Journal of Air Pollution and Health (Spring 2016); 1(2):123-136

Review Article

Available online at http://japh.tums.ac.ir

CRITICAL REVIEW OF AIR POLLUTION HEALTH EFFECTS WITH SPECIAL CONCERN ON RESPIRATORY HEALTH

Morteza Abdullatif Khafaie[1], Chittaranjan S. Yajnik[2], Sundeep S. Salvi[3], Ajay Ojha[4]*

[1] Environmental Technologies Research Center & Department of Public Health, School of Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[2] King Edward Memorial Hospital Research Center, Pune, Maharashtra, India
[3] Chest Research Foundation (CRF), Pune, Maharashtra, India
[4] Technogreen Environmental Solutions, Pune, Maharashtra, India

ARTICLE INFORMATION

Article Chronology:

Received 11 November 2015
Revised 14 February 2016
Accepted 12 March 2016
Published 31 May 2016

Keywords:

air pollution; health effect; mechanism; respiratory system

CORRESPONDING AUTHOR:

m.khafaie@live.com
Tel: (+98 61) 33362536
Fax: (+98 61) 33361544

ABSTRACT:

Searching, PubMed (accessed Nov. 10, 2015) for "Air pollution" and "Health" resulted in 26,156 citations. Since the 1930 Meuse Valley episode in Belgium, Donora 1948 and the London fog of December 1952, the number of studies showing adverse health effects of short and long term exposure to outdoor air pollution has grown. This review looks at historical air pollution studies to get a general overview of the overall health effects that can be attributed to bad air quality. Then we specifically reviewed the important respiratory effects, the plausible mechanism and population at greater risk. Further research is central concern of researcher and policy maker to assess the plausible biological mechanisms of air pollution effects and identifying specific air pollutant that would be more dangerous

REVIEW

Historical perspective

1930 Meuse valley episode of Belgium

On December 4 and 5, a high atmospheric pressure and mild winds created an immobile fog in a narrow valley in Belgium, which entrapped pollutants and caused 60 deaths. Most of the deaths were in the small town of Engis [1].

Donora 1948

On October 26, accumulation of industrial pollutants from a local smelting plant over Donora, Pennsylvania, leads to an environmental disaster. The incident caused 20 sudden
deaths, 400 hospitalizations and affected half the residents [2].

London smog of December 1952

Demonstrated a turning point in the history of air pollution. From December 5 to 9, a dense fog loaded with pollutants from local stoves and industrial plants more or less paralyzed the entire city where black smoke and SO_2 concentration

Please cite this article as: Khafaie MA, Yajnik CS, Salvi SS, Ojha A. Critical review of air pollution health effects with special concern on respiratory health. Journal of Air Pollution and Health. 2016; 1(2): 123-136.

exceed 3000 μg/m^3. There was a 48% increase in all hospital admissions and a 163% increase in respiratory disease related admissions. During and shortly after the incident, the numbers of deaths were significantly elevated. A retrospective analysis indicated that there were approximately 12000 more deaths from December 1952 through February 1953 [3].

Bhopal episode of Madhya Pradesh

At midnight on Dec. 2nd and 3rd, India witnessed the worst industrial disaster in the world. The accidental released 40 tons of Methyl Iso Cyanate (MIC) spilled over from the Union Carbide factory in Bhopal, killing 2,500 to 6,000 people and making more than 20,000 people ill [4].
These events motivated nations around the world to put in place laws to limit the effects of air pollutants. The Clean Air Act and Air Quality Act in the United States, established in1963 and 1967 are especially notable.

General review of air pollution health effect

The associations between air pollution and health issues are derived from epidemiological studies (episode, time series, crossover, and cohort), toxicological studies and controlled human studies. A variety of acute physiological effects, including, induction of pulmonary and systemic inflammation [5], endothelial dysfunction[6], thrombosis [7, 8], arrhythmia[9], and blood pressure [10] reported which may contribute to long-term consequences of cumulated exposure [11] such subclinical indicators of, insulin resistance [12], metabolism disorder (i.e. diabetes [13-15]), respiratory [16, 17] and cardiovascular disease [18]. These morbidities ultimately lead to shorter life expectancies (see Table 1) [19].
In broad view, epidemiological air pollution studies looking at the temporal as well as spatial variations in concentrations of air pollution. We discussed the evidence that air pollution is associated with acute (i.e. outcome from episode and time series) and chronic health related event (i.e. cross-sectional and cohort) in human populations.

Short term health effect

Broadly two research approaches have been used to evaluate short term health effects of air pollution. One approach investigates whether the incidence of health related events (e.g. incidence of

Table 1. Respiratory and cardiovascular health effect of air pollution

	Lung	Heart/vasculature
Acute	- Forced expiratory volume and flows - Inflammatory mediators - Air way remodeling - Upper/lower respiratory symptoms, - Exacerbations, hospitalization - School/work absences - hospitalization	- Heart rate, blood pressure - Blood coagulation factor, vascular reactivity, inflammation - Vessel structure - Thrombosis, myocardial infarction, stroke, - Hospitalization - Death
Chronic	- Reduced lung growth - Reduced small airway function, - Chronic bronchitis - Asthma - Lung cancer - Reduced life expectancy	- Reduced life expectancy (premature cardiovascular death) - Atherosclerosis

deaths, hospitalization, subclinical Pathophysiological responses) can be correlated to episodes or daily fluctuations of air pollution in a population. This method generally uses available data on daily counts of health related events and relates these to ambient concentrations of air pollution on the same or previous days measured by central monitors situated in the study area. Alternative perspectives are individual-level studies, such as panel (group of individual followed over time) and case-crossover (comparing pollution at an index time close to the event with concentration at other referents times), which are of more complex design.

Mortality

Studies reporting daily changes in death counts attributable to short- term changes in air pollution are increasing. Evidence from a large number of time-series studies shows very clearly that air pollution is positively associated with increased mortality. For instance, a meta-analysis of time-series studies estimates that a 10μg/m^3 increase in daily $PM_{2.5}$ levels increases the daily cardiovascular mortality (RR= 0.4%- 1.0%) [20]. The most important studies of this kind are National Morbidity, Mortality, and Air Pollution Study (NMMAPS), which looked at a few cities in the U.S. [21-23] and a number of countries [24]; Air Pollution and Health: A European Approach (APHEA and APHEA-2) projects [25, 26]; a few time-series studies have also confirmed similar finding from Asia [27, 28]. The overall evidence from time-series analyses conducted worldwide confirms the existence of a small and consistent association between increased mortality and short-term elevations in number of air pollutants. Risks attributed to air pollution are not equally distributed within a population, with some, such as the elderly and those with "existing coronary artery or structural heart disease", more likely to be susceptible [29]. Also it has been noted that short term elevations in daily PM levels lead to a greater absolute risk for CVD-related mortality (69%) than for all other causes such pulmonary (28%) diseases [30]. Copper, et al. [31] conducted a time series study to find out impact of particulate air pollution on daily mortality in Delhi. They analyzed mortality data, 25% of total death in Delhi. They observed about 2.3% increase in daily non-accidental deaths per 10 μg/m^3 increase in total particulates, and also significant increase in deaths from respiratory and cardiovascular causes for selected age groups. Since studies from other countries showed an increase in death (6%) simultaneously, they attributed this difference to the fact that a larger proportion of deaths occur at younger age.

