The Effect of Industrial vs. Rural Environment in the Respiratory Status of Schoolchildren

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Abstract

Introduction: This is the first study in Greece where specific methodology is used controlling for all known confounders on the morphology of the children's spirometric curve in industrial vs. rural area.

Materials and Methods: A parental questionnaire and a spirometry test in 62 children in Oinofyta (Industrial area) and 42 in Makrakomi (Rural Area) (5th and 6th Grades, 11-12 years).

Results: Higher rates in the industrial area for children's history of asthma and asthma related symptoms were observed. Subnormal spirometric curve rates in Oinofyta was 25.8% vs. 12.2% in Makarakomi (P=0.074). Similarly, the number of children who had FVC (Forced Vital Capacity) <90% was higher in Oinofyta than in Makrakomi (P=0.046). After adjusting for confounding factors, statistically significant differences were observed in asthma diagnosis and related symptoms, in subnormal spirometric curves and spirometric indices between children in the two study groups.

Conclusion: Industrial residential area is significantly associated with children's history of asthma and reduced pulmonary function.

Keywords: Childhood asthma, Industrial area, Respiratory health

1. Introduction

Bronchial asthma is a very common chronic disease in childhood and its prevalence has been increasing during the past decades, as shown by a considerable number of studies, where asthma and allergies in childhood are more pronounced in most developed countries (Asher et al., 2006; Maziak et al., 2003; Pearce et al., 2000). The aetiology of the disease seems to be multifactorial and still remains under discussion (Anthracopoulos et al. 2001; Pearce & Douwes, 2006). The environmental factors which greatly contribute to the development of the disease

is air pollution - industrial and traffic related - as well as indoor environmental factors (pet allergens, mould, dust mite, passive smoking) (Lau et al., 2000; Kattan et al., 1997; Nelson et al., 1999; Eggleston, 2000). In Europe the effect of air pollution on children's health is of a great interest. In June 2004, the European Environment and Children's Health Action Plan was set by the World Health Organization, the aim of which was to reduce mortality and morbidity related to environmental air pollution in fetus, children and adolescents (Fuentes-Leonarte et al., 2008). According to Valent et al. (2004) the rate of children's deaths (0-4 year-old) caused by air pollution is 1.8-6.4% and they are related mostly to lower respiratory tract morbidities. Air pollution consists of Particulate Matter (PM) which may be characterized as PM_{10} : coarse, $PM_{2,5}$: fine and ultrafine PM according to its aerodynamic diameter (Sioutas et al. 2005) and of other air pollutants which are ozon (O₃), nitrogen dioxide (NO₂), carbon monoxide (CO) and sulphur dioxide (SO₂). Children's exposure to air pollutants is associated with infant mortality, deficits in lung growth and asthma development, as well as asthma exacerbations and hospitalizations (Kim, 2004). The prevalence of asthma and asthma related symptoms are statistically significant associated with SO₂, NO₂ and PM₁₀ concentrations (Zhang et al., 2002; Clark et al., 2010), as well as O3 and CO concentrations (Hwang & Lee, 2010).

A number of cohort studies performed to date have demonstrated that residing in an industrial area may result in elevated prevalence of asthma diagnosis and asthma-related symptoms in children (Cara et al., 2010; Priftis et al., 2007; Sichletidis et al., 2005). Moreover, other cohort studies demonstrate that children residing in an industrial area have reduced lung function as indicated by spirometric values (Carta et al., 2007; Ranzi et al., 2004; Wichmann et al., 2009). It has been reported that children's residency near a petroleum refinery and therefore elevated ambient SO₂ concentration has been associated with the number of asthma related admissions or hospitalizations in these children (Smargiassi et al., 2009). Aylin et al. (2001) reached to the same conclusion when they studied on children residing near a coke-mining site. It should also be noted that as heavy metals are widely used in industry, children's exposure to them is increased by residency in such an area and especially in mine tailings (Moreno et al. 2010). Such an exposure can lead to asthma diagnosis and asthma related symptoms in children (Wilhelm et al., 2007; Patel et al., 2009; Hirshon et al., 2008).

