ASSOCIATION BETWEEN EXPOSURES OF PARTICULATE MATTER 2.5 AND POLLEN ANTIGENS WITH ACUTE PRECIPITATION OF RESPIRATORY SYMPTOMS: A PROSPECTIVE STUDY IN ADULTS OF A CITY IN INDIA AND AHPCO AS A REMEDY

BY:

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ABSTRACT

In India, air pollution has been the fifth leading cause of death. Studies have conferred serious health outcomes in people living in polluted areas with fine particulate matter (PM 2.5) values exceeding permissible limits. Particulate matter with such lesser aerodynamic diameter poses greater respiratory risk factor due to its propensity to reach deep down the lungs and come in contact with the blood. Both short and long term exposures are linked to serious respiratory outcomes. At this outset, a prospective study was conducted on the adult residents of a known polluted area, who developed acute respiratory symptoms on exposure to PM 2.5 and grass pollen grains over a period of more than a year. The study tried to probe the association between PM 2.5 and grass pollen exposure with daily clinic visits due to precipitation of acute respiratory symptoms and its probable relation with seasonal variation throughout the year. A prospective observational study was conducted in a part of city of Howrah in state of West Bengal of Eastern India. The study area was important for having all the four sources of PM 2.5. The study included all the permanent adult residents (aged >20 yrs. to <70 yrs.) exposed to both ambient air pollutant and grass pollen persistently throughout the year (1-32 pollen/day/mm^3). Data of the airborne grass pollen samples were collected using Burkard volumetric sampler and pollen count was obtained. A 24 hours Ambient PM 2.5 level of the study area was gathered from the official website of State Pollution Control Board. Private clinics of 32 experienced medical practitioners were identified in the locality and daily clinic visits of patients with acute precipitation of allergic upper respiratory inflammation like allergic rhinitis or allergic rhino conjunctivitis or allergic pharyngitis were noted. Data collected were statistically analyzed. Daily mean concentrations of PM 2.5 in this area was found to be 251.23 $\mu g/m^3$ which was quite above the permissible limit as enumerated by NAAQS. Daily mean concentration of pollen grains was found to be 6.77 per cubic meter. The mean PM 2.5 levels followed a trend as the concentrations reached the lowest averages during the

summer season, slightly increasing during the monsoon, and reaching its peak during post monsoon and winters. Similarly average grass pollen concentration was found to be minimum in summer or pre-monsoon time, while being at peak in winters. Maximum grass pollen concentration has been observed in monsoon and winters. Average daily clinic visits due to acute precipitation of respiratory symptoms were found to be maximum in winter followed by post and pre-monsoon respectively. Management of respiratory symptoms included oral antihistamines and local steroids. There was significant and positive association between personal exposure to both PM 2.5 and grass pollen with clinic visit due to precipitating respiratory symptoms. Severe AQI was observed in winter and post monsoon time. ($p<0.005$). The present study showed mean particulate matter concentration throughout the study period being far above the permissible standard limits. Increased aeroallergen concentration in this study site was also found prevalent. A seasonal variation of particulate matter and aeroallergen concentration was found to be significantly associated with precipitating respiratory symptoms amongst the residents of this area which upsurges a serious respiratory health concern. Stringent pollution control measures shall help to combat these deteriorating air quality issues thereby promising a healthier, safer and cleaner environment.

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CHAPTER I

INTRODUCTION

Ambient or outdoor air pollution is a major cause of death and disease globally, accounting for an estimated 4.2 million deaths per year due to stroke, heart disease, lung cancer and chronic respiratory diseases. The health effects ranges from increased hospital admissions and emergency room visits to increased risk of premature death. Around 91% of the world's population lives in places where air quality levels exceed WHO permissible limits. While ambient air pollution affects developed and developing countries alike, low- and middle-income countries experience the highest burden, with the greatest toll in the Western Pacific and South-East Asia regions, as mentioned by WHO. According to the latest air quality database, 97% of cities in low and middle income countries and 49% cities of high income countries do not meet WHO air quality guidelines (WHO, 2018). As urban air quality declines, the risk of stroke, heart disease, lung cancer, and chronic or acute respiratory diseases including asthma, increases for the people who live in those areas particularly in the vulnerable groups of extreme of ages.

While ambient air pollution originates from natural sources like forest fires and dust storms, the anthropogenic sources remains the major contributor of ambient air pollution which include fuel combustion from motor vehicles, heat and power generation, industrial facilities, municipal and agricultural waste sites and waste incineration/burning, residential

cooking, heating, and lighting with polluting fuels. The pollutants with the strongest evidence of precipitating adverse health effects include particulate matter (PM), ozone (O_3), nitrogen dioxide (NO_2) and sulphur dioxide (SO_2) (Ghorani-Azam A., Riahi-Zanjani B., Balali-Mood M. 2016**)**

The major concern of air pollution is the aerosol in the form of particulate matter (PM), also known as particulate pollution. Particulate matter (PM) are inhalable and respirable particles of varied size and shape composed of sulfate, nitrates, ammonia, sodium chloride, black carbon, mineral dust and water. Sources of PM include solid-fuel combustion products from households and industry, as well as other industrial activities. Particles having a diameter of less than 10 microns (PM 10), including fine particles less than 2.5 microns (PM 2.5) pose the greatest risks to health, as they can reach deep down into our lungs and comes in contact to our blood. While long term exposure to PM 2.5 has been linked with health issues like increased respiratory symptoms, decreased lung function, aggravated asthma, development of chronic respiratory disease in the form of chronic bronchitis and chronic obstructive lung diseases affecting more in extreme age groups. Short term exposure to particulate material can also aggravate chronic lung disease by precipitating asthma attacks, acute bronchitis, respiratory infections, and heart attacks and or irregular hearts on an existing heart disease. (Xing YF, 2016). Primary source of outdoor PM 2.5 is fuel combustion during transportation and energy production by thermal power or others. Indoor PM 2.5 sources including cooking, smoking and cleaning activities. Air pollutants encountered indoors include particulate matter, gases such as ozone, nitrogen dioxide, carbon monoxide, volatile organic compounds, passive smoke, and outdoor

ambient air. The sources of indoor air pollutions are electrical appliances, heaters, household cleaners.

In India, air pollution has been the fifth leading cause of death. According to a 2014 statistics by WHO, New Delhi was found to have worst air of 16,000 cities surveyed worldwide. Studies have conferred serious health outcomes in people living in polluted areas with PM 2.5 values exceeding permissible limits. Increased risk of lung cancer were observed to be 40% in Mumbai, 45% in Lahore, 50% in Jakarta, 58% in Peshawar, 60 % in Delhi, 80% in Allahabad. In the same go increased risk of stroke due to particulate matter 2.5 exposure were observed up to highest 170% in Allahabad to 160% in Peshawar and 130% in Mumbai. The effect of particulate matter 2.5 was believed to have more adverse effect on human health including myocardial infarction/heart attack; lung cancer with an increased level of 10 microgram/m^3 in comparison to particulate matter PM 10. WHO database on PM 2.5 annual mean concentration of 500 cities of the world whose measurement reach or surpass the permissible limits revealed that the top five cities polluted by PM concentration were Zabol (Iran), Gwalior (India), Allahabad (India) and Riyadh (Saudi Arabia). From 5th to the next 100th positions included different cities of Southeast Asian countries like China, India, Iran, Saudi Arabia, Pakistan, Bangladesh, Kuwait, Afghanistan, Qatar **(**Ghosh, N., et al., 2018).

Another prime problem in air quality has been aeroallergens which include airborne fungal spores and pollens, which are one of the major causes of allergies and asthma. Allergens are caused by substances that can trigger a reaction which include aeroallergens like pollen, mold spores, dander-animal droppings, mite fecal pellet, dust particles, plant fibers-products, burnt residues and other offenders like food, medications and insect venom/bite

(Richard M. Hyde, 2017). Pollen grains are one of the earliest identified aeroallergens and major cause of bronchial asthma and allergic rhinitis (Singh, & Mathur. 2017). Symptoms caused by pollen allergens include sneezing, watery eyes, nasal obstruction, itchy eyes and nose, and coughing (Stanley, & Linksens. 1974). Allergy symptoms to fungal spores also include respiratory problems, nasal-sinus congestion, watery eyes, sore throat, coughing, asthma, and skin irritations (Harris, 2017).

In an attempt to address the dearth of studies concerning environment toxicology, the present study tried to probe the association of PM 2.5 and perennial grass pollen in the respiratory health of residents in a particular poor air quality area. The present study selected Howrah city of eastern part of India (Belilias road area of Howrah), which is known for being an industrial area with metal processing mills, thus being a potential anthropogenic source of air pollutants. This area is also a predominant aeroallergen source of perennial grass pollens, which may affect the respiratory health of the inhabitants. Thus a prospective study was conducted on the adult residents of this area who developed acute respiratory symptoms on exposure to PM 2.5 and grass pollen grains over a period of more than a year. The present study tried to probe the association between PM 2.5 and grass pollen exposure with daily clinic visits with acute respiratory symptoms.

CHAPTER II

AIMS & OBJECTIVES

Aim:

- To probe the association between PM 2.5 and grass pollen exposure with daily clinic visits with acute respiratory symptoms.

Objectives:

Primary objective:

- To find the association between PM 2.5 and grass pollen exposure with daily clinic visits with acute respiratory symptoms.

Secondary-objective:

- To find the seasonal variation of PM 2.5 and grass pollen concentrations throughout the year
- To find association of PM 2.5 and grass pollen concentrations with seasonal variations in a year

CHAPTER III

REVIEW OF LITERATURE

Ambient Air Pollution: A Global Concern

Air pollution has been a significant public health problem, responsible for a growing range of health effects that are well documented from the results of an extensive research effort conducted in many regions of the world. A vast population of the developed and developing countries breathe air that does not meet the quality standards as set by World Health Organization Air Quality Guidelines. Air pollution has become a growing concern in the past decade, with an increasing number of acute air pollution episodes in many cities worldwide. Being associated with a broad spectrum of acute and chronic illness, such as lung cancer, chronic obstructive pulmonary disease (COPD) and cardiovascular diseases, ambient air pollution has been responsible for 4.2 million deaths as of 2016. Worldwide, ambient air pollution is estimated to cause about 16% of the lung cancer deaths, 25% of chronic obstructive pulmonary disease (COPD) deaths, about 17% of ischemic heart

disease and stroke, and about 26% of respiratory infection deaths. Globally, air pollution it is estimated to cause about 29% of lung cancer deaths, 43% of COPD deaths, about 25% of ischemic heart disease deaths and 24% of stroke deaths.