Hospitalization rate (clinical symptom)

Associations between daily measurements of the pollutants and daily admissions to the hospital for a variety of health related problem are also generally positive and significant. For instance, Dominici et.al. [32], investigated data from large number of U.S. cities (n=204), counties with 11.5 million individuals older than 65 years. Daily changes in $PM_{2.5}$ levels were associated with a range of cardiovascular and respiratory hospital admission. Different levels of association reported from different region (stronger in the Northeast than in other regions). It was suggested that these differences reflected variations in particle composition and pollution sources, but still more investigation is needed to explain this heterogeneity.

Subclinical pathophysiological response

Subclinical physiological changes occur in individuals in response to the inhalation of air pollution that do not become clearly noticeable. There are evidences that even short-term exposure to air pollution can result in changes to biomarkers of inflammation (local and systemic), oxidative stress, endothelial cell activity, vascular dysfunction, blood pressure, heart rate variability, etc. [33]. Reported associations usually vary from place to place. This disparity in finding could be explained by variations in the characteristics of

air pollution, exposure assessment methods, environments of exposure coupled with diversity in time frames, and host factors. However, this finding supports previous observable outcome (e.g. death, MI) and provides insight into the plausible mechanism whereby air pollution affects health.

Long term health effect

Some studies reporting long-term exposure to air pollution have inverse and statistically significant associations with life expectancy. Early population-based cross-sectional studies from as early as 1970 in U.S. metropolitan areas reported that mortality rates are associated with annual concentrations of $PM_{2.5}$ or SO_2 [34-36]. However, the studies were limited in controlling for individual factors, which could have potentially confounded the air pollution effects. The other main research approach is prospective studies which usually follow a group of subjects (cohort) for a number of years and provide important information about the amount of life lost or chronic health events due to air pollution. The evidence from two American studies from 1993 suggests that cardiovascular deaths increase when people live in areas with higher levels of air pollution. However, because prospective studies require collecting information on a large number of people and following them prospectively for long periods of time, they are costly, time consuming, and, therefore, much less common.

Although air pollution studies of short-term health effect (i.e. time series, panel, and cross-over) provide a vast amount of information about the role of pollution in inducing or accelerating the progress of chronic disease [36] , they are significantly less useful for estimating the health impact in terms of amount of life lost or additional admission to the hospital. Studies of long-term air pollution and health effect can be classified into three main types:

1)Studies of different occupational groups with different occupational exposure to pollutions; the unit of investigation is the occupational group (such as traffic police officers) and health issue (disease such as lung cancer). These types of studies do not deal with a mixture of pollutants. For instance, Wiwanitkit estimated the risk of cancer for traffic police officers is about 1.8 per 100000 per year [37].

2)Trend studies or studies of fixed populations with long-term changes in exposure to air pollution; before and after differences in pollution are related to before and after differences in health-related issues. Studies of this kind are follow-ups of the Harvard Six Cities study, which clearly showed a reduction in fine particulate air pollution was associated with improved overall mortality [38].

3)Studies of different population with different levels of long-term exposure to air pollutants; such studies provide information on each population's exposure (i.e. long-term exposure to traffic-related air pollution) and health related events (development of diabetes) [39].

All types of studies of long-term health effect of air pollution (named above) have some limitations such; a) Measurements of exposure to pollutants are extrapolated to a whole population, b) Air pollution involves a mixture of possible harmful components that shows a degree of association with each other and with other factors (such as temperature, barometric pressure and rainfall), and c) Observation of health related events between people exposed to different levels of air pollution are likely to be confounded by all the other socio-economic and cultural difference that might also explain different levels of disease.

Respiratory health effect

The respiratory system is the main portal of air pollution entry and as a biochemically active tissue involving mediators that induce both local and systemic effects after exposure [40]. Therefore the lung is the first organ affected within hours or after years of exposure. Growing evidence suggests that air pollution contributes to the large global burden of respiratory and allergic diseases, including asthma, chronic obstructive pulmonary disease, pneumonia, and possibly

tuberculosis [41]. This section will discuss the effects exposure to outdoor air pollution on the respiratory tract including lung function, pulmonary exacerbation, and disease rate (i.e. Asthma and COPD).

Lung function

Lung function is an important measure of chronic respiratory and systemic inflammation, as well as premature cardio-respiratory morbidity and mortality [42]. These same outcomes have been associated with ambient air pollution [43]. Therefore lung function is an important link in the investigation of effects of ambient air pollution. Over the past 20 years, many publications have investigated long-term effects of ambient air pollution on lung function with most finding adverse effects. There is strong evidence for an adverse effect of air pollution on lung function growth from cross-sectional studies [44-47] supported by longitudinal studies conducted in Europe [48-50] and the United States [51-53] but the size of the effect and which pollutants are responsible remains unclear (i.e. the extent to which long-term exposure to outdoor air pollution accelerates adult decline in lung function, increasing the risk of chronic respiratory disease and cause death by cardiovascular disease, is unclear).

In adults, the evidence for long-term air pollution effects is mostly based on cross-sectional comparisons [54, 55]. The Swiss SAPALDIA study is currently the only notable longitudinal study reporting significant associations between long-term exposure to air pollution and decline in lung function [56], whereas the earlier longitudinal studies had substantial limitations [57-60]. There is great diversity in study designs, types of air pollutants, exposure assessment, and measures of lung function. These limit the comparability of studies and hamper quantitative summaries. Results from longitude studies are conflicting. Nine years follow up of 5610 European multi-national adult, in European Community Respiratory Health Survey (ECRHS) by aim of testing the effect of long-term air pollution and its association with both lung function level and change in lung function, results in null association neither for average lung function levels nor change on lung function with city- specific annual mean $PM_{2.5}$ [61]. Where Swiss study on Air Pollution and Lung Disease in adults (SAPALDIA) exposure to air pollution not only associated with adverse effect on lung function [62] but it have beneficial impact when there is improvement in air quality [63] and respiratory symptoms.

