

# Environmental Toxicants and Allergic Disorder

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**Abstract:** Air pollution affecting the quality of life worldwide has been accelerating in recent decades and is widely regarded as a threat to both public health and economic progress. The relationship between air pollution and the development and severity of asthma and other allergic diseases has been proved by epidemiological studies. Allergic disease in India is on an uprising trend, both in outbreak and severity. Approximate 20-30% population suffers from allergic diseases. There are 37.5 million cases of Asthma in India, with 40-50% being pediatric allergic disease cases. The main objective of this work is to study the various environmental factors that impact the manifestation and course of allergic diseases, i.e., asthma, allergic rhinitis, atopic dermatitis. The main emphasis has been paid to particulate matter (PM), gaseous materials such as ozone (O<sub>3</sub>), sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>) as well as Heavy Metals and pollutants generated by vehicular traffic and industry. Controlled urbanization, and scientific industrialization is urgent call to reduce this burden. The creation of awareness with reduced exposure to biomass and fossil fuels may pave the way to eradicate this burning problem.

**Keywords:** environment; toxin; atopic dermatitis; contact allergy; Asthma; allergic rhinitis.

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## 1. Introduction

Allergic reactions refer to abnormal adaptive immune responses associated with a hypersensitivity reaction, including hay fever, asthma, systematic anaphylaxis, or contact dermatitis. Allergic hypersensitivity may be categorized as IgE-mediated and not mediated by IgE. Here IgE mediated allergic inflammations their consequences, development; characteristics have been given priority. Production of IgE antibodies in response to even low doses of allergens, with atopy with a familial tendency, is affiliated to IgE-mediated mechanism that yields for development of typical syndromes, such as rhinoconjunctivitis, or eczema/dermatitis, asthma, etc. [1].

Allergic (atopic) diseases result from the interaction between individual genetic reciprocity outpouring and environmental factors. Environmental factors, in summation with a genetic tendency of a patient, may subscribe to the development of extrinsic forms of atopic dermatitis or asthma, which are associated with sensitization to environmental factors and the appearance of antigen-specific serum IgE. Contact allergy may be affected by genetically determined alterations in the production of pro- and anti-inflammatory cytokines [2-6].

Allergen non-infectious environmental substance that most commonly induces hypersensitivity type- 1 reaction. Conventional sources of allergens comprised of grass and tree pollens, dander of animal (aberration from skin and fur), house-dust-mite fecal particles, insect toxins, latex, certain foods (notably tree nuts, peanuts, fish, shellfish, milk and eggs, etc.), and some medicines [7].

A toxin is a chemical or a set of chemicals that may set on injury or cause an unwarranted risk of injury to those exposed to it. For instance, DEHP (diethyl hexyl phthalate) at the high concentration present in indoor dust is responsible for wheezing among preschool children. Heavy metals like Lead(Pb), cadmium(Cd), mercury(Hg), aluminum (Al), arsenic(As) are found in the air, drinking water, food, and other products, and their exposure act as environmental toxins. Nitrogen dioxide (NO<sub>2</sub>) and ozone (O<sub>3</sub>), like gaseous substances and particulate matter (PM), generated by car traffic and industry, also have a toxic effect in a generation to allergic disorders [8,9].

Urbanized air pollution has been a great concern for the last few decades as an important external, environmental causative agent. This review focus mainly paid on particulate matter (PM), Diesel exhaust particulate (DEP), and gaseous materials, such as ozone (O<sub>3</sub>) and nitrogen dioxide (NO<sub>2</sub>)[10], as causative agents of allergic disorders.

## **2. Role of Environmental Pollutants on Allergic Disorder**

### *2.1. Role of air pollutants.*

Epidemiological studies show a strong alliance between air pollution and the development and nourishment of asthma and other allergic diseases.

It has been revealed by experiments with an animal that hypersensitivity –mediated by IgE to ovalbumin proclaim more efficiently when the animals were illuminated together with diesel exhaust particles (DEP) or O<sub>3</sub> [11]. It is appraised that modifying the epithelium by air pollutants may escalate allergic reactions by influencing immunity and elevating the allergenicity. Recent literature data show that pollutants and allergens are operable not only additively but may also aggravate allergic reactions [12].

