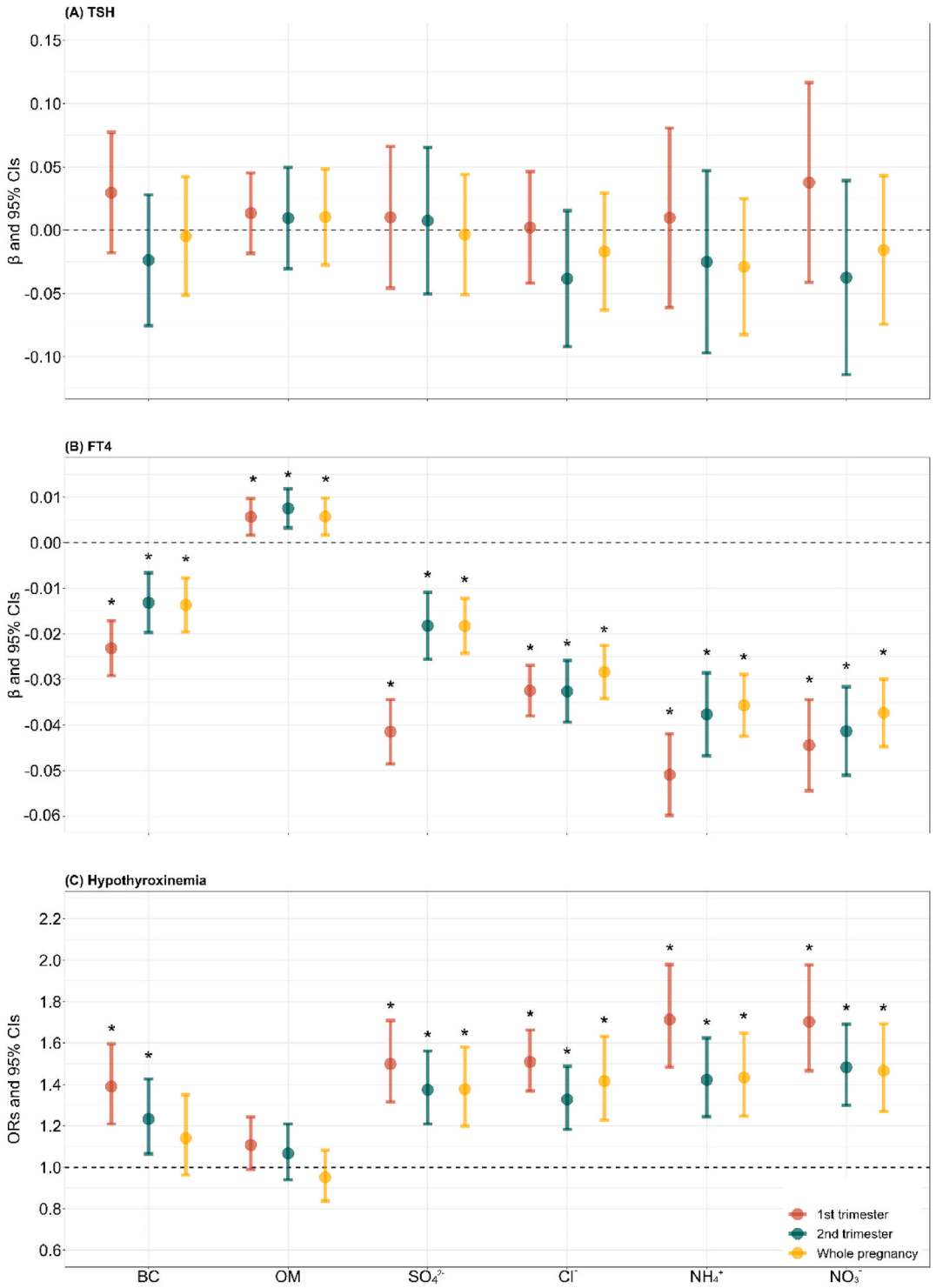

Fig. 1. Associations between chemical constituents of $PM_{2.5}$ (per IQR increase) and thyroid functions of pregnant women during different exposure windows. Models adjusted for age, educational level, employment status, alcohol status, smoking status, passive smoking, maternal folic acid status, living areas, BMI, gestational age, maternal TPOAb status, season of conception, and ambient temperature.

should not be overlooked as their weights, during a certain exposure window in pregnancy, exceeded the calculated cutoff value.

