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Environmental pollution and human fertility: investigating the relationship between PM2.5 exposure and assisted reproductive technology outcomes

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Abstract

Objective To investigate the impact of seasonal variations in particulate matter with an aerodynamic diameter of 2.5 µm or less (PM2.5) exposure on assisted reproductive technology (ART) outcomes.

Methods This retrospective study, conducted at the First People's Hospital of Shangqiu, analyzed data from 13,476 patients who underwent ART procedures between February 2018 and December 2022. Patients were categorized based on seasonal PM2.5 exposure levels. A generalized additive model (GAM), linear regression analysis, and multivariate logistic regression were used to assess the relationship between PM2.5 exposure and ART outcomes, including oocyte and embryo quality, pregnancy rates, live birth rates, and miscarriage rates.

Results Significant differences were observed in oocyte number, metaphase II (MII) oocyte number, transferable embryos, and good-quality embryos across seasonal PM2.5 exposure subgroups. Pregnancy rates and live birth rates also demonstrated statistically significant variations. Linear regression analysis revealed a consistent negative correlation between PM2.5 concentrations and key ART outcomes. Multivariate logistic regression analysis, adjusting for age and seasonal variations, confirmed a significant negative association between PM2.5 exposure and both pregnancy rates (OR = 0.995, 95% CI: 0.994–0.996, $p < 0.001$) and live birth rates (OR = 0.996, 95% CI: 0.995–0.997, $p < 0.001$). However, no significant relationship was found between PM2.5 exposure and miscarriage rates. GAM analysis further identified a nonlinear, threshold-like association between pregnancy outcomes and predictive factors, with significantly higher live birth rates observed in spring, summer, and autumn compared to winter.

Conclusions The study complements existing evidence that exposure to PM2.5 can lead to decreased success rates of pregnancy and live births, as well as significantly impact the outcomes of ART. Future research should focus on developing strategies to mitigate the adverse effects of environmental pollution on ART success rates.

Keywords PM2.5 exposure, Environmental factors, Seasonal variations, Pregnancy rates, Live birth, Assisted Reproductive Technology

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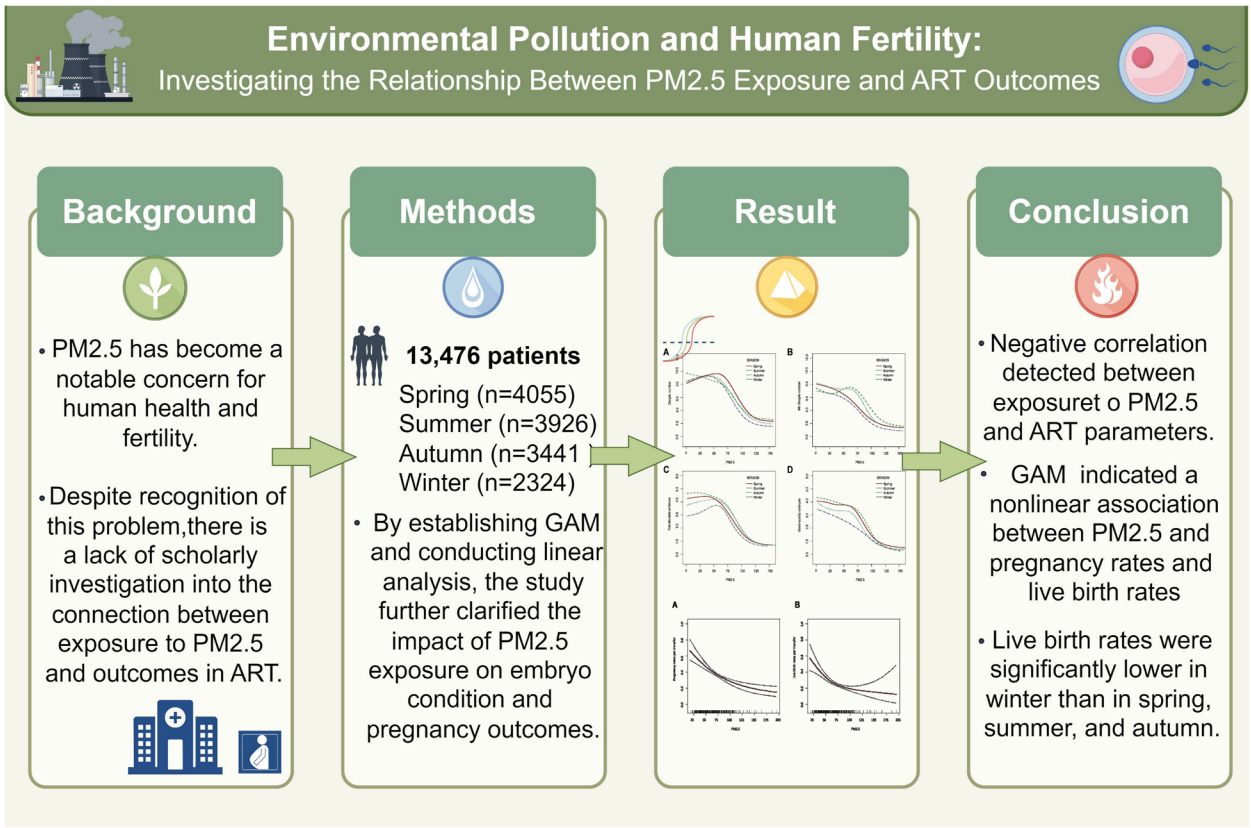
Graphical Abstract



Introduction

In recent decades, environmental pollution has emerged as a significant concern for human health and fertility [1, 2]. Fine particulate matter (PM2.5) has been identified as a prominent pollutant with documented adverse effects on the respiratory and cardiovascular systems [3, 4]. However, the impact of PM2.5 on reproductive health, specifically on the outcomes of Assisted Reproductive Technology (ART), has not been extensively studied. ART procedures have garnered heightened interest as a method for addressing infertility, with their success rates being susceptible to a variety of influencing factors [5, 6]. While established factors such as age, lifestyle, and genetic predisposition are recognized as significant determinants of ART outcomes [7], the potential impact of environmental exposures, particularly air pollution, has been relatively understudied.

Previous studies have hinted at a potential link between air pollution and reproductive health outcomes, including decreased fertility rates and increased risks of pregnancy complications [8, 9]. For instance, Leathersich et al. found that elevated PM2.5 exposure in the three months preceding oocyte retrieval correlates with reduced live birth rates. Specifically, live birth odds decreased by 34% in the highest PM2.5 quartile compared to the lowest [10]. Zhou et al. found that exposure to ambient airborne PM2.5 increases the risk of female infertility, highlighting the critical role of PM2.5 and/or air pollution in ovarian dysfunction through mitochondria-dependent and NF-κB/IL- 6-mediated pathways [11]. Similarly, Dai et al. demonstrated that exposure to PM2.5 causes damage to male reproductive function, in addition to its direct impacts on the respiratory and cardiovascular systems [12]. Another study demonstrates that air pollution exposure is linked to reduced rates of clinical pregnancy, biochemical pregnancy, and live birth. To enhance pregnancy outcomes, limiting air pollution exposure at least three months prior to IVF treatment is recommended [13]. A meta-analysis by Wang et al. found a positive association between adverse pregnancy outcomes (APOs) and PM2.5 exposure, with the degree of increased risk varying according to pregnancy-specific

factors [14]. Nevertheless, the aforementioned studies primarily focused on the potential impact of PM2.5 on infertility risk within the general population and are limited by small sample sizes. The mechanisms driving these associations and the effects of seasonal variations in PM2.5 exposure on reproductive outcomes remain inadequately elucidated. Given the prevalence of seasonal fluctuations in PM2.5 levels, it is plausible that they could variably influence reproductive health.