We hypothesized that respiratory health and pulmonary function in children residing in an industrial heavily polluted area would be adversely affected, when compared with children residing in a rural area. To test this hypothesis we compared respiratory symptoms and spirometric indices of a cohort of children permanently residing in an industrial area to those of a cohort of children with similar demographic characteristics living in a rural environment in Greece. This is the first study in Greece where this type of association is examined, as well as this is the only study in Greece where a population of this size is permanently residing in an industrial area and exposed to industrial air pollution from birth till the time of the study.

2. Materials and methods

2.1 Study area

The study was conducted in two distinctly different types of environment: an industrial and a rural residential area. The municipality of Oinofyta (Viotia Prefecture) was chosen as the industrial environment (Figure 1), located 50 km North of Athens, Greece. The number of industries in Oinofyta region increased significantly after 1984, when according to a new law, restrictions were imposed on the establishment of various industries within Attica prefecture, thus an industrial zone within Oinofyta region was formed. All children parents who participated in the study reported that their home is within 5km from the industrial area. According to the Technical Chamber of Greece (2009) about 700 industries are operating in the Oinofyta region, of which 500 generate liquid industrial waste and various emissions (Greece TCo, 2009). Oinofyta as the industrial zone of Attica host numerous industrial types of activity such as mining, detergents, pesticides, and other chemical production, leather production, aluminium, pharmaceuticals, food production and fodders according to the National Technical University of Athens and registry of industries held by the Oinofyta municipal office.

It should be noted that in 1969 a ministerial decision permitted industries to deposit their waste in the Asopos river, which runs through Oinofyta. Data concerning the concentration of air pollutants are not readily available, but citizens are complaining about the large number of industries located in the area, the black smoke produced by industries' smokestucks and its odour especially in summer when children spend most time outdoors. Moreover, measurements in drinking water have shown that the concentration of hexavalent chromium is 41-156 μ g/lt (Linos et al. 2011) which in some cases exceeds the official limits set by the United States Environmental Protection Agency equal to 100 μ g/lt and the European Union equal to 50 μ g/lt.

The provincial area of Makrakomi (Fthiotida Prefecture, Figure 2) was chosen as the rural area. It is situated approximately 200 km North of Athens and about 30 km of the nearest large town which is Lamia. Makrakomi

is an agricultural village, where at a radius of 30km there is no industry located. According to our research none of Makrakomi children parents, who participated in the study, are occupied in an industry (0%), whereas in Oinofyta region the rate of children mothers who report to be occupied in an industry is 25% and for their fathers the rate is 60.7% (P<0.001).

It must be considered that both Oinofyta and Makrakomi are two small and isolated villages, with only one elementary school in each, as generally happens in Greek villages. In order to ensure the conformity of the study population, we limited our study in these two areas of residency.

2.2 Study Population

Children attending the 5th and 6th Grade of Oinofyta and Makrakomi elementary schools, 11 and 12 years, were recruited. The age (11 and 12 years - not younger) was chosen in order to ensure childrens' cooperation. Eligible study participants had to be permanent residents in both study areas from birth until the date of spirometry test. Moreover, they had to show competence in performing acceptable forced expiratory flow-volume maneuvers. Children were excluded from the study if they had any upper or lower respiratory tract infection at the time when spirometry was performed or in case of any myoskeletal deformity. None child attending 5th and 6th Grade of both elementary schools, had any reported history of diagnosed cystic fibrosis, primary ciliary dyskinesia, bronchiectasis or prematurity.

A total of 73 children are registered in the 5th and 6th grades of Oinofyta and 62 in the Makrakomi elementary school respectively. All registered children and their parents in both schools received an invitation letter for participation to the study on respiratory health without disclosing the study hypothesis, after an informative lecturer to childrens' parents, teachers and authorities in both study areas. A specifically designed questionnaire (according to the questionnaire used in the International Study of Asthma and Allergies in Childhood – ISAAC) was developed for the study which was distributed to the parent/guardian of each pupil. Parents were instructed to complete the questionnaire and deliver it to the study's main researcher.

A written informed consent form was signed by the parents or guardians of each participating pupil regarding the completion of a questionnaire, a clinical examination and spirometry test. The study has been approved by the Athens University Ethics Committee and the Ministry of Education.

Spirometry tests were performed during normal school hours having made prior arrangements with the school's headmaster and the teachers. Spirometry test was performed within two weeks parents completed the administered questionnaire (before or after).

Overall, 62 out of 73 children in Oinofyta (84.5%) and 42 out of 62 children in Makrakomi (67.7%), completed the questionnaire and performed a technically acceptable maneuver during the spirometric effort.

