


Systemic Review

Air pollution enhances susceptibility to novel coronavirus (COVID-19) infection – an impact study

S. Maheswari^{1,*}, Rajarajan Pethannan¹ and Shanthi Sabarimurugan^{2,3}¹Department of Microbiology, Centre for Research & PG Studies, Indian Academy Degree College - Autonomous, Bangalore, India²Theranostics, GenesisCare, WA, Australia³School of Biomedical Sciences, Faculty of Health and Medical Sciences, The University of Western Australia Perth, WA, Australia*Correspondence: mahehrp@gmail.com

Received: July 19, 2020 Accepted: September 22, 2020

Abstract

On concurring to the current evidence, the myriad of vulnerable COVID-19 (Coronavirus Disease 19) transmission is acquiring through human-to-human transmission through droplets, which is depicting devastating pandemic. Urbanization and industrialization are the major contributing factors to the on-going change in global climate, with increased air pollution and poor air quality. As the global climate and air quality deteriorate, air pollutants remain as a fundamental concern to public health. Air pollution has been globally acknowledged as a major influence and exacerbating factor for human morbidity and mortality influenced on various respiratory diseases such as lung cancer, bronchitis, chronic obstructive pulmonary diseases, pneumonia, asthma, and influenza. Patients by long-term exposure to polluted air leads to chronic lung and heart conditions are less able to fight off lung infections and likely to die. Polluted air in developed countries is causing heart and lung damage and is responsible for early deaths in a year. This is also likely the case for COVID-19. The more severe impact by COVID-19 on city dwellers and those exposed to toxic fumes leads to the primary health damage such as respiratory infections than on others. The health damage inflicted on people by long-standing air pollution in cities is likely to increase the death rate by COVID-19. By lowering air pollution levels probability to reduce the spread of most vulnerable viruses by aerosol to fight against any possible future pandemics.

Keywords: COVID-19, air pollutants, respiratory diseases, SARS, MERS

Introduction

COVID-19 (Coronavirus disease 19) are enveloped single stranded RNA, which is currently exclaiming tremendous challenge throughout the world. This infectious pneumonia and fibrosis causing illness are spreading through droplets and direct contact with infected victims. The droplets are smudging with polluted air and the viruses are favourably immobilising in polluted air until it reaches a succeeding host in a need of an hour. Seemingly, Air pollution is now considered as the most substantial environmental cause of disease, with 4.2 million premature deaths in 2016 [1]. The differential effect of air pollution on health, which is particularly deleterious for older people and people with limited resources, is of significant concern to global health organizations [2]. Europe, the United States and other parts of the world have shown that ambient air pollution has adverse effects on morbidity and mortality [3]. Outdoor fine particulate air pollution is estimated to be responsible for about 3% of global adult cardiopulmonary-related mortality. Air pollution is likely to have similar adverse effects in developing countries, with Asian countries contributing approximately with two-thirds of the global burden [4]. The impact of air pollution on respiratory health in China has recently received significant attention since air pollutants have been associated with multiple adverse effects on human health, particularly respiratory and cardiovascular health [5]. In addition, residents of different regions have variable sensitivity to potential health effects of air pollutants [6]. Air pollution continues to rise at an alarming rate which affects the economy and quality of life. About 92% of the population breathes in air not according to the world health organization (WHO) limits, among which China tops the list as the worst country in outdoor air pollution, followed by India and Russia also in terms of the number of deaths annually [7]. Major cause of illness in ancient China by atypical climate variations and also excessive physical strain