New studies should use individual-level exposure assessment to clarify the role of traffic and to exclude potential community-level confounding. Further research is also needed to identify specific pollution sources which are more hazardous, and groups which are more susceptible. Table 2 summarizes the results of studies dealing with long-term exposure to air pollution and measures of lung function.

Table 2. Summary of long-term exposure to air pollution and lung function

Population	Design	Place/Years	Pollutant	Level/Resolution	Key finding	Ref.
N= 2841 ~ 48 years	Cross-sectional	central Italy/ 1991-93	Traffic-related	Group/ distance from main road	Alteration in - lung function	[64]
N=? Age >16	Cross-sectional	UK/1995-7, and 2001	PM_{10}, NO_2 , SO_2, O_3	Individual/ postcodes	- Decrease FEV_1	[65]
N=1983 children	Prospective	China/?	PM_{10}, NO_2, SO_2	Group/ geographical area	Decrease in growth rates of - FEF - FEV	[66]
N=5610 European	prospective	Europe/ 1991–93 and 2000–2002	$PM_{2.5}$	Group/ central monitor	- null	[61]

Table 2. Summary of long-term exposure to air pollution and lung function

Population	Design	Place/Years	Pollutant	Level/Resolution	Key finding	Ref.
N=5682 female	prospective	Tokyo / 1987 to 1994	NO_2, SPM	Group/residence area	- symptoms - Decrease in FEV_1	[59]
N≅ 167o 25- 59 years	prospective	Southern California	SO_x PM, NO_x	Group/geographic area	- FEV1 decline	[58]
N=1414 Adult	prospective	Cracow (1968-1981)	sulfur	Group/residence area	- Low FEV_1 - FEV_1 decline rate	[60]
N=1001 preadolesc	prospective	Poland/?	SPM, SO_2	Group/geographic area	- Lower lung function - Slower growths	[49]
N= ? Children	cross-sectional	United States/1980-1981	TSP, PM_{15}, $PM_{2.5}$, SO_2, O_3, NO_2	Group/geographic area	Increased risk of - Chronic cough - Bronchitis - Chest illness	[44]
N= ? ages 6–24	cross-sectional	United States/?	TSP, NO_2, SO_2	Group/geographic area	- FVC - FEV_1 - Peak expiratory flow	[45]

Asthma and chronic obstructive pulmonary disease (COPD)

Even though, the number of reports showing association between short-term exposure to air pollution and exacerbation of chronic obstructive pulmonary disease (COPD) and Asthma increasing but limited number of prospective cohort indicating long-term impact of air pollution on the development of these diseases and related symptoms. Cross-sectional studies based on large number of population from the USA(n=13369) [67], Switzerland (n=4470) [68], and Austria (n=843) [69] reporting increased risk of respiratory outcomes (disease and symptoms) and air pollution, where other study from Canada (n>1600) only showed lower levels of lung function among children living in more polluted area (SO_2, O_3) [70]. We have summarized result from studies dealing with long-term exposure to air pollution and respiratory outcomes (see Table 3).

Table 3. Long-term exposure to air pollution and respiratory disease and symptoms

Population	Design	Place/Year	Pollutants	Level/Resolution	Key finding	Ref.
N~4000 1-2 years	Prospective	Netherland 1996-7 1998-9	NO_2 $PM_{2.5}$ soot	Individual/home address	traffic-related air pollution was associated with self-reported prevalence of respiratory illness,	[71]
N=3535 children	Prospective	Southern California /?	Ozone NO_2 PM	Group/geographical area	Incidence of new diagnoses of asthma is associated with heavy exercise in communities with high concentrations of ozone	[72]
N=4757 55 years women	Cross sectional	Germany /1985–1994	NO_2 PM_{10}	group/8 km grid & distance from nearest major road	long-term exposure with air pollution from industrial sources and traffic had an adverse effect on pulmonary function, COPD	[73]
N~4000 First 4 years	Prospective birth cohort	Netherlands/ 1996-1997 1999-2000	NO_2, $PM_{2.5}$, soot	Individual/home address (land-use regression model)	Traffic-related air pollutants were positively associated with wheeze, asthma diagnosis, respiratory infections and sensitisation to food allergens	[74]

Table 3. Long-term exposure to air pollution and respiratory disease and symptoms

Population	Design	Place/Year	Pollutants	Level/Resolution	Key finding	Ref.
N=2,860 4 years N=3,061 6 years	Prospective birth cohort	Munich metropolitan area/Dec 2005	NO_2, $PM_{2.5}$	Individual/ home address & distance from the nearest main road	Strong positive associations were found between the distance to the nearest main road and atopic diseases (asthmatic bronchitis, hay fever, eczema), and sensitization	[75]
n = 4089 Children	Prospective birth cohort	Sweden/?	NOx, PM_{10}	Individual/home addresses (dispersion modeling)	Early life Exposure to traffic related air pollution influence the development of airway disease and sensitization	[76]
N=57,053	Prospective	Denmark /1993- 2006	NO_2 NOx	Individual/ indicators of traffic near the residential address at recruitment	Positive association between first-ever hospital admission for COPD and 35-year accumulated exposure to traffic-related air pollution at home address and modifying effects of asthma and diabetes.	[77]
N=3863 8 years.	Prospective	Netherlands /1996–1997	NO_2 $PM_{2.5}$ Soot	Individual/ land-use regression models	Levels of traffic-related air pollution was positively associated with incidence and prevalence of asthma, and the prevalence of asthma-related symptoms in children	[78]
10106 white preadolescent	Cross-sectional	United States /1974 and 1977	TSP TSO_4 SO_2	Group/geographic area	Frequency of cough, rates of bronchitis and a composite measure of lower respiratory illness were associated with air pollutants during the year preceding the health examination and lifetime mean TSP concentration	[79]
N=10,251 age 8-12	cross-sectional	United States and Canada	PM_{10}	Group/geographic area	Living in area with High levels of pollution were significantly associated with prevalence of bronchitis	[80]

Mechanism of air pollution health effect

Ambient air contains various pollutants such as diesel exhausts which contain free radicals or highly oxidative gases (e.g. O_3 or NO_x). The release of reactive oxygen species from lung cells upon contact with inhaled particles ,where toxic substances such as metals are adsorbed, attack and oxidize other cell component in the lungs [81]. This leads to tissue injury and the influx of inflammatory cells to the sites of injury [82]. Activated inflammatory cells also generate and release large quantity of free radical [83]. In the absence of anti-oxidants, these free radicals attack local tissue and component and cause cell injury in the lung with the development of histological pulmonary inflammatory foci [11]. Extensive numbers of experimental studies have shown that lung epithelial cells and alveolar macrophages generate a rich milieu of inflammatory mediators when exposed to atmospheric particles. Furthermore increased oxidative stress production and development of inflammation in the lungs may transduce to the systemic tissues. Systemic inflammatory reactions, mediated through cytokines and chemokines, have been described in vitro [84], in vivo [85, 86], and in chamber studies with human subjects [87] (see Table 4).

