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# Long-Term Exposure to Outdoor Air Pollution and its Effect on Children's Health

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## Abstract

Air pollution is one of the major environmental determinants for human health. Globally, about 300 million children are exposed to highly toxic air, defined as levels six or more times exceeding international guidelines. There is growing epidemiologic evidence for adverse health impact of expsore to outdoor air pollution on children. Outdoor air pollution is linked not only with mortality in children, but also with an array of adverse health outcomes, including the respiratory health related conditions such as pneumonia, asthma and bronchitis, as well as with neurodevelopmental disorders such as autism spectrum disorders (ASD), adverse pregnancy outcomes, and metabolic diseases. Previous studies have focused on the effects of short-term exposure to air pollution, but recently there are increasing evidence on the effects of long-term exposure to air pollution on children's health. In this review, the adverse effects of long-term exposure to outdoor air pollution in children in terms of different health outcomes is discussed.

### Keywords: Long-term; Air pollution; Children, Health effect

## **Abbreviations**

ASD: Autism Spectrum Disorders; UNICEF: United Nations Children's Fund; WHO: World Health Organization; PM: Particulate Matter;  $O_3$ : Ozone; Sox: Sulphur Oxides; NOx: Nitrogen Oxides; CO: Carbon Monoxide; US EPA: United States Environment Protection Agency; IARC: International Agency for Research on Cancer; NO<sub>2</sub>: Nitrogen Dioxide; SO<sub>2</sub>: Sulfur Dioxide; PM10 (particles larger than 2.5 micrometers and smaller than 10 micrometers in diameter); PM2.5 (particles 2.5 micrometers in diameter and smaller); OR: Odd Ratio; CI: Confidence Interval; ESCAPE: European Study of Cohorts for Air Pollution Effects; FEVI: Forced Expiratory Volume in 1 sec; LBW: Low Birth Weight; PTB: Preterm Birth; IQR: Interquartile Range

# Introduction

Exposure to outdoor air pollution is a major threat to child health. According to a new report from the United Nations Children's Fund (UNICEF), an estimated 2 billion children around the world live in areas where outdoor pollution exceeds minimum air-quality guidelines set by the World Health Organization (WHO). Among them, 300 million children are exposed to toxic levels of outdoor air pollution, and those living in low- and middle-income countries are most at risk [1].

Exposure to outdoor air pollution is an increasing risk to children, who are physiologically vulnerable to air pollution. Outdoor criteria air pollutants are linked not only with mortality in children, but also with an array of adverse health outcomes, including the respiratory health related conditions such as pneumonia, asthma and bronchitis, as well as with neurodevelopmental disorders such as Autism spectrum disorders (ASD) [2]. In addition to the above, there are emerging epidemiological evidence that exposure to outdoor air pollution is associated with adverse pregnancy outcomes, alteration in the immune system and metabolic diseases in children [3]. These effects have been reported in short-term studies, which have shown the associations between day-to-day variations in air pollution and health, and in long-term studies, which have followed exposed cohorts over time [4-7]. Compared to short-term effects, long-term health effects of air pollution are less studied. In the present review, the adverse health outcomes associated with long-term exposure to criteria air pollutants in children are highlighted.

# What is Air Pollution?

The term "Air pollution" refers to a complex mixture of compounds that vary greatly vary with regard to its major emission sources and atmospheric condition. Generally, the criteria air pollutants

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(which include particulate matter [PM], ozone [O<sub>2</sub>], sulphur oxides [SOx] and nitrogen oxides [NOx]), lead [Pb], carbon monoxide [CO]) according to the United States Environment Protection Agency (US EPA), are monitored in air-quality networks) on the basis of their potential to cause adverse health and/or environmental effects in most of the countries [8]. The International Agency for Research on Cancer (IARC) has classified outdoor air pollution, as a whole, as a group 1 carcinogen based on findings form lung and bladder cancer [9]. PM, CO,  $O_3$ , nitrogen dioxide (NO<sub>2</sub>) and sulfur dioxide (SO<sub>2</sub>) are the pollutants of major public health concern among the air pollutants. However, PM affects more people than any other pollutant. The term "particulate matter" refers to the complex heterogeneous mixture of solid particles and/or droplets of variable size found in suspension in the air. According to the US EPA [10], particle pollution can be categorized as inhalable coarse particles or PM10 (particles larger than 2.5 micrometers and smaller than 10 micrometers in diameter) and fine particles or PM2.5 (particles 2.5 micrometers in diameter and smaller).

# Children, More Vulnerable to Air Pollution than adults

Millions of children are exposed to air pollution well above the WHO guidelines level, especially living in the world's largest cities in developing countries [11]. Children are considered as being one of the groups most vulnerable to the adverse health-related effects of outdoor air pollution [12] because there are many differences between children and adults in the ways that they respond to air pollution. Firstly, Children have a larger lung surface area and inhale a higher volume of air per kilogram of body weight than adults [13]. Compared to adults, children breathe 50% more air per kilogram of body weight when normally breathing, thus taking more air pollution than adults. Secondly, children have a higher exposure to air pollution because they spend more time outdoors and engage in a greater level of physical activity than adults [14]. Thus, their air intake into the lungs is much greater than adults. In addition, children do not necessarily respond to air pollution in the same way as adults. Adults exposed to low levels of the pollutant ozone will experience symptoms such as coughing, soreness in their chests, sore throats, and sometimes headaches. Children, on the other hand, may not feel the same symptoms as adults, which does not mean that children are less sensitive to air pollution.