associated with climate variations [8]. The climatic variations influence mortality and morbidity rates and the infectious disease transmission such as acute respiratory infections (ARIs) [9]. Pneumonia is caused by a combination of risk factors related to the host, the environmental pollutants and the infection [10]. People inhale infectious dust by direct contact, face-to-face contact or contaminant in patient room is deliberately accustomed to polluted air than unpolluted air. WHO described an ambient air quality database that looked that the human health is exposed to tiny particulate matters of 2.5 μm ($\text{PM}_{2.5}$) and 10 μm (PM_{10}) that are even very small enough to enter through the respiratory system and lead to serious health consequences [1]. In several urbanised areas of the world, air pollution patterns are changing with weather conditions and climate scenarios which have a significant effect on respiratory health both independently and synergistically. Synoptic air masses i.e., humidity, temperature, cloud cover, visibility, air pressure and wind speed have been associated with increases in mortality and morbidity but specific evidence for respiratory causes by viral infection is occasional and there is no clear evidence that these variables may have an independent effect apart from temperature [11]. Respiratory tract infections occur most often when the ambient temperature was at or below 0 °C. Average daily temperature was significantly associated with upper respiratory tract infections and lower respiratory tract infections episodes and separately for common cold and pharyngitis. A decrease in temperature increases the risk for common cold and pharyngitis. Furthermore, a lower absolute humidity increased the risk of upper respiratory tract infections and pharyngitis. The association between temperature, humidity and lower respiratory tract infections was non-linear [12]. Only limited information is available on the combined effect of viral infection, cold weather, and air pollution on mortality rate, but there is some evidence that air pollution and the weather may also affect the mortality rates associated with viral epidemics [13]. Therefore, to prevent avoidable deaths, evidence on the individual and combined effects of viral infections, cold temperatures, and air pollution on mortality would enable public health authorities to promote interventions such increasing vaccination coverage among elderly people and implementing measures to mitigate the effects of environmental risk factors.

Emergence of Coronavirus

Coronaviruses belong to the family *Coronaviridae*; subfamily *Coronavirinae* which can circulate in a diverse array of avian and mammalian and reservoirs, including humans, bats, cats, pigs, rodents, dogs, and birds [14]. Coronaviruses (CoV) are classified into four genera as Alpha-, Beta-, Gamma-, and Deltacoronavirus [15]. Severe acute respiratory syndrome-related coronavirus (SARS-CoV) and Middle East respiratory syndrome-related coronavirus (MERS-CoV) are highly pathogenic coronavirus emerged into human populations, other human coronaviruses (HCoVs) including HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoV-HKU1 are circulated in human populations for hundreds of years, causing mild respiratory illness to which approximately 5–30% are common colds [16]. In 2019, a new coronavirus was identified as the cause of a disease outbreak that originated in China. The virus is known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease it causes is called COVID-19. In March 2020, WHO declared the COVID-19 outbreak a pandemic. SARS-CoV and MERS-CoV are originated in bats, and it is likely that SARS-CoV-2 did as well. SARS-CoV spread from infected civets to people, while MERS-CoV spread from infected dromedary camels to people. Scientists are trying to determine how SARS-CoV-2 spread from an animal reservoir to people. Coronaviruses are enveloped, positive-strand RNA viruses between 70 and 120 nm in size. The characteristics of crown – like appearance of coronavirus are due the spike glycoproteins that radiate from the virus envelope of the spherical particles.

Mode of transmission of Coronavirus

Respiratory infections are transmitted through different sizes of droplets. Droplet particles which are larger than 5-10 μm in diameter are respiratory droplets, whereas those smaller than 5 μm in diameter are droplet nuclei [17]. COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes. Droplet transmission occurs when a person is in in close contact (within 1 m) with someone who has respiratory symptoms (e.g., coughing or sneezing) and is therefore at risk of having mucosae (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets [18]. Transmission may also occur through fomites in the immediate environment around the infected person [19]. Therefore, transmission of the COVID-19 virus can occur by direct contact with infected people and indirect contact with surfaces in the immediate environment or with objects used on the infected person. In the context of COVID-19, airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed; e.g., endotracheal intubation, bronchoscopy, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation [20]. There is some evidence that COVID-19 infection may lead to intestinal infection and be present in faeces. However, to date only one study has cultured the COVID-19 virus from a single stool specimen [21]. There have been no reports of faecal–oral transmission of the COVID-19 virus to date. MERS-CoV is also transmitted from close person-to-person contact (primarily in health care settings during the symptomatic phase of the disease), although instances of this transmission were significantly less during the height of the MERS epidemic. The transmission occurs through respiratory secretions from

coughing and sneezing, whereas primary cases of the virus have been traced to close contact with infected dromedary camels, the animals identified as the reservoir host for MERS-CoV [17]. Similarly, the transmission of SARS-CoV occurred during close person-to-person contact, via respiratory droplets from sneezing or coughing at a rapid rate, although not as quickly as the current outbreak of COVID-19. Furthermore, fomites, fecal transmission and handling of animals (killing, selling or preparing wild animals) were less common methods of transmission [22].