After conducting a series of sensitivity tests, including fitting the constituent-$PM_{2.5}$ joint model (Table S9), the single-constituent residual model (Table S10), and the residual model (Table S11), adjusting for pre-existing hypertension and diabetes (Table S12) or pregnancy complications (Table S13) in the primary model, and estimating the inhalation concentrations of $PM_{2.5}$ and its chemical components (Table S14), we observed that the associations between $PM_{2.5}$ and its constituents and thyroid function among pregnant women remained largely unchanged.

4. Discussion

To our knowledge, our study is not only the largest but also the first one to comprehensively examine the associations of exposure to $PM_{2.5}$

Table 3
Associations between WQS model regression indices and thyroid functions of pregnant women during different exposure windows.

Thyroid functions during pregnancy	β (ORs) and 95%CIs	*P* values
TSH during pregnancy		
1st trimester	0.018 (−0.024, 0.061)	0.425
2nd trimester	0.014 (−0.010, 0.045)	0.273
Whole pregnancy	0.012 (−0.023, 0.052)	0.326
FT4 during pregnancy		
1st trimester	**−0.031 (-0.036, -0.026)**	**<0.001**
2nd trimester	**−0.026 (-0.030, -0.023)**	**<0.001**
Whole pregnancy	**−0.024 (-0.028, -0.020)**	**<0.001**
Hypothyroxinemia during pregnancy		
1st trimester	**1.552 (1.312, 1.821)**	**<0.001**
2nd trimester	**1.453 (1.194, 1.691)**	**<0.001**
Whole pregnancy	**1.402 (1.152, 1.713)**	**<0.001**

β, ORs, and 95% CIs in bold represent significance at $P < 0.05$. β and ORs estimates represent mean differences in components of $PM_{2.5}$ when the WQS indices were increased by quartile.
Models adjusted for age, educational level, employment status, alcohol status, smoking status, passive smoking, maternal folic acid status, living areas, BMI, gestational age, maternal TPOAb status, season of conception, and ambient temperature.

and its chemical components with thyroid function in pregnant women across different exposure windows. This study revealed that exposure to $PM_{2.5}$ and its constituents across different exposure windows in the gestational period were significantly associated with a reduction in FT4 level, as well as an increased risk of hypothyroidism. Of note, in addition to the separate effect of $PM_{2.5}$ and its constituents, a potential mixed effect of chemical constituents of $PM_{2.5}$ was found to exert a detrimental effect on the thyroid function of pregnant women.

Prior epidemiological studies, conducted at 1st trimester or the whole pregnancy, consistently reported a significant association between particulate matter and a decrease in FT4 level (Zhao et al., 2019; Ghassabian et al., 2019; Janssen et al., 2017). Moreover, a mendelian randomization study established a causative link between $PM_{2.5}$ and the risk of hypothyroidism by identifying specific single nucleotide polymorphisms that are associated with $PM_{2.5}$ concentration (Zhang et al., 2022b). Findings of our study were in line with these studies. Our study further revealed that women who tested positive for TPOAb were particularly susceptible to thyroid disruption triggered by $PM_{2.5}$ exposure during pregnancy. This vulnerability might arise from their reduced ability to synthesize TH, making them unable to compensate for the detrimental impact of air pollution on FT4 level (McLachlan and Rapoport, 2007; Vanderpump et al., 1995). For the disruption of thyroid function by $PM_{2.5}$ constituents, one cohort study, carried out among 433 pregnant women in Nanjing, China, uncovered that maternal exposure to BC and NH_4^+ during the early pregnancy was associated with a reduction of FT4 concentration. The effect estimates were −0.14 (−0.29, −0.01) for BC (per unit increase) and −0.19 (−0.33, −0.05) for NH_4^+ (per unit increase) (Wang et al., 2019). However, it did not observe any significant associations between $PM_{2.5}$ and its constituents with maternal TSH level, which is consistent with our findings. Another Chinese study found that exposure to inorganic metal ions of $PM_{2.5}$ constituents, such as Zn, K, and Mn, was associated with a decrease in FT4 level in 329 pregnant women (Zhou et al., 2022). Although the sample size, types of $PM_{2.5}$ constituents, and methodologies employed for exposure estimation varied, these findings confirm our results and suggest that the 1st trimester of pregnancy is a critical period of vulnerability to exposure to $PM_{2.5}$ and its constituents.

