Indoor Air Pollution Effects On Pediatric Asthma Are Submicron Aerosol Particles Dependent

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Indoor air pollution effects on pediatric asthma are submicron aerosol particles dependent

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Short title: Indoor air pollution effects on pediatric asthma

Abbreviations:

PNC: Particle number concentrations
PMC: Particle mass concentrations
OPS: Optical Particle Sizer
CPC: Condensation particle counter
PM: particulate matter
$PM_{2.5}$: -particles less than or equal to 2.5 μm
PM_{10} - particles less than or equal to 10 μm
PM_1 - submicron particles, less than or equal to 1 μm

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Article summary:

Up to day, only a few studies evaluated the influence of the school environment on the respiratory health of younger school-age children. At the same time, there is a shortage of studies analyzing the effects of different size range aerosol pollutants. When children enter the first grade of primary school, they are relatively naive to air pollution other than in the home environment. Therefore, children in this age group were chosen as the target group. Our study aimed to evaluate indoor air pollution particle number and mass concentrations in primary schools and the impact of different size range particles on asthma morbidity among younger school-age children.

Author contributions:
Izabele Juskiene, Nina Prokopciuk and Arunas Valiulis designed the study and wrote the paper. All authors revised it critically for important intellectual content. All authors contributed to the article and approved the submitted version.

Abstract

The school environment is crucial for the child's health and wellbeing. On the other hand, the data about the role of school's aerosol pollution on the etiology of chronic non-communicable diseases remain scarce.

Objectives: To evaluate the level of indoor aerosol pollution in primary schools and its relation to the incidence of doctor's diagnosed asthma among younger school-age children.

Methods: The cross-sectional study was carried out in 11 primary schools of Vilnius during one year of education from autumn 2017 to spring 2018. Particle number (PNC) and mass (PMC) concentrations in the size range of 0.3-10 µm were measured using an Optical Particle Sizer (OPS, TSI model 3330). The annual incidence of doctor's diagnosed asthma in each school was calculated retrospectively from the data of medical records.

Results: The total number of 6-11 years old children participated in the study was 3638. The incidence of asthma per school ranged from 1.8 to 6.0%. Mean indoor air pollution based on measurements in classrooms during the lessons was calculated for each school. Levels of PNC and PMC in schools ranged between 33.0-168.0 part/cm^3 and 1.7-6.8 µg/m^3, respectively. There was a statistically significant correlation between the incidence of asthma and PNC as well as asthma and PMC in the particle size range of 0.3-1 µm ($r=0.66$, $p=0.028$) and ($r=0.71$, $p=0.017$) respectively. No significant correlation was found between asthma incidence and indoor air pollution in the particle size range of 0.3-2.5 and 0.3-10 µm.

Conclusions: We concluded that the number and mass concentrations of indoor air aerosol pollution in primary schools in the particle size range of 0.3-1 µm are primarily associated with the incidence of doctor's diagnosed asthma among younger school age-children.

Keywords: Asthma · Indoor aerosol pollution · Particle number concentration · Particle mass concentration · Particle size range · Primary school · Children

Introduction

Asthma is a chronic multifactorial disease, where genetic predisposition and environmental factors that interact and influence gene expression play an important role [1, 2, 3]. It seems environmental factors have different etiologic weight for children of different ages [4, 5]. It was earlier reported that increased prevalence of asthma is associated with the projected increase in the urban population [6]. By 2050 it is estimated that more than two-thirds of the world population will live in urban areas [7]. There is a greater prevalence of paediatric asthma in urban compared to rural populations [8], which may be partly explained by *hygiene theory* [9] and a higher level of air pollution, especially concentrations of particulate matter (PM) in the size range less than or equal to 2.5 μm ($PM_{2.5}$) [10-14]. At the same time only few studies have compared the effects of particles of different sizes, including submicron particles (PM_1, less than or equal to 1 μm), on child health [15, 16, 17]. It is essential to continue research on the effects of air pollution on child health and develop strategies to combat the burden of chronic non-communicable diseases [18, 19, 20, 21, 22].

Children when they enter the first grade of primary school are relatively naive to air pollution other than in the home environment. They spend more time at school (up to 4-8 hours usually in the same class) than anywhere else except their own home. School is a new environment for these children in terms of environmental pollution. Primary school children could be more susceptible to pollution because of incomplete immune system maturation and rapid lung growth [23].

Up to the present day, only a few studies evaluated the influence of the school environment on the respiratory health of younger school-age children [24-27]. Data on the effect of various sub-spectra of aerosol pollution are still scarce, while it should be needed for better understanding the mechanism of damage of the airways in children [15, 16, 17].