Respiratory diseases related to air pollution

The vapour of air pollutants is prone to be absorbed by human tissues or dissolved in body fluids, mainly relying on their hydrophilicity and hydrophobicity. PM₁₀ particles with larger size (~10 µm) can reach the proximal airways and be mostly eliminated by mucociliary clearance. PM_{2.5} is a notable risk factor for health, and can invade more deeply into the lungs [23]. People inhaling PM_{2.5} at high concentration are more prone to develop chronic respiratory diseases. In long-term exposure to PM_{2.5} develops a chronic inflammatory stimulus, especially in unhealthy population [24], whereas short term PM_{2.5} exposure may also increase susceptibility to infections which damages human airways, potentially facilitating viral infections. Also, exposure to PM_{2.5} pollutants weakens the immune response by making the human body less effective in fighting against the virus-caused diseases [25]. PM₁₀ are so small and when breathed in they penetrate deep into the lungs. When exposed to high concentrations of PM₁₀ can result in a number of health impacts such as coughing and wheezing to asthma attacks and bronchitis to high blood pressure, strokes, heart attack and premature death. Adverse health effects of air pollutants have been shown on multiple respiratory diseases, including respiratory infections, asthma, chronic obstructive pulmonary disease (COPD), lung cancer, even in combination with stroke and heart diseases [26-28]. The adverse impact of air pollutants can be highlighted especially in individuals with pre-existing lung infections or other lung diseases, because they are likely at greater risk, and children, possibly because children have a relatively larger lung surface area and more outdoor physical activities with a greater chance to expose to air pollution. Both major outdoor and indoor pollutants, including ozone (O₃), carbon monoxide (CO), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), PM₁₀, PM_{2.5}, dust mite, pollen, pet dander, and smoke, contribute to more severe allergic responses [29]. Specifically, allergic immunoglobulin E (IgE) responses to pollen or ovalbumin can be triggered by diesel exhaust particles (DEP) exposure and airway responsiveness in asthmatic patients with house dust mite challenge can be potentiated by short-term exposure to NO₂ [30].

Coronavirus threat greater for polluted cities

Air pollution can lead to hypertension, diabetes and respiratory diseases, conditions that link to higher mortality rates (comorbidity) for COVID-19. The European Public Health Alliance (EPHA) warned those who are living in polluted cities are more at risk for COVID-19 [31]. According to the U.S. Environmental Protection Agency (US EPA), breathing air with a high concentration of NO₂ can irritate airways in the human respiratory system [31]. NO₂, which is released when coal, oil, gas, and diesel are burned, is dreadful for the lungs. In addition, climatic pollutants reduce lung function and increase wheezing, asthma attacks, inflammation in airways, and hospitalizations. Exposures to air pollutants over short periods can exacerbate respiratory diseases, particularly asthma, leading to respiratory symptoms (such as coughing, wheezing or difficulty breathing). The development of asthma and potentially increased susceptibility to respiratory infections are due to the longer exposure to elevated concentrations of NO₂. Patients with long-term exposure to air pollution and with chronic lung and heart condition are unable to fight off lung infections and are more likely to die. This is likely also the case for COVID-19 [32].

COVID-19 is now widely diffused in many other European countries, particularly Spain and Germany, nevertheless with evident international dissimilarities which cannot be explained only by different health policies and systems. In particular, since the virus began to spread in Italy, Lombardy and Emilia-Romagna recorded a substantial high level of lethality when compared with other countries but also than other Italian regions. In less than a month, Italy which had only three cases of the COVID-19 had the highest number of infected cases and deaths than China. The number of infected cases rose by 50% by March 2020 alone with a mortality rate of 4%. The northern regions of Lombardy, Veneto and Emilia-Romagna have been most affected by the outbreak of COVID-19. In which 85% of infected patients are in this region and 92% of deaths so far. COVID-19 has been confirmed in all 20 regions of the country. The air pollution in northern Italy might be a factor for highest death rates. The European Environment Agency (EEA) has recently introduced an aggregated index named as air quality index (AQI), reflecting the potential impact of air quality on health, driven by the pollutants in geographical regions [33]. The AQI is based on concentration values for up to five key pollutants, including: PM₁₀, PM_{2.5}, O₃, SO₂ and NO₂. According to the AQI the area covering Lombardia and Emilia-Romagna results to be the most polluted area in Italy and one of the most polluted in Europe [34]. At the same time, the fatality rate only in two Italian regions: given the pandemic dimension of COVID-19, it will be interesting to evaluate if, similarly, a higher lethality will be also recorded in the most polluted regions worldwide [35]. According to Swiss air monitoring platform, IQA 24 of Europe's 100 most polluted cities are in Italy. Studies have shown a high correlation between mortality rates from respiratory condition and pollution in Italy and this could be one of the factors for increasing the high mortality rate by COVID-19 in Italy [36]. One COVID-19 hotspot in northern Italy had particularly high levels of PM₁₀ – microscopic particles of pollution due to large

road traffic. Mortality data for COVID-19 is incomplete but preliminary numbers shows that the majority of patients are elderly or have pre-existing chronic conditions such as heart or lung disease.

