Impact of Air Pollution on Allergic Rhinitis and Asthma: Consensus Statement by Indian Academy of Pediatrics

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ABSTRACT

Justification: Rising air pollution is an ever-growing threat to many human diseases. Poor air quality has been directly correlated with respiratory allergies with a disproportionate affection among the pediatric age group. A clear understanding of common air pollutants and their potential contribution in allergic rhinitis and asthma is lacking. **Objective:** To formulate a consensus statement for appropriate understanding among pediatricians and general practitioners about the effects of air pollution on respiratory allergies and their prevention. **Process:** A group of experts (Pediatric pulmonologists and allergy specialists) from across India were appointed by the Indian Academy of Pediatrics (IAP) to formulate a consensus statement on 'Allergy and Air pollution'. A virtual meeting was conducted on 6th April 2020 to discuss in detail regarding various issues related to the subject and a writing committee was formed with broad consensus. After extensive literature review and multiple virtual sessions, the current document was prepared and circulated via email to the representatives from central IAP and IAP environment chapter. All the experts approved the consensus with minor modifications after a detailed discussion on 29th September 2020 on a virtual platform. **Recommendations:** Air pollution is the emerging contributor to respiratory allergies due to various mechanisms including oxidative stress and compromised mucociliary clearance. Children are more vulnerable to both outdoor and indoor pollution, due to their unique physiological characteristics. Knowledge about pollutant particle size and air quality index will help in demarcating level and extent of airway involvement. Relevant environmental history in difficult allergic rhinitis and asthma cases, along with conventional pharmacological measures, is warranted. Multipronged approach, targeted at community, physician and individual levels, needs to be emphasized to improve air quality and reduce economic and psychological burden of respiratory allergies.

Keywords: *Air quality index, Allergy, Asthma, Pollution, Rhinitis.*

Increasing levels of air pollution and its impact on health has emerged as an area of immense concern across the world. Air pollution was found to be responsible for 16% of global deaths, of which 92% was in low- and middle-income countries (LMICs) [1]. There is ample evidence emerging on the role that poor air quality could adversely affect child health. Children remain a vulnerable group to the effects of air pollution due to their outdoor play activity, breathing higher concentration of pollutants, more mouth breathing behaviour, higher minute ventilation, an ineffective nasal filtering capacity, and an underdeveloped detoxification and antioxidant defence systems [2]. There is a simultaneous increase in the prevalence of respiratory allergies worldwide [3], with the prevalence of wheeze ranging from 7-20% and allergic rhinitis between 11-24% [4]. This increase correlated with demographic changes of the cities including urbanization, air pollution and environmental tobacco smoke [5]. Hence, a pediatrician needs to

be aware about the impact of air pollution on allergic rhinitis and asthma, the two most common chronic conditions that one addresses in daily clinical practice. By understanding the interaction between air quality and allergy, patient management can be improved with targeted preventive and therapeutic measures.

PROCESS

A group of experts (Pediatric pulmonologists and allergy specialists) from across India were appointed by the Indian Academy of Pediatrics (IAP) to formulate a consensus statement on 'Allergy and Air pollution'. A virtual meeting was conducted on 6th April 2020 to discuss in detail regarding various issues related to the subject and a writing committee was formed with broad consensus. After extensive literature review and multiple virtual sessions, the current document was prepared and circulated via email to the representatives from central IAP and IAP environment chapter. All the experts approved the consensus with minor modifications after a detailed discussion on 29th September 2020 on a virtual platform.

Terminology

Commonly used terms, which a pediatrician needs to know, in the context of air pollution and allergy are:

Allergen: An allergen is a protein component which produces an immunologically potent reaction in which the immune system perceives a threat in susceptible individuals, which otherwise is harmless to a majority of people. An allergen is responsible for initiating an allergic reaction.

Pollutant: Pollutants contaminate the environment and render the natural resources toxic or unsuitable for use when it crosses permissible limits. Air pollutants have been known to augment the allergenicity of certain pollens and fungal spores, but are directly non-immunogenic.

