Chapter 10
Impact of Air Pollution Hazards on Human Development

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Abstract Air pollutants like carbon monoxide (CO), ozone (O_3), nitrogen oxides (NO, NO_2, NO_x), lead (Pb), mercury (Hg), sulfur dioxide (SO_2), polycyclic aromatic hydrocarbons (PAHs), and particulate matter ($PM_{2.5}$ and PM_{10}) have known to exhibit harmful effects on different organs and systems in human body. Increasing exposure to air pollution in children is a global public health concern as children are extremely vulnerable to air pollution due to their dynamic growth. Under age five mortalities due to air pollution are increasing worldwide thus making it necessary to take prompt action on protecting children's environmental health. Air pollutants like PM_{10}, $PM_{2.5}$, SO_2, O_3, NO_2, CO are known to be strongly associated with adverse birth outcomes like low birth weight, preterm birth, and small for gestational age. Air pollution is found to be linked with neurocognitive development in children. NO_2 was found to be associated with psychomotor development in children, while $PM_{2.5}$ and PM_{10} were found to be associated with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). Studies have reported an association between air pollution especially PM and NO_2 and childhood obesity/insulin resistance. Thus, more advanced research is needed to implement effective strategies safeguarding children's health.

Keywords Air pollution · PM_{10} · $PM_{2.5}$ · SO_2 · O_3 · NO_2 · CO · Prenatal · Postnatal · Human development

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10.1 Introduction

Children around the globe are exposed to air pollution. Of the global population, 92% live in areas with ambient air pollution levels that exceed World Health Organization (WHO) limits, including billions of children. Air pollution causes approximately 600,000 deaths of children under 5 years of age annually and increases the risk for respiratory infections, asthma, and adverse birth outcomes. Growing evidence also suggests that air pollution can adversely affect children's cognitive development, and early exposure might induce the development of chronic diseases in adulthood [1, 2]. Although historically air pollution has been thought of as a respiratory toxicant, recent evidence has broadened our understanding of its full range of effects. These associations may or may not be causal but clearly warrant additional study [3].

Ambient air pollution can result from the combustion of fossil fuels (including domestic heating, cooking and lighting, power generation, and motor vehicle exhaust), industrial processes, waste incineration, as well as natural processes (thunderstorms and volcanic eruptions) [training module]. Key ambient air pollutants include carbon monoxide (CO), ozone (O_3), nitrogen oxides (NO, NO_2, NO_x), lead (Pb), mercury (Hg), sulfur dioxide (SO_2), polycyclic aromatic hydrocarbons (PAHs), and particulate matter ($PM_{2.5}$ and PM_{10}) [1].

Def. Particulate Matter
Small particulate matter with a diameter of less than 10 microns is termed PM10, and its subset, PM2.5, are particles with a diameter of 2.5 microns or less, and both are widely used indicators of ambient air quality. The size of particulate matter determines where in the body the pollutant is deposited; particles larger than PM10 are typically filtered out through the nose while smaller particles can reach the lower airways. However, children typically breathe through their mouth, bypassing the nasal filtration mechanism, and these pollutants are able to penetrate deep into the child's lungs and the cardiovascular system [1].

The "WHO air quality guidelines" (Table 10.1) were proposed to help reduce the severe impact that air pollution can have on human health. The guidelines offer global guidance on the thresholds and limits for key air pollutants.

This chapter primarily reviews the impact of air pollution on infant mortality, fetal growth, and birth outcomes. Neurobehavioral diseases, such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) also are reviewed in this chapter as these diseases too have been linked to childhood, air pollution exposure. Conditions, such as obesity or insulin resistance, also are included in this review. These conditions are important to include as they have the potential to develop into metabolic syndrome or diabetes mellitus in later life.

Past and current research have proven that it is crucial to cover this matter, and more advanced research is needed. Unfortunately, humans cannot avoid the

Table 10.1 WHO air quality guideline values [1]

Pollutant	Common source of exposure	WHO guideline values
Particulate matter (PM) Fine particulate matter (PM2.5) Coarse particulate matter (PM10)	A direct source, such as construction sites, unpaved roads, fields, smokestacks or fires; secondary reactions of chemicals such as sulfur dioxide and nitrogen oxides of pollutants emitted from power plants, industries, and automobiles	10 μg/m^3 annual mean25 μg/m^3 24-h mean 20 μg/m^3 annual mean50 μg/m^3 24-h mean
Ozone (O_3)	Secondary pollutant formed by chemical reaction of volatile organic compounds (VOCs) and NO_x in the presence of sunlight	100 μg/m^3 8-h mean
Nitrogen dioxide (NO_2)	Combustion processes from heating, power generation, and engines in vehicles and ships	40 μg/m^3 annual mean 200 μg/m^3 1-h mean
Sulfur dioxide (SO_2)	Burning of sulfur-containing fossil fuels for domestic heating, power generation, and motor vehicles	20 μg/m^3 24-h mean 500 μg/m^3 10-min mean

negative impact of ambient and household air pollution since inhalation is a continuous activity that occurs in everyday life. Moreover, a breadth of research has provided evidence suggesting children, compared to adults, are uniquely susceptible to air pollution exposure as, is well understood, infants and children are undergoing critical and rapid cellular, system and organ growth, organization, and development.

Consequently, this chapter reviews the health effects of air pollution exposure on children including infant mortality, birth outcomes, neurocognitive development, and childhood obesity. This review includes relevant published studies, prioritizing systematic reviews, meta-analyses, and recent studies—primarily those published within the last 10 years. In addition, each section will present definitions of key health outcomes, biological mechanisms, and a brief summary.

