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Fine Particulate Matter ($PM_{2.5}$) and Health Effects: An Unbridle Problem in Iran

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Abstract

Particulate matter (PM) is a complex mixture of solid and liquid particles from various sources. Fine PM or $PM_{2.5}$ is defined as a mass with a size of less than 2.5 μm in aerodynamic diameter and has a large contribution to the world increasing annually. Iran is a developing country set in the Middle East that is not secured from this pollutant mainly due to its industries, desert dust and the travel of dust from the neighboring countries. Poor air quality caused by $PM_{2.5}$ can induce multiorgan dysfunction including cardiovascular disease, respiratory impairment, and other adverse effects that lead to morbidity and even death. Since $PM_{2.5}$ is a risk factor for health problems, the comprehension of the detailed molecular mechanisms of $PM_{2.5}$ including oxidative stress and inflammation would be beneficial. The aim of this review is gathering information from epidemiological studies about the health effects of this pollutant in Iran for the sake of a healthy environment and proposing solutions which can be applied to every country that is concerned about the air quality. **[GMJ.2017;6(2):81-94] DOI: 10.22086/GMJ.V6I2.755**

Keywords: Particulate Matters; Air Pollution; Health Effects

Introduction

Nowadays, air quality and air pollution are big challenges around the world. The classification of atmospheric particulate matters (PMs) is as follows PM10 (dp<10 μm), fine PM or $PM_{2.5}$ (dp<2.5 μm), and ultrafine PM (dp< 0.1 μm) in aerodynamic diameter [1].

Among the air pollutants, $PM_{2.5}$ is the most important pollutant deteriorating air quality [2], and it is putative due to its wide range of origins including combustion engines, power plants, industry, home energy consumption, cultivation, smokes from biomass burning, and natural sources like desert dust. Also, $PM_{2.5}$ is associated with a variety of health disorders (cardiovascular, respiratory, endocrine, cancers, etc.) as mentioned in epidemiological cohort studies [3-5]. The $PM_{2.5}$ can cause death and have health impaction at very low concentration levels [6-9].

People living in the Middle East are exposed to $PM_{2.5}$ [10], and Iran is one of the countries of the Middle East encountering a serious environmental problem because of the rapid growth in urban population, industries, desert dust, and deserts in its neighborhood [11]. Although the air quality index (AQI) in Iran differs from the standards of environmental

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protection agency [12], everyone agrees on the disaster of $PM_{2.5}$ for Iran and other countries where the AQI ranges between 50-150 for $PM_{2.5}$, which equals a 24-hour average of 12 to 55.4 μg/m³.
The $PM_{2.5}$ is not in accordance with the standards set by World Health Organization (WHO) which shows that public health is in danger in main provinces of Iran [13-15].
The purpose of this study is to evaluate and overview the hazards of $PM_{2.5}$ in Iran and to propose solutions to make better decisions to solve this problem.

Epidemiology

The $PM_{2.5}$ is noticed around the world mainly due to its impact on mortality rate and hospital admission; on the report of WHO it was responsible for 3.7 million deaths in 2012 [16, 17]. Atkinson *et al*. [18] suggested that the association of $PM_{2.5}$ with respiratory mortality (1.51%) was larger than the percent reported for cardiovascular mortality (0.84%) and all-age, all-cause mortality ranged from 0.25% to 2.08% with an overall estimate of 1.04% which declared the public health importance of $PM_{2.5}$. However, a larger part of the population is affected by cardiovascular diseases (CVD) than by respiratory diseases.
Not only cardiovascular and respiratory mortalities are attributable to $PM_{2.5}$ [19-21], but also it is a major risk factor for premature deaths globally [4]. However, PMs is the consequence of urbanization. Previous research in California demonstrated that surprisingly the mortality rate due to chronic exposure to $PM_{2.5}$ was higher in rural areas [22].
According to the study conducted in Mashhad (one of the cities with high $PM_{2.5}$ levels in Iran), total mortality rate related to $PM_{2.5}$ was 1.61% (600 cases in a year due to short-term exposure) and results of the relative risks (RR) for the increase in total mortality and hospitalization caused by $PM_{2.5}$ indicated that with every 10 μg/m³ increase in $PM_{2.5}$ concentration, there was 0.3% increase in RR [23].
Also, dust is a powerful source of $PM_{2.5}$ in Iran that is located in the dust belt, so dust can contaminate the atmosphere of cities and change the cloud characteristics and even soil properties [24-28]. The outdoor concentrations of $PM_{2.5}$ are strongly correlated with indoor concentrations of $PM_{2.5}$ in the schools which are built near the main roads in Iran [29]. The $PM_{2.5}$ is one of the pollutants in dust which attenuates the air quality in metropolises of Iran. Hence, vulnerable groups such as children and older adults would be in danger [13].
Two studies conducted in Tabriz revealed that in February, there is the maximum daily mass concentration of total suspended $PM_{2.5}$ (96.6μg/m³) and annual average concentration is 85.3 μg/m³ that mostly comes from natural sources especially soil and Urmia lake bed [15,30,31].
However, a study in Ahvaz (a city in Iran with many dust events) indicated that the average concentration of $PM_{2.5}$ is 69.5μg/m³ and the peak concentration is in May and early July [32]. By evaporation of the water from semi-arid lakes, dust contains $PM_{2.5}$ are created and transported by winds for thousands of kilometers [33,34]. A study claimed that the dust in Iran is similar to the dust around the world in their characteristics [35]. Unfortunately, there was 12 percent reduction in the air quality of Iran from the year 2002 until 2012 [36].

Mechanism

Several mechanistic pathways linking air pollution exposure to adverse health outcomes have been described [5]. The inhalation of air pollution can alter the autonomic balance leading to sympathetic activation which can for example cause changes in heart rate or impaired heart rate variability. Secondly, nanoparticles or their constituents may translocate into the circulation leading to direct harmful effects on the cardiovascular system. Thirdly, $PM_{2.5}$ can induce detrimental effects by the impact of oxidative stress and inflammation (Figure-1).
The $PM_{2.5}$ contains metals which can alter antioxidant enzymes, eg, glutathione (GSH) resulting in increasing reactive oxygen species (ROS), lipid peroxidation and redox imbalance. On the other hand, nuclear factor erythroid-2-related factor-2 (Nrf-2) translocation to the nucleus increases due to the ROS produc-

tion and attenuate the activity of antioxidant enzymes by changing their transcription [37]. Also, ROS overproduction occurs by altering electron transport chain and through Haber-Weiss and Fenton reactions in the cell cytosol [31, 38-40]. The ROS formation leads to the damage of DNA and proteins which can be the cause of cancers or apoptosis [41-43].

Inhaled PMs are capable of production of proinflammatory cytokines and adhesion molecules such as tumor necrosis factor (TNFα), interleukin-6 (IL-6).

Inflammation leads to activate the ataxia telangiectasia and rad3-related-tumor protein53 (ATR-TP53) axis and induces autophagy. Also, TP53 triggers autophagy in response to DNA damage [44-48].

However, DNA damage induced by $PM_{2.5}$ causes apoptosis, ROS elevation increases AMP-activated protein kinase (AMPK) and mechanistic target of rapamycin (mTOR) inhibition due to the activation of AMPK cause proliferation and inhibition of autophagy [49]. The $PM_{2.5}$-induced IL-8 expression occurs via activation of Toll-like receptor-2 (TLR2) [50]. The ROS increases transformation of procaspase-1 to caspase-1, and caspase-1 increases IL-18. The ROS activates nuclear factor kappa B (NF-κB) and causes insulin resistance and IL-1β promotion. The IL-18 and IL-1β augmentation, transcription, and cleavage in endothelial progenitor cells (EPCs) accelerate EPC depletion [51].