Table 4. Result from studies investigating association between air pollution and inflammatory components responses

Population	Exposure type	Outcomes	Result	Ref.
Healthy young subjects	Air pollutants during the 1997 Southeast Asian forest fires	Cytokines	Elevate levels of - IL-1, IL-6 - GM-CSF	[88]
N=38 healthy subject	Particles concentrated air	Cells and fluid obtained by bronchoalveolar lavage	Increased - fibrinogen	[87]
N= 79 Honduran women cooking with traditional or improved cook stoves	Indoor and personal monitoring of CO and PM_{10}	Pulmonary function and respiratory symptoms C-reactive protein	Null	[91]
Normal hamster	Concentrated ambient particulates, residual oil fly ash, and their water-soluble and particulate fractions	Intracellular oxidant production in alveolar macrophages	Increased in - TNF-alpha - AMs macrophage	[86]
in VITRO, AM & human bronchial epithelial cells	Ambient coarse & fine PM	Inflammation & oxidant stress	Inhibited - mRNA & protein Decreased - TLR4 in the macrophages	[84]
45 schoolchildren with persistent asthma	Personal active sampler exposures	Exhaled nitric oxide	- Increase F_{ENO}	[92]

These findings, also, have been supported by population base studies [88] (see Table 5). Systemic effect of air pollution may either be result from indirect release of inflammatory mediators into the blood or they could be the result of translocation of particles or their chemical constituents into the systemic circulation with direct action at the target sites [33, 89]. Additional experiments show that air pollution exposure could induce autonomic nervous system imbalance [90]. However, inflammation in the lungs, caused by deposited particles, can be seen as a key process that could mediate adverse effects on the cardiovascular system.

Table 5. Studies investigated short-term air pollution effect on C-reactive protein

Population	Place/Years	Pollutant(s)	Outcomes	Key finding	Ref.
N=112 60+ years	UK/1996-1998	Personal exposure and city center measurements of PM_{10}	Repeated Measurement: Hemoglobin, Pecked Cell Volume, Red Cell Count, platelets, white cell count, IL-6, CRP, Fibrinogen, Factor VII	Decrease in Hb, PCV, RCC, Platelets, Factor VII. & Increase in CRP	[93]
N=631 male MONICA Augsburg Cohort	Southern Germany/ 1984-85 & 1987-88	-1985episode -SO_2, TSP, and CO	Repeated measurement CRP	CRP concentration increased during 1985 episode. Also elevated CRP, were associated with SO_2, and TSP	[94]

Table 5. Studies investigated short-term air pollution effect on C-reactive protein

Population	Place/Years	Pollutant(s)	Outcomes	Key finding	Ref.
N= 9 male Healthy Nonsmoking, 23-30 years	North Carolina/ 2001	-In-vehicle $PM_{2.5}$ -Central $PM_{2.5}$ -Road side $PM_{2.5}$	Repeated measurement: CRP	HRV, ectopic beats, blood inflammatory and coagulation markers, and MCV showed increase associated with in-vehicle exposure to $PM_{2.5}$	[95]
N=88 elderly	Utah (U.S)/ 1999-2000	Central $PM_{2.5}$	Repeated measurement: Heart Rate, (SDNN, SDANN, r-MSSD), CRP, Monocytes	$PM_{2.5}$ were negatively associated with HRV,and CRP but not with changes in WBC, RBC, platelets, or whole-blood viscosity.	[96]
N=57 male with CHD	Erfurt (Germany)/2000-2001	Central UFP 0.01-0.1 $PM_{2.5,10}$,Gaseous , EC, and OC	Repeated measurement: CRP, SAA, Factor VII, vWf, Fibrinogen, ICAM-1 ,E-selectin	ICAM-1 and CRP were associated with all of pollutants ambient except EC and OC, with a higher association on lags 1 and 2 respectively.	[97]
N=6814 45- 84 years MESA	U.S/ 2000-2002	Central $PM_{2.5}$	CRP	Only average 30 and 60 days exposure to $PM_{2.5}$ were weakly associated with CRP and no other lags days	[98]
N=710 male Normative Aging Study	Boston ,U.S/ 2000 -2004	Central site near the examination site. PN, BC, $PM_{2.5}$,SO_2	WBC, CRP, SR, and Fibrinogen	PN and BC had greater association with inflammatory markers, than $PM_{2.5}$ and SO_2. Elder (>78 years.) and obese were the more vulnerable subject to this effect. Also a suggestion for a protective effect of Statin use on effect of particles on inflammatory markers observed	[99]
N=1003 35-80 post-MI	Greece, Germany, Spain, Finland, Italy, and Sweden/ 2003- 2004	Central, $PM_{2.5,\ 10}$, gaseous (SO_2, NO_2, NO, CO, O_3), PNC, BS, BC	Repeated measurement: IL-6, CRP, Fibrinogen	Elevated PNC 12- 17 hrs before the clinical visit increased IL-6. Cumulative exposure, to PM_{10} & $PM_{2.5}$ were associated with an increase in fibrinogen and not CRP	[100]
N=76 young, healthy students	Taipei/ 2004 2005	Air monitoring station $PM_{2.5\ \&\ 10}$ SO_2, NO_2, CO, and O_3	Repeated measurement of CRP, 8-OHdG, PAI-1, Plasma tPA, and HRV	Ambient air pollution were associated with increases in hs-CRP, 8-OHdG, fibrinogen, and PAI-1, and decreases in HRV indices	[101]
N=3659	Tel-Aviv/ 2003 & 2006	City central monitored PM_{10}, SO_2, NO_2, CO, and O_3	Fibrinogen, CRP, and WBC	In the male, negative correlation between NO_2, SO_2, and CO, and fibrinogen in several lag days, and PM_{10} at day 7	[102]
N=1696 pregnant women	U.S/ 1997-2001	Nearest monitoring station, PM_{10} & $PM_{2.5}$, CO, NO_2, SO_2, and ozone	CRP	Increase PM_{10} and $PM_{2.5}$ prior to the blood sample was associated with high CRP.	[103]
N= 1700 Diabetes patients	Pune India 2007	City central monitoring station; PM_{10}, SO_2, NO_x	CRP	SO_2 and oxides of nitrogen (NOx) in ambient air, were associated with increased in CRP.	[104]

Who is at greater risk

Vulnerability and susceptibility to the adverse health effects of air pollution could be related either to variation in exposure between individual and groups or to the degree to which individuals or groups may respond to a given exposure. For instance, people living or working (e.g. bus drivers, traffic police officers) along highly trafficked roads are a vulnerable group. Susceptible group includes children (because they breathe a greater volume of air relative to their body weigh), elderly subjects (especially subjects with pre-existing heart or lung disease) and poorly educated populations.

