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**Abstract Title**

Maternal Exposure to Ambient Air Pollution During Pregnancy and the Risk of Congenital Surgical Anomalies and Necrotizing Enterocolitis: A Population-Based Retrospective Matched Cohort Study

**Authors**

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**Background**

Air pollution, including fine particulate matter (PM<sub>2.5</sub>) and ground-level ozone (O<sub>3</sub>), has been linked to adverse pregnancy outcomes, but effects on congenital surgical anomalies (CSA) and necrotizing enterocolitis (NEC) remain incompletely characterized. We examined associations of PM<sub>2.5</sub> and O<sub>3</sub> exposure with CSA and NEC.

**Objective**

To examine associations between maternal exposure to fine particulate matter (PM<sub>2.5</sub>) and ground-level ozone (O<sub>3</sub>) during pregnancy and the risk of congenital surgical anomalies (CSA) and necrotizing enterocolitis (NEC), including identification of trimester-specific windows of vulnerability using Distributed Lag Non-linear Models (DLNMs).

**Methods**

Using population-based data, we compared maternal PM<sub>2.5</sub> (2002–2021) and O<sub>3</sub> (2012–2020) exposures between CSA/NEC cases and controls. Multivariable logistic regression and Distributed Lag Non-linear Models (DLNMs) assessed average and trimester-specific exposure associations, adjusted for maternal age, household income quintile, and residential area.

**Results**

Average pregnancy PM<sub>2.5</sub> was associated with increased gastroschisis risk (OR=1.15, 95%CI=1.01–1.31) and inversely associated with congenital lung malformations (CLM; OR=0.65, 95%CI=0.43–1.00). DLNM analyses for PM<sub>2.5</sub> identified second-trimester exposure as associated with increased risk of NEC (OR=1.89, 95%CI=1.23–2.89) and reduced risk of CLM (OR=0.23, 95%CI=0.08–0.72). Third-trimester

exposure was associated with reduced esophageal atresia risk (OR=0.26, 95%CI=0.15–0.45), as was total pregnancy exposure (OR=0.31, 95%CI=0.14–0.68). In pooled analysis, second-trimester exposure was associated with increased risk (OR=1.30, 95%CI=1.07–1.57), while third-trimester exposure was associated with reduced risk (OR=0.69, 95%CI=0.49–0.97). For O<sub>3</sub>, significant associations were limited to pooled analysis: third-trimester (OR=2.42, 95%CI=1.13–5.16) and total-pregnancy exposure (OR=3.73, 95%CI=1.69–8.26) were associated with increased overall CSA/NEC risk.

## **Conclusion**

Maternal PM<sub>2.5</sub> and O<sub>3</sub> exposures during pregnancy were associated with select CSA and NEC, with trimester-specific vulnerability windows identified through DLNM analyses. These findings suggest ambient air pollution may be a modifiable environmental risk factor for congenital surgical conditions.