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Review Article

Allergic and environmental causes of asthma in children

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ABSTRACT

Estimates show that asthma is highly prevalent across the different communities, and recent reports showed that by 2015, 300 million patients will be affected by asthma, and projections show that additional 100 million individuals will furtherly be affected by 2025. Many factors can attribute to the development of asthma, including genetic, environmental, and allergic causes. They have essential roles in the pathogenesis and development of the condition. Exposure to the different environmental factors has been an area of research for a long time to identify the potential factors that can cause sensitization and asthma development, especially among children that are more exposed to these factors because of their physical structure and daily outdoor activities. In the present literature review, we aim to provide a thorough discussion about the allergic and environmental causes of asthma in children. Our evidence indicates that exposure to different environmental factors including indoor and outdoor pollutants can significantly increase the risk of asthma. Furthermore, maternal exposure to certain pollutants in the prenatal period was also reported to be significantly associated with developing asthma in children around the age of 5 years old. Exposure to these substances increases the inflammatory and airway reactions leading to the development of asthma. Accordingly, healthcare authorities should plan for adequate interventions to reduce the exposure to these compounds among children and reduce the risk of developing asthma and respiratory tract morbidities.

Keywords: Asthma, Etiology, Environmental, Allergy, Pollutants, Pediatrics, Children

INTRODUCTION

Estimates show that asthma is highly prevalent across the different communities, and recent reports showed that by 2015, 300 million patients will be affected by asthma, and projections show that additional 100 million individuals will furtherly be affected by 2025.[1] Western communities have the highest rates of asthma. However, evidence shows that the disease burdens most global communities. In western communities, the prevalence has been estimated to be around 10%. On the other hand, the prevalence of the condition is much lower in developing countries being <1%.[2]

As a result of the increasing trends of urbanization, evidence shows that the incidence of asthma is increasing. Many factors can attribute to the development of asthma, including genetic, environmental, and allergic causes, and both have essential roles in the pathogenesis and development of the condition. Exposure to the different environmental factors has been an area of research for a long time to identify the potential factors that can cause sensitization and asthma development, especially among children that are more exposed to these factors because of their physical structure and daily outdoor activities.[3-5] In the present literature review, we aim to provide a thorough discussion about the allergic and environmental causes of asthma in children.

LITERATURE REVIEW

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 10th of October 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, according to the database. To avoid missing poetential studies, a further manual search for papers was done through Google Scholar, while the reference lists of the initially included papers. All relevant papers were screened for useful information, with no limitations posed on date, language, age of participants, or publication type.

DISCUSSION

Many allergic and environmental factors can attribute to the development of pediatric asthma. These include both indoor and outdoor factors that have been variously confirmed among the various studies in the literature in this concern. Furthermore, evidence indicates the significance of certain prenatal factors that also aid the prognosis and trigger the pathology of asthma. These factors will be adequately discussed in the following paragraphs. Exposome representing external exposures have been significantly associated with the development and pathology of asthma, and therefore, the condition can be adequately managed by applying proper interventional approaches on patients at high risk for developing this condition. Mild respiratory infections and allergic sensitization are marked as synergistic and dependent risk factors in developing asthma in children. The presence of the microbiome significantly induces the development of asthma in early infancy, which can also be adequately prevented by applying environmental modifications. Early exposure to these elements in early childhood can significantly add to the development of innate immunity.[6] However, lost biodiversity in the human microbiome and reduced microbial exposure in the early life of the exposed children have been significantly associated with improved sanitation, urbanization, and vaccinations. On the other hand, evidence indicates that the development of these changes has adversely influenced the development of asthma and allergic sensitization.

