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Association between ambient PM_1 and semen quality: A cross-sectional study of 27,854 men in China

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ABSTRACT

Background: Exposure to ambient fine and respirable particulate matter is associated with poor sperm quality, but evidence for particulate matter with an aerodynamic diameter ≤ 1 μm (PM_1) is scarce. We aimed to estimate the association between PM_1 exposure and sperm concentration, sperm count, sperm total motility, and sperm progressive motility in Chinese men.

Methods: We conducted a cross-sectional study of 33,221 men attending an infertility clinic in Hubei, China, between 2014 and 2020. Daily concentrations of PM_1 data were estimated from a validated spatiotemporal artificial intelligence model. We used multivariate linear regression to estimate the association between PM_1 exposure and sperm parameters during the spermatogenesis period after adjusting for age, body mass index (BMI), education, ever having fathered a child, and season of semen collection. In addition, we performed stratified analysis to assess whether the association was varied by age, BMI, and educational attainment.

Results: A total of 27,854 participants were included in the final analysis. An interquartile range (17.2 μg/m^3) increase in PM_1 during the entire period of semen development was associated with declined semen concentration [-4.39% (95% CI: −7.67%, −1.12%)] and sperm count [–23.56% (95% CI: −28.95%, −18.18%)], reduced total motility [-0.86% (95% CI: −1.66%, −0.06%)] and progressive motility [-2.22% (95% CI: −3.00%, −1.43%)]. The associations were homogeneous across subgroups defined by age and education, but were more pronounced among men with underweight for sperm concentration and sperm count. We identified a critical exposure window of 0–9 lag days, 10–14 lag days, and 70–90 lag days before semen collection for sperm count and progressive motility.

Conclusions: Among men attending an infertility clinic in China, exposure to PM_1 was associated with poor semen quality, especially during the 70–90 days before ejaculation. These results suggest that exposure to PM_1 might be a novel risk factor for impaired semen quality.

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Table 1
Summary characteristics of the study participants (N = 27,854) and statistics of air pollutants in Hubei, China.

Characteristics	N (%) Mean ± SD
Demographics	
Age, years	
≤ 30	8700 (31.1%)
31–39	4305 (15.5%)
≥ 40	14,848 (53.3%)
Unknown	1 (0.0%)
BMI, kg/m^2	
< 18.5	1101 (4.0%)
18.5–23.9	12,822 (46.0%)
24.0–27.9	10,417 (37.4%)
≥ 28.0	3225 (11.6%)
Unknown	289 (1.0%)
Education	
College and higher	12,388 (44.5%)
High school	3359 (12.1%)
Middle school and lower	12,086 (43.4%)
Unknown	21 (0.1%)
Ever having fathered a child	
No	13,435 (48.2%)
Yes	3973 (14.3%)
Unknown	10,446 (37.5%)
Abnormal sperm quality[a]	10,128 (36.4%)
Season[b]	
Spring	6445 (23.1%)
Summer	9077 (32.6%)
Autumn	7291 (26.2%)
Winter	5041 (18.1%)
Air pollutants (μg/m^3)	
PM_1	27.6 ± 11.8
CO	1.0 ± 0.2
SO_2	15.1 ± 9.0
NO_2	32.6 ± 13.3
O_3	100.7 ± 25.1

Abbreviations: N = number of counts; SD = standard deviation; BMI = body mass index; PM_1 = particulate matter with aerodynamic diameter ≤ 1 μm; NO_2 = nitrogen dioxide; SO_2 = sulfur dioxide; O_3 = ozone; CO = carbon monoxide.

[a] Abnormal sperm quality was classified as being below the World Health Organization reference values: sperm concentration (15×10^6/mL), total sperm count (39×10^6/sample), progressive motility (32% motile sperm) and total motility (40% motile sperm).

[b] Season of sperm collection was defined as Spring (March to May), Summer (June to August), Autumn (September to November), and Winter (December to February).

1. Introduction

Infertility has become a global public health concern. It was estimated that approximately 10% of couples experienced infertility globally (Fainberg and Kashanian 2019). Pure men factors accounted for ~ 50% of infertility cases, and among men factors, poor semen quality is one of the key contributing factors, including low sperm concentration, abnormal sperm morphology, or low sperm motility (World Health Organization WHO, 2018). There has been a global decline in sperm quality in recent years (Levine et al., 2017; Lv et al., 2021; Punjani et al., 2023; Virtanen et al., 2017; Wang et al., 2017). For example, a systematic review and *meta*-analysis reported that sperm concentration and sperm count declined by 52.4% and 59.3% between 1973 and 2011, respectively (Levine et al. 2017).

Emerging studies have examined whether exposure to particulate matter (PM) may impair semen quality, but findings have been mixed, with some studies reporting that poor semen quality is associated with exposure to PM (Carré et al. 2017; Guan et al. 2020; Huang et al. 2019; Lao et al. 2018; Sun et al. 2020; Wu et al. 2017; Yu et al. 2022; Zhao et al. 2022; Zhou et al. 2018), or not associated with exposure to PM (Chen et al. 2019; Hansen et al. 2010; Nobles et al. 2018). In addition, most prior studies focused on fine particulate matter ($PM_{2.5}$) or respirable particulate matter (PM_{10}), but evidence for PM with an aerodynamic diameter ≤ 1 μm (PM_1) is scarce. PM_1 is potentially more toxic than $PM_{2.5}$ and PM_{10} because PM_1 has a larger surface area to mass ratio than $PM_{2.5}$ and PM_{10}, potentially comprising more toxins, metals, and organic compounds, and it could reach a deeper place in human lungs and deposit in blood vessels (Dioni et al. 2011; Guo et al. 2022). Thus, it is possible that exposure to PM_1 might impair semen quality.