#### *2.1.1. Effect of ozone.*

O<sub>3</sub>, the ‘summer smog’ being the main stuff of photochemical oxidants and might share up to 90% of total oxidant levels, and inhaled O<sub>3</sub> at the rate of 60% is absorbed within the upper airways the residual within the lower part of the respiratory tract. In the case of both adults and children, respiratory morbidity increased additively with increased air levels of O<sub>3</sub> and NO<sub>2</sub>, resulting in more hospital admissions [13].

##### *2.1.1.1. Effect of ozone on asthma.*

Asthma is a long-standing disease of the lungs characterized by narrowing and inflammable airways, and it gets too hard to breathe. The degranulation of mast cells triggers it by releasing mediator reactions that develop in the lower respiratory tract. The bronchial smooth muscles contraction turns out to be bronchoconstriction. Airways edema, mucus secretion, and inflammation contribute to airway obstruction. Airborne and blood-borne allergens, such as pollens, dust, fumes, insect product, or viral antigens, trigger an asthmatics attack.

People with asthma may be more rigorously affected by ozone than those without asthma and be more reactionary or sensitive to ozone and therefore perceive changes in lung function and respiratory symptoms. Emergency hospitalization in the USA against asthma was more repeating for days when ozone concentrations were high (generally above 110 ppb as a 1-hour average of 60 ppb as a 7-hour average) compared to days with low ozone concentrations. Similarly, admissions for asthma in some places were higher when ozone levels were squatted, with effects generally being larger in the warm season than the cold season [12].

The epidemiological experiment of ozone exposures in human volunteers in a controlled way where markers of asthma status were measured after clean air and after ozone exposures shows that ozone worsens airway inflammation, increase the airway response to an inhaled allergen, and also elevate nonspecific airway responsiveness, each of which is likely to indicate worsening asthma.

In variant studies, it has been found that there is a greater inflow in polymorphonuclear leukocytes (PMNs) in people having asthma exposed to ozone and larger changes in other markers of airway inflammation in comparison to individuals without asthma. Another study reflects that the counts of eosinophils increased by ozone in the bronchoalveolar lavage (BAL) fluid of individuals having asthma; on the other hand, zero eosinophils in the BAL of individuals without asthma [12,13].

#### *2.1.1.2. Effect of ozone on Atopic dermatitis (AD).*

Atopic dermatitis: (Allergic eczema) is an inflammatory disease of skin frequently associated with a family history of atopy, observed most frequently in young children. Serum IgE level remains elevated. The individual develops skin eruption that is erythematous and filled with pus. AD have Th2 cells and eosinophils in increased number at the affected site. Various cytokines, including IL-3, IL-5 contribute to the growth of eosinophils. Strong soaps and detergents, skincare products, makeup Pollen and mold, Animal dander, Perfumes, and fabrics, like wool or scratchy materials, are the strong environmental factors that fire atopic dermatitis.

Atopic dermatitis (AD) is an inflammatory skin disease that colonized *Staphylococcus aureus* (*S. aureus*) and impaired immune imbalance. Recent research shows that topical ozone therapy may effectively treat multiple skin diseases, including AD, as an alternative treatment. However, the pathway of action is not well established [14].

#### *2.1.1.3. Effect of Ozone on allergic rhinitis.*

O<sub>3</sub> is the most detrimental air pollutant that acts as a threat to ecosystems and humanity. Oxides of nitrogen and other Volatile organic compounds (VOCs) of automobile exhaust produced ground-level ozone [15], B.J. Kim *et al.* proved through a survey conducted in 1743 school children selected from metropolitan cities and industrial areas during 2 years by using a geometric information system with the 5-year mean concentration of air pollutants that there is an ecological association of allergic rhinitis, asthma, and atopic dermatitis and ambient O<sub>3</sub>; as a result, a total of 1,340 children (male: female ratio, 51.4:48.6) with a mean (SD) age of 6.84 (0.51) years were taken in the analysis. Each child underwent allergy evaluation at the time of enrolment and a 2-year follow-up. After 2 years, the appearance of wheezing was decreased significantly, whereas the outbreak of allergic rhinitis showed a considerable increase in the lifetime. Children are residing in industrial areas found to be more inclined to

allergic rhinitis combined with ozone. Thus ozone exposure was coupled with current wheeze and allergic rhinitis [16].