Major forms of air pollution include aerosols, tiny airborne solid and liquid particles that are released by Earth's surface both naturally and as a by-product of human activities (Simmon, & Voiland, 2010). There are two types of aerosols, primary and secondary. Primary aerosols are made by the activity of human beings which are directly released by motor vehicles (carbon monoxide), factories (Sulphur dioxide), while secondary aerosols are mainly the combustion products of different primary aerosols. 90% of aerosols are attributed to the natural sources like volcanoes, forest fires, plants, and oceans (Simmon, & Volland, 2010**).** Volcanoes release large amounts of ash, sulfur dioxide and other gases into the air. Partially burned organic compounds originate from forest fires. Some plant produce gases that react with other substances such as smoke, causing the production of aerosols in the air. Micro-algae acting on the ocean produce sulfurous gas known as di-methyl-sulfide which is converted into sulfate in the atmosphere **(**Simmon, & Voiland**,** 2010). 10% aerosols are contributed by man-made or anthropogenic sources, produced by biomass burning, fossil fuel combustion, and automobiles. Other sources of anthropogenic aerosols are incinerators, smelters, and power plants **(**Simmon, & Voiland, 2010). Fossil fuel combustion results in sulfate aerosols, from large amount of liberated sulfur dioxide which reacts with water vapor and other gasses in the atmosphere. Biomass burning, burning of farm waste and vegetation to clear land, produces smoke which contains organic carbon and black carbon. The majority of sulfates, nitrates, black carbon, and other particles are products of automobile, incinerators, smelters (metal smelting), and power

plants. Other forms of aerosols, such as dust aerosols, arise from alteration of the land surface by deforestation (cutting or burning down of all trees in an area), overgrazing (letting animals pass through crops), drought, and excessive irrigation **(**Simmon, & Voiland, 2010**).**

National Ambient Air Quality Standards

The U.S. National Ambient Air Quality Standards (NAAQS) are standards for harmful pollutants, established by the United States Environmental Protection Agency (EPA) under authority of the Clean Air Act. The standards are listed in 40 C.F.R. 50. ***Primary standards*** are designed to protect human health, with an adequate margin of safety, including sensitive populations such as children, the elderly, and individuals suffering from respiratory diseases. ***Secondary standards*** are designed to protect public welfare (including effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility, and climate), damage to property, transportation hazards, economic values, and personal comfort and well-being from any known or anticipated adverse effects of a pollutant. A district meeting a given standard is known as an **"attainment area"** for that standard, and otherwise a **"non-attainment area"**. EPA set NAAQS for six major pollutants as listed hereunder. These six pollutants are also the ***criteria pollutants***. **(Table 1).**

Table 1: NAAQS for Six Major Pollutants				
Pollutant	Type	Standard	Averaging Time	Form
Sulfur dioxide (SO_2)	Primary	75 ppb	1-hour	99th Percentile of 1-hour daily maximum concentrations, averaged over 3 years
	Secondary	0.5 ppm (1,300 µg/m³)	3-hour	Not to be exceeded more than once per year
Particulate matter (PM 10)	Primary and Secondary	150 µg/m³	24-hour	Not to be exceeded more than once per year on average over 3 years
Fine particulate matter (PM 2.5)	Primary	12 µg/m³	annual	Annual mean, averaged over 3 years
	Secondary	15 µg/m³	annual	Annual mean, averaged over 3 years
	Primary and Secondary	35 µg/m³	24-hour	98th percentile, averaged over 3 years
Carbon monoxide (CO)	Primary	35 ppm (40 mg/m³)	1-hour	Not to be exceeded more than once per year
	Primary	9 ppm (10 mg/m³)	8-hour	Not to be exceeded more than once per year
Ozone (O_3)	Primary and Secondary	0.12 ppm (235 µg/m³)	1-hour[b]	expected number of days per calendar year, with maximum hourly average concentration greater than 0.12 ppm, is equal to or less than 1
	Primary and Secondary	0.070 ppm (140 µg/m³)	8-hour	Annual fourth-highest daily maximum 8-hour concentration,

				averaged over 3 years
Nitrogen dioxide (NO_2)	Primary and Secondary	0.070 ppm (140 µg/m³)	8-hour	Annual fourth-highest daily maximum 8-hour concentration, averaged over 3 years
Lead (Pb)	Primary and Secondary	0.15 µg/m³	Rolling 3 months	Not to be exceeded

Indoor and outdoor pollution sources

According to the 2014 WHO report, in 2012 air pollution caused deaths of around 7 million people globally. Worldwide, the main sources of outdoor pollutants are fuel combustion from vehicular transportation, construction and agricultural operations, power plants and industries. Primary pollutants coming from these sources are: carbon monoxide (CO), nitrogen dioxide (NO_2), Sulphur dioxide (SO_2) and polycyclic aromatic hydrocarbons (PAHs). Ozone (O_3) is classified as secondary pollutant since it is formed by reaction between NO_2 and volatile organic compounds (VOCs) in the presence of heat and sunlight. Sulfur oxide pollutants are compounds such as sulfur dioxide (SO_2), a poisonous colorless gas that can form naturally or anthropogenically, and sulfur trioxide (SO_3), which is highly poisonous, highly reactive and extremely corrosive (Environmental Pollution Centers, 2017). The most common sulfur oxide pollutant is sulfur dioxide, which comes from industrial processing plants: coal, oil, cement, metal, wood, copper, and electric power plants. Long term exposure to sulfur dioxide can cause severe health problems such as acute respiratory problems, chronic bronchitis, emphysema, coughing, stomach pain, nausea, menstrual disorders, hypothyroidism, headache, convulsion and dizziness (Environmental Pollution Centers, 2017). Nitrogen oxide gases are compounds of nitrogen

and oxygen with the most common forms being nitric oxide (NO), nitrogen dioxide (NO_2) and nitrous oxide (N_2O). The causes of nitrogen oxide pollution are car exhausts, electric power plants, burning of various fuels, cigarette smoking, electroplating, and welding (Environmental Pollution Centers, 2017). Carbon monoxide (CO) a known pollutant that is a colorless, odorless and tasteless toxic gas, is present everywhere at all times. It is produced by anything that burns fuel. Carbon dioxide (CO_2) which produces naturally and anthropogenically, contributes to air pollutants, and is toxic if inhaled or in direct contact in enclosed areas (Environmental Pollution Centers, 2017). VOCs (Volatile organic compounds) are important in everyday life, they are compounds containing carbon and can easily turn from solids into vapors or gases contributing to air pollution leading to serious health problems. VOCs can also contain fluorine, bromine, sulfur, nitrogen, and other elements (Environmental Pollution Centers, 2017).

Elemental mercury is another form of toxic air pollutant. Mercury is natural chemical element in rock in earth's crust and is in deposits of coal. Mercury exists in several forms: elemental or metallic mercury, inorganic mercury compounds, methyl mercury and other organic compounds (US Environmental Protection Agency [EPA], "Basic Information", 2017). Main concern is elemental mercury which forms toxic gas in room temperature. Elemental mercury is a shiny silver-white metal and is liquid at room temperature. Evaporate from liquid mercury becomes a toxic, colorless, odorless gas (EPA, "Basic Information," 2017). The emission of mercury can happen naturally through volcanoes and forest fires, and with human activities by burning of oil, wood, coal, and other fossil fuels, and waste containing mercury. Mercury toxicity can damage brain, kidney, heart, lungs, and immune system.

The major concern of air pollution is the aerosol in the form of particulate matter (PM), also known as particulate pollution. Particulate matter (PM) are inhalable and respirable particles of varied size and shape composed of sulfate, nitrates, ammonia, sodium chloride, black carbon, mineral dust and water. Sources of PM include solid-fuel, industrial activities and combustion products from households and industry.

Particulate Matter

PM is a mixture of solid and liquid particles suspended in air and it can have different sizes, shapes and chemical composition; it is divided into different categories depending on the aerodynamic diameter of the particles. The particle size influences the capability of the PM to penetrate deeply in the lung. Primary and secondary PM present in atmosphere can be transported over long distances and their removal may occur via rainfall, gravitational sedimentation or coagulation with other particles.PM is usually made up of primary and secondary PM from both anthropogenic and natural sources. While primary form is directly emitted from different sources like agricultural and industrial processes, vehicles, construction sites and forest fires, secondary form is derived from complex chemical reactions of gases in the atmosphere. (Table 2-(US Environmental Protection Agency). Particulate Matter (PM) Basic. (2016).

Table 2: Characteristics and Sources of Various PM Fractions

PM fraction	Characteristics	Sources
PM 10 (*Inhalable PM*)	• diameter ≤ 10 μm • able to penetrate into both upper and lower respiratory tract	Outdoor Sources like Vehicular traffic, Organic matter and fossil fuel combustion and Power stations/industry
PM(10-2.5) (*Coarse particles*)	• diameter ranging from 2.5 to 10 μm • able to penetrate into the upper respiratory tract	Outdoor Sources like Marine aerosol, Soil erosion, Volcanic eruptions

PM 2.5 (*Fine PM*)	• diameter ≤ 2.5 μm • able to penetrate into the alveoli	Outdoor Sources like Windblown dust from roadways, agriculture and construction, Bushfires/dust storms
PM 0.1 (Ultrafine PM)	• diameter ≤ 0.1 μm • able to penetrate into alveolar region.	Indoor Sources like Woodstoves, Organic matter and fossil fuel combustion, Tobacco Smoke

WHO Guideline on PM

The latest update of air quality guidelines (AQG) for PM from the WHO in 2005 showed that the PM10 values were limited to an annual mean of 20μg/m^3 and a 24-hour mean of 50μg/m^3, while the values of PM 2.5 were limited to an annual mean of 10 μg/m^3 and a 24-hour mean of 25μg/m^3 (not to be exceeded for more than 3 days/year).

Effect of PM Exposure on Respiratory Diseases

Epidemiological evidences show that both short- and long-term PM exposure have a close association with the development of respiratory diseases, such as COPD, asthma, lung cancer and pneumonia (Conti, S., et al., 2017; Zeng, Q., et al., 2017). Studies have demonstrated that PM exposure increases the mortality of patients with respiratory diseases (Atkinson, R.W., et al., 2015; Atkinson, R.W., et al., 2014; Pun, V.C., et al**.,** 2017). In China, a nationwide analysis showed that the mortality from respiratory diseases increased 0.29% with a 10 μg/m^3 increment in PM 2.5 every 2days (Chen, R., et al., 2017). PM exposure also increases respiratory symptoms and medication use, and decreases pulmonary function**.** Though the risk extends to the entire population, those in extreme age groups are more susceptible.

COPD

Short-term exposure to PM could exacerbate the disease process of COPD. Several studies have showed that PM 10 or PM 2.5 with a 10 $\mu g/m^3$ increase in concentration could lead to reduced forced vital capacity (FVC), forced expiratory volume during the first second (FEV1), FEV1/FVC ratio and peak expiratory flow (PEF) (Bloemsma, L.D., et al., 2016; Liu, S., et al., 2016). PM 2.5 even showed a stronger harm on the lung function of COPD patients than PM 10 possible owing to its smaller size which makes it easier to be inhaled into the small airways and the alveoli of the lung. As for PM 10, Zhu et al. showed that an increase of 10 $\mu g/m^3$ PM10 was significantly associated with increased COPD-related hospital admissions (2.7%) and increased COPD mortality (1.1%) **(**Zhu, R., et al., 2013). A study by Pun et al., 2017. showed that long-term PM 2.5 exposure was related with 10% increased risks of COPD mortality in older residents.

Asthma

Association between PM exposure and the risk of asthma incidence or lifetime prevalence in childhood aged from 1 to 18 years has been studied which reveals that PM 10 or PM 2.5 exposure has been a risk factor for the development of asthma in children. Meta-analysis showed PM exposure led to an adverse impact on the exacerbation of asthma, especially in children and in warm season.

Lung Cancer

Both PM 2.5 and PM 10 has substantially contributed to increased lung cancer mortality. Effect of PM components on lung cancer incidence which compared eight elements like copper (Cu), iron (Fe), potassium (K), nickel (Ni), sulfur (S), silicon (Si), vanadium (V)

and zinc (Zn) in PM 10 and PM 2.5, found that Cu from PM 2.5 and Zn, S, Ni and K from PM 10 had positive associations with the incidence of lung cancer (Raaschou-Nielsen, O. et al., 2016). However, smoking has been an important risk factor for lung cancer and is considered to be a potential confounder for PM and lung cancer mortality.

Pneumonia

Various studies have demonstrated a positive association of PM with morbidity and mortality of pneumonia. Short-term exposure of PM 10 and PM 2.5 were found associated with increase in ED (emergency department) visits due to upper respiratory infection and pneumonia. Increase in hospital admission for pneumonia with PM 10 levels were also noted in some studies, specifically in warm seasons. Population from extreme ages and those with comorbidities were found more susceptible. The elderly, children under five years of age, and those with special comorbidities were found more susceptible to pneumonia. Short-term exposures of both PM 10 and PM 2.5 increased the ED visits in children under five years old for PM 10 per 10 $\mu g/m^3$ and 1.8% for PM 2.5 per 10 $\mu g/m^3$. (Wang, J., et al., 2018)

PM 10 Vs PM 2.5

Particulate matters with aerodynamic diameter smaller than 10 μm have a greater impact on human health. PM 2.5 having small diameters are capable of carrying toxic stuffs, passing through the filtration of nose hair, reaching the end of the respiratory tract with airflow and accumulate there by diffusion, thereby causing damage due to air exchange in the lungs.