Only children who participated in the spirometry test and delivered the completed questionnaire, were included in the study. In case of any of the two was missing, the main researcher contacted the family by phone reminders and letters. Moreover, children were excluded if they were not permanent residents in both study areas. There is no indication that there was any relationship between participation in the study and impaired pulmonary function or history of asthma in any of the children.

2.3 Questionnaire

A parental questionnaire was distributed at school requesting information on the child's respiratory health, i.e. the child ever been diagnosed with asthma, ever used asthma medication or ever been hospitalized because of an asthma exacerbation and the prevalence of asthma related symptoms in the last 12 months. Furthermore parents were asked to answer questions concerning demographic and household characteristics, number of siblings, a family history of asthma, parental education and occupation, their socioeconomic status, children's perinatal history of prematurity and their birth weight, their exposure to indoor air pollutants, such as second hand smoking before and after birth, pet ownership, indoor humidity, exposure to heating and cooking fuels. Questions on children being exposed to traffic related air pollution were also included.

2.4 Spirometry

Spirometry was performed at the two elementary schools during morning school hours, between February and March 2011, using the computerized spirometer Spirolab III Ver 2.5 SN 303142 (Device characteristics: Volume Range: 10L, Flow Range: 16L/s, Volume accuracy: +/- 30% or 50mL, Flow accuracy +/- 5% or 200 mL/s). Spirometry was deffered for another day if the child had suffered an upper or lower respiratory tract infection within the last week or had used a bronchodilator within 2 days. Values were expressed as percentage of predicted for gender and height (Quanjer, 1983). All efforts were taken to ensure that there was no difference in the performance of technically acceptable maneuvers between the two study groups. Spirometry tests were

performed by the same researchers in both areas, trained in performing and evaluating the test and spirometry testing was standardized.

2.5 Statistical Analysis

The relationship between diagnosed asthma, bronchodilator use, hospitalization because of an asthma exacerbation or an abnormal spirometric curve, against area of residence and potential confounding variables, was tested using the Fisher's exact test or Pearson chi-square test when applicable, due to the small sample size. Moreover, children in each area were placed in two categories according to their predicted spirometric percent values (<90% and >90%), and tested with Pearson χ^2 test. For the binary dependent variables, logistic regression modeling was applied adjusting for potential confounders. Specifically, to control for the potential effect of the studied confounders on the relationship between children's spirometric indices, as well as their asthma related symptoms and city of residence, logistic regression analysis was performed using the confounding factors for which statistically significant difference was observed between the two study areas as independent variables in each examined model. They were included concurrently in all regression analyses performed. As dependent variables were used reported bronchitis, dry cough, asthma diagnosis, breathlessness in the last 12 months, the child ever been diagnosed with asthma, ever used asthma medication or ever been hospitalized because of an asthma exacerbation, as well as the aforementioned spirometric values <90% in each examined model.

We verified the assumptions of normality of all variables and the level of statistical significance was set at 0.05. Analysis was carried out using the statistical software SPSS 17.0.

3. Results

The mean age of children who participated in the study was 10.93 years in Oinofyta and 10.78 years in Makrakomi region. The male/female ratio in the industrial and rural area was almost identical (0.77/1 and 0.75/1 respectively). The distribution of potentially confounding risk factors and statistical differences between the two study areas (Oinofyta and Makrakomi) is shown in Table 1. In Oinofyta region the rate of children who had a family history of asthma was 4.9% and in Makrakomi was 2.4% and no statistically significant difference was observed between the two areas of residency. Moreover, no statistically significant difference was observed between the two study groups regarding the number of children's siblings. The difference in reported exposure to traffic related air pollution, maternal and paternal occupation in an industry and parental occupation in agriculture or livestock was statistically significant between the study areas (P=0.012, P<0.001, P<0.001, P=0.007 respectively), whereas no statistically significant difference was observed for exposure to passive smoking, exposure to prenatal smoking and children's close contact to pets and interior plants. The difference in exposure to humidity and heating fuels was borderline (P=0.052, P=0.156 respectively).