10.2 Infant Mortality

10.2.1 Air Pollution Effects on Infant Mortality

Maternal exposure to air pollutants during pregnancy has been linked to infant mortality, which is defined below.

Def 2.1. Infant Mortality
Infant mortality is the death of an infant before his or her first birthday. The infant mortality rate is the number of infant deaths for every 1000 live births. In addition to giving us key information about maternal and infant health, the infant mortality rate is an important marker of the overall health of a society. In 2016, the infant mortality rate in the USA was 5.9 deaths per 1000 live births (https://www.cdc.gov/reproductivehealth/maternalinfanthealth/infantmortality.htm).

Numerous epidemiological studies have demonstrated the link between air pollution and adverse outcomes, including hospitalizations, emergency room visits, decreased lung function, increased risks of cardiovascular diseases, and mortality [4–7]. However, most of these studies are adult-focused and relatively few studies have examined the detrimental effects of air pollution on infant health.

Exposure to air pollution may result in increased risk of infant mortality because infants are possibly more susceptible to air pollution due to the immaturity of their lungs and immune system [8]. Therefore, a keen interest in preventing infant mortality attributable to air pollution is required. However, tentative conclusions from two systematic reviews suggest that although inferences on particulate matter and infant mortality due to respiratory causes are sufficient, the evidence of an association between particulate matter and infant mortality from other causes is still inconsistent and insufficient. More research is needed to clarify the link [9, 10]. As the systematic reviews were conducted in 2004 and 2005, an up-to-date review may be helpful for further identification of the association between particulate matter and infant mortality. Hence, to introduce the recent scientific research on this issue and summarize the evidence, included in this review are studies published after 2010 which investigated the effects of particulate matter on infant mortality.

Jung et al. [11] reported the effects of pre- and postnatal exposure to $PM_{2.5}$ on infant mortality using 2010–2015 retrospective birth cohort data obtained from the Statistics Korea. A total of 2,628,904 infants with 1509 deaths were identified. The mean $PM_{2.5}$ concentrations were calculated using CMAQ data for the following exposure periods: each trimester, gestation, postnatal period, and pre- and postnatal periods. The study indicated that a higher risk of infant mortality was associated with exposure to $PM_{2.5}$ during prenatal and postnatal periods.

Yorifuji et al. [12] analyzed the association between infant mortality and acute exposure to $PM_{2.5}$, SPM (suspended particulate matter), and $PM_{7–2.5}$ in Tokyo, Japan. The studied population included 2086 infants who died in the 23 urbanized wards of the Tokyo Metropolitan Government between January 2002 and December 2013. Infant mortality was further categorized by age at death (infant, neonatal, and post-neonatal mortality) and cause of death (cardiac diseases, respiratory diseases, perinatal circumstances, congenital and chromosomal abnormalities, and sudden infant death syndrome [SIDS]). This study reported the increased risks of infant mortality, post-neonatal mortality, and mortality due to respiratory diseases per a 10 μg/m^3 increase in $PM_{2.5}$. In addition, $PM_{7–2.5}$ was associated with a 21% increased risk of post-neonatal mortality. The risks of post-neonatal mortality and mortality due to respiratory diseases increased by 10% and 25%, respectively, for a 10 μg/m^3 increase in PM_7. The study also highlighted the elevated risks of infant and post-neonatal mortality even when $PM_{2.5}$ and SPM concentrations were below Japanese air quality guidelines.

Carbajal-Arroyo et al. [13] studied the effect of PM_{10} and O_3 on infant mortality in Mexico City, Mexico. Daily mortality data were obtained for infants under 1 years of age (1–11 months old) living in the 14 municipalities of Mexico City between January 1, 1997 and December 31, 2005. Infant mortality was stratified by cause of death (respiratory diseases) and socioeconomic status (high, medium, and low). PM_{10} was significantly associated with all-cause mortality with a one-day lag and a two-day lag by 5.5% and 6.6%, respectively, for a 38.7 μg/m^3 (interquartile range [IQR]) increase in PM_{10}. The risk of respiratory mortality increased by 9.8%

at a two-day lag with the same PM_{10} increase level. Cumulative exposure to PM_{10} from day zero to day two was found to be associated with an increased risk of infant mortality by 6.3% per IQR change. The effects of PM_{10} were assessed within the first and fourth quartiles of O_3 concentrations. The results showed elevated risks of infant mortality at lag 0, lag 1, lag 2, and lag 0–2 at the highest O_3 quartile ($\geq$130.5 ppb). When stratified by socioeconomic status, infant mortality and respiratory mortality significantly increased in the low SES group with respect to the concentration of PM_{10}. O_3 was also associated with respiratory mortality in the low SES group.

Son et al. [14] conducted a cohort study, examining the association between long-term exposure to TSP (total suspended particles), PM_{10}, $PM_{10-2.5}$, and $PM_{2.5}$ and infant mortality in South Korea. The studied population included 359,459 births with 225 deaths. Infants who died in the neonatal period (<28 days) were excluded from the analysis. Infant mortality was categorized by cause of death (all-cause, respiratory, and SIDS). The window of exposure included both prenatal (gestation and each trimester) and postnatal periods. Gestational exposure to PM_{10} increased the risks of infant mortality from all-cause and respiratory cause in normal birth weight infants per IQR change (6.93 $\mu g/m^3$). Gestational exposure to TSP and $PM_{2.5}$ also significantly elevated the risks of all-cause mortality in normal birth weight infants per IQR change (8.91 $\mu g/m^3$ and 3.15 $\mu g/m^3$, respectively). Gestational exposure to TSP, PM_{10}, and $PM_{2.5}$ increased the risk of respiratory-related mortality per IQR increase. When stratified by each trimester, these increases were only statistically significant for exposure during the first trimester.