Irritant: An irritant is a substance, mainly chemical, which may cause injury to mucosal tissues even after a single exposure. Prolonged exposure may result in airway diseases like asthma or skin disorders like contact dermatitis/eczema.

Trigger: Trigger is a stimulus, which when comes in contact with the immune system, initiates a physiological exaggerated response, which can be a manifestation of a disease. Allergens, pollutants and irritants can be triggers of an allergic reaction.

Inducers: Inducers are agents which enable the complex interaction of a pollutant and the immunological mechanism. These may be (1) exogenous, either microbial (pathogen-associated molecular patterns, that function through dedicated receptors, and virulence factors) or non-microbial (allergens, irritants, toxic compounds) and (2) endogenous such as signals produced by stressed or damaged tissues [6].

Particulate matter (PM): It is a predominant air pollutant which is frequently used as a proxy indicator of air pollution. In urban areas, it includes dust, smoke, and liquid droplets emitted into the air mainly by vehicles, factories, and construction activities. Coarse particles are PM ≥2.5 microns (μm) to 10 μm

(PM10) in aerodynamic diameter, while fine particles are <2.5 μm (PM2.5). Ultrafine particles have sizes up to 100 nanometers (nm) (PM0.1). Collectively, the PM less than 10 μm are called respirable PM. Coarse particles get deposited in the upper airway, whereas fine and ultrafine PM can reach up to the alveoli.

Air Quality Index (AQI): This index has been developed for disseminating easy information about complex parameters of air quality as a single number. Calculation of AQI is usually computed from the concentration of six major pollutants – Ozone (O_3), PM, Nitric oxide (NO_2), Sulphur dioxide (SO_2), Carbon monoxide (CO) and Lead (Pb), Further data availability, averaging period, monitoring frequency and measurement methods are used**.** However, PM (PM10, PM2.5) used in AQI is the most commonly used marker of exposure to air pollution.

Sources of Air Pollution

Pollutants can be classified into household air pollution (HAP) or ambient air pollution (AAP), primary (if directly emitted into the atmosphere), or secondary (if these react or interact therein, e.g. ozone-O_3) based on their source and derivation. Table 1 enumerates various sources of air pollutants. The AQI derived from these pollutants is categorized as per their ill effects on human health. The Indian standards for 24-hr air quality is, however, relaxed when compared to United States Environmental Protection Agency (USEPA) or WHO standards because of underlying higher background pollution (i.e. is dust and natural sources) which poses a challenge to achieve USEPA air quality standards in a very short time [7]. An updated knowledge of AQI and its impact on health can help a clinician to provide quality care to his patients.

Pathophysiology

Exposure to air pollutants enhances the airway responsiveness to aeroallergens via several mechanisms as shown in **Fig. 1**. The pathophysiological mechanisms [12] include: 1) Traffic-related pollutants and global warming triggered pollen allergens release, 2) enhancement of antigenic properties of biological aerosols (e.g. plant-derived components and pollens) by air pollutants after adhering to their surface, 3) increased penetration of allergens and subsequent airway sensitization by the compromised mucociliary clearance, 4) transport of free allergens to lower airways after binding to particulate pollutants like smoke, dust, and diesel exhaust particles (DEP), 5) changes in the epithelial structure and microflora through oxidative stress and inflammatory reactions leading to allergic immune response, 6) co-localization of adjuvants and allergens on PM creating multivalent epitopes to cross-link several IgE receptors, and triggering an exaggerated IgE response, 7) chemical modification and oligomerization of allergens by reactive oxygen and nitrogen species (ROS/RNS), thus enhancing their immunogenicity with biological

aging, 8) epigenetic changes causing DNA methylation in the promoter region of immune effector genes by cigarette smoke.

How does air pollution affect asthma and allergic rhinitis?