- Oxidant-antioxidant activity is a key characteristics of susceptibility: it appears likely that an individual's sensitivity to pollution is related, in part, to their pulmonary antioxidant defenses. This could involve modification effect of variation in gens or condition (such obesity, elderly, pre-existing disease) which involved is in inflammatory processes, defense against reactive oxygen species formed by particulate matters, or enzymes involved in the detoxification toxic compounds present in ambient air.
- Obesity is a metabolic condition that influences immune function [105]. It plays significant role in pro-inflammatory mediators' production in adipose tissue that contributes to a low-grade state of systemic inflammation [106]. Consequently, oxidant- antioxidant imbalances and alterations in physiological systems can largely influence the response of the lungs to inflammatory stimuli such air pollution [107].
- Aging: it is also accompanied by changes in the functions of leukocytes and antioxidant defenses. Lowering of the antioxidant defenses in the elderly could predispose them to amount inappropriate and harmful inflammatory responses.

CONCLUSIONS

The National Research Council (NRC) declared that there needs to be more research on the long-term health effects of air pollution exposure in two areas: first the effects of PM in combination with gaseous pollutants (such as nitrogen dioxide), and the effects on potentially susceptible groups. Also SAPALDIA and Health Effects Institute (HEI) also recommend further studies to address unresolved issues, such as why some persons suffer more from the exposure to air pollution than others.

However, Asian studies on adverse health effects of air pollution are limited to a few cross sectional studies. That is because monitoring of air quality in most cities is irregular, incomplete and inaccessible, and hospital based health records and incomplete death records available with municipal authorities. No Asian prospective study has been published on the impacts of air pollution on respiratory health especially on susceptible group such diabetic's patient since this would require an assessment of individual exposures.

FINANCIAL SUPPORTS

The study was supported by the Welcome Trust (London, U.K.).

COMPETING INTERESTS

No potential conflicts of interest relevant to this article were reported

ACKNOWLEDGEMENTS

This review is part of PhD thesis report from Interdisciplinary School of Health Sciences, University of Pune. M.A.K. discussed, and edited the manuscript. C.S.Y., S.S.S. and A.O. edited the manuscript. The authors acknowledge the contributions of K. Kumaran (King Edward Memorial Hospital) and Gayathri Vaidyanathan (Environment and Energy Publishing's Energywire-Washington DC) in improving the language.

ETHICAL CONSIDERATIONS

"Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors."

REFERENCES

[1] Nemery B, Hoet PH, Nemmar A. The Meuse Valley fog of 1930: an air pollution disaster. The Lancet. 2001;357(9257):704-8.
[2] Helfand WH, Lazarus J, Theerman P. Donora, Pennsylvania: an environmental disaster of the 20th century. American journal of public health. 2001;91(4):553.
[3] Bell ML, Davis DL. Reassessment of the lethal London fog of 1952: novel indicators of acute and chronic consequences of acute exposure to air pollution. Environmental health perspectives. 2001;109(Suppl 3):389-94.
[4] Bucher JR. Methyl isocyanate: A review of health effects research since Bhopal. Fundamental and Applied Toxicology. 1987;9(3):367-379.
[5] Mazzoli-Rocha F, Fernandes S, Einicker-Lamas M, Zin WA. Roles of oxidative stress in signaling and inflam-

mation induced by particulate matter. Cell biology and toxicology. 2010;26(5):481-98.
[6] Alexandra S, Lucas N, Margaret CH, Martin C, Ronald WW, Wayne CA, et al. Endothelial Dysfunction: Associations with Exposure to Ambient Fine Particles in Diabetic Individuals. Environmental Health Perspectives. 2008;116(12):1666–1674.
[7] Franchini M, Mannucci PM. Thrombogenicity and cardiovascular effects of ambient air pollution. Blood. 2011;118(9):2405-12.
[8] Mutlu GM, Bryce PJ, Budinger GRS. Linking air pollution exposure with thrombosis. Blood. 2011;118(9):2636-7.
[9] Link MS, Dockery DW. Air pollution and the triggering of cardiac arrhythmias. Current opinion in cardiology 2010;25(1):16-22.
[10] Hoffmann B, Luttmann-Gibson H, Cohen A, Zanobetti A, de Souza C, Foley C, et al. Opposing effects of particle pollution, ozone and ambient temperature on arterial blood pressure. Environmental health perspectives. 2012;120(2):241-46.
[11] Gomez-Mejiba SE, Zhai Z, Akram H, Pye QN, Hensley K, Kurien BT, et al. Inhalation of environmental stressors & chronic inflammation: autoimmunity and neurodegeneration. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 2009;674(1):62-72.
[12] Sun Q, Yue P, Deiuliis J, Lumeng C, Kampfrath T, Mikolaj M, et al. Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity. Circulation. 2009 2009;119(4):538-46.
[13] Brook RD, Jerrett M, Brook JR, Bard RL, Finkelstein MM. The relationship between diabetes mellitus and traffic-related air pollution. Journal of Occupational and Environmental Medicine / American College of Occupational and Environmental Medicine 2008;50(1):32-8.
[14] Marquez EB, Diaz BR, Gurian PL. Understanding the associations between statewide diabetes prevalence and air pollution emissions. Diabetes care 2004;27(6):1515-7.
[15] Lockwood AH. Diabetes and air pollution. Diabetes care 2002;25(8):1487-8.
[16] Ristovski ZD, Miljevic B, Surawski NC, Morawska L, Fong KM, Goh F, et al. Respiratory health effects of diesel particulate matter. Respirology (Carlton, Vic.). 2012;17(2):201-12.
[17] van Eeden SF, Yeung A, Quinlam K, Hogg JC. Systemic response to ambient particulate matter: relevance to chronic obstructive pulmonary disease. Proceedings of the American Thoracic Society. 2005;2(1):61-7.
[18] Sun Q, Hong X, Wold LE. Cardiovascular effects of ambient particulate air pollution exposure. Circulation. 2010;121(25):2755-65.
[19] Fann N, Lamson AD, Anenberg SC, Wesson K, Risley D, Hubbell BJ. Estimating the National Public Health Burden Associated with Exposure to Ambient PM2.5 and Ozone. Risk analysis : an official publication of the Society for Risk Analysis. 2012;32(1):81-95.
[20] Pope CA, 3rd, Dockery DW. Health effects of fine particulate air pollution: lines that connect. Journal of Air and Waste Management Association. 2006;56(6):709-42.
[21] Dominici F, McDermott A, Zeger SL, Samet JM. National maps of the effects of particulate matter on mortality: exploring geographical variation. Environ Health Perspect 2003;111(1):39-44.
[22] Peng RD, Dominici F, Pastor-Barriuso R, Zeger SL, Samet JM. Seasonal analyses of air pollution and mortality in 100 US cities. American Journal of Epidemiology. 2005;161(6):585-94.
[23] Samet Jm Fau - Dominici F, Dominici F Fau - Curriero FC, Curriero Fc Fau - Coursac I, Coursac I Fau - Zeger SL, Zeger SL. Fine particulate air pollution and mortality in 20 US cities, 1987-1994. New England Journal of Medicine. 2000;343(24):1742-9
[24] Dominici F, Peng RD, Ebisu K, Zeger SL, Samet JM, Bell ML. Does the effect of PM10 on mortality depend on PM nickel and vanadium content? A reanalysis of the NMMAPS data. Environmental Health Perspective. 2007;115(12):1701-3.
[25] Analitis A, Katsouyanni K, Dimakopoulou K, Samoli E, Nikoloulopoulos AK, Petasakis Y, et al. Short-term effects of ambient particles on cardiovascular and respiratory mortality. Epidemiology. 2006;17(2):230-3.
[26] Katsouyanni K. Ambient air pollution and health. British Medical Bulletin. 2003;68(1):143-56.
[27] Omori T, Fujimoto G, Yoshimura I, Nitta H, Ono M. Effects of particulate matter on daily mortality in 13 Japanese cities. Journal of Epidemiology. 2003;13(6):314-22.
[28] Wong CM, Vichit-Vadakan N, Kan H, Qian Z. Public Health and Air Pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality. Environmental Health Perspectives. 2008;116(9):1195-202.
[29] Pope CA, Muhlestein JB, May HT, Renlund DG, Anderson JL, Horne BD. Ischemic heart disease events triggered by short-term exposure to fine particulate air pollution. Circulation. 2006;114(23):2443-8.
[30] Dominici F. Time-series analysis of air pollution and mortality: a statistical review. Research report (Health Effects Institute). 2004(123):3-27; discussion 29-33.
[31] Cropper ML, Simon NB, Alberini A, Sharma P. The health effects of air pollution in Delhi, India. World Bank Policy Research WorkingPaper. 1997(1860).
[32] Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, et al. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. Jama. 2006;295(10):1127-34.
[33] Brook RD, Rajagopalan S, Pope CA, Brook JR, Bhatnagar A, Diez-Roux AV, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation. 2010;121(21):2331-78.