In the United States nationwide study estimates the relationship between long-term exposure to PM_{2.5} and COVID-19 death rates. The statistically significant evidence that an increase of 1 g/m³ in long-term PM_{2.5} exposure is associated with a 15% increase in the COVID-19 mortality rate. Therefore, a small increase in long-term exposure to PM_{2.5} leads to a large increase in COVID-19 death rate of a magnitude that is 20 times the one estimated for all-cause of mortality [37]. This analysis provides a timely characterization of the relationship between historical exposures to air pollution COVID-19 deaths in the United States. Research on how modifiable factors may exacerbate COVID-19 symptoms and increase mortality risk is essential to guide policies and behaviours to minimize fatality related to the outbreak.

According to the global air pollution observatory maintained by WHO (http://www.who.int/gho/phe/outdoor_air_pollution/en/), 13 of the world's 20 cities with the highest annual levels PM_{2.5} are in India, in which New Delhi is leading the cities within India [38]. Due to increasing economic activity and industrialization across the country, a progressive worsening of ambient air pollution (AAP) in these Indian cities is nearly certain. The Indian Central Pollution Control Board revised the annual average PM₁₀ to 60 µg/m³ which is lower than the Interim Target 1 (IT-1) guideline value of 70 µg/m³ recommended by the WHO [38, 39]. The annual average PM₁₀ levels reported by Central Pollution Control Board (CPCB; > 90 µg/m³) is routinely higher than the recommended guideline values across most locations in India. The CPCB recommended annual average value for PM_{2.5} (40 µg/m³) is higher than WHO recommended value (35 µg/m³) and similar to PM₁₀, the annual average PM_{2.5} levels are higher than the guideline values in most locations throughout India [39]. The situation is similar for NO₂ and SO₂, with the annual levels for these pollutants exceeding, by a substantial margin, the 24-h WHO-AQG (Air Quality Guidelines) levels. A systematic review of the literature on the health effects of ambient air pollution in Asia published by the Health Effects Institute (HEI) identified 43 studies carried out between 1980 and 2008, which reported adverse health effects of air pollution in India [40]. These studies, largely concentrated in the cities of Delhi and Mumbai, reported that the prevalence of diminished lung function, acute and chronic respiratory symptoms such as cough and wheeze, and asthma in children and adults increased in areas with elevated levels of air pollution. More time-series studies reported that increased rates of natural all-cause mortality with short-term (daily) exposure to PM₁₀ in Chennai, Ludhiana, and Delhi, India. In India, people living in major cities with long-term exposure to air pollutants along with chronic lung and heart condition are unable to fight off lung infections and are more likely to die. So, in India there is a huge scramble of COVID-19 infections in major polluted cities.

Air pollution and case fatality of SARS and MERS

Air pollution was associated with increased risk of dying from SARS-CoV which claimed 349 lives with 5,327 probable cases reported in China in November 2002 [41]. It might be long-term or short-term exposure to certain air pollutants which could compromise lung function, therefore increased SARS-CoV fatality. Both long-term and short-term exposure to air pollution had associated with a variety of adverse health effects including acute respiratory inflammation, asthma and COPD [42]. In SARS patients, the predisposition of respiratory epithelium leads to severe respiratory symptoms and an increased risk of death due to air pollution. The adverse effect of fatality rate was due to exposure of PM₁₀ [43]. In the United States on the long-term effects of air pollution showing that every 10 µg/m³ elevation in PM₁₀ accounted for 6% of increased risk of cardiopulmonary mortality [44]. Exposure to PM₁₀ was also linked to asthma and bronchitis. Exposure to air pollutants, such as PM₁₀, might influence the prognosis of SARS and lead to increased risk of deaths. Also, SARS victims in regions with moderate air pollution levels were 84% more likely to die than with low air pollution [45]. According to the WHO, in Saudi Arabia in September 2012 MERS-CoV was reported and spread to 27 countries. People infected with MERS-CoV developed symptoms such as fever, cough, shortness of breath and severe acute respiratory illness. Also in Saudi Arabia, the major cities are severely polluted by particulate matter which exceed WHO guidelines. Sand and dust storms as well as other sources of air pollution such as industrial activities, fuel combustion, and traffic emissions contribute to elevated levels of particulate matter in the country [46], all of which contribute to reduced visibility. Sandstorms, dust storms, and air pollution in Saudi Arabia and elsewhere have been associated with increased morbidity and mortality, including from respiratory disease [47]. In January 2020, WHO confirmed 2,519 MERS-CoV cases and 866 deaths (fatality rate of 34.37%). Among all reported cases in people, about 80% have occurred in Saudi Arabia [48].