The “Harvard six Cities Study”, published in 1993 (Dockery D.W., et al., 1993) revealed that PM 2.5 was one of the causative factors of human non-accidental death. In this study, PM 2.5 was positively related to daily mortality of humans, particularly the elderly, evidence supporting the linear relationship between non-accidental death and PM 2.5 was established.

Increased PM concentration in the air may directly lead to an elevated morbidity and mortality of a population **(**Nemery, B. et al., 2001; Helfand, W.H., et al., 2001**).** A study by Orru, H., et al., (2011) showed that PM 2.5 decreased the average life span by 8.6 months**.** A multi nation study by Analitis, A., et al., (2006) found that respiratory mortality increased by 0.58% for every 10 $\mu g/m^3$ increase of PM 10. Even an increase by 10 $\mu g/m^3$ of daily PM 2.5 have been postulated to increase the prevalence rate of respiratory diseases by 2.07%, and hospitalization rate by 8% respectively **(**Zanobetti, A., et al., 2009; Dominici, F., et al., 2006). Positive correlations with respiratory symptoms were noted specifically in the elderly, pregnant women, adolescents, infants, patients with a history of cardiopulmonary problems and other susceptible populations **(**Huynh, M., et al., 2006**;** Martinelli, N., et al., 2012; de Oliveira, B.F., et al., 2012). Yadav et al**.,** revealed that the morbidity of asthma, influenza and acute respiratory tract infection increased notably during outbreaks of smog.

The Underlying Mechanism

Various mechanisms have been proposed to explain the adverse effect of PM on respiratory diseases. Particulate matter is supposed to enter and deposit in the lung with breathing to directly or indirectly cause the oxidant stress, pro-inflammation, epigenetic modifications,

apoptosis, DNA damage and even carcinogenesis in the lung cells. These biological dysfunctions eventually contribute to the increased morbidity and mortality of respiratory diseases.

Oxidative Stress

Cellular redox equilibrium is essential for maintenance of normal biological process. Under physical conditions, cells produce a variety of antioxidants to neutralize the reactive oxygen species and oxygen radicals. Exogenous and endogenous stimuli often disturb the balance between oxidation and anti-oxidation making excessive ROS accumulation form oxidant stress. Oxidant stress has been demonstrated as an important mechanism in PM induced respiratory diseases and excessive ROS acts as a key mediator to initiate pro-inflammation, physical barrier disruption, cell death and carcinogenesis (Li, N., et al., 2003).

Cellular Death

Cell death is another prime mechanism for PM-induced respiratory diseases. The oxidative stress, inflammation cascades and DNA damage are considered to participate into PM-induced cell death. Different cell death types like apoptosis, autophagy and necrosis have been demonstrated to be associated with PM exposure in lung cells.

Epigenetic Changes

The PM-induced epigenetic changes focus on DNA methylation and histone modification (Kim HJ et al, 2017). Baccarelli et al., found that PM exposure caused a decrease in repeated-element methylation. Chen et al. showed that PM 2.5 exposure decreased the NOS2A DNA methylation and increased Fractional Expiratory nitric-oxide (FENO) in

COPD patients. Several studies also showed that PM could affect histone modification **(**Liu, C. et al., 2015).

Indoor Environment Quality

Indoor environment is also an important source of health risk factors, particularly considering that most people spend around 90% of their time indoors. The indoor environment quality depends on the air that penetrates from outdoor and on the presence of indoor air pollution sources. To improve energy efficiency, modern dwellings are often thermally insulated and scarcely ventilated, possibly resulting in deterioration of the air quality. Moreover, indoor environment is influenced by building systems, construction techniques, contaminant sources and occupants' behavior. The most frequently investigated risk factors for indoor pollution are Environmental Tobacco Smoke (ETS), biomass fuel, cleaning products and biological allergens. **(**Cincinelli et al., 2017**)**

Biological allergens

Biological allergens originate from a wide range of animals, insects, mites, plants, or fungi **(**Bousquet, J. et al., 2008**).** Indoor allergens are mainly originated from house dust mites, furred pets (primarily cat and dog dander), cockroaches, moulds, plants and rodents (Hulin, M. et al., 2012). Primary sources for outdoor allergens include plants, fungi, molds and yeasts. **(**Baldacci, S. et al., 2015**)** (Table 3).

Table 3: Various Allergens and their Sources	
Sources	**Allergens**
Dust, beds, carpets	House dust mites
Pets, birds, insects, rodents	Specific allergens (i.e. Fel d1)
Cockroaches	Specific allergens (i.e. Bla g1)
Dampness	Moulds
Plants	Pollens
Virus, bacteria	Biological contaminants

Airborne biological particles are released from sources into the air by wind, rain, mechanical disturbance, or active discharge mechanisms; once particles have been launched into the air, their concentration decreases with increasing distance from the point of liberation. Particle dispersion is largely dependent on air mass movement, turbulence and thermal convection following the physical laws that apply to all airborne particulate **(**Lacey, M.E., West, J.S., 2006**).** Pollen and fungal spores are one of the major aeroallergen causing allergies and asthma **(**Ghosh, Saadeh, Gaylor, & Aurora., 2006**).**

Pollens

The male gametophyte of seed plants is pollen. In order to reproduce, it has to be produced by seed producing plants like gymnosperms (having vascular system) or angiosperms (vascular plants). Gymnosperms produce pollen in cones, while angiosperms produce them in the anthers **(**Ghosh, et al., 2017**).** One of the earliest identified aeroallergens are pollen grains, which are found to be the major causes of allergic rhinitis and bronchial asthma **(**Singh, Mathur, 2017**).** Atopic allergic rhinitis is called Hay fever. They present with itchy nose (flag sign) and eyes, sneezing-nasal obstruction, red watery eyes, and or coughing.

Following past first exposure causing sensitization repeat exposures lead to this type of allergic reactions **(**Stanley, & Linskens., 1974**)**.The different types of pollen include oak pollen, ragweed, plants, weeds, sagebrush, redroot pigweed, and lamb's quarters. Also includes Tumbleweed, English plantain, grasses, and trees. Trees producing pollen are oak, ash, elm, hickory, pecan, box elder, and mountain cedar **(**Ghosh et al., 2017**).** The most significant aeroallergen pollen in Texas Panhandle include grass pollen, short ragweed, pine, common sunflower, hairy sunflower, buffalo Bur, purple nightshade, and lamb's quarters **(**Ghosh et al., 2017**).**

Fungal spores

Spore forming fungi reproduce both sexually and asexually (Hudson. 1986).Most commonly allergy causing molds are filamentous fungi which belongs to three phylum: Zygomycota, Ascomycota and Deuteromycota. They are differentiated by the way they reproduce. Zygomycota fungi have the ability to reproduce sexually or asexually. Ascomycota reproduces sexually while Deuteromycota reproduces asexually **(**Zukiewiez-Sobezak. 2013**).** Fungi are formed from microscopic thread like structures known as Hyphae. An entire mass of hyphae makes up the mycelium, which is formed in soil, leaf litter, or decaying wood **(**Stephenson. 2010**)**. Fungal spore develops seasonally. High number of mold spores formed during summer because of the nutrients in soil, favorable temperature and humidity. Outdoor allergenic fungi include the genera: *Cladosporium, Alternaria, Botrytis, Epicoccum, Fusarium, Aspergillus* and *Penicillium* **(**Zukiewiez-Sobezak, 2013**).** ~10% people are highly allergic to mold **(**Harris. 2017**).** Allergic reactions to mold include respiratory problems, nasal and sinus congestion, watery eyes, sore throat, coughing, asthma, and skin irritations **(**Harris, 2017**).** People at high risk to mold exposure

are extremes of ages, atopic persons, pregnant women, and immune-deficient patients with cell mediated and or humoral immune deficiency (IgA/IgG deficiency). IgA is specific for Sino-Pulmonary system. The most significant fungal spores in Texas Panhandle include *Alternaria, Ascospores* (Pezizales), *Drechslera, Stachybotrys, Cladosporium, Carvularia,* Teliospores (*Ustilago*) **(**Ghosh et al., 2017**).**

Pathogenesis of allergy and hypersensitivity with antigens of pollen, fungal spores, and other respirable antigens:

Allergic reactions occur when an individual, who has produced IgE antibody in response to an innocuous antigen, or allergen, subsequently encounters the same allergen. The allergen then activates IgE-binding mast cells in the exposed tissue, thereby leading to allergic response.

The most common and traditional classification for hypersensitivity reactions (Gell and Coombs classification) divides the hypersensitivity reactions into the following 4 variants namely,

Type I reaction- commonly known as immediate hypersensitivity reactions, involve IgE mediated release of histamine and other mediators from mast cells and basophils.

Type II reaction- commonly known as cytotoxic hypersensitivity reactions involve IgG or IgM antibodies bound to cell surface antigens, with subsequent complement fixation.

Type III reaction- commonly known as immune-complex reactions involve circulating antigen-antibody immune complexes depositing in post-capillary venules, with subsequent complement fixation.

Type IV reaction- commonly known as delayed hypersensitivity reactions, cell-mediated immunity are mediated by T cells rather than by antibodies.

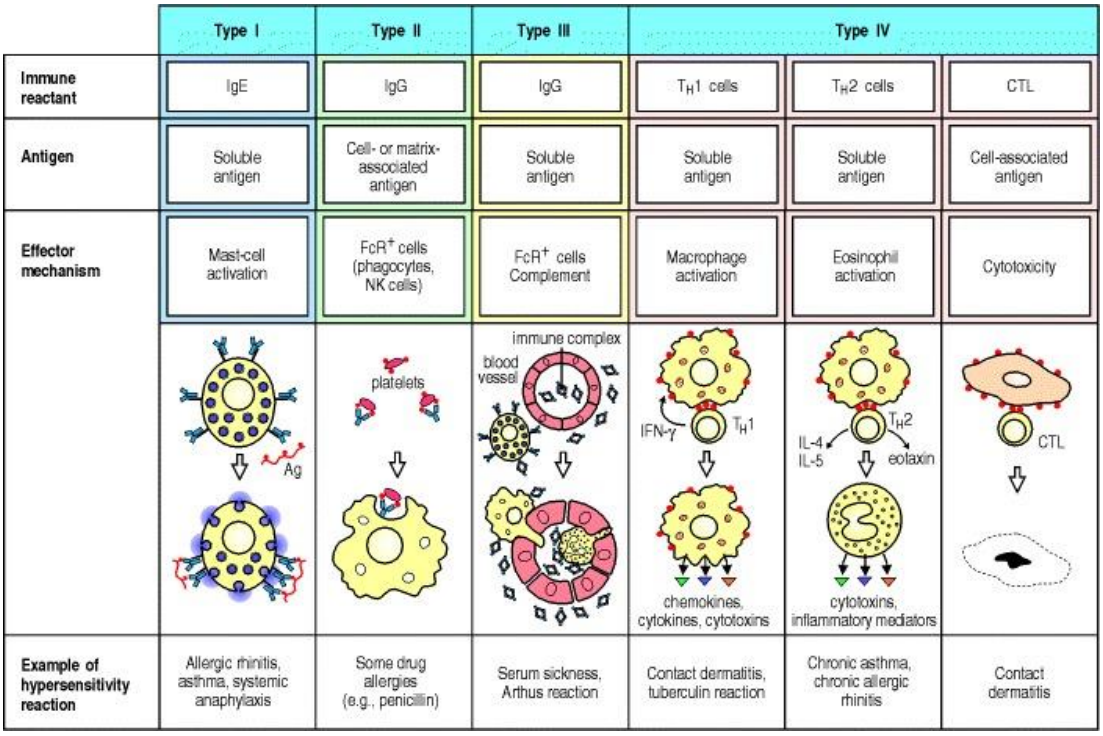


Figure 1: Types of Hypersensitivity Reactions *(Image Courtesy: Immunobiology: The Immune System in Health and Disease. 5th edition. Janeway, CA Jr, Travers P, Walport M, et al. New York: Garland Science; 2001.)*

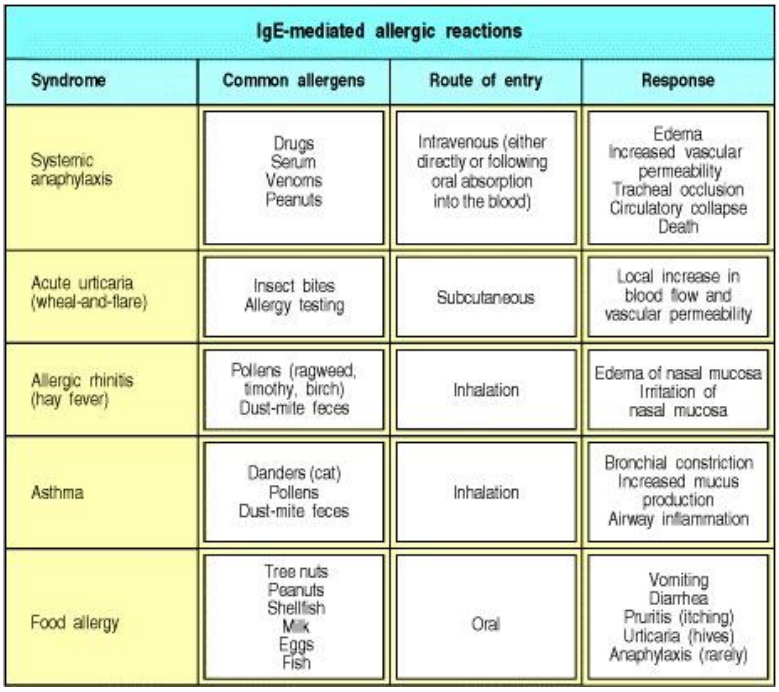
Allergic reactions manifest clinically as IgE mediated reactions like anaphylaxis, allergic asthma, urticaria, angioedema, allergic rhinitis, some types of drug reactions, and atopic dermatitis. Atopy is the genetic predisposition of an individual to make IgE antibodies in response to allergen exposure.