Although a definitive mechanism explaining the impact of particulate matter on thyroid function disruption has not been fully elucidated, the existing evidence suggests several potentially plausible pathways. Animal experiments have demonstrated that $PM_{2.5}$ exposure not only results in disruption of the hypothalamic-pituitary-thyroid axis but also reduces thyroid peroxidase levels during TH synthesis, consequently inhibiting iodine activation and further decreasing circulating TH levels (Dong et al., 2021). Furthermore, oxidative stress and inflammatory responses induced by $PM_{2.5}$ exposure may also contribute to abnormal thyroid function (Kang et al., 2021; Gangwar et al., 2020; Mancini et al., 2016). An example of this is observed in $PM_{2.5}$-exposed rats, where elevated levels of reactive oxygen species and malondialdehyde hindered the iodination process and effective uptake of iodide ions in the thyroid gland, ultimately impacting the biosynthesis of TH (Dong et al., 2021). Also, the activation of thyroxine can be blocked by specific inflammatory factors such as IL-6, which in turn promotes the development of nonthyroidal illness syndrome (Wajner et al., 2011). $PM_{2.5}$ toxicity is also related to its sources and relative abundance. The most abundant ions in $PM_{2.5}$ are SO_4^{2-} (typically from fossil fuel burning), NO_3^- (usually from vehicular emissions), and NH_4^+ (mostly from residential and agricultural sources) (Liang et al., 2022). Inhalation of these inorganic ions can disrupt thyroid function by generating high levels of reactive oxygen species and inflammatory pathways (Dong et al., 2021; Ying et al., 2014; Oberdörster et al., 2004). Carbonaceous aerosol (OM and BC) is another important component in $PM_{2.5}$ in urban atmospheres. Previous studies conducted in Fujian Province have revealed that carbonaceous aerosols constitute 40% of the $PM_{2.5}$ mass, and predominantly originate from incomplete combustion of biomass and fossil fuels, including emissions from vehicle tailpipes, industrial sources, and residential burning of biofuels (Zhang et al., 2011; Liang et al., 2016). At the population level, inhalation of OM and BC has been linked to systemic inflammation activation (by inhibiting DNA methylation), production of reactive oxygen species, and increased platelet activation biomarkers (including C-reactive protein, interleukin 1-6, and tumor necrosis factor) (Delfino et al., 2008; Lei et al., 2019). These biological changes interfere with the effective absorption of iodine ions by the thyroid gland and affect the synthesis of TH (Sun et al., 2009; Ogino et al., 2017).

To date, no study has evaluated the mixed effect and relative contributions of $PM_{2.5}$ components on thyroid function impairment in pregnant women. However, an increasing number of studies have noticed that humans are exposed to mixtures of air pollutants rather than a single pollutant at a time. Using the WQS model, a Chinese study examined the combine effect of $PM_{2.5}$ and its constituents in early life on obesity in adults (Yang et al., 2023). Likewise, a study conducted in the U.S. found that exposure to $PM_{2.5}$ components had a composite effect on fetal neurodevelopment (Chiu et al., 2023). Similar to the aforementioned studies, this study adopted the novel approach of mixture analysis that took into account the combined effect of various $PM_{2.5}$ components across different exposure windows during pregnancy. Our findings demonstrated that, in the context of mixed exposure, the various chemical components of $PM_{2.5}$ exerted different contributions to thyroid function impairment during the early to mid-pregnancy stage. This study has some reference value, as it reminds us that co-occurring pollutants may interact in complex ways to compound the hazardous effect on thyroid function in pregnant women. Nevertheless, slight discrepancies existed between the findings of single pollutant analysis and those of mixture analysis. For example, in single pollutant analysis, both NO_3^- and NH_4^+ exerted the most significant influence on maternal FT4 level. Whereas, in mixed pollutant analysis, SO_4^{2-}, NO_3^-, NH_4^+, and Cl^- all emerged as crucial factors warranting attention (over the WQS cutoff value). One possible reason for this disparity is that the health effect resulting from pollutants exposure vary depending on the exposure context (single versus mixed exposure), which is in line with previous studies (Guo et al., 2023; Li et al., 2024). Additionally, differences in analytical approaches also constitute a significant factor. These findings suggested that environmental research should not only focus on the health effect resulting from single pollutant exposure but should also address the health effect arising from both single and multiple pollutant exposures. This is imperative as human populations inhabit environments characterized by intricate mixtures of exposure.