Our study aimed to assess indoor air pollution levels in primary schools and the impact of different sizes of aerosol particles on the incidence of asthma in younger school age children. We hypothesised that aerosol particles of different sizes can play different roles in the etiology and course of bronchial asthma in children.

Materials and methods

Sampling sites and description of schools

This cross-sectional study was carried out in Vilnius, Lithuania, (54º41′17″N, 25º15′ 8″E). Primary school children (children in the age range of 6-11 years, grades 1-4) were enrolled in our study. The number of pupils involved in the study was 3638 (total number of primary school children in Vilnius was 27019). Invitations were sent to 107 Vilnius schools to participate in the study, 25 have responded and agreed to participate. Every second school was randomly included in the study. One of the selected schools did not have primary classes and was rejected. Finally, 11 schools were selected to participate in the study. A unique number was assigned for each school to protect the privacy of study participants. Detailed characteristics of schools are presented in **Table 1**. Schools numbered 1, 5, 7, 10 were located in the downtown area, schools numbered 2, 3, 4, 6, and 8 were located in the peripheral part of the city and those numbered 9 and 11 were located in the suburbs**.**

Table 1. Characteristic of study schools.

Collecting of clinical and air pollution data

The annual incidence of doctor-diagnosed asthma among 6-11 years old pupils in each study school was calculated based on clinical records of health care providers collected by the National Institute of Hygiene. According to national legislation, personal codes of children and codes of diagnoses based on the Australian Modification of the International Statistical Classification of Diseases and Related Health Problems (ICD-10-AM) were received in the National Institute of Hygiene. The asthma incidence per school was calculated using the data of doctor's diagnosed asthma cases in the group of children of 6-11 years and the total number of this age group children in the school. For the study purposes, depersonalized data was provided. To determine aerosol particle number concentration (PNC) and particle mass concentration (PMC) in primary schools, a condensation particle counter (CPC; TSI model 3007, PNC in size range of 0.01 to >1.0 µm) and an optical particle sizer (OPS, TSI model 3330, PNC in size range of 0.3–10.0 µm) were used. The PMC was calculated by OPS software with the predefined particle density of 1 g/cm^3. Before measurements, the instruments were checked for contamination by using high-efficiency particulate arrestance filters. The data collection period was for one school year. The first measurements were done in October 2017 and the last in May 2018. In the schools, series of 10 minutes measurements of aerosol pollution were carried out in the classrooms during the lessons from 9 to 14 hours. The devices were placed on the school desk at the back of the classroom. Mean indoor air pollution per school was calculated based on the measurements in classrooms during the lessons only. Due to the detection of sources of aerosol pollution, indoor measurements were also carried out near the cafeterias and in the corridors. The outdoor particle concentrations were also measured in the school environment. For these data, see our previous publications [28, 29].

Statistical analysis

Descriptive statistics were used to estimate the aerosol pollution levels. The Linear Regression Model was used to determine the dependence of respiratory diseases on air pollution (aerosol particle number and mass concentrations). Pearson's correlation was used to evaluate the correlation between aerosol particle number and mass concentrations and asthma incidence. Dependence of the annual asthma incidence on PNC and PMC can be expressed by linear function: $y = a + b \cdot X$
The coefficient of proportionality (slope) (b) shows absolute average increase of asthma incidence (in percent), when particle number or mass concentration increases by 1 particles/cm³ or 1 μg/m³ respectively.
A P-value of < 0.05 was considered significant. Statistical analysis was performed using the statistical program IBM SPSS Statistics 23.

Results

Air pollution and incidence of asthma in primary schools

Data on average annual (2017-2018) particle number and mass concentrations (OPS, from 0.3 to 10 μm), as well as the incidence of doctor's diagnosed asthma in each of 11 participating primary schools, are presented in **Fig. 1A.** The incidence of asthma of 6-7 years old children in 11 Vilnius schools involved in our survey was between 1.8 to 6.0 % per school. The mean annual particle number concentration varied between 36-172 particles/cm³, with the minimum value at school No. 8 and highest at school No. 1. The mean annual particle mass concentration varied between 52-179 μg/m³, with the lowest value at school No. 4 and the highest at school No. 3.

Fig. 1. Incidence of doctor's diagnosed asthma and average annual aerosol particle number and mass concentrations in participating primary schools **(A)** and 5th and 95th percentiles of particle number concentration **(B)** in participating primary schools; (PNC – particle number concentration, PMC – particle mass concentration).