Given the public health significance of infertility and the toxic potential of PM_1, we sought to evaluate the association of PM_1 with sperm parameters among 33,221 Chinese men from an infertility clinic between 2014 and 2020. We also examined whether the association was varied by age, body mass index, and educational attainment.

2. Method

2.1. Study population

We included participants from our established studies on environmental chemical exposure and male reproductive health, which have been reported elsewhere (Wang et al. 2015; Yang et al. 2017; Zeng et al. 2014). Briefly, we recruited 33,221 male partners in couples who attended the Reproductive Center of Tongji Hospital for semen examination in Wuhan, Hubei, China, between January 2014 and December 2020, with complete outcome records and residential addresses. We excluded 4,660 men with self-reported azoospermia or reproductive dysfunction associated with decreased semen quality (e.g., vasectomy, epididymitis, vesiculitis, varicocele, injury of the testis, endocrine diseases). We additionally excluded 707 participants with missing PM_1 concentration during the spermatogenesis period. We included 27,854 participants in the final analytic sample. The demographic differences between the included and total population were presented in **Table S1**. We used a standardized and structured questionnaire to collect demographic information for each participant at each visit, including age, educational attainment, ever having fathered a child, and health conditions, such as vasectomy. Clinical examinations at each visit were conducted by registered nurses. We calculated body mass index (BMI) as weight in kilograms divided by height in meters squared. The Ethics Committee of Tongji Medical College approved the study. Each participant signed written informed consent before participation.

2.2. Semen sample collection and study outcome

Semen was collected and analyzed in accordance with the World Health Organization (WHO) guidelines (World Health Organization WHO, 2010), as detailed elsewhere (Wang et al. 2015). Briefly, each man was asked to masturbate into a sterile plastic specimen cup in an enclosed room near the semen analysis room. The semen samples were liquefied in a heating chamber, and the semen volume was assessed utilizing a serologic pipette. Micro-cell slide and computer-aided semen examination were used to measure sperm concentration, sperm progressive motility, and sperm non-progressive motility. Sperm count was calculated as semen volume multiplied by sperm concentration; sperm total motility was defined as progressive motility plus non-progressive motility. Two professional technicians conducted all semen sample analyses under blinded conditions, respectively, and were supervised by the Quality Control Center of Hubei Province. We did not find any statistically significant difference between these two professionals in quality control results (Wang et al. 2015).

2.3. Environmental exposure data

We obtained 1 km × 1 km daily grid ambient PM_1 (Wei et al. 2019) and maximum 8-hour averages ozone (O_3) (Wei et al. 2022a), and 10 km × 10 km daily grid ambient sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and carbon monoxide (CO) (Wei et al. 2022b; Wei et al. 2023) in Hubei province during 2014–2020 from the ChinaHighAirPollutant

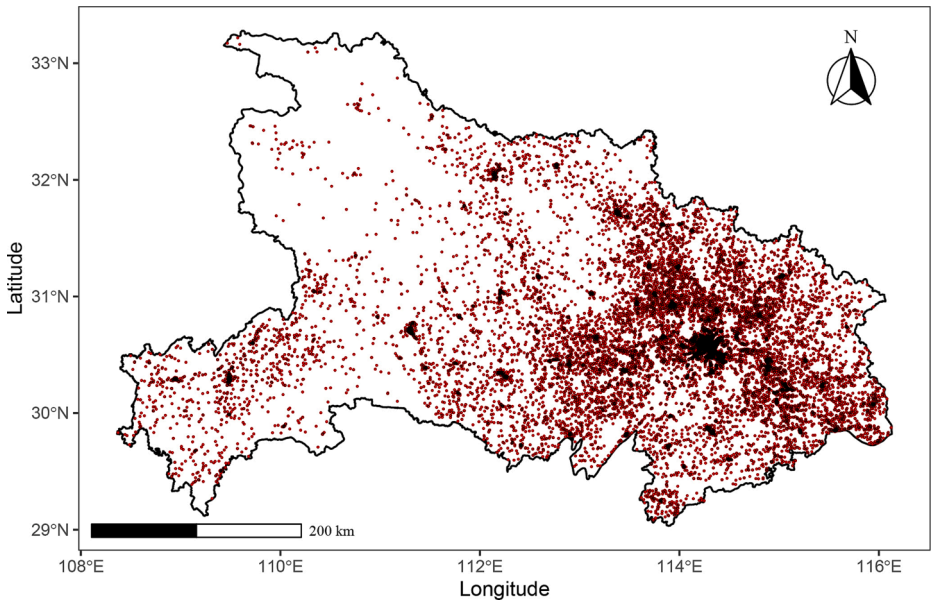

Fig. 1. Spatial distribution of the included study participants (N = 27,854).