Pathophysiology

Though immediate hypersensitivity reactions are mainly mediated by IgE, but T and B cells also play important roles in the development of these antibodies. (Buelow, 2015) CD4+ T-cells are broadly divided into 3 classes namely effector T-cells, memory T-cells, and T-regulatory (Treg) cells. Effector T-cells are further subdivided based on the cytokines produced (TH1, TH2, TH17).

Cellular Components	Functions
Effector T Cells TH1 (produce IFNγ, IL2) TH2 (IL-4, IL-13) TH17(IL-17, IL-21, IL-22)	 Promote a cell-mediated immune response Act on B-cells to promote the production of antigen-specific IgE To help fight extracellular pathogens, to produce antimicrobial peptides, to promote neutrophil inflammation essential for immunity at the skin and mucosal surfaces
Memory T-cells	Rapidly differentiate into effector T-cells in secondary immune responses
CD4+CD25+FOXP3+ Treg cells	Essential in peripheral tolerance and serve to suppress dysregulated immune responses. Inhibit TH2 cytokine production through the secretion and action of IL-10 and TGF-beta Important in allergen tolerance

The allergic reaction first requires sensitization to a specific allergen in an atopic individual. The allergen is then processed by an antigen-presenting cell (APC) which migrates to lymph nodes, where they prime naïve TH cells that bear receptors for the specific antigen. After antigen priming, naïve TH cells differentiate into TH1, TH2, or TH17 cells based upon antigen and cytokine signaling.



IgE-mediated allergic reactions			
Syndrome	**Common allergens**	**Route of entry**	**Response**
Systemic anaphylaxis	Drugs Serum Venoms Peanuts	Intravenous (either directly or following oral absorption into the blood)	Edema Increased vascular permeability Tracheal occlusion Circulatory collapse Death
Acute urticaria (wheal-and-flare)	Insect bites Allergy testing	Subcutaneous	Local increase in blood flow and vascular permeability
Allergic rhinitis (hay fever)	Pollens (ragweed, timothy, birch) Dust-mite feces	Inhalation	Edema of nasal mucosa Irritation of nasal mucosa
Asthma	Danders (cat) Pollens Dust-mite feces	Inhalation	Bronchial constriction Increased mucus production Airway inflammation
Food allergy	Tree nuts Peanuts Shellfish Milk Eggs Fish	Oral	Vomiting Diarrhea Pruritis (itching) Urticaria (hives) Anaphylaxis (rarely)

Figure 2: IgE Mediated Allergic Reactions (*Image Courtesy: Immunobiology: The Immune System in Health and Disease. 5th edition., Janeway CA Jr, Travers P, Walport M, et al., New York: Garland Science; 2001*.)

The antigen-specific IgE antibodies can then bind to high-affinity receptors located on the mast cells surface and basophils. Re-exposure to the antigen can result in the antigen binding to and cross-linking the bound IgE antibodies causing release and formation of chemical mediators from cells. The major mediators and their functions are described in Table 4, which follows.

Table 4: Various Mediators and their Functions	
Preformed mediators	
Histamine	Acts on histamine 1 (H1) and histamine 2 (H2) receptors to cause contraction of smooth muscles of the airway and GI tract, increased vasopermeability and vasodilation, enhanced mucus production, pruritus, cutaneous vasodilation, and gastric acid secretion.
Tryptase	cleave C3, C3a, and C5 in addition to playing a role in airway remodeling. Tryptase is found in all human mast cells but in few other cells and thus is a good marker of mast cell activation.
Proteoglycans	Includes heparin and chondroitin sulfate. Heparin plays a role in the production of alpha-tryptase.
Chemotactic factors	An eosinophilic chemotactic factor of anaphylaxis causes eosinophil chemotaxis; an inflammatory factor of anaphylaxis results in neutrophil chemotaxis. Eosinophils release major basic protein and, together with the activity of neutrophils, can cause significant tissue damage in the later phases of allergic reactions.
Newly formed mediators	
Arachidonic acid metabolites	
Leukotrienes	Produced via the lipoxygenase pathway
Leukotriene B4	Neutrophil chemotaxis and activation, augmentation of vascular permeability
Leukotrienes C4 and D4	Potent broncho-constrictors, increase vascular permeability, and cause arteriolar constriction
Leukotriene E4	Enhances bronchial responsiveness and increases vascular permeability
Leukotrienes C4, D4, and E4	Comprise what was previously known as the slow-reacting substance of anaphylaxis
Cyclooxygenase Products	
Prostaglandin D2	Produced mainly by mast cells; broncho-constrictor, peripheral vasodilator, coronary and pulmonary artery vasoconstrictor,

	platelet aggregation inhibitor, neutrophil chemoattractant, and enhancer of histamine release from basophils
Prostaglandin F2-alpha	Broncho-constrictor, peripheral vasodilator, coronary vasoconstrictor, and platelet aggregation inhibitor
Thromboxane A2	Causes vasoconstriction, platelet aggregation, and bronchoconstriction
Platelet-activating factor (PAF)	Increases vascular permeability, causes bronchoconstriction, and causes chemotaxis and degranulation of eosinophils and neutrophils.
Adenosine	Potentiates IgE-induced mast cell mediator release.
Bradykinin	Kininogenase released from the mast cell can act on plasma kininogens to produce bradykinin. An additional (or alternative) route of kinin generation, involving activation of the contact system via factor XII by mast cell–released heparin, has been described. Bradykinin increases vasopermeability, vasodilation, hypotension, smooth muscle contraction, pain, and activation of arachidonic acid metabolites.
Cytokines	
IL-4	Stimulates and maintains TH2 cell proliferation and switches B cells to IgE synthesis
IL-5	Maturation, chemotaxis, activation, and survival of eosinophils. IL-5 primes basophils for histamine and leukotriene release.
IL-6	Promotes mucus production.
IL-13	Same effects as IL-4.
Tumor necrosis factor-alpha	Pro-inflammatory cytokine which activates neutrophils and eosinophils and increases monocyte chemotaxis.

Clinical Responses caused by these Mediators:

Urticaria/angioedema: Release of these mediators in the superficial layers of the skin can cause pruritic wheals with surrounding erythema. Angioedema is the swelling of the affected area; it tends to be painful rather than pruritic and is caused when deeper layers of the dermis and subcutaneous tissues are involved.

Allergic rhinitis: Release of these mediators in the upper respiratory tract can result in sneezing, itching, nasal congestion, rhinorrhea, and itchy or watery eyes.

Allergic asthma: Release in the lower respiratory tract can cause bronchoconstriction, mucus production, and inflammation of the airways, resulting in chest tightness, shortness of breath, and wheezing.

Anaphylaxis: Systemic release results in symptoms in multiple organ systems and is considered anaphylaxis. Gastrointestinal system can be affected with nausea, abdominal cramping, bloating, and diarrhea. Systemic vasodilation and vaso-permeability may result in significant hypotension (anaphylactic shock).

Allergic reactions can manifest as immediate reactions, late-phase reactions, or chronic allergic inflammation.

Immediate/acute-phase reactions occur within seconds to minutes immediately after allergen exposure. Few mediators (released from mast cells and basophils) cause eosinophil and neutrophil chemotaxis. These cells along with monocytes and T cells are believed to cause the late-phase reactions that can occur hours after antigen exposure and after the signs or symptoms of the acute-phase reaction have resolved. Late-phase reaction

can manifest redness and mucosal swelling, nasal discharge, airway narrowing, sneezing, coughing, and wheezing, which can last a few hours and usually resolve within 24-72 hours. Continuous or repeated exposure to an allergen can result in chronic allergic inflammation. Affected tissue sites contain T cells and eosinophils, which can further release many mediators causing tissue damage and thus increase inflammation. Repeated allergen challenge can result in increased levels of antigen-specific IgE, which can cause further release of IL-4 and IL-13, increasing the propensity for TH2 cell/IgE–mediated responses.

Management Approaches

Management of allergic symptoms like allergic rhinitis, allergic rhino-conjunctivitis essentially consists of 3 major categories of treatment:

(1) Environmental Control Measures and Allergen Avoidance

(2) Pharmacological management, and

(3) Immunotherapy

Environmental Control Measures and Allergen Avoidance

Environmental control measures and allergen avoidance involve both the avoidance of known allergens and avoidance of nonspecific, or irritant, triggers. Environmental control measures should be undertaken, however identification of specific triggers is needed prior that.

Pollens and outdoor molds

Generally tree pollens are present in the spring, grass pollens from the late spring through summer, and weed pollens from late summer through fall, though exceptions to these seasonal patterns also exist. Thus an effective measure can be reduction of outdoor exposure during the season in which a particular type of pollen is predominant. Pollen counts are on a higher mark usually on dry, sunny, windy days. Outdoor exposure can thus be minimized during this time. Keeping the windows and doors of the house and car closed as much as possible during the pollen season can be helpful. Taking a shower after outdoor exposure can be helpful by removing pollen stuck to the hair and skin. Despite all of these measures, pollen allergic patients usually continue to be symptomatic during the pollen season and usually require other management approaches.

Indoor allergens

For dust mites, use of impermeable covers for mattress and pillows helps reduce exposure. Periodical washing of bed linen in warm water and efficient vacuum cleaning of carpets and rugs can help. Since dust mites thrive at indoor humidity above 50%, dehumidification and air conditioning may be helpful. Reduction of excessive humidity and removal of standing water may serve as control measures for mold allergy. Control measures for dust mites can also mitigate mold spores. In case of animal allergy, complete avoidance is the best option. In event of unavoidable situations, confinement of the animal to a non-carpeted room and keeping it entirely out of the bedroom may be beneficial. Use of high-efficiency particulate air (HEPA) filters is effective in reducing cat allergen levels in the home.

Occupational allergens -To combat occupational allergens, use of mask or respirator is advocated.

Nonspecific triggers -Exposure to smoke, strong perfumes and scents, fumes, rapid changes in temperature, and outdoor pollution can be nonspecific triggers in patients with allergic rhinitis and can thus be avoided.

Pharmacotherapy

Most cases of allergic rhinitis respond to pharmacotherapy. Patients with intermittent symptoms are often treated with oral antihistamines, decongestants, or both as needed. For chronic conditions, regular intranasal steroid spray may be more useful. In addition, ocular antihistamine drops, intranasal antihistamine sprays, intranasal cromolyn, intranasal anticholinergic sprays, and short courses of oral corticosteroids may also provide relief.

