

Very Early Pregnancy Loss: The Role of PM_{2.5} Exposure in IVF-ET Outcomes

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Air pollution, particularly fine particulate matter (PM_{2.5}), has long been recognized as a significant global environmental and public health concern. The detrimental effects of PM_{2.5} on human health are well-documented, with implications for respiratory, cardiovascular, and metabolic health.^{1–3} However, its potential impact on reproductive health, particularly on very early pregnancy outcomes, is an area of growing research interest. In this issue of *Environment & Health*, Lan and colleagues make a notable contribution to the field, offering key insights into the effects of PM_{2.5} on early pregnancy outcomes, particularly among women undergoing assisted reproductive technology (ART).⁴

Lan et al. undertook a large multicenter retrospective cohort study,⁴ examining 141,040 IVF-ET cycles from eight fertility centers across China. Their findings provide compelling evidence that increased PM_{2.5} exposure, both before and after embryo transfer, significantly reduces the success rate of very early pregnancy (VEP). This multicenter study used both biochemical and clinical pregnancy outcomes as end points, while also applying high-resolution PM_{2.5} data to enhance the precision of exposure assessment and provide a more detailed examination of sensitive windows in the reproductive process. Moreover, through stratified analysis, the study identified women undergoing fresh cycles and single embryo transfers as particularly vulnerable to the adverse effects of PM_{2.5} exposure.

The findings of epidemiologic studies investigating the impact of air pollution on ART outcomes have been inconsistent, with variability in study design, sample size, and exposure assessment contributing to the discrepancies.^{5–7} The large sample size and robust methodology employed by Lan et al. provide valuable evidence that adds clarity to the field, offering new insights by pinpointing specific time windows during which PM_{2.5} exposure is most detrimental to early pregnancy outcomes.⁴ These results are consistent with toxicological evidence suggesting that PM_{2.5} can induce oxidative stress, inflammation, and immune system dysregulation—mechanisms that are known to impair reproductive function.⁸ By validating these findings in a human population, the study reinforces the biological plausibility of a causal relationship between PM_{2.5} exposure and early pregnancy loss, further strengthening the case for more stringent air quality regulations, particularly in urban areas, where infertility treatments such as IVF-ET are becoming increasingly prevalent.

Another key issue is the identification of susceptible subpopulations. Lan et al.'s findings suggest that women undergoing fresh cycles and single embryo transfers are at higher risk, potentially due to altered endometrial receptivity in fresh cycles and the lower likelihood of success associated with single embryo transfers. Fresh cycles, compared to frozen ones, often involve hormonal imbalances and suboptimal endometrial conditions,⁹ potentially exacerbated by environmental stressors like air pollution. Additionally, single embryo transfers are often chosen to reduce the risk of multiple pregnancies. However, the potential adverse effects of air pollution may pose added challenges for this subpopulation during critical reproductive windows. These insights have important clinical implications, suggesting that targeted interventions may be necessary to mitigate the effects of air pollution during critical reproductive periods, particularly for these vulnerable subgroups.

The study underscores the importance of considering environmental factors, such as air pollution, when counseling patients undergoing IVF-ET. Given the substantial emotional and financial burden that ART places on couples, any modifiable factor that can improve the likelihood of a successful pregnancy should be carefully considered. Fertility clinics, especially those located in regions with high PM_{2.5} concentrations, may need to implement additional strategies to protect their patients. Such strategies could include adjusting the timing of embryo transfers to coincide with periods of lower air pollution or enhancing indoor air filtration systems within fertility clinics to minimize patients' exposure to harmful pollutants during sensitive reproductive windows.

In China, where air pollution remains a significant public health challenge, this study could inform the development of more rigorous environmental policies aimed at safeguarding reproductive health. The identification of specific time windows during which PM_{2.5} exposure is most harmful suggests that targeted interventions—such as improving air quality near fertility centers or offering temporary accommodations with cleaner air for IVF patients—could signifi-

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cantly reduce the risk of early pregnancy loss. Furthermore, the findings of Lan et al. may have broader implications for addressing declining birth rates in China and other industrialized nations facing similar challenges. Collectively, as infertility rates rise,¹⁰ particularly in regions with high levels of air pollution, research exploring the relationship between environmental factors and in vitro reproductive outcomes is essential for guiding future efforts to enhance reproductive success and protect public health.