(CHAP) dataset (available at https://weijing-rs.github.io/product.html), which refers to the long-term, full-coverage, high-resolution, and high-quality ground-level air pollutants datasets for China. The CHAP dataset was generated using developed spatiotemporal artificial intelligence models from big data combining multiple data sources, including ground-based measurements, satellite remote sensing products, atmospheric reanalysis, and model simulations. The performance of the model to estimate these five air pollutants was assessed by a 10-fold cross-validation approach with coefficients of determination (R^2) ranging from 0.80 for NO_2 to 0.93 for O_3 (Wei et al. 2019; Wei et al. 2022a; Wei et al. 2022b; Wei et al. 2023). We assigned the daily concentration of each air pollutant for each participant based on their geocoded residential addresses. Spermatogenesis takes ~ 90 days and includes three essential periods: epididymal storage (0–9 days before semen ejaculation), sperm motility development (10–14 days before semen ejaculation), and spermatogenesis (70–90 days before semen ejaculation) (Hansen et al., 2010; Zhao et al., 2022). For each participant, we calculated the average concentration of air pollutants during the 0 ~ 90 days of sperm development and each essential period of sperm development. We also obtained daily ambient temperature data from the meteorological bureau of China. We calculated the average ambient temperature during 0–90 days before the date of semen collection derived from the nearest monitoring stations for each participant.

2.4. Statistical analysis

Given that sperm count and sperm concentration were right-skewed, we transformed these two sperm parameters using a natural logarithm to approximate a normal distribution. Descriptive analysis was applied to summarize characteristics with the number or proportion for demographic variables, including age (≤30, 31–39, ≥ 40 years, unknown), BMI (<18.5, 18.5–23.9, ≥ 28.0 kg/m^2, unknown), education (college and higher, high school, middle school and lower, unknown), ever having fathered a child (yes, no, unknown), and season of sperm collection (spring [March to May], summer [June to August], autumn [September to November], and winter [December to February]). We used mean and standard deviation to describe statistics of air pollution, and used median (upper and lower quartiles) to describe sperm parameters.

We used multivariate linear regression to examine the association between exposure to PM_1 and sperm parameters during the sperm development period (0–90 days) after adjusting for age, BMI, education, ever having fathered a child, season of semen collection, and daily ambient temperature. We presented results as effect estimates per interquartile range (IQR) increase in ambient PM_1 concentration (continuous) or effect estimates in the upper four quintiles of PM_1 concentration compared with the lowest quintile. Specifically, the effect estimates for sperm count and sperm concentration were presented as percent change (%) and those for total motility and progressive motility were expressed as absolute change (%). We tested the linear trend of effect estimates across quintiles by extracting the median values of ambient PM_1 to each quintile and coding this new variable as a continuous variable in models.

To investigate the exposure–response relationship for the association between exposure to PM_1 and sperm parameters, we fitted ambient PM_1 using a restricted cubic spline with three knots located at the 10th, 50th, and 90th percentiles of PM_1 levels in the models. We applied analysis of variance (ANOVA) to assess whether the exposure–response curve was departed from linear.

To explore the critical exposure windows, we also examined the association of lag 0–9, 10–14, and 70–90 days exposure with semen quality using multivariate linear regression model. We included all three exposure windows in the same model to reduce bias introduced by seasonal trends in PM_1 that induced correlation between exposure windows (Wilson et al. 2017). Based on prior studies on the association between PM and semen quality (Wu et al. 2022; Xu et al. 2023), we further conducted stratified analysis to test whether the association was differed across subgroups defined by age, BMI, and educational attainment. We used the two-sample *t* test to assess whether the associations were homogeneous across subgroups.

To assess the robustness of our findings, we conducted three main sensitivity analyses. First, to examine whether the adverse effects of PM_1 on sperm quality were independent of other pollutants, we constructed two-pollutant models. In the two-pollutant models, we adjusted for the other pollutant one at a time when the Spearman correlation between PM_1 and the co-pollutant < 0.8 to avoid collinearity (**Fig S3**) (Sun et al. 2019; Sun et al. 2016). Second, to test whether the association was also observed in men with normal sperm quality, we repeated the main analyses among participants with semen quality ≥ the WHO referenced values: sperm concentration (15 × 10^6/mL), total sperm count (39 × 10^6/sample), sperm progressive motility (32% motile), and sperm total

Table 2
Effect estimates of semen parameters associated with an interquartile range (IQR) increase in PM_1 exposure during the sperm development period.