The present study aims to address this critical gap by investigating the impact of seasonal fluctuations in PM2.5 exposure on ART outcomes. Our hospital situated in central China with a warm temperate climate characterized by four distinct seasons and complex sources of PM2.5 including industrial emissions, traffic emissions, agricultural activities, and biomass combustion, provides a representative context for this investigation [15–17]. A previous study demonstrated that embryo transfers performed with embryos retrieved during the summer season were associated with a 30% higher likelihood of live birth compared to those retrieved in the autumn and winter [18]. To mitigate the potential confounding effects of seasonal and temperature variations on the study outcomes, we stratified patients according to the season in which they underwent treatment, and utilizing robust statistical models such as GAM, linear regression analysis, and multivariate logistic regression analysis, this study aims to clarify the relationship between PM2.5 exposure and key ART parameters, thereby enhancing our understanding of the impact of environmental exposures on reproductive health outcomes.

Methods

Study design and patient population

This retrospective cohort study was conducted at the First People's Hospital of Shangqiu. The study population comprised 13,476 patients who underwent ART procedures and received fresh cycle IVF transfers between February 1, 2018, and December 30, 2022. The patients were divided into four seasonal groups based on the day of ovarian stimulation: the Spring group with 4,055 patients (March–May), the Summer Group with 3,926 patients (June–August), the Autumn Group with 3,441 patients (September–November), and the Winter Group with 2,324 patients (December–February). Within each seasonal group, patients were further stratified based on PM2.5 exposure levels into three categories: < 50 μg/m3, 50–75 μg/m3, and > 75 μg/m3, the exposure period for PM2.5 was from the initiation of ovarian stimulation to the day of pregnancy test, spanning approximately 30 days, and the 30-day exposure window was selected based on the critical period of folliculogenesis and early embryo implantation.

The geographic coordinates (latitude and longitude) of both air quality monitoring stations and participants' residential addresses were obtained through the widely utilized online coordinate identification system (https://lbs.amap.com/tools/picker?spm), a geospatial service platform in China demonstrating an average positioning accuracy of 10–50 m in urban areas. Daily average PM2.5 concentrations ($\mu g/m^3$) were acquired from ground-based monitoring stations administered by the China National Environmental Monitoring Center (CNEMC). PM2.5 concentrations were measured using a beta-attenuation monitor (BAM- 1020), with the limit of detection (LOD) and limit of quantification (LOQ) determined as 0.8 $\mu g/m^3$ and 2.4 $\mu g/m^3$, respectively. These thresholds were calculated according to the instrument's technical manual, ensuring compliance with the Chinese National Ambient Air Quality Standards. Individual PM2.5 exposure levels were determined through a two-step spatiotemporal matching approach combining spatial matching with temporal alignment. The analyzed PM2.5 composition comprised sulfate, nitrate, ammonium, organic carbon (OC), elemental carbon (EC), along with heavy metals such as lead (Pb) and cadmium (Cd). To assess spatial interpolation accuracy, we conducted a leave-one-out cross-validation (LOOCV) by iteratively excluding each monitoring station and comparing predicted versus observed PM2.5 concentrations. The model performance showed a root mean square error (RMSE) of 3.9 $\mu g/m^3$ and mean R^2 of 0.72. The study protocol adhered to the ethical principles of the Declaration of Helsinki and was approved by the Institutional Review Board of The First People's Hospital of Shangqiu (No: SYY2023112). As a retrospective study, the Ethical Committee of the First People's Hospital of Shangqiu waived the requirement of informed consent.

Inclusion criteria were as follows: (1) having a menstrual cycle between 25 and 35 days and (2) residing in Henan, China. Exclusion criteria included: (1) cycles involving preimplantation genetic testing (PGT), (2) recipient cycles, donor cycles, and frozen-thawed cycles, (3) cycles with no oocytes retrieved or interrupted oocyte retrieval, (4) chromosomal abnormalities in either partner of the couple, and (5) cycles with incomplete data. Additionally, patients with endocrine and metabolic disorders, pelvic tuberculosis, or congenital uterine malformations were excluded.

Outcome measures

The primary outcome measures were the clinical pregnancy rates and the live birth rates. Clinical pregnancy was defined as the presence of one or more pregnancy sacs observed via ultrasound examination, encompassing normal intrauterine pregnancies, ectopic pregnancies,

intrauterine simultaneous pregnancies, as well as instances where only the pregnancy sac was visible without a fetal heartbeat [19]. The clinical pregnancy rates were calculated as the ratio of clinical pregnancy cycles to the total number of transplant cycles, expressed as a percentage. The live birth rates were determined as the proportion of live births at 28 weeks of gestation or beyond, also expressed as a percentage [20]. Secondary outcome measures included oocyte count, metaphase II (MII) oocyte count, number of transferable embryos and good-quality embryos, the definition of good-quality embryos encompasses first-grade and second-grade embryos according to the Gardner blastocyst grading system. These outcomes were compared across different PM2.5 level subgroups and seasons using statistical tests appropriate for the data distribution. Additionally, the abortion rate was considered as a secondary measure. All abortion cases were characterized by spontaneous embryonic arrest, which is clinically defined as pregnancy termination occurring before 28 weeks of gestation, accompanied by a fetal weight below the threshold of 1000 g [21]. The abortion rate was calculated as the ratio of abortion cycles to the number of clinical pregnancy cycles, expressed as a percentage.

ART procedures

Patients underwent ovulation induction primarily using either an agonist or antagonist protocol. Embryo quality assessment was systematically performed at 72 h post-oocyte retrieval using standardized morphological evaluation criteria, and embryo transfer was routinely performed on day 3 after oocyte retrieval, while blastocyst transfer was conducted on day 5 post-retrieval. Following the transfer of embryos or blastocysts, patients received luteal phase support through progesterone administration. Pregnancy testing was performed 14 days after embryo transfer by measuring serum beta-human chorionic gonadotropin (β-hCG) levels. A positive β-hCG test indicated a successful pregnancy, whereas a negative test signified non-conception.

For patients undergoing the agonist protocol, pituitary down-regulation was achieved through intramuscular administration of 3.75 mg long-acting GnRH agonist (Diphereline, Ipsen Pharma, France) during the early follicular phase (menstrual cycle days 2–3). Ultrasound examinations and serum hormone assessments (LH, FSH, progesterone) were performed to confirm down-regulation criteria. Ovarian stimulation commenced with individualized gonadotropin dosing (72.5–300 IU/day) based on comprehensive patient characteristics including age, AFC, BMI, and prior ovarian response. Final oocyte maturation was triggered using dual medication: 2000 IU urinary-derived hCG (Livzon Pharmaceutical Group, China) combined with 250 μg recombinant hCG (Ovidrel, Merck Serono, Germany), administered when ≥3 dominant follicles reached 17–18 mm in diameter. Transvaginal oocyte retrieval was systematically performed 36–37 h post-trigger under ultrasound guidance.

For patients undergoing the antagonist protocol, initiated ovarian stimulation with daily gonadotropin injections (Puregon, Organon, Netherlands; 72.5–300 IU) beginning on cycle days 2–3. Cetrorelix acetate (Cetrotide, Pierre Fabre Medicament, France) was introduced when lead follicle diameter attained 12–14 mm, with daily dosages titrated between 0.25–0.75 mg based on follicular growth dynamics.Triggering medication consisted of 5000 IU urinary hCG (Livzon) supplemented with 2000 IU urinary hCG or 250 μg recombinant hCG, administered upon observing ≥2 follicles ≥17 mm. Oocyte retrieval procedures were conducted 35–37 h post-trigger using standardized aspiration techniques (17-gauge needle, 100–120 mmHg vacuum pressure).