There are several studies that show children to have losses in lung functions even when they don't cough or feel discomfort. It is because children have a different response to exposure to air pollution as their immune system and lungs are not fully developed. The lung is not fully formed at birth and 80% of alveoli are formed after birth with changes in the lung continuing through adolescence [15]. For example, the number of bronchial alveoli in the human lung is about 24 million at birth and increases to 257 million at age 4 [13]. This results in greater permeability of the epithelial layer in young children. While the child's lung is developing, the child's immune system is also immature at birth and develops during the first years of life. Immature type of lung of infants and young children makes children more vulnerable to air pollution.

# Long Term Effects of Air Pollution Exposure in Children

There is a vast body of evidence for the adverse effects of air pollution on children's health [14]. A European review estimated that all cause deaths attributable to outdoor air pollution was between 1.8% and 6.4% for children of 0–4 years age [16]. Apart from infant and childhood mortality [17-19], numerous epidemiological studies show associations between air pollution and morbidity outcomes for children, including development and exacerbations of asthma and allergies [20-22], lung function decrements [23,24], adverse pregnancy outcomes [25,26], birth defects [27] and neurodevelopmental disorders [28,29]. In this review, long term effects of air pollution exposure are mainly discussed. Long-term exposure studies usually use cohort or prospective design; however, many of them use crosssectional design as well.

### Mortality outcomes

Outdoor air pollution has been linked to increased mortality in children [30]. All cause deaths attributable to outdoor air pollution was estimated between 1.8% and 6.4% for children of 0–4 years age in an European review study [16]. Exposure to air pollutants has been associated with sudden infant death syndrome [31-33]. In a systematic review of the literature on the association between outdoor air pollution and infant mortality, Glinianaia et al [19] observed a consistent and significant association between PM and postneonatal mortality due to respiratory causes, as well as sudden infant death syndrome. Other studies also have showed a significant association between outdoor air pollution and mortality in children under five years of age [34].

### Adverse respiratory health outcomes

It is revealed in several evidences that the long-term childhood air pollution exposure plays a role in the development of respiratory health related diseases such as asthma and allergies [35,36]. A recent systematic review and meta-analysis of birth cohort studies examined the effects of childhood traffic related air pollution exposure on asthma and found increased longitudinal childhood exposure to PM2.5 was associated with increasing risk of asthma in childhood [Odd ratio (OR) 1.14, 95% Confidence Interval (CI): 1.00 –1.30 per 2 µg/m<sup>3</sup> increase] [20]. Another meta-analysis evaluated the associations between longterm exposure to motor vehicle air pollutants and wheeze and asthma in children. According to this study, exposure to NO<sub>2</sub> (OR: 1.05, 95% CI: 1.00-1.11), and CO (OR: 1.06, 95% CI: 1.01-1.12) were positively associated with a higher prevalence of childhood asthma Moreover, SO, was positively associated with a higher prevalence of wheeze (OR: 1.04, 95% CI: 1.01-1.07), NO2 was positively associated with a higher incidence of asthma (OR: 1.14, 95% CI: 1.06-1.24), and PM was positively associated with a higher incidence of wheeze (OR: 1.05, 95% CI: 1.04-1.07) in children [35].

The effects of long-term exposure to air pollution have been also reflected on respiratory health related diseases other than asthma and allergies. A meta-analysis performed for 10 European birth cohorts within the European Study of Cohorts for Air Pollution Effects (ESCAPE) project found significant association between air pollution and early childhood pneumonia [37]. According to that study, combined OR was 1.30 (95% CI: 1.02 -1.65) per 10-µg/m<sup>3</sup> increase in NO<sub>2</sub> and 1.76 (95% CI: 1.00 -3.09) per 10-µg/m<sup>3</sup> increase in PM10. Moreover, a review summarized more than 50 publications on the effects of outdoor air pollution on lung function, an important objective marker of respiratory health of children and concluded that overall there is evidence for adverse effects on lung function measures [38]. Combining data from ESCAPE, another study showed longterm exposure to air pollution may result in lung function decline in schoolchildren; with changes for forced expiratory volume in 1 sec (FEV1) being -0.86% (95% CI: -1.48, -0.24%) for a 20-µg/m<sup>3</sup> increase in NOx and –1.77% (95% CI: –3.34, –0.18%) for a 5-µg/m³ increase in PM2.5 [23].

#### Adverse pregnancy outcomes

Pregnancy outcomes including low birth weight (LBW) and preterm birth (PTB) are important indicators of the health of the newborns babies and may result in increased neonatal morbidity and mortality in childhood. Outdoor levels of criteria air pollutants have been associated with adverse pregnancy outcomes, including PTB, LBW, intrauterine growth retardation [19], abnormal birth length, abnormal head circumference [20] and small size for gestational age [21]. Studies conducted in different countries such as China, the Czech Republic, Brazil, Mexico, and the United States observed a significant association between outdoor air pollution and birth outcomes, specifically LBW, PTB, intrauterine growth retardation, and fetal mortality [39-43]. However, no specific trimester has been identified as the most vulnerable period of gestation during which air pollution might be most harmful to the fetus.