Semen quality parameters	Effect estimates (95% CI)[a]	
	Crude model[b]	Adjusted model[c]
Sperm concentration		
Q1 (median 14.6 μg/m^3)	[Reference]	[Reference]
Q2 (median 19.4 μg/m^3)	−2.94 (-5.94, 0.06)	−3.78 (-6.91, −0.65)
Q3 (median 25.3 μg/m^3)	0.01 (-3.22, 3.25)	−2.78 (-6.69, 1.12)
Q4 (median 33.0 μg/m^3)	1.92 (-1.52, 5.37)	−2.04 (-6.93, 2.85)
Q5 (median 44.5 μg/m^3)	−0.84 (-4.68, 3.00)	−6.81 (-12.90, −0.72)
Continuous PM_1 exposure (per IQR increase)[d]	0.28 (-1.60, 2.17)	−4.39 (-7.67, −1.12)
P for trend[e]	0.45	0.07
Sperm count		
Q1 (median 14.6 μg/m^3)	[Reference]	[Reference]
Q2 (median 19.4 μg/m^3)	−6.35 (-10.52, −2.19)	−10.72 (-15.19, −6.26)
Q3 (median 25.3 μg/m^3)	−3.41 (-8.11, 1.28)	−16.69 (–23.02, −10.36)
Q4 (median 33.0 μg/m^3)	−4.62 (-9.82, 0.59)	−25.33 (–33.59, −17.08)
Q5 (median 44.5 μg/m^3)	−13.26 (-19.03, −7.49)	−40.03 (-50.02, −30.05)
Continuous PM_1 exposure (per IQR increase)[d]	−6.27 (-9.08, −3.45)	–23.56 (-28.95, −18.18)
P for trend[e]	<0.001	<0.001
Total motility		
Q1 (median 14.6 μg/m^3)	[Reference]	[Reference]
Q2 (median 19.4 μg/m^3)	−0.86 (-1.59, −0.12)	−0.92 (-1.69, −0.15)
Q3 (median 25.3 μg/m^3)	−0.15 (-0.95, 0.64)	−0.81 (-1.77, 0.14)
Q4 (median 33.0 μg/m^3)	1.32 (0.48, 2.17)	−0.04 (-1.24, 1.16)
Q5 (median 44.5 μg/m^3)	−0.30 (-1.24, 0.64)	−2.20 (-3.69, −0.71)
Continuous PM_1 exposure (per IQR increase)[d]	0.40 (-0.06, 0.86)	−0.86 (-1.66, −0.06)
P for trend[e]	0.12	0.02
Progressive motility		
Q1 (median 14.6 μg/m^3)	[Reference]	[Reference]
Q2 (median 19.4 μg/m^3)	−1.30 (-2.01, −0.58)	−1.60 (-2.34, −0.85)
Q3 (median 25.3 μg/m^3)	−0.64 (-1.41, 0.14)	−2.00 (-2.93, −1.06)
Q4 (median 33.0 μg/m^3)	0.68 (-0.15, 1.50)	−1.73 (-2.90, −0.56)
Q5 (median 44.5 μg/m^3)	−1.04 (-1.96, −0.12)	−4.41(-5.86, −2.95)
Continuous PM_1 exposure (per IQR increase)[d]	−0.05 (-0.50, 0.40)	−2.22 (-3.00, −1.43)
P for trend[e]	0.92	<0.001

Abbreviations: Q: quintile; IQR: interquartile range; CI: confidence interval.
[a] The sperm count and sperm concentration were in percent change and sperm total motility and sperm progressive motility were in absolute change.
[b] Models included ever having fathered a child.
[c] Models were additionally adjusted for age (≤ 30, 31-39, ≥ 40 years, unknown), body mass index (<18.5, 18.5-23.9, 24.0-27.9, ≥ 28.0 kg/m^2, unknown), ever having fathered a child (yes, no, unknown), educational attainment (middle school and lower, high school, college and higher, unknown), season of sperm collection (spring, summer, autumn, and winter), and average daily ambient temperature during 0-90 days.
[d] An IQR increase in PM_1 exposure at the residential address is 17.2 μg/m^3.
[e] Test for trend is based on the median value for each quintile.

motility (40% motile) (World Health Organization WHO, 2010). Third, to assess the robustness of results, we separately fitted ambient PM_1 using a restricted cubic spline with three and four knots located equally over the range of PM_1. We performed all analyses in R software (Version 4.2.1). All tests were 2-sided, and $P < 0.05$ was considered statistically significant.

3. Result

3.1. Descriptive statistics

The summary characteristics of the participants were presented in Table 1. Between 2014 and 2020, a total of 27,854 men were included in the final analysis, of whom more than half (53.3%) were over 40 years old. The participants were more likely to never have fathered a child (48.2%), to had an education of college or higher (44.5%), or have a BMI ranging from 18.5 to 24.0 kg/m^2 (46.0%). The spatial distribution of study participants is shown in Fig. 1 and **Fig S1**.

The annual average concentration of PM_1 decreased from 2014 to 2020 in Hubei, China (**Fig S2**). Ambient PM_1 was positively correlated with NO_2, CO, and SO_2, but was negatively correlated with O_3, with a Spearman correlation coefficient < 0.8 for all pollutants (**Fig S3**).

The median of sperm quality parameters was 129.5 million per sample for sperm count, 52.0 million/mL for sperm concentration, 47.0% for total motility, and 42.0% for progressive motility **(Table S2).**

3.2. PM_1 and sperm quality parameters

Exposure to PM_1 was associated with reduction in sperm count and progressive motility during the entire period of semen development (Table 2). Compared with the first quintile of PM_1 in the fully adjusted models, effect estimates of sperm concentration and sperm count associated with the fifth quintiles of PM_1 were −6.81% (95% CI: −12.90%, −0.72%) and −40.03% (95% CI: −50.02%, −30.05%), respectively. The corresponding effect estimates for total motility and progressive motility were −2.20% (95% CI: −3.69%, −0.71%) and −4.41% (95% CI: −5.86%, −2.95%). An IQR (17.2 μg/m^3) increase in PM_1 was associated with a 4.39% (95% CI: 1.12%, 7.67%), 23.56% (95% CI: 18.18%, 28.95%), 0.86% (95% CI: 0.06%, 1.66%), and 2.22% (95% CI: 1.43%, 3.00%) reduction in sperm concentration, sperm count, total motility, and progressive motility, respectively.

To examine the relationship between PM_1 exposure and sperm parameters, we fitted ambient PM_1 using a restricted cubic spline with three knots located at the 10th, 50th, and 90th percentiles in the models (Fig. 2). The exposure–response curves showed a decreasing trend with higher PM_1 concentrations associated with reduced sperm parameters.