A significant strength of this study lies in exploring the separate and

mixture effect of $PM_{2.5}$ and its constituents in different exposure windows during pregnancy on thyroid function. This is instrumental in identifying critical periods of vulnerability to mixture components and developing specific strategies to mitigate early-life air pollution exposure. Nevertheless, this study possesses certain constraints. First, despite our comprehensive consideration of various covariates that could potentially influence thyroid function during pregnancy, the presence of unmeasured confounders remains a possibility, potentially impacting the study outcomes. Second, information on relocation history during pregnancy was not collected in the FJBCS. Thus, individual $PM_{2.5}$ exposure was estimated based on participants' address gathered at the time of enrollment in the FJBCS, which might lead to exposure misclassification bias. However, according to traditional Chinese customs, pregnant women typically refrain from moving residences during pregnancy. Therefore, this study assumes that the residential addresses of pregnant women will remain unchanged throughout the study period. Third, no data regarding iodine intake levels were collected in the FJBCS, and overlooking this confounding factor may introduce a certain degree of bias. Fourth, although ambient $PM_{2.5}$ is closely related to the indoor $PM_{2.5}$ exposure (a lower proportion of outdoor $PM_{2.5}$ concentrations in the presence of indoor pollution sources and a higher proportion in the absence of indoor pollution sources) (Lunderberg et al., 2023; Xie et al., 2022), the impact of indoor air pollution cannot be ignored completely. Fifth, this study primarily examined exposure to $PM_{2.5}$ components from respiratory sources, without considering the effect of ions from the gastrointestinal tract (e.g., from food and drinking water) on pregnant women's health. Given that the gastrointestinal tract is also a significant route for substance entry into the body, future research should focus on the effect of pollutants from the gastrointestinal tract on the health of pregnant women. Finally, as an observational study, the findings on the associations between exposure to $PM_{2.5}$ and its constituents in pregnancy and the thyroid disruption cannot be interpreted as a causal relation.

5. Conclusion

Exposure to $PM_{2.5}$ and its constituents was linked to impaired thyroid function in pregnant women, whether in isolation or in combination. The detrimental impact was most notable during the 1st trimester of pregnancy. This study provided a novel perspective on the impact of $PM_{2.5}$ constituents on health in pregnancy, emphasizing the necessity of investigating the relationship between particulate matter exposure and thyroid dysfunction in pregnant women across various exposure windows, as well as under the context of mixed exposure.

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CRediT authorship contribution statement

Yudiyang Ma: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Chong Miao:** Writing – review & editing. **Jing Wei:** Data curation. **Bin Sun:** Writing – review & editing, Software. **Haibo Li:** Writing – review & editing, Data curation. **Yaohua Tian:** Writing – review & editing, Data curation, Conceptualization. **Yibing Zhu:** Writing – review & editing, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2024.143610.

Data availability

Data will be made available on request.