Antihistamines

H1 antagonists are useful in acute types of allergy presenting with symptoms of rhinitis, urticaria, and conjunctivitis **(**Simons and Simons, 2011**).** They suppress symptoms due to the histamine released by the antigen-antibody reaction.

First Generation Antihistamines

The older, first-generation H1 antagonist are effective in reducing most allergic rhinitis symptoms but produces a number of adverse effects mainly anticholinergic effects. Some patients tolerate the adverse effects with prolonged use, though cognitive impairment may be experienced. Bedtime dosing may help drowsiness, though sedation and cognition impairment may continue until the next day. The second-generation antihistamines are

however non-sedating in most patients and are thus preferred as first-line therapy, owing to fewer side effects as compared to first generation ones.

Chlorpheniramine: First-generation agent which competes with histamine on H1-receptor sites on effector cells in blood vessels and respiratory tract.

Diphenhydramine: Common first-generation agent which competes with histamine on H1-receptor sites on effector cells in blood vessels and respiratory tract and is used for symptomatic relief of allergic symptoms due to histamine release.

Hydroxizine: It is an effective first-generation agent though frequently produces sedation in lower doses. It antagonizes H1 receptors in periphery and may suppress histamine activity in subcortical region of CNS.

Second-generation antihistamines (Non-sedating antihistamines):

They compete with histamine for H1 receptor sites in the blood vessels, GI tract, and respiratory tract, which, in turn, inhibits physiologic effects usually induced by histamine at H1 receptor sites. They are efficacious in controlling symptoms of allergic rhinitis like sneezing, rhinorrhea, itching. Some produced low rate sedation, while anticholinergic symptoms are grossly absent.

Topical azelastine and olopatadine are nasal sprays antihistamines that are effective in reducing allergic symptoms like sneezing, itching, rhinorrhea, congestion. On combination with a topical nasal corticosteroid, azelastine is also effective at managing both allergic and non-allergic rhinitis.

Second-generation oral antihistamines include cetirizine, levocetirizine, desloratadine, fexofenadine, and loratadine.

Cetirizine: It competes with histamine for H1 receptors in GI tract, blood vessels, and respiratory tract, reducing hypersensitivity reactions.

Levocetirizine: It is an active enantiomer of cetirizine, indicated for seasonal and perennial allergic rhinitis.

Fexofenadine: It competes with histamine for H1 receptors in GI tract, blood vessels, and respiratory tract, reducing hypersensitivity reactions.

Loratadine: It selectively inhibits peripheral histamine H1 receptors and is well tolerated.

Desloratadine: It is a long-acting tricyclic histamine antagonist selective for H1-receptor which relieves nasal congestion and systemic effects of seasonal allergy. It is a major metabolite of loratadine, which after ingestion is extensively metabolized to active metabolite 3-hydroxydesloratadine.

Combinations like **Pseudoephedrine/loratadine, Pseudoephedrine/fexofenadine, Cetirizine/ Pseudoephedrine** are also in use**.** Pseudoephedrine stimulates vasoconstriction by direct activation of alpha-adrenergic receptors of the respiratory mucosa, inducing bronchial relaxation and increasing heart rate and contractility by beta-adrenergic stimulation.

Leukotriene receptor antagonists

Leukotriene receptor antagonists are alternative to oral antihistamine for treatment of allergic rhinitis. One of the leukotriene receptor antagonists, montelukast has been approved for treatment of seasonal and perennial allergic rhinitis.

Montelukast: It is a selective leukotriene receptor antagonist that inhibits the cysteinyl leukotriene (CysLT 1) receptor. It selectively prevents action of leukotrienes released by mast cells and eosinophils.

Mast Cell Stabilizers

It produces mast cell stabilization and anti-allergic effects that inhibit degranulation of mast cells. Having no direct anti-inflammatory or antihistaminic effects, it may be used just before exposure to a known allergen. Treatment with this agent may be started one to two weeks before and continued daily to prevent seasonal allergic rhinitis. It has excellent safety profile and is thought to be safe for use in children and pregnancy.

Cromolyn sodium: It is indicated for seasonal or perennial allergic rhinitis. For patients with isolated and predictable periods of allergen exposure, administration is advised just before the exposure.

Decongestants

Decongestants stimulate vasoconstriction by direct activation of alpha-adrenergic receptors of the respiratory mucosa. Pseudoephedrine produces weak bronchial relaxation and is not effective for treating asthma. It increases heart rate and contractility by stimulating beta-adrenergic receptors, and increases blood pressure by stimulating alpha adrenergic

receptors. Pseudoephedrine is helpful for nasal and sinus congestion. Expectorants may thin and loosen secretions, thus preparations are available containing combinations of various decongestants, expectorants, or antihistamines.

Nasal corticosteroids

The intranasal steroids are divided into three generations based on their bioavailability. First generation corticosteroids, such as, beclomethasone, are more bioavailable and tend to produce more systemic adverse effects than newer intranasal corticosteroids and second- and third-generation.

Nasal steroid sprays are effective and safer monotherapy for allergic rhinitis, since it controls the major symptoms like sneezing, itching, rhinorrhea and congestion. In October 2013, the FDA approved once-daily triamcinolone acetonide nasal spray as an over-the-counter treatment for nasal allergy symptoms in children aged 2 years or older, adolescents, and adults. Flonase was approved by FDA to be available over the counter on July 24, 2014, and Rhinocort was recently approved on March 23, 2015.

Local adverse effects of nasal steroid sprays are minor irritation or nasal bleeding, which resolve with temporary discontinuation of the medication. They may also find use for vasomotor rhinitis or mixed rhinitis and can help to control nasal polyps.

Intranasal Beclomethasone: It is a corticosteroid with potent anti-inflammatory properties which elicits effects on various cells, including mast cells, eosinophils and inflammatory mediators like histamine, eicosanoids, leukotrienes, and cytokines.

Intranasal Budesonide: It is efficacious, safe for allergic rhinitis and may decrease number and activity of inflammatory cells, resulting in decreased nasal inflammation.

Fluticasone: Intranasal Fluticasone is a corticosteroid indicated for seasonal and perennial allergic rhinitis, which relieves nasal symptoms associated with allergic rhinitis and alsoimproves allergic eye symptoms.

Triamcinolone: Intranasal triamcinolone is efficacious and safe for allergic rhinitis, may decrease number and activity of inflammatory cells, resulting in decreased nasal inflammation.

Intranasal Mometasone: Intranasal mometasone reduces intraepithelial eosinophilia and inflammatory cell infiltration.

Nasal corticosteroids and antihistamine combinations

Here the antihistamine component inhibits the histamine release, which is responsible for causing the allergic response while the corticosteroid component inhibits inflammatory reactions. These combinations help in better compliance.

Intranasal Azelastine/fluticasone: Intranasal steroids and intranasal antihistamine combinations are more effective than using the individual component alone. However some patients may experience unpalatability.

Intranasal antihistamines: They are effective alternative to oral antihistamines in treating allergic rhinitis.

Intranasal Olopatadine: It is indicated for relief of symptoms of seasonal allergic rhinitis.

Intranasal anticholinergic agents

Intranasal anticholinergic agents are used for reducing rhinorrhea in patients with allergic or vasomotor rhinitis. It can be used alone or in conjunction with other medications.

Ipratropium: It is chemically related to atropine and has anti-secretory properties, and when applied locally, inhibits secretions from serous and seromucous glands lining the nasal mucosa. It has poor absorption by nasal mucosa; therefore, not associated with adverse systemic effects. However local adverse effects (eg, dryness, epistaxis, irritation) may occur.

Immunotherapy

Another way of management is immunotherapy which is a long-term process where noticeable improvement is often not observed for the initial 6-12 months, and therapy should be continued for 3-5 years. However carefully caution should be exercised for considering the risks and benefits of immunotherapy in each patient and weigh the risks and benefits of immunotherapy against the risks and benefits of the other management options to avoid serious reactions.

Immunotherapy is often combined with pharmacotherapy and environmental control and is an effective measure in conditions of severe disease forms non-responsive to other management approaches and complicated by comorbid conditions. Immunotherapy should only be performed by trained individuals who undertake appropriate precautions, and are equipped for addressing potential adverse events. Focused monitoring for signs of severe systemic or local allergic reaction is required after first dose administration, which should be given in supervision of a physician in a healthcare setting.

Sublingual Immunotherapy (SLIT)

Immunotherapy with daily sublingual (SL) tablets may be able to replace weekly injections in some individuals, depending on the offending allergens and are initiated 4 months before the specific allergen season.

Grass pollens allergen extract: SLIT is indicated for grass pollen–induced allergic rhinitis (with or without conjunctivitis) confirmed by positive skin test or in vitro testing for grass pollen–specific IgE antibodies for any of the 5 grass species contained in the product. In April 2014, the FDA approved a sublingual form (Oralair) consisting of 5 calibrated grass pollen extracts namely Perennial Ryegrass (*Lolium perenne*), Kentucky bluegrass (*Poa pratensis*), Timothy grass (*Phleum pratense*), Orchard grass (*Dactylis glomerata*), and Sweet Vernal grass (*Anthoxanthum odoratum*).

Timothy grass pollen allergen extract: SLIT for Timothy grass was also approved in April 2014 for adults and children aged 5 years or older, indicated for allergic rhinitis (with or without conjunctivitis) confirmed by positive skin test or in vitro testing for Timothy grass pollen-specific IgE antibodies.

Ragweed allergen extract: SL immunotherapy is indicated for allergic rhinitis (with or without conjunctivitis) confirmed by positive skin test or in vitro testing for ragweed (*Ambrosia artemisiifolia*) grass pollen-specific IgE antibodies. SLIT for ragweed was also approved in April 2014 for adults aged 18 years or older.

House dust mite immunotherapy: SLIT was approved by the FDA in 2017 for dust mite-induced allergic rhinitis with or without conjunctivitis, confirmed by in vitro testing for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house

dust mites, or skin testing to licensed house dust mite allergen extracts, in people of age group 18-65 years. SLIT can produce significant clinical improvement in elderly patients with allergic rhinitis caused by house dust mites, according to a study by Bozek et al which observed a group of patients aged 60-75 years with allergic rhinitis, as well as allergies to *Dermatophagoides pteronyssinus* and *D farinae*.

However, limitations do exist. SLIT may not be appropriate for everyone such as those affected by multiple allergens may not obtain relief of all of their symptoms by taking immunotherapy for only a single or more allergens. SLIT is more convenient than weekly injections in those with limited, specific allergies that match the SL product. Whether SLIT will be effective for non-pollen allergens other than dust mites needs further research.

