MAZUR, Sylwia, DĄBROWSKA, Natalia, MADERA, Magdalena, ZDUNEK, Roksana, MARCINKOWSKI, Krzysztof, STRUS, Karolina, KUBLIŃSKA, Aleksandra and NAGÓRSKA, Emilia. Asthma - a healthcare, environment and green transformation - associated disease. Quality in Sport. 2024;18:53276. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.18.53276
https://apcz.umk.pl/QS/article/view/53276

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 08.07.2024. Revised: 22.07.2024. Accepted: 25.07.2024. Published: 26.07.2024.

Asthma - a healthcare, environment and green transformation - associated disease

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Abstract

Air pollution both anthropogenic and from natural sources impacts human health and is a rising problem for healthcare around the world. Key pollutants, such as particulate matter, carbon monoxide, ozone, nitrogen dioxide, and sulphur dioxide, contribute especially to respiratory illnesses. This review examines recent studies in the field of asthma and air pollution correlation, particularly mechanisms of air pollution-related damage, asthma symptoms exacerbations and the risk of developing the disease due to poor air quality. Studies show that pollutants affect the immune system by triggering pro-inflammatory responses and oxidative stress, particularly in individuals with asthma. The review present findings of exacerbation of asthma symptoms and increased frequency of asthma attacks along with

higher rates of hospital admissions and emergency room visits due to exposure to common air pollutants. Additionally, prenatal and early-life exposure to traffic-related air pollution proved to significantly increase the risk of developing asthma in children. The review also critically identifies data gaps and methodological inconsistencies in some investigations. The complex relationship between air pollution and asthma is for sure an interesting field to explore furtherly. Analysed materials emphasize the critical need for global measures to reduce air pollution, including stricter air quality regulations and public awareness initiatives.
Key words: air pollution, asthma

Introduction

Air pollution can be defined as the presence of harmful to humans substances in the air surrounding the population[1] . Pollutants are emitted by cars, heating, power plants, agriculture, and many more in the industrial field. Natural phenomena add to the mixture too when fires, volcanic eruptions or even desert dust movement occurs [2]. The most commonly assessed pollutants are presented in Table 1.

Table 1. Air pollutants [1],[2],[6],[8].

Particulate matter (PM)	Have the greatest impact on human health. The most common indicator of air quality. It is a mixture of solid and liquid particles suspended in the air such as sulfates, nitrates, ammonia, sodium chloride, black carbon, mineral dust, and water. -**PM10** inhalable particles that have 10 μm or less. -**PM2.5** - fine particles with diameter ≤2,5 μm -**UFP**- ultrafine particles ≤0,1 μm
Carbon monoxide (CO)	Gas is released mostly from the combustion of different fuels. It is colorless and odorless.
Ozone (O3)	The ground level one (not the ozone layer in

	the upper atmosphere). It is a result of the reaction of gases in the sunlight and a major component of photochemical smog.
Nitrogen dioxide (NO2)	Product of fuel combustion mostly from industrial sectors.
Sulfur dioxide (SO2)	Colourless but with a distinctive odour. Released from fuel and mineral ores combustion.

Studies sometimes focus solely on traffic-related air pollution (TRAP) which is a mixture of gases and particles emitted from motor vehicle use. The majority of it is a direct tailpipe emission but evaporation of fuel, resuspension of dust, abrasion of the road, and wear of brakes and tires are also taken into consideration [3]. As the World Health Organization reports approximately 2.3 billion people by cooking on open fires and old stoves fuelled i.e. by kerosene, biomass, or coal are highly exposed to household air pollution which in 2020 contributed to 3.2 million deaths [4]. Other proportions of indoor air pollution include smoking, heating, allergens such as animal fur, mold or dust, and quality of ventilation [5]. Ambient (outdoor) air pollution affects indoor air quality and contrariwise [1]. The WHO's collective reports reveal that in 2019, 99% of humans were living in places where air quality guidelines levels were not kept and air pollution (both ambient and household) is associated with 6.7 million premature deaths each year and 140 million disability-adjusted life-years (DALYs) [6], [7]. The increase in air pollutant exposure and its consequences is especially observed in low and middle-income countries. Together with the process of population aging and lifestyle changes bad air quality escalates morbidity and mortality from noncommunicable cardiovascular and respiratory diseases- major causes of global mortality. Air pollution has an impact on the rise of the disease burden from lower respiratory tract infections and other causes of death in children and infants including preterm births [8].