References

Burrow, G.N., Fisher, D.A., Larsen, P.R., 1994. Maternal and fetal thyroid function. N. Engl. J. Med. 331 (16), 1072–1078.
Carrico, C., Gennings, C., Wheeler, D.C., Factor-Litvak, P., 2015. Characterization of weighted quantile sum regression for highly correlated data in a risk analysis setting. J. Agric. Biol. Environ. Stat. 20 (1), 100–120.
Cheng, E.S., Chan, K.H., Weber, M., Steinberg, J., Young, J., Canfell, K., Yu, X.Q., 2022. Solid fuel, secondhand smoke, and lung cancer mortality: a prospective cohort of 323,794 Chinese never-smokers. Am. J. Respir. Crit. Care Med. 206 (9), 1153–1162.
Chiu, Y.M., Wilson, A., Hsu, H.L., Jamal, H., Mathews, N., Kloog, I., Schwartz, J., Bellinger, D.C., Xhani, N., Wright, R.O., et al., 2023. Prenatal ambient air pollutant mixture exposure and neurodevelopment in urban children in the Northeastern United States. Environ. Res. 233, 116394.
Delfino, R.J., Staimer, N., Tjoa, T., Polidori, A., Arhami, M., Gillen, D.L., Kleinman, M.T., Vaziri, N.D., Longhurst, J., Zaldivar, F., et al., 2008. Circulating biomarkers of inflammation, antioxidant activity, and platelet activation are associated with primary combustion aerosols in subjects with coronary artery disease. Environ. Health Perspect. 116 (7), 898–906.
Derakhshan, A., Peeters, R.P., Taylor, P.N., Bliddal, S., Carty, D.M., Meems, M., Vaidya, B., Chen, L., Knight, B.A., Ghafoor, F., et al., 2020. Association of maternal thyroid function with birthweight: a systematic review and individual-participant data meta-analysis. Lancet Diabetes Endocrinol. 8 (6), 501–510.
Dong, X., Wu, W., Yao, S., Li, H., Li, Z., Zhang, L., Jiang, J., Xu, J., Zhang, F., 2021. PM (2.5) disrupts thyroid hormone homeostasis through activation of the hypothalamic-pituitary-thyroid (HPT) axis and induction of hepatic transthyretin in female rats 2.5. Ecotoxicol. Environ. Saf. 208, 111720.
Gangwar, R.S., Bevan, G.H., Palanivel, R., Das, L., Rajagopalan, S., 2020. Oxidative stress pathways of air pollution mediated toxicity: recent insights. Redox Biol. 34, 101545.
Ghassabian, A., Pierotti, L., Basterrechea, M., Chatzi, L., Estarlich, M., Fernández-Somoano, A., Fleisch, A.F., Gold, D.R., Julvez, J., Karakosta, P., et al., 2019. Association of exposure to ambient air pollution with thyroid function during pregnancy. JAMA Netw. Open 2 (10), e1912902.
Ghosh, R., Causey, K., Burkart, K., Wozniak, S., Cohen, A., Brauer, M., 2021. Ambient and household PM2.5 pollution and adverse perinatal outcomes: a meta-regression and analysis of attributable global burden for 204 countries and territories. PLoS Med. 18 (9), e1003718.
Guo, B., Huang, S., Li, S., Han, X., Lin, H., Li, Y., Qin, Z., Jiang, X., Wang, Z., Pan, Y., et al., 2023. Long-term exposure to ambient PM2.5 and its constituents is associated with MAFLD. JHEP reports : innovation in hepatology 5 (12), 100912.
Howe, C.G., Eckel, S.P., Habre, R., Girguis, M.S., Gao, L., Lurmann, F.W., Gilliland, F.D., Breton, C.V., 2018. Association of prenatal exposure to ambient and traffic-related air pollution with newborn thyroid function: findings from the children's health study. JAMA Netw. Open 1 (5), e182172.
Janssen, B.G., Saenen, N.D., Roels, H.A., Madhloum, N., Gyselaers, W., Lefebvre, W., Penders, J., Vanpoucke, C., Vrijens, K., Nawrot, T.S., 2017. Fetal thyroid function, Birth weight, and in utero exposure to fine particle air pollution: a Birth cohort study. Environ. Health Perspect. 125 (4), 699–705.
Kang, Y.J., Tan, H.Y., Lee, C.Y., Cho, H., 2021. An air particulate pollutant induces neuroinflammation and neurodegeneration in human brain models. Adv. Sci. 8 (21), e2101251.
Keil, A.P., Buckley, J.P., O'Brien, K.M., Ferguson, K.K., Zhao, S., White, A.J., 2020. A quantile-based g-computation approach to addressing the effects of exposure mixtures. Environ. Health Perspect. 128 (4), 47004.
Lei, X., Chen, R., Wang, C., Shi, J., Zhao, Z., Li, W., Yan, B., Chillrud, S., Cai, J., Kan, H., 2019. Personal fine particulate matter constituents, increased systemic inflammation, and the role of DNA hypomethylation. Environ. Sci. Technol. 53 (16), 9837–9844.
Li, C., Martin, R.V., van Donkelaar, A., Boys, B.L., Hammer, M.S., Xu, J.W., Marais, E.A., Reff, A., Strum, M., Ridley, D.A., et al., 2017. Trends in chemical composition of

