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Air pollution susceptibility in children with asthma and obesity: tidal volume as key player?

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Shareable abstract (@ERSpublications)
The higher susceptibility to air pollution of asthmatic children with a higher BMI can (partly) be explained by differences in breathing patterns that result in a higher (alveolar) lung deposition of $PM_{2.5}$ https://bit.ly/3FuNpxM

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Decades of research have clearly shown that higher levels of air pollution have deleterious effects on respiratory and cardiovascular health [1, 2]. In addition, more recent studies have shown that air pollution is also associated with health outcomes that seem less obvious candidates, such as higher systemic inflammation [3], worse kidney function [4], worse cognitive abilities [5] and, very recently, higher incidence and mortality of COVID-19 [6, 7]. Importantly, these health effects of air pollution are also seen in regions with relatively low levels of air pollution, indicating that the current WHO air quality guidelines [8] are insufficient to prevent the negative health effects of air pollution.

Interestingly, the health effects of air pollution differ between individuals. This indicates that people are not equally susceptible to these health effects. For example, older and younger age, the presence of specific diseases, such as asthma or COPD, smoking [9] and specific genetic markers [10] have been associated with larger air pollution health effects. Another susceptibility-increasing factor is a higher body mass index (BMI). For example, a Chinese study in children has shown that higher levels of air pollution are associated with worse lung function and these effects are significantly larger in overweight and obese children [11]. Also, in children with asthma, air pollution effects on respiratory symptoms are larger in overweight and obese asthmatic children [12]. In addition, higher air pollution exposure is also associated with a higher obesity risk in children [13], resulting in a vicious circle and risk accumulation for negative health effects of air pollution.

Obesity has been widely recognised as both a risk factor and disease modifier in children and adults with asthma. The prevalence of asthma and obesity has increased significantly over the past decades. With an estimated prevalence of 10% in the paediatric population, asthma is the most prevalent chronic disease among children globally. The prevalence rate of obesity among children increased by about 50% between 1980 and 2013 in both developed and developing countries [14]. Asthma and obesity have a known intimate relationship and distinct phenotypes of overweight asthmatic subjects are distinguished: the "obese asthmatic" with prevalent (typically allergic) asthma with obesity-worsening asthma complaints (*i.e.* more frequent and more severe exacerbations), and the "asthmatic obese" in which asthma seems to have developed as a consequence of obesity [15]. Up to 23% to 27% of new asthma cases in children with obesity seem to be directly attributable to obesity [16]. Regardless of the asthma phenotype, obesity leads to more frequent and severe exacerbations, lung function changes, reduced response to asthma medication and lower quality of life [17–20]. Importantly, obesity also makes these asthmatic patients more susceptible to environmental exposures such as air pollution.

To date, it is not clear why subjects with a higher BMI are more susceptible to the health effects of air pollution. One of the hypothesised mechanisms is that both air pollution and obesity are associated with an increase in inflammation and oxidative stress. The cumulative effects of these will lead to larger air pollution effects in obese subjects. Indeed, the study by Dubowsky *et al*. [21] shows that subjects with diabetes, obesity and hypertension have larger increases in markers of systemic inflammation after air pollution exposure. Another hypothesis focuses on differences in lung volumes and breathing patterns between normal weight and overweight/obese subjects. These differences may lead to higher lung deposition of air pollutants. Evidence for this mechanism has been shown in healthy children [22].

In this issue of the *European Respiratory Journal*, Afshar-Mohajer *et al*. [23] have tried to shed more light on the possible mechanism to explain the greater susceptibility to air pollution in subjects with obesity. They focused on asthmatic children, since this is a group that already experiences a larger impact of air pollution exposure. They used data from a cohort of 174 asthmatic children to investigate the association of BMI with differences in breathing patterns and deposition of inhaled particles with a 50% cut-off aerodynamic diameter of 2.5 µm ($PM_{2.5}$). They show that children with a higher BMI have higher tidal volumes and minute ventilation than children with a lower BMI. By using a computational particle dosimetry model for $PM_{2.5}$, they show that higher tidal volumes caused a higher fractional deposition of $PM_{2.5}$ in the lungs, and especially in the alveolar region. A 20% decrease of functional residual capacity (FRC) in obese children was taken into account in a sensitivity analysis showing that the higher fractional deposition was independent of the FRC. The authors conclude that the higher tidal volumes in children with a higher BMI lead to higher susceptibility to air pollution.

The strength of this paper is that the authors used a combination of investigational methods to assess their hypothesis that higher tidal volumes in obese children will lead to higher $PM_{2.5}$ deposition in the respiratory system. Breathing pattern data were collected in a rather large group of asthmatic children with about equal numbers of obese and non-obese children. Breathing patterns were measured using a full-face mask, preventing the alterations in breathing patterns due to wearing a nose clip and the use of a mouthpiece. These breathing patterns were the input for the multi-path particle dosimetry model, which is an often used dosimetry model in children. A novel aspect of the study was that not only total fractional deposition of $PM_{2.5}$ was estimated but also regional deposition. These analyses showed that the deposition in the upper respiratory tract and the tracheobronchial tract (up to the 16th airway generation) was not dependent on the tidal volume, and thus was not dependent on BMI. However, deposition in the alveolar region was higher with higher tidal volumes, indicating that $PM_{2.5}$ penetrates deeper into the lung. Since a deeper penetration of particles probably leads to higher oxidative stress and pro-inflammatory responses [3], this suggest that children with a higher BMI are more at risk for these effects.