10.2.2 Biological Mechanism

The biological mechanism by which particulate matter influences infant mortality has not been elucidated. It is plausible that particulate matter may induce oxidative stress, inflammation, and reduction of cell proliferation in different parts of the body [15–17] and thus adversely influence infant health.

10.2.3 Summary

Studies examining the association between particulate matter and infant mortality are few in number and are mostly concerned with short-term exposure. The present review suggests that particulate matter has an influence on infant mortality. However, more research is needed to enhance our understanding of the long-term effects of particulate matter on infant mortality. Furthermore, to advance our current understanding, refined analysis on the composition of particulate matter needs to be explored, as does the timing of exposure and how the specific components of particulate matter affect infant mortality. Even so, based on the current evidence, adequate public health interventions to prevent infants from particulate matter exposure can be delivered to the public (Table 10.2).

Table 10.2 Effects of particulate matter on infant mortality

Air pollution	Health outcome measurement (age)	Effect size	Reference (study design)
PM2.5 SPM PM7–2.5 Postnatal	Infant mortality (under 1-year-old)	Per 10 μg/m^3 increase in PM2.5 Infant mortality: AOR = 1.06(95% CI = 1.10–1.12) Post-neonatal mortality: AOR = 1.10 (95% CI = 1.02–1.19) Respiratory diseases: AOR = 1.30 (95% CI = 1.01–1.67) PM7 Post-neonatal mortality: AOR = 1.10 (95% CI = 1.03–1.16) Respiratory diseases: AOR = 1.25 (95% CI = 1.02–1.54) PM7–2.5 Post-neonatal mortality: AOR = 1.21 (95% CI = 1.03, 1.42)	Yorifuji et al. [12] (time-stratified, case-crossover design conditional logistic regression)
PM10 O3 Postnatal	Infant mortality (1- to 11-month-old infant)	Per 38.7 μg/m^3 (IQR) increase in PM10 Infant mortality at lag 1: AOR = 1.055 (95% CI = 1.011–1.102) Infant mortality at lag 2: AOR = 1.066 (95% CI = 1.021–1.114) Infant mortality at lag 0–2: AOR = 1.063 (95% CI = 1.001–1.132) Respiratory diseases lag 2: AOR = 1.098 (95% CI = 1.021–1.180) PM10 within O3 (quartiles first and fourth) At the highest O3 quartile (≥130.5 ppb) Infant mortality at lag 0: AOR = 1.145 (95% CI = 1.016–1.290) Infant mortality at lag 1: AOR = 1.139 (95% CI = 1.014–1.279) Infant mortality at lag 2: AOR = 1.131 (95% CI = 1.012–1.262) Infant mortality at lag 0–2: AOR = 1.261 (95% CI = 1.078–1.474)	Carbajal-Arroyo et al. [13] (time-stratified, case-crossover design conditional logistic regression)

TSP PM10 PM10–2.5 PM2.5 Prenatal Postnatal	Infant mortality Infant, omitted infants who died in the neonatal period (<28 days)	Per IQR increase in gestational exposure TSP (8.91 μg/m^3)—All (normal birth weight): AHR = 1.44 (95% CI = 1.06–1.97) PM10 (6.93 μg/m^3)—All (normal birth weight): AHR = 1.65 (95% CI = 1.18–2.31) PM2.5 (3.15 μg/m^3)—All (normal birth weight): AHR = 1.53 (95% CI = 1.22–1.90) First trimester (normal birth weight): AHR = 1.15 (95% CI = 1.04–1.28) Per IQR increase in gestational exposure Respiratory diseases (normal birth weight) TSP (8.91 μg/m^3)—All: AHR = 3.78 (95% CI = 1.18–12.13) First trimester: AHR = 2.08 (95% CI = 1.26–3.43) PM10 (6.93 μg/m^3)—All: AHR = 6.20 (95% CI = 1.50–25.66) First trimester: AHR = 2.19 (95% CI = 1.30–3.70) PM2.5 (3.15 μg/m^3)—All: AHR = 3.15 (95% CI = 1.26–7.85) First trimester: AHR = 1.58 (95% CI = 1.14–2.19)	Son et al. [14] (cohort Cox proportional hazards)

AOR adjusted odds ratio, *AHR* adjusted hazard ratio

10.3 Birth Outcomes

The role of the environment on the health of children has been widely researched, with findings suggesting an association between air pollution and various birth outcomes. Infants are most likely to be affected by the hazardous environment during the prenatal period.

The impacts of air pollution on birth outcomes are not trivial because air toxicants, among others, can be passed through the placenta from the mother to the fetus [18–20]. Therefore, during pregnancy, the environment that the fetus lives in and the toxicants that the fetus is exposed to are primarily dependent on the mother [18, 19]. Mothers' exposure to air pollution can be from within the home, known as household air pollution, or from outdoors, known as ambient air pollution [18, 19].

Moreover, birth outcomes are linked to morbidity, mortality, disability, and disease, with the consequences potentially being experienced through to adult life [18, 21]. Air pollution also has the potential to have societal impacts including an increased use of healthcare facilities after birth [18]. These examples highlight the importance of understanding the association between air pollution and birth outcomes as the consequences can be experienced by the individual and society as a whole, and this burden is entirely preventable.

Air pollution may influence common complications of pregnancy. Two of these complications are small for gestational age (SGA), which results from intrauterine growth retardation, and premature birth (PB). These conditions can occur independently or together, and both can result in low birth weight (LBW) [18].