global and regional population-weighted fine particulate matter estimated for 25 years. Environ. Sci. Technol. 51 (19), 11185–11195.
Li, H., Miao, C., Xu, L., Gao, H., Bai, M., Liu, W., Li, W., Wu, Z., Zhu, Y., 2022a. Maternal pre-pregnancy body mass index, gestational weight gain trajectory, and risk of adverse perinatal outcomes. Int. J. Gynaecol. Obstet.: the official organ of the International Federation of Gynaecology and Obstetrics 157 (3), 723–732.
Li, H., Miao, C., Liu, W., Gao, H., Li, W., Wu, Z., Cao, H., Zhu, Y., 2022b. First-trimester triglyceride-glucose index and risk of pregnancy-related complications: a prospective Birth cohort study in southeast China. Diabetes, Metab. Syndrome Obes. Targets Ther. 15, 3705–3715.
Li, D., Xiong, J., Cheng, G., 2024. Long-term exposure to ambient PM(2.5) and its components on menarche timing among Chinese adolescents: evidence from a representative nationwide cohort. BMC Publ. Health 24 (1), 707.
Liang, C.S., Duan, F.K., He, K.B., Ma, Y.L., 2016. Review on recent progress in observations, source identifications and countermeasures of PM2.5. Environ. Int. 86, 150–170.
Liang, R., Chen, R., Yin, P., van Donkelaar, A., Martin, R.V., Burnett, R., Cohen, A.J., Brauer, M., Liu, C., Wang, W., et al., 2022. Associations of long-term exposure to fine particulate matter and its constituents with cardiovascular mortality: a prospective cohort study in China. Environ. Int. 162, 107156.
Liu, F., Liu, C., Liu, Y., Wang, J., Wang, Y., Yan, B., 2023a. Neurotoxicity of the air-borne particles: from molecular events to human diseases. J. Hazard Mater. 457, 131827.
Liu, J., Zhao, K., Qian, T., Li, X., Yi, W., Pan, R., Huang, Y., Ji, Y., Su, H., 2023b. Association between ambient air pollution and thyroid hormones levels: a systematic review and meta-analysis. Sci. Total Environ. 904, 166780.
Lunderberg, D.M., Liang, Y., Singer, B.C., Apte, J.S., Nazaroff, W.W., Goldstein, A.H., 2023. Assessing residential PM(2.5) concentrations and infiltration factors with high spatiotemporal resolution using crowdsourced sensors. Proc. Natl. Acad. Sci. U. S. A 120 (50), e2308832120.
Ma, Y., Hu, Q., Yang, D., Zhao, Y., Bai, J., Mubarik, S., Yu, C., 2022. Combined exposure to multiple metals on serum uric acid in NHANES under three statistical models. Chemosphere 301, 134416.
Ma, Y, Li, D, Cui, F, Wang, J, Tang, L, Yang, Y, Liu, R, Tian, Y, 2024. Air pollutants, genetic susceptibility, and abdominal aortic aneurysm risk: a prospective study. Eur. Heart J. 45 (12), 1030–1039. https://doi.org/10.1093/eurheartj/ehad886.
Mancini, A., Di Segni, C., Raimondo, S., Olivieri, G., Silvestrini, A., Meucci, E., Currò, D., 2016. Thyroid hormones, oxidative stress, and inflammation. Mediat. Inflamm. 2016, 6757154.
McLachlan, S.M., Rapoport, B., 2007. Thyroid peroxidase as an autoantigen. Thyroid : official journal of the American Thyroid Association 17 (10), 939–948.
Modesto, T., Tiemeier, H., Peeters, R.P., Jaddoe, V.W., Hofman, A., Verhulst, F.C., Ghassabian, A., 2015. Maternal mild thyroid hormone insufficiency in early pregnancy and attention-deficit/hyperactivity disorder symptoms in children. JAMA Pediatr. 169 (9), 838–845.
Oberdörster, G., Sharp, Z., Atudorei, V., Elder, A., Gelein, R., Kreyling, W., Cox, C., 2004. Translocation of inhaled ultrafine particles to the brain. Inhal. Toxicol. 16 (6–7), 437–445.
