THE NEW ARMENIAN MEDICAL JOURNAL
Vol.16 (2022), No 2 p.76-90
DOI: https://doi.org/10.56936/18290825-2022.16.2-76

HOSPITAL ADMISSIONS DUE TO SHORT-TERM EXPOSURE TO AIR POLLUTION: A SCOPING REVIEW

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Received 11.03.2022; accepted for printing 30.05.2022

Abstract

Context: Annually thousands of people lose their lives due to air pollution. Today, air pollution in most countries, especially developing countries, is a public health problem and millions of dollars spent to treat patients who admitted to the emergency department due to exposure to air pollutants. Study on hospital admissions is a method for the impact survey of ambient air pollution on a human. Evidence Acquisition: In this study reviewed the effects of air pollutants (No2, SO2, PM2.5, PM10, CO, PAH and VOCs) on human health, with a focus on hospital admission after short-term exposure. In the articles literature that reviewed Short-term exposure to ambient air pollutants including No2, SO2, PM2.5, PM10 and CO led to hospital admission (except for PAH and VOCs). We systematically searched international datasets to identify relevant studies, including PubMed, Scopus, Cochrane library, CINAHL, ISI Web of Science, Science Direct from inception, PROSPERO and EMBASE using medical purposed subject headings (Mesh) terms. Result: The most common cause of hospital admission after short-term exposure to air pollution was cardiovascular and respiratory diseases. The health effects of air pollution on studied groups in dry and warm weather were higher than in wet and cold weather. In studies with more pollutants, the share of each pollutant in hospital admission was clearer. Conclusion: The costs of treatment were far higher than the cost of prevention. The effectiveness of preventive methods was more than therapeutic methods. The history of exposure to ambient air pollutants and their impact on hospital admission rate due to short-term exposure to air pollutants require separate studies in this field. More accurate identification of the toxicological mechanisms seemed to be necessary after the short-term exposure to deal with acute poisoning due to air pollution.

Keywords: *air, pollution, hospital admissions, emergency service, public health*

Introduction

Many different factors can lead to decreased life expectancy, increased disability and disease development. At birth life expectancy was estimated by World Health Organization, 71.4 years of the worldwide population in 2015 [*WHO 2015*].

Healthy life expectancy at birth was 63.1 years globally in 2015. In 2014, 7 million premature deaths in each year were associated with air pollu-

Cite This Article as:
Ebrahimi SM, Motamed H, Kalantar H, Kalantari A, Rahim F;Hospital Admissions Due to Short-term Exposure to Air Pollution: A scoping review; NAMJ v.16 (2022) no.6, p. 76-90;
DOI: https://doi.org/10.56936/18290825-2022.16.2-76

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tion [*WHO 2014a*]. 2012 annually reports confirmed, an estimation of 6.5 million deaths as a result of indoor and outdoor air pollution (more than 10% of the world's deaths) [*WHO 2012*].

Air pollution is one of the significant causes for noncommunicable diseases such as cardiac disease, cerebrovascular accident, Chronic Obstructive Pulmonary Disease (COPD), and lung malignancy. Air pollution also leads to susceptibility of acute lung infection. The WHO's report about the status of noncommunicable diseases in 2010 revealed that these diseases are the most important causes of mortality worldwide. The major etiology of non-communicable diseases leading to death in 2008 were cardiovascular disorders (48%), Cancers (21%) and then Lung disorders [*WHO 2014b*]. In WHO's report, the statistics regarding cardiovascular and respiratory diseases are significant. In 2014, about 90% of countries people lived in area of low air quality on the basis of standards of WHO [*WHO 2021*].