### 2.1.2. Particulate matter.

#### 2.1.2.1. *Effect of Particulate matter on asthma.*

Particulate matter (PM) is a heterogeneous amalgamation of small particles and liquid droplets suspended in the air. Depending on size, it is of three types a) Coarse PM (diameter, 2.5–10  $\mu\text{m}$ ) b) Fine ( $\leq 2.5 \mu\text{m}$ ),c) and ultrafine ( $\leq 0.1 \mu\text{m}$ ), obtained from road dust, abraded soil, construction debris. In urban areas, Diesel exhaust and Combustion of fossil fuel products are the major source of particulate matter (PM). Particle matter of 2.5  $\mu\text{m}$ (PM<sub>2.5</sub>), diesel particles, and sand dust bring about pulmonary inflammation, especially allergic asthma. PM enters the lungs through the nose and throat and has an adverse effect on another organ. As per San-Nan Yang *et al.*, exposure to PM<sub>2.5</sub> may be more toxic to exhort allergic asthma and also responsible for the deterioration of lung function. PM from fossil fuel combustion can set on oxidative stress commenced by reactive oxygen species (ROS) that turn to airway inflammation. Adjuvant effects are shown by several particulates like polystyrene particles, crystalline silica, and carbon nanotubes. Humoral immune responses can selectively be stimulated by aluminum especially through Th2 immune responses, featured by the IL-4 and IL-5 production and the induction of IgE and IgG1[16-18].

#### 2.1.2.2. *Effect of Particulate matter on acute rhinitis.*

Several studies show no consistent correlation between acute rhinitis and exposure to PM<sub>2.5</sub>. Meta-analysis of birth cohorts found no increased risk for AR from exposure to PM<sub>2.5</sub>. Asian birth cohorts published data reflect that long-term exposure and the onset of AR are scarce. Asian studies during 2000-2018 established that PM could not induce AR. Hence it may be concluded as an inconsistent relationship between Acute Rhinitis and PM[14, 18].

#### 2.1.2.3. *Effect of particulate matter on atopic dermatitis.*

As per Young- Min Kim *et al.* effects of particulate matter (PM) on AD symptoms by weather type were investigated for 17 months between August 2013 and December 2014. It has been viewed that among the 7 types of weather PM<sub>2.5</sub> and PM<sub>10</sub> caused the development of AD symptoms significantly in dry moderate (DM) days, but insignificant to the other weather types[19].

### 2.1.3. Effect of Diesel exhaust particles.

Up to 90% of the airborne PM is contributed by Diesel exhaust particulate (DEP), which is liable for respiratory changes, fatigue, nausea, disturbances of lung functions, etc. Prolonged exploration of DEP yields chronic cough, sputum production, and decline in lung function. According to published data DEP have both adjuvant activity and enhancing effects. Adjuvant activity means sensitization against common allergens, and enhancement means the development of allergic symptoms in the sensitized patient. DEP is small enough to invade deep into the respiratory tract and elapsed allergic symptoms. 30% of inhaled DEP can be deposited in the alveolar region, and a large proportion is phagocytized by alveolar macrophages [Table 1] [20,21].

It is epidemically proven that childhood exposure to diesel exhaust (DEP) generates allergies. Mice with open exposure to (DEP) were hypersensitive to ovalbumin (OVA), reported by airways inflammation with elevated serum OVA-specific IgE levels, and increased pulmonary and systemic Th2 and type 17 helper T cell (Th17) cytokine levels[22,23].

#### 2.1.3.1. Effect of Diesel exhaust particles on allergic rhinitis.

DEP worked through reactive oxygen species-mediated pathways and increased permeability of nasal epithelial cells. This may promote allergen delivery into subepithelial tissues subscribed to the intensity of immediate allergic responses[24].