[34] Lave LB, Seskin EP. Air pollution and human health. Science 1970;169(3947):723-33.
[35] Evans JS, Tosteson T, Kinney PL. Cross-sectional mortality studies and air pollution risk assessment. Environment international. 1984;10(1):55-83.
[36] McMichael AJ, Anderson HR, Brunekreef B, Cohen AJ. Inappropriate use of daily mortality analyses to estimate longer-term mortality effects of air pollution. International Journal of Epidemiology. 1998;27(3):450-3.
[37] Wiwanitkit V, Suwansaksri J, Soogarun S. Cancer risk for Thai traffic police exposed to traffic benzene vapor. Asian Pac J Cancer Prev. 2005;6(2):219-20.
[38] Laden F, Schwartz J, Speizer FE, Dockery DW. Reduction in fine particulate air pollution and mortality: Extended follow-up of the Harvard Six Cities study. American Journal of Respiratory and Critical Care Medicine. 2006;173(6):667-72.
[39]` Andersen ZJ, Raaschou-Nielsen O, Ketzel M, Jensen SS, Hvidberg M, Loft S, et al. Diabetes incidence and long-term exposure to air pollution: a cohort study. Diabetes care. 2012;35(1):92-8.
[40] Bates ML, Bascom R. Air Pollution and the Pulmonary Vasculature. Textbook of Pulmonary Vascular Disease: Springer; 2011. p. 963-77.
[41] Laumbach RJ, Kipen HM. Respiratory health effects of air pollution: Update on biomass smoke and traffic pollution. Journal of Allergy and Clinical Immunology. 2012;129(1):3-11.
[42] Sin D, Wu L, Man S. The relationship between reduced lung function and cardiovascular mortality: a population-based study and a systematic review of the literature. CHEST Journal. 2005;127(6):1952–59.
[43] Pope Cr, Dockery D. Health effects of fine particulate air pollution: lines that connect. Journal of the Air Waste Management Association. 2006;56(6):709–42.
[44] Dockery D, Speizer F, Stram D, Ware J, Spengler J, Ferris BJ. Effects of inhalable particles on respiratory health of children. American Review of Respiratory Disease. 1989;139(3):587-594.
[45] Schwartz J. Lung function and chronic exposure to air pollution: a cross-sectional analysis of NHANES II. Environmental Research. 1989;50(2):309-21.
[46] Peters J, Avol E, Gauderman W. A study of twelve Southern California communities with differing levels and types of air pollution. II. Effects on pulmonary function. American Journal of Respiratory and Critical Care Medicine. 1999;159(3):768-75.
[47] Khafaie A. M, Salvi SS, Khafaie B, Ojha A, Yajnik CS. The impact of air pollution on respiratory health among diabetes and non-diabetes subject in Pune, India. Environment and Health—Bridging South, North, East and West. Environmental Health Perspective; .2013: p. P-1-25-16.
[48] Frischer T, Studnicka M, GARTNER C, Tauber E, Horak F, Veiter A, et al. Lung function growth and ambient ozone: a three-year population study in school children. American journal of respiratory and critical care medicine. 1999;160(2):390-6.
[49] Jedrychowski W, Flak E, Mróz E. The adverse effect of low levels of ambient air pollutants on lung function growth in preadolescent children. Environmental Health Perspectives. 1999;107(8):669-74.
[50] Horak FJ, Studnicka M, Gartner C. Particulate matter and lung function growth in children: a 3-yr follow-up study in Austrian schoolchildren. European Respiratory Journal. 2002;19(5):838-45.
[51] Gauderman WJ, Gilliland GF, Vora H, Avol E, Stram D, McConnell R, et al. Association between air pollution and lung function growth in southern California children: results from a second cohort. Am J Respir Crit Care Med 2002;166(1):76-84.
[52] Avol EL, Gauderman WJ, Tan SM, London SJ, Peters JM. Respiratory effects of relocating to areas of differing air pollution levels. American Journal of Respiratory and Critical Care Medicine. 2001;164(11):2067-72.
[53] Gauderman WJ, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, et al. The effect of air pollution on lung development from 10 to 18 years of age. New England Journal of Medicine. 2004;351(11):1057-67.
[54] Ackermann-Liebrich U, Leuenberger P, Schwartz J, Schindler C, Monn C, Bolognini G, et al. Lung function and long term exposure to air pollutants in Switzerland. Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) Team. American journal of respiratory and critical care medicine. 1997;155(1):122-9.
[55] Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann H-E, et al. Long-term air pollution exposure and living close to busy roads are associated with COPD in women. Respir Res. 2005;6(1):152.
[56] Downs SH, Brändli O, Zellweger J-P, Schindler C, Künzli N, Gerbase MW, et al. Accelerated decline in lung function in smoking women with airway obstruction: SAPALDIA 2 cohort study. Respiratory research. 2005;6(1):45.
[57] van der Lende R, Kok T, Peset R, Quanjer P, Schouten J, Orie N. Longterm exposure to air pollution and decline in VC and FEV1: Recent results from a longitudinal epidemiologic study in the Netherlands. CHEST Journal. 1981;80(1- Supplement):23S–26S.
[58] Tashkin D, Detels R, Simmons M, Liu H, Coulson AH, Sayre J, et al. The UCLA population studies of chronic obstructive respiratory disease: XI. Impact of air pollution and smoking on annual change in forced expiratory volume in one second. American Journal of Respiratory and Critical Care Medicine. 1994;149(5):1209–17.
[59] Sekine K, Shima M, Nitta Y, Adachi M. Long term effects of exposure to automobile exhaust on the pulmonary function of female adult in Tokyo, Japan. Occupational Environmental Medicine. 2004;61(4):350–7.
[60] Jedrychowski W, Krzyzanowski M. Ventilatory lung function and chronic chest symptoms among the inhabitants of urban areas with various levels of acid aerosols: prospective study in Cracow. Environmental Health Perspectives. 1989;79:101–7.