Statistical analysis

All statistical analyses were performed using R (version 4.3.2) and SPSS 26.0 (IBM, Armonk, NY, USA) software. For seasonally grouped data, the Shapiro–Wilk test was employed to verify data normality. Continuous variables were expressed as medians with interquartile ranges, while categorical variables were presented in terms of ratios (%). One-way ANOVA was utilized for comparisons of continuous variables among multiple groups, Chi-square tests for comparisons of categorical variables, and Kruskal–Wallis tests for post hoc comparisons. PM2.5 concentrations were analyzed as continuous variables in all regression models, Statistical significance was set at $p < 0.05$.

Linear regression analysis was conducted to quantify the relationship between PM2.5 concentrations and key ART parameters, specifically oocyte number, MII oocyte number, transferable embryos, and good-quality embryos, regression coefficients (β) and 95% confidence intervals (CIs) were reported. Multivariate logistic regression analysis was performed to quantify the relationship between PM2.5 concentrations and pregnancy rates and the live birth rates, adjusting for age and seasonal variations, to account for potential confounders. Odds ratios (ORs) and 95% CIs were calculated to assess the associations' strength and direction. Furthermore, GAM were employed to explore threshold and nonlinear associations between pregnancy outcomes and predictive factors. Additionally, logistic regression analysis was conducted to investigate seasonal variations in ART outcomes, comparing pregnancy rates, live birth rates, and miscarriage rates across seasons, with winter as the

reference, adjusted ORs and 95% CIs were reported to quantify seasonal effects.

Result

The study conducted a retrospective analysis of patient data from the First People's Hospital of Shangqiu, encompassing the period from February 1st, 2018, to December 30 th, 2022. A total of 13, 476 patients were included in the study, with 4,055 patients comprising the Spring group, 3,926 patients in the Summer Group, 3,441 patients in the Autumn Group, and 2,324 patients in the Winter Group. Within each seasonal group, patients were further stratified based on PM2.5 exposure levels into three categories: < 50 μg/m3, 50–75 μg/m3, and > 75 μg/m3.

In the Spring and Summer groups, the differences in age, education, BMI, and basal hormone levels among the PM2.5 subgroups were not clinically significant $p > 0.05$). However, in the Spring group, basal E2 levels ($p = 0.035$) and P levels ($p = 0.005$) exhibited significant variations across the PM2.5 categories. In the Summer group, significant differences were observed in basal P levels ($p = 0.049$), T levels ($p = 0.008$), and AMH levels ($p = 0.022$) across the PM2.5 categories (Table 1). In the Autumn

Table 1 Comparison of baseline parameters of different concentrations of PM2.5 between spring group and summer group

Season	Spring Group, $N = 4055$				Summer Group, $N = 3926$			
PM2.5 Group	**< 50 μg/m^3 N = 2220 (55%)[1]**	**50–75 μg/m^3 N = 784 (19%)[1]**	**> 75 μg/m^3 N = 1051 (26%)[1]**	***p*-value[2]**	**< 50 μg/m^3 N = 2067 (53%)[1]**	**50–75 μg/m^3 N = 793 (20%)[1]**	**> 75 μg/m^3 N = 1066 (27%)[1]**	***p*-value[2]**
Infertility years	3.00 [2.00, 6.00]	4.00 [2.00, 6.00]	3.00 [2.00, 6.00]	0.861	4.00 [2.00, 6.00]	4.00 [2.00, 7.00]	3.00 [2.00, 6.00]	0.142
Age				0.113				0.112
< 30 years	588 (26.49%)	226 (28.83%)	244 (23.22%)		455 (22.01%)	205 (25.85%)	282 (26.45%)	
30–35 years	678 (30.54%)	241 (30.74%)	339 (32.25%)		685 (33.14%)	232 (29.26%)	317 (29.74%)	
36–40 years	474 (21.35%)	149 (19.01%)	245 (23.31%)		445 (21.53%)	170 (21.44%)	252 (23.64%)	
> 40 years	480 (21.62%)	168 (21.43%)	223 (21.22%)		482 (23.32%)	186 (23.46%)	215 (20.17%)	
Education				0.741				0.623
Hish school and lower	1,288 (58.02%)	456 (58.16%)	612 (58.23%)		1,155 (55.88%)	448 (56.49%)	571 (53.56%)	
College graduate	846 (38.11%)	289 (36.86%)	398 (37.87%)		816 (39.48%)	313 (39.47%)	443 (41.56%)	
Post-graduate	86 (3.87%)	39 (4.97%)	41 (3.90%)		96 (4.64%)	32 (4.04%)	52 (4.88%)	
BMI				0.241				0.089
< 23.9 kg/m	1,357 (61.13%)	480 (61.22%)	649 (61.75%)		1,217 (58.88%)	452 (57.00%)	637 (59.76%)	
23.9–29.9 kg/m	697 (31.40%)	237 (30.23%)	324 (30.83%)		699 (33.82%)	280 (35.31%)	329 (30.86%)	
29.9–35 kg/m	37 (1.67%)	11 (1.40%)	27 (2.57%)		51 (2.47%)	13 (1.64%)	27 (2.53%)	
> 35 kg/m	129 (5.81%)	56 (7.14%)	51 (4.85%)		100 (4.84%)	48 (6.05%)	73 (6.85%)	
Basal FSH (IU/L)	7.34 [6.12, 9.27]	7.21 [5.95, 9.31]	7.43 [6.05, 9.33]	0.531	7.41 [5.98, 9.63]	7.27 [5.96, 9.47]	7.40 [6.00, 9.69]	0.735
Basal E2 (ng/L)	36.11 [24.25, 49.78]	38.28 [24.69, 53.31]	35.66 [24.26, 49.29][b]	0.035	36.01 [23.89, 52.38]	35.61 [24.03, 55.36]	34.83 [23.63, 50.38]	0.263
Basal P (μg/L)	0.45 [0.30, 0.67]	0.50 [0.34, 0.71][a]	0.47 [0.32, 0.68]	0.005	0.46 [0.32, 0.68]	0.47 [0.33, 0.67]	0.45 [0.29, 0.65][b]	0.049
PRL (ng/L)	14.84 [10.72, 20.76]	15.25 [11.20, 21.32]	14.75 [10.69, 19.85]	0.112	14.95 [10.87, 20.40]	14.45 [10.92, 19.78]	14.66 [10.65, 20.41]	0.683
Basal LH (IU/L)	4.87 [3.47, 6.52]	4.92 [3.61, 6.55]	4.81 [3.30, 6.51]	0.305	4.61 [3.34, 6.21]	4.61 [3.36, 6.29]	4.72 [3.52, 6.58]	0.085
T(ng/mL)	0.23 [0.14, 0.33]	0.24 [0.17, 0.33]	0.24 [0.15, 0.35][a]	0.002	0.21 [0.14, 0.31]	0.23 [0.15, 0.32]	0.21 [0.14, 0.31][a]	0.008
AMH (ng/mL)	1.77 [0.59, 2.86]	1.84 [0.61, 2.97]	1.69 [0.59, 2.85]	0.573	1.62 [0.60, 2.69]	1.83 [0.66, 2.82][a]	1.89 [0.55, 2.97][a]	0.022
AFC(n)	8.00 [3.00, 14.00]	9.00 [3.00, 14.00]	9.00 [3.00, 14.00]	0.716	8.00 [3.00, 13.00]	8.00 [3.00, 13.00]	9.00 [3.00, 14.00]	0.201

BMI Body mass index, *FSH* Follicular-stimulating hormone, *E2* Estradiol, *P* Progesterone, *LH* Luteinizing hormone, *AMH* Anti-Müllerian hormone, *AFC* Antral Follicle Countin

[a] $P < 0.05$, vs. PM2.5 < 50 μg/m^3

[b] $P < 0.05$, vs. PM2.5 50–75 μg/m^3

[1] Median [IQR]; or n (%)

[2] Kruskal-Wallis rank sum test; or Pearson's Chi-squared test

and Winter groups, no statistically significant differences were observed in age, education, or BMI among the PM2.5 subgroups ($p > 0.05$). In the Autumn group, significant differences were noted in basal E2 levels ($p = 0.009$), PRL levels ($p = 0.036$), and P levels ($p = 0.038$) across the PM2.5 categories. In contrast, no significant differences were found in any of the indices in the Winter group (Table 2).