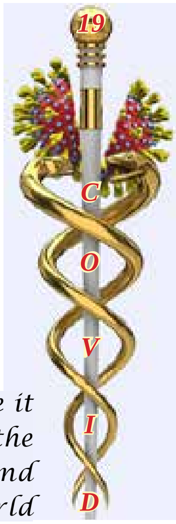
After Revolution of Industry, using different fuel types, mining and industrial activities are the major causes of air pollution [*Phalen RF, Phalen RN, 2012*]. Urban environmental pollutants that are associated with respiratory disorders include gases, vapors and particulate matters with different aerodynamic diameters. The increased level of air pollutants in air is among the most reported reasons for hospital admissions in patients with acute respiratory diseases. Dust entering into atmosphere through deserts, and also gases and vapors from motor vehicles or industrial processes are among the main causes of air pollution [*Pande J et al.,2002; Tsai S et al.,2014; López-Villarrubia E et al.,2016*], which are believed to increase the risks of cardiovascular diseases [*Vedal S., 1997*]. Cardiovascular diseases include any kind of disease that affects the circulatory system. They include heart, cerebrovascular, renal and arterial diseases [*Poloniecki J et al.,1997; Pearson T et al.,2002*]. A positive correlation has been observed in the Emergency hospital admissions with lung diseases and exposure to NO_2 and O_3 gases Generally, exposure of short-term for concentrations higher than normal of air pollutants make people more susceptible to air pollution and cause serious mortality and morbidity effects include aging, childhood diseases, cardiopulmonary, flu and asthma [*Saldiva P et al.,1995; Vedal S., 1997; Sarnat S et al., 2015*].

Opportunistic infections such as Cryptococcosis and similar opportunistic pathogens, are health dilemma specially in patients with compromised immune system. [Hashemi et al., 2014] Lung disease and bronchial asthma incidence of worldwide are rising and in most societies and habitants of cities are at a higher risk of developing these diseases [*D'Amato G et al., 2010*]. There have been several pieces of evidence supporting the relationship between the air pollution exposure either the increase in respiratory diseases from the last six decades so far [*Falcon-Rodriguez C et al., 2016*]. The exposure to air pollution aspects of the London fog of December 1952 caused 4000 deaths. This event attracted the attention of scientific communities to the problem of air pollution all over the globe [*Ling SH, van Eeden SF, 2009*]. A high correlation has been found between air pollution and morality [*Dockery D et al., 2000*]. Thus, reducing the concentration of air polluters in air is believed to reduce mortality which, in turn, can lead to saving economic expenses on treating the related diseases for every society [*El-Fadel M, Massoud M, 2000*]. Attacks of acute asthma, which can be exacerbated directly as a sequence of air pollution, leads to costs for health systems in orther to patients hospitalization, mortality and morbidity [*Motamed H et al., 2017*]. Exacerbation of asthma is cuiprit in medical staff workload, due to approximately 50% increase in asthma patients hospital admissions frequency [*Motamed H et al., 2018*]. This scoping review investigated the air pollution influences and airborne particles on mortality and morbidity in respiratory, cardiovascular and cerebrovascular diseases in hospital admissions during the past 30 years. It also examined the relationship between the pollen of plants and other natural contaminants that are associated with public health based on scientific findings.

EVIDENCE ACQUISTION:

A. *Inclusion and Exclusion criteria*

<u>*Inclusion criteria:*</u> All published



To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world original articles reporting on the association of air pollution with the hospital admissions. Exclusion criteria: any reviews (Narrative, Systematic review, scoping review, Meta-analysis review and umbrella review), letters to the editor without original data, commentaries and editorials, Case series, case reports and other single arm studies were excluded.

Participants : For this scoping review, no limitations were identified to the air population used in research, and all participants ' ages, genders, races, or regions. All, including newborns, infants, adults, pregnant women, and the elderly, is suffering from health outcomes linked to air pollution exposure.

Outcome measures: Finally, the effects of air pollution exposure on respiratory diseases, cardiovascular diseases, asthma, ischemic heart disease, chronic obstructive pulmonary disease (COPD), acute myocardial infarction and were discussed.

B. Search strategy

We systematically searched international datasets to identify relevant studies, including PubMed, Scopus, Cochrane library, CINAHL, ISI Web of Science, Science Direct from inception, PROSPERO and EMBASE using medical subject headings (Mesh) terms, such as "PM_{10}", "$PM_{2.5}$", "Black carbon", "Elemental carbon", " O_3", "volatile organic pollutant", "nitrogen oxide", "Toxic air pollutant", "Ozone", "carbon monoxide", "sulfur dioxide", "nitrogen dioxide", "total suspended particle", "particulate matter". The search is included in the period from 1980 to 2019. We also manually searched through the reference lists of potentially selected studies to find relevant papers.

C. Data extraction method and quality assessment

Screening was done by two reviewers (H.M. and H.K.) independently, considering selection criteria; then, the data were extracted and cross-checked. Any inconsistencies were resolved by consultation with a third reviewer (S.M.E.). The information including author name, publication year and location, Target group and outcomes were extracted. Quality assessments of the selected studies were individually performed by two researchers using the Newcastle-Ottawa Scale (NOS) tool for observational study [*Peterson J et al., 2011*].