Asthma is a chronic inflammatory disease affecting airways. Recurrent symptoms of coughing, wheezing, tachypnoea, or even chest tightness sensations are caused by reversible airflow obstructions and bronchospasms [7]. It is one of the most common respiratory diseases with 260 or even 334 million patients affected worldwide. Since they are one of the main body boundaries airways are constantly exposed to the environment [5]. Numerous studies have been conducted to investigate the impact of air pollution on asthma exacerbation,

symptoms, onset, or mortality [7], [9], [10]. The mechanisms responsible for inducing new-onset asthma include oxidative stress following inflammation affecting the mucous membrane of the respiratory tract. Further remodeling and immune changes induce sensitization and asthma symptoms appear [11]. Variables such as time of exposure, type of pollution, and different population groups were investigated and this review aims to summarize and analyse those studies [5], [11].

Aim

The aim of this study is to gather and analyse the studies about the impact of air pollution on asthma. The mechanisms of air pollution-related damage, asthma symptoms exacerbations and the risk of developing the disease due to poor air quality.

Methods

Freely accessible database PubMed was searched using the keywords: 'air pollution' and 'asthma'. Only articles published between 2016-2024 and with full text written in English were taken into consideration. Articles were furtherly chosen based on title, next abstract. Finally, 24 were included in the study.

Results

- **Mechanisms of air pollution-related damage**

How does air pollution affect our immune system? Glencross et al. [12] investigated this matter. Primarily pollutants affect the respiratory tract upon inhalation, impacting the immune system at the interface of the airways. Inhaled pollutants interact with epithelial and immune cells in the airways, triggering cellular signaling pathways that can lead to immune responses

and disease. The immune system comprises various specialized cells that interact with each other and non-immune cells like epithelial cells. In the lungs, innate immune cells such as alveolar macrophages and neutrophils respond quickly to inhaled pathogens, while dendritic cells beneath the epithelium sample antigens. Ambient urban air pollution includes gases like ozone, VOCs, CO, and NOx, as well as particulate matter (PM) of varying sizes (PM10, PM2.5, UFPM), which penetrate different parts of the respiratory tract. These pollutants stimulate immune cells via mechanisms such as Toll-Like Receptors and reactive oxygen species pathways, leading to pro-inflammatory responses. PM, especially, is known to induce oxidative stress, reducing antioxidant defenses and causing cellular damage. Air pollution affects these immune responses by disrupting the function of multiple cell types, leading to disease. A healthy immune system must balance effective responses to infections and neoplastic cells with tolerance to the body's tissues. Environmental factors, such as early-life exposure to pollutants, increase the risk of asthma and chronic airway diseases, starting in utero. Studies show [13], [14] that ambient pollutants trigger cellular signaling pathways, promoting pro-inflammatory and Th2 responses while disrupting antimicrobial defenses, correlating with increased disease incidence. Recent studies [1], [15] suggest that both gaseous and particulate components of air pollution can disrupt immune homeostasis, particularly affecting individuals with conditions like asthma. The complexity of PM composition and its geographic variability further complicates the impact of air pollution on health, necessitating ongoing research to fully understand and mitigate these effects.