10.3.1 Fetal Growth

Maternal exposure to air pollution can cause fetal growth stunting, which, in turn, is linked to the outcomes of LBW and SGA [22]. These birth outcomes have been associated with an increased risk of cardiovascular morbidity and mortality later in life and emerging evidence suggests an increased risk of developmental delays and lower intelligence [18, 23]. See the definitions below.

Def 3.1 Low Birth Weight (LBW) and Small for Gestational Age (SGA) As defined by WHO, low birth weight is a weight at birth of less than 2500 grams (5.5 lb) (http://apps.who.int/iris/bitstream/10665/43184/1/9280638327.pdf). LBW is a significant public health issue worldwide, and it is associated with a range of short- and long-term health effects. It is estimated that 15%–20% of all births worldwide are LBW, which represents more than 20 million births per year (http://www.who.int/nutrition/topics/globaltargets_lowbirthweight_policybrief.pdf).

In comparison, SGA refers to babies who are smaller than usual for the number of weeks of pregnancy, most commonly defined as having a birth weight below the 10th percentile of the recommended gender-specific birth weight for gestational age and gender [24]. Both LBW and SGA can be linked to preterm birth (PB) [18].

10.3.1.1 Low Birth Weight

Traffic-related air pollution is a major contributor to ambient air quality, and a study by Aguilera et al. investigated the effect of prenatal exposure to traffic-related air pollution on birth weight. The study used geographic information system (GIS) models on birth weight in 570 newborns from the INMA Sabadell cohort. A significant association between aromatic hydrocarbons (benzene, toluene, ethylbenzene, m/p-xylene, and o-xylene) and LBW was found, highlighting the negative impact traffic-related air pollutants can have on birth outcomes [3].

10.3.1.2 Low Birth Weight

Using spatiotemporal exposure metrics, a prospective cohort study, examining the relationship between LBW and exposure to various air pollutants (CO, NO, NO_2, $PM_{2.5}$, PM_{10}, O_3, and SO_2), found that residences within 50 m of highways were associated with an 11% increase in LBW (95% CI = 1.01–1.23). While ambient air pollution levels were detected to be relatively low, compared to air quality standards and international guidelines, the importance of reducing ambient air pollution and effective urban planning is evident [25].

While many studies on air pollution and LBW have looked at exposure throughout pregnancy, Darrow et al. [26] focused on exposure late in pregnancy. This five-country analysis, conducted between 1994 and 2004, found that ambient levels of NO_2, SO_2, $PM_{2.5}$, elemental carbon, $PM_{2.5}$ and water-soluble metals were all significantly associated with reductions in birth weight (−4 to −16 g per IQR increase in pollutant concentrations). Furthermore, this association was generally stronger in Hispanic and non-Hispanic black infants compared to non-Hispanic white infants, indicating a physiological difference between different ethnic groups.

Through a review of current literature, a number of additional studies show an association between air pollution and LBW (https://www.ncbi.nlm.nih.gov/pubmed/26918840, https://www.ncbi.nlm.nih.gov/pubmed/26137887, https://www.ncbi.nlm.nih.gov/pubmed/26046983).

10.3.1.3 Small for Gestational Age (SGA)

Gray et al. [27] assessed the association between $PM_{2.5}$ and O_3 exposure to individual- and area-based SES indicators and SGA from 2002 to 2006. Daily measurements of $PM_{2.5}$ and O_3 were calculated through a spatial hierarchical Bayesian

model. The researchers found that $PM_{2.5}$ air pollutants as well as maternal race, education, and neighborhood household income were associated with SGA (OR = 1.03, 95% CI = 1.02–1.05 per IQR). Despite the link between $PM_{2.5}$ air pollutants and SGA, O_3 showed inconsistent effects, substantiating the need for further research in this area. Woodruff et al. [28] reported disparities in air pollution exposure during pregnancy based on a multi-pollutant index by race, but not educational attainment in the USA. While in a study in Toronto, Buzzelli and Jerrett [29] found higher NO_2 exposure among both those with lower incomes and those with higher status occupations.

Stieb et al. [30] found that NO_2 was associated with adverse birth outcomes like SGA. Another study in Ohio showed that exposure to $PM_{2.5}$ in the last trimester was associated with an increased risk of SGA [31]. Ha et al. [32] found that elemental carbon exposure showed a 4% increase in SGA. Others studies have reported significant positive associations between NO_2 and LBW, SGA, or reduced birth weight [33, 34]. An association of a larger magnitude of $PM_{2.5}$ with SGA and term birth weight (but not with term LBW) was observed among births to mothers born in Canada [30].

Le et al. [35] investigated the link between SGA and exposure to SO_2, CO, NO_2, O_3, and PM_{10} during the first month and third trimester of pregnancy. The study found an association between SGA and CO levels that exceeded 0.75 ppm (OR = 1.14, 95% CI = 1.02–1.27) and NO_2 exceeding 6.8 ppb (OR = 1.11, 95% CI = 1.03–1.21) exposure in the first month, and PM_{10} exceeding 35 $\mu g/m^3$ (OR = 1.22, 95% CI = 1.03–1.46) and O_3 (OR = 1.11, 95% CI = 1.02–1.20) exposure in the third trimester.

Overall, there is growing evidence of the link between air pollution and the SGA birth outcome; however, many studies still present limited findings, thus highlighting the need for further research.

10.3.2 Preterm Birth (PB)

Maternal exposure to air pollutants during pregnancy has also been linked with preterm birth (PB), which is defined below.

Def 3.2 Preterm Birth (PB)
WHO defines PB as babies born alive before 37 weeks of gestation [5]. It is estimated that each year, 15 million babies are born preterm, with PB complications being the leading cause of death among children under 5 years of age (responsible for nearly one million deaths annually) (http://www.who.int/mediacentre/factsheets/fs363/en/).