RESULTS

Overall, a total of 4,032relevant studies were initially found.

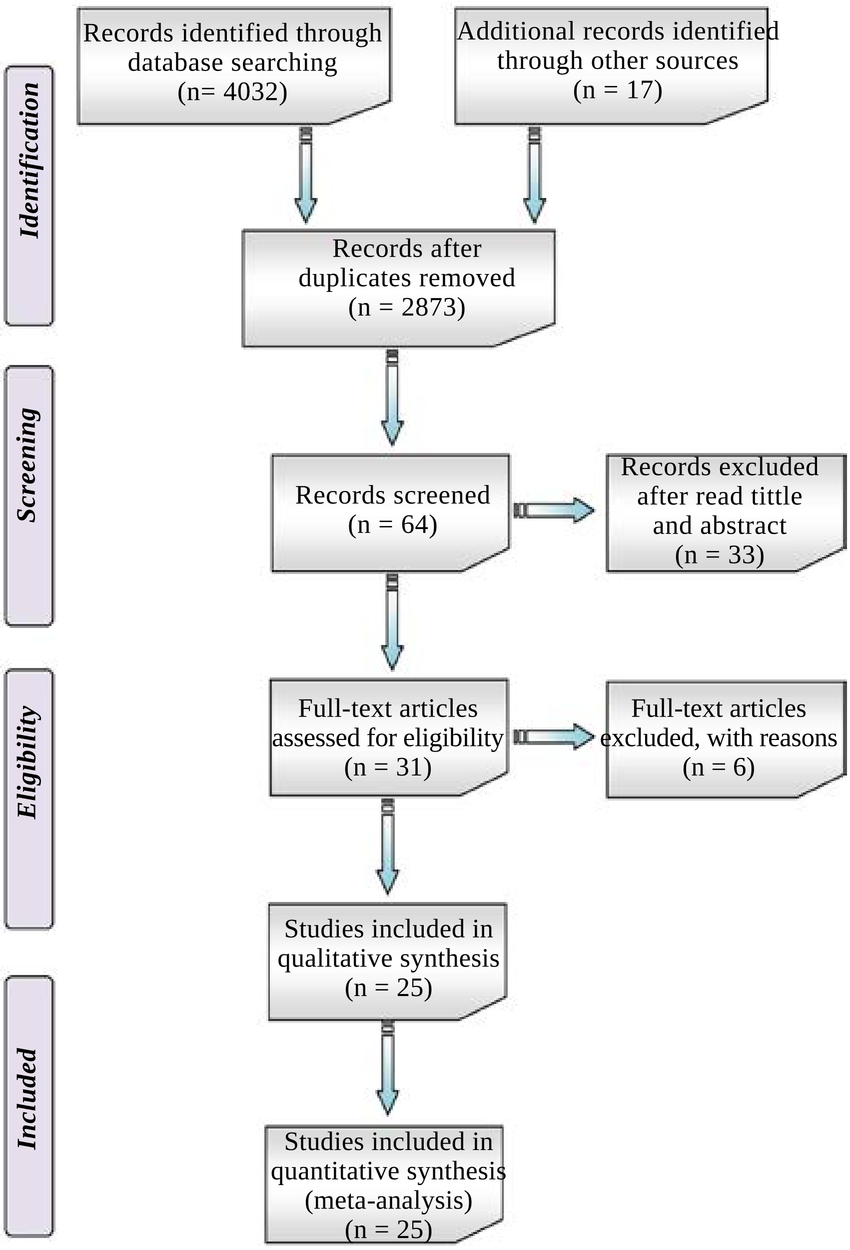


FIGURE 1. *Study Flow Diagram showing how to extract articles*

After the title–abstract screening 4,007 studies were excluded, and 25 studies were used for the scoping review. Figure 1 shows outlines the search method and the number of studies identified and selected during each phase of the search.

