Exposure to ambient air pollution and early manifestation of type 1 diabetes: results from an observational cohort study

Research Letter

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The incidence of type 1 diabetes (T1D) is increasing worldwide, especially in children aged 0–4 years, decreasing the mean age at diagnosis. Several environmental risk factors for T1D-related islet autoimmunity have been identified, including exposure to respiratory infections in very early life. In young children, ambient air pollution may exacerbate inflammation and promote respiratory diseases. We hypothesised that exposure to high levels of ambient air pollution is associated with earlier onset of T1D.

We analysed data of DiMelli, a population-based register monitoring incident diabetes in children and youths in Bavaria, Germany, since 2009. At the registration of each patient, a structured questionnaire is completed by the attending physician, and a blood sample is drawn, which is used to determine islet autoantibodies to insulin, GAD, IA-2, or ZnT8. Here, we used data for 671 patients registered up to May 2013 (mean age at diagnosis: 9.6 years) who were positive for at least one islet autoantibody and whose residential addresses were available from the questionnaire.

The concentrations of particulate matter (PM) with an aerodynamic diameter of <10 μm (PM$_{10}$), nitrogen dioxide (NO$_2$), PM$_{2.5}$ and PM$_{2.5}$ absorbance, Normalized Difference Vegetation Index (NDVI) as a measure of greenness, and distance to the nearest major at the residential addresses of patients were obtained from various sources (see online supplement). These served as possible explanatory variables in linear regression and quantile regression models using the 10$^{th}$, 30$^{th}$, 50$^{th}$ (median), 70$^{th}$, and 90$^{th}$ percentiles of age at diagnosis as the dependent variables. Models were adjusted for sex, parental education, family history of T1D, and patient’s body mass index at diagnosis, and additionally for level of urbanisation in sensitivity analyses.

Exposure to high levels of PM$_{10}$ and NO$_2$ was associated with a shift in the 10$^{th}$ percentile of the age at diagnosis to lower values (−1.40 [95% CI: −2.24, −0.56] years per 2 SD increase in PM$_{10}$; −1.28 [95% CI: −2.14, −0.42] years per 2 SD increase in NO$_2$), but not for higher percentiles or for the mean age at diagnosis (figure 1). Considering that the 10$^{th}$ percentile of
the age at diagnosis was 3.29 years in the whole dataset, the first 10% of children with high exposure (+2 SDs) to PM$_{10}$ were predicted to develop T1D by the age of 1.89 years (i.e., 3.29 − 1.40), while the 10$^{th}$ percentile in children with low exposure (−2 SDs) was estimated to be 4.69 years (i.e. 3.29 + 1.40). No clear associations were observed for PM$_{2.5}$, PM$_{2.5}$ absorbance, NDVI, or the distance to the nearest major road. If we included the level of urbanisation as an additional confounder, similar results were obtained, except for the association between PM$_{2.5}$ and the 10$^{th}$ percentile of age at diagnosis (−1.37 [95% CI: −1.97, −0.77] per 2 SD increase). Boxplots of the inflammatory markers (IL)-1β, IL-6, IL-8, and tumour necrosis factor (TNF) indicated no clear associations with manifestation age and PM$_{10}$ exposure level (supplementary figure).

Our findings indicate that high exposure to the traffic-related air pollutants PM$_{10}$, NO$_2$ and possibly PM$_{2.5}$ accelerates the manifestation of T1D, but only in very young children. Interestingly, findings from a previous study suggested that PM$_{10}$ was associated with an increased risk of T1D in children aged < 5 years. Our results were independent of urbanisation level, indicating that air pollutants, not urbanisation-related lifestyle habits or e.g. higher temperatures in urbanized areas, might be responsible for the observed associations. However, we did not observe any clear associations with inflammatory markers to show that air pollution accelerates the onset of T1D by inducing a more severe inflammatory state in young children.
References


Figure legends

Figure 1. Point estimates and 95% confidence intervals for differences in the age at diagnosis of type 1 diabetes (T1D) per 2 SD increases in PM$_{10}$, NO$_2$, NDVI, PM$_{2.5}$ and PM$_{2.5}$ absorbance, and per 500 m increase in distance to the nearest major road, with adjustment for sex, parental education, family history of T1D, and body mass index. The dots represent specific quantile regression estimates and are connected by dashes to visualise trends by age quantiles. The horizontal grey lines represent the linear regression coefficients and their respective confidence intervals. The horizontal line depicts $y = 0$ as a reference.

Supplemental figure. Boxplots of the inflammatory markers IL-1$\beta$, IL-6, IL-8 (each on a logarithmic scale), and TNF by age group and low, medium, and high exposure to PM$_{10}$ (defined as the lowest quartile, interquartile range, and highest quartile of exposure). Box: interquartile range; whiskers: $1.5 \times$ interquartile range; circles: outliers. The category limits correspond to the 0.1, 0.3, 0.7, and 0.9 quantiles of age at diagnosis in the dataset.
Figure 1.
Supplemental figure.