As mentioned above, Le et al. [35] found a significant association between PB and SO_2 and O_3, but surprisingly not CO. This prospective cohort study included 164,905 singleton births among a large Black population in Detroit, Michigan between 1990 and 2001. Air pollutants were measured with three fixed site ambient air monitors located in densely populated urban areas. PB was associated with SO_2 (OR = 1.07, 95% CI = 1.01–1.14) exposure in the last month, with hourly O_3 exceeding 92 ppb (OR = 1.08, 95% CI = 1.02–1.14) exposure in the first month. This study also noted the importance of accounting for individual risk factors such as maternal smoking, maternal race, and long-term trends in air pollution levels and adverse birth outcomes. Additionally, the results showed that infants born to Black mothers had an approximately twofold higher risk of PB than those who were born to White mothers; however, further research is needed to support this finding.

Another study supporting the association between PB and air pollution [36] is a population-based case–control study in Los Angeles County, California. This study used three exposure data sources to examine the risks of PB among mothers exposed to high levels of traffic-related air pollutants during pregnancy. The odds of PB increased 6–21% per IQR increase in all pregnancy exposures to $PM_{2.5}$ as well as other traffic-related pollutants, while there was a 30% per interquartile increase in PAH (OR = 1.3, 95% CI = 1.15–1.47).

A retrospective cohort study in Brisbane, Australia supports the above findings, demonstrating an association between PB and air pollution [37]. This study assessed average maternal exposures to ambient PM_{10}, O_3, and NO_2 air pollutants of 28,200 singleton live births between 2000 and 2003, during the first 3 months after the last menstrual period and the last 3 months prior to birth. This study found that exposure to PM_{10} and O_3 in the first trimester was strongly associated with an increased risk of PB (OR = 1.15, 95% CI = 1.06–1.25 and OR = 1.26, 95% CI 1.10–1.45, respectively).

With the rate of PB across 184 countries ranging from 5% to 18% and evidence indicating an association with ambient air pollution, reducing exposure to ambient air pollution has the potential to drastically reduce the prevalence of PB (http://www.who.int/mediacentre/factsheets/fs363/en/).

10.3.3 Summary

Air pollution is strongly linked to LBW, PB, and SGA birth outcomes. As each of these birth outcomes has the potential to have a severe impact on the health of the child throughout his or her lifetime, it is critically important for all countries to ensure compliance with the WHO air quality guidelines (http://apps.who.int/iris/bitstream/10665/43184/1/9280638327.pdf). As air pollution has the potential to impact individual as well as societal health, this review highlights the importance of better understanding the association between air pollution and birth outcomes.

10.4 Neurocognitive Development

Neural development is a process that includes proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis of neurons [38]. Prenatal development is a critical window for the growth of the central nervous system (CNS) [39, 40]. Three recent systematic reviews have provided moderate evidence that air pollution affects children's neurodevelopment, which cannot be ignored [39, 41]. The evidence as a whole suggests that vehicular pollution contributes to cognitive impairment, thus emphasizing that government bodies and individuals should take prompt measures to control air pollution [42]. In this review, the effects of prenatal and postnatal air pollution exposure on children's neurodevelopment are considered separately. Only studies on ambient air pollution are included as well as studies on several cognitive functioning tests along with global intelligence quotients (IQ) and behavioral disorders, such as autism, ASD, and ADHD.

Def 4. Neurodevelopment, ASD, ADHD
Neurodevelopment is a process that includes the proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis of neurons [38]. Autism spectrum disorder (ASD) is a developmental disorder that affects communication and behavior. Although autism can be diagnosed at any age, it is said to be a "developmental disorder" because symptoms generally appear in the first 2 years of life (https://www.nimh.nih.gov/health/topics/autism-spectrum-disorders-asd/index.shtml). Attention-deficit/hyperactivity disorder (ADHD) is a brain disorder marked by an ongoing pattern of inattention and/or hyperactivity–impulsivity that interferes with functioning or development (https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml).

10.4.1 Children's Neurocognitive Function–Prenatal Exposure

Lertxundi et al. [43] assessed children at the age of 15 months on the Bayley Scales of Infant Development (BSID) and concluded that prenatal $PM_{2.5}$ and NO_2 exposures were associated with significant decreases in neurocognitive scores.

Guxens et al. [40] suggested that exposure to fine particles during fetal life was related to structural alterations of the cerebral cortex in children's brains, and these alterations partially mediated the association between exposure to fine particles during fetal life and children's impaired inhibitory control.

A pooled analysis of six European prospective studies examining the association of prenatal exposure to $PM_{2.5}$, PM_{10}, and NO_2 with cognitive development [44] identified small deficits in global cognition, language development, and psychomotor

development with an increase in pollution exposure. However, only the association between increased NO_2 and a deficit in psychomotor development was significant. Among urban youth, Peterson et al. [45] conducted an MRI study exploring the effects of prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) on the development of white brain matter, cognition, and behavior in later childhood. Results indicated that prenatal PAH air pollutant exposure is associated with cognitive and behavioral disturbances in childhood and disrupts the development of left-hemisphere white matter, which contributes to slower processing speed, ADHD symptoms, and externalizing problems in urban youth.

10.4.2 Children's Neurocognitive Function–Postnatal Exposure

In a Spanish, longitudinal study, Freire et al. [46] showed that high exposure to air pollution was associated with a modest decrease on the McCarthy Scales of Children's Abilities (MSCA) at 5 years of age. In another prospective birth cohort study, Suglia et al. [47] observed that an IQR increase in log-transformed black carbon exposure was associated with a reduction in scores of several subscales of the Kaufman Brief Intelligence Test (K-BIT) and the Wide Range Assessment of Memory and Learning (WRAML) at 9 years of age.