THE TYPES OF AIR POLLUTANTS IN AMBIENT AIR

Black carbon, elemental carbon, organic carbon matter

Black carbon is a compound with aerodynamic diameter less than 2.5 micron, which contains carbon in different shapes. It is made by incomplete biofuels and fossil fuels combustion and their emissions as soot in the air [*Anenberg S et al., 2012*]. Major sources of organic carbon are fossil fuels and biomass. Generally, these pollutants result from burning agricultural land around cities after the harvest [*Fine P et al., 2002*]. Elemental carbon is one of primary compounds for burning [*Zanobetti A et al., 2014; Winquist A et al., 201*] which could lead to emergency admission for cardiopulmonary illnesses, COPD and asthma (Table 1).

Ozone (O_3) is a strong oxidative in troposphere and it is made by reactions associated with the effects of sunlight on CO_2 nitrogen and hydrocarbons [*Brunekreef B, Holgate S, 2002*]. Several evidence show ozone emissions in the earth (tropospheric ozone) can lead to disorders in normal pulmonary function and respiratory system, irritation, inflammation and hyperactivity [*Uysal N, Schapira R, 2003*]. In their study, Hui-Fen Chiu et al in Taipei, Taiwan confirmed that increasing ozone concentration in ambient air increases the relative

TABLE 1.

Air pollution and its adverse effects on health.

Adverse health effect	Pollutant	Location	References
Respiratory diseases	PM_{10}	Spain (Canary Islands)	[López-Villarrubia E et al.,2016]
	$PM_{2.5}$	USA	[*Bravo M et al., 2017*]
	Black carbon	USA	[*Winquist A et al., 2015*]
	Elemental carbon	UK	[*Winquist A et al., 2015*]
	O_3	USA	[*Malig B et al., 2016*]
	NO_2	Spain (Canary Islands)	[López-Villarrubia E et al.,2016]
Cardiovascular diseases	SO_2	China	[*Qin X-D et al., 2015*]
	NO_2	China	[*Qin X-D et al., 2015*]
	PM_{10}	China	[*Qin X-D et al., 2015*]
	O3	China, Iran	[*Qin X-D et al., 2015*]
	Elemental Carbon	USA	[*Winquist A et al., 2015*]
	Black Carbon	USA	[*Winquist A et al., 2015*]
Asthma	PM_{10}	Taiwan, USA	[*Guo Y et al., 1999; Malig B et al., 2013*]
	$PM_{2.5}$	USA	[*Malig B et al., 2013*]
	O_3	USA, Taiwan	[*Guo Y et al., 1999; Malig B et al., 2016*]
	NO_2	Taiwan	[*Guo Y et al., 1999*]
	NO_x	Taiwan	[*Guo Y et al., 1999*]
	NO_2	Denmark	[*Andersen Z et al., 201*]
	O_3	USA	[*Malig B et al., 2016*]
Acute myocardial infarction	O_3	Taiwan, USA	[*Koken P et al., 2003; Chiu H et al., 2017*]

risk of hospitalization due to myocardial infarction (Table 1) [*Chiu H et al., 2017*].

Nitrogen oxides (NOx) is one of traffic-related air pollutants which is considered as a compound in acidic rain [*Carslaw D, 2005*]. Thus, nose and throat irritation, shortness of breath and bronchoconstriction happen as a result of Nitrogen dioxide and other nitrogen oxides exposure of outdoor and indoor air pollutions [*Guo Y et al., 1999; Carslaw D, 2005; Naeher L et al., 2007; Perez-Padilla R et al., 2010; Andersen Z et al., 2011*]. Nitric oxide (NO) is converted to NO_2 by strong oxidizers like ozone in environmental conditions (Table 1) [*Brunekreef B, Holgate S, 2002; Mauzerall D et al., 2005*].

Sulfur dioxide (SO_2) is considered as an irritant to under respiratory system and alveolar pulmonary. It is also a compound in acidic rain [*Gao S et al., 2001; Perez-Padilla R et al., 2010*]. Respiratory symptoms like noise and throat irritation, bronchoconstriction and shortness of breath are often observed especially in patients with respiratory diseases after exposure to SO2 in indoor and outdoor air pollutions (Table 1) [*Balmes J et al., 1987; Fine J et al., 1987; Gokirmak M et al., 2003; Zhen W et al., 2013*].

Carbon monoxide (CO) concentration is increased in the air. O3 concentration is also increased when inversion happens in the air [*Koken P et al., 2003*]. Since people are usually exposed to low concentration of CO in the ambient air, it could lead to cardiovascular and neurobehavioral poisoning [*Raub J et al., 2000*] (Table 1).