Table 2 presents the prevalence of children ever having any history of asthma diagnosis, asthma medication use and asthma hospitalization. The prevalence of the last 12 months reported bronchitis, dry cough, breathlessness, and diagnosis of an asthma episode is also shown. It is apparent that the prevalence of children having had bronchitis and a diagnosis of asthma in the last 12 months was higher in Oinofyta region, but there was no statistically significant difference between the industrial and rural area of residency. The prevalence of dry cough in the last 12 months was higher in Makrakomi region (rural area) and the prevalence of breathlessness in the last 12 months was similar in the two study areas. Furthermore, when the variables of the child "ever had asthma", "ever used asthma medication" and "ever been hospitalized because of an asthma exacerbation" were examined, they are more prevalent for children living in Oinofyta region but no statistically significant difference was found.

Successful spirometry was performed in children of both study areas and the spirometric curve was evaluated by a pediatrician and a pneumonologist. Complete agreement was achieved by the observers in all evaluations. According to our statistical analysis we demonstrated that the rate of children having performed an abnormal spirometric curve was 25.8% in Oinofyta (Industrial region) and 12.2% in Makrakomi region (Rural area) (P=0.074). We performed Pearson χ^2 test after creating two groups of children's spirometric values - percent predicted – those with values <90% and those with values >90% for FVC, FEF25, FEF50 (Forced Expiratory Flow 50%) and PEF. Table 3 shows the number of children in both study areas, with FVC, FEF25, FEF50 and PEF values <90%. The rate of children having had values <90% for these spirometric indices were higher in the industrial area than the rural area and for FVC the difference was statistically significant (P=0.046).

To control for the potential effect of known confounders on the relationship between children's pulmonary function as well as their asthma related symptoms and city of residence, logistic regression analysis was performed using the confounders for which a statistically significant difference between the two study areas was shown as independent variables in each examined model. As shown in Table 1, these confounding factors were

exposure to passive smoking, traffic related air pollution, heating fuels, humidity at home and parental occupation. They were included concurrently in all regression analyses performed controlling for age and gender as well.

Specifically, multivariate logistic regression analysis was performed using as dependent variables a) the child ever had an asthma diagnosis, b) ever used asthma medication and c) ever been hospitalized because of an asthma exacerbation and as main independent variable the city of residence controlling for age, gender and the potential effect of exposure to passive smoking, traffic related air pollution, heating fuels and humidity in home as well as parental occupation. Furthermore, logistic regression analysis was used after setting as dependent variables FVC, FEF25, FEF50 and PEF values <90% and independent the aforementioned confounding factors and the area of residency. The results concerning the area of residency are shown in Tables 4 and 5. There was a significant correlation between the child ever been diagnosed with asthma, ever used asthma medication and residing in an industrial area. Furthermore, a significant correlation was noted between the child having had FEF25 and PEF<90%, as well as performance of an abnormal spirometric curve and industrial area of residency. Although we have shown that industrial area of residency may affect children's spirometric indices, as well as their asthma related symptoms in the last 12 months and their history of asthma diagnosis, asthma medication use and hospitalization, the studied confounding factors seem to also play an important role in children's respiratory health, which remains to be studied in the future.

4. Discussion

We studied two cohorts of children, 11 and 12 years of age, attending 5th and 6th grade of Oinofyta elementary school (industrial area) and Makrakomi elementary school (rural area) by means of questionnaire completed by the children's parents/guardians and spirometry testing. Our results show that industrial area of residency may affect children's pulmonary function, as indicated by measured spirometric values, as well as their respiratory health - history of asthma diagnosis and asthma related symptoms - although no statistically significant difference was evident between the industrial and the rural study areas. After adjusting for confounding factors, such as exposure to reported passive smoking (Oberg et al., 2011; Cheraghi & Salvi, 2009; Goodwin & Cowles, 2008), traffic related air pollution (Li et al., 2011), heating fuels (Qian et al., 2004) and humidity at home (Nguyen et al., 2010; Hagmolen of Ten Have et al., 2007), as well as parental occupation, we concluded that statistically significant difference exists for the children ever having asthma diagnosis and ever used asthma medication. We can therefore assume that these confounding factors play an important role in the respiratory status of schoolchildren, which may be the scope of a later research, focusing on how these factors contribute to the incidence of children's asthma symptoms and how they affect children's pulmonary function as shown by spirometric percent predicted values. Regarding these percent predicted values we demonstrated that children residing in the industrial area were more likely to have FVC, FEF25, FEF50 and PEF<90% with FVC presenting an adverse statistically significant difference for the industrial (Oinofyta) study area compared with the rural one (Makrakomi). After adjusting for the aforementioned confounding factors the statistically significant difference was no longer evident for FVC percent predicted value, but was noted for FEF25 and PEF. This observation can lead again to a conclusion that the studied confounding factors affect children's percent predicted spirometric values. Also, a statistically significant difference was present between children's abnormal spirometric curve and residing in an industrial area, which remained after logistic regression analysis was performed.