CHAPTER IV
MATERIALS & METHODS

Study design, area and population

A prospective observational study was conducted in a part of city of Howrah in state of West Bengal of Eastern India. The study area (Belilias road, Kadamtala) consisted of two municipal wards (Ward no 21 & 22) with an area of 0.4024 sq km (Ward No 21) and 1.098 sq km (Ward no 22). As per Census 2011, the wards had a population of 11,285 (ward no 21) and 16,873 (ward no 22) respectively. (Fig 3, 4)

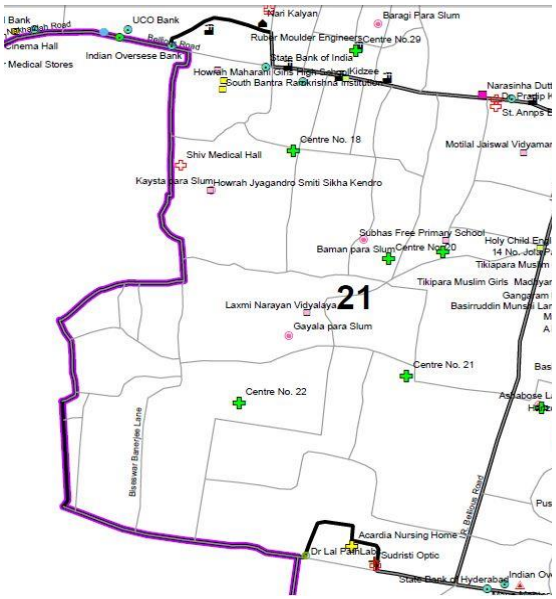


Fig 3: Geographical Map of Ward no 21

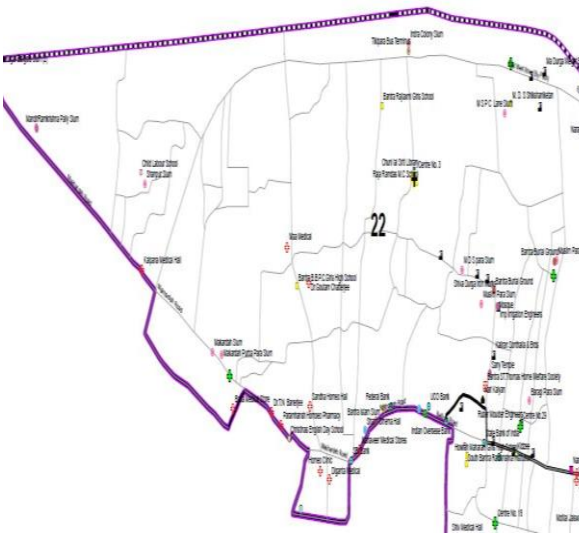


Fig 4: Geographical Map of Ward no 22

Apart from thick population, this area was important for having all the four sources of PM 2.5, which includes area source (restaurant, bakeries), point source (industries including steel-iron mills), on road mobile sources (commercial & private vehicles on public roadways), off road mobile sources (adjacent running trains, generators, construction equipment).The study included all the permanent adult residents (aged >20 yrs. to <70 yrs.) exposed to both ambient air pollutant and grass pollen persistently throughout the year (1-32 pollen/day/mm^3). Residents currently taking ≥10 mg OD prednisone or equivalent systemic corticosteroid, inability to perform complete respiratory symptom questionnaire, pregnant ladies and patients with unstable cardiac status i.e. recent history of Heart attack, chronic heart disease, and patients with hereditary (IgA) or acquired immune deficiency were excluded from the study.

Study Technique:

Study and Analysis of Aeroallergens-

Data of the airborne grass pollen samples (Family Poaceae) were collected using Burkard volumetric sampler that accurately determines the composition of the atmosphere.

Dominant pollen species in this area was *Cynodon dactylon* (L.) Pers, commonly known as Bermuda grass.

The Burkard trap takes samples at the same rate as the inhalation of pollen by normal human. Unit includes the sampling head, a metal drum, and a clock as a part of head. The turning of the clock leads the drum make a complete revolution in seven days at 2mm per hour (Figure 5-1 & 5-2).

Figure 5-1: Burkard Volumetric Spore Trap on the roof top of NSB, at the West Texas A&M University, Canyon, Texas. Fig. 5-2: Researcher P. Banerjee working with the Burkard Volumetric Spore Trap.

To collect the samples, the drum was prepared by placing it on the mounting stand and secured with a bolt. A small piece of double-sided tape was placed at the orifice starting positions between the two lines, and a clear one-sided tape with the sticky side up was attached on the double sided tape starting on the black line in the middle, winding the tape all the way around the drum and ended in the black line in the middle of the orifice start position. To place the drum in the spore trap, the head of the spore trap was fixed in place with a pin to prevent the wind from swinging the wind vane. The sampling head (lid assembly) was pulled straight up from the sampler by pressing down and rotating the locking arm 180 degree. The clock was then wound fully counter clockwise and the new drum was placed on the clock. The drum and the clock were then secured and placed back on the spore trap.

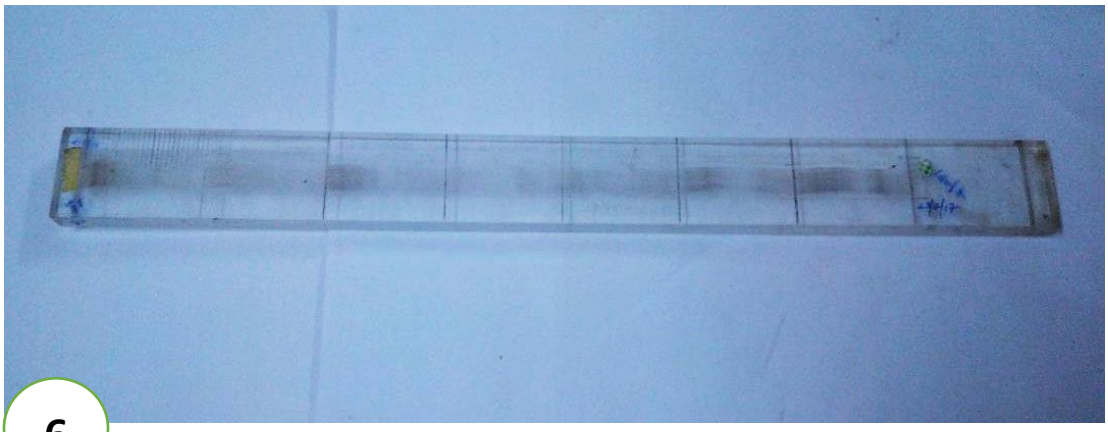


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Figure 6: Scaled Tape (Weekly) of Captured Pollen

The slides were prepared after the seven days' revolution by removing the tape from the drum and cutting them into seven 48 mm pieces. Each daily tape segments were fixed onto microscope slides. The tape (Figure 6) was mounted on the microscope slides by placing a few drops of distilled water on a clean slide, and placing the tape on the slide, making sure there were no air bubbles. A clean glass rod was used to stain the tape with the polyvinyl alcohol (PVA) stain. The slide was then complete and ready for observation under microscope after placing a 50mm glass coverslip over the slide. The slides were then observed under compound microscope. The slides were observed at magnifications of 4X, 10X, and 40X. The images were captured and pollens were identified at 40X magnifications. (Figure 7)

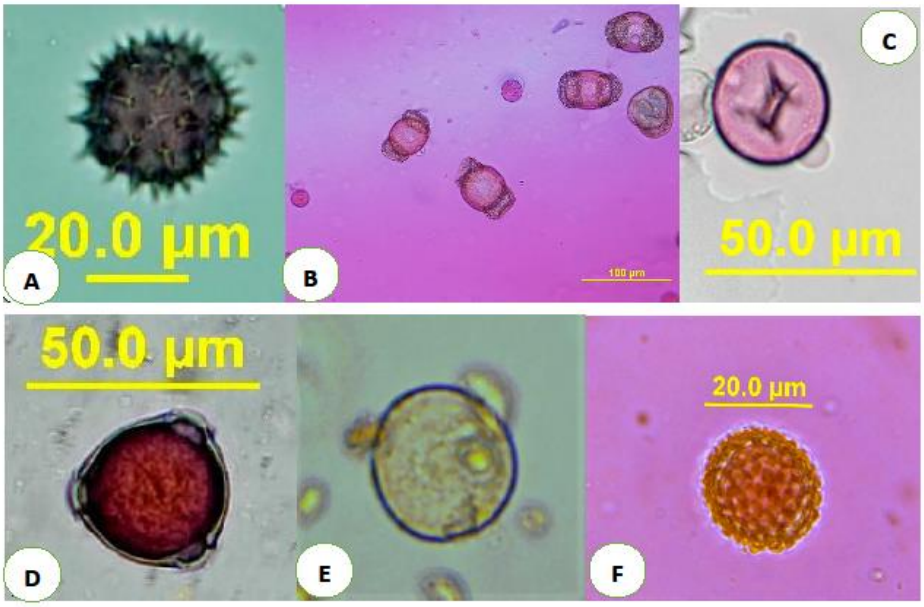

Figure 7: Microscopic pictures of captured pollen Figure 7A. ***Gaillardia pulchella, B. Pinus strobus, C. Juniperous macropoda, D. Solanum rostratum, E.*** **Grass pollen (Poaceae),** ***F. Ambrosia artemisiifolia***

Pollens were counted along five standardized latitudinal transverses using a Vernier micrometer scale on the microscope mechanical stage and graticule (100 micro meter) attached to the ocular of the microscope. Pollen counts were then converted into pollens per cubic meter of air sampled for each 24-hour period (pollen/mm^3/day). The pollen counts are only a small sample of the total numbers captured. Therefore, a correction factor must be used to attain a more precise representation of the actual concentration of the pollen grains per cubic meter of air. The scale that measures distances to the 1/100 division of 1mm is the graticule. Stage micrometer was used to calibrate the graticule, the correction factor for the microscope was 2.889. The following formula was used to obtain the daily mean concentration of pollen grains per cubic meter: N * CF = 0.28/ Width of one transverse (mm)

Ambient Air Pollutant Level

A 24 hours Ambient PM 2.5 level of the study area was gathered from the official website of West Bengal State Pollution Control Board, which determined local PM 2.5 values.

Daily Clinic Visit

Private clinics of 32 experienced (of at least 15 years duration) medical practitioner were identified in this locality and daily clinic visits of patients with acute (less than 7 days duration) precipitation of allergic upper respiratory inflammation like allergic rhinitis or allergic rhino conjunctivitis or allergic pharyngitis were noted.

Statistical Analysis:

Data collected was checked for completeness and then statistically analyzed. Descriptive data were represented as mean, standard deviation and range. Different levels were expressed at 95% Confidence Interval. A P-value of less than 0.05 were considered statistically significant. Mean values were compared with hypothesis testing as found applicable. Correlation analysis was attempted between PM 2.5 levels and aeroallergen with clinic visit.

CHAPTER V

RESULTS AND ANALYSIS

From March 2015 to June 2016, a descriptive summary of the daily ambient air quality in terms of 24 hours mean PM 2.5 concentration was obtained. In the entire study period under consideration, daily mean concentrations of PM 2.5 in this area was found to be 251.23 $\mu g/m^3$ which was quite above the permissible limit as enumerated by National Ambient Air Quality Standards (NAAQS). Daily mean concentration of pollen grains was found to be 6.77 per cubic meter as measured with help of using Burkard spore trap. (Figure 8, 9).

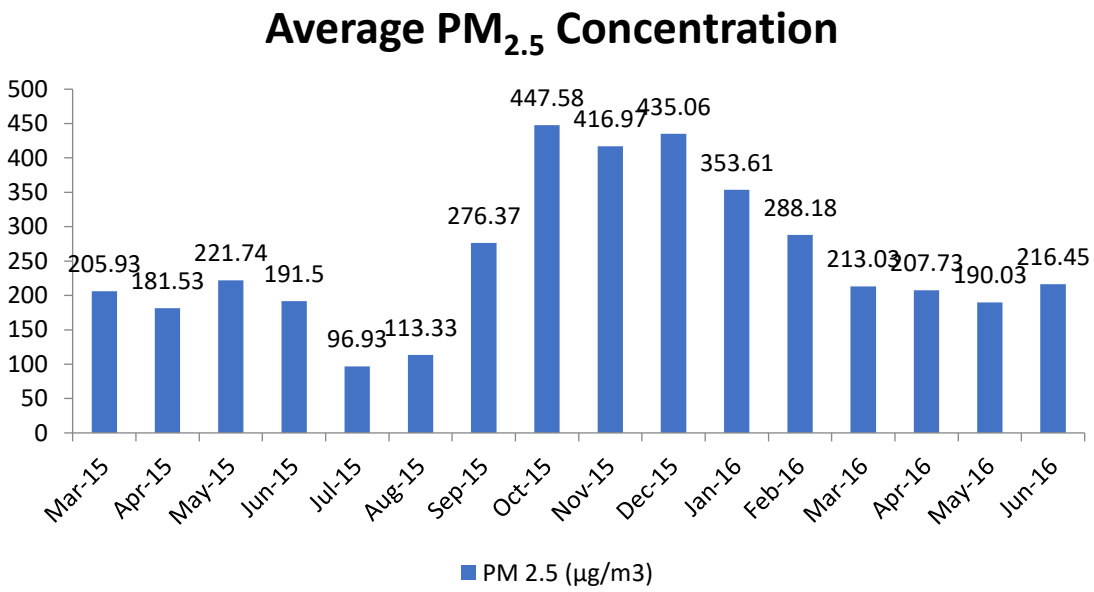

Figure 8: Average Monthly PM 2.5 Concentration (24 Hours) for the entire study duration