Serafini et al. [13] focus in the review on outdoor air pollution. Health effects are caused by reactive oxygen and nitrogen species (ROS, RNS), leading to oxidative stress and activating inflammatory pathways (Nrf2, MAPK, NF-κB), as well as epigenetic alterations like histone modifications, microRNA expression, and DNA methylation. Exposure to air pollutants primarily occurs through inhalation, ingestion, and skin contact, affecting various systems of the human body such as the immune system.

Allergic asthma, the most prevalent type of asthma, is typically characterized by a sensitivity to environmental allergens [16]. Diagnosis is reinforced when there is a clear connection between allergen exposure and asthma symptoms. Meta-analysis of 6163 children from four European birth cohorts (Sweden, Germany, the Netherlands) conducted by Melen et al. [17], explored the association between air pollution exposure and allergic sensitization. Median air pollution levels varied across cohorts, ranging from 12.4 μg/m3 to 23.2 μg/m3 for NO2 and

from 8.1 μg/m3 to 17.2 μg/m3 for PM2.5. However, concentrations of PMcoarse were similar among the cohorts. While there wasn't a consistent link between air pollutants and overall allergic sensitization up to age 16, exposure was associated with specific allergens like birch pollen, grass pollen Phl p 1, and cat Fel d 1. Sensitization to a combination of common inhalant and food allergen extracts varied across the cohorts, with different prevalence rates at ages 4-6, 8-10, and 15-16. At ages 4 to 6 years, prevalence ranged from 24.1% to 40.4% . At ages 8 to 10 years, it ranged from 34.8% to 47.9% . At ages 15 to 16 years, it ranged from 41.8% to 51.2%. Although no consistent evidence was found for the association between air pollution and sensitization to common allergens, statistically significant positive associations were observed in the cohort from the Netherlands. Notably, higher odds of sensitization against birch pollen were linked to several air pollution markers at the time of sampling. Despite adjustments, associations remained statistically significant. Additionally, no differences in age-specific associations were noted. Overall, while the study didn't consistently find a link between air pollution and allergic sensitization, specific analyses hinted at heightened risks related to birch pollen and certain pollutants, what might lead to an increased risk of developing asthma [18].

In investigations using postmortem samples from organ donors, it was consistently noted that lymph nodes near the lungs contained dark particulate matter, which was distinct from those near the gut [19]. This observation prompted a closer examination of how these particles affect immune cells and the structure of lymph nodes in these regions. The research from this study revealed that as individuals age, particulates tend to accumulate more in lymph nodes associated with the lungs, disrupting their normal functions. Specifically, these particles interfere with the activity of certain immune cells, reducing their ability to clear harmful substances. Additionally, the accumulation of particulates in lung-related lymph nodes disrupts their architecture, impairing their ability to filter toxins. These findings highlight the direct harm inflicted by environmental pollutants on the immune system, particularly in organs connected to the respiratory system. Many questions remain unanswered, including how these particles are contained and whether targeting specific immune cells could aid in their removal. Further research is crucial to fully comprehend the impact of inhaled particles on immune cells within the lungs.

Exacerbations

Research consistently shows that air pollution significantly exacerbates asthma symptoms and increases the frequency of asthma attacks. In "Impact of Air Pollution on Asthma Outcomes," Tiotiu et al.[1] highlight how traffic-related pollution, nitrogen dioxide, and second-hand smoke are critical risk factors for both the development and worsening of asthma, particularly in children. The study emphasizes that exposure to these pollutants can induce asthma symptoms, trigger exacerbations, and decrease lung function. This is particularly concerning for vulnerable populations, such as children and those with pre-existing respiratory conditions.

Similarly, Orellano et al.[20], in their systematic review and multilevel meta-analysis, detail the impact of outdoor air pollutants on asthma exacerbations. They found that exposure to particulate matter (PM), ozone (O3), and nitrogen dioxide (NO2) is associated with a significant increase in asthma attacks in both children and adults. The meta-analysis confirms that these pollutants not only exacerbate asthma symptoms but also lead to higher rates of hospital admissions and emergency room visits due to severe asthma attacks .