The $PM_{2.5}$ promote more inflammation and proliferation via NF-κB and ROS-mediated signal transducer and activator of transcription-3 (STAT3) activation [52].

Some studies showed that using extracellular signal-regulated kinase-1/2 (ERK1/2) inhibitor and/or protein kinase B (AKT) inhibitor which block ERK/AKT/ NF-κB pathway can reduce the number of adhesion molecules such

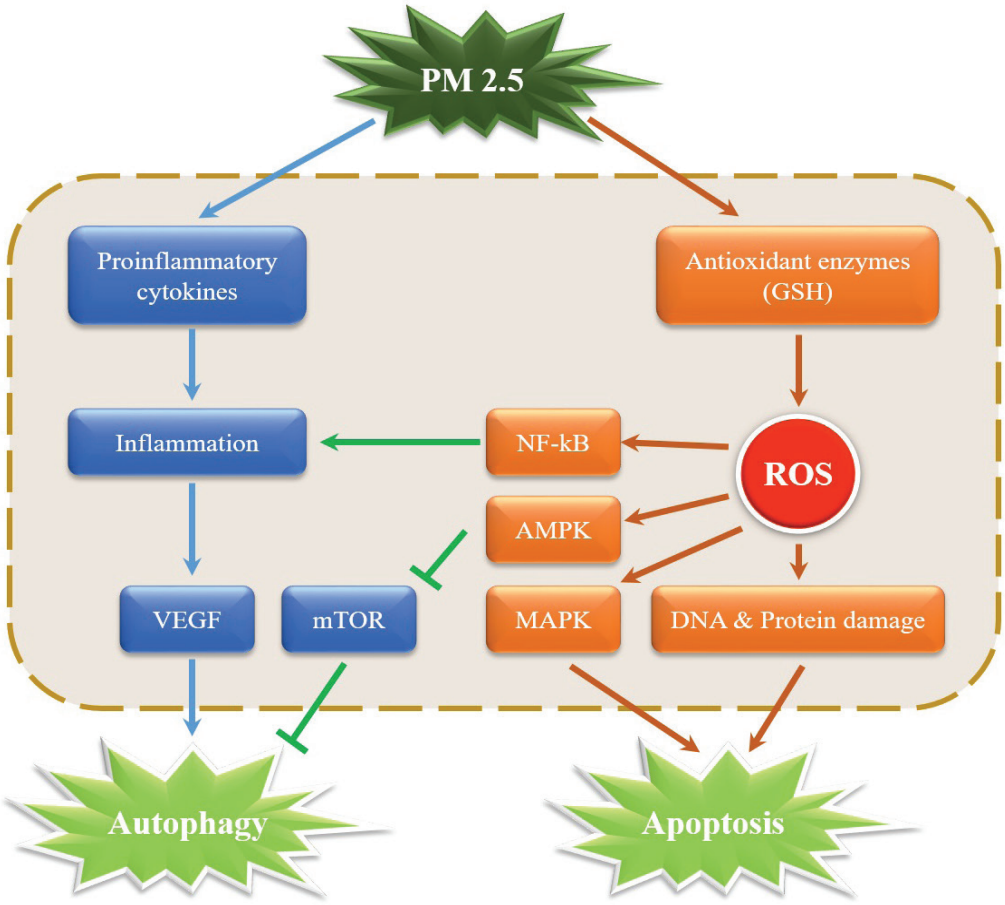

Figure 1. Mechanism of $PM_{2.5}$ induced autophagy and apoptosis by various pathways in cell

as intercellular adhesion molecule-1(ICAM-1) and vascular adhesion molecule-1(VCAM-1) production due to the oxidative stress [53].
Cao *et al*. suggested that ROS elevation caused by $PM_{2.5}$ activates mitogen-activated protein kinase (MAPK) and causes apoptosis in rat cardiac cells [54]. The $PM_{2.5}$ effects on EGFR/PI3K/AKT and NLRP (ie, NACHT, LRR and PYD domains-containing protein) and leads to inflammation [55]. Besides, $PM_{2.5}$ accelerates regulatory T cell (Treg) generation by altering forkhead box P3 (Foxp3) gene transcription [56)]. The $PM_{2.5}$ disrupts the metabolism of xenobiotics through Aryl hydrocarbon receptor (AhR) and increases transforming growth factor β (TGFβ) [57].

Cardiovascular Impairment

Studies showed that there is a significant correlation between air pollution ($PM_{2.5}$) and CVD [58, 59].
Recent studies indicated that $PM_{2.5}$ could decrease heart rate variability (HRV) a marker for cardiac parasympathetic tone modulation which may correlate with cardiac morbidity and sudden death [60,61]. The $PM_{2.5}$ exacerbates the autonomic nervous system and can lead to cardiac arrhythmia [62]. Furthermore, polymorphisms in glutathione S-transferase enzyme-1(GSTM1) and HFE (hemochromatosis) genes impairs HRV [63-65]. The HRV depressing is associated with aging, and low HRV causes CVD and coronary disease [66, 67]. As mentioned above, proinflammatory cytokine release occurs due to the exposure to $PM_{2.5}$. TNF-α and IL-6, two inflammatory markers associated with increased $PM_{2.5}$ [5], increase the risk of myocardial infarction (MI) and out-of-hospital cardiac arrest [68-70].
Also, IL-6 increases C-reactive protein (CRP). The CRP is an indicator of inflammation in CVD as a rapid response to air pollution. With every 100 $\mu g/m^3$ in $PM_{2.5}$ concentration, blood CRP level increases to 8.1 mg/L [71]. In this case, Dabass *et al*. suggested that $PM_{2.5}$ is not significantly correlated with biomarkers of CVD, though can increase these biomarkers in the presence of metabolic disease [72].
Another adverse effect of $PM_{2.5}$ is shortening prothrombin time and increasing fibrinogen, tissue factor, hypercoagulable state, and thrombosis [73, 74]. The $PM_{2.5}$ activates platelets at high shear rates through phosphoinositide 3-kinase/AKT (PI3Kβ/AKT) and glycogen synthase kinase 3 (GSK3) pathway and ultimately causes emboli [75].
Macrophages devour any xenobiotic that is foreign to them including $PM_{2.5}$ and result in increasing adhesion molecules. The ROS leads to inflammation, endothelial damage, and apoptosis; thrombus formation, vascular damage, EPC depletion, high levels of endothelin-1 and imbalance between supply and demand occurs. Hence, all these events explain vascular pathologies, hypertension and coronary artery disease related to the $PM_{2.5}$ [76-79].
In Tehran the capital city of Iran which trapped by air pollution with the largest population-there was a significant relationship between the exposure to $PM_{2.5}$ and changes in HRV in 2010.
Tehran is one of the most populated cities in the world, and approximately 20% of total population of Iran lives in Tehran; thus, the HRV, cardiac morbidities and mortalities should be more taken into consideration. Davoodi *et al*. conducted a study on 21 young people who had exposure to the polluted air and compared it to their situation in the clean air. Besides, they applied continuous Holter monitoring of electrocardiogram (ECG) and determined QT interval; they suggested that air pollution may increase nonsustained supraventricular tachycardia [80, 81]. Another study in Tehran demonstrated that tachycardia, cardiac dysfunction, endothelial damage and more atherosclerosis happens under the high $PM_{2.5}$ concentration circumstances [82-84].