Maternal transmission in utero initiates the development of the microbiome.[7] Developing atopy has been associated with gut microbiota during infancy. It should be noted that this process is associated with the process of colonization of certain strains of these microbes. In this context, a previous related investigation indicated that at 6 years of age, allergic sensitization was significantly predictable at the age of 1 month by the state of reduced diversity compared with the stool flora at this age.[8] On the other hand, another investigation demonstrated that the diversity of infantile gut microbiota is significantly inversely proportional to the increased risk of developing atopic sensitization.[9] Another investigation also demonstrated that the risk of allergic sensitization and wheezing was significantly correlated with colonization in the infantile gut with *Clostridia* species.[10] On the other hand, the authors of this investigation also demonstrated that reduced risk of allergy was significantly correlated with the colonization by other species including *Lactobacillus* and *Bacteriodes* species. The increased risk of asthma development has also been correlated with the status of airway colonization during childhood. The development of asthma at the age of five was reported to be significantly correlated with the colonization of the airways by *Streptococcus* species at the age of 2 months.[11] The same association was also reported with the colonization of *Mycobacterium catarrhalis*, *Haemophilus influenza*, and *S. pneumoniae* at the age of 1 month when no symptoms were observed on these children.[12] Reduced infantile colonization by *Bacteroides* and *Bifidobacterium* species was significantly associated with the administering of antibiotics during childhood.[13] Accordingly, adequate attention should be provided in these situations to reduce the significance and frequency of bacterial colonization by reducing the exposure to the different associated risk factors. Some of these factors include environmental exposure, medication administration, and nutrition. For instance, previous investigations have demonstrated the significance of certain environmental media on the development of bacterial colonization. Less asthma and atopy were significantly associated with children living in farms more than others that were not due to the increased microbial exposure in these environments.[14] Accordingly, the risk of developing asthma has been significantly inversely proportional to the increased microbial diversity.

Indoor and outdoor air quality can also lead to the development and exacerbation of asthma. It is widely known that most people are aware that outdoor air quality comprises major risk factors to the general health and can significantly predispose to the development of asthma. However, not many general populations are aware that indoor air pollution can also have a significant risk on the overall general health among the different communities. The increased use of consumer products and different materials, changing behaviors, and increasing urbanization rates have been associated with significant variations in indoor and outdoor qualities.[15] For instance,

several chemicals can aid in a significant reduction in indoor air quality and might include nitrogen oxides, O_3, carbon monoxide, volatile organic compounds, radon, fibers, and other biological agents, including the different microbiological species.[16] These factors can be influenced by their outdoor frequency, and/or the presence of an indoor resource.[15]

Children are mainly at increased risk of being exposed to these compounds due to their unique physical characteristics, and being characterized by spending more time indoors.[17,18] Different biological investigations have recently aimed at investigating the impact of the different environmental factors on the development of asthma and other allergic diseases. A previous review article by Kanchongkittiphon et al summarized evidence regarding the association between asthma development and exacerbation and the exposure to the different indoor pollutants and allergens.[19] For instance, asthma secondary to dust mite sensitization might develop as a result of exposure to indoor dust mites. This has been attributed to the presence of protease in the indoor dust mites, which acts by activating protease-activated receptor-2 leading to the significant release of the different inflammatory mediators (like interleukin-6 and 8) and triggering an innate immune response, which is done by activating the protease-activated receptor-2 within the airway epithelial cells.[20] The previous review by Kanchongkittiphon et al also demonstrated the impact of being exposed to the different chemical pollutants, like di(2-Ethylhexyl) phthalate, 2-ethyl-1-hexanol, and formaldehyde, on the development of asthma and its relation with airway inflammation in the pediatric population.[19] In the same context, another investigation by Patelarou et al also found that most of the currently present volatile organic compounds were found to have a significant risk on the development of asthma.[21] It has been reported that benzene, ethylbenzene, and toluene are associated with the highest risk of developing and exacerbating asthma in children. Schools and playgrounds also represent important sources for the different environmental and allergic causes that can predispose to wheezings and asthma development since children usually spend much time in these areas.