In the Spring and Summer Groups, no statistically significant differences were observed in terms of Total Gn dose and duration of Gn use across the PM2.5 level subgroups ($P > 0.05$). However, notable disparities emerged in oocyte number, MII oocyte number, transferable embryos, and good-quality embryos among the PM2.5 level subgroups ($p < 0.001$ for all pairwise comparisons). Similarly, pregnancy rates and live birth rates demonstrated statistically significant variations ($p < 0.001$), with lower rates observed in the subgroups exposed to higher PM2.5 levels. It is worth noting that while miscarriage rates did not differ significantly within the Spring group ($p = 0.950$), they did exhibit statistical significance in the Summer Group ($p = 0.003$). (Table 3).

In the Autumn and Winter Groups, no statistically significant disparities were found in Total Gn doses and

Table 2 Comparison of baseline parameters of different concentrations of PM2.5 between autumn group and winter group

Season	Autumn group, $N = 3441$				Winter group, $N = 2324$			
PM2.5 group	**< 50 μg/m³ N = 1864 (54%)[1]**	**50–75 μg/m³ N = 749 (22%)[1]**	**> 75 μg/m³ N = 828 (24%)[1]**	***p*-value[2]**	**< 50 μg/m³ N = 953 (41%)[1]**	**50–75 μg/m³ N = 668 (29%)[1]**	**> 75 μg/m³ N = 703 (30%)[1]**	***p*-value[2]**
Infertility years	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	4.00 [2.00, 6.00]	0.515	4.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 7.00]	0.714
Age				0.472				0.064
< 30 years	449 (24.09%)	187 (24.97%)	214 (25.85%)		336 (26.82%)	123 (26.28%)	133 (22.06%)	
30–35 years	512 (27.47%)	234 (31.24%)	227 (27.42%)		299 (23.86%)	136 (29.06%)	170 (28.19%)	
36–40 years	453 (24.30%)	171 (22.83%)	199 (24.03%)		338 (26.98%)	121 (25.85%)	175 (29.02%)	
> 40 years	450 (24.14%)	157 (20.96%)	188 (22.71%)		280 (22.35%)	88 (18.80%)	125 (20.73%)	
Education				0.677				0.381
Hish school and lower	1,039 (55.74%)	395 (52.74%)	469 (56.64%)		634 (50.60%)	239 (51.07%)	332 (55.06%)	
College graduate	750 (40.24%)	322 (42.99%)	325 (39.25%)		570 (45.49%)	214 (45.73%)	246 (40.80%)	
Post-graduate	75 (4.02%)	32 (4.27%)	34 (4.11%)		49 (3.91%)	15 (3.21%)	25 (4.15%)	
BMI				0.763				0.142
< 23.9 kg/m	1,167 (62.61%)	463 (61.82%)	505 (60.99%)		764 (60.97%)	269 (57.48%)	384 (63.68%)	
23.9–29.9 kg/m	585 (31.38%)	227 (30.31%)	266 (32.13%)		363 (28.97%)	150 (32.05%)	178 (29.52%)	
29.9–35 kg/m	39 (2.09%)	20 (2.67%)	21 (2.54%)		36 (2.87%)	22 (4.70%)	13 (2.16%)	
> 35 kg/m	73 (3.92%)	39 (5.21%)	36 (4.35%)		90 (7.18%)	27 (5.77%)	28 (4.64%)	
Basal FSH (IU/L)	7.53 [6.01, 9.66]	7.47 [6.04, 9.53]	7.50 [6.18, 9.84]	0.996	7.49 [6.17, 9.52]	7.28 [6.15, 9.83]	7.30 [5.94, 9.96]	0.615
Basal E2 (ng/L)	35.93 [24.57, 53.98]	35.58 [25.36, 51.50]	33.91 [23.68, 49.57][ab]	0.009	35.32 [23.71, 51.10]	35.61 [23.01, 50.15]	38.08 [25.70, 51.28]	0.117
Basal P (μg/L)	0.47 [0.30, 0.67]	0.47 [0.31, 0.65]	0.50 [0.32, 0.68][ab]	0.036	0.45 [0.30, 0.61]	0.47 [0.30, 0.66]	0.45 [0.30, 0.64]	0.384
PRL (ng/L)	14.70 [10.52, 20.86]	15.12 [10.45, 21.61]	16.13 [11.00, 21.53][a]	0.038	14.00 [10.36, 19.63]	14.69 [10.67, 20.08]	14.38 [10.62, 19.28]	0.532
Basal LH (IU/L)	4.54 [3.32, 6.38]	4.86 [3.56, 6.40]	4.55 [3.46, 6.26]	0.051	4.84 [3.46, 6.33]	5.00 [3.68, 6.83]	4.70 [3.53, 6.52]	0.075
T(ng/mL)	0.23 [0.15, 0.32]	0.23 [0.14, 0.31]	0.23 [0.15, 0.32]	0.847	0.22 [0.14, 0.31]	0.22 [0.14, 0.32]	0.20 [0.14, 0.30]	0.763
AMH (ng/mL)	1.58 [0.49, 2.66]	1.69 [0.58, 2.72]	1.66 [0.57, 2.85]	0.092	1.53 [0.55, 2.69]	1.82 [0.67, 2.72]	1.70 [0.66, 2.58]	0.081
AFC(n)	7.00 [3.00, 13.00]	8.00 [3.00, 13.00]	8.00 [3.00, 13.00]	0.057	7.00 [3.00, 13.00]	8.50 [4.00, 13.00]	8.00 [3.00, 14.00]	0.038

BMI Body mass index, *FSH* Follicular-stimulating hormone, *E2* Estradiol, *P* Progesterone, *LH* Luteinizing hormone, *AMH* Anti-Müllerian hormone, *AFC* Antral Follicle Countin

[a] $P < 0.05$, vs. PM2.5 < 50 μg/m³

[b] $P < 0.05$, vs. PM2.5 50–75 μg/m³

[1] Median [IQR]; or n (%)

[2] Kruskal–Wallis rank sum test; or Pearson's Chi-squared test

Table 3 Comparison of controlled ovulation induction and pregnancy outcomes of different concentrations of PM2.5 between spring group and summer group