To explore the critical exposure windows, we examined the associations during each key period of sperm development. We found that the association was more pronounced during the spermatogenesis (Table 3). For example, an IQR increase in PM_1 exposure decreased sperm count levels by 6.80% (95% CI: 2.92%, 10.68%), 4.10% (95% CI: 0.94%, 7.27%), and 17.74% (95% CI: 12.90%, 22.58%) during the 0–9 lag days, 10–14 lag days, and 70–90 lag days, respectively.

3.3. Subgroup analyses

We conducted subgroup analyses to identify the susceptible subpopulations to PM_1 **(**Fig. 3**)**. We found that the association was more pronounced among men with a BMI < 18.5 kg/m^2 for sperm concentration and sperm count. For example, an IQR increase in PM_1 was associated with a 33.62% (95% CI: 13.28%, 53.96%) reduction in sperm concentration among men with a BMI < 18.5 kg/m^2 versus 1.63% (95% CI: −7.55%, 10.80%) among men with a BMI ≥ 28.0 kg/m^2.

3.4. Sensitivity analysis

We conducted three main sensitivity analyses to confirm the robustness of our findings. We found that effect estimates were similar with additional adjustment for CO, SO_2, O_3, and NO_2 one at a time in the two-pollutant models (Table 4). We further restricted to men with normal semen quality defined by the WHO guidelines, and the effect estimates were stronger than those obtained among men with abnormal semen quality. For example, the effect estimate of sperm count was

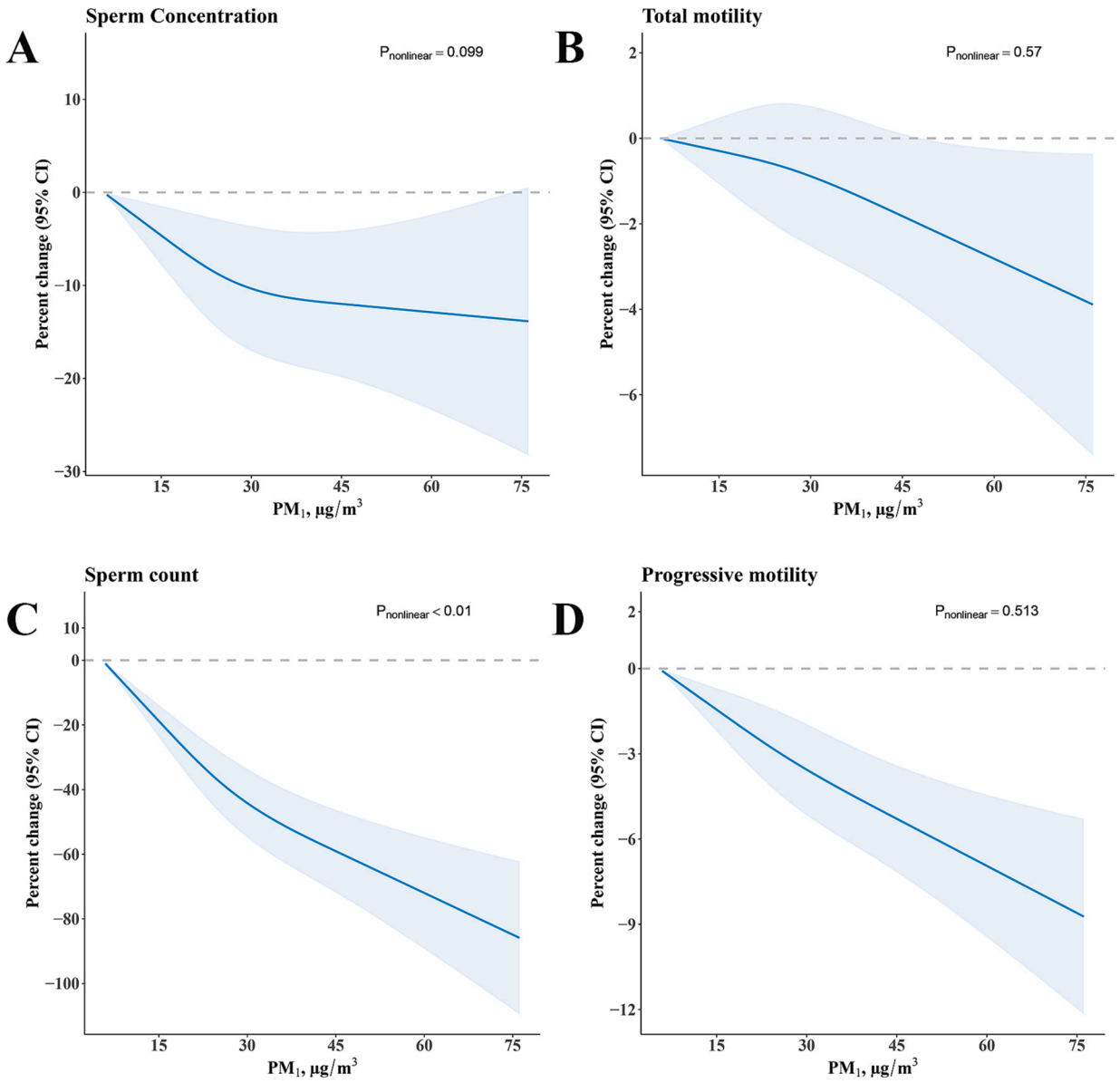

Fig. 2. The exposure–response curves for the association between exposure to PM_1 and (A) sperm concentration, (B) sperm count, (C) total motility, and (D) progressive motility during the entire sperm development. Models were adjusted for age (≤30, 31–39, ≥ 40 years, unknown), body mass index (<18.5, 18.5–23.9, 24.0–27.9, ≥ 28.0 kg/m^2, unknown), ever having fathered a child (yes, no, unknown), educational attainment (middle school and lower, high school, college and higher, unknown), season of sperm collection (spring, summer, autumn, and winter), and average daily ambient temperature during 0-90 days. $P_{nonlinear}$ < 0.05 indicates a nonlinear relationship.