Ogino, K., Nagaoka, K., Okuda, T., Oka, A., Kubo, M., Eguchi, E., Fujikura, Y., 2017. PM2.5-induced airway inflammation and hyperresponsiveness in NC/Nga mice. Environ. Toxicol. 32 (3), 1047–1054.
Shen, Y., Yu, G., Liu, C., Wang, W., Kan, H., Zhang, J., Cai, J., 2022. Prenatal exposure to PM(2.5) and its specific components and risk of hypertensive disorders in pregnancy: a nationwide cohort study in China. Environ. Sci. Technol. 56 (16), 11473–11481.
Siegel, E.L., Ghassabian, A., Hipwell, A.E., Factor-Litvak, P., Zhu, Y., Steinthal, H.G., Focella, C., Battaglia, L., Porucznik, C.A., Collingwood, S.C., et al., 2023. Indoor and outdoor air pollution and couple fecundability: a systematic review. Hum. Reprod. Update 29 (1), 45–70.
Sun, Q., Yue, P., Deiuliis, J.A., Lumeng, C.N., Kampfrath, T., Mikolaj, M.B., Cai, Y., Ostrowski, M.C., Lu, B., Parthasarathy, S., et al., 2009. Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity. Circulation 119 (4), 538–546.
van Donkelaar, A., Martin, R.V., Li, C., Burnett, R.T., 2019. Regional estimates of chemical composition of fine particulate matter using a combined geoscience-statistical method with information from satellites, models, and monitors. Environ. Sci. Technol. 53 (5), 2595–2611.
Vanderpump, M.P., Tunbridge, W.M., French, J.M., Appleton, D., Bates, D., Clark, F., Grimley Evans, J., Hasan, D.M., Rodgers, H., Tunbridge, F., et al., 1995. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. Clinical endocrinology 43 (1), 55–68.
Wajner, S.M., Goemann, I.M., Bueno, A.L., Larsen, P.R., Maia, A.L., 2011. IL-6 promotes nonthyroidal illness syndrome by blocking thyroxine activation while promoting thyroid hormone inactivation in human cells. J. Clin. Invest. 121 (5), 1834–1845.
Wang, X., Liu, C., Zhang, M., Han, Y., Aase, H., Villanger, G.D., Myhre, O., Donkelaar, A. V., Martin, R.V., Baines, E.A., et al., 2019. Evaluation of maternal exposure to PM (2.5) and its components on maternal and Neonatal thyroid function and Birth weight: a cohort study. Thyroid : official journal of the American Thyroid Association 29 (8), 1147–1157.
Wei, J., ZhanqingLyapustin, AlexeiSun, LinPeng, YiranXue, WenhaoSu, TianningCribb, Maureen, %J., 2021. Remote Sensing of Environment: an Interdisciplinary Journal: **reconstructing 1-km-resolution high-quality PM2.5 data records from 2000 to 2018 in China: spatiotemporal variations and policy implications**. Rem. Sens. Environ.: An Interdisciplinary Journal 252 (1).
Wei, J., Liu, S., Li, Z., Liu, C., Qin, K., Liu, X., Pinker, R.T., Dickerson, R.R., Lin, J., Boersma, K.F., et al., 2022. Ground-level NO(2) surveillance from space across China for high resolution using interpretable spatiotemporally weighted artificial intelligence. Environ. Sci. Technol. 56 (14), 9988–9998.
Wei, J., Li, Z., Chen, X., 2023. Separating Daily 1 km PM_(2.5) inorganic chemical composition in China since 2000 via deep learning integrating ground, satellite, and model data. Environ. Sci. Technol. ES&T 57 (46), 18282–18295.
Xie, Y., Wang, Y., Zhang, Y., Fan, W., Dong, Z., Yin, P., Zhou, M., 2022. Substantial health benefits of strengthening guidelines on indoor fine particulate matter in China. Environ. Int. 160, 107082.
Xue, J., Wan, Y., Kannan, K., 2016. Occurrence of bisphenols, bisphenol A diglycidyl ethers (BADGEs), and novolac glycidyl ethers (NOGEs) in indoor air from Albany, New York, USA, and its implications for inhalation exposure. Chemosphere 151, 1–8.