Particulate matters (PM) are Liquid, solid or a combination form which are air suspended (i.e., airborne) [*Brunekreef B, Holgate S, 2002*]. Its particles are categorized in three categories: coarse, fine, ultrafine. Fine particles include $PM_{2.5}$ and PM_{10}. Since respiratory diseases are highly associated with air pollutants with aerodynamic diameter less than 2.5 micrometer, several pieces of evidences have shown the links between diseases with larger particulate matter (diameters between 2.5-10 micrometers) [*Malig B et al., 2013*]. According to Ly M.T. Luong L et al in Hanoi, Vietnam increase in concentration of PM10, PM2.5 and PM1 increased hospital admissions due to respiratory problems in young children [*Luong L et al., 2017*]. According to Mercedes A. Bravo et al, increase in short-term exposure to PM2.5 in the non-urban areas of the United States (With high population) increased the of hospitalization due to pulmonary problems and in urban areas increased hospitalizations were due to cardiovascular problems (Table 1) [*Bravo M et al., 2017*].

VOLATILE ORGANIC COMPOUNDS (VOCS)

Airborne carbonic chemicals which evaporate in natural temperature and pressure of the atmosphere. So, VOCs are categorized based on their boiling points. These compounds have high vapor pressure in room temperature and their distribution are due to high level of human activities such as fossil fuel consumption, direct evaporation of fuels and solvents, and chemical processes in industries [*Pankow J, 1967; Atkinson R, 2000; Bilde M, Pandis S,2001*]. The most important volatile organic compounds in the ambient air pollution are toluene, ethylene, benzene or BTEX. Benzene in these compounds is recognized as a carcinogen compound by IARC [*Tomatis L et al., 1989; Hayes R et al., 2001; Ho K et al., 2002; Boeglin M et al., 2006; Jia C et al., 2008*]. Toluene is one of the crude oil distillation products and is one of the most commonly used in industry [*Cherubini F, 2010*]. The most common way to be exposed to Toluene is through the inhalation of ambient air pollution [*Czaplicka M, Klejnowski K, 2002; Bono R et al., 2003*]. Major sources of produced xylene isomers is reformate of oil compounds and hydrocarbons. Disproportionation of Toluene is one of its production source [*EPA, 1994*]. Volatile organic compounds can be one of the causes of leukemia, exposure to these compounds and the measurement of a series of biomarkers after exposure indicates that these compounds interfere with the gene expression of the cells involved in the formation of leukemia and thus a potential induced for Leukemia [*Sarma S et al., 2010; Sarma S et al., 2011*]. Bente Oftedal et al confirmed that relationship between 7 traffic-related air pollutants (PM10, NO2, O3, SO2, Benzene, Formaldehyde and Toluene) and hospital admission , Benzene have more relationship to respiratory diseases [*Oftedal B et al., 2003*]. Toluene, ethylene benzene and Xylene isomers have toxic properties especially influencing central nervous system. Toluene changes gene expression in the central nervous system [*Olson B et al., 1985; Filley C et al., 2004; Hester S et al., 2011*]. Acute exposure to Toluene causes headache, dizziness, drowsiness, tremor headache, dizziness, drowsiness, tremor and unconsciousness [*IPCS, 200*]. The exposure to benzene in concentrations lower than the concentration of anesthetic may lead to loss of normal heartbeat rhythm or sudden death. Sometimes exposure to benzene causes problems like thrombocytopenia, leukopenia, blood cancer and pancytopenia [*Carbonari D et al., 2016*]. Skin exposure to benzene may also lead to irritation of the skin All of these signs and symptoms can be among the reasons for hospital admission. Generally, acute exposure to benzene affects the central nervous system, while exposing to it via inhalation causes dizziness, drowsiness, headache and nausea [*ASTDR, 2014*] (Table 1).