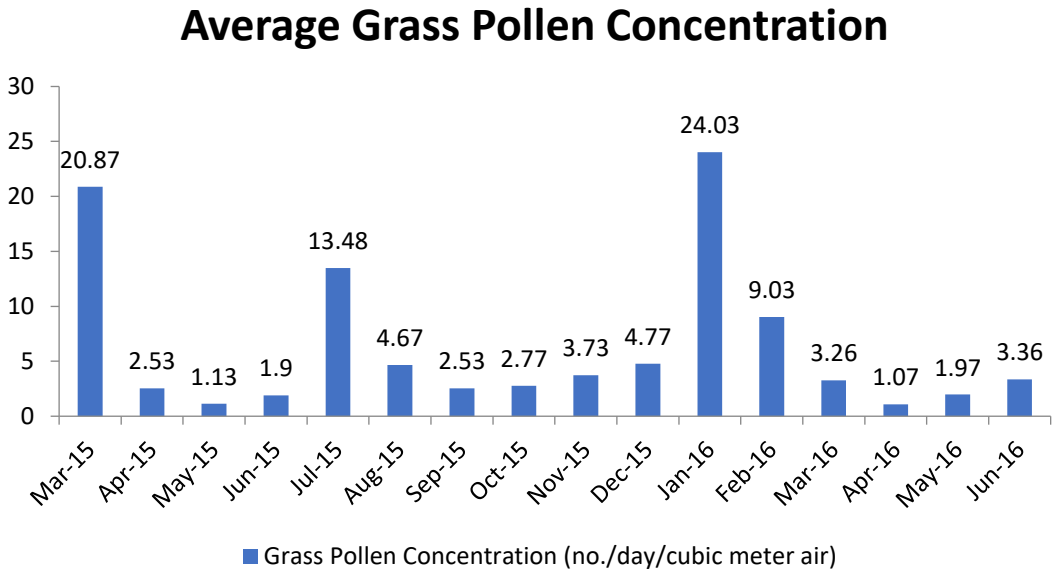

Figure 9: Average Monthly Grass Pollen Concentration for the entire study duration

The study identified 32 experienced medical practitioners around the study locality, whose clinics were under the purview and daily clinic visits with acute precipitation of respiratory

symptoms like allergic rhinitis or allergic rhino conjunctivitis or allergic pharyngitis were probed. Monthly mean clinic visits were represented. (Fig 10)

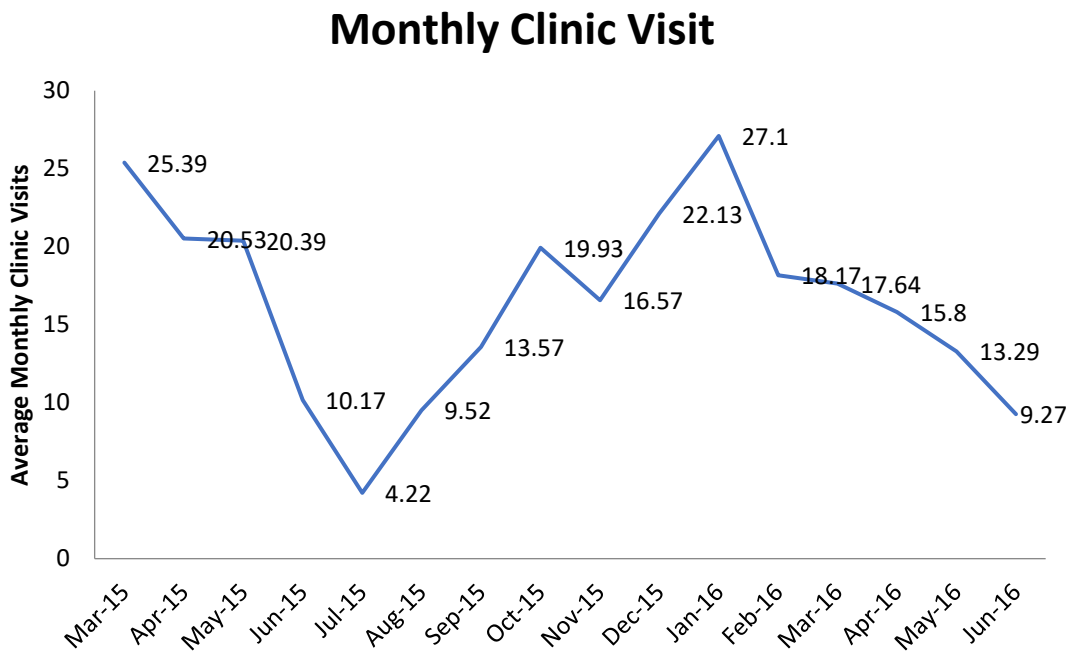

Figure 10: Mean Monthly Clinic Visits with acute precipitation of respiratory symptoms

Ambient air quality and precipitation of respiratory symptoms in terms of seasonal variation

The concentrations of fine particulate matter as well as pollens were observed to vary in different seasons. The mean PM 2.5 levels followed a similar trend as the concentrations reached the lowest averages during the summer season, slightly increasing during the monsoon, and reaching its peak during post monsoon and winters. Similarly average grass pollen concentration was found to be minimum in summer or premonsoon time, while being at peak in winters. Maximum grass pollen concentration has been observed in monsoon and winters. Average daily clinic visits due to acute precipitation of respiratory

symptoms were found to be maximum in winter followed by post and pre monsoon respectively. (Table 5)

Table 5:Daily PM 2.5, grass pollen concentration and precipitation of respiratory symptoms in terms of seasonal variation

	Mean	Minimum	Maximum	SD
Daily 24 hours PM 2.5 Concentration				
Pre Monsoon	198.52	91	419	84.40
Monsoon	153.435	25	562	121.30
Post Monsoon	432.52	205	601	81.47
Winter	314.56	33	572	121.36
Average Grass Pollen Concentration				
Pre Monsoon	1.85	0	6	1.47
Monsoon	6.95	0	28	6.52
Post Monsoon	3.25	0	7	1.48
Winter	10.29	1	38	9.46
Average Daily Clinic Visits with Acute Precipitation of Respiratory Symptoms				
Pre Monsoon	17.07	0	35	8.28
Monsoon	9.05	0	24	5.81
Post Monsoon	18.28	9	28	4.27
Winter	21.31	6	43	7.00

Management of acute precipitations of respiratory symptoms like allergic rhinitis or allergic rhino conjunctivitis or allergic pharyngitis included oral antihistamines and local steroids. Oral antihistamines have been used for 50 years. The second generation of oral antihistamines provides lower anticholinergic and sedative side effects and is more efficient, with a significant reduction of symptoms such as runny nose, nasal itching and sneezing. Nasal steroids are more effective than antihistamines for controlling nasal obstruction.

There was significant and positive association between personal exposure to PM 2.5 and clinic visit with precipitating respiratory symptoms. (Pearson's Correlation- 0.340, p= 0.000)Similarly positive correlation was also found with exposure to grass pollen and daily clinic visit. (Pearson's Correlation- 0.274, p= 0.000).

As per NAAQS, there are six AQI categories, namely Good, Satisfactory, Moderately polluted, Poor, Very Poor, and Severe considering measured short term (24 hours) ambient concentrations of eight pollutants (PM 10, PM 2.5, NO_2, SO_2, CO, O_3, NH_3, and Pb). Based on the corresponding standards and likely health impact, a sub-index is calculated for each of these pollutants. The worst sub-index reflects overall AQI. As for PM 2.5, a sub-index and its likely health impacts for different AQI categories has been represented. (Table 6)

Table 6: Health Impacts for various AQI Categories

AQI Category	PM 2.5 (24 Hrs)	Associated Health Impacts
Good	0 – 30	Minimal impact
Satisfactory	31 – 60	May cause minor breathing discomfort to sensitive people.
Moderately Polluted	61 – 90	May cause breathing discomfort to people with lung disease such as asthma, and discomfort to people with heart disease, children and older adults.
Poor	91 – 120	May cause breathing discomfort to people on prolonged exposure, and discomfort to people with heart disease.
Very poor	121 – 250	May cause respiratory illness to the people on prolonged exposure. Effect may be more pronounced in people with lung and heart diseases.
Severe	>250	May cause respiratory impact even on healthy people, and serious health impacts on people with lung/heart disease. The health impacts may be experienced even during light physical activity.

Based on these categorization, AQI was interpreted in terms of PM 2.5 levels in all seasons, which showed significantly severe AQI in winter and post monsoon time. ($p<0.005$) (Figure 11)

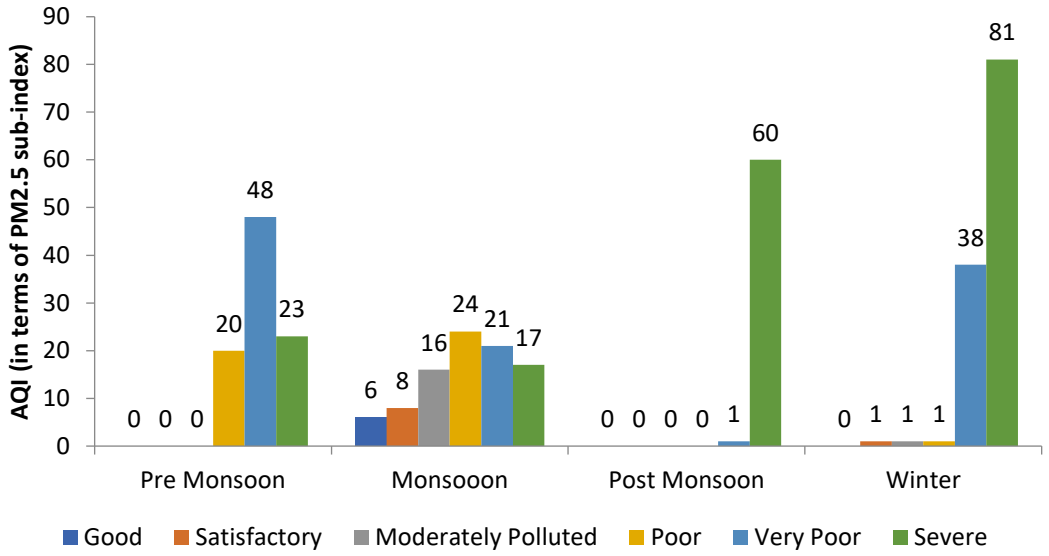

Figure 11: Air Quality Index in terms of PM 2.5 Concentration (as per seasonal variations).

CHAPTER VI

DISCUSSION

Past decades have witnessed a gradual change in air pollution spectra from its classical type being caused by sulfur dioxide and large dust particles to modern type characterized by nitrogen oxides, organic compounds, ozone, and ultrafine particles (Schäfer & Ring, 1997). Particulate matter has been the prime component of indoor and outdoor air pollution. PM, a complex, multi-pollutant mixture of solid and liquid particles suspended in gas, originates from a variety of manmade and natural sources. While natural pollution sources includes pollen, spores, bacteria, plant and animal debris, and suspended materials, man-made sources involves industrial emissions and combustion byproducts. On the other hand indoor sources consists of cigarette smoking, cooking, wood and other materials burned in stoves and fireplaces, cleaning activities that re-suspend dust particles, and the infiltration of outdoor particles into the indoor environment (McCormack et al., 2008).Vehicle emissions are the predominant source of fine PM in urban areas, where most people live globally **(**Ristovski et al., 2011). Airborne PM 10 is a complex mixture of materials with a carbonaceous core and associated materials such as organic compounds, acids, and fine metal particles (Pagan et al., 2003).