The 5th and 95th percentiles of particle number concentrations (OPS, from 0.3 to 10 µm) are presented in **Fig. 1B**. The highest values of 95th percentiles are in schools No 1 and No 10 (393 and 502 particles/cm^3, respectively) and the lowest in schools No. 8 and No. 9 (64 and 131 particles/cm^3, respectively). The 5th percentiles varied between 12 particles /cm^3 in schools No. 9 and No.11 and 92 particles/cm^3 in school No. 1.

Annual (2017-2018) data on PNC (OPS, from 0.3 to 1 µm) are presented in **Table 2**. The mean particle number concentration in 11 schools ranged between 33-168 part/cm^3.

Table 2. Annual (2017-2018) data on PNC (OPS, from 0.3 to 1 µm) in participating primary schools.

During the 2017–2018 school year, the highest annual PNC (CPC) values in classrooms were determined in schools No. 10 and No. 11 (**Table 3**). The main sources responsible for the elevated levels of indoor air pollution were local cafeterias (particle concentrations up to 30,000 part/cm^3. In schools No.1-4, the main sources responsible for the elevated levels of indoor air pollution were cafeterias, but also to a lesser degree an elevated outdoor air pollution. The mean annual PNC varied in the range of 3475-8035 particles/cm^3. The highest values of 95th percentiles are in schools No. 3 and No. 11 (21374 and 22956 particles/cm^3, respectively) and the lowest in schools No. 7, No. 8 and No. 9 (7577, 7328 and 6538 particles/cm^3, respectively). The 5th percentiles varied between 1198 particles /cm^3 in schools No. 11 and 4757 particles/cm^3 in school No. 1.

Table 3. Annual (2017-2018) data on PNC (CPC, from 0.01 to >1.0 µm) in participating primary schools.

Relationship between the concentrations of aerosol particles of different size range and asthma

There was a positive but not significant correlation (r=0.55, p=0.08) between PNC in the size range of 0.3-10 µm and asthma. There was no correlation between asthma incidence and the total number concentrations (CPC) of aerosol particles. No correlation was also found between PMC in the size range of 0.3-2.5 µm and asthma.

On the other hand, a significant correlation was found between asthma incidence and submicron (0.3-1 µm) aerosol particle number (r=0.66, p=0.028) **(Fig. 2A)** and mass (r=0.71, p=0.017) (**Fig. 2B**) concentrations.

Fig. 2. Correlation between aerosol particle number (**A**) and mass (**B**) concentrations in size range of 0.3-1 µm and incidence of doctor's diagnosed asthma among pupils in study schools.

The obtained data of regression analysis give rather reliable results. Thus, P-values are <0.05, which indicates the reliability of the coefficients. The coefficients of determination ($R^2= 0.44$ for PNC, $R^2=0.50$ for PMC) demonstrate that up to 50 perc. of the values correspond to the data of linear regression.

According to the linear regression equation, an increase in the mass concentration of aerosol particles by 1 µg/cm3 leads to the increase in the incidence of asthma by 0.6%, while an increase in the number concentration by 1 particle/cm^3 leads to the increase in the incidence of asthma by 0.03%.

Discussion

Despite the comprehensive research of the role of air pollution in the etiology of asthma during the last decades, we still have more questions than answers [10, 11, 13, 16, 30, 31]. The research data focussing mainly on $PM_{2.5}$, PM_{10} (particles less than or equal to 10 µm) remain contradictory [32, 33, 34, 35]. Air pollution data used in epidemiological studies are usually obtained from stationary air pollution monitoring stations and extrapolated to the child's living environment [30, 32, 36, 37, 38]. There is also a lack of research done in the populations on the new social and environmental life threshold, including the first years of entering kindergarten or primary school.

Our study in primary school children setting shows that in a relatively low polluted region of Eastern Europe, there are big differences in aerosol pollution between schools within one middle-size city. Data on PNC and PMC in schools ranged between 33.0-168.0 part/cm^3 and 1.7-6.8 µg/m^3, respectively. A statistically significant correlation was found between PNC and PMC in the size range of 0.3-1 µm and incidence of asthma of younger school age children. In contrast to previous study of French primary schools [27], no significant correlation was found between PMC in the particle size range of 0.3-2.5 or 0.3-10 µm and the incidence of asthma among pupils.