Polycyclic aromatic hydrocarbons (PAHs)

Chemical substances classified in categories hydrocarbon (carbon & hydrogen) which makes multiple aromatic rings. These compounds cause incomplete combustion of organic chemical in motor vehicles. This compounds also lead to lung cancer [*Xia Z et al., 2013; Okona-Mensah K et al., 2005*]. Some samples of aromatic hydrocarbon like benzo (b) fluoranthene, benzo (a) pyrene, Chrysene indeno (1 2 3-c d) pyrene have mutagenic, genotoxic and carcinogenic effects on laboratory animals. Some of PAHS like (Benzo [a] pyrene) are categorized in one group of cancer by IARC [*Straif K et al., 2005*]. Abedi Ardekani et al conducted a study in rural areas in the Easter north of Iran (2003-2007). She found high level of colored monoclonal antibody 8 E 11 in non-tumoral epithelium of esophageal squamous cell carcinoma patients compared to the control groups. Thus, PAHs was identified as a reason for esophageal carcinogenesis in the Eastern north of Iran (Table 1) [*Abedi-Ardekani B et al., 2010*].

The effect of temperature and humidity on hospital admitions due to air pollution

Hospital admissions due to ambient air short term pollutants exposure are presented generally by cardiovascular and pulmonary acute symptoms. Temperature and dry weather exacerbate air pollution and lead to higher hospital admissions [*Katsouyanni K et al., 2001; Aga E et al., 2003; Sunyer J et al., 2003; Leitte A et al., 2009; Tramuto F et al., 2011; Qiu H et al., 2013; Jayamurugan R et al., 2013; Rodopoulou S et al., 2014; Malig B et al., 2016; Samoli E et al., 2016*] (Table 1).

Conclusion:

The exposure to air pollutants causes economic and hygienic costs on every government and it can lead to different kinds of side effects in susceptible age and special groups such as children, the elderly, pregnant women, respiratory and cardiovascular cases. The economic costs of due to air pollutants on healthcare system associated with the number of people at risk and the rate of mortality and morbidity in every society.

Air pollution health costs caused by motor vehicle traffic were 916 million dollars in Swiss. Also, the economic cost due to premature birth associated with PM2.5 (in 2010) was 760 million dollar of 4.3 milliard dollars spent for health care in the USA. Childhood illness can effect on the person's life due to the physical, psychological and social consequences of it [*Quah E, Boon T, 2003; Boesch H-J et al., 2008*]. In 2001, the total economic costs due to the health effects of particulates in Shanghai urban districts estimated about 625.40 million$ [*Rai P, 2015*]. Damages due to emissions and exposure for PM2.5, SO2, NOx, NH3, and volatile organic compound from electric power plants, oil and gas Industry, coal mining totaled 131 billion$, with emissions of SO2 from power generation play the largest role to environmental and social harms in 2011 [*Jaramillo P, Muller N, 2016*]. Asthma is a respiratory disorder and its clinical aspects are different based on the environmental factors and individual genetic background [*Lemanske RF, Busse W, 2010*]. Air pollution has extensive effects on families with low economic social class relative to families with high economic social class [*Kan H, Chen B, 2004*]. Air pollution can exacerbate asthma in children and impose indirect costs on the health, education and economy systems of governments. Since the air pollution has become a major health problem in the world can defined for morbidity and mortality caused by air pollution Health indexes base on world Health Organization standards. According to WHO air quality guidelines, the limited average exposure to O_3, PM2.5, PM10, NO_2 and SO_2 are shown

TABLE2.

The limits recommended by WHO for exposure to pollutants.

Pollutant	Exposure limit ($\mu g/m^3$)	Type of mean concentration
PM2.5	10	Annual average
	25	24- hrs average
PM10	20	Annual average
	50	24- hrs average
Ozone	100	8- hrs average
Nitrogen dioxide	40	Annual average
	200	1- hrs average
Sulfur dioxide	20	Annual average
	500	10- min average

in Table 2 [*WHO, 2005*].

Although long term and cohort studies investigated the acute effects of air pollutants on morbidity and mortality, but recently several studies have shown that changes in the pollutants concentration can lead to increased hospital admissions due to cardiovascular and respiratory problems [*Brunekreef B, Holgate S, 2002*]. Gharehchahi E et al (2008-2009) conducted a research for the effects of air pollution on people health in Shiraz, Iran. The results showed extra hospitalization (1163 extra cases) as a result of respiratory illness following PM10 exposure in 2009. Meanwhile, the maximum number of extra hospital admissions due to respiratory illnesses and COPD were due to SO2 exposure in 2008, which were 520 and 900 excess cases, respectively. In conclusion, increased morbidity risk rates were assessed due to air pollutants acute exposure [*Gharehchahi E et al., 2013*]. As the results indicated, when the pollutants concentration increased, hospital admissions increased accordingly and led to higher levels of ambulance dispatches due to acute effect of air pollutants [*Sajani S et al., 2014; Michikawa T et al., 2015; Tasmin S et al., 2016*].