Lung Impairment

The $PM_{2.5}$ passes the barriers deeply into the alveoli where it can exert respiratory problems [85]. It gives rise to cough hypersensitivity by increasing the expression of a non-selective cation channel [86]. Increasing asthma and asthma-like airway inflammation, reflect the danger of $PM_{2.5}$ for the respiratory system [87, 88].

The $PM_{2.5}$ is a risk factor for lung cancer and increases mortality from lung cancer [89, 90]. Sometimes, chemical components such as polycyclic aromatic hydrocarbons attach to the $PM_{2.5}$ and go deep into the alveoli acting as a carcinogen [91].

The higher rate of phagocytosis, oxidative stress, and inflammation post $PM_{2.5}$ exposure could impair immunity of the respiratory system which can lead to aggregation of microbes and infection. This process adds to decreasing cardiovascular function resulting in exacerbation of chronic obstructive pulmonary disease (COPD) [92]. The ROS and the activation of metabolic enzymes may induce pneumonia [93].The $PM_{2.5}$ correlates with the onset of asthma and higher asthma morbidity; also decreasing forced expiratory volume in 1 second (FEV1) due to the asthma is more noticeable in comparison with non-polluted air condition [94]. The presence of $PM_{2.5}$ aggravates respiratory symptoms such as chest pain, dyspnea, sore throat, and wheezing [83, 95].

In Iran, a cross-sectional study gathered meteorological and air pollution information from 31 air quality monitoring station in Tehran and compared cardiovascular (68.36%) and respiratory admission (31.64%). This study showed that $PM_{2.5}$ increases respiratory hospital admissions and also it is correlated with more respiratory admissions to emergency [96].

Neurodegenerative Impairment

A survey carried out on animals suggested that PM progresses to the brain through the nose and absorption from the digestive tract [97]. It revealed that lipid peroxidation and level of CRP had been associated with Parkinson's disease (PD) [98].

The $PM_{2.5}$ correlates with neuroinflammation in the central nervous system, while some cohort studies showed that fine PM does not have potential effects on PD [99, 100]. Liu *et al*. observed a higher prevalence of PD among non-smoking women who inhaled $PM_{2.5}$ [101].

Microglia (the resident innate immune cell in the brain) express TLRs on their surface which $PM_{2.5}$ can attach these receptors leading to a chronic activation of microglia. Chronic microglial activation results in more ROS production as a protective mechanism. However, the subsequent inflammation triggers a neuronal loss [102].

In an area covered with air pollutant, solar rays do not reach the earth properly, and vitamin D deficiency is prevalent among the people in such areas. Vitamin D deficiency is a risk factor for cognitive impairments. High concentration of lipids and poor level of vitamin D play a critical role in Alzheimer's disease (AD) [103]. Cyclooxygenase-1 (COX-1) and COX-2 increase during prolonged inhalation of particulate matter which reflects early changes in the brain in AD [104].

A pilot study in Iran suggested that there is a relationship between hypertension and AD [105]. The $PM_{2.5}$ also is a trigger of stroke and raises the number of the emergency admissions posts cerebrovascular accident. A retrospective cross-sectional study in Iran indicated that increasing concentration of $PM_{2.5}$ over 2 weeks and long-term changes in this pollutant elevates the risk of stroke admission 1.09 times [106].

Endocrine Disorders

According to the fact that the prevalence of diabetes is considerable in Iran and $PM_{2.5}$ increases the risk of diabetes due to the insulin resistance along with aggravating the metabolic imbalance; it is more important to pay more attention to the air quality in Iran [107, 108].

Another effect of $PM_{2.5}$ on the endocrine system is damaging the blood-testis barrier, oligospermia, and impairing testicular function as shown in animal studies [109]. There is some evidence that states the interaction between $PM_{2.5}$ and AhR [57]. Furthermore, AhR- dependent apoptosis diminishes follicular maturation and has negative effects on the female reproductive system [110].

Having a child is one of the most vital issues in Iranian culture. Therefore, the clear mechanism of endocrine disruption by $PM_{2.5}$ through AhR and other pathways remain to be understood. There is no extensive study conducted on the relationship between $PM_{2.5}$ and

endocrine disorders in Iran; so, future studies should be done to fill our knowledge gaps.

Other Adverse Effects

Hypercoagulable state, hemodynamic problems, endothelial dysfunction, oxidative stress, and inflammation are five possible reasons for low birth weight children and infant mortality (add references for this statement). The $PM_{2.5}$ competes with growth factors (add references for this statement); also, impairs the passage of nutrient and oxygen across the placenta which causes preterm birth.
Eosinophilic rise and nasal inflammation induce asthmatic allergy during childhood [111, 112].
Treg proliferation is the result of activation of Foxp3 transcription factor via TGFβ induction that happens following $PM_{2.5}$ exposure. Besides, AhR promotes Treg differentiation that acts as an immunosuppressive agent [56, 113]. Genotoxic effects of $PM_{2.5}$ as a fundamental aspect of various cancers and other disorders should be fully determined in Iran [114]. Finally, the detrimental effects of $PM_{2.5}$ on gastrointestinal tract is another dilemma which should be surveyed broadly because of its intestinal absorption and evidence gave for more hospitalization due to the peptic ulcer disease after $PM_{2.5}$ exposure [115].
In Iran, some studies conducted on particulate matter and defined the adverse effect of these matters (Table-1).

Suggestions

Since a mild to the moderate rise of $PM_{2.5}$ would be harmful to a vulnerable group including old age people and children, one suggestion is to install air cleaners in the schools for school-aged children and nursing homes for elderly care [88]. Forasmuch as the mechanisms of $PM_{2.5}$ is somewhat known; a possible solution is using the agents which modulate these mechanisms, for example, applying antioxidants like vitamin A, C, and E or β carotene may be beneficial in alleviating inflammation. However, more studies are necessary to prove this claim [116, 117].
Soy oil and fish oil supplements (rich in Omega-3) are the best sources to decrease oxidative stress. These polyunsaturated fatty acids should be more consumed in cities which are established in the deserts of Iran where far from the sea [118].
As discussed above wide range of disorders are related to $PM_{2.5}$ (Figure-2); as a consequence wide range of treatments are enable for attenuating these effects.
Controlling HRV, hypertension, diabetes by the use of β blockers, antihypertensive agents, and managing diabetes is approximately a kind of constitutional treatment [119].
Other environmental interventions including using air purifiers, assessment of $PM_{2.5}$ concentration by calibrator machines, the foundation of industries away from metropolises, seeding more plants, and using new technologies which are less harmful to the atmosphere are programs that should be performed by the government. For example, Tehran was equipped with subway system several years ago. Thus the concentration of pollutants is a key factor for the quality of underground stations [120].
On the other hand, people should follow some advice: avoid going out or exercising at high concentrations of $PM_{2.5}$ (based on the daily reports), more use of public transports, more walking and cycling instead of using private cars and motorcycles, and ultimately cooperating with the government in order to improve air quality and advance healthy air [121, 122].
Characterization of $PM_{2.5}$ and visibility measurement with professional satellites is another way to determine more accurate concentrations of this pollutant which can predict the exposure in Iran and the countries in its neighborhood [123, 124]. So, it could be helpful for civilization, migration, living and programming.