–23.56% (95% CI: −28.95%, −18.18%) among all participants (main results) and −21.88% (95% CI: −26.85%, −16.91%) among men with normal semen quality only. Results were not materially different when we varied number and location of knots of the spline function for PM_1 in the sensitivity analysis (Fig S4).

4. Discussion

Among 27,854 men enrolled in an infertility clinic in China, we found that exposure to ambient PM_1 was associated with a decrease in sperm concentration and sperm count, total motility and progressive motility. We found no evidence of effect modification by age and education, but we found that the association was more pronounced among men with a BMI ≤ 18.5 kg/m^2 for sperm concentration and sperm count. We found that the lag 0–9, lag 10–14, and lag 70–90 days exposure were all associated with a reduction in sperm count and sperm progressive motility, with the strongest association for lag 70–90 days exposure. The results were robust in the two-pollutant models after adjusting for co-pollutant or among men with normal semen quality defined by the WHO guidelines.

To our knowledge, this is the largest study to examine the adverse effects of ambient PM_1 exposure on sperm quality parameters, including sperm count, sperm concentration, sperm total motility, and sperm progressive motility. Our findings of a significant association between PM_1 and reduction in sperm count, sperm concentration, sperm total motility, and sperm progressive motility were in contrast with an analysis among 1,310 Chinese men in Guangzhou, a megacity of South China, the only study so far that examined the association between PM_1 and semen quality (Yu et al. 2022). This study used a random forest model to estimate daily PM_1 concentration and found no evidence of any association of PM_1 exposure with sperm concentration, sperm count, sperm total motility, and sperm progressive motility. The

Table 3
Effect estimates of semen quality parameters associated with an interquartile range increase in PM_1 exposure during specific time windows of sperm development.

Exposure time window, lag days[b]	Effect estimate (95% CI)[a]			
	Sperm concentration (% changes in millions/mL)	Sperm count (% changes in millions/sample)	Total motility (%)	Progressive motility (%)
0 ~ 9	0.32 (-2.06, 2.70)	−6.80 (-10.68, −2.92)	−0.61 (-1.20, −0.03)	−1.09 (-1.66, −0.52)
10 ~ 14	−0.81 (-2.80, 1.19)	−4.10 (-7.27, −0.94)	−0.05 (-0.54, 0.44)	−0.52 (-1.00, −0.04)
70 ~ 90	−2.26 (-5.22, 0.70)	−17.74 (−22.58, −12.90)	−0.10 (-0.82, 0.63)	−1.19 (-1.90, −0.49)

[a] Models were adjusted for age (≤30, 31–39, ≥ 40 years, unknown), body mass index (<18.5, 18.5–23.9, 24.0–27.9, ≥ 28.0 kg/m^2, unknown), ever having fathered a child (yes, no, unknown), educational attainment (middle school and lower, high school, college and higher, unknown), season of sperm collection (spring, summer, autumn, and winter), and average daily temperature during 0–90 days.
[b] Exposure time windows included three key periods of sperm development: epididymal storage (0–9 lag days), sperm motility development (10–14 lag days), spermatogenesis (70–90 lag days).

inconsistencies in results across these two studies may be due to differences in sample size (1,310 vs. 27,854) and accuracy in estimated daily PM_1 concentration (random forest models with $R^2 = 0.72$ vs. spatiotemporal artificial intelligence models with $R^2 = 0.77$).

Although it is not directly comparable, our findings are broadly stronger than the results from the emerging studies that examined the association of poor semen quality with $PM_{2.5}$ or PM_{10} (Dai et al. 2022; Guan et al. 2020; Xu et al. 2023; Zhao et al. 2022). For example, in a recent *meta*-analysis synthesizing 11 studies that examined the association between PM and sperm quality, Xu et al. (2023) reported that each 10 μg/m^3 increase in PM_{10} was associated with a 2.18% (95% CI: 0.10%, 4.21%) reduction in sperm concentration, 2.76% (95% CI: 0.10%, 5.35%) reduction in total sperm count, 0.75% (95% CI: 0.43%, 1.08%) reduction in total motility, and 0.31% (95% CI: 0.06%, 0.56%) reduction in progressive motility. The corresponding effect reduction associated with a 10 μg/m^3 increase in $PM_{2.5}$ was 2.00% (95% CI: −1.00%, 6.00%), 3.00% (95% CI: −2.00%, 8.00%), 1.06% (95% CI: 0.31%, 1.82%), and 0.55% (95% CI: 0.09%, 1.01%), respectively. In our study, a 10 μg/m^3 increase in PM_1 was associated with 2.61% (95% CI: 0.01%, 4.64%), 15.62% (95% CI: 11.67%, 19.87%), 0.05% (95% CI: 0.03%, 0.96%), and 1.29 % (95% CI: 0.83%, 1.74%) reduction in sperm concentration, sperm total count, total motility, and progressive motility, respectively.