A Spanish longitudinal study [48] found that children exposed to higher levels of $PM_{2.5}$, black carbon, and ultrafine particles at school performed worse on tests of working memory and attentiveness than those exposed to lower levels. After 12 months, the gap widened significantly among those in the highly exposed group. Another longitudinal study [49] demonstrated a non-linear relationship between air pollution exposure and attention abilities. The second and third quartiles of black carbon exposure were associated with more errors and slower reaction times on the Connors' Continuous Performance Task. However, this relationship was heavily reduced among those in the highest quartile of black carbon exposure.

10.4.3 Prenatal and Postnatal Air Pollution Exposure and ASD and ADHD

Becerra et al. [50] reported an increased risk of ASD with increased NO_x, O_3, and $PM_{2.5}$ exposure. Similarly, three other studies assessed the association between pre- and postnatal exposure to $PM_{2.5}$ and ASD [51–53]. Another study in Spain [54] found that higher exposure to NO_2 during pregnancy is associated with impaired attentional function, especially increased inattentiveness, in children aged 4–5 years.

Postnatal exposure to NO_2 is also associated with increased inattentiveness, although it is difficult to completely dissociate the effects of pre- and postnatal

exposure since they are highly correlated. Jung et al. [55] reported increased odds of ASD in relation to postnatal exposure to CO, NO_2, O_3, and SO_2. Based on case–control studies, several systematic reviews on autism have described fairly consistent evidence showing an association between air pollution, especially prenatal exposure to PM, and an ASD diagnosis [56–58].

However, several European studies have not demonstrated any association between prenatal exposure to NO_2, $PM_{2.5}$, or PM_{10} and autistic traits [59] or between pre- and postnatal exposure to NO_x, PM_{10}, and ASD and ADHD [60]. A cross-sectional American study [61] also did not find any association between pre- and postnatal exposure to NO_x and PM_{10} and ADHD, respectively. Furthermore, a population-based nested case–control study in Israel [62] revealed that exposure to NO_2 during the postnatal period may be more relevant to ASD than prenatal exposure.

10.4.4 Biological Mechanism

The potential cellular mechanisms known to be responsible for CNS damage are neuroinflammation, oxidative stress, glial activation, and white matter injury [63, 64].

Further research is still needed on the specific components of air pollution that are responsible for CNS damage and the molecular mechanisms involved in humans [39].

10.4.5 Summary

Although current studies did determine the critical period of exposure (pre- or postnatal) for the occurrence of ASD [39], the evidence of an association between pre- or postnatal exposure to $PM_{2.5}$, PM_{10}, and ASD and ADHD is limited (Tables 10.3 and 10.4).

10.5 Childhood Obesity

Childhood obesity is emerging as a major public health problem that is on the increase worldwide [65]. The rates of overweight and obesity among youths have been shown to be highly prevalent in many countries, especially in the USA where the rate increased to about 32% in 2003–2006 [66, 67]. Childhood obesity can develop into serious diseases such as metabolic or cardiovascular disorders, and the rapid increase of its prevalence can be attributed to environmental factors in childhood [68, 69]. There has been growing interest in discovering the wider determinants of childhood obesity, but much more needs to be clarified, including the identification of distal and modifiable factors such as air pollution and traffic delays [65].

Table 10.3 Effects of air pollution on neurodevelopment

Air pollution	Health outcome measurement (age)	Effect size	Reference (study design)
NO_2 Prenatal	Psychomotor development (1–6 years)	−0.68 (−1.25 to −0.11)	Guxens et al. [44] Prospective studies
Aerosol samples measure $PM_{2.5}$, NO_2 Prenatal	Neurodevelopment *BSID* (15 months)	1 μg/m^3 increase in $PM_{2.5}$ in motor score (−0.14; −1.75, −0.53) 1 μg/m^3 increase in NO_2 in mental score (−0.29; −0.47, −0.11)	Yorifuji et al. [12] Longitudinal
SPM Prenatal	Survey questions about behavioral problems (8 years)	1.06 (95% CI: 1.01, 1.11) interrupting others, 1.09 (95% CI: 1.03, 1.15) failure to pay attention, 1.06 (95% CI: 1.01, 1.11) for lying, 1.07 (95% CI: 1.02, 1.13) for causing public disturbance	Suglia et al. [47] Prospective
Quartiles of average black carbon exposure estimated using LUR mean 0.56 μg/m^3 Postnatal	Cognitive functioning *K-BIT, WRAML* (8–11 year)	An interquartile range (0.4 μg/m^3) *Vocabulary* (−2.2, −5.5 to 1.1); *matrices* (−4.0, −7.6 to −0.5); *Composite* (−3.4, −6.6 to −0.3); *verbal* (−1.3, −4.8 to 2.2); *Visual* (−5.4, −8.9 to −1.9); *learning* (−2.8, −6.6 to 1.1); *General index* (−3.9,-7.5 to −0.3)	Freire et al. [46] Longitudinal
Home outdoor NO_2 concentration Estimated using LUR Postnatal 15.40 μg/m^3 15.40–24.75 μg/m^3 424.75 μg/m^3	Neurodevelopment *MSCA* (*Spanish*) (5 years) 0% female	Medium NO_2 exposure (β = −1.07, −9.99 to 7.85) High NO_2 exposure (β = −4.19, −14.02 to 5.64)	
Exposure to $PM_{2.5}$, black carbon and ultrafine particles at school *Ultrafine particles* 8034cm^3 (indoor) 11,939 cm^3 (outdoor)	Working memory *n-back attentional network* (7–10 years)	*Working memory (2-back):* Change from −5.3 (−1.6, 5.1) points to −9.9 (−16, −3.5) points *Working memory (3-back):* Change from −1.4 (−10, 7.1) points to −5.8 (−11, −0.74) points. *Inattentiveness:* Change from 5.2 (— 6.2, 17) points to 5.2 (0.68, 9.7) points (higher score = poorer performance).	Sunyer et al. [48] Longitudinal (Spain)