Furthermore, Nassikas et al.[21] examine the specific impact of ozone pollution on asthma exacerbations in New England. Their study reveals a clear correlation between higher ozone levels and increased incidences of asthma-related emergency room visits and hospitalizations. This study underscores the regional impact of air pollution, demonstrating that even in areas with relatively stringent air quality regulations, ozone pollution remains a significant trigger for asthma exacerbations .

A comprehensive study[7] using a multisite time-series design across ten U.S. states found significant links between short-term exposure to various air pollutants and increased emergency department (ED) visits for asthma. The pollutants examined included PM2.5, PM10–2.5, key PM2.5 components (such as EC, OC, sulfate, and nitrate), and gaseous pollutants (O3, NOx, NO2, SO2, and CO). The analysis revealed that pollutants like NOx, NO2, CO, SO2, PM10–2.5, nitrate, and sulfate had a more substantial impact on children and adolescents, while PM2.5, EC, and OC affected both young and older populations significantly. Ozone had a more pronounced effect on adults compared to children .

Collectively, these studies underscore the urgent need for global measures to mitigate air pollution. Reducing exposure to both outdoor and indoor pollutants is crucial for improving

asthma outcomes and decreasing the healthcare burden associated with asthma exacerbations. Implementing stricter air quality regulations, promoting cleaner transportation options, and increasing public awareness about the harmful effects of air pollution are essential steps in protecting public health, especially for those with asthma .

- **The risk of developing asthma**

The risk of developing asthma is significantly heightened by exposure to air pollution, particularly in urban areas with heavy traffic. Pollutants such as nitrogen dioxide (NO2), particulate matter (PM2.5 and PM10), and volatile organic compounds (VOCs) have been strongly linked to increased asthma incidence in children and adults. [15]

A systematic review was conducted [22] to investigate whether prenatal exposure to air pollution contributes to the development of wheezing and asthma in children. The review included epidemiological studies published up to June 6, 2017, sourced from MEDLINE and Web of Science databases. The analysis focused on the association between prenatal exposure to various air pollutants, excluding tobacco smoke, and the incidence or prevalence of wheezing or asthma from birth to 14 years of age. Eighteen studies met the inclusion criteria, highlighting variability in exposure assessment methods. The meta-analysis revealed significant associations between prenatal exposure to NO2, SO2, and PM10 and increased risk of wheezing and asthma in childhood. Specifically, the pooled odds ratios (OR) were 1.04 for polycyclic aromatic hydrocarbons (PAH), 1.04 for NO2, 1.4 for PM2.5 for childhood wheeze, and 1.07 for NO2, 1.02 for SO2, and 1.08 for PM10 for childhood asthma. The review found minimal heterogeneity for PAH and SO2 but noted some heterogeneity for PM10, PM2.5, and NO2. However, there was insufficient evidence to link prenatal exposure to black carbon (BC), CO, and O3 with childhood wheezing and asthma, indicating a need for further studies to explore these associations in more detail.

Comprehensive meta-analysis[23] conducted using data from 27 studies sourced from Elsevier, LISTA (EBSCO), and Web of Science databases indicates that traffic-related air pollution (TRAP) significantly increases asthma risk among children, with meta-odds ratios (meta-OR) of 1.07 for PM2.5, 1.11 for NO2, 1.21 for benzene, and 1.06 for total volatile organic compounds (TVOCs). Sensitivity analyses confirmed these associations. Additionally, regional analyses revealed higher odds ratios for PM2.5 and NO2 in Asia compared to Europe and North America, suggesting regional differences in TRAP impacts. The study underscores the need for further research on the role of organic pollutants in TRAP and their association

with childhood asthma, as well as efforts to disentangle the effects of TRAP from other pollutant sources.

