



## Effects of ambient air pollution on respiratory tract complaints and airway inflammation in primary school children



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### HIGHLIGHTS

- Acute effects of ambient air pollution were investigated in school-aged children.
- Ambient ozone levels were associated with upper respiratory tract complaints.
- Exhaled NO levels were associated with various upper respiratory tract complaints.

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### ABSTRACT

Respiratory health effects of ambient air pollution were studied in 605 school children 9 to 13 years in Eskişehir, Turkey. Each child performed a fractional exhaled nitric oxide (FE<sub>NO</sub>) measurement and a lung function test (LFT). Self-reported respiratory tract complaints (having cold, complaints of throat, runny nose and shortness of breath/wheezing) in the last 7 days and on the day of testing were also recorded. As acute health outcomes were investigated, weekly average ambient concentrations of ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>) and sulfur dioxide (SO<sub>2</sub>) were determined by passive sampling in the school playgrounds simultaneously with the health survey. Effects of air pollution on respiratory tract complaints and exhaled NO/lung function were estimated by multivariate logistic regression and multivariate linear mixed effects models, respectively.

Upper respiratory tract complaints were significantly ( $p < 0.05$ ) associated with weekly average O<sub>3</sub> concentrations during the health survey (adjusted odds ratios (OR) of 1.21 and 1.28 for a 10  $\mu\text{g m}^{-3}$  increment for having cold and a runny nose on day of testing, respectively). FE<sub>NO</sub> levels were significantly ( $p < 0.05$ ) increased in children with various upper respiratory tract complaints (ratio in FE<sub>NO</sub> varied between 1.16 and 1.40). No significant change in FE<sub>NO</sub> levels was detected in association with any of the measured pollutants ( $p \geq 0.05$ ). Lung function was not associated with upper respiratory tract complaints and FE<sub>NO</sub> levels. Peak Expiratory Flow (PEF) levels were negatively associated with weekly average O<sub>3</sub> levels for children without upper respiratory tract complaints. In summary, elevated levels of air pollutants increased respiratory tract complaints in children.

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### 1. Introduction

Respiratory tract complaints, which are mostly related to infections of largely viral etiology, are important contributors of morbidity and mortality in childhood (WHO, 2005). Common risk factors for respiratory tract complaints are poor sanitation, low birth weight and poverty in addition to environmental factors such as indoor and outdoor air pollution (WHO, 2005; Karevold et al., 2006). Previous studies provide evidence that ambient air pollution including particles, ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>) and sulfur dioxide (SO<sub>2</sub>) may be associated

with increased upper and lower respiratory complaints in children (Dockery and Pope, 1994; Hoek and Brunekreef, 1995; Keles and Ilicali, 1998; Boezen et al., 1999; Brauer et al., 2002; Fischer et al., 2002; Sanchez-Carrillo et al., 2003; Brauer et al., 2007; Rodriguez et al., 2007; Amarillo and Carreras, 2012). Although effect estimates are mainly small, the population attributable risks are high related to the high prevalence respiratory tract complaints in childhood (WHO, 2005).

Airway inflammation is a complex response of the immune system to a perceived threat such as infectious agents, irritants and allergens in the airways. A number of respiratory diseases such as asthma, chronic bronchitis, bronchiectasis and cystic fibrosis are associated with airway inflammation (Alving et al., 1993; Shelhamer et al., 1995). There has been an increasing number of studies investigating the role of air pollutants in exacerbating airway inflammation (Holguin et al., 2007; Barraza-Villarreal et al., 2008; Liu et al., 2009; Renzetti et al., 2009;

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Romieu et al., 2009; Chen et al., 2012). Children might be more likely to be affected by inflammation produced by air pollutants, as their airways are smaller in diameter. Children are sensitive to the effects of air pollution due to several other physiological reasons (WHO, 2005). Therefore, assessing airway inflammation is important for understanding the underlying mechanisms of respiratory diseases and preventing them.

Use of exhaled gas measurements to assess airway inflammation is an easy and non-invasive method. Measurement of fractional concentrations of orally exhaled nitric oxide ( $FE_{NO}$ ) is used as a sensitive biomarker of airway inflammation since the early 1990s (Gustafsson et al., 1991). Nitric oxide (NO) is produced from L-arginine by enzymes in the airway epithelial cells and partly exhaled. Standards for measurement of exhaled NO in human breath have been developed (American Thoracic Society/European Respiratory Society, 2005). Average levels of NO measured in exhaled air vary between 5 and 15 ppb in healthy individuals (Aerocrine, 2007). Main conditions that influence levels of  $FE_{NO}$  are demographic/anthropometric factors (gender, age and body size), indoor and outdoor allergens, atopy, smoking, acute airway infections and presence of chronic respiratory diseases such as asthma (Alving et al., 1993; Kharitonov et al., 1995; Steerenberg et al., 1999; Tsang et al., 2001; Malmberg et al., 2006; Kovesi et al., 2008).

Exposure to ambient air pollution is related to several health outcomes such as reduced lung function, exacerbation of asthma and increased acute and chronic respiratory/allergic diseases in children (Kunzli et al., 2000; Brunekreef and Holgate, 2002). Fewer studies investigated the effect of air pollution on airway inflammation in children and biologic mechanisms are not fully understood (Delfino et al., 2006; Holguin et al., 2007; Murata et al., 2007; Chen et al., 2012). The main objectives of this study are to determine if (i) respiratory tract complaints and (ii) increased exhaled NO levels (as a biomarker of airway inflammation) are associated with exposure to ambient air pollution in children.