#### 2.1.4. Effect of NO<sub>2</sub>.

An oxidant gas, nitrogen dioxide (NO<sub>2</sub>), contaminates both outdoor and indoor air is a potential risk factor for asthma.

A cohort study carried out by Masayuki Shima *et al.* on 842 school children in Japan found that outbreaks of wheeze, bronchitis, and asthma enhanced significantly with increases of indoor NO<sub>2</sub> concentrations among girls, but no effect among boys. The asthma episode increased among children living in areas with outdoor NO<sub>2</sub> concentrations high. It suggests outdoor NO<sub>2</sub> may be important for onset asthma, particularly among children, and girls are affected with respiratory syndrome by the influence of Indoor NO<sub>2</sub> concentrations [25].

#### 2.1.5. Effect of sulfur dioxide.

A case-control study on Residents of Macassar, South Africa, was made by Roslynn Baatjies *et al.* where residents exposed to sulfur dioxide vapors (SO<sub>2</sub>) arose from an ignited sulfur stockpile, which produced hourly SO<sub>2</sub> levels of 20–200 ppm and the risk factors related to persistent lower respiratory symptoms (LRS) or asthma even six years later acute exposure to high SO<sub>2</sub> levels was measured. The previous history of pulmonary tuberculosis (PTB) collaborated with persistent LRS/asthma was found more chest tightness during the incident[26,27].

Hence, individuals persisted in LRS/asthma even six years after acute SO<sub>2</sub> exposure; initial chest tightness and a previous history of PTB at peak exposure were strong indicators of persistent LRS/asthma [26].

A PubMed search also observed during 2014 that airway epithelial cell function affected by SO<sub>2</sub> and SO<sub>2</sub>-associated amplification of allergic inflammation leading to asthma exacerbations and airway dysfunction[28].

#### 2.1.6. Effect of EDCs (Endocrine Disrupting Chemicals).

EDCs found in the air, water, and the soil, and many came into the picture since World War- II are ubiquitous in the environment and have unwitting effects on human health, piercing the inflammatory response via aryl hydrocarbon receptors are reported as potential modulators of the immune system and allergic responses in allergic disease. Indoor dust consists of diethyl hexyl phthalate (DEHP) accompanied with wheezing in preschool children. Other ubiquitous like p-octylphenol, alkylphenol, induce strong Th2 polarization via suppression of type 1 helper T cell (Th1) and enhancement of Th2 immune responses, respectively [29,30].

2.1.6.1. Effect of NP( Nonylphenol).

Nonylphenol is structurally similar to 17β-estradiol is one of the common EDCs developed relatively more severe OVA-induced allergic lung inflammation. NP augments the expression of TNF-α and suppresses IL-10 production in a range of physiological doses, accompanied by activation of the MKK3/6-p38 signaling pathway. This raises allergic inflammation in the lung as a murine model of Asthma (Table 1) [31].

**Table 1.** Possible mechanisms of the effects of environmental toxins on allergic inflammation.

Environmental Toxin	Effects on allergic inflammation
Alkyl Phenol	Suppress the Th1 immune response. Augments the Th2 response. Increases TNF-α in DC. Decreases IL-10, INF-α and INF- β.
Nonylphenol	Th2-skewing of DC Increases IL-6, and TNF-α expression in DC Decreases IFN-γ expression in T cell
Phthalate/DEHP	Enhances Th2 differentiation Increases Th2 cytokines Increases IgE Decreases IFN-α and IFN-β expression in DC
Tobacco Smoke	Increases IgE Sensitization, Decreases IFN-γ expression Decreases NK Cell activity Increases IL-4 & IL-5.
Heavy Metal Lead	Decrease INF-γ expression
Mercuric Chloride	Increases IgE production, Increases IL-4 expression, Increases IgE-dependent mediators in basophil.
Diesel Exhaust Particle	Increases IgE production Increases Th2/Th17 cytokine levels.
Pesticides	Interferes with Th1/Th2 balance.