Conflicting data on the influence of ultrafine particles of <0.1 μm (UFPs) on child health has been earlier reported [24, 25,39]. Paunescu et al. found no associations of UFPs with lung function parameters or exhaled nitric oxide (FeNO) in children [24]. The other study by Clifford et al. from Australia UFPs PNC was measured in 25 schools and modelled at homes using a Land Use Regression model [24]. It was found that UFPs are positively associated with an increase in FeNO and C reactive protein among atopic pupils. In contrast, Samali et al. reported UFP effects on respiratory hospital admission among children till 14 years of age [39]. Indoor and outdoor measurements of PM and gaseous pollutants have been carried out in 12 Korean schools [26]. There was a positive association between current asthma and outdoor UFP, as well as between wheezing and outdoor NO_2. Yang et al. reported that in terms of risk of asthma and asthma related-symptoms among 2-17 years old children, the strength of positive associations with $PM_{2.5}$ or PM_1 is similar [40]. However, in a recent retrospective study by Zhang et al., it was found that increased risk of the onset of asthma in children is associated with early-life exposure to PM_1. PMC of PM_1 has a stronger association with asthma if compared to larger particles of $PM_{2.5}$ and PM_{10} [41].

In vivo studies on rats showed that PM_1 altered morphometric measures of the lung parenchyma, depressed macrophage functions related to defence against respiratory infections, and increased lung permeability [42]. *In vivo* experimental studies on the regional deposition of PM_1 are scarce. An *ex vivo* study assessed regional deposition patterns of radioactive polydisperse aerosols size ranges 0.15-0.5 μm, 0.25-1 μm and 1-9 μm. Using a polydisperse radioactive aerosol, marked with ^{99}Tc, deposition was studied using an original respiratory tract model [43]. The deposited fractions obtained for thoracic and extra-thoracic regions were 89 ± 4% and 11 ± 4% for 0.15-0.5 μm, 78 ± 5% and 22 ± 5% for 0.25-1 μm and 35 ± 11% and 65 ± 11% for 1-9 μm, respectively. It was suggested that an accumulation mode of 0.1-1 μm particles could be responsible for a greater negative impact on children's respiratory health [15,17]. We have found a submicron spectrum of aerosol pollution in contrast to larger size range particles related to the incidence of asthma in children. It could be speculated that interaction between submicron particles of aerosol pollution and aeroallergens as well as bacteria/viruses can be the further target of paediatric asthma research.

Aerosol particles in the 0.1-1 μm range have a long lifetime in the atmosphere (1-3 weeks), and dry deposition is minimal [44, 45]. This mode has relatively large mass and number concentrations with proportionally larger amounts of harmful substances. However, there are few studies comparing the effects of accumulation mode particles on children's health [16, 17]. The most substantial impact on respiratory health among young children were observed for the mass concentration of PM_1 and the number concentration of particles 0.5-1 μm [16]. Braniš et al. found the strongest association between accumulation mode PNC in the size range of 205–487 μm and hospital admissions due to respiratory diseases [17].

Andersson et al. reported that preschool children with severe wheeze had impaired airway epithelial proliferative responses following damage by respiratory viruses and house dust mite aeroallergens [46]. The reduced expression of epithelial growth factor receptors in severe preschool wheezers, together with lower wound healing response to epithelial cytokine IL-33, may lead to a damaged epithelial barrier function and contribute to the development of airway remodelling. Some other studies have shown that airway remodelling occurs even in children with mild asthma [47, 48]. It is still unclear when asthma remodelling and other morphologic changes of the airways can appear and which trigger lead the way [49, 50, 51]. We hypothesize that the accumulation mode of particles equal to or less than 1 μm, in contrast with larger size range particles, can activate mechanisms of asthma not only through the maintenance of chronic inflammation in the airways but also by direct engagement in the fibrosis process of asthma remodelling. Saglani et al. found that pathologic features of asthma in adults and school-aged children develop in preschool children with recurrent wheeze between the age of 1-3 years [49].

The variations in findings in terms of air pollution and the origin of asthma in children are still not completely understood [52, 53, 54]. The results suggest that asthma initiation and/or modulation effects and the relationships with air pollution may be complex and nonlinearly dependent [15, 55].

It was some limitations of our study. We neither measured air pollution in the home environment of pupils nor analyzed the chemical compounds and the main trace elements of aerosol pollutants. Data on the incidence of asthma in children were obtained retrospectively from the records of health care providers. It is important to carry out a prospective study with a more extensive data collection and a comprehensive assessment of particulate and gaseous pollution effects in the school environment.

Conclusion

We concluded that the number and mass concentrations of indoor aerosol pollution in primary school in the particle size range of 0.3-1.0 μm, compared to particles of a larger size range, are associated with the incidence of doctor's diagnosed asthma in younger school-age children. Since children spend so much time at school, focusing on the school environment is very important.

What is Known: Both indoor and outdoor aerosol pollution is associated with bronchial asthma in children.

What is New: The incidence of bronchial asthma among younger school age children is related to indoor air quality in primary schools. Aerosol pollutants in the size range of 0.3–1 μm in contrast to bigger size range particles can play major role in the etiology of bronchial asthma in children.

