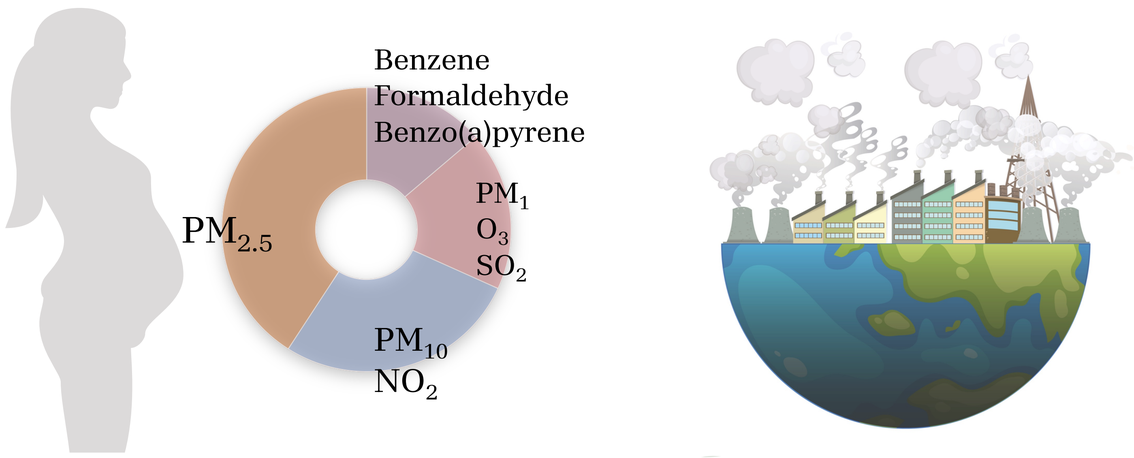
Effetto degli Inquinanti Atmosferici sulla Riserva Ovarica: Una Revisione Sistematica

Roberta Zupo[1*], Fabio Castellana[1], Rodolfo Sardone[2], Giovanni De Pergola[3], Filomena Corbo[4], Maria Lisa Clodoveo[1]

[1] Department of Interdisciplinary Medicine (DIM), University of Bari Aldo Moro, Piazza Giulio Cesare 11, 70100 Bari, Italy; [2] Unit of Statistics and Epidemiology, Local Health Authority of Taranto, 74121 Taranto, Italy; [3] Center of Nutrition for the Research and the Care of Obesity and Metabolic Diseases, National Institute of Gastroenterology IRCCS "Saverio de Bellis", 70013 Castellana Grotte, Italy; [4] Department of Pharmacy-Drug Sciences, University of Bari "Aldo Moro", 70125 Bari, Italy