2.1.7. Effect of phthalates.

Phthalates are broadly used in manufacture in plastic, insect repellent, synthetic fiber, lubricant, phthalic paint and varnishes, adhesive, air freshener easily contaminant indoor air. Wheezing in preschool children is caused by diethyl hexyl phthalate (DEHP) present in indoor dust. Phthalates are compounds that make plastics more flexible reported to be associated with rhinitis, eczema, and asthma. DEHP is present in all PVC products. According to a cohort study, exposition to PVC flooring during pregnancy caused to be a critical factor for the onset of asthma in children. DEHP can suppress CpG-induced IFN-α/ IFN-β expression. Suppression of the histone H3K4 trimethylation at the IRF7 gene promoter region, compressed the CpG-induced interferon regulatory factor (IRF)-7 expression, via DEHP can, translocation of H3K4-specific trimethyltransferase considered to be the best pathway of its action. DEHP also suppresses IFN-γ while enhancing IL-13 production by CD4+ T cells (Table 1) [32].]

2.1.8. Effect of Tobacco smoke.

Almost every organ in the body of a smoker's effect by harmful chemicals contains in Cigarette smoke. Tobacco smoke is one of the indoor air pollutants that cause higher allergy and asthma rates. Passive cigarette smoke induces asthma and wheezing in children and young people by at least 20%. The risk of IgE sensitization is increased by tobacco smoke. The inferential mechanism of Tobacco smoke is to diminish the Th1 response by suppressing IFN-γ production and activity of a natural killer cell. Still, it exaggerates the Th2 response by increasing production of IL-4, IL-5, and other pro-inflammatory cytokines that result in growing allergic responses [33].

2.1.9. Effect of molds.

According to Targonski *et al.*, asthma deaths in Chicago increased two-fold when the concentration of *Alternaria* molds was higher than 1000 spores per cubic meter.

*Penicillium* and *Alternaria* are Outdoor molds, and *Cladosporium* indoor dust are risk factors for the development of AR [34,35]; epidemiological informatics also proclaimed the cause-and-effect relationship between molds and development and exacerbation of asthma in children, and AR, respectively [36].

## 2.2. Role of water pollutants.

Pesticides' main water pollutants of agricultural origin come through runoff from the agricultural field and industrial wastewater in the water body, posing a health risk to humans.

### 2.2.1. Effect of pesticides.

Pesticides are meant to control pests and to monitor pest-related diseases in agriculture, forestry, fishery, also applicable in the food industry. Infiltration of pesticides through agril products to utero reported being high risk for asthma in childhood. There has been evidence of strong alignment between occupational exposure to pesticides and asthma, especially in the field of agriculture. During pregnancy, if the fetus is exposed to certain pesticides, hay fever and allergies are found in the offspring, and especially male offspring (Table 1) [37,38].

#### 2.2.1.1. Organophosphorus pesticide toxicity.

Childhood asthma is found to be more common in early life, coming in contact with organophosphorus pesticides (OP). Airway hyperreactivity and bronchospasm prevails in the general population as respiratory dysfunction in cases where OP is associated with occupational compulsion. OPs induce airway hyperactivity by blocking autoinhibitory M2 muscarinic receptors present on parasympathetic nerves that innervate airway smooth muscle [39,40].

### 2.2.2. Effect of heavy metals.

Heavy metals in surface water are a global environmental crisis derived from natural and anthropogenic sources. Metal mining, smelting, use of fertilizer, sewage discharge are the prime anthropogenic source of surface water pollution. Bedrock weathering as a natural source enters into agril input through irrigation paves the way of entry for heavy metals in the food chain, thus cave health hazards. Exposure at the Prenatal and early postnatal stages to heavy metals, such as mercury and lead thought to be skewed immune responses. Th2 bias and elevated production of IgE or Th2-related cytokines were reported as the way to immune response.

#### 2.2.2.1. Effect of lead.

Lead caused in mice to promote a Th2 reaction and suppresses IFN- $\gamma$  expression[41].