Conclusion

Iran is a country in the Middle East which wrestles with the $PM_{2.5}$ pollution.
Many studies suggested that $PM_{2.5}$ can be the cause of mortalities and morbidities in Iran and even trigger many diseases due to the multi-organ damage. Despite the discovery of mechanisms of adverse effects worldwide

Table 1. Overview Over the Iranian Studies on Particulate Matter

Authors	Publication Date	City	Source of Exposure	Outcomes
Sanobari *et. al.* [13]	2007	Tabriz	Vehicle (traffic)	Non-standard AQI
Shahsavani *et. al.* [28]	2010	Ahvaz	Dust	Maximum $PM_{2.5}$ in May and early July
Davoodi *et. al.* [77]	2010	Tehran	Polluted air	CVD
Poursafa *et. al.* [81]	2010	Tehran	Polluted air	Cardiac dysfunction
Givehchi *et. al.* [9]	2011	Tehran	Dust	Unsuitable atmosphere
Zarasvandi *et. al.* [31]	2011	Khuzestan	Dust	Unhealthy atmosphere
Hojati *et. al.* [23]	2012	Zagros	Dust	Poor atmosphere
Naddafi *et. al.* [78]	2012	Tehran	Polluted air	CVD
Masoumi *et. al.* [22]	2013	Zanjan	Dust	Poor atmosphere
Mohammadyan *et. al.* [24]	2013	Sari	Vehicle (traffic)	Increased indoor concentrations of $PM_{2.5}$
Rashki *et. al*. [30]	2013	Sistan	Dust	Uncontrolled dust storms
Arfaeinia *et. al.* [12]	2014	Tehran, Isfahan, Shiraz	Polluted air	Non-standard AQI
Gholampour *et. al.* [25]	2014	Tabriz	Urmia lake bed	Maximum $PM_{2.5}$ in February
Gholampour *et. al.* [26]	2014	Tabriz	Dust	Increased total mortality
Shahi *et. al.* [93]	2014	Tehran	Polluted air	Increased hospital admissions
Kamani *et. al.* [116]	2014	Tehran	Subway system	High $PM_{2.5}$ of underground stations
Gholampour *et. al.* [29]	2015	Tabriz	Urmia lake bed	Uncontrolled dust storms
Hassanvand *et. al*. [88]	2015	Tehran	Polluted air	Lung carcinogenesis
Hamedian *et. al.* [11]	2016	Tehran	Polluted air	Non-standard AQI
Miri *et. al.* [21]	2016	Mashhad	Polluted air	Increased mortality and morbidity rate
Saniei *et. al.*[32]	2016	Tehran	Dust	Reduced AQI
Alimohammadi *et. al.* [103]	2016	Tehran	Polluted air	Increased emergency admission
Bonyadi *et. al.* [117]	2016	Mashhad	Variable sources	Increased total mortality

CVD: Cardiovascular Disease; **AQI:** Air Quality Index

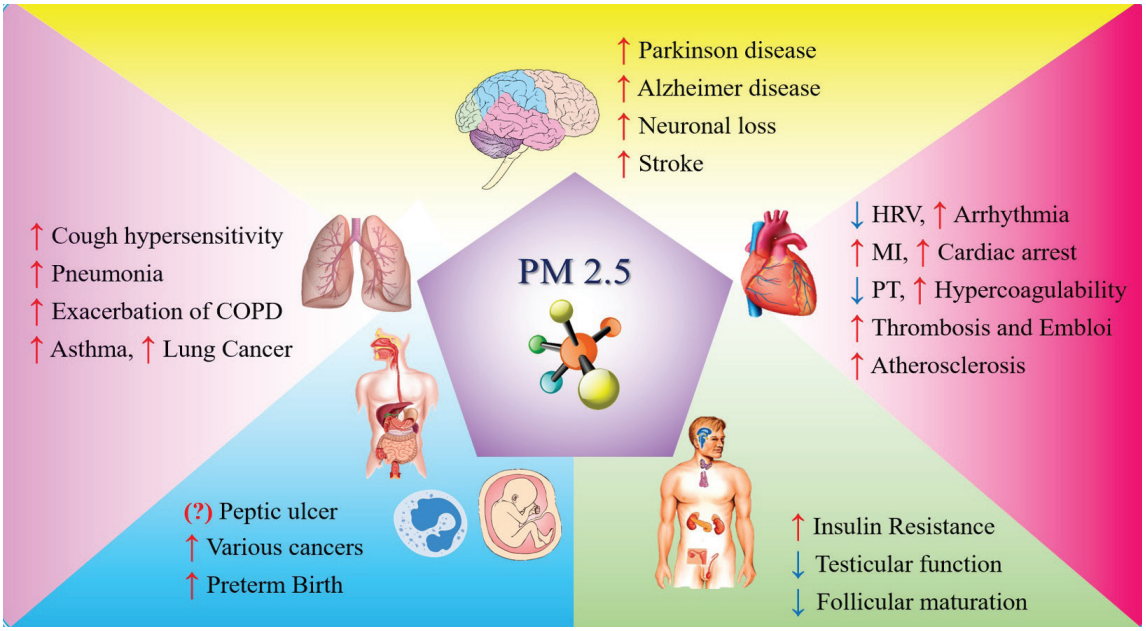

Figure 2. Effect of $PM_{2.5}$ on the vital organs and systems.

such as inflammation and oxidative stress, no study demonstrates which mechanism is prominent in Iran to better overcome the detrimental effects.

Increasing $PM_{2.5}$ is a major concern for public health effect. Since the countries are affected by each other in the air pollution, and Iran nearly is in the center of other countries in the Middle East geographically, new strategies should be scheduled to attenuate the amount of $PM_{2.5}$ concentration and mitigate its detrimental effects. The accurate assessment and finding characterization $PM_{2.5}$ in Iran are the priorities that should be tightly performed.

There are some solutions to improve air quality and clean environment that WHO, the government of Iran and every individual should attempt to apply. Finally, more and more studies must be done to fill our knowledge gaps.

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Conflict of Interests

The authors declare that they have no conflict of interests.

References

1. Wegesser TC, Pinkerton KE, Last JA. California wildfires of 2008: coarse and fine particulate matter toxicity. Environ Health Perspect. 2009;117(6):893-7
2. Kim KH, Kabir E, Kabir S. A review on the human health impact of airborne particulate matter. Environ Int. 2015;74:136-43.
3. Giannadaki D, Lelieveld J, Pozzer A. Implementing the US air quality standard for PM $_{2.5}$ worldwide can prevent millions of premature deaths per year. Environ Health. 2016;15(1):88.
4. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380(9859):2224-60.