Conclusions

WHO reported significant inflammation in the airways due to the toxic gas NO₂ at concentrations above 200 µg/m³ [49]. Rather, pollution particles may also be a vector for pathogens, as well as exacerbating existing health problems. There is also clear evidence that people exposed to highly polluted air have substantially higher risk of mortality rate in other coronavirus viruses – related diseases. There is no research that has proven a direct relationship between air pollution and COVID-19 infections. Apparently recent research establishing smoking, which affects the functioning of the lung, an important factor for COVID-19 develops into pneumonia. In 2012, MERS-CoV outbreak in Saudi Arabia reported that

tobacco smokers were more likely to contract the mortality rate by the virus. Confinement measures thus protect in two ways, by reducing the risk of COVID-19 infection and by easing pollution from road traffic and significant industrial activities. The concentration of PM_{2.5} and PM₁₀ and CO will also reduce in future due to lockdown.

Conflict of interest

The authors declare that there is no conflict of interest.

CRediT author statement

SM: Conceptualization, Methodology, Software, Data curation, Writing- Original draft preparation, Visualization, investigation, Supervision, Writing- Reviewing and Editing; RP: Data curation, Writing- Original draft preparation, Supervision, Writing- Reviewing and Editing; SS: Conceptualization, Methodology, Software, Supervision, Writing- Reviewing and Editing.

ORCID

S. Maheswari: 0000-0003-3500-1284

P. Rajarajan: 0000-0002-7745-4276

References

- [1] World Health Organization (WHO). Ambient air pollution: Health impacts. [cited Aug 5, 2019]. Available from: <http://www.who.int/airpollution/ambient/health-impacts/en/>.
- [2] 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;69:660–665.
- [3] Pope CA, Turner MC, Burnett RT, Jerrett M, Gapstur SM, Diver WR, et al. Relationships between fine particulate air pollution, cardiometabolic disorders, and cardiovascular mortality. *Circ Res* 2015;116(1): 108-15.
- [4] Cohen AJ, Ross Anderson H, Ostro B, Pandey KD, Krzyzanowski M, Kunzli N. The global burden of disease due to outdoor air pollution. *J Toxicol Environ Health Part A* 2005; 68: 1301–1307.
- [5] Ran L, Ning J, Qichen L. Impact of air pollutants on outpatient visits for acute respiratory outcomes. *Int J Environ Res Public Health* 2017;14(1):47.
- [6] Liu HY, Bartonova A, Schindler M. Respiratory disease in relation to outdoor air pollution in Kanpur, India. *Arch Environ Occup Health* 2013;68(4):204–17
- [7] World Health Organization (WHO) (2016). Air Pollution [cited Sep 27, 2016]. Available from: <https://www.who.int/news/item/27-09-2016-who-releases-country-estimates-on-air-pollution-exposure-and-health-impact>
- [8] Sampaio J. Historia da medicina tradicional china. Leon: Fundacion Europea de Medicina Tradicional China, Fundacion Universitaria Iberoamericana (FUNIBER), Universidad de Leon 2008. (Spanish)
- [9] Nair H, Simoes EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JS. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. *Lancet*. 2013; 381(9875):1380-90.
- [10] Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. *Bull World Health Organ* 2008;86(5),408-416.
- [11] Abe T, Tokuda Y, Ohde S, Ishimatsu S, Nakamura T, Birrer RB. The relationship of short-term air pollution and weather to ED visits for asthma in Japan. *Am J Emerg Med* 2009;27:153–159.
- [12] Ikaheimo TM, Juvonen R, Jokelainen J, Harju T, Peitso A, Bloigu A, et al. Cold temperature and low humidity are associated with increased occurrence of respiratory tract infections. *Respir Med* 2009;103,456-462
- [13] Analitis A, De Donato F, Scortichini M, Lanki T, Basagana X, Ballester F. synergistic effects of ambient temperature and air pollution on health in Europe: results from the PHASE project. *Int J Environ Res Public Health* 2018;15(9):1856.