In more than 27 studies, it has been shown that an acute increase in air pollution plays a significant role in asthma flare-ups [13,14]. Nearly 15% of flare-ups in asthmatic children were found to be attributed to TRAP (Traffic-related air pollution) [15], especially in those whose homes were close to roadways with a heavy truck density [16]. Hence, children exposed to higher levels of NO_2, Ozone, PM 2.5 and PM 10 for a longer duration have lower lung function and lung growth [17]. With increased life expectancy, they might unmask asthma in the future and also have the potential of developing chronic obstructive pulmonary disease (COPD) [18]. Furthermore, prenatal exposure to NO_2, SO_2, PM 2.5, and PM 10 can affect the lung growth in a foetus, which can be associated with an increased risk of asthma in childhood.

Other contributing factors include exposure to mosquito coil, incense sticks and environmental tobacco smoke (ETS). Burning of one mosquito coil produces as much PM 2.5 as 100 cigarettes and as much hydrocarbon as 50 cigarettes [19]. Incense sticks burning produces polyaromatic hydrocarbons, benzene, carbon monoxide and PM 2.5. In a study in Cardiff during Easter , the pollution inside a church due to incense burning showed a marked increase in ultrafine PM, PM2.5 and PM 10. The oxidative stress was 25-30 times higher than that of cigarette smoking [20]. Exposure to cigarette smoke can trigger asthma symptoms, can lead to a flare up and even affect a prenatal fetus. Prevalence of infant passive smoking is 10% in Sweden, 60% in Greece, 40% in USA and 50-70% in South East Asia. Second hand smoke (SHS) is as detrimental to health as active smoking. It contains more than 4000 chemicals, of which 250 are harmful. In addition, there is a strong correlation with childhood obesity, asthma and ambient air pollution [21]. Higher exposure to early life TRAP increased the rate of change of childhood BMI [22], a known co-morbidity of difficult to control asthma in children.

Many epidemiological and clinical trials reveal that patients with Allergic Rhinitis, when exposed to pollutants, have worsening of their symptoms [23]. In a randomised controlled trial involving 253 adults with seasonal allergic rhinitis (SAR) to ragweed pollen, it was observed that controlled exposure to DEP and ragweed pollen in a special exposure unit, significantly increased SAR symptoms compared to ragweed exposure alone. This effect persisted beyond the end of the DEP + pollen exposure period [24].

CONSENSUS STATEMENT

Evaluation of Impact of Air Pollution in a Child

A pediatrician must take a detailed environmental history (Box 1) in every child with asthma or allergic rhinitis during the initial contact. Investigations are needed in select situations and currently documented in research settings only. Measures of inflammation like Fractional Excretion of Nitric Oxide (FENO) or

functional assessment with spirometry or Impulse Oscillometry (IOS) should be monitored [25]. Airway FENO level is a surrogate marker of eosinophilic inflammation and corticosteroid sensitivity in bronchial asthma [26]. It was found that annual increase in PM2.5, PM 10 and NO2 level were associated with significantly higher FENO level [27]. The impact of air pollution on lung function testing needs more evidence to establish correlation. Measurements of metabolites of polycyclic aromatic hydrocarbons (PAH) and cotinine/creatinine ratio in urine may guide to the amount of air pollution and second hand smoke exposure [28].

Prevention and Counselling

A multipronged strategy should be applied at various levels of the healthcare infrastructure to prevent the effects of air pollution on children. Medical organisations need to make efforts in the field of research and publication to disseminate knowledge among healthcare professionals, colleagues, students and the community on air pollution and its effects. Pediatricians must counsel and advice caregivers about various measures which can be utilised to prevent the effects of air pollution on child health.

Measures to Reduce Outdoor Air Pollution and/or Its Effects

Face mask: For the community at large, wearing any mask is recommended when the AQI score exceeds 200 or at PM2.5 concentrations of 150 mcg/m^3 and above [36]. Although, N95 mask is most effective for filtering PM2.5 particles, a reusable 3-layer cotton cloth mask can suffice for many children.

Clean fuels for vehicles: Encourage use of newer and lesser polluting fuels, with less exposure to diesel fumes [29]. Electric vehicles can be a welcome initiative.

Restriction of outdoor activities: Advice to keep children indoors when AQI is poor or pollen count is high [30].