BSID-II Bayley scale of infant development – Revised, *CPT* Connors' continuous performance test, *DMST* digit memory span test, *DSST* digit symbol substitution test, *ETS* environmental tobacco smoke, *HECT* hand-eye coordination test, *IQ* intelligence quotient, *KBIT* Kaufman brief intelligence test, *MSCA* McCarthy scales of children's abilities, *NO_2* nitrogen dioxide, *OR* odds ratio; will be added

Table 10.4 Effects of air pollution on ASD and ADHD

Air pollution	Health outcome measurement (age)	Effect size	Reference (study design)
Per interquartile range (IQR) Particulate matter ≤2.5 μm Prenatal (entire pregnancy)	ASD DSM-IV-R (6–7 years)	OR = 1.15 (95% CI: 1.06–1.24) Per 4.68 μg/m^3 increase	Becerra et al. [50] Case–control
Per IQR increase $PM_{2.5}$ Prenatal and postnatal	ADOS (not provided)	*Postnatal* OR = 1.57 (95% CI: 1.22–2.03) *9 months of pregnancy* OR = 1.63 (95% CI: 1.08–2.47) *Third trimester* OR = 1.42 in PM2.5 (95% CI: 1.09–1.86)	Raz et al. [51] Nested case–control
Nitrogen dioxide, $PM_{2.5,}$ PM_{10} Prenatal, postnatal, and during the first year of life	ADI-R ADOS (2–5 years)	AOR, 1.81 (95% CI: 1.37–3.09) AOR, 2.08 (95% CI: 1.93–2.25) AOR, 2.17 (95% CI: 1.49–3.16) AOR, 2.06 (95% CI: 1.37–3.09) AOR, 2.12 (95% CI: 1.45–3.10) AOR, 2.14 (95% CI: 1.46–3.12).	Volk et al. [52] Case–control
$PM_{2.5}$ Prenatal and postnatal	ADOS SCQ (3–7 years)	*Postnatal year two* AOR = 1.45 (95% CI = 1.01–2.08) *Pre-pregnancy through year 2* OR = 1.51 (95% CI = 1.01–2.26)	Talbott et al. [53] Case–control
PM10: Per 10 μg/m^3 increase CO: Per 100 ppb in CO NO_2, O_3: Per 10 ppb Increase postnatal SO_2: Per 1 ppb in SO_2 Multi-pollutant models	ICD-9-CM 6.26 (2.91 years)	59% risk increase l (95% CI 1.42–1.79), 37% risk increase (95% CI 1.31–1.44), 340% risk increase (95% CI 3.31–5.85), 17% risk increase level (95% CI 1.09–1.27)	Jung et al. [55] Prospective cohort (I)
NO_x $PM_{2.5}$ PM_{10} Prenatal	Autistic traits A-TAC (4–10 years)	Borderline/clinical range *Per each 10 μg/m^3 increase in NO_2* OR = 0.94 (95% CI: 0.81–1.10) *PM2.5, PM10*: NS	Guxens et al. [59] Birth cohorts and child cohort
NO_x PM_{10} Prenatal	ASD, ADHD A-TAC (9–12 years)	NO_x 5–95% difference, odds ratios (ORs) of 0.92 (95% CI: 0.44–1.96) for ASD 0.90 (95% CI: 0.58–1.40) for ADHD *PM10* ORs of 1.01 (95% CI: 0.52–1.96) for ASD 1.00 (95% CI: 0.68–1.47) for ADHD	Gong et al. [60] Birth cohort (I)

Although only a few epidemiological studies have investigated the association of air pollution with childhood obesity, two recent systematic reviews concluded that outdoor air pollution significantly contributes to the development of obesity in childhood [70, 71]. However, additional evidence is required indicating an association between air pollution and childhood obesity. According to one systematic review, the evidence on this issue is "insufficient" because of the small number of studies [72].

This review includes studies of ambient air pollution only and childhood obesity, which is defined by weight-for-length or body mass index (BMI) and metabolic syndrome.

Def 5. Childhood Obesity
The body mass index (BMI) is a measure used to determine childhood overweight and obesity. Overweight is defined as a BMI at or above the 85th percentile and below the 95th percentile for children and teens of the same age and sex. Obesity is defined as a BMI at or above the 95th percentile for children and teens of the same age and sex. The BMI is calculated by dividing a person's weight in kilograms by the square of height in meters. For children and teens, the BMI is age- and sex-specific and is often referred to as BMI-for-age. A child's weight status is determined using an age- and sex-specific percentile for the BMI rather than the BMI categories used for adults. This is because a child's body composition varies as he or she ages, and it varies between boys and girls. Therefore, the BMI levels among children and teens must be expressed relative to other children and teens of the same age and sex (https://www.cdc.gov/obesity/childhood/defining.html).