5. Rückerl R, Schneider A, Breitner S, Cyrys J, Peters A. Health effects of particulate air pollution: a review of epidemiological evidence. Inhal Toxicol. 2011;23(10):555-92.
6. Maté T, Guaita R, Pichiule M, Linares C, Díaz J. Short-term effect of fine particulate matter ($PM_{2.5}$) on daily mortality due to diseases of the circulatory system in Madrid (Spain). Sci Total Environ. 2010; 408(23):5750-7.
7. World Health Organization. Health effects of particulate matter. Policy implications for countries in Eastern Europe. Caucasus and central Asia. World Health Organization Regional Office for Europe, Copenhagen. 2013. (Accessed 2013, at http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2013/health-effects-of-particulate-matter.-policy-implications-for-countries-in-eastern-europe,-caucasus-and-central-asia-2013)
8. Shi L, Zanobetti A, Kloog I, Coull BA, Koutrakis P, Melly SJ, et al. Low-concentration $PM_{2.5}$ and mortality: estimating acute and chronic effects in a population-based study. Environ Health Perspect. 2016; 124(1):46-52.
9. Pinault L, Tjepkema M, Crouse DL, Weichenthal S, van Donkelaar A, Martin RV, et al. Risk estimates of mortality attributed to low concentrations of ambient fine particulate matter in the Canadian community health survey cohort. Environ Health. 2016 ;15:18.
10. Givehchi R, Arhami M, Tajrishy M. Contribution of the Middle Eastern dust source areas to PM 10 levels in urban receptors: case study of Tehran, Iran. Atmos Environ. 2013;75:287-95.
11. United States Census Bureau. World population. 2009 (Accessed Aug 16, 2013, at http://www. census.gov/population/international/data/worldpop/table_population.php.)
12. Hamedian AA, Javid A, Zarandi SM, Rashidi Y, Majlesi M. Air Quality Analysis by Using Fuzzy Inference System and Fuzzy C-mean Clustering in Tehran, Iran from 2009–2013. Iran J Public Health. 2016; 45(7):917-25.
13. Arfaeinia H, Kermani M, Aghaei M, Asl FB, Karimzadeh S. Comparative investigation of health quality of air in Tehran, Isfahan and Shiraz metropolises in 2011-2012. Journal of Health in the Field. 2017;1(4): 37-44.
14. Sanobari F, Banisaeid S. Determination of atmospheric particulate matter and heavy metals in air of Tabriz City, Iran. Asian J Chem. 2007;19(6):4143-50.
15. Gholampour A, Nabizadeh R, Naseri S, Yunesian M, Taghipour H, Rastkari N, et al. Exposure and health impacts of outdoor particulate matter in two urban and industrialized area of Tabriz, Iran. J Environ Health Sci Eng. 2014;12(1):27.
16. Esposito K, Petrizzo M, Maiorino MI, Bellastella G, Giugliano D. Particulate matter pollutants and risk of type 2 diabetes: a time for concern? Endocrine. 2016;51(1):32-7.
17. Bravo MA, Ebisu K, Dominici F, Wang Y, Peng RD, Bell ML. Airborne fine particles and risk of hospital admissions for understudied populations: effects by urbanicity and short-term cumulative exposures in 708 US counties. Environ Health Perspect. 2017; 125(4): 594–601.
18. Atkinson RW, Kang S, Anderson HR, Mills IC, Walton HA. Epidemiological time series studies of $PM_{2.5}$ and daily mortality and hospital admissions: a systematic review and meta-analysis. Thorax. 2014;69(7):660-5.
19. Ostro B, Lipsett M, Reynolds P, Goldberg D, Hertz A, Garcia C, et al. Long-term exposure to constituents of fine particulate air pollution and mortality: results from the California Teachers Study. Environmental Health Perspectives. Environ Health Perspect. 2010;118(3):363-9.
20. Lepeule J, Laden F, Dockery D, Schwartz J. Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. Environ Health Perspect. 2012;120(7):965-70.
21. Cesaroni G, Badaloni C, Gariazzo C, Stafoggia M, Sozzi R, Davoli M, et al. Long-term exposure to urban air pollution and mortality in a cohort of more than a million adults in Rome. Environ Health Perspect. 2013;121(3):324-31.
22. Garcia CA, Yap PS, Park HY, Weller BL. Association of long-term $PM_{2.5}$ exposure with mortality using different air pollution exposure models: impacts in rural and urban California. Int J Environ Health Res. 2016;26(2):145-57.
23. Miri M, Derakhshan Z, Allahabadi A, Ahmadi E, Conti GO, Ferrante M, et al. Mortality and morbidity due to exposure to outdoor air pollution in Mashhad metropolis, Iran. The AirQ model approach. Environ Res. 2016;151:451-57.
24. Masoumi A, Khalesifard HR, Bayat A, Moradhaseli R. Retrieval of aerosol optical

and physical properties from ground-based measurements for Zanjan, a city in Northwest Iran. Atmos Res. 2013;120:343-55.
25. Alessandrini ER, Stafoggia M, Faustini A, Gobbi GP, Forastiere F. Saharan dust and the association between particulate matter and daily hospitalisations in Rome, Italy. Occup Environ Med. 2013;70(6):432-4.
26. Mallone S, Stafoggia M, Faustini A, Gobbi GP, Marconi A, Forastiere F. Saharan dust and associations between particulate matter and daily mortality in Rome, Italy. Environ Health Perspect. 2011;119(10):1409-14.
27. Stafoggia M, Zauli-Sajani S, Pey J, Samoli E, Alessandrini E, Basagaña X, et al. Desert dust outbreaks in Southern Europe: contribution to daily PM10 concentrations and short-term associations with mortality and hospital admissions. Environ Health Perspect. 2016;124(4):413-9.
28. Hojati S, Khademi H, Cano AF, Landi A. Characteristics of dust deposited along a transect between central Iran and the Zagros Mountains. Catena. 2012;88(1):27-36.
29. Mohammadyan M, Shabankhani B. Indoor PM 1, PM $_{2.5}$, PM 10 and outdoor PM $_{2.5}$ concentrations in primary schools in Sari, Iran. Arh Hig Rada Toksikol. 2013;64(3):371-7.
30. Gholampour A, Nabizadeh R, Yunesian M, Naseri S, Taghipour H, Rastkari N, et al. Physicochemical characterization of ambient air particulate matter in Tabriz, Iran. Bull Environ Contam Toxicol. 2014;92(6):738-44.
31. de Paula Ribeiro J, Kalb AC, Campos PP, De La Cruz AR, Martinez PE, Gioda A, et al. Toxicological effects of particulate matter (PM $_{2.5}$) on rats: Bioaccumulation, antioxidant alterations, lipid damage, and ABC transporter activity. Chemosphere. 2016;163:569-77.
32. Shahsavani A, Naddafi K, Haghighifard NJ, Mesdaghinia A, Yunesian M, Nabizadeh R, et al. The evaluation of PM 10, PM $_{2.5}$, and PM 1 concentrations during the Middle Eastern Dust (MED) events in Ahvaz, Iran, from April through September 2010. J Arid Environ. 2012;77:72-83.
33. Gholampour A, Nabizadeh R, Hassanvand MS, Taghipour H, Nazmara S, Mahvi AH. Characterization of saline dust emission resulted from Urmia Lake drying. J Environ Health Sci Eng. 2015;13:82.
34. Rashki A, Eriksson PG, Rautenbach CD, Kaskaoutis DG, Grote W, Dykstra J. Assessment of chemical and mineralogical characteristics of airborne dust in the Sistan region, Iran. Chemosphere. 2013;90(2):227-36.
35. Zarasvandi A, Carranza EJ, Moore F, Rastmanesh F. Spatio-temporal occurrences and mineralogical–geochemical characteristics of airborne dusts in Khuzestan Province (southwestern Iran). J GEOCHEM EXPLOR. 2011;111(3):138-51.
36. Saniei R, Zangiabadi A, Sharifikia M, Ghavidel Y. Air quality classification and its temporal trend in Tehran, Iran, 2002-2012. Geospat Health. 2016 ;11(2):442.
37. Deng X, Rui W, Zhang F, Ding W. $PM_{2.5}$ induces Nrf2-mediated defense mechanisms against oxidative stress by activating PIK3/AKT signaling pathway in human lung alveolar epithelial A549 cells. Cell Biol Toxicol. 2013;29(3):143-57.
38. Donaldson K, Stone V, Borm PJ, Jimenez LA, Gilmour PS, Schins RP, et al. Oxidative stress and calcium signaling in the adverse effects of environmental particles (PM 10). Free Radic Biol Med. 2003;34(11):1369-82.
39. Huang Q, Zhang J, Peng S, Tian M, Chen J, Shen H. Effects of water soluble PM $_{2.5}$ extracts exposure on human lung epithelial cells (A549): a proteomic study. J Appl Toxicol. 2014;34(6):675-87.
40. Maciejczyk P, Zhong M, Lippmann M, Chen LC. Oxidant generation capacity of source-apportioned $PM_{2.5}$. Inhal Toxicol. 2010;22 Suppl 2:29-36.
41. Méndez-Armenta M, Nava-Ruiz C, Fernández-Valverde F, Sánchez-García A, Rios C. Histochemical changes in muscle of rats exposed subchronically to low doses of heavy metals. Environ Toxicol Pharmacol. 2011;32(1):107-12.
42. Chen HM, Lee YH, Wang YJ. ROS-triggered signaling pathways involved in the cytotoxicity and tumor promotion effects of pentachlorophenol and tetrachlorohydroquinone. Chem Res Toxicol. 2015;28(3):339-50.
43. Ghio AJ, Carraway MS, Madden MC. Composition of air pollution particles and oxidative stress in cells, tissues, and living systems. J Toxicol Environ Health B Crit Rev. 2012;15(1):1-21.
44. Xu X, Wang H, Liu S, Xing C, Liu Y, Aodengqimuge, et al. TP53-dependent autophagy links the ATR-CHEK1 axis activation to proinflammatory VEGFA production in human bronchial epithelial cells exposed to fine particulate matter

