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מרצה

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בברכה,

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The possible association between exposure to air pollution and adverse pregnancy outcomes

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**Introduction:** Over the last decade, there is growing evidence that exposure to air pollution may be associated with adverse health outcomes and some populations appear to be more susceptible than others. Moreover, the possibility that exposure to air pollution may be associated with adverse birth outcomes such as congenital malformations (CM), small for gestational age (SGA), low birth weight (LBW) and preterm birth (PTB) has been considered. Understanding the possibly harmful effects of prenatal exposure to air pollution is important not only for the immediate impact on pregnancy outcomes but also for long term health sequelae. The current study is one of the first nation-wide studies in Israel to provide evidence-based data on the impact of air pollution on birth outcomes. Moreover, to the best of our knowledge the current study is the first to examine the effect air pollution on pregnant women who conceived following assisted reproductive technology (ART) treatments. This information is necessary for policy health makers to reinforce the need for action to reduce exposure to environmental pollutants.

**Objectives:** To evaluate the possible association between exposure to air pollution during pregnancy and adverse birth outcomes among children born following assisted reproductive technology (ART) and spontaneously conceived (SC) pregnancies.

**Methods:** This is an historical cohort study comprising 207,825 SC infants and 8,905 ART conceived infants during the period 1997-2004. Air pollution data was obtained from the air monitoring stations database on: sulfur oxides (SO\textsubscript{2}), particulate matter <10 µm (PM\textsubscript{10}), nitrogen oxides (NO\textsubscript{x}) and ozone (O\textsubscript{3}). Using a Geographic Information System (GIS) and the Kriging procedure, exposure to different air pollutants during each pregnancy trimester and for the entire pregnancy was assessed for each woman according to her residential location. Logistic and Cox proportional hazards regression models were used in order to evaluate the adjusted risk for adverse pregnancy outcomes including congenital malformations (CM), small for gestational age (SGA), low birth weight (LBW) and preterm birth (PTB). In addition, Air Quality Indexes (AQIs) for adverse birth outcomes were calculated based on analyses of numerous epidemiological studies assessing relative risks (RR) of adverse birth outcomes associated with 10µg/m\textsuperscript{3} normalized increases of time averaged air concentrations, pertinent
to different air pollutants. As widely accepted for various short term air concentrations health effects, the regional AQI is determined in this study by exposure to the "worse" air pollutant long term concentrations (and all-pregnancy health effects), considering not only the concentrations themselves but also the particular RRs associated with them.

**Results:** Higher levels of SO₂ exposure were not associated with an increased risk of any of the adverse outcomes under investigation. Increased levels of PM₁₀ exposure in the entire pregnancy were associated with an increased risk for CM and PTB OR 1.06 (95%CI 1.01-1.11) and OR 1.05 (95%CI 1.02-1.08) per 10µg/m³ respectively. Higher levels of NOₓ exposure in the entire pregnancy were associated with increased risk of CM and PTB OR 1.06 (95%CI 1.01-1.10) and OR 1.05 (95%CI 1.02-1.08) per 10ppb increase respectively. Higher levels of O₃ exposure in the entire pregnancy were associated with an increased risk for SGA; OR 1.03 (95%CI 0.99-1.08) and for LBW; OR 1.10 (95%CI 1.02-1.18) per 10ppb increase. In the ART group compared to the spontaneously conceived pregnancies, higher levels of SO₂ were associated with slightly higher risk for CM and PTB. Higher levels of O₃ exposure were associated with a slightly higher risk for all adverse outcomes in the ART group. Concerning the AQI - the feasibility, under certain assumptions, of creating an AQI for adverse birth outcomes has been demonstrated. Also, Israeli and international long term air concentration criteria have been quantitatively checked in comparison with the proposed AQIs and turned out to be mainly within the "moderate" range. Besides, five years average (2001-2005) air concentrations of different pollutants in an Israeli town have been analyzed and yielded possible adverse birth outcomes by rather conservative implementation of the ranges of adverse birth outcomes as obtained from the literature survey, as function of 10µg/m³ increases in particular pollutant's air concentrations, PM10, and to a lesser extent, NOx were apparently the main contributors to adverse birth outcomes.

**Conclusion:** Our initial results suggest that exposure to higher levels of air pollution during pregnancy may be associated with various adverse pregnancy outcomes. Although not significant, suggestion of higher impact of air pollution in the ART pregnancies was observed particularly for O₃ exposure. Further studies are warranted, including more accurate exposure assessment data and a larger sample size for ART pregnancies, in order to confirm these associations.