Measures to Reduce Indoor Air Pollution

Reduce molds, dust and dust mites concentration: This can be achieved by washing bedding on weekly intervals using hot water at 54^{O}C or by employing commercially available mite-proof bedding. Feather dusters disperse dust and allergens and thus should be avoided. Moist cloth should be preferred over dry ones for wiping dirt [31]. Vacuum cleaners should be sealed tightly to avoid a dust leak. Cleaning products with a high composition of volatile organic compounds (VOC), scents, or odours should be avoided.

Home ventilation and use of air purifiers: An air purifier can be used in cases where significantly poor air quality is documented. To help choose an air purifier, the patient can be advised to choose one with a Clear Air Delivery Rate (CADR) of more than 600, and with a Minimum Efficiency Reporting Value (MERV) of the High Efficiency Particulate Air (HEPA) filter more than 14. One must however replace and clean filters periodically and install the machine away from walls or furniture.

Cooking fuels: Use of clean fuels for cooking like LPG should be encouraged at home. Biomass fuels and stoves should be avoided.

Cessation of smoking (both active and passive): Exposure to ETS should be reduced in all forms. Public health measures like bans on smoking in public places and media education campaign on benefits of cessation are useful [32].

Cessation of use of mosquito coils, agarbatti and dhup sticks in households [33].

Furniture with pressed wood need to be avoided: These types of furniture can emit high levels of VOC, formaldehyde and carbamide (urea) [34]. Formaldehyde is commonly used to bond the adhesives in pressed wood products. It is a hazardous pollutant that can pose a serious threat to health if exposed for a long period of time. The rate at which formaldehyde is released into the air is accelerated by heat and humidity, so avoid placing new pieces of furniture over or near a heat source.

Renovation and painting of the house needs to be done during a holiday break when children are out of home.

Selecting a school or building a new house needs to be considered very carefully so that it is at least 100 meter away from the main road.

Measure to Build Lung Capacity

Yoga and relaxation therapy: These have been found to increase the peak expiratory flow rate in children as well as improve the lung function and quality of life in adults.

Exercise and other physical activities: Regular aerobic activity has the potential to improve lung capacity and reduce bronchial hyper responsiveness

Management of Asthma and Allergic Rhinitis in the Presence of Pollution

Although the principles of management in children with asthma and allergic rhinitis remain the same, focus needs to be laid on exposure to air pollution as a trigger of flare-ups and cause for poorly controlled symptoms. In addition to avoidance of exposure of pollutants on high pollution days, asthma flare-ups can be prevented by using maintenance dose of inhaled corticosteroid therapy (ICS) on a regular basis [35]. Studies suggest that this approach has shown to decrease an adverse response to pollutant exposure [36]. Some additional measures like use of reliever medication or stepping up of ICS for few days during poor air quality monitored by AQI and pollen calendar is advisable, although there are limited studies to support this. Stepping down of ICS and outdoor activities should be discouraged on days with a high AQI or high pollen count.

Management of allergic rhinitis with intranasal corticosteroids (INCS) and antihistamines should be based on the severity of symptoms and treatment should be continued on days of poor air quality as per the AQI. Despite recent discoveries on mechanistic biomarkers and signal pathways of cellular oxidative stress injury secondary to pollutant exposure, efficacy studies on pharmacological therapy of AR patients

exposed to specific pollutants is currently lacking [37]. In adults, fexofenadine demonstrated efficacy and a well-tolerated safety profile in ragweed AR patients exposed to ragweed associated to Diesel Exhaust Particles (DEP) in an environmental exposure unit. There was improved nasal symptom scores following ragweed plus DEP exposure when pre-treated with fexofenadine compared to the placebo group [38,39]. However, paediatric focused clinical studies are needed to address the need of managing allergies caused or aggravated by air pollution. In children with poorly controlled asthma or allergic rhinitis despite high doses of conventional medication, the contribution of air pollution needs to be considered and evaluated in detail.