Several review articles and meta-analysis studies have been conducted to summarize the association between air pollution and elevated risk in pregnancy outcomes. For example, results from a meta-analysis study suggested a 9% increase in risk of LBW for a 10µg/m<sup>3</sup> increase in PM2.5 (combined OR, 1.09; 95% CI, 0.90-1.32) and a 15% increase in risk of PTB for each 10-µg/m<sup>3</sup> increase in PM2.5 (combined OR, 1.15; CI, 1.14-1.16) [26]. In addition, a study pooling data from 12 European countries showed air pollution during pregnancy is associated with restricted fetal growth and OR for LBW was1.18 (95% CI 1.06-1.33) per 5µg/m3 increase in PM2.5 [44]. In a study meta-analyzing data from studies across the world (across 14 centers from 9 countries using a common analytical protocol) found the LBW was positively associated with PM and OR was 1.10 (95% CI: 1.03, 1.18) per10µg/m3 increase in PM2.5 [45]. Stieb et al. (2012) found the pooled ORs for LBW ranged from 1.05 (0.99-1.12) per 10µg/m3 PM2.5 to 1.10 (1.05-1.15) per 20µg/m3 PM10 based on entire pregnancy exposure. However, this study reported less consistent results for O<sub>2</sub> and SO<sub>2</sub> for both pregnancy outcomes [46]. Hence, there is good evidence of adverse effects of air pollution on pregnancy outcomes.

### Increased risk of birth defects

Long-term exposure to air pollution during pregnancy has been considered to increase risk of birth defects. A study conducted in Southern California found odds for cardiac ventricular septal defects increased in a dose-response fashion with increasing CO exposure (OR for  $2^{nd}$  quartile CO = 1.62, 95% CI: 1.05, 2.48; OR for  $3^{rd}$  quartile CO = 2.09, 95% CI: 1.19, 3.67; OR for  $4^{th}$  quartile CO = 2.95, 95% CI: 1.44, 6.05) in second-month of pregnancy [27]. Moreover, the authors reported the risks for aortic artery and valve defects, pulmonary artery and valve anomalies, and conotruncal defects increased with second-month O<sub>2</sub> exposure.

### Adverse neurodevelopmental outcomes

Recently, a growing body of evidence also suggests the adverse neurodevelopmental effects of air pollution [47,48]. There are accumulating number of studies focused on ASD, a brain development disorders with heterogeneous disorder with genetic and environmental factors and characterized by impaired social interaction and communication, and by restricted and repetitive behaviors [49]. Prenatal exposure to PM2.5 was found to be associated with increased odds of ASD, with an adjusted OR of 1.57 (95% CI:

1.22, 2.03) per interquartile range (IQR) increase in PM2.5 (4.42µg/ m<sup>3</sup>) in a case-control study of participants in the Nurses' Health Study II (NHS II), a prospective cohort of 116,430 U.S. female nurses [28]. A study in California showed regional exposure measures of NO2, PM2.5 and PM10 were also associated with autism during gestation and the first year of life [49]. Moreover, a recent study was conducted in Taiwan showing the associations between long-term exposure to air pollution and newly diagnostic ASD. According to that study, there were an approximately 59% risk increase per 10 ppb increase in O<sub>2</sub> (95% CI 1.42-1.79), 37% risk increase per 10 ppb in CO (95% CI 1.31-1.44), 340% risk increase per 10 ppb increase in NO2 level (95% CI 3.31-5.85), and 17% risk increase per 1 ppb in  $\mathrm{SO}_2$  level (95% CI 1.09-1.27) [50]. In Quanzhou, China, a study was performed to assess the neurobehavioral performance for participants from two primary schools with different air pollution level and revealed that children living in the polluted area showed poor performance on all testing [51].

### **Metabolic disorders**

There is now emerging evidence that air pollution is also associated with indicators related to metabolic disorders such insulin resistance and obesity in children [52,53]. In a large study involving more than 9000 Chinese children, exposure to outdoor air pollutants (PM10, NO<sub>2</sub>, SO<sub>2</sub> and O<sub>3</sub>) was associated with increased risks for childhood obesity and hypertension [54]. Another study of 10-year-old children in two prospective German birth cohorts showed insulin resistance increased by 17.0% (95% CI 5.0, 30.3) and 18.7% (95% CI 2.9, 36.9) for two-fold standard deviation increase in NO<sub>2</sub> and PM10, respectively [53].

# Conclusion

There is increasingly strong evidence from epidemiological studies that long-term exposure to outdoor air pollution is associated significant adverse effects in children in terms of different health outcomes, i.e. increases in the risk of death and chronic disease in children, worse pregnancy outcomes, and adverse neurodevelopmental outcomes. More research is needed to be conducted to emphasize the development and implementation of air pollution reduction policies to protect the health of the children.

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