Other researchers also demonstrated that residing in an industrial area results in elevated prevalence of asthma diagnosis and asthma-related symptoms in children. Specifically, Cara et al. (2010) in their cohort study in Romania demonstrated that the prevalence of asthma symptoms was higher for children residing in an industrial area (OR: 7.2, 95% CI: 3.6-14.3) as reported by the completion of a parental questionnaire. The statistically significant difference remained after adjusting for confounding factors. The fact that industrial area of residency may adversely affect children's respiratory health, could be explained by the increased air pollutants' concentration in these areas. Other researchers have compared air pollutants' concentration measurements in their study areas of interest. Wichmann et al. (2009) reported that children residing near a petroleum refinery were more likely to have asthma (OR: 2.76, 95% CI: 1.96-3.89), asthma exacerbations (OR: 1.88, 95% CI: 1.25-1.83), wheezing (OR: 1.93, 95% CI: 1.39-2.67), chest tightness (OR: 1.77, 95% CI: 1.23-2.55) and breathlessness (OR: 1.72, 95% CI: 1.29-2.41). They included in their analysis the air pollutants' concentration for particulate matter (PM10, PM2.5 Kat PM0.5) and volatile organic compounds and proved that were elevated in the industrial area. The fact that children's exposure to air pollutants may result in respiratory symptoms in children is proved by various researchers in US (Mann et al., 2010; Yu et al., 2000; Gent et al., 2003), Australia (Rodriguez et al., 2007; Jalaludin et al., 2004) and China (Zhang et al., 2002). In our study, as elevated levels of hexavalent chromium have been measured in drinking water, one can hypothesize that industrial waste may be

contaminated with this heavy metal and the respiratory status of the exposed children has been affected. However, no measurements of heavy metals and especially hexavalent chromium in ambient air or in contaminated ground are readily available. Results from other studies, also, demonstrated that children's pulmonary function, is directly associated with their area of residency (urban vs. rural environment). Wichmann et al. (2009) showed a 13% reduction of FEV₁ for children residing near a petroleum refinery industry and similar were findings concerning PEF values (Ranzi et al., 2004). Moreover, industrial air pollution is directly associated with pulmonary function during childhood. In US, Gauderman et al. (2002), Delfino et al. (2004), Dales et al. (2009) demonstrated that increased air pollutants' concentration lead to FEV₁ value reduction during childhood. Jalaludin et al. (2000) studied on ozone concentration effect on children with a wheezing history and concluded that a statistically significant associated that FEV₁ and FEF values were significantly associated with PM₁₀ concentration.

However, the interpretation of our results regarding the association of industrial residency with respiratory symptoms and lung function in childhood, is limited by the fact that any data concerning air pollutants' concentrations was available. In addition, unreported variables such as sensitization in aeroallergens and IgE test performance (Priftis et al., 2007; Ogershok et al., 2007) in both areas and socioeconomic factors may constitute confounders on respiratory symptomatology and lung function. The relatively small study sample size is a limitation which was mostly imposed by financial and time constraints as well as difficulties in securing the prompt cooperation from the official educational authorities as well as the consent of the parents. On the other hand, we focused our study in two small isolated villages with distinct characteristics of industrial and rural environment. Due to these reasons and given the fact that this is the first type of this study in Greece, we decided to carry on with a cross-sectional study in order to create a baseline for further research to determine the causative relationship between asthma related symptoms and industrial area of residency.

Moreover, we used specific methodology to control for the aforementioned confounders on the morphology of the children's spirometric curve in industrial vs. rural area for the first time in a study of this type in Greece. We intend in the immediate future to use specific data on air pollutants' concentration in both study areas and correlate them with children's history of asthma, asthma related symptoms and pulmonary function in the two residential areas to further test our hypothesis.