Although the biological mechanism for the association between PM_1 exposure and semen quality is not yet clear, oxidative stress and inflammatory reactions, and disruption of endocrine activity have been proposed to be the underlying pathways. In vitro, Zhang et al. (2018) reported that exposure to PM inhibited cell viability and increased the reactive oxygen species (ROS) levels, leading to the release of lactate dehydrogenase and DNA damage (Zhang et al. 2018). Exposure to PM could also induce apoptosis via mitochondrial apoptosis resulting from oxidative stress and the disruption of the process of spermatogenesis (Liu et al. 2019). In addition, exposure to PM might damage the integrity of blood-testis barrier through ROS-mediated autophagy and thus disturb the development of sperm (Wei et al. 2018). Animal studies also suggested that exposure to PM could induce the alteration of DNA damage and histopathology in testes by triggering inflammatory actions (Zhou et al. 2019), such as increasing the expression of angiotensin-converting enzyme 2 (Lin et al. 2018).

We found that the association was stronger among underweight men for sperm concentration and sperm count. Previous studies suggested that being underweight was associated with low sperm concentration and sperm count, possibly due to malnutrition (Guo et al. 2019; Ma et al. 2019). Malnutrition is known as a detrimental factor for

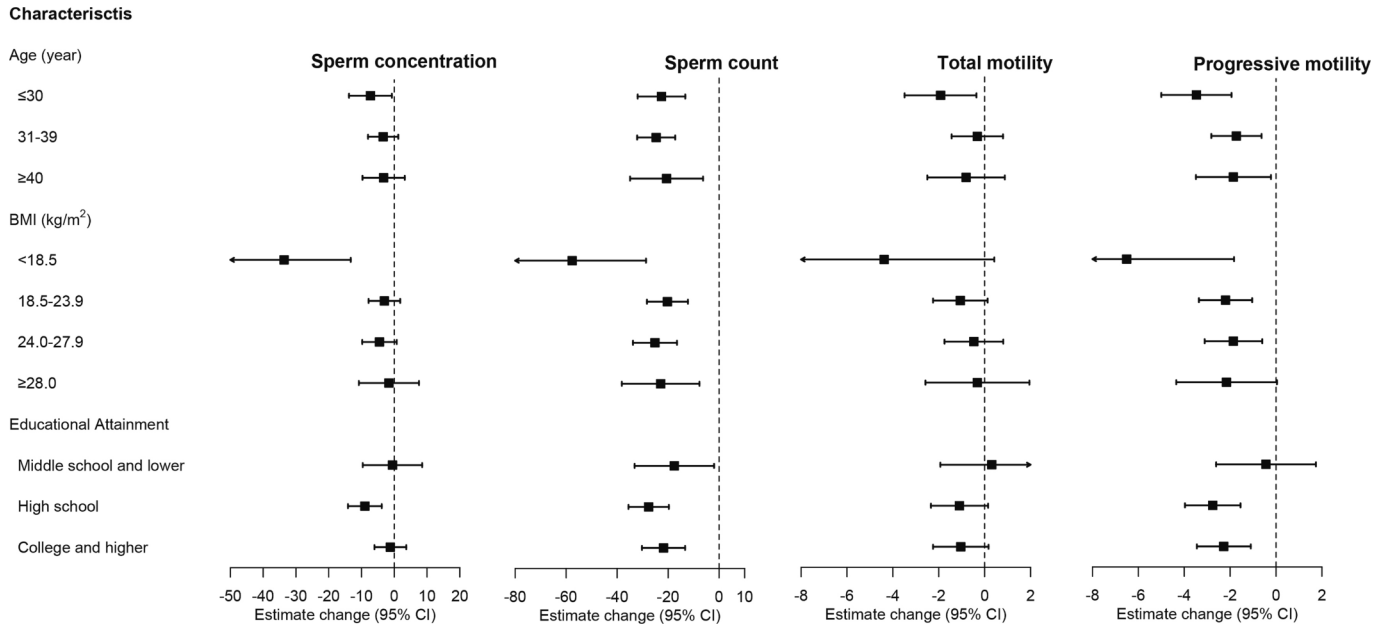

Fig. 3. Percent change of sperm quality associated with an interquartile range increase in PM_1 during the entire sperm development, stratified by age, body mass index, and educational attainment. Abbreviation: The multivariate linear model was used for adjusting age (≤30, 31–39, ≥ 40 years, unknown), body mass index (<18.5, 18.5–23.9, 24.0–27.9, ≥ 28.0 kg/m^2, unknown), ever having fathered a child (yes, no, unknown), educational attainment (middle school and lower, high school, college and higher, unknown), season of sperm collection (spring, summer, autumn, and winter), and average daily ambient temperature during 0-90 days.

Table 4
Percent changes or changes in semen quality parameters associated with an interquartile range increase in PM_1 after adjusting for co-pollutants during the entire period or among men with normal sperm quality.