CONCLUSION

Air pollution has a significant impact on respiratory allergies in children through various mechanisms. Physicians managing children with allergic rhinitis and/or asthma regularly need to be well versed with the pathophysiology, evaluation and management, and be able to suggest targeted preventive measures. More research in pediatric patients is needed to enhance our knowledge and practices in this field. A detailed document is available for those who wish to gain more evidence based knowledge in the impact of air pollution on allergic rhinitis and asthma at Indian Academy of Pediatrics (IAP) website (*www.iapindia.org*).

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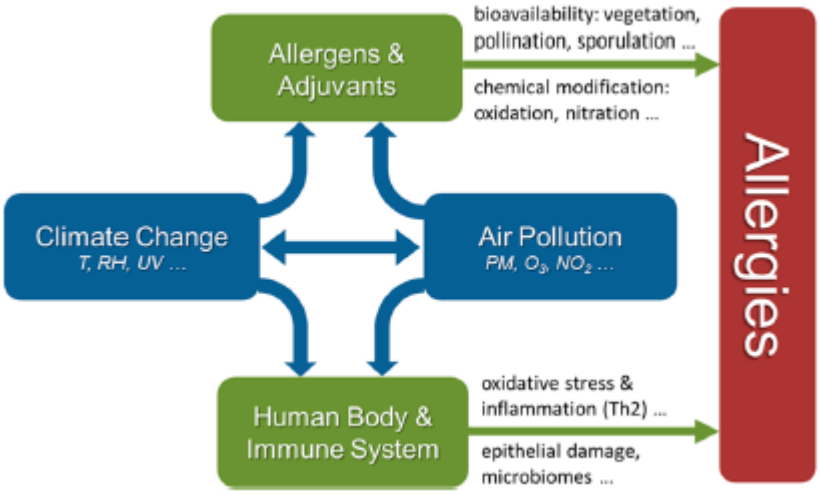
Table I Types of Air Pollution and Their Sources

Ambient air pollution (AAP)	
Pollutants	Sources
Particle matter(especially PM 2.5, PM 10, ultrafine PM)	Fuel combustion (vehicles, factories, residential heating, dust and construction)
Ground level Ozone	Fuel combustion, chemical reaction between oxides of nitrogen and Volatile organic compounds (VOCs) emitted from natural sources and/or due to human activities.
Carbon monoxide	Vehicles, combustion of wood, fossil fuels
Nitrogen oxides (NO, NO3)	
Sulphur oxides	Fuel or industrial combustion.
Lead & Mercury	Industrial activity, coal burning, diesel batteries, radiators, waste incinerators, metals, ore, Industries, Thermometers
Polycyclic Aromatic hydrocarbons (PAC)	forest fires, incineration, and engines, coal and tar residue
Household Air Pollution (HAP)	
PM, CO, NO2	Fuel combustion(cooking, incense, candle and mosquito repellent coil burning) and human bioactivity
Second hand tobacco smoke	Smokers
Pesticides, Solvents, Benzene & VOC	Paints, floor finishes, furniture, polyurethane foam
Allergens	Allergens from furred pets, dust mites, cockroaches, rodents and molds.
Building related	
-radon	Rock formation underneath buildings
-asbestos	

Prepared using information from references [8, 9, 10,11]



*Reproduced with permission (11)*Abbreviations: UV- Ultraviolet, PM- Particulate matter, O3- Ozone, NO2- Nitrous oxide, Th2- Type 2 Helper cells, T- Temperature, RH- Relative Humidity

Fig. 1 Pathophysiology of the interplay of air pollution and allergies

Box 1 Evaluation by Environmental History – Questions to be asked by a Pediatrician

Indoor Home Environment

- Does the home have a separate kitchen? What fuel is used for cooking?
- Is there any smoker at home?
- Do you use mosquito coil, agarbatti or insecticide spray?
- Was there any recent renovations at home, civil work, painting or wood work? What is the type of wood used?

Home Surroundings

- How far is the home located from main road?
- Is there any construction work near home?
- Any garbage dump, weeds or farm fields with post-harvest burning
- Are there any industries or mills close to home?
- Does the child have aggravation of symptoms during Diwali or Holi?

School related

- How does the child travel to school?
- How far is the school located from main road?
- Is there any construction work near school or any renovations in school?