In conclusion, our study's results indicate that industrial residency may be associated with an increased prevalence of asthma and respiratory symptoms, as well as reduced pulmonary function in childhood in Greece although statistically significant difference was not demonstrated in all cases. These findings and our small sample size suggest that larger cohort studies investigating the role of exposure to industrial air pollution and residency in an industrial area on children's respiratory status are required to verify the relationships.

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	City					
	Oinofyta (industrial)		Makrakomi (rural)		P value	
	n	%	n	%		
Family history of asthma	3	4.9%	1	2.4%	0.644	
>3 siblings	3	4.8%	4	9.5%	0.436	
Any smoking at home	30	54.5%	22	53.7%	0.931	
Mother smoked during pregnancy	4	6.7%	3	7.1%	1.000	
Exposure to traffic related air pollution	6	9.7%	12	28.6%	0.012	
Wood/coal stove for heating	1	1.6%	4	9.5%	0.156	
Humidity/Mould in home	21	33.9%	7	16.7%	0.052	
Close contact to interior plants	13	21%	9	21.4%	1.000	
Close contact to pets	14	23%	9	21.4%	1.000	
Maternal occupation in an industry	16	25.8%	0	0%	< 0.001	
Paternal occupation in an industry	37	60.7%	0	0%	< 0.001	
Paternal occupation in agriculture or livestock	0	0%	5	19.2%	0.007	

Table 1. Distribution of children's exposure to confounding risk factors in the two study areas

	City				
	Oinofyta (industrial)		Makrakomi (rural)		P value
	n	%	n	%	
Bronchitis in the last 12 months	7	11.3%	3	7.1%	0.736
Dry cough in the last 12 months	5	8.1%	4	9.5%	1.000
Asthma diagnosis in the last 12 months	2	3.2%	1	2.4%	1.000
Breathlessness in the last 12 months	3	4.8%	2	4.8%	1.000
Ever had asthma	11	17.7%	4	9.5%	0.272
Ever used asthma medication	11	17.7%	4	9.5%	0.272
Ever been hospitalized	4	6.5%	1	2.4%	0.646

Table 2. Prevalence of related asthma symptoms in children by type of residency (Industrial vs. Rural)

Table 3. Prevalence of reduced pulmonary indices in children by type of residency (Industrial vs. Rural)

		City				
		Oinofyta (industrial)		Makrakomi (rural)		P value
		n	%	n	%	
FVC	<90%	41/62	66.1%	19/42	46.3%	0.046
FEF25	<90%	49/62	79.0%	27/42	65.9%	0.137
FEF50	<90%	21/62	33.9%	11/42	26.8%	0.450
PEF	<90%	49/62	79.0%	29/42	70.7%	0.336

Table 4. Results of multiple logistic regression analysis examining the effect of area of residence on respiratory health indicators (for each of them a separate model was performed) controlling for studied confounding factors¹

Oinofyta Residency (Industrial area)						
	P value	value Odds Ratio		95% Confidence Interval		
			Lower	Upper		
Bronchitis in the last 12 months	0.943	1.161	0.020	68.191		
Dry cough in the last 12 months	0.254	9.962	0.192	516.348		
Asthma diagnosis in the last 12 months	0.998	5.907E13*	.000			
Breathlessness in the last 12 months	0.955	3.727E90*	.000			
Ever had asthma diagnosis	0.016	33.063	1.899	575.584		
Ever used asthma medication	0.016	33.063	1.899	575.584		
Ever been hospitalized	0.996	2.062E34*	.000			

1 Age, Gender, exposure to passive smoking, traffic related air pollution, heating fuels, humidity at home and parental occupation in an industry.

*Non-applicable, due to the small sample size

Oinofyta Residency (Industrial area)						
	P value	Odds Ratio	95% Confidence Interval			
		Natio	Lower	Upper		
FVC<90%	0.619	1.452	0.334	6.315		
FEF25<90%	0.023	17.603	1.480	209.335		
FEF50<90%	0.734	1.335	0.253	7.036		
PEF<90%	0.029	15.383	1.332	177.664		
Abnormal spirometric curve*	0.045	3.747	1.032	13.598		

Table 5. Results of multiple logistic regression analysis examining the effect of area of residence on spirometric indices (for each of them a separate model was performed) controlling for studied confounding factors¹

1 Age, Gender, exposure to passive smoking, traffic related air pollution, heating fuels, humidity at home and parental occupation in an industry.

* Subjective assessment by a pediatrician and a pulmonologist