A systematic review and meta-analysis conducted by Khreis et al. [24] investigated the link between children's exposure to traffic-related air pollution and the development of asthma. This comprehensive research reviewed studies that assessed the risk of asthma incidence or lifetime prevalence in children exposed to TRAP from birth to 18 years old. The analysis included 41 studies, revealing significant associations between asthma development and various pollutants: black carbon (BC), nitrogen dioxide (NO2), nitrogen oxides (NOx), and particulate matter (PM2.5 and PM10). The findings showed that increased levels of these pollutants correlated with higher asthma risk, with risk estimates of 1.08 for BC, 1.05 for NO2, 1.03 for PM2.5, and 1.05 for PM10. Despite variability in asthma definitions, exposure assessment methods, and confounder adjustments among the studies, the results consistently supported the hypothesis that TRAP exposure during childhood contributes to asthma development. The study highlights the need for standardized methods in future research to further validate these associations and understand the underlying mechanisms .

The study conducted by Gehring et al. [25] indicates that exposure to air pollution is linked to the development of asthma from childhood through adolescence and into early adulthood. This research builds on previous European birth cohort studies by bridging the gap between findings from childhood and adolescent cohorts and those from adult cohorts. While the statistical power to analyze age-specific associations is limited, the estimates for NO2 and PM2.5 exposure at birth remain consistent from age four into early adulthood. Larger cohort studies are needed to confirm these results.

While only a few studies have examined the impact of air pollution on asthma development throughout all stages of youth, consistent evidence points to traffic-related pollutants like NO2 and PM2.5 as major contributors to asthma. The study underscores the importance of early-life exposure, reinforcing the evidence for these associations. Despite some limitations, such as the inability to separate analyses between atopic and nonatopic asthma and potential exposure misclassification due to the use of spatial land-use regression models, the findings align with previous research. Overall, early-life exposure to air pollution, particularly from motorized traffic, significantly increases the risk of developing asthma, highlighting the long-term impact of air pollution on respiratory health.

A retrospective cohort study [26] conducted on 39,782 preschoolers in seven cities in China investigated the combined effects of temperature and air pollution on childhood asthma. The study estimated exposure to three temperature indicators and three key ambient air pollutants

(PM10, SO2, and NO2) using the inverse distance weighted (IDW) method. The results indicated a significant association between traffic-related NO2 exposure and increased asthma prevalence, with odds ratios (ORs) of 1.17, 1.19, and 1.16 for lifetime, pregnancy, and postnatal exposure, respectively. Additionally, higher temperatures were positively associated with asthma risk, particularly during the first year of life, with ORs of 1.89, 1.47, and 1.15 for lifetime, pregnancy, and postnatal periods. Extreme heat days (EHD) further increased asthma risk, while extreme cold days (ECD) did not show a significant association. The study revealed a synergistic effect of high air pollutant levels and high temperatures, especially among boys and younger children, emphasizing the importance of considering both environmental factors in asthma risk assessments. These findings highlight the need for integrated strategies to mitigate the effects of both air pollution and temperature on childhood asthma.

A nationwide study in Denmark [27] investigated the link between early-life exposure to ambient air pollution and the development of asthma in children aged 0-19 years. The study included data from over one million children born between 1998 and 2016, analyzing their exposure to various pollutants such as PM2.5, PM10, NO2, nitrogen oxides, elemental carbon, organic carbon (OC), sulfur dioxide, ozone, sulfate, nitrate, ammonium, secondary organic aerosols, and sea salt. Using Cox proportional hazard models, the researchers found that increased prenatal exposure to most pollutants, excluding ozone and sea salt, was associated with a higher risk of developing asthma. The hazard ratio for an interquartile range increase in PM2.5 and NO2 exposure was 1.06 and 1.04, respectively, with the PM2.5 association remaining stable after adjusting for NO2. Additionally, a 0.5 μg/m3 increase in prenatal OC exposure, primarily from biomass, was associated with an increased asthma risk (HR 1.08). These findings highlight that early-life exposure to various air pollutants significantly contributes to asthma development in children.