($PM_{2.5}$). Autophagy. 2016;12(10):1832-1848.
45. Mitkus RJ, Powell JL, Zeisler R, Squibb KS. Comparative physicochemical and biological characterization of NIST interim reference material PM $_{2.5}$ and SRM 1648 in human A549 and mouse RAW264. 7 cells. Toxicol In Vitro. 2013;27(8):2289-98.
46. Dieme D, Cabral-Ndior M, Garçon G, Verdin A, Billet S, Cazier F, et al. Relationship between physicochemical characterization and toxicity of fine particulate matter (PM $_{2.5}$) collected in Dakar city (Senegal). Environ Res. 2012;113:1-13.
47. Martinelli N, Olivieri O, Girelli D. Air particulate matter and cardiovascular disease: a narrative review. Eur J Intern Med. 2013;24(4):295-302.
48. Westberg H, Elihn K, Andersson E, Persson B, Andersson L, Bryngelsson L, et al. Inflammatory markers and exposure to airborne particles among workers in a Swedish pulp and paper mill. Int Arch Occup Environ Health. 2016;89(5):813-22.
49. Wang Y, Lin Z, Huang H, He H, Yang L, Chen T, et al. AMPK is required for $PM_{2.5}$-induced autophagy in human lung epithelial A549 cells. Int J Clin Exp Med. 2015;8(1):58-72.
50. Yan Z, Wang J, Li J, Jiang N, Zhang R, Yang W, et al. Oxidative stress and endocytosis are involved in upregulation of interleukin□8 expression in airway cells exposed to $PM_{2.5}$. Environ Toxicol. 2015;31(12):1869-78.
51. Haberzettl P, McCracken JP, Bhatnagar A, Conklin DJ. Insulin sensitizers prevent fine particulate matter-induced vascular insulin resistance and changes in endothelial progenitor cell homeostasis. Am J Physiol Heart Circ Physiol. 2016;310(11):H1423-38.
52. Jin XT, Chen ML, Li RJ, An Q, Song L, Zhao Y, et al. Progression and inflammation of human myeloid leukemia induced by ambient $PM_{2.5}$. Arch Toxicol. 2016;90(8):1929-38.
53. Rui W, Guan L, Zhang F, Zhang W, Ding W. $PM_{2.5}$-induced oxidative stress increases adhesion molecules expression in human endothelial cells through the ERK/AKT/NF-κB-dependent pathway. J Appl Toxicol. 2016;36(1):48-59.
54. Cao J, Qin G, Shi R, Bai F, Yang G, Zhang M, et al. Overproduction of reactive oxygen species and activation of MAPKs are involved in apoptosis induced by $PM_{2.5}$ in rat cardiac H9c2 cells. J Appl Toxicol. 2016;36(4):609-17.
55. Jin Y, Wu Z, Wang N, Duan S, Wu Y, Wang J, et al. Association of EGF Receptor and NLRs signaling with Cardiac Inflammation and Fibrosis in Mice Exposed to Fine Particulate Matter. J Biochem Mol Toxicol. 2016;30(9):429-37.
56. Xie Y, Gong C, Bo L, Jiang S, Kan H, Song W, et al. Treg responses are associated with $PM_{2.5}$-induced exacerbation of viral myocarditis. Inhal Toxicol. 2015;27(6):281-6.
57. Líbalová H, Krčková S, Uhlířová K, Kléma J, Ciganek M, Rössner P, et al. Analysis of gene expression changes in A549 cells induced by organic compounds from respirable air particles. Mutat Res. 2014;770:94-105.
58. Franchini M, Mannucci PM. Air pollution and cardiovascular disease. Thromb Res. 2012;129(3):230-4.
59. Lai CY, Lai CH, Chuang HC, Pan CH, Yen CC, Lin WY, et al. Physicochemistry and cardiovascular toxicity of metal fume $PM_{2.5}$: a study of human coronary artery endothelial cells and welding workers. Sci Rep. 2016 ;6:33515.
60. Hampel R, Breitner S, Schneider A, Zareba W, Kraus U, Cyrys J, et al. Acute air pollution effects on heart rate variability are modified by SNPs involved in cardiac rhythm in individuals with diabetes or impaired glucose tolerance. Environ Res. 2012;112:177-85.
61. Schneider A, Hampel R, Ibald-Mulli A, Zareba W, Schmidt G, Schneider R, et al. Changes in deceleration capacity of heart rate and heart rate variability induced by ambient air pollution in individuals with coronary artery disease. Part Fibre Toxicol. 2010 ;7:29.
62. O'Neal WT, Soliman EZ, Efird JT, Judd SE, Howard VJ, Howard G, et al. Fine particulate air pollution and premature atrial contractions: The Reasons for Geographic and Racial Differences in Stroke study. J Expo Sci Environ Epidemiol. 2017;27(3):271-275.
63. Xie Y, Bo L, Jiang S, Tian Z, Kan H, Li Y, et al. Individual $PM_{2.5}$ exposure is associated with the impairment of cardiac autonomic modulation in general residents. Environ Sci Pollut Res Int. 2016 ;23(10):10255-61.
64. Schwartz J, Park SK, O'neill MS, Vokonas PS, Sparrow D, Weiss S, et al. Glutathione-S-transferase M1, obesity, statins, and autonomic effects of particles: gene-by-drug-by-environment interaction. Am J Respir Crit Care Med. 2005;172(12):1529-33.
65. Weichenthal SA, Pollitt KG, Villeneuve PJ. PM $_{2.5}$, oxidant defence and cardiorespiratory