Season	Spring group, $N = 4055$				Summer group, $N = 3926$			
PM2.5 group	**< 50 μg/m³ N = 2220 (55%)[1]**	**50–75 μg/m³ N = 784 (19%)[1]**	**> 75 μg/m³ N = 1051 (26%)[1]**	***p*-value[2]**	**< 50 μg/m³ N = 2067 (53%)[1]**	**50–75 μg/m³ N = 793 (20%)[1]**	**> 75 μg/m³ N = 1066 (27%)[1]**	***p*-value[2]**
Total Gn dose	2,700.00 [1,912.50, 3,600.00]	2,700.00 [1,925.00, 3,487.50]	2,850.00 [2,100.00, 3,600.00][ab]	0.145	2,850.00 [2,100.00, 3,525.00]	2,925.00 [2,000.00, 3,612.50][a]	2,700.00 [1,950.00, 3,450.00][ab]	0.116
Gn using days	12.00 [10.00, 14.00]	12.00 [10.00, 14.00]	12.00 [10.00, 14.00]	0.671	12.00 [10.00, 13.00]	12.00 [11.00, 14.00][a]	12.00 [10.00, 14.00][ab]	0.101
Oocyte number (n)	7.00 [5.00, 9.00]	8.00 [4.00, 10.00][a]	2.00 [1.00, 3.00][ab]	< 0.001	7.00 [5.00, 9.00]	7.00 [4.00, 10.00][a]	2.00 [1.00, 4.00][ab]	< 0.001
MII oocyte number (n)	6.00 [4.00, 7.00]	6.00 [3.00, 8.00][a]	1.00 [1.00, 3.00][ab]	< 0.001	6.00 [4.00, 7.00]	6.00 [3.00, 9.00][a]	1.00 [1.00, 3.00][ab]	< 0.001
Transferable embryos (n)	2.00 [2.00, 4.00]	2.00 [1.00, 4.00][a]	1.00 [1.00, 2.00][ab]	< 0.001	2.00 [2.00, 4.00]	2.00 [1.00, 3.00][a]	1.00 [1.00, 2.00][ab]	< 0.001
Good-quality embryos (n)	2.00 [1.00, 4.00]	2.00 [1.00, 4.00][a]	1.00 [1.00, 1.00][ab]	< 0.001	2.00 [1.00, 4.00]	2.00 [1.00, 4.00][a]	1.00 [1.00, 1.00][ab]	0.012
Pregnancy rates per transfer				< 0.001				< 0.001
Yes	1,058 (47.66%)	279 (35.59%)[a]	213 (20.27%)[ab]		1071 (51.88%)	268 (33.82%)[a]	221 (20.73%)[ab]	
No	1,132 (50.10%)	505 (64.41%)	838 (79.73%)		996 (48.12%)	525 (66.18%)	845 (79.27%)	
Miscarriage rates				0.950				0.003
Yes	79 (7.45%)	22 (7.89%)	17 (7.98%)		88 (8.22%)	23(8.58%)	34 (15.38%)[ab]	
No	979 (92.55%)	257 (92.11%)	196(92.02%)		983 (91.78%)	245(91.42%)	187 (84.62%)	
Live birth rates per transfer				< 0.001				< 0.001
Yes	979 (44.10%)	257 (32.78%)[a]	196 (18.65%)[ab]		983 (47.50%)	245 (30.90%)[a]	187 (17.54%)[ab]	
No	1,241 (55.90%)	527 (67.22%)	855 (81.35%)		1084 (52.50%)	548 (69.10%)	879 (82.46%)	

Gn:gonadotropin; MII, metaphase II

[a] $P < 0.05$, vs. PM2.5 < 50 μg/m³

[b] $P < 0.05$, vs. PM2.5 50–75 μg/m³

[1] Median [IQR]; or n (%)

[2] Kruskal–Wallis rank sum test; or Pearson's Chi-squared test

duration of Gn use across the PM2.5 level subgroups. Nevertheless, considerable differences were observed in oocyte number, MII oocyte number, transferable embryos, and good-quality embryos among the PM2.5 level subgroups within both seasons ($p < 0.001$), except for transferable embryos in Winter ($p = 0.013$). Pregnancy rates and live birth rates also demonstrated statistically significant differences ($p < 0.001$), with lower rates associated with higher PM2.5 levels. Miscarriage rates did not exhibit any significant differences in either season ($p = 0.609$ for Autumn and $p = 0.065$ for Winter). (Table 4).

The results of the linear regression analysis reveal a statistically significant negative correlation between PM2.5 concentrations and four key parameters: oocyte number, MII oocyte number, transferable embryos, and good-quality embryos, this association remains consistent across all seasons (Fig. 1 and 2). In the spring season, linear regression analyses adjusted for basal E2, basal P, and T levels demonstrated that each unit increase in PM2.5 exposure was associated with significant reductions in oocyte number (β = − 0.034, 95% CI: − 0.039 to − 0.030, $p < 0.001$), MII oocyte number (β = − 0.026, 95% CI: − 0.028 to − 0.024, $p < 0.001$), transferable embryos (β = β = − 0.015, 95% CI: − 0.017 to − 0.013, $p < 0.001$), good-quality embryos (β = − 0.015, 95% CI: − 0.018 to − 0.013, $p < 0.001$). In the summer season, linear regression analyses adjusted for basal P, T, and AMH levels demonstrated that each unit increase in PM2.5 exposure was associated with significant reductions in oocyte number (β = − 0.043, 95% CI: − 0.049 to − 0.038; $p < 0.001$), MII oocyte number (β = − 0.031, 95% CI: − 0.036 to − 0.027; $p < 0.001$), transferable embryos (β = − 0.023, 95% CI: − 0.027 to − 0.019; $p < 0.001$), and high-quality embryos (β

Table 4 Comparison of controlled ovulation induction and pregnancy outcomes of different concentrations of PM2.5 between Autumn group and Winter group

Season	Autumn Group, $N = 3441$				Winter Group, $N = 2324$			
PM2.5 Group	**< 50 μg/m³ N = 1864 (54%)[1]**	**50–75 μg/m³ N = 749 (22%)[1]**	**> 75 μg/m³ N = 828 (24%)[1]**	***p*-value[2]**	**< 50 μg/m³ N = 953 (41%)[1]**	**50–75 μg/m³ N = 668 (29%)[1]**	**> 75 μg/m³ N = 703 (30%)[1]**	***p*-value[2]**
Total Gn doses	2,712.50 [2,025.00, 3,550.00]	2,850.00 [2,000.00, 3,600.00]	2,875.00 [2,000.00, 3,600.00]	0.583	2,850.00 [2,100.00, 3,600.00]	3,000.00 [2,212.50, 3,606.25]	2,800.00 [2,072.25, 3,600.00]	0.351
Gn using days	12.00 [10.00, 14.00]	12.00 [10.00, 14.00]	12.00 [10.00, 14.00]	0.104	12.00 [10.00, 14.00]	13.00 [10.00, 14.00][a]	12.00 [10.00, 14.00][ab]	0.131
Oocyte number (n)	7.00 [5.00, 9.00]	7.00 [4.00, 9.00][a]	2.00 [1.00, 3.00][ab]	< 0.001	7.00 [5.00, 9.00]	7.00 [4.00, 9.00][a]	2.00 [1.00, 3.00][ab]	< 0.001
MII oocyte number (n)	6.00 [4.00, 7.00]	6.00 [3.00, 8.00][a]	1.00 [1.00, 2.00][ab]	< 0.001	6.00 [4.00, 7.00]	6.00 [3.00, 8.00][a]	1.00 [1.00, 2.00][ab]	< 0.001
Transferable embryos (n)	3.00 [2.00, 4.00]	2.00 [1.00, 3.00][a]	1.00 [1.00, 1.00][ab]	< 0.001	3.00 [2.00, 4.00]	2.00 [1.00, 3.00][a]	1.00 [1.00, 1.00][ab]	0.013
Good-quality embryos (n)	2.00 [1.00, 4.00]	2.00 [1.00, 4.00][a]	1.00 [1.00, 1.00][ab]	< 0.001	2.00 [1.00, 4.00]	2.00 [1.00, 4.00][a]	1.00 [1.00, 1.00][ab]	0.008
Pregnancy rates per transfer				< 0.001				< 0.001
Yes	935 (50.16%)	371 (49.53%)	168 (20.29%)[ab]		423 (44.39%)	277 (41.47%)	215 (30.58%)[ab]	
No	929 (49.84%)	378 (50.47%)	660 (79.71%)		530 (55.61%)	391 (58.53%)	488 (69.42%)	
Miscarriage rates				0.609				0.065
Yes	83 (8.89%)	32 (8.62%)	11 (6.55%)		38 (8.98%)	21 (7.58%	14 (6.51%)	
No	852 (91.11%)	339 (93.45%)	157 (93.45%)		385 (91.02%)	256 (92.42%)	201 (93.49%)	
Live birth rates per transfer				< 0.001				< 0.001
Yes	852 (45.70%)	339 (45.29%)	157 (19.01%)[ab]		385 (40.40%)	256 (38.32%)	201 (28.59%)[ab]	
No	1012 (54.30%)	410 (54.71%)	671 (80.99%)		568 (59.60%)	412 (61.68%)	502 (81.41%)	