Exposure	Evidence base	Strength of association	Strength of evidence (GRADE)
PM1	two studies	PM1-AMH association by adjusted multivariable linear mixed effect model. For every 10 µg/m3 increment in PM1, the AMH changed by −8.8% (95% CI, −12.1% to −5.3%), significant	⊕ low
		In fully adjusted regression models, each one-IQR increase in PM1 was associated with −0.89 (95% confidence interval (CI): −1.43, −0.35, P-value ≤ 0.01) decrease in serum level of AMH.	
PM2.5	eight studies	PM2.5-AMH association by adjusted multivariable linear mixed effect model. For every 10 µg/m3 increment in PM2.5, the AMH changed by −2.1% (95% CI, −3.5% to −0.6%), significant	⊕⊕ moderate
		Logistic regression models were employed to assess the association between quartiles of exposure to PM2.5 and the risk of POR. Women in the highest quartile of PM2.5 exposure during 6 months (OR: 1.44, 95%CI: 1.06, 1.96) and 12 months (OR: 1.54, 95%CI: 1.10, 2.14) before oocytes pick up had a higher risk of POR compared with those in the lowest quartile, significant.	
		In multivariable models, an interquartile range (IQR) increase in 1- and 12-month average PM2.5 was associated with 3% (95% CI: − 0.07, 0.00) and 10% (95% CI: −0.18, −0.01) lower AMH ratio, respectively.	
		In adjusted multivariable models a 2 µg/m3 increase in average PM2.5 exposure was associated with a 6.2% (95% CI -11.8, −0.3) lower AFC.	
		In fully adjusted models, each one-IQR increase in PM2.5 was associated with a −1.11 (95% CI: −1.67, −0.55, P-value ≤ 0.01) decrease in serum level of AMH.	
		In adjusted models, AMH levels were inversely related to PM2.5 (Rho = −0.062, P = 0.021)	
		Women with diminished ovarian reserve (DOR) had high levels of exposure to PM2.5 (P = 0.003) compared with those without DOR and who had low exposure.	
		Every 2 µg/m increase in estimated PM2.5 exposure was associated with a -7.2% (95% confidence interval = -10.4%, -3.8%) lower antral follicle count	
PM10	five studies	PM10-AMH association by adjusted multivariable linear mixed effect model. For every 10 µg/m3 increment in PM10, the AMH changed by −1.9% (95% CI, −3.3% to −0.5%), significant	⊕⊕ moderate
		Logistic regression models were employed to assess the association between quartiles of exposure to PM10 and the risk of POR. Women in the third quartile of PM10 exposure for 3 months (OR: 0.82, CI 95%: 0.70, 0.97) and 6 months (OR: 0.78, 95%CI: 0.66, 0.91) before oocytes pick up had a higher risk of POR compared with those in the lowest quartile, significant.	
		In multivariable models, an interquartile range (IQR) increase in 1-month average PM10 was associated with a decrease (beta coefficient = −0.06, 95% confidence interval: −0.11, 0.00, Table 2) in AMH ratio.	
		In adjusted models, AMH levels were inversely related to PM10 (Rho = −0.088, P = 0.001), significant	
		Women with diminished ovarian reserve (DOR) had high levels of exposure to PM10 (P = 0.01) compared with those without DOR and who had low exposure.	
Benzene	one study	Benzene-AMH association by adjusted linear models. A negative association of AMH with benzene (percentage reduction in AMH per interquartile range [IQR] increase = 5.5%, 95% CI = 1.0 to 9.8), significant.	⊕ very low
Formaldehyde	one study	Formaldehyde-AMH association by adjusted linear models. A negative association of AMH with formaldehyde (percentage reduction in AMH per interquartile range [IQR] increase =6.1%, 95% CI = 1.6 to 10), significant.	⊕ very low
O3	two studies	O3-AMH association by adjusted multivariable linear mixed effect model. For every 10 µg/m3 increment in O3, the AMH changed by -4.5 (95% CI, -7.1 to -1.9), significant	⊕ low
		Women in the third quartile of O3 exposure for 3 months (OR: 1.19, 95%CI: 1.00, 1.42) and 12 months (OR: 1.28, 95%CI: 1.08, 1.53) before oocytes pick up were more likely to have a POR compared with the first quartile, significant.	
SO2	two studies	Logistic regression models were employed to assess the association between quartiles of exposure to SO2 and the risk of POR. Women in the third quartile of SO2 exposure for 6 months (OR: 2.10, 95%CI 1.67, 2.64) and 12 months (OR: 2.53, 95%CI 2.01, 3.19) before oocytes pick up had a higher risk of POR compared with those in the lowest quartile, significant.	⊕ low
		In linear adjusted models, every 10 µg/m3 increase in SO2 concentration level during the entire development stage of antral follicle was associated with a −0.01 change in AFC (95% confidence interval: −0.016, −0.002), significant.	
NO2	five studies	NO2-AMH association by adjusted multivariable linear mixed effect model. For every 10 µg/m3 increment in NO2, the AMH changed by -4.5 (95% CI, -7.1, -1.9), significant.	⊕⊕ moderate
		Multivariable-adjusted linear regression to estimate the percent change in AMH in relation to ambient residential NO2 (quartile exposure). Women in the highest quartile of NO2 exposure had higher estimated AMH concentrations (Q4 vs. Q1, 42.9%; 95% CI = -3.4, 111.4) compared with the lowest quartile, not significant.	
		In linear adjusted models, negative associations were observed between AFC and quartiles of NO2 levels: Q2 (−0.138 change, 95%CI: -0.198, -0.078), Q3 (−0.058 change, 95%CI: -0.170, 0) and Q4 (−0.068 change, 95%CI: -0.127,-0.009) compared with Q1, significant.	
		In adjusted models, AMH levels were inversely related to NO2 (Rho = −0.111, P < 0.001), significant.	
		Women with diminished ovarian reserve (DOR) had high levels of exposure to NO2 (P < 0.001) compared with those without DOR and who had low exposure.	
BaP	one study	In adjusted logistic regression models, per one-unit increase in the log-transformed BaP concentration was significantly correlated with a 2.191-fold increased risk of POF (OR: 2.191, 95%CI: 1.6-2.9, p < 0.05).	⊕ very low

Introduzione: Sempre più evidenze scientifiche indicano l'esistenza di un'associazione tra l'inquinamento atmosferico e la riduzione del potenziale riproduttivo umano. Questo studio si proponeva di esaminare sistematicamente l'associazione tra inquinanti atmosferici e riserva ovarica femminile.



Materiali e Metodi: La letteratura è stata esplorata in sei banche dati elettroniche fino a gennaio 2024. Lo screening dei 75 articoli in linea con i criteri di inclusione ha portato alla selezione di 12 studi osservazionali che hanno valutato l'effetto degli inquinanti ambientali sui marcatori della riserva ovarica nella donna. Il protocollo dello studio è stato registrato su PROSPERO (CRD42023474218).

Risultati: Il disegno degli studi selezionati è risultato essere trasversale (2 su 10), di coorte retrospettivo (7 su 10), di coorte prospettico (2 su 10) e caso-controllo (1 su 10). La popolazione in studio era equamente distribuita tra asiatici (60%) e americani (50%) con una minoranza italiana (10%). I risultati principali hanno mostrato un maggior numero di evidenze per gli inquinanti ambientali PM2.5, PM10 e NO2, mentre un basso numero di evidenze per PM1, O3, SO2 e un numero molto basso di evidenze per benzene, formaldeide e benzo(a)pirene, pur mostrando consistentemente dati significativi di associazione inversa. La qualità metodologica complessiva degli studi selezionati è stata valutata moderata secondo i 14 domini del toolkit NIH.

Discussione: L'aumento dell'esposizione agli inquinanti atmosferici è associato a una riduzione della riserva ovarica femminile e, sebbene le evidenze siano più forti per inquinanti come PM2,5, PM10 e NO2, sono necessarie ulteriori prove per poter trarre conclusioni sulla causalità. Alla luce di questi risultati, è auspicabile una transizione su larga scala dai combustibili fossili all'energia pulita e rinnovabile come strategia vincente per prevenire l'inquinamento e allo stesso tempo mitigare il cambiamento climatico, ottenendo così un doppio beneficio per la salute del pianeta.