Sensitivity analysis	Sperm concentration (% changes in millions/mL)	Sperm count (% changes in millions/sample)	Total motility (%)	Progressive motility (%)
Main results	−4.39 (-7.67, −1.12)	−23.56 (-28.95, −18.18)	−0.86 (-1.66, −0.06)	−2.22 (-3.00, −1.43)
Co-pollutant adjustment				
CO	−3.85 (-9.41, 1.70)	0.06 (-8.04, 8.16)	−0.33 (-1.69, 1.03)	0.61 (-0.72, 1.93)
SO_2	−3.30 (-6.66, 0.06)	−11.49 (-16.84, −6.14)	−1.31 (-2.13, −0.48)	−1.90 (-2.70, −1.10)
O_3	−6.19 (-9.21, −3.17)	−13.87 (-18.30, −9.44)	−1.29 (-2.03, −0.55)	−1.96 (-2.68, −1.24)
NO_2	−6.70 (-9.64, −3.76)	−20.69 (-25.24, −16.14)	−0.51 (-1.23, 0.21)	−1.11(-1.82, −0.41)
Among men with normal semen quality[a]	−9.74 (-12.48, −7.01)	−21.88 (-26.85, −16.91)	−1.82 (-2.43, −1.21)	−3.22 (-3.82, −2.62)

Abbreviations: PM_1 = particulate matter with aerodynamic diameter ≤ 1 μm; NO_2 = nitrogen dioxide; SO_2 = sulfur dioxide; O_3 = ozone; NO_2 = nitrogen dioxide. Models were adjusted for age (≤30, 31–39, ≥ 40 years, unknown), body mass index (<18.5, 18.5–23.9, 24.0–27.9, ≥ 28.0 kg/m^2, unknown), ever having fathered a child (yes, no, unknown), educational attainment (middle school and lower, high school, college and higher, unknown), season of sperm collection (spring, summer, autumn, and winter), and average daily ambient temperature.

[a] Men with normal semen quality was defined as men with sperm quality ≥ the World Health Organization reference values: sperm concentration (15 × 10^6/mL), total sperm count (39 × 10^6/sample), progressive motility (32% motile sperm) and total motility (40% motile sperm).

spermatogenesis by decreasing testosterone levels (Chik et al. 1989). The pathogenesis of malnutrition for the adverse effects of air pollutant on sperm quality might be speculated through increased oxidative stress, adipose tissue inflammation, elevated risk for chronic comorbidities, and insufficient exercise (An et al. 2018).

We found that the effects of PM_1 on sperm quality were more pronounced among men with normal sperm quality. Our findings were consistent with a study conducted in Nanjing, China (Wu et al. 2022), which reported a significant reduction in total motility and progressive motility associated with exposure to $PM_{2.5}$ among men with normal sperm quality but the association was not found in the semen abnormal group. This observation indicates that the general population may be more sensitive to PM_1 exposure.

To our knowledge, our study was the first to examine the critical exposure windows for the detrimental effects of PM_1 on sperm quality. We found that exposure to PM_1 was linked with declined sperm count and sperm progressive motility during the episodes of epididymal storage, sperm motility development, and spermatogenesis. Our findings were consistent with the four studies that identified critical exposure windows for $PM_{2.5}$ or PM_{10} and sperm parameters in China (Dai et al. 2022; Guan et al. 2020; Sun et al. 2020; Zhao et al. 2022). The study conducted in Wuhan, China suggested that the critical exposure window for PM_{10} and semen quality was during the 6th to 12th sperm development weeks (Sun et al. 2020). In an analysis of 33,876 men in Shanghai, China, the authors found that exposure to $PM_{2.5}$ was associated with sperm motility reduction during the epididymal storage, sperm motility development, and spermatogenesis, with more pronounced effects during the episodes of spermatogenesis (Zhao et al. 2022).

Our study has five main limitations. First, although we adjusted for a wide range of potential confounders, we might miss some unmeasured confounders, such as smoking status, alcohol consumption, and mental stress. Thus, we cannot exclude the possibility of residual confounding. Second, approximately 40% of the participants did not provide information about whether they ever had fathered a child, and therefore the interpretation of the results of this subgroup should be cautious. Third, we used ambient PM_1 as a proxy for personal exposure, we did not take individual movement into account. In our analysis, we also did not take PM_1 from indoor solid fuel use and biomass fuel use into account. However, these nondifferential exposure misclassifications might bias our results toward null association. Fourth, our participants were recruited from one infertility clinic, thus our findings might not be generalizable to general men or to other countries. Fifth, our participants included men with reproductive problems who might have abnormal reproduction cycles. In addition, we did not consider the delayed effects of PM_1 on semen quality. These might influence the results of PM_1 over the key periods of sperm development. On the other hand, our study is the largest analysis to date to examine the association between PM_1 exposure and sperm parameters including sperm concentration, sperm count, sperm total motility, and sperm progressive motility.

5. Conclusion

In summary, among 27,854 men who attended an infertility clinic in Hubei, China, we found that exposure to ambient PM_1 (especially during the 70–90 day before ejaculation) was associated with a reduction in sperm concentration, sperm count, sperm total motility, and sperm progressive motility. Our findings might be beneficial to the prevention of male infertility.

CRediT authorship contribution statement

Yangchang Zhang: Writing – original draft, Methodology, Data curation, Visualization, Investigation. **Jing Wei:** Writing – original draft, Writing – review & editing. **Chong Liu:** Writing – review & editing. **Wangnan Cao:** Writing – review & editing. **Zhenyu Zhang:** Writing – review & editing. **Yufeng Li:** Writing – review & editing, Supervision. **Qiang Zeng:** Writing – review & editing, Supervision. **Shengzhi Sun:** Conceptualization, Resources, Methodology, Supervision, Writing - original draft, Writing - review & editing.

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.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.107919.

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