In classrooms, exposure to different substances was introduced in the literature, including pinene, formaldehyde, PM, and CO, which can significantly lead to the development of asthma in these children.[22] Further evidence also indicates that exposure to PM_{10} and high benzene were significantly associated with the development of nocturnal cough among school children.[22,23] Similar findings were also reported for the development of asthma when children were exposed to formaldehyde and $PM_{2.5}$, and volatile organic substances.[24] Accordingly, a previous investigation reported that the indoor air quality is different among the different schools based on the building characteristics of each, the exposure to the outdoor air pollutants, and the frequency of maintenance and cleaning.[22] In this context, some European studies showed that school children living in industrial regions developed more asthma-related symptoms than other children that lived in other areas, indicating the importance of exposure to air pollution among these children.[25,26] Molds within the school environment were also significantly associated with upper respiratory and asthma symptoms as wheezes and coughing.[27] On the other hand, a previous investigation by Cavaleiro Rufo indicated that lower sensitization rates were observed among children at schools with increased diversities.[28]

Evidence also indicates the increased ability of the different endocrine-disrupting compounds on the induction and progression of asthma. A previous investigation by Wang et al reported that these compounds might play role in the development of asthma through altering DNA methylation by inducing significant epigenetic changes.[29] It has been reported that they play an important role in inducing a state of airway hyperresponsiveness and inflammation, and regulating the immune response and increasing the risk of developing asthma and related symptoms. Stimulation of the airway C-fiber sensory nerve fibers was also reported to be a significant characteristic of these compounds, which can remarkably influence a transient receptor potential expression of the cation channels. This has been associated with the increased synthesis and release of neuropeptides at these nerve endings leading to the incidental increase in airway manifestations and symptoms like cough by increasing mucus secretion, airway irritation, and bronchoconstriction.[30,31] This has been furtherly indicated by previous investigations that confirmed the roles of these channels, indicating the essential roles that the autonomic nervous system plays in airway regulation and maintenance of the physiologic functions.[32,33] Exposure to bisphosphate A and phthalates has been correlated with the development of asthma. Previous investigations that were conducted in European countries indicated a significant association between the development of asthma and the in-house concentrations of these compounds.[34,35] Previous studies have also found a significant correlation between asthma allergic symptoms and the in-house concentration of benzyl butyl phthalate.[34] In children ≤12 years old, a previous meta-analysis demonstrated that the risk of asthma was significantly correlated with the presence and concentration of the different PVC surface materials.[36] On the other hand, an investigation by Donohue et al demonstrated that maternal exposure to bisphenol A during pregnancy was found to be in a significant inverse association with the development of asthma symptoms among children of the exposed mothers at 5 years of age.[37] On the other hand, at ages 3, 5, and 7 years old, the same authors reported that the different concentrations of the compound were positively associated with the development of asthma. This has been furtherly indicated in another investigation by Gascon et al. [38] that indicated that frequent maternal exposure to high-molecular-weight phthalates and bisphenol A was associated with a

significantly high risk of asthma development. Additional two studies also assessed the urinary concentrations of these compounds as significant biomarkers that can remarkably assess the development of asthma based on maternal exposure within the prenatal period.[39,40] There is no doubt that the exposure to these compounds within the external settings offers exposure to the increased concentration and more elevation in the risk of developing asthma and respiratory symptoms. Besides, evidence furtherly indicates that spending more frequent time outdoors significantly increases the risk of asthma among children. Urbanization also plays a major role and previous reviews have adequately discussed these issues. Further research is still needed to elaborate on the best interventions that should be applied to children at high risk of exposure and developing asthma.[5,14,41]

CONCLUSION

Our evidence indicates that exposure to different environmental factors including indoor and outdoor pollutants can significantly increase the risk of asthma. Furthermore, maternal exposure to certain pollutants in the prenatal period was also reported to be significantly associated with developing asthma in children around the age of 5 years old. Exposure to these substances increases the inflammatory and airway reactions leading to the development of asthma. Accordingly, healthcare authorities should plan for adequate interventions to reduce the exposure to these compounds among children and reduce the risk of developing asthma and respiratory tract morbidities.

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