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Table 1. Characteristic of study schools.

School number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Year of construction	1970	1965	1979	1970	1977	1969	1973	1988	1980	1972	1962
Number of children*	419	392	444	388	264	229	234	305	270	547	146
Location in city	downtown	periphery	periphery	periphery	downtown	periphery	downtown	periphery	suburbs	downtown	suburbs
Ventilation type of classrooms	natural	natural	natural	natural	natural	natural	natural	natural	natural	natural	natural
Food cooking inside school	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

* data of 2017-2018 years, children in the age range of 6 – 11

Fig. 1. Incidence of doctor's diagnosed asthma and average annual aerosol particle number and mass concentrations in participating primary schools **(A)** and 5th and 95th percentiles of particle number concentration **(B)** in participating primary schools; (PNC – particle number concentration, PMC – particle mass concentration).

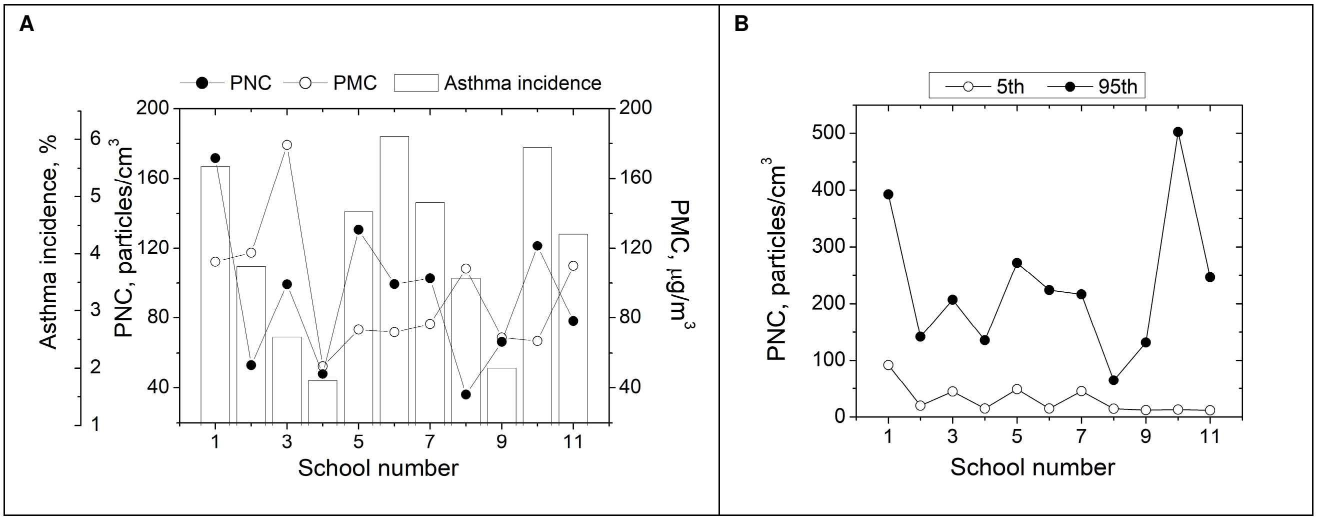

Table 2. Annual (2017-2018) data on PNC (OPS, from 0.3 to 1 µm) in participating primary schools.

	Particle number concentrations in classrooms				
School No.	Mean	Max	Min	95th	5th
1	168	504	84	390	89
2	50	146	17	139	17
3	92	261	36	176	41
4	46	140	12	133	12
5	128	280	46	268	47
6	97	271	13	222	13
7	100	220	42	216	43
8	33	250	9	58	11
9	64	189	10	130	10
10	120	646	9	501	11
11	75	348	9	245	10

Table 3. Annual (2017-2018) data on PNC (CPC, from 0.01 to >1.0 µm) in participating primary schools.

	Particle number concentrations in classrooms				
School No.	Mean	Max	Min	95th	5th
1	7567	14507	4527	12004	4757
2	5776	17205	1657	10724	1771
3	7158	24158	2723	21374	2934
4	8035	16149	2828	15577	3014
5	6855	12379	3592	11035	4048
6	6682	11319	3896	10792	4448
7	4636	8335	2034	7577	2081
8	5488	8638	3206	7328	3401
9	3475	6853	1784	6538	1895
10	4108	30999	1734	16445	1980
11	3735	30995	1105	22956	1198

Fig. 2. Correlation between aerosol particle number (**A**) and mass (**B**) concentrations in size range of 0.3-1 µm and incidence of doctor's diagnosed asthma among pupils in study schools.