[1] Median [IQR]; or n (%)

[2] Kruskal–Wallis rank sum test; or Pearson's Chi-squared test

Gn:gonadotropin; MII, metaphase II

[a] $P < 0.05$, vs. PM2.5 < 50 μg/m³

[b] $P < 0.05$, vs. PM2.5 50–75 μg/m³

= − 0.013, 95% CI: − 0.016 to − 0.010; $p = 0.013$). For the autumn season, after adjustment for basal E2, basal P, and PRL, each PM2.5 unit increase correlated with decreased oocyte retrieval (β = − 0.032, 95% CI: − 0.035 to − 0.030; $p < 0.001$), reduced MII oocytes (β = − 0.025, 95% CI: − 0.028 to − 0.023; $p < 0.001$), fewer transferable embryos (β = − 0.010, 95% CI: − 0.011 to − 0.009; $p < 0.001$), and diminished high-quality embryos (β = − 0.010, 95% CI: − 0.011 to − 0.008; $p < 0.001$). In winter season analyses adjusted for AFC, PM2.5 elevation per unit significantly predicted reduced oocyte numbers (β = − 0.020, 95% CI: − 0.023 to − 0.016; $p < 0.001$), decreased MII oocytes (β = − 0.017, 95% CI: − 0.019 to − 0.015; $p < 0.001$), fewer transferable embryos (β = − 0.015, 95% CI: − 0.017 to − 0.013; $p = 0.034$), and reduced high-quality embryos (β = − 0.009, 95% CI: − 0.012 to − 0.005; $p = 0.013$) (Table 5).

To further explore the relationship between PM2.5 and pregnancy outcomes, a multivariate logistic regression analysis was conducted, incorporating age and seasonal variations as potential confounders. The analysis indicates that age significantly impacts pregnancy rates ($p < 0.001$), miscarriage rates ($p = 0.002$), and live birth rates ($p < 0.001$). With regard to PM2.5 exposure, a statistically significant negative association is noted with pregnancy rates (OR = 0.995, 95% CI: 0.994 ~ 0.996, $p < 0.001$), a negative association emerges with live birth rates (OR = 0.996, 95% CI: 0.995 ~ 0.997, $p < 0.001$). The adjusted GAM revealed a non-linear association between PM2.5 exposure and both pregnancy rates and live birth rates, while PM2.5 exhibited a negative correlation with these outcomes, the relationship was not characterized by a simple linear pattern (Fig. 2). The association between PM2.5 exposure and miscarriage

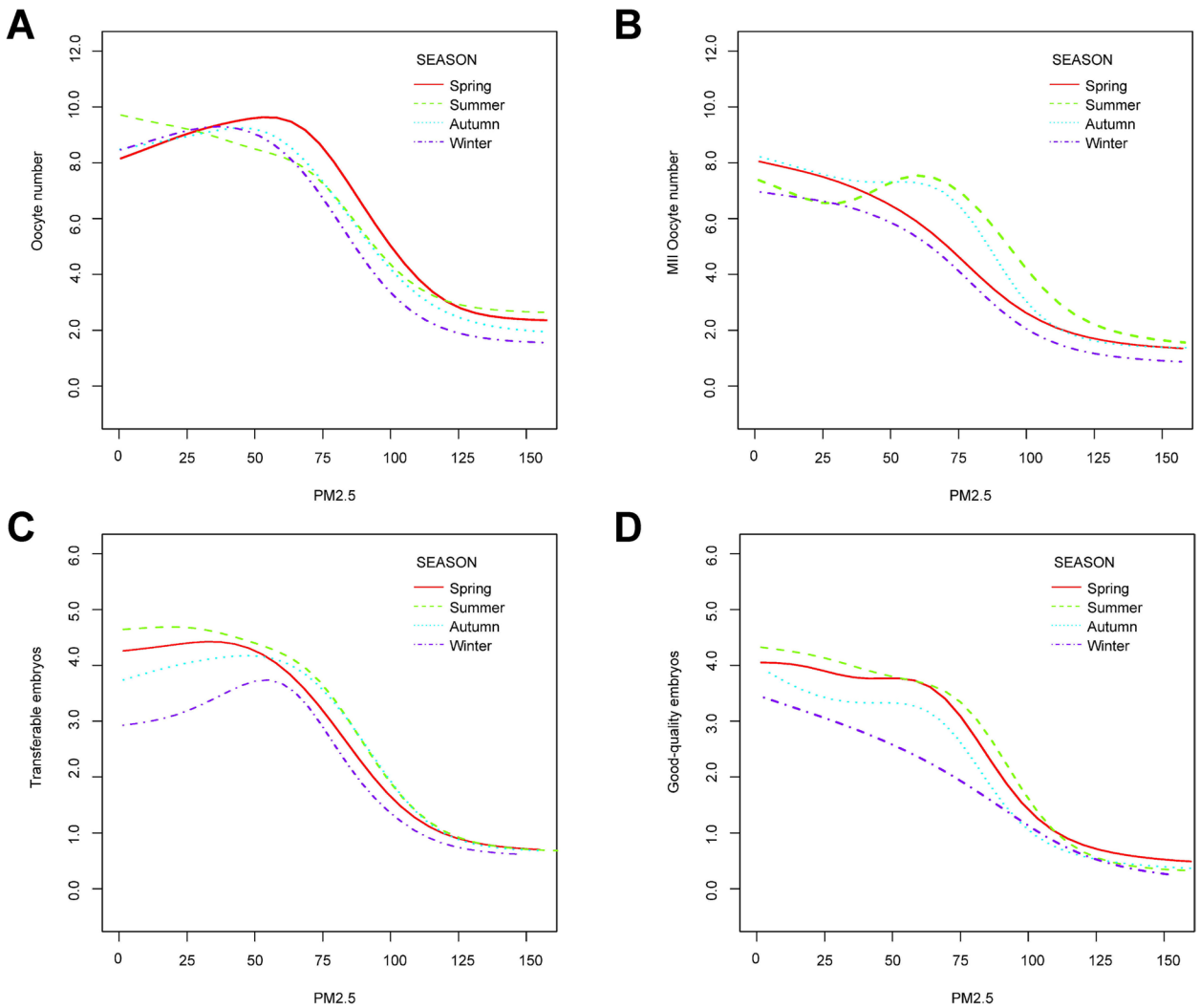


Fig. 1 Linear relationship between PM2.5 and oocyte number (**A**), MII oocyte number (**B**), transferable embryos (**C**) and good-quality embryos (**D**) in different seasons, in which the solid red line represents spring group, the dotted green line represents summer group, the dotted blue line represents autumn group, and the dotted purple line represents winter group

rates did not demonstrate statistical significance (OR = 1.016, 95% CI: 0.894 ~ 1.127, $p = 0.281$). Additionally, seasonal variations are found to have an influence on pregnancy outcomes. Compared to winter, both spring (OR = 1.192, 95% CI: 1.060 ~ 1.341, $p = 0.003$) and summer (OR = 1.080, 95% CI: 0.959 ~ 1.217, $p = 0.205$) exhibit higher pregnancy rates per transfer, with spring showing statistical significance. Similarly, live birth rates are significantly elevated in spring (OR = 1.141, 95% CI: 1.006 ~ 1.295, $p = 0.040$), summer (OR = 1.063, 95% CI: 1.015 ~ 1.207, $p = 0.035$) and autumn (OR = 1.142, 95% CI: 1.002 ~ 1.300, $p = 0.046$) when compared to winter. However, no significant seasonal differences were observed for miscarriage rates.(Table 6).