The study presented here is a part of a project, supported by the MATRA programme of the Dutch government, carried out in Eskişehir to assess the adverse effect of air pollution on children's health between the years of 2007 and 2010. This paper presents the results of the health survey on a subpopulation of the project. Two other papers within the same project presented health survey results of the whole population from Eskişehir (Altuğ et al., 2013) and genotoxic effects on a smaller group of those children (Demircigil et al., 2013). A detailed evaluation of ambient air quality before and during the health survey has been reported (Gaga et al., 2012).

## 2. Materials and methods

### 2.1. Study area and population

Eskişehir is an intermediate size urban area in Turkey located in the northwest part of central Anatolia, with a population of approximately 600,000 inhabitants. Domestic heating (for  $SO_2$  and PM) and traffic (for  $NO_x$  and VOCs), rather than industry were the main sources contributing to ambient air pollution in the city (Özden et al., 2008; Gaga et al., 2012). Even though coal usage in domestic heating has been gradually replaced with natural gas since 1996, approximately half of the residences still use coal for heating (Çınar, 2003; Özden et al., 2008; Gaga et al., 2012). Eskişehir is not a heavily industrialized city. The main industrial activities in the vicinity of the residential area are a sugar factory, a locomotive engine factory and a plane engine factory (locations shown in Fig. 1). Small and medium sized plants are present in the industrial zone which is located in the southeastern part of the city. Ceramics and food industry are dominant industrial activities in the industrial zone. Natural gas is used for energy production in almost all industrial plants in this zone (Çınar, 2003; Özden et al., 2008; Gaga and Ari, 2011; Gaga et al., 2012).

The study area was classified into three regions: suburban (R1), urban (R2) and urban-traffic (R3). Regions were selected based on the

results of an extensive passive sampling campaign in 2008 (Gaga et al., 2012), population density data and former emission inventory studies in the residential area of Eskişehir (Özden et al., 2008). Traffic volume data of major streets in each region were gathered from data belonging to the Municipality of Eskişehir. Traffic measurements were carried out by the municipality manually at 33 major arterial roads in the city.

Sixteen public primary schools were randomly selected from the three regions in order to perform the health survey. Fig. 1 shows the location of the selected primary schools in each region.

Region 1 (R1) represents the suburban area in the outer zone of Eskişehir. Population density ( $2750 \text{ capita km}^{-2}$ ) and traffic density (traffic volume of  $<5000 \text{ vehicles day}^{-1}$  measured at major roads closest to selected schools) are the lowest in this area. Region 2 (R2) represents the urban area with higher population density ( $5000 \text{ capita km}^{-2}$ ) and similar traffic volume ( $<5000 \text{ vehicles day}^{-1}$ ) compared to Region 1. Region 3 (R3) is in the city center (urban-traffic area), which has the highest population density ( $18,000 \text{ capita km}^{-2}$ ) and a busier road network. Measured traffic volume of major roads in this region varies between 10,000 and 30,000 vehicles  $\text{day}^{-1}$ . The total road length within a buffer zone (for 2 km distance) for each school was determined using a GIS (ArcGIS 9.2). The average of calculated total road lengths (525 km, 669 km and 1351 km for R1, R2 and R3, respectively) was highest for the urban-traffic area and lowest in the sub-urban area.

605 primary school children in the 4th and 5th grade were selected from 16 public primary schools. These children were recruited from the larger population of the MATRA project subjects ( $n = 1880$ ) that were examined by the International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire in May 2008 in order to determine prevalences of symptoms of asthma, rhinitis and eczema (ISAAC, 1998). The standardized ISAAC questionnaire was directly translated into Turkish and no additional validation study was carried out. Questions on various environmental risk factors (parental smoking habits at home, coal/wood stove usage for domestic heating, parental education) were added to the questionnaire. The ISAAC questionnaire was correctly answered by 521 (86.1%) of 605 children. The health survey of this study was carried out at the end of the winter season and a few weeks before the start of the pollen season. Schools were visited by two teams to perform sequentially anthropometric measurements, health interview, exhaled NO measurements and lung function tests from March 2, 2009 to March 17, 2009. Self-reported respiratory tract complaints (having cold, complaints of throat, runny nose and shortness of breath/wheezing) in the last 7 days and on the day of testing were recorded before an exhaled nitric oxide measurement and a lung function test. The health survey was approved by the local ethical committee of Mustafa Kemal University, Faculty of Medicine in agreement with the Helsinki declaration (09/04/2008, No 4/22).

### 2.2. Ambient air monitoring

The exposure of each child to air pollution was derived from a passive sampling campaign conducted in the playground of each selected primary school. Ambient measurements were carried out for two weeks (from February 27 to March 13, 2009) simultaneous with the health survey. The average temperature was  $4.6^\circ\text{C}$  (daily averages varying between 0 and  $12^\circ\text{C}$ ) and westerly winds were prevalent during the sampling period. Air pollution levels measured included weekly average concentrations of ozone ( $O_3$ ), nitrogen dioxide ( $NO_2$ ) and sulfur dioxide ( $SO_2$ ). Daily mean concentrations of particulate matter ( $PM_{2.5}$  and  $PM_{10}$ ) were also measured at 4 active monitoring stations during the health survey. PM data was not included into the statistical analysis since PM measurements were not school-based. The details of the methodology of air quality measurements can be found elsewhere (Gaga et al., 2012).

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