

RESEARCH LETTER

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Association between long-term occupational exposure to PM₁₀ and allergic diseases in subway workers

To the Editor,

Persistent or repetitive exposure to environmental pollutants, in particular, exposure to ambient particulate matter with a median aerodynamic diameter of $<10\mu\text{m}$ (PM₁₀) in air pollution, cigarette smoking and other irritants is associated with an increased risk of development and exacerbation of allergic diseases.^{1–3} Inflammation and oxidative stress play a central role in the pathophysiology of allergic diseases and could be measured using biomarkers.^{4,5} For that purpose, exhaled breath condensate (EBC), a noninvasively collected biological matrix, allows the measurement of different biomarkers of oxidative stress directly in the lung.⁶

Within the Franco-Swiss project 'Respiratory disease Occupational Biomonitoring Collaborative Project' (ROBoCoP), we assessed whether a long-term occupational exposure to subway PM₁₀ is associated with the prevalence of allergic diseases and whether the latter are associated with biomarkers measured in EBC of subway workers.⁷

We adopted a cross-sectional study design with an aetiological focus, combining a retrospective exposure assessment and contemporary outcome measurements to meet the temporality condition. Participants were randomly selected from a 15,000-subway worker cohort. All data and biological samples were collected from March through May 2021 according to the study protocol.⁷ The outcomes variables (i.e., current asthma, current rhinitis and current eczema) were assessed using an electronic self-administered questionnaire addressed to workers who consented to participate. Moreover, atopic sensitization defined as a positive skin prick test to one or more of the tested allergens, according to the recommendations from the European Academy of Allergology and Clinical Immunology, was assessed by an occupational physician at the company occupational medicine centre. Finally, EBC samples were collected, during 20min of tidal breathing using Turbo-Deccs® (Medivac, Parma, Italy) and nose clips, according to the latest recommendations.⁶

Individual inhaled PM₁₀ mass (iPM₁₀) per work shift was estimated using a company-specific job-exposure-matrix (JEM) based on PM₁₀ measurements conducted from 2004 through 2019.⁸ iPM₁₀ was modelled as a function of PM₁₀ exposure averaged over the participant's employment in the Parisian subway, inhalation rate and filtration efficiency of the respiratory protections used. A detailed description of these methods and results is available elsewhere.⁹

Associations between iPM₁₀, health outcomes and biomarkers, were assessed using multivariable logistic regression models adjusted for potential confounders.

Among 287 participants, 35% reported a current rhinitis and 12% a current eczema and 5% a current asthma. Mean exposure duration of PM₁₀ was 23.3 years at a mean estimated concentration of $76.7\mu\text{g}/\text{m}^3$. This corresponds to an iPM₁₀ of $0.6\mu\text{g}/\text{shift}$.

The first research hypothesis tested in this study was that iPM₁₀ will be positively associated with the prevalence of at least one of the three allergic diseases. We found that iPM₁₀ was associated with the prevalence of current asthma among locomotive operators. The adjusted OR was equal to 1.05 [95%CI=1.00–1.10] per 10ng/shift, corresponding to 5%-increase in current asthma risk per every 10ng/shift PM₁₀ inhaled (Table 1). Among station agents, the association between iPM₁₀ and the prevalence of current asthma was not statistically significant. However, station agents were found to be at higher risk of current asthma when compared to locomotive operators (aOR=7.47 [95%CI=1.02–54.74]). No interaction was found between iPM₁₀ and job. Moreover, exposure duration was not associated with asthma prevalence.

The second research hypothesis tested in this study was that biomarkers measured in EBC would be associated with the prevalence of the outcomes considered. We found an association of nitrite concentration in EBC with atopic and poly-atopic sensitization, and current asthma (aOR=2.95 [95%CI=1.21–7.19], 3.94 [95%CI=1.35–11.54] and 9.13 [95%CI=1.23–67.96] per $\mu\text{mol}/\text{L}$, respectively). Nitrate level was negatively associated with current eczema but not associated with current asthma and current rhinitis (Table 1). More detailed information on study results is available at the Unisanté data repository (<https://doi.org/10.16909/dataset/47>).

Among the study strengths, the use of an original retrospective exposure assessment strategy is noteworthy. This strategy combines the JEM-based estimates of external exposure to subway PM₁₀ with inhalation rates accounting for age, sex and physical activity of participants and the filtration efficacy of respiratory protection used at the workplace. The JEM used in this study is the first and unique JEM for subway PM available in the world.⁸ It enables, for the first time, assessing the health effects of subway PM₁₀ exposure accumulated during more than 23 years of employment. Although personal

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exposure monitoring is considered the reference method, it is challenging to implement in Parisian subway, where workers are not allowed wearing measurement devices for security reasons. Another strength of this study is the 84%-response rate. Moreover, EBC sample analysis was robust, with only 0.4% results below the limit of detection and very few results below the limit of quantification.