A limitation of the paper is that although the authors showed that, in this model, a set 20% reduction of the FRC in obese patients did not significantly influence deposition, the FRC was still estimated and not measured in individual study participants, which is feasible nowadays. Furthermore, as discussed by the authors, the evidence is indirect and future studies are needed with direct measurement of regional particle deposition. This will be challenging for both practical and ethical reasons.

The higher deposition of $PM_{2.5}$ in subjects with obesity is a very important observation and, especially in children with asthma, this may have clinical consequences. Children with asthma carry already two risk factors that make them more susceptible to air pollution, *i.e.* their younger age and their asthma. This study shows that if they are also obese, a third susceptibility factor is present. Undoubtedly, efforts to lower air pollution levels to control the negative health effects should continue and be enforced. But in addition, the health effects could be diminished if we can prevent or treat physical determinants, such as a high BMI, that increase susceptibility to air pollution. This study underlines the importance of primary prevention of overweight in children, and also indicates that secondary prevention may be beneficial for the course of disease in children with asthma.

Conflict of interest: None declared.

References

1 Hayes RB, Lim C, Zhang Y, *et al.* PM2.5 air pollution and cause-specific cardiovascular disease mortality. *Int J Epidemiol* 2020; 49: 25–35.

2 Khreis H, Kelly C, Tate J, *et al.* Exposure to traffic-related air pollution and risk of development of childhood asthma: a systematic review and meta-analysis. *Environ Int* 2017; 100: 1–31.

3 Arias-Pérez RD, Taborda NA, Gómez DM, *et al.* Inflammatory effects of particulate matter air pollution. *Environ Sci Pollut Res Int* 2020; 27: 42390–42404.
4 Jeong SM, Park JH, Kim HJ, *et al.* Effects of abdominal obesity on the association between air pollution and kidney function. *Int J Obes* 2020; 44: 1568–1576.
5 Aretz B, Janssen F, Vonk JM, *et al.* Long-term exposure to fine particulate matter, lung function and cognitive performance: a prospective Dutch cohort study on the underlying routes. *Environ Res* 2021; 201: 111533.
6 Brandt EB, Mersha TB. Environmental determinants of coronavirus disease 2019 (COVID-19). *Curr Allergy Asthma Rep* 2021; 21: 15.
7 Curtis L. $PM_{2.5}$, NO_2, wildfires, and other environmental exposures are linked to higher Covid 19 incidence, severity, and death rates. *Environ Sci Pollut Res Int* 2021; 28: 54429–54447.
8 Krzyzanowski M. WHO air quality guidelines for Europe. *J Toxicol Environ Health A* 2008; 71: 47–50.
9 Schraufnagel DE, Balmes JR, Cowl CT, *et al.* Air pollution and noncommunicable diseases: a review by the forum of international respiratory societies' environmental committee, part 1: the damaging effects of air pollution. *Chest* 2019; 155: 409–416.
10 Fuertes E, van der Plaat DA, Minelli C. Antioxidant genes and susceptibility to air pollution for respiratory and cardiovascular health. *Free Radic Biol Med* 2020; 151: 88–98.
11 Xing X, Hu L, Guo Y, *et al.* Interactions between ambient air pollution and obesity on lung function in children: the Seven Northeastern Chinese Cities (SNEC) study. *Sci Total Environ* 2020; 699: 134397.
12 Lu KD, Breysse PN, Diette GB, *et al.* Being overweight increases susceptibility to indoor pollutants among urban children with asthma. *J Allergy Clin Immunol* 2013; 131: 1017–1023.
13 Vrijheid M, Fossati S, Maitre L, *et al.* Early-life environmental exposures and childhood obesity: an exposome-wide approach. *Environ Health Perspect* 2020; 128: 67009.
14 GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, *et al.* Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med* 2017; 377: 13–27.
15 Bantulà M, Roca-Ferrer J, Arismendi E, *et al.* Asthma and obesity: two diseases on the rise and bridged by inflammation. *J Clin Med* 2021; 10: 169.
16 Lang JE, Bunnell HT, Hossain MJ, *et al.* Being overweight or obese and the development of asthma. *Pediatrics* 2018; 142: e20182119.
17 Forno E, Han YY, Mullen J, *et al.* Overweight, obesity, and lung function in children and adults—a meta-analysis. *J Allergy Clin Immunol Pract* 2018; 6: 570–581.
18 Borrell LN, Nguyen EA, Roth LA, *et al.* Childhood obesity and asthma control in the GALA II and SAGE II studies. *Am J Respir Crit Care Med* 2013; 187: 697–702.
19 van Gent R, van der Ent CK, Rovers MM, *et al.* Excessive body weight is associated with additional loss of quality of life in children with asthma. *J Allergy Clin Immunol* 2007; 119: 591–596.
20 Forno E, Lescher R, Strunk R, *et al.* Decreased response to inhaled steroids in overweight and obese asthmatic children. *J Allergy Clin Immunol* 2011; 127: 741–749.
21 Dubowsky SD, Suh H, Schwartz J, *et al.* Diabetes, obesity, and hypertension may enhance associations between air pollution and markers of systemic inflammation. *Environ Health Perspect* 2006; 114: 992–998.
22 Bennett WD, Zeman KL. Effect of body size on breathing pattern and fine-particle deposition in children. *J Appl Physiol (1985)* 2004; 97: 821–826.
23 Afshar-Mohajer N, Wu TD, Shade R, *et al.* Obesity, tidal volume, and pulmonary deposition of fine particulate matter in children with asthma. *Eur Respir J* 2022; 59: 2100209.