#### 2.2.2.2. Effect of mercury.

Mercuric chloride conduces increases IL-4 levels and a higher IgE production. According to Chih-Hsing Hung, MD, Ph.D., Department of Paediatrics, the increased probability of wheezing at 24 months old is related significantly to ambient vanadium and nickel concentrations. Heavy metals out of Heavy traffic like Cd, Cr, Fe, and Mn also correlated

with coughing. Interferon- $\gamma$  (IFN- $\gamma$ ) expression Inhibition suppresses Th1 development and promotes Th2 development by augmenting interleukin 4 expressions, increasing IgE, and IgE-dependent basophil-mediated inflammation is the possible mechanism through which heavy metal works.[42,43]. Exposure to heavy metals at the prenatal stage may affect the development of asthma and allergic diseases in childhood [44,45]. The maternal serum concentration of lead (Pb), cadmium (Cd), and manganese have a detrimental effect on Asthma and allergy.

#### *2.2.2.3. Effect of nickel.*

Nickel used in costume jewelry, coins, mobile phone, and orthodontic materials is ubiquitous, exposed to a considerable amount leads to asthma and causes contact dermatitis, hypersensitivity, cytotoxicity, and DNA damage [46]. Nickel is the most affluent factor of metal allergy. Items containing nickel and long-term use of it with direct contact to the skin lead to corrosion by sweating. Being absorbed as nickel ions induce an allergenic effect thus, sensitized persons evolve contact dermatitis. After penetration, Ni active epithelial cells produce chemokines and cytokines. T cell being activated duplicate themselves and reaches “threshold” value after 48–72 hrs and develops a rash that can exacerbate as acute[47].

### **3. India and Allergic Disorders**

Allergy and allergic disorders are manifested through a complex interaction between environmental, genetic, and multiple lifestyle factors. Our India enriched with 1.3 billion populations, i.e., 1/5<sup>th</sup> of the global population having a great diversity in terms of socioeconomic strata, environment, types of infections, diet, culture, aero-biology, etc., opens the fields of epidemiological studies on allergic disease.

Published literature in this respect comes from high-income English-speaking countries, which differ widely from low-middle income countries such as India as there prevail fundamental differences in environmental, genetic, and lifestyle factors [48-51].

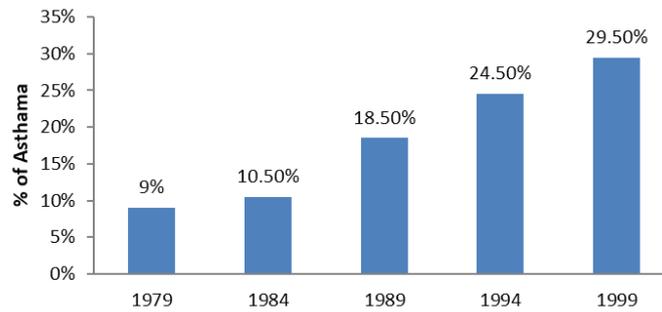
#### *3.1. Asthma.*

In 2016 around 37.9 million asthma cases were estimated globally, but cases of Asthma in India were 2.4-fold higher. Second round Indian Human Development Survey (IHDS-II) in 2011–12 involving all states and union territories excluding Andaman and Nicobar Islands and Lakshadweep shows that overall outbreak of asthma increased from 41.9/1000 to 54.9/1000 population between 2004–5 and 2011-12 and also unlock that manifestation higher in poorer Indian states, Northern states but low rates in North-Eastern states. It also reveals that asthma was estimated significantly higher with lower literacy, homes using unclean fuels, i.e., population with the lower socioeconomic background. Firewood, kerosene, and cow dung are used by 80%, 78%, and 52%, respectively, as fuels out of an estimated 65 million cases. It could be avoidable if firewood and kerosene/cow dung is not being used.