[61] Götschi T, Sunyer J, Chinn S, de Marco R, Forsberg B, Gauderman JW, et al. Air pollution and lung function in the European Community Respiratory Health Survey. International journal of epidemiology. 2008;37(6):1349-58.
[62] Künzli N, Ackermann-Liebrich U, Brändli O, Tschopp J, Schindler C, Leuenberger P, et al. Clinically "small" effects of air pollution on FVC have a large public health impact. Eur Respir J. 2000;15(1):131-6.
[63] Downs SH, Schindler C, Liu LJ, Keidel D, Bayer-Oglesby L, Brutsche MH, et al. Reduced exposure to PM10 and attenuated age-related decline in lung function. New England Journal of Medicine. 2007;357(23):2338-47.
[64] Nuvolone D, Della Maggiore R, Maio S, Fresco R, Baldacci S, Carrozzi L, et al. Geographical information system and environmental epidemiology: a cross-sectional spatial analysis of the effects of traffic-related air pollution on population respiratory health. Environ Health. 2011;10(1):12.
[65] Forbes LJL, Kapetanakis V, Rudnicka AR, Cook DG, Bush T, Stedman JR, et al. Chronic exposure to outdoor air pollution and lung function in adults. Thorax. 2009;64(8):657–63.
[66] He Q, Wong T, Du L, Jiang Z, Gao Y, Qiu H, et al. Effects of ambient air pollution on lung function growth in Chinese schoolchildren. Respiratory Medicine 2010;104(10):1512-20.
[67] Dockery DW, Cunningham J, Damokosh AI, Neas LM, Spengler JD, Koutrakis P, et al. Health effects of acid aerosols on North American children: respiratory symptoms. Environmental Health Perspectives. 1996;104(5):500-5.
[68] Braun-Fahrländer C, Vuille JC, Sennhauser FH, Neu U, Künzle T, Grize L, et al. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren. SCARPOL Team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution, Climate and Pollen. American Journal of Respiratory and Critical Care Medicine. 1997;155(3):1042-9.
[69] Studnicka M, Hackl E, Pischinger J, Fangmeyer C, Haschke N, Kuhr J, et al. Traffic-related NO2 and the prevalence of asthma and respiratory symptoms in seven year olds. European Respiratory Journal 1997;10(10):2275-8.
[70] Stern B, Jones L, Raizenne M, Burnett R, Meranger JC, Franklin CA. Respiratory health effects associated with ambient sulfates and ozone in two rural Canadian communities. Environmental Research. 1989;49(1):20-39.
[71] Brauer M, Hoek G, Vliet PV, Meliefste K, Fischer PH, Wijga A, et al. Air Pollution from Traffic and the Development of Respiratory Infections and Asthmatic and Allergic Symptoms in Children. American Journal of Respiratory and Critical Care Medicine. 2002;166(8):1092-8.
[72] McConnell R, Berhane K, Gilliland F, London S, Islam T, Gauderman W, et al. Asthma in exercising children exposed to ozone: a cohort study. The Lancet 2002;359(9304):386-91.
[73] Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann H-E, et al. Long-term air pollution exposure and living close to busy roads are associated with COPD in women. Respir Res. 2005;6(1):152.
[74] Brauer M, Hoek G, Smit H, De Jongste J, Gerritsen J, Postma DS, et al. Air pollution and development of asthma, allergy and infections in a birth cohort. European Respiratory Journal. 2007;29(5):879–88.
[75] Morgenstern V, Zutavern A, Cyrys J, Brockow I, Koletzko S, Krämer U, et al. Atopic Diseases, allergic sensitization, and exposure to traffic-related air pollution in children. American Journal of Respiratory and Critical Care Medicine. 2008;177(12):1331-7.
[76] Nordling E, Berglind N, Melén E, Emenius G, Hallberg J, Nyberg F, et al. Traffic-related air pollution and childhood respiratory symptoms, function and allergies. Epidemiology. 2008;19 (3):401-8.
[77] Andersen ZJ, Hvidberg M, Jensen SS, Ketzel M, Loft S, Sorensen M, et al. Chronic Obstructive Pulmonary Disease and Long-Term Exposure to Traffic-related Air Pollution. American Journal of Respiratory and Critical Care Medicine 2011;183(4):455-61.
[78] Gehring U, Wijga AH, Brauer M, Fischer P, de Jongste JC, Kerkhof M, et al. Traffic-related Air Pollution and the Development of Asthma and Allergies during the First 8 Years of Life. American Journal of Respiratory and Critical Care Medicine. 2010;181(6):596-603.
[79] Ware J, Ferris Jr B, Dockery D, Spengler J, Stram D, Speizer FE. Effects of ambient sulfur oxides and suspended particles on respiratory health of preadolescent children. The American Review of Respiratory Disease. 1986;133(5):834-42.
[80] Raizenne M, Neas LM, Damokosh A, Dockery DW, Spengler JD, Koutrakis P, et al. Health effects of acid aerosols on North American children: pulmonary function. Environmental Health Perspectives. 1996;104(5):506-514.
[81] Li N, Wang M, Oberley TD, Sempf JM, Nel AE. Comparison of the pro-oxidative and proinflammatory effects of organic diesel exhaust particle chemicals in bronchial epithelial cells and macrophages. The Journal of Immunology. 2002;169(8):4531-41.
[82] Happo M, Salonen R, Hälinen A, Jalava P, Pennanen A, Dormans J, et al. Inflammation and tissue damage in mouse lung by single and repeated dosing of urban air coarse and fine particles collected from six European cities. Inhalation toxicology. 2010;22(5):402-16.
[83] Sørensen M, Daneshvar B, Hansen M, Dragsted LO, Hertel O, Knudsen L, et al. Personal PM2.5 exposure and markers of oxidative stress in blood. Environmental Health Perspectives. 2003;111(2):161-6.
[84] Becker S, Mundandhara S, Devlin RB, Madden M. Regulation of cytokine production in human alveolar macrophages and airway epithelial cells in response