Among limitations, the absence of PM₁₀ measurements prior to 2004 and post-2020 is noteworthy; the missing PM₁₀ levels had to be extrapolated. The number of asthma cases was limited and by design, only prevalence of current asthma could be analysed. Indeed, in studies relying on self-reported data, information bias might arise. Therefore, we focussed on current effects of allergic diseases, with diagnosis and/or symptoms within the last year. Finally, the study sample was small, and these study findings need further confirmation.

This study showed for the first time the relationship between long-term exposure to subway PM₁₀ and prevalence of asthma in some categories of subway workers. This finding is important for occupational allergology practice pointing out the risk of allergic asthma in the underground railway settings and the need of its screening and appropriate management. The study also confirmed nitrite in EBC as a biomarker of atopy and current asthma, indicating the diagnostic interest of this biomarker. The use of such noninvasively measured biomarkers may facilitate further research in occupational allergology.

KEYWORDS

asthma, atopy, exhaled breath condensate, nitrite, PM₁₀ exposure

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Summary box

- In locomotive operators, subway PM₁₀ exposure is associated with asthma prevalence.
- Nitrite in exhaled breath condensate is associated with prevalent allergic diseases.

participating in the study. Open access funding provided by Universite de Lausanne.

AUTHOR CONTRIBUTIONS

IGC, PW, JAP, JJS and GS was involved in conceptualization; RF, IGC and PW were involved in Methodology; RF, TC and PW were involved in software and formal analysis; AD, KS, VJ and JAP were involved in validation; AD, KS, VJ and JJS were involved in investigation; TC was involved in data curation; RF, JJS and IGC were involved in writing—original draft preparation; All authors were involved in writing—review and editing; IGC was involved in project administration and funding acquisition. All authors have read and agreed to the published version of the manuscript.

FUNDING INFORMATION

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data are not publicly available due to ethical and privacy restrictions.

TABLE 1 Relationship between mean inhaled PM₁₀ mass per work shift (iPM₁₀), biomarker concentration in EBC and health outcomes.

Logistic regression adjusted model (n = 240)	Current asthma			Current rhinitis			Current eczema		
	aOR	95%-CI	p ^a	aOR	95%-CI	p ^a	aOR	95%-CI	p ^a
iPM ₁₀ in locomotive operators (per 10 ng/shift)	1.05 ^b	1.00–1.10	.04	0.98 ^b	0.96–1.00	.13	0.99 ^b	0.96–1.02	.55
iPM ₁₀ in station agents (per 10 ng/shift)	1.05 ^b	0.98–1.13	.19	0.95 ^b	0.91–0.98	<.01	0.99 ^b	0.94–1.05	.83
Job category (ref: locomotive operators)	7.47	1.02–54.74	.05	1.14	0.63–2.08	.67	0.63	0.26–1.51	.30
Exposure duration (per year)	0.94	0.85–1.04	.25	1.07	1.02–1.12	.01	1.02	0.96–1.10	.50
Sex (ref: male)	2.18	0.48–9.93	.31	0.73	0.38–1.39	.34	0.65	0.26–1.65	.36
Atopic sensitization (ref: no)	3.87	1.09–13.73	.04	1.17	0.66–2.09	.59	0.50	0.19–1.30	.16
EBC biomarkers ^c									
n = 280									
Nitrite (μmol/L)	9.13	1.23–67.96	.03	1.20	0.51–2.84	.67	0.53	0.15–1.85	.32
Nitrate (μmol/L)	0.70	0.12–3.97	.69	2.19	0.79–6.10	.13	0.25	0.08–0.75	.01

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; EBC, exhaled breath condensate; iPM₁₀, mean inhaled; PM₁₀, mass per shift; p, p-value; PM₁₀, particulate matter less than 10 microns.

^aAssociations with a p-value of <.05 are bolded.

^bInteraction not significant.

^cLogistic regression models adjusted are adjusted on age, sex, and smoking status.

INSTITUTIONAL REVIEW BOARD STATEMENT

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the French Personal Protection Committees South-Est IV (N°2020-A03103-36), Declaration of conformity to the French National Commission for Computing and Freedoms (CNIL) N° 2,220,108 (protocol code ID RCB 2020-A03103-36).

INFORMED CONSENT STATEMENT

Informed consent was obtained from all subjects involved in the study.

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