In metropolitan cities polluted form the pollution of industries and traffic vehicles, people are usually exposed to dust and air pollution. Thus, the number of hospital admissions due to air pollution is very high in these cities. Tehran, Karaj, Ahvaz, Mashhad, Tabriz, Zabol, Zahedan, Abadan and Khoramshahr are most polluted cities in Iran. Ahvaz which is located in the western south of Iran is one of most polluted cities in the country and world and its pollution level is more than Beijing and London. So far, air pollution in this city has led to increased hospital admissions. There are oil and gas reservoirs, oil industry and oil installations. Some issues like drying wetlands and ponds near the city of Ahvaz, the indiscriminate construction of dams on Dez and Karoon rivers, climate change and limited annual rainfall, and also the loss of vegetation due to human activities are the most important factors of dust phenomenon in Ahvaz. Also, significant transfer of dust from Iraq which is neighboring Khuzestan province increases dust in the ambient air in Ahvaz. Abadan and Khoramshahr, other major cities in Khuzestan Province, are not exception to this phenomenon. Besides, Zabol city in western area of Iran is another high level polluted city worldwide and in the country. The most important origin of dust particles in Zabol is due to drying Hamun Lake. However, the most important air pollutant origin in Iran metropolitan cities like Tehran and Mashhad is due to motor vehicles traffic. In effect, in these cities, the concentration of 100 to 150 microgram/m^3 is considered unhealthy for sensitive groups like children, the elderly, pregnant women and patients with cardiovascular and respiratory diseases. $PM_{2.5}$ concentrations in Tehran was even higher than this range from 11th to 18th in November, 2016. Based on the Air Quality Index (AQI) EPA, PM2.5 concentration higher than 150 microgram/m^3 is unhealthy for all people [*Rashki A et al., 2013; EPA, 2014; Mawer C, 2014; Goudarzi G et al., 2016; Maleki H et al., 2016*]. Jesse D Berman et al confirmed that droughts in western United States increase mortality [*Berman J et al., 2017*]. In studies related to air pollution some limitations such as time, cost, the large number of air pollutants, large number of unknown environmental and human confounding variable, the wide range of health effects caused by air pollutants has diminished the comprehensiveness of the studies and has limited the scope of the study. Also in studies that measure the health effects of air pollutants can felt absence of one or more common health index that all researchers can use. Therefore, it is not possible compare and assess with high confidence the effects of toxicology and clinical studies together.

Toxicological Mechanisms

The biological mechanisms of response to air pollutants, especially PM that leads to increased morbidity and mortality in exposed peoples are not clear. Seaton et al suggested inhalation of fine particles leads to the release of inflammation mediators and a mild inflammatory response in lung. This can, in turn, lead to the exacerbation of respiratory diseases, changes in blood coagulation and finally respiratory and cardiovascular diseases [*Seaton A et al., 1995*]. The damage to the mucosal membrane of airway due to the effects of air pollutants on immune cells leads to secretion of IgE and a severe allergic response and causes increased airway sensitivity; consequently increases the prevalence of respiratory allergies in cities (6) [*D'Amato G et al., 2010*]. And causes increased airway sensitivity; consequently, increases the prevalence of respiratory allergies in cities. Systematic response to fine particles include releasing cytokine and changing the natural performance of cardiac autonomic function may be part of pathophysiological mechanism by fine particulate air pollution [*Pope 3rd C, 2000*]. Stephan F et al suggested broad ranges of different activation of alveolar macrophages in blood by short period of air pollution (PM10) exposure to produce cytokines which have pro inflammatory effects. They assumed that cytokines play an important role in pathogenesis of cardiopulmonary systems and function as a systematic response associated with air pollution [*van Eeden S et al., 2001*]. Small size of ultrafine particles (less than 100 nanometer) facilitates the uptake of cells and transcytosis by endothelial and epithelial cells, and also facilitates its entry into circulatory system (lymph and blood) to reach the target organs consist of lymph nodes, spleen, bone marrow, heart. Finally it can by entering the cell and impairment in performance of target organ cell mitochondria through oxidative stress response leads to cell death [*Oberdörster G et al., 2005*]. After entering the body, Benzene goes to liver as its primary metabolism is in the liver. The first phase of metabolism is oxidation and the result is Benzene oxide produced by P450 cytochrome. At least there are two metabolic pathways after oxidation:

1. Benzene oxide formation through the P-450 cytochrome enzyme depends on the function of oxidases. Epoxide is changed to phenol by hydroxylation. The phenol then is excreted as a sulphate conjugate or is glucuronidase or transformed to benzoquinone and hydroquinone. Hydroquinone, Phenol, glucuronide, and hydroquinone sulphate are markers of these enzymatic process.
2. An NADPH mediated process of Transformation of benzene oxide to malondialdehyde, resulting in catechol production by the intermediate benzene glycol [*Ong C-N, Lee B-L, 1994; Wang B et al., 2007*].

In respiratory exposure to Toluene, (about 65%), after four hours, lots of it is excreted in the urine in the form of Hippuric acid metabolites. This show that Toluene solvent is rapidly metabolized in body after 20 hour exposure [*Löf A et al., 1993*]. Air pollutants like NO2, black carbon and PM2.5 can lead to heart arrhythmia [*Peters A et al., 2000*]. Obesity, respiratory and cardiovascular diseases are considered as the risk factors for the exposure to pollutants and are intensified as a result of exposure to pollutants. Also there are below components nitrogen oxide (NOx), particulate matter (PM), carbon monoxide (CO), polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs) in cities with more vehicles [*Sarnat S et al., 2015*].

A strong relationship was also identified between emergency department visits and respiratory, cardiovascular and cerebrovascular problems resulted from exposure to particulate matters with different diameters aerodynamics and some gases [*Peters A et al., 2000; Phalen R, Phalen R, 2012; Dohrenwend P et al., 2013*].

According to the review of Paula Valencia Moulton et al, air pollutants exposure can create oxidative stress risk factors (chronic) which could, in turn, lead to Alzheimer's [*Qin X-D et al., 2015*]. In a case study conducted by Jonathan O. Anderson (2011), exposure to PM was found to be associated with oxidative stress factors, respiratory problems, increased use of drugs, decreased pulmonary function, increased mortality and recurrent health care utilization. The burden of disease such as severe attack of asthma leads to massive health resources consumption and costs and large load of resonances. [*Shah A et al., 2013*] According to this review, available data for cerebrovascular disease caused by the PM were not significant enough [*Moulton PV, Yang*

W, 2012]. Gennaro D'Amato et al (2014) also reported that human sensitivity to allergens can increase with chemical compounds, Aerosols like Exhaust Smoke, Ozone, Nitrogen Dioxide and suspended particles [*Anderson J et al., 2012*]. Loss of products and services provided by the workforce (Commodity or services) by the illness of the workers and the workforce is one of costs due to air pollution. With the increase in air pollution level, the rate of morbidity and mortality increases. One of the major air pollutant costs is the government healthcare system load, as it can increase costs of hospital emergency department visits worldwide, especially in days with more air pollution concentration. Cardiovascular and respiratory diseases are among reasons for hospital admissions acute cardiovascular and respiratory disease are one of the most serious causes for emergency department visits when the concentration of air pollution like CO, PM2.5, PM10, NO_2, SO_2 is very high [*Boesch H-J et al., 2008*]. Air pollution was found to be highly associated with hospitalization and deaths due to heart failure [*D'Amato G et al., 2014*].

Air pollution and its annually related Emergency Department visits, probably can be used as an public health index for health system strategies. Related Emergency Department visits should be differentiate in case of chronic respiratory/cardiovascular disease to clarify the difinitive role of air pollution subsequences; more studies should be conducted for this purpose. Preventive measures such as increasing air pollution standards of motor vehicles and industries, such as environmental dust control can lead to improve of health subsequences.

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THE NEW ARMENIAN MEDICAL JOURNAL

Vol.16 (2022). No 2

The Journal is founded by
Yerevan State Medical
University after M. Heratsi.

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Our journal is registered in the databases of Scopus, EBSCO and Thomson Reuters (in the registration process)

Scopus EBSCO Thomson Reuters

Copy editor: Tatevik R. Movsisyan

Printed in "VARM" LLC
Director: Ruzanna Arakelyan
Armenia, 0018, Yerevan,
Tigran Mec 48, 43
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