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Notes

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REFERENCES

- (1) Hao, Y.; Balluz, L.; Strosnider, H.; Wen, X. J.; Li, C.; Qualters, J. R. Ozone, Fine Particulate Matter, and Chronic Lower Respiratory Disease Mortality in the United States. *Am. J. Respir Crit Care Med.* **2015**, *192* (3), 337–41.
- (2) Brook, R. D.; Newby, D. E.; Rajagopalan, S. The Global Threat of Outdoor Ambient Air Pollution to Cardiovascular Health: Time for Intervention. *JAMA Cardiol.* **2017**, *2* (4), 353–354.
- (3) Diabetes, G. B. D.; Air Pollution, C. Estimates, trends, and drivers of the global burden of type 2 diabetes attributable to PM(2.5) air pollution, 1990–2019: an analysis of data from the Global Burden of Disease Study 2019. *Lancet Planet Health* **2022**, *6* (7), e586–e600.
- (4) Lan, C.; Guan, Y.; Luo, H.; Ma, X.; Yang, Y.; Bao, H.; Hao, C.; He, X.; Zhang, H.; Gao, N.; Lin, W.; Ren, M.; Wu, T.; Wang, C.; Ni, X.; Shen, C.; Zhang, J.; Ma, J.; Zhang, R.; Bi, Y.; Zhuang, L.; Miao, R.; Song, Z.; An, T.; Liu, Z.; Pan, B.; Fang, M.; Liu, J.; Bai, Z.; Meng, F.; Chen, Y.; Lu, X.; Gao, Y.; Cao, Y.; Lu, Q.; Wang, B. Observed Effects on Very Early Pregnancy Linked to Ambient PM2.5 Exposure in China among Women Undergoing In Vitro Fertilization Embryo Transfer. *Environmental & Health* **2024**, 4c00107 DOI: [10.1021/envhealth.4c00107](https://doi.org/10.1021/envhealth.4c00107).
- (5) Carre, J.; Gatimel, N.; Moreau, J.; Parinaud, J.; Leandri, R. Influence of air quality on the results of in vitro fertilization attempts: A retrospective study. *Eur. J. Obstet Gynecol Reprod Biol.* **2017**, *210*, 116–122.
- (6) Boulet, S. L.; Zhou, Y.; Shriber, J.; Kissin, D. M.; Strosnider, H.; Shin, M. Ambient air pollution and in vitro fertilization treatment outcomes. *Hum. Reprod.* **2019**, *34* (10), 2036–2043.
- (7) Zeng, X.; Jin, S.; Chen, X.; Qiu, Y. Association between Ambient Air Pollution and Pregnancy Outcomes in Patients Undergoing In Vitro Fertilization in Chengdu, China: A retrospective study. *Environ. Res.* **2020**, *184*, 109304.
- (8) Gai, H. F.; An, J. X.; Qian, X. Y.; Wei, Y. J.; Williams, J. P.; Gao, G. L. Ovarian Damages Produced by Aerosolized Fine Particulate Matter (PM(2.5)) Pollution in Mice: Possible Protective Medications and Mechanisms. *Chin Med. J. (Engl)* **2017**, *130* (12), 1400–1410.
- (9) Devroey, P.; Bourgain, C.; Macklon, N. S.; Fauser, B. C. Reproductive biology and IVF: ovarian stimulation and endometrial receptivity. *Trends Endocrinol Metab* **2004**, *15* (2), 84–90.
- (10) Qiao, J.; Wang, Y.; Li, X.; Jiang, F.; Zhang, Y.; Ma, J.; Song, Y.; Ma, J.; Fu, W.; Pang, R.; Zhu, Z.; Zhang, J.; Qian, X.; Wang, L.; Wu, J.; Chang, H. M.; Leung, P. C. K.; Mao, M.; Ma, D.; Guo, Y.; Qiu, J.; Liu, L.; Wang, H.; Norman, R. J.; Lawn, J.; Black, R. E.; Ronsmans, C.; Patton, G.; Zhu, J.; Song, L.; Hesketh, T. A Lancet Commission on 70 years of women's reproductive, maternal, newborn, child, and adolescent health in China. *Lancet* **2021**, *397* (10293), 2497–2536.