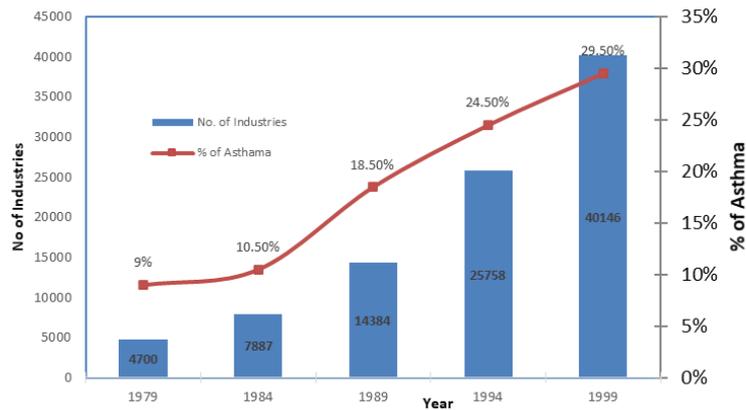
Study on Asthma in Children by International Study of Allergy and Asthma in Children (ISAAC) evaluated that India has a relatively lower outbreak in comparison to high-income English-speaking countries. In India, children of age group 6–7 years and 13–14 years were found to have asthma symptoms 3.5% and 4.5%, respectively. The asthma symptom in the older age group was 6.0% overall for wheeze, 9.5% for “wheeze on exertion”, and 14% for nocturnal cough, whereas the capital city of Chandigarh, in Punjab state, shows having lower

rate at 3.5% for asthma, 4.2% for wheeze, and 8% for “exertional wheeze” and nocturnal cough in the age group 13–14 years [52-58].

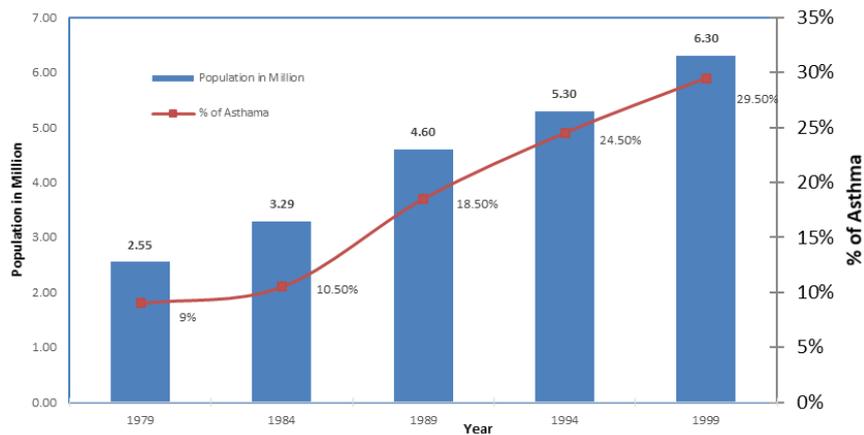
A study on under 18yrs children, in 2 decades, since 1979-1999 in India reveals the effect of industrialization, increased population by migration of rural peoples, and increased automobiles as follows: a) Increased prevalence of asthma as passing through years (Figure 1); b) Rising industrialization shows a clear depiction of an increased outbreak of Asthma (Figure 2); c) Increased population density, including migrated labors, shows a steady growth of Asthma (Figure 3); d) Pollution from automobiles acts as an addendum in an increased outbreak of Asthma (Figure 4).



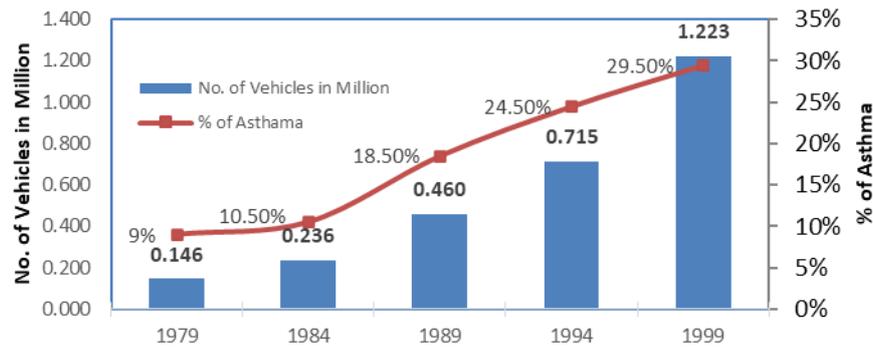
**Figure 1.** Increasing incidence of asthma with years.