Yang, Y., Ruan, Z., Wang, X., Yang, Y., Mason, T.G., Lin, H., Tian, L., 2019. Short-term and long-term exposures to fine particulate matter constituents and health: a systematic review and meta-analysis. Environ. Pollut. 247, 874–882.
Yang, S., Hong, F., Li, S., Han, X., Li, J., Wang, X., Chen, L., Zhang, X., Tan, X., Xu, J., et al., 2023. The association between chemical constituents of ambient fine particulate matter and obesity in adults: a large population-based cohort study. Environ. Res. 231 (Pt 2), 116228.
Yin, P., Brauer, M., Cohen, A.J., Wang, H., Li, J., Burnett, R.T., Stanaway, J.D., Causey, K., Larson, S., Godwin, W., et al., 2020. The effect of air pollution on deaths, disease burden, and life expectancy across China and its provinces, 1990-2017: an analysis for the Global Burden of Disease Study 2017. Lancet Planet. Health 4 (9), e386–e398.
Ying, Z., Xu, X., Bai, Y., Zhong, J., Chen, M., Liang, Y., Zhao, J., Liu, D., Morishita, M., Sun, Q., et al., 2014. Long-term exposure to concentrated ambient PM2.5 increases mouse blood pressure through abnormal activation of the sympathetic nervous system: a role for hypothalamic inflammation. Environ. Health Perspect. 122 (1), 79–86.
Yu, G., Ao, J., Cai, J., Luo, Z., Martin, R., Donkelaar, A.V., Kan, H., Zhang, J., 2020. Fine particular matter and its constituents in air pollution and gestational diabetes mellitus. Environ. Int. 142, 105880.
Yu, W., Ye, T., Zhang, Y., Xu, R., Lei, Y., Chen, Z., Yang, Z., Zhang, Y., Song, J., Yue, X., et al., 2023. Global estimates of daily ambient fine particulate matter concentrations and unequal spatiotemporal distribution of population exposure: a machine learning modelling study. Lancet Planet. Health 7 (3), e209–e218.
Zhang, F., Zhao, J., Chen, J., Xu, Y., Xu, L., 2011. Pollution characteristics of organic and elemental carbon in PM2.5 in Xiamen, China. J. Environ. Sci. 23 (8), 1342–1349.
Zhang, X., Huels, A., Makuch, R., Zhou, A., Zheng, T., Xia, W., Gaskins, A., Makuch, J., Zhu, Z., Zhu, C., et al., 2022a. Association of exposure to ambient particulate matter with maternal thyroid function in early pregnancy. Environ. Res. 214 (Pt 2), 113942.
Zhang, Y., Liu, S., Wang, Y., Wang, Y., 2022b. Causal relationship between particulate matter 2.5 and hypothyroidism: a two-sample Mendelian randomization study. Front. Public Health 10, 1000103.
Zhao, Y., Cao, Z., Li, H., Su, X., Yang, Y., Liu, C., Hua, J., 2019. Air pollution exposure in association with maternal thyroid function during early pregnancy. J. Hazard Mater. 367, 188–193.
Zhou, Y., Zhu, Q., Wang, P., Li, J., Luo, R., Zhao, W., Zhang, L., Shi, H., Zhang, Y., 2022. Early pregnancy PM(2.5) exposure and its inorganic constituents affect fetal growth by interrupting maternal thyroid function. Environ. Pollut. 307, 119481.
Zhu, Y., Ma, Y., Tang, L., Li, H., Miao, C., Cao, H., Tian, Y., 2023. The adverse impact of maternal ozone exposure on fetal growth in utero and the interaction with residential greenness. J. Hazard Mater. 461, 132562.
Zhu, Y., Ma, Y., Tang, L., Li, H., Miao, C., Cao, H., Tian, Y., 2024. The adverse impact of maternal ozone exposure on fetal growth in utero and the interaction with residential greenness. J. Hazard. Mater. 461, 132562. https://doi.org/10.1016/j.jhazmat.2023.132562.