In summary, e xtensive research consistently demonstrates that exposure to air pollution, especially from traffic-related sources, significantly increases the risk of developing asthma in children from prenatal stages through early adulthood. These findings emphasize the critical need for integrated strategies to mitigate the impact of air pollution on respiratory health, highlighting the importance of early-life exposure assessments and standardized research methods to better understand and address this growing public health concern.

Discussion

Overall, the findings highlight the complex relationship between air pollution and respiratory health, underscoring the need for ongoing, detailed research to address data gaps and methodological inconsistencies [22, 23, 24, 12,]. In the research conducted by Glencross et al. [12], it was stated that the composition of particulate matter (PM) varies by location, making it difficult to fully grasp its health effects. Other studies [22] showed no consistent and sufficient evidence concerning the association between air pollution and sensitization to common allergens as well as prenatal exposure to black carbon, CO, and O3 with childhood wheezing and asthma, indicating a need for further studies to explore these associations in more detail. Unlike [26, 27], no large groups of participants were examined in the studies [25], highlighting the need for larger participant groups to confirm any presented results. The large study conducted by Lu et al. [26] is the first to systematically demonstrate a temperature-pollution synergy on the risk of asthma development. While significant associations between NO2 exposure and asthma in preschoolers align with findings from previous studies, reinforcing the study's validity, this study only included data for PM10, SO2, and NO2, lacking information on other relevant pollutants like PM2.5, CO, and O3. Additionally, important factors such as green space, nutrition, and medication, which could influence asthma, were not included in the study. Moreover, the data from Beijing was incomplete, which may affect the generality of the findings. Using an administrative cohort with no selective participation in the research conducted by Pedersen et al. [27] reduces selection bias. However, exposures during commuting or at the workplace were not considered, resulting in possible differential exposure misclassification. Approximately 11% of the study population was not included in the final analysis due to missing smoking status data, although this absence is likely random.

In the era of climate change and the green transformation, particularly noticeable within the borders of the European Union, a lot of fake news and misconceptions are being produced and shared every day. One key policy should encompass a comprehensive educational campaign aimed at increasing awareness of air pollution-related diseases, such as asthma. This campaign should aim not only to encourage public opinion to exert even greater pressure for further and more complex actions to prevent potential emissions but also to halt environmental degradation in the coming years. To provide the public with clearer and more reliable answers, it is essential to broaden research, prepare a more universal research environment and enlarge participant groups in future studies.

Conclusion

Research consistently shows air pollution worsens asthma, especially in children, with various pollutants exacerbating symptoms and increasing attacks. Urban pollution significantly raises asthma risk, especially in early life. Mitigating pollution's effects is crucial, alongside raising awareness. Educational campaigns are needed to advocate for emission prevention and environmental protection, particularly within the European Union amidst climate change and green initiatives.

Authors contributions

Conceptualization: Sylwia Mazur and Magdalena Madera; Methodology: Sylwia Mazur, Natalia Dąbrowska, Krzysztof Marcinkowski; Software: Emilia Nagórska; Check: Magdalena Madera, Emilia Nagórska and Krzysztof Marcinkowski; Formal analysis: Karolina Strus; Investigation: Karolina Strus and Aleksandra Kublińska; Resources: Roksana Zdunek; Data curation: Roksana Zdunek and Natalia Dąbrowska; Writing - rough preparation: Sylwia Mazur, Aleksandra Kublińska and Emilia Nagórska; Writing - review and editing: Krzysztof Marcinkowski and Natalia Dąbrowska; Visualization: Magdalena Madera; Supervision: Roksana Zdunek; Project administration: Sylwia Mazur.

All authors have read and agreed with the published version of the manuscript.

Conflict of interest The authors report no conflict of interest.

Financial disclosure The study did not receive any funding.

Institutional Review Board Statement Not applicable.

Informed Consent Statement Not applicable.

Data Availability Statement Not applicable.

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