health: a review. Environ Health. 2013;12(1):40.
66. Reardon M, Malik M. Changes in heart rate variability with age. Pace. 1996 ;19(11):1863-6.
67. Carney RM, Freedland KE. Depression and heart rate variability in patients with coronary heart disease. Cleve Clin J Med. 2009; 76(Suppl 2): S13–S17.
68. Haikerwal A, Akram M, Del Monaco A, Smith K, Sim MR, Meyer M, et al. Impact of fine particulate matter ($PM_{2.5}$) exposure during wildfires on cardiovascular health outcomes. J Am Heart Assoc. 2015 ;4(7):e001653.
69. Marchini T, Wolf D, Michel NA, Mauler M, Dufner B, Hoppe N, et al. Acute exposure to air pollution particulate matter aggravates experimental myocardial infarction in mice by potentiating cytokine secretion from lung macrophages. Basic Res Cardiol. 2016;111(4):44.
70. Pei Y, Jiang R, Zou Y, Wang Y, Zhang S, Wang G, et al. Effects of fine particulate matter ($PM_{2.5}$) on systemic oxidative stress and cardiac function in ApoE−/− mice. Int J Environ Res Public Health. 2016 ;13(5):484.
71. Ostro B, Malig B, Broadwin R, Basu R, Gold EB, Bromberger JT, et al. Chronic $PM_{2.5}$ exposure and inflammation: determining sensitive subgroups in mid-life women. Environ Res. 2014 ;132:168-75.
72. Dabass A, Talbott EO, Venkat A, Rager J, Marsh GM, Sharma RK, et al. Association of exposure to particulate matter ($PM_{2.5}$) air pollution and biomarkers of cardiovascular disease risk in adult NHANES participants (2001–2008). Int J Hyg Environ Health. 2016;219(3):301-10.
73. Bonzini M, Tripodi A, Artoni A, Tarantini L, Marinelli B, Bertazzi PA, et al. Effects of inhalable particulate matter on blood coagulation. J Thromb Haemost. 2010;8(4):662-8.
74. Mutlu GM, Green D, Bellmeyer A, Baker CM, Burgess Z, Rajamannan N, et al. Ambient particulate matter accelerates coagulation via an IL-6–dependent pathway. J Clin Invest. 2007;117(10):2952-61.
75. Laurent PA, Séverin S, Hechler B, Vanhaesebroeck B, Payrastre B, Gratacap MP. Platelet PI3Kβ and GSK3 regulate thrombus stability at a high shear rate. Blood. 2015;125(5):881-8.
76. Niu J, Liberda EN, Qu S, Guo X, Li X, Zhang J, et al. The role of metal components in the cardiovascular effects of $PM_{2.5}$. PloS one. 2013;8(12):e83782.
77. Giorgini P, Di Giosia P, Grassi D, Rubenfire M, D Brook R, Ferri C. Air pollution exposure and blood pressure: an updated review of the literature. Curr Pharm Des. 2016;22(1):28-51.
78. Meng X, Zhang Y, Yang KQ, Yang YK, Zhou XL. Potential Harmful Effects of $PM_{2.5}$ on Occurrence and Progression of Acute Coronary Syndrome: Epidemiology, Mechanisms, and Prevention Measures. Int J Environ Res Public Health. 2016;13(8):748.
79. Ying Z, Xu X, Chen M, Liu D, Zhong M, Chen LC, et al. A synergistic vascular effect of airborne particulate matter and nickel in a mouse model. Toxicol Sci. 2013;135(1):72-80.
80. Davoodi G, Sharif AY, Kazemisaeid A, Sadeghian S, Farahani AV, Sheikhvatan M, et al. Comparison of heart rate variability and cardiac arrhythmias in polluted and clean air episodes in healthy individuals. Environ Health Prev Med. 2010;15(4):217-21.
81. Naddafi K, Hassanvand MS, Yunesian M, Momeniha F, Nabizadeh R, Faridi S, et al. Health impact assessment of air pollution in megacity of Tehran, Iran. Iranian J Environ Health Sci Eng. 2012;9(1):28.
82. Nasser Z, Salameh P, Nasser W, Abou Abbas L, Elias E, Leveque A. Outdoor particulate matter (PM) and associated cardiovascular diseases in the Middle East. Int J Occup Med Environ Health. 2015;28(4):641-61.
83. Ediagbonya TF, Tobin AE. Air pollution and respiratory morbidity in an urban area of Nigeria. Greener J Environ Manag Pub Saf. 2013;2(1):9-15.
84. Poursafa P, Kelishadi R. Air pollution, platelet activation and atherosclerosis. Inflamm Allergy Drug Targets. 2010;9(5):387-92.
85. Pope CA, Dockery DW. Health effects of fine particulate air pollution: lines that connect. Journal of the air & waste management association. J Air Waste Manag Assoc 2006;56(6):709-42.
86. Lv H, Yue J, Chen Z, Chai S, Cao X, Zhan J, et al. Effect of transient receptor potential vanilloid-1 on cough hypersensitivity induced by particulate matter $_{2.5}$. Life Sci. 2016;151:157-66.
87. Ogino K, Nagaoka K, Okuda T, Oka A, Kubo M, Eguchi E, et al. $PM_{2.5}$-induced airway inflammation and hyperresponsiveness in NC/Nga mice. Environ Toxicol.