Physical properties of PM include mass, surface area, and number/size/distribution of particles, as well as physical state which influence the respiratory health in different ways

(Ristovski et al., 2011). Airborne PM inhalation increases respiratory and cardiac mortality and morbidity, and produces a range of adverse respiratory health outcomes such as asthma, lung function decline, lung cancer, and chronic obstructive pulmonary disease (COPD) (Ayres et al., 2008, Ristovski et al., 2011). Aggravation of asthma, with the exacerbation correlating with levels of environmental particles was also noted (Schwartz et al., 1993). PM triggers a series of biological processes including innate immunity inflammation, oxidative stress, apoptosis and autophagy, and an imbalance of T helper cells, all of which are associated with pathological changes in allergic respiratory diseases. It is well known that particulates of different aerodynamic diameters and chemical compositions can result in different inflammatory responses in the respiratory tract. As an adjuvant inducing lung inflammation to allergens or respiratory viruses, PM inhalation aggravates respiratory symptoms in patients with chronic airway diseases, but the mechanisms underlying this response remain poorly understood. Another significant contributor in this regard are aeroallergens like grass pollens, fungal spores, and other respirable antigens. The present study thus tried to probe the association of particulate matter (PM 2.5) emission and grass pollen exposure with acute presentations of respiratory tract inflammations in daily clinic visits.

The area chosen as the study area was a thick populated area embracing all the four sources of PM 2.5, namely area source, point source, on road and off road mobile sources. This 16 month study revealed that the average 24 hours PM 2.5 concentration was far beyond the permissible limits for ideal ambient air quality index. However this data can be attributed to the nearby industries and emission sources which have significantly contributed towards

the air quality worsening. Aeroallergens like grass pollen, in addition to this particulate matter have also been a complementary contributor to this concern.

In the entire 16 month study period, daily mean concentrations of PM 2.5 in this study area were found to be 251.23μg/m^3 which was quite above the permissible limit as enumerated by National Ambient Air Quality Standards (NAAQS). Daily mean concentration of grass pollen grains was found to be 6.77 per cubic meter as measured with help of using Burkard spore trap. The concentrations of fine particulate matter as well as pollens were observed to vary in different seasons. The mean PM 2.5 levels followed a similar trend as the concentrations reached the lowest averages during the summer season, slightly increasing during the monsoon, and reaching its peak during post monsoon and winters. Average daily (24 hours) PM 2.5 was found maximum at 432.52 $\pm$ 81.47 μg/m^3 in post monsoon season followed by 314.56 $\pm$ 121.36 μg/m^3 in winter.

Similarly average grass pollen concentration was found to be minimum in summer or premonsoon time, while being at peak in winters. Maximum grass pollen concentration has been observed in monsoon and winters. Average grass pollen concentration was found maximum at 10.29 $\pm$ 9.46 in winter season followed by 6.95 $\pm$ 6.52 m^3 in monsoon.

The study identified 32 experienced medical practitioners around the study locality, whose clinics were under the purview and daily clinic visits with acute precipitation of respiratory symptoms like allergic rhinitis or allergic rhino conjunctivitis or allergic pharyngitis were monitored and noted. Mean daily clinic visits was maximum at 21.31$\pm$ 7 for winters followed by 18.27 $\pm$ 4.27 in post and 17.07 $\pm$ 8.28 in pre monsoon respectively.

Management of acute precipitations of respiratory symptoms like allergic rhinitis or allergic rhino -conjunctivitis or allergic pharyngitis included oral antihistamines (first and second generation) along with intranasal corticosteroids. While the management of allergic rhinitis mainly involves environmental control measures and allergen avoidance include keeping exposure to allergens such as pollen, dust mites, and mold to a minimum, patients are often successfully treated with pharmacologic approach with oral antihistamines, decongestants, or both. Oral antihistamines have been used for 50 years. The second generation of oral antihistamines provides lower anticholinergic and sedative side effects and is more efficient, with a significant reduction of symptoms such as runny nose, nasal itching and sneezing. Nasal steroids are more effective than antihistamines for controlling nasal obstruction. For severe disease, poor response to other management options, and the presence of comorbid conditions or complications; immunotherapy is considered, often combined with pharmacotherapy and environmental control. While patients with intermittent symptoms are often treated adequately with oral antihistamines, decongestants, or both as needed, patients with chronic symptoms needs regular use of an intranasal steroid spray. The newer, second-generation (ie, non-sedating) antihistamines are usually preferable to avoid sedation and other adverse effects associated with the older, first-generation antihistamines. Ocular antihistamine drops, intranasal antihistamine sprays, intranasal cromolyn, intranasal anticholinergic sprays, and short courses of oral corticosteroids may also provide relief.

The study showed significant and positive association between personal exposure to PM 2.5 and clinic visit with precipitating respiratory symptoms. PM 2.5 is not only deposited in extra-thoracic airways but also penetrates deeper into the alveoli through air flow and

diffusion. Hence, PM 2.5 can induce various symptoms of pulmonary inflammation and structure impairment. PM 2.5 causes imbalance of T helper cells. High concentrations of PM 2.5 up-regulate TNFα and the Th2-mediated cytokines IL-4 and IL-10, while down-regulating the Th1-mediated cytokine IFNγ, which leads to an imbalance of the Th1/Th2 ratio. PM 2.5 was shown to significantly increase the expression of IL-13 and IL-17. Exposure to PM 2.5 is associated with oxidative stress and impaired lung function. A burst of reactive oxygen species induced by PM 2.5 was found in the neutrophils of asthmatic patients. Becker et al., (2005) revealed that PM 2.5 induces oxidative stress responses by inducing TNF-a, IL-6, and cyclooxygenase-2 (COX-2) expression in alveolar macrophages and human bronchial epithelial cells. Exposure to PM 2.5 can also induce apoptosis and autophagy. It has been postulated that PM 2.5 induces apoptosis and autophagy via three pathways in human lung epithelial cells: the TNF-a signaling pathway; the intrinsic apoptosis pathway via caspase-8 and caspase-3 signaling; and the cell autophagy pathway via caspase-9, caspase-3, and B-cell lymphoma 2 (BCL2).

Grass pollen exposure represents a major public health burden for patients with seasonal allergic rhinitis and asthma (Hill et al., 1979;Erbas et al., 20012 **).** Although grass pollen is generally regarded as the major outdoor aeroallergen source, there are limited studies posing its association with allergenic effects. Our study showed positive correlation between grass pollen exposure and daily clinic visit due to respiratory symptoms precipitation. Relationships between pollen counts and allergy symptoms are, however, likely to be complex, and influenced not only by severity of sensitization and cumulative exposure over the season, but also priming by exposure to tree pollens earlier in the season **(**Katelaris, **2000***)*. Whereas extended exposure to pollen could lead to chronic symptoms

with sustained nasal congestion, short duration exposure at high concentration could lead to more acute symptoms of rhinorrhea and sneezing, presenting as same-day and lagged effects. Owing to widespread presence in the outdoor air, pollens are difficult to avoid, however their reduction of outdoor exposure during the season in which a particular type of pollen is present can be an acceptable measure. Pollen counts tend to be on higher magnitude on dry, sunny, windy days. During this time, outdoor exposure can be limited though pollen counts are also influenced by a multitude of other factors. During the pollen season, closing the windows and doors of the house and car to the possible extent may be of some help. A shower taken after outdoor exposure may help remove the pollens stuck to the hair and the skin. Despite these measures, patients allergic to pollens usually remain symptomatic during this season and usually require some other form of management.

Local, current pollen counting and reporting, based on standardized methodology would assist with management of allergen exposure for patients at risk of symptom exacerbation due to pollen allergy. Although season timing is unlikely to be affected, different spore trap heights, type of spore trap (Burkard or Rotorod), sampling (weekly tapes or daily slides) and counting methodologies (including magnification and number of transects) may impact on seasonal counts. Projecting response of grass pollen and allergic disease to climate change requires repeated local pollen counts over many seasons with continual monitoring and validation of start and end dates. Late-season peaks may be particularly important for allergic disease, as earlier exposures can prime sufferers for symptoms, while later-season pollen may be more allergenic, and species composition and thus allergenic composition may differ. Identifying the species composition of these peaks, for example by molecular

characterization and phonologic studies, is imperative for predicting and understanding seasonal pollen allergic disease, which remains as a further avenue of research.

As per NAAQS, there are six AQI categories, namely Good, Satisfactory, Moderately polluted, Poor, Very Poor, and Severe considering measured short term (24 hours) ambient concentrations of eight pollutants (PM 10, PM 2.5, NO_2, SO_2, CO, O_3, NH_3, and Pb). Based on the corresponding standards and likely health impact, a sub-index is calculated for each of these pollutants. The worst sub-index reflects overall AQI. As for PM 2.5, a sub-index and its likely health impacts for different AQI categories were analyzed. In terms of PM 2.5 levels in all seasons, severe AQI were observed in winter and post monsoon time, suggesting respiratory impact even on healthy people, and serious health impacts on people with lung/heart disease. However the availability of a larger data set would allow for more rigorous analysis to fully unravel seasonal and region-specific associations in the future.

CHAPTER VII

CONCLUSION

The present study showed mean particulate matter concentration throughout the study period being far above the permissible standard limits. Increased aeroallergen concentration in this study site was also found prevalent. A seasonal variation of particulate matter and aeroallergen concentration was found to be significantly associated with precipitating respiratory symptoms amongst the residents of this area which upsurges a serious respiratory health concern. Stringent pollution control measures shall help to combat these deteriorating air quality issues thereby promising a healthier, safer and cleaner environment.

AHPCO as a remedy for the PM 2.5

A decade research in aerobiology and biotechnology developed an air purification system that uses Advanced Hydrated Photo Catalytic Oxidation (AHPCO) and Plasma Nanotechnology to reduce indoor aeroallergen to improve air quality and better food preservation. Air Oasis air purifiers utilize a new generation AHPCO technology that does not rely on filters or air passing through the air purifier. Innovations in technology continue to have massive impact on business and society. Technology is a process and a body of knowledge as much as a collection of artifacts. Biology is no different—and we are just beginning to comprehend the challenges inherent in the next stage of biology as a

human technology. It is this critical moment, with its wide-ranging implications, that Robert Carlson considers in *Biology Is Technology*. He offers a uniquely informed perspective on the endeavors that contribute to current progress in this area—the science of biological systems and the technology used to manipulate them. My co-researchers in Dr. Ghosh's Lab have been assessing the AHPCO and Plasma Nanotechnology for net reduction of bacteria, fungi, VOCs with the specific effect on Methicillin resistant S*taphylococcus aureus* (MRSA) and PM 2.5. A 5-year research project carried out at the BSA Hospital and Coulter Animal Hospital in Amarillo, Texas evidenced a gradual reduction of airborne bacteria, aeroallergens and VOCs in the indoor air thereby improving the air quality significantly when specialized air purification units were used in the Microbiology and Mycology Laboratories of the BSA Hospital.

Evaluations on safety measures showed no side effect on human cell cultures. Indoor aeroallergens such as, airborne fungal spores, airborne bacteria and animal dander reduced significantly on using the air purification units to improve indoor air quality and alleviating breathing ailments.

The air purification system developed with novel AHPCO and Plasma Nanotechnology efficiently reduced the indoor particulate matters, fungal spores and animal dander in course of progressive time interval. The major conclusive points from our research are summarized below. Investigation on assessing the efficiency of the AHPCO and Plasma Nanotechnology used in Air Oasis air purifiers showed the improvement of the Indoor Air Quality (IAQ) by--

Reducing the indoor particulate matters and aeroallergen concentration

Reducing the MRSA, (Methicillin Resistant *Staphylococcus aureus*) concentration

Reducing the VOCs (Volatile Organic Compounds)

Improving the odor from cigarette smoke

Assessing the safety measures showed no harmful effect of the AHPCO Air Purification system on the living system and cell culture. From their work it can be recommended that the AHPCO and the Plasma Nanotechnology may be used to reduce the indoor PM 2.5 concentration efficiently (Ghosh et al. 2017, 2018).

LIST OF ABBREVIATIONS

AQI : Air Quality Index

COPD: Chronic Obstructive Pulmonary Disease

CysLT : Cysteinyl Leukotriene Receptor

EPA : Environmental Protection Agency

ETS : Environmental Tobacco Smoke

FDA : Food And Drugs Administration

FEV : Forced Expiratory Volume

FVC : Forced Vital Capacity

HDM : House Dust Mites

NAAQS : National Ambient Air Quality Standards

OD : Once Daily

PAHs : Polycyclic Aromatic Hydrocarbons

PM : Particulate Matter

ROS : Reactive Oxygen Species

SLIT : Sublingual Immunotherapy

VOCs : Volatile Organic Compounds

WHO : World Health Organization

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