Discussion

The correlation between PM2.5 exposure and the outcomes of ART treatment remains a subject of ongoing debate in current research. Prior studies have predominantly concentrated on the influence of air pollution on natural conception, often with small sample sizes and employing singular research approaches [22–24]. Consequently, these studies have not adequately captured the nuanced impacts of PM2.5 exposure on embryonic conditions and the associated outcomes of ART. The findings of this study demonstrate a consistent adverse relationship between PM2.5 levels and important ART outcomes, including oocyte number, MII oocyte number, transferable embryos, and good-quality embryos.

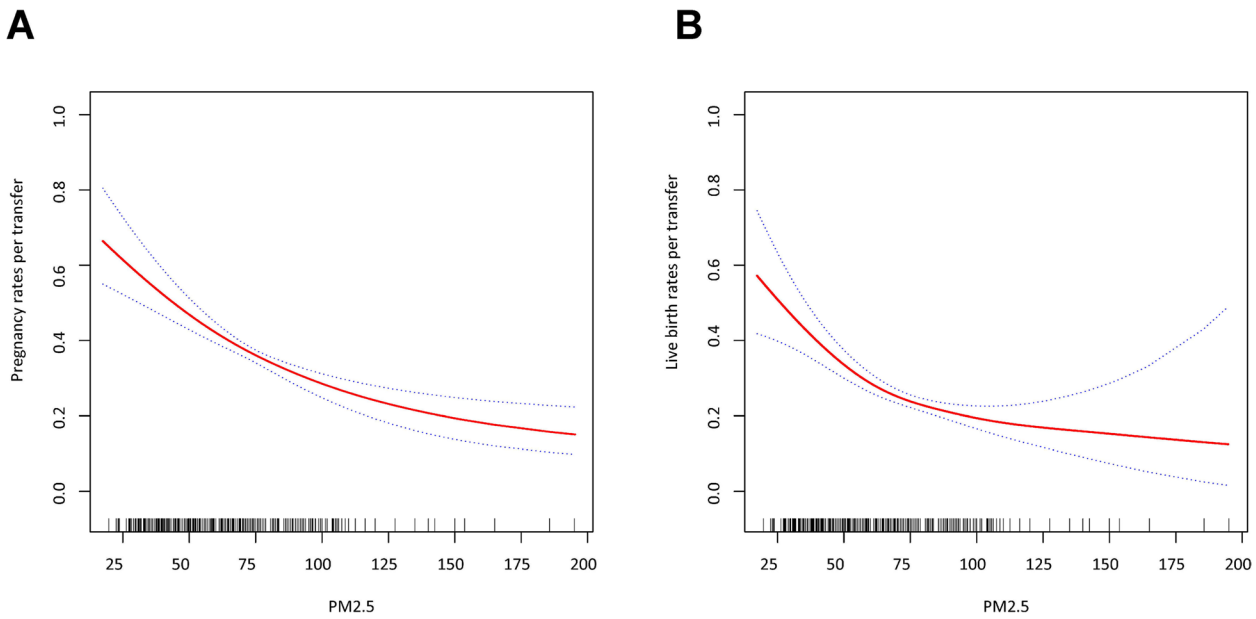


Fig. 2 Association between PM2.5 and pregnancy rates (**A**), live birth rates (**B**). The generalized additive model (GAM), adjusted for age and seasonal factors, demonstrated a nonlinear association between PM2.5 exposure and both pregnancy and live birth rates ($P < 0.001$). Solid red line represents the smooth curve fit between variables. Blue line represents the 95% of confidence interval from the fit

Table 5 Linear regression between pm2.5 and ovulation induction and embryo condition

Item	Oocyte number		MII Oocyte number		Transferable embryos		Good-quality embryos	
	β (95% CIs)	*p*-value	β (95% CIs)	*p*-value	β (95% CIs)	*p*-value	β (95% CIs)	*p*-value
PM2.5 μg/m^3 (Spring)	− 0.034 (− 0.039 ~ −0.030)	< 0.001	− 0.026 (− 0.028 ~ −0.024)	< 0.001	− 0.015 (− 0.017 ~ −0.013)	< 0.001	− 0.015 (− 0.018 ~ −0.013)	< 0.001
PM2.5 μg/m^3 (Summer)	− 0.043 (− 0.049 ~ −0.038)	< 0.001	− 0.031 (− 0.036 ~ −0.027)	< 0.001	− 0.023 (− 0.027 ~ −0.019)	< 0.001	− 0.013 (− 0.016 ~ −0.010)	0.013
PM2.5 μg/m^3 (Autumn)	− 0.032 (− 0.035 ~ −0.030)	< 0.001	− 0.025 (− 0.028 ~ −0.023)	< 0.001	− 0.010 (− 0.011 ~ −0.009)	< 0.001	− 0.010 (− 0.011 ~ −0.008)	< 0.001
PM2.5 μg/m^3 (Winter)	− 0.020 (− 0.023 ~ −0.016)	< 0.001	− 0.017 (− 0.019 ~ −0.015)	< 0.001	− 0.015 (− 0.017 ~ −0.013)	0.034	− 0.009 (− 0.0012 ~ −0.005)	0.013

CI Confidence interval, *MII* Metaphase II, *β* Beta coefficients, *E2* Estradiol, *P* Progesterone, *T* Testosterone, *AMH* Anti-Müllerian Hormone, *PRL* Prolactin, *AFC* Antral Follicle Count

PM2.5 Spring group: Adjustments excluded basal E2, basal P, and T

PM2.5 Summer group: Adjustments excluded basal P, T, and AMH

PM2.5 Autumn group: Adjustments excluded basal E2, basal P, and PRL

PM2.5 Winter group: Adjustments excluded AFC

GAM results indicate statistically significant differences in pregnancy rates and live birth rates across PM2.5 level subgroups, further highlighting a threshold and nonlinear association between pregnancy outcomes and these independent predictive factors, these findings align with the growing body of evidence implicating air pollution, particularly PM2.5, as a significant determinant of human fertility and reproductive health. The period of PM2.5 exposure in our study spans from the initiation of controlled ovarian stimulation to the pregnancy test (approximately 30 days). This period was prioritized as a critical window of susceptibility for oocyte development and embryo implantation, with potential mechanistic impacts on ART outcomes through disrupted gamete-endometrial interplay. When considering seasonal variations, an interesting trend emerges: live birth rates are significantly lower in winter compared to spring, summer, and autumn, this suggests a seasonal influence on ART outcomes, potentially linked to PM2.5 in winter, temperature and

Table 6 Multivariate logistic regression analysis of PM 2.5 and pregnancy outcomes

Item	Pregnancy rates per transfer		Miscarriage rates		Live birth rates per transfer	
	OR (95% CIs)	*p*-value	OR (95% CIs)	*p*-value	OR (95% CIs)	*p*-value
Age	0.885 (0.879 ~ 0.891)	< 0.001	0.981 (0.970 ~ 0.993)	0.002	0.874 (0.867 ~ 0.880)	< 0.001
PM2.5 μg/m^3	0.995 (0.994 ~ 0.996)	< 0.001	1.016 (0.894 ~ 1.127)	0.281	0.996 (0.995 ~ 0.997)	< 0.001
Season						
Winter	Reference		Reference		Reference	
Spring	1.192 (1.060 ~ 1.341)	0.003	1.212 (0.976 ~ 1.506)	0.082	1.141 (1.006 ~ 1.295)	0.040
Summer	1.080 (0.959 ~ 1.217)	0.205	1.088 (0.872 ~ 1.359)	0.454	1.063 (1.015 ~ 1.207)	0.035
Autumn	1.102 (0.975 ~ 1.245)	0.121	0.917 (0.723 ~ 1.159)	0.467	1.142 (1.002 ~ 1.300)	0.046

CI Confidence interval

other unknown factors. However, the exact mechanism behind this remains unclear, necessitating further research to elucidate the underlying pathways, it is worth noting that the relationship between PM2.5 and miscarriage rates did not reach statistical significance. Nonetheless, these findings emphasize the critical need to consider environmental factors, particularly PM2.5 exposure, in the context of ART treatments. Additionally, the potential for seasonal variations to influence reproductive outcomes should not be overlooked.