to ambient air pollution particles: further mechanistic studies. Toxicology and Applied Pharmacology. 2005;207(2):269-75.
[85] Goldsmith C-AW, Ning Y, Qin G, Imrich A, Lawrence J, Murthy GK, et al. Combined air pollution particle and ozone exposure increases airway responsiveness in mice. Inhalation Toxicology. 2002;14(4):325-47.
[86] Imrich C-AWGA, Ning HDY. Analysis of air pollution particulate-mediated oxidant stress in alveolar macrophages. Journal of Toxicology and Environmental Health Part A. 1998;54(7):529-45.
[87] Ghio AJ, Kim C, Devlin RB. Concentrated ambient air particles induce mild pulmonary inflammation in healthy human volunteers. American Journal of Respiratory and Critical Care Medicine. 2000;162(3):981-8.
[88] van EEDEN SF, Tan WC, Suwa T, Mukae H, Terashima T, Fujii T, et al. Cytokines involved in the systemic inflammatory response induced by exposure to particulate matter air pollutants (PM10). American Journal of Respiratory and Critical Care Medicine. 2001;164(5):826-30.
[89] Mills NL, Donaldson K, Hadoke PW, Boon NA, MacNee W, Cassee FR, et al. Adverse cardiovascular effects of air pollution. Nature clinical practice. Cardiovascular Medicine. 2009;6(1):36-44.
[90] Brook RD, Urch B, Dvonch JT, Bard RL, Speck M, Keeler G, et al. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. Hypertension. 2009;54(3):659-67.
[91] Clark ML, Peel JL, Burch JB, Nelson TL, Robinson MM, Conway S, et al. Impact of improved cookstoves on indoor air pollution and adverse health effects among Honduran women. International Journal of Environmental Health Research. 2009;19(5):357-68.
[92] Delfino RJ, Staimer N, Gillen D, Tjoa T, Sioutas C, Fung K, et al. Personal and ambient air pollution is associated with increased exhaled nitric oxide in children with asthma. Environmental Health Perspectives. 2006;114(11):1736-43.
[93] Seatona A, Soutara A, Crawfordb V, Eltonc R, McNerlanb S, Cherriea J, et al. Particulate air pollution and the blood. Thorax. 1999;54(11):1027-32.
[94] Peters A, Frohlich M, Doring A, Immervoll T, Wichmann H-E, Hutchinson W, et al. Particulate air pollution is associated with an acute phase response in men; results from the MONICA-Augsburg Study. European Heart Journal. 2001;22(14):1198-204.
[95] Riediker M, Cascio WE, Griggs TR, Herbst MC, Bromberg PA, Neas L, et al. Particulate matter exposure in cars is associated with cardiovascular effects in healthy young men. American Journal of Respiratory and Critical Care Medicine. 2004;169(8):934-40.
[96] Pope Iii CA, Hansen ML, Long RW, Nielsen KR, Eatough NL, Wilson WE, et al. Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects. Environmental Health Perspectives. 2004;112(3):339-45.
[97] Rückerl R, Ibald-Mulli A, Koenig W, Schneider A, Woelke G, Cyrys J, et al. Air pollution and markers of inflammation and coagulation in patients with coronary heart disease. American Journal of Respiratory and Critical Care Medicine. 2006;173(4):432-441.
[98] Roux AVD, Auchincloss AH, Astor B, Barr RG, Cushman M, Dvonch T, et al. Recent exposure to particulate matter and C- reactive protein concentration in the multi-ethnic study of atherosclerosis. American Journal of Epidemiology. 2006;164(5):437-48.
[99] Zeka A, Sullivan JR, Vokonas PS, Sparrow D, Schwartz J. Inflammatory markers and particulate air pollution: characterizing the pathway to disease. International Journal of Epidemiology. 2006;35(5):1347-54.
[100] Ruckerl R, Phipps RP, Schneider A, Frampton M, Cyrys J, Oberdorster G, et al. Ultrafine particles and platelet activation in patients with coronary heart disease--results from a prospective panel study. Particle and Fibre Toxicology. 2007;4:1.
[101] Chuang KJ, Chan CC, Su TC, Lee CT, Tang CS. The effect of urban air pollution on inflammation, oxidative stress, coagulation, and autonomic dysfunction in young adults. American Journal of Respiratory and Critical Care Medicine. 2007;176(4):370-6.
[102] Steinvil A, Kordova-Biezuner L, Shapira I, Berliner S, Rogowski O. Short-term exposure to air pollution and inflammation-sensitive biomarkers. Environmental Research. 2008;106(1):51-61.
[103] Lee PC, Talbott EO, Roberts JM, Catov JM, Sharma RK, Ritz B. Particulate air pollution exposure and C-reactive protein during early pregnancy. Epidemiology. 2011;22(4):524-31.
[104] Khafaie MA, Salvi SS, Ojha A, Khafaie B, Gore SS, Yajnik CS. Systemic inflammation (C-reactive protein) in type 2 diabetic patients is associated with ambient air pollution in Pune City, India. Diabetes Care. 2013;36(3):625-30.
[105] Kawasaki N, Asada R, Saito A, Kanemoto S, Imaizumi K. Obesity-induced endoplasmic reticulum stress causes chronic inflammation in adipose tissue. Scientific Reports. 2012;2.
[106] Emanuela F, Grazia M, Marco de R, Maria Paola L, Giorgio F, Marco B. Inflammation as a Link between Obesity and Metabolic Syndrome. J Nutr Metab 2012;2012:476380.
[107] Mancuso P. Obesity and lung inflammation. Journal of Applied Physiology. 2010;108(3):722-8.