10.5.1 Air Pollution Effects on Childhood Obesity

Fleisch et al. [73] assessed the weights and lengths of US infants at birth and 6 months of age and examined the association of prenatal $PM_{2.5}$ and black carbon with fetal growth and infant weight gain among participants of the project Viva cohort. Results showed lower fetal growth among infants exposed to the highest quartile of black carbon during the third trimester compared to the lowest quartile group. In addition, although effect estimates were imprecise, the highest quartile of black carbon or $PM_{2.5}$ exposure during the third trimester was also shown to be positively associated with 0–6 months weight-for-length gain. Furthermore, compared with the lowest quartile of neighborhood traffic density, infants of the highest quartile had a greater weight-for-length gain from 0–6 months of age, and they had greater odds of weight-for-length $\geq$ the 95th percentile at 6 months of age.

Kim et al. [74] indicated that higher exposure to early life near-roadway air pollution (NRAP) increased the rate of change of childhood BMI and resulted in a higher attained BMI at 10 years of age that was independent of later childhood

exposures. These findings suggest that elevated early life NRAP exposure contributes to an increased risk of obesity in children. Moreover, results indicated that increased first year of life near-road freeway NO_x exposures are associated with an increased velocity of childhood BMI growth trajectory and higher attained BMI at 10 years. Furthermore, increased childhood near-roadway exposures from non-freeway sources were associated with increased BMI growth and a higher BMI at 10 years.

In another longitudinal study in the USA, Rundle et al. [75] suggested that prenatal exposure to the PAH of ambient traffic-related pollution was associated with an increased BMI and obesity at 5 and 7 years of age. When the prenatal PAH exposure levels were divided into three groups based on the concentrations of exposure, children of mothers in the highest exposure group had a higher BMI z-score and a relative risk of 1.79 for obesity at 5 years of age. They also had a higher BMI z-score, a higher percentage of body fat, and a relative risk of 2.26 for obesity at 7 years of age, compared with children of mothers in the lowest group of PAH exposure.

Huang et al. [76] assessed the association of air pollutants (PM_{10}, SO_2, NO, and NO_2) at different growth phases (in utero, in infancy, and in childhood) with a BMI at ~9, ~11, ~13, and ~15 years of age in a population-representative birth cohort from Hong Kong, "Children of 1997." This study found that associations were sex-specific based on better model fit when including sex interaction terms. Among boys, higher NO_2 in childhood was associated with higher BMI at ~9, ~13, and ~15 years of age using a multi-pollutant model.

The GINIplus and LISAplus birth cohorts study [77] showed insulin resistance increased by 17.0% (95% CI 5.0, 30.3) and 18.7% (95% CI 2.9, 36.9) for every 2-SD increase in ambient NO_2 and particulate matter $\leq$10 μm in diameter, respectively, indicating that traffic-related air pollution may increase the risk of insulin resistance. Given the ubiquitous nature of air pollution and the high incidence of insulin resistance in the general population, the associations examined here may have potentially important public health effects despite the small/moderate effect sizes observed.

10.5.2 Biological Mechanism

It is plausible that air pollutants are potent oxidizers that act either directly on lipids and proteins or indirectly through the activation of intracellular oxidant pathways [78, 79]. Oxidative stress caused by exposure to air pollutants may therefore play a major role in the development of insulin resistance [77, 80]. Another hypothesis is one centered on environmental obesogens, which are chemical simulators of metabolic hormones or brain neurotransmitters [81, 82]. The hypothesis builds on the existing science that chemicals in air pollution have the potential to interfere with

endocrine and metabolic systems and may change growth patterns and induce weight gain, obesity, and obesity-related diseases such as metabolic syndromes and cardiovascular diseases (CVD) [72, 74, 82–84].

10.5.3 Summary

Epidemiological studies examining the associations between exposure to air pollution and childhood obesity with insulin resistance are scarce. The present review may suggest a positive association between outdoor air pollution, especially PM and NO_2, and the development of obesity or insulin resistance in children. These air pollutants may disrupt normal development and thus result in increased weight-for-length gain, mean BMI growth, and differences in attained BMI at specific ages [74–76]. Many research questions remain, and further studies are needed to fill the data gaps to stimulate focused research and advance the field. Taking into account the current knowledge on the adverse effects of obesogen chemicals on childhood health, the child obesity epidemic should be considered a multifactorial complex disorder necessitating an emphasis on public health interventions for environmental protection [82] (Table 10.5).

Table 10.5 Effects of air pollution on child obesity

Air pollution	Health outcome measurement (age)	Effect size	Reference (study design)
$PM_{2.5}$ and black carbon Prenatal	Fetal growth and infant weight gain (6 months)	The highest (vs. lowest) quartile of neighborhood traffic density: Increased weight-for-length gain z-score change, (β) = 0.25 (0.01 to 0.49) Greater odds of weight-for-length ≥95th percentile at 6 months (OR) = 1.84 (1.11 to 3.05)	Fleisch et al. [73] Cohort (USA)
Polycyclic aromatic hydrocarbon (PAH) Prenatal	BMI (body mass index) (age 5 and 7 years)	The highest (vs. lowest) prenatal PAH: Higher BMI z-score At 5 years (β) = 0.39 (0.08–0.70) At 7 years (β) =0.30 (0.01–0.59) risks of obesity At 5 years (RR) = 1.79 (1.08–2.98) At 7 years (RR) = 2.26 (1.28–4.00)	Rundle et al. [75] Cohort (USA)
Ambient NO_2 and particulate matter ≤10 μm At birth	HOMA of insulin resistance (HOMA-IR) (10-year-old children)	Insulin resistance increased by 17.0% (95% CI 5.0, 30.3) and 18.7% (95% CI 2.9, 36.9) for every 2SDs increase in ambient NO_2 and particulate matter ≤10 μm in diameter	Thiering et al. [77] Two birth cohorts (Germany)

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