The negative correlation between PM2.5 exposure and ovulation induction, as well as embryo condition, is a significant concern in our research. Although the precise mechanisms remain unclear, potential pathways include the direct toxic effects of PM2.5 on oocyte quality and embryo development, as well as indirect effects mediated through systemic inflammation and oxidative stress [25, 26]. Due to their small size, PM2.5 particles can penetrate deeply into the bloodstream, directly threatening oocyte and embryo development. A study demonstrates that PM2.5 induces ROS generation, mitochondrial dysfunction, DNA damage, and early apoptosis, which collectively contribute to a decline in oocyte quality and affect subsequent embryonic development potential [27]. Additionally, studies on rat models have shown that PM2.5 exposure leads to placental pathological changes and adverse perinatal outcomes, suggesting that inflammation and vascular thrombosis may disrupt normal reproductive processes [28]. Moreover, elemental contaminants within PM2.5, such as iron and sulfur, have been linked to neurotoxicity and oxidative stress, potentially contributing to reproductive toxicity, these elements may contribute to the disruption of oocytes cellular homeostasis [29]. Collectively, these findings align with our research, confirming that PM2.5 exerts toxic effects on oocytes and embryos, directly disrupting cellular processes and ultimately impairing fertility outcomes [11, 30].

Systemic inflammation and oxidative stress induced by PM2.5 exposure may indirectly contribute to adverse outcomes in ART. Inflammation and oxidative stress are known to have deleterious effects on reproductive health, affecting oocyte maturation, fertilization, and embryo implantation [25, 31]. A recent study revealed that the inflammatory cytokines released in response to PM2.5 exposure can interfere with hormonal signaling and reproductive tissue function, further compounding the negative effects on reproductive health [32]. Another critical factor affecting embryo quality involves compromised semen parameters [12, 33]. A study demonstrates that PM2.5 exposure has been linked to testicular damage and decreased sperm quality through mechanisms involving the NALP3 inflammasome and miR- 183/96/182 cluster targeting FOXO1. This exposure results in increased inflammation in the testes, decreased sperm densities, and reduced testosterone levels, further highlighting the detrimental impact of PM2.5 on male fertility [34]. Furthermore, the toxic components present in PM2.5, such as polycyclic aromatic hydrocarbons and heavy metals, can accumulate in the testes and interfere with normal spermatogenesis. These toxicants can disrupt the delicate hormonal balance required for sperm production and maturation, leading to a decrease in sperm count and quality [35, 36]. PM2.5-induced oxidative stress can damage sperm DNA, affecting their fertilizing potential [37, 38]. Both previous studies and our current investigation have demonstrated that PM2.5 exposure may induce irreversible damage to oocyte quality through oxidative stress mechanisms. Furthermore, it can exacerbate the impact on embryo quality by compromising male sperm quality, ultimately leading to decreased success rates in ART pregnancies and live births.

The findings of the GAM analysis indicate significant variations in pregnancy and live birth rates among distinct subgroups based on PM2.5 levels, along with a

non-linear threshold relationship between PM2.5 exposure and these reproductive outcomes. This association is consistent with existing research highlighting the role of PM2.5 as a significant factor in fertility and reproductive health. Possible mechanisms for this relationship include disturbances in hormonal equilibrium, inflammation, oxidative stress, and epigenetic alterations, all of which may impact uterine receptivity and embryo development [39, 40]. Exposure to PM2.5 has been found to disrupt the normal physiological processes of the endometrium, leading to changes in its receptivity [41, 42]. Specifically, PM2.5 may alter the expression of key molecules involved in embryo implantation, such as adhesion molecules and growth factors, thereby impeding the successful attachment of the embryo to the endometrial lining. Additionally, PM2.5-induced oxidative stress and inflammation can damage endometrial cells, further compromising endometrial receptivity [39, 43]. Future investigations into the impact of PM2.5 on ART outcomes should extend their focus to include the effects of PM2.5 on endometrial receptivity, rather than solely concentrating on oocyte and embryo quality. Elucidating these mechanisms and developing effective interventions are crucial for mitigating the adverse effects of air pollution on reproductive health.

The seasonal variations observed in this study are particularly intriguing. Specifically, live birth rates exhibited a notable decline in winter compared to spring, summer, and autumn. These findings suggesting a seasonal influence on reproductive outcomes, albeit the precise mechanisms behind this remain enigmatic. Some researchers have speculated that vitamin D levels may play a pivotal role, vitamin D is a cornerstone of reproductive health [44], and its levels are known to fluctuate with the seasons, reaching lower points during winter. While the exact mechanisms are still elusive, it is conceivable that vitamin D deficiency, coupled with heightened PM2.5 exposure, could exacerbate the detrimental effects on ART outcomes [45, 46]. However, it is worth noting that the relationship between vitamin D and ART outcomes remains contentious and merits further exploration. Moreover, it is well-documented that PM2.5 levels tend to escalate during winter in comparison to other seasons [47, 48]. This seasonal surge in PM2.5 concentrations can be attributed to several contributing factors, such as the increased utilization of fossil fuels for heating, adverse meteorological conditions conducive to pollutant accumulation, and reduced pollutant dispersion due to lower atmospheric mixing heights [49]. These converging factors could potentially explain the diminished pregnancy and live birth rates observed during winter.

The strengths of this study are underscored by its utilization of a large sample size and a meticulously designed methodology that allowed for the stratified analysis of a comprehensive dataset spanning five years and accounting for seasonal variations. Nevertheless, several limitations warrant consideration. First, the retrospective nature of our data collection introduces inherent risks of selection bias that may compromise the accuracy of associations identified between PM2.5 exposure and ART outcomes. Second, while the study accounted for potential confounders such as age and seasonal variations, other factors such as lifestyle habits, pregnancy comorbidities, and socioeconomic status may have exerted an influence on the results [50, 51]. Moreover, the dynamic physiological changes during pregnancy may involve unaccounted biological variables that could influence reproductive outcomes. A critical methodological constraint arises from the lack of complete monitoring data for atmospheric pollutants beyond PM2.5. These undetected environmental exposures may constitute undetected confounders, potentially introducing latent bias into our regression models. Subsequent research employing prospective cohort designs with refined exposure quantification across multiple pollutants is necessary to verify these observational relationships.

Our study complements existing evidence that exposure to PM2.5 can lead to decreased success rates of pregnancy and live births, as well as significantly impact the outcomes of ART. Notably, live birth rates exhibited a notable decline in winter compared to spring, summer, and autumn. These findings underscore the critical importance of considering environmental pollution, particularly PM2.5 exposure, in the realm of ART treatments, and the potential for seasonal variations to modulate reproductive outcomes. In light of this, clinicians and policymakers should remain cognizant of the potential ramifications of air pollution on fertility when counseling patients and formulating public health strategies.

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Authors' contributions
F.L. and Y.M.G. conceived of and designed the experiments. F.L. and M.M.L. selected and supervised suitable patients. F.L and Y.J.K. provided overall supervision. F.L., Y.C. drafted the manuscript. All authors reviewed this manuscript.

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Data availability
The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, all data is available from the

corresponding author on reasonable request. The important and representative information are available in the quotations and tables available in the manuscript.

Declarations

Ethics approval and consent to participate

The study protocol adhered to the ethical principles of the Declaration of Helsinki and was approved by the Institutional Review Board of The First People's Hospital of Shangqiu (No: SYY2023112). As a retrospective study, the informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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