**Figure 2.** Correlation of incidence of asthma with industrialization.



**Figure 3.** Correlation of incidence of asthma with population density.



**Figure 4.** Correlation of incidence of asthma with vehicular emission.

### 3.1.2. Risk factors.

In recent days, multiple environmental and lifestyle factors that India has changed regarding socioeconomic criteria are recognized for allergic disorders. The high compulsion of indoor and outdoor air pollution, Tobacco Smoke (ETS), is a major concern in rural and urban families. Adolescents living with smoker parents had a higher chance and morbidity due to asthma than non-smoking parents.

India has one of the highest air pollution loads globally [59]. Biomass fuels, and fossil fuels, vehicular exhausts are the main sources. Nearly 55.5% of the population uses solid fuels, and some states use 75% of the same. Nearly 77% of the Indian population is exposed to an annual weighted mean particulate matter (PM) 2.5 levels of  $> 40\text{mcg}/\text{m}^3$ , that exceed threshold limit of  $< 10\text{mcg}/\text{m}^3$  as recommended by WHO. (PM) 2.5 levels high  $> (125\text{mcg}/\text{m}^3)$ , in Uttar Pradesh, Haryana, New Delhi, and Bihar. PM2.5 directly has an adverse effect on respiratory diseases like Asthma and COPD, as well as mortality [59]. Salvi *et al.* reported The common triggers for asthmatics in India were dust (49%) and air pollution (49%), while only 5% reported pollen as a trigger[60]. Sensibility to aspergillus at a high rate (51%) and allergic bronchopulmonary aspergillosis(38%) has been found in Indian patients admitted with acute asthma [60-63].

### 3.2. Allergic rhinitis.

Since the last few decades, an outbreak of allergic rhinitis has gradually been risen in India, especially in older children aged 13–14 years than in children of 6–7-year-old, as reported in ISAAC phase-I and phase-III studies[64,65]. The coexistence of Allergic rhinitis and asthma was found in 70–80% of Indian patients [66]. Allergic rhinitis has an adverse effect on health quality in Indian patients [66,67]. House dust mite, mold spores, cockroaches, and pollen are Common aeroallergens to allergic rhinitis and Asthma in India [68]. Eastern India exposed that 96% of patients with naso-bronchial allergy showed sensibility to predominant house dust mite. Pollen, another catalyst, has two seasons in India: tree pollen during February–April and grass pollen during September and December with allergenicity [69]. Cannabis, Parthenium, Cassia, Holoptelea, Brassica, Cocos, and grasses are important allergens [70-72].

### 3.3. Atopic dermatitis.

The outburst of atopic dermatitis (AD), as per ISAAC studies, is wide-ranging (3.0–20.5%) globally[73,74]. ISAAC phase I and III data examination has reported that the appearance of AD is rising worldwide, especially in younger children[73,74]. The outburst of

AD in India is minor compared to other countries as evolved by the same reports as no serious increment in India. All the centers participating in ISAAC phase I study (except Kottayam in Kerala) reported a prevalence between 2.4% and 6% in 12 months. In ISAAC phase III, most of the participating Indian centers booked low rates (<5%) of AD, similar to phase I data [75].

#### 4. Conclusion

A serious fraction of the pediatric group in a population is affected by allergic diseases in most countries. Many environmental factors and toxins are implicated in childhood allergic diseases. Hence, intervention to impart environmental pollution control is important as they are a major cause of allergic diseases. This, in turn, is required to abate the impaired human resources and economic stress which is needed for a healthy nation. Prevention of Disease by abrogation of prenatal and neonatal environmental risk factors may significantly reduce the outbreak of pediatric allergies. As pregnant women and children are most vulnerable, adequate protection from allergy-related immunotoxicity may be taken care of, along with attention to oxidative stress and epigenetic mechanisms. They are considered possible factors of allergic disease and asthma. Policy on urbanization, industrialization, aviation, road traffic, etc., being the source of pollution (including NO<sub>2</sub> and P M<sub>2.5</sub>), may be chalked out with expert views. The provision of uniform civil education for a healthy lifestyle and to avoid pollutants from the indoor and outdoor environment may be an easy way to minimize the concerning risk factor, especially for the future citizens of our country.

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#### Conflicts of Interest

The authors declare no conflict of interest.

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