- [14] Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. *Nat Rev Microbiol* 2009;7: 439–450.
- [15] De Groot R. Family – Coronaviridae. In: King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ, editors. *Virus Taxonomy*. Elsevier; 2012. 806–828.
- [16] Corman VM, Muth D, Niemeyer D. Chapter eight - hosts and sources of endemic human coronaviruses. In: Kielian M, Mettenleiter TC, Roossinck MJ, editors. *Advances in virus research*. Vol. 100. Academic Press; 2018. 163–188.
- [17] World Health Organization (WHO). (2014). Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. [cited Apr 15 2014]. Available from: https://apps.who.int/iris/bitstream/handle/10665/112656/9789241507134_eng.pdf?sequence=1
- [18] Huang C, Wang Y, Li X. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 2020;395:497–506.
- [19] Ong SW, Tan YK, Chia PY, Lee TH, Ng OT, Wong MS. Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. *JAMA* 2020 [Epub ahead of print]
- [20] World Health Organization (WHO). Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations. [cited Mar 29, 2020]. Available from: <https://www.who.int/news-room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations>
- [21] Zhang Y, Chen C, Zhu S. Isolation of 2019-nCoV from a stool specimen of a laboratory-confirmed case of the coronavirus disease 2019 (COVID-19). *China CDC Weekly*. 2020;2(8):123–4.
- [22] Yeung MC, Xu RH. SARS: Epidemiology. *Respirol* 2003;8:S9–S14
- [23] Falcon-Rodriguez CI, Osornio-Vargas AR, Sada-Ovalle I, Segura-Medina P. Aeroparticles, composition, and lung diseases. *Front Immunol* 2016;7:3.
- [24] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al.. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–513.
- [25] Conticini E, Frediani B, Caro D. Can atmospheric pollution be considered a cofactor in extremely high level of SARS-CoV-2 lethality in northern Italy? *Environ Pollut* 2020;114465.
- [26] Hu G, Zhong N, Ran P. Air pollution and COPD in China. *J Thorac Dis* 2015;7:59-66.
- [27] Kurt OK, Zhang J, Pinkerton KE. Pulmonary health effects of air pollution. *Curr Opin Pulm Med* 2016;22:138-143.
- [28] Li L, Yang J, Song YF, Chen PY, Ou CQ. The burden of COPD mortality due to ambient air pollution in Guangzhou, China. *Sci Rep* 2016;6:25900
- [29] Saadeh R, Klaunig J. Children's inter-individual variability and asthma development. *Int J Health Sci (Qassim)* 2015; 9:456-467.
- [30] Tunnicliffe WS, Burge PS, Ayres JG. Effect of domestic concentrations of nitrogen dioxide on airway responses to inhaled allergen in asthmatic patients. *Lancet* 1994;344:1733-1736
- [31] European Public Health Alliance. Clean air – latest developments COVID–19. [cited Mar 16, 2020]. Available from: [Epha.org/coronavirus-threat – greater- - for – polluted – cities/](https://epha.org/coronavirus-threat – greater- - for – polluted – cities/)
- [32] Lerner S. Million people in the U.S. could die if Coronavirus goes unchecked. [cited Mar 17, 2020]. Available from: <https://theintercept.com/2020/03/17/coronavirus-air-pollution/>
- [33] Barbrioglio E. Europe's 100 most polluted cities. [cited Feb 29, 2020]. Available from: <https://www.forbes.com/sites/emanuelbarbiroglio/2020/02/29/cities-in-poland and italy-among-europes-100-most-polluted/#77eaacd058fd>.

- [34] Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with COVID19 in Wuhan, China. *Clin Infect Dis* 2020;71(15):762-768; Available from: <https://doi.org/10.1093/cid/ciaa248>.
- [35] Conticini E, Frediani B, Caro D. Can atmospheric pollution be considered a co-factor in extremely high level of SARS-CoV-2 lethality in Northern Italy? *Environ Pollut* 2020;261:114465
- [36] Godin M. Why is Italy's Coronavirus outbreak so bad? [cited Mar 10, 2020]. Available from: <https://time.com/5799586/italy-coronavirus-outbreak/>
- [37] Wu X, Nethery RC, Sabath BM, Braun D, Dominici F. Exposure to air pollution and COVID-19 mortality in the United States. [cited Apr 27, 2020]. Available from: <https://www.medrxiv.org/content/10.1101/2020.04.05.20