2017;32(3):1047-54.
88. Jhun I, Gaffin JM, Coull BA, Huffaker MF, Petty CR, Sheehan WJ, et al. School Environmental Intervention to Reduce Particulate Pollutant Exposures for Children with Asthma. J Allergy Clin Immunol Pract. 2017;5(1):154-159.e3.
89. Fu J, Jiang D, Lin G, Liu K, Wang Q. An ecological analysis of PM2. 5 concentrations and lung cancer mortality rates in China. BMJ Open. 2015;5(11):e009452.
90. Ferecatu I, Borot MC, Bossard C, Leroux M, Boggetto N, Marano F, et al. Polycyclic aromatic hydrocarbon components contribute to the mitochondria-antiapoptotic effect of fine particulate matter on human bronchial epithelial cells via the aryl hydrocarbon receptor. Part Fibre Toxicol. 2010;7:18.
91. Hassanvand MS, Naddafi K, Faridi S, Nabizadeh R, Sowlat MH, Momeniha F, et al. Characterization of PAHs and metals in indoor/outdoor PM 10/PM $_{2.5}$/PM 1 in a retirement home and a school dormitory. Sci Total Environ. 2015;527-528:100-10.
92. Ni L, Chuang CC, Zuo L. Fine particulate matter in acute exacerbation of COPD. Front Physiol. 2015;6:294.
93. Li R, Kou X, Xie L, Cheng F, Geng H. Effects of ambient PM2. 5 on pathological injury, inflammation, oxidative stress, metabolic enzyme activity, and expression of c-fos and c-jun in lungs of rats. Environmental Science and Pollution Research. Environ Sci Pollut Res Int. 2015;22(24):20167-76.
94. Ren J, Li B, Yu D, Liu J, Ma Z. Approaches to prevent the patients with chronic airway diseases from exacerbation in the haze weather. J Thorac Dis. 2016;8(1):E1-7
95. Olujimi OO, Ana GR, Ogunseye OO, Fabunmi VT. Air quality index from charcoal production sites, carboxyheamoglobin and lung function among occupationally exposed charcoal workers in South Western Nigeria. Springerplus. 2016;5(1):1546.
96. Shahi AM, Omraninava A, Goli M, Soheilarezoomand HR, Mirzaei N. The effects of air pollution on cardiovascular and respiratory causes of emergency admission. Emerg (Tehran). 2014;2(3):107-14.
97. Hawkes CH, Del Tredici K, Braak H. Parkinson's disease: the dual hit theory revisited. Ann N Y Acad Sci. 2009;1170:615-22.
98. Andican G, Konukoglu D, Bozluolcay M, Bayülkem K, Firtiına S, Burcak G. Plasma oxidative and inflammatory markers in patients with idiopathic Parkinson's disease. Acta Neurol Belg. 2012;112(2):155-9.
99. Palacios N, Fitzgerald KC, Hart JE, Weisskopf MG, Schwarzschild MA, Ascherio A, et al. Particulate matter and risk of Parkinson disease in a large prospective study of women. Environ Health. 2014;13:80.
100. Calderón-Garcidueñas L, Leray E, Heydarpour P, Torres-Jardón R, Reis J. Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond. Rev Neurol (Paris). 2016;172(1):69-80.
101. Liu R, Young MT, Chen JC, Kaufman JD, Chen H. Ambient air pollution exposures and risk of Parkinson disease. Environ Health Perspect 2016;124(11):1759-1765.
102. Block ML, Elder A, Auten RL, Bilbo SD, Chen H, Chen JC, et al. The outdoor air pollution and brain health workshop. Neurotoxicology. 2012;33(5):972-84.
103. Calderón-Garcidueñas L, Franco-Lira M, D'angiulli A, Rodríguez-Díaz J, Blaurock-Busch E, Busch Y, et al. Mexico City normal weight children exposed to high concentrations of ambient PM $_{2.5}$ show high blood leptin and endothelin-1, vitamin D deficiency, and food reward hormone dysregulation versus low pollution controls. Relevance for obesity and Alzheimer disease. Environ Res. 2015;140:579-92.
104. Bhatt DP, Puig KL, Gorr MW, Wold LE, Combs CK. A pilot study to assess effects of long-term inhalation of airborne particulate matter on early Alzheimer-like changes in the mouse brain. PLoS One. 2015;10(5):e0127102
105. Foroughan M, Farahani ZG, Shariatpanahi M, Vaezinejad M, Kamerani A, Ali A, et al. Risk factors of Alzheimer's disease among Iranian population. Curr Alzheimer Res. 2008;5(1):70-2.
106. Alimohammadi H, Fakhri S, Derakhshanfar H, Hosseini-Zijoud SM, Safari S, Hatamabadi HR. The effects of air pollution on ischemic stroke admission rate. Chonnam Med J. 2016;52(1):53-8.
107. Haghdoost AA, Rezazadeh-Kermani M, Sadghirad B, Baradaran HR. Prevalence of

type 2 diabetes in the Islamic Republic of Iran: systematic review and meta-analysis. East Mediterr Health J. 2009;15(3):591-9.
108. Liu C, Bai Y, Xu X, Sun L, Wang A, Wang TY, et al. Exaggerated effects of particulate matter air pollution in genetic type II diabetes mellitus. Part Fibre Toxicol. 2014;11:27.
109. Yan C, Cao XN, Shen LJ, Liu DY, Peng JP, Chen JJ, et al. Long-term exposure to PM2. 5 from automobile exhaust results in reproductive dysfunction in male rats. Zhonghua Nan Ke Xue. 2016;22(2):104-9.
110. Cavallini A, Lippolis C, Vacca M, Nardelli C, Castegna A, Arnesano F, et al. The Effects of Chronic Lifelong Activation of the AHR Pathway by Industrial Chemical Pollutants on Female Human Reproduction. PLoS One. 2016;11(3):e0152181.
111. Feng S, Gao D, Liao F, Zhou F, Wang X. The health effects of ambient $PM_{2.5}$ and potential mechanisms. Ecotoxicol Environ Saf. 2016;128:67-74.
112. Kumar N. The Exposure Uncertainty Analysis: The Association between Birth Weight and Trimester Specific Exposure to Particulate Matter (PM2. 5 vs. PM10). Int J Environ Res Public Health. 2016;13(9).
113. Gandhi R, Kumar D, Burns EJ, Nadeau M, Dake B, Laroni A, et al. Activation of the aryl hydrocarbon receptor induces human type 1 regulatory T cell–like and Foxp3+ regulatory T cells. Nat Immunol. 2010;11(9):846-53.
114. Sancini G, Farina F, Battaglia C, Cifola I, Mangano E, Mantecca P, et al. Health risk assessment for air pollutants: alterations in lung and cardiac gene expression in mice exposed to Milano winter fine particulate matter ($PM_{2.5}$). PLoS One. 2014;9(10):e109685.
115. Wong CM, Tsang H, Lai HK, Thach TQ, Thomas GN, Chan KP, et al. STROBE-Long-Term Exposure to Ambient Fine Particulate Air Pollution and Hospitalization Due to Peptic Ulcers. Medicine (Baltimore). 2016;95(18):e3543.
116. Mukaddes E. Oxidative stress and benefits of antioxidant agents in acute and chronic hepatitis. Hepat Mon. 2012;12(3):160-7.
117. Tong H. Dietary and pharmacological intervention to mitigate the cardiopulmonary effects of air pollution toxicity. Biochim Biophys Acta. 2016;1860(12):2891-8.
118. Romieu I, Garcia-Esteban R, Sunyer J, Rios C, Alcaraz-Zubeldia M, Velasco SR, et al. The Effect of Supplementation with Omega-3 Polyunsaturated Fatty Acids on Markers of Oxidative Stress in Elderly Exposed to $PM_{2.5}$. Environ Health Perspect. 2008;116(9):1237-42.
119. de Hartog JJ, Lanki T, Timonen KL, Hoek G, Janssen NA, Ibald-Mulli A, et al. Associations between $PM_{2.5}$ and Heart Rate Variability Are Modified by Particle Composition and Beta-Blocker Use in Patients with Coronary Heart Disease. Environ Health Perspect. 2009;117(1):105-11.
120. Kamani H, Hoseini M, Seyedsalehi M, Mahdavi Y, Jaafari J, Safari GH. Concentration and characterization of airborne particles in Tehran's subway system. Environ Sci Pollut Res Int. 2014;21(12):7319-28.
121. Bonyadi Z, Ehrampoush MH, Ghaneian MT, Mokhtari M, Sadeghi A. Cardiovascular, respiratory, and total mortality attributed to PM2. 5 in Mashhad, Iran. Environ Monit Assess. 2016;188(10):570.
122. Wang C, Tu Y, Yu Z, Lu R. PM2. 5 and cardiovascular diseases in the elderly: An overview. Int J Environ Res Public Health. 2015;12(7):8187-97.
123. Masri S, Garshick E, Coull BA, Koutrakis P. A novel calibration approach using satellite and visibility observations to estimate fine particulate matter exposures in Southwest Asia and Afghanistan. J Air Waste Manag Assoc. 2017;67(1):86-95.
124. Habil M, Massey DD, Taneja A. Personal and ambient $PM_{2.5}$ exposure assessment in the city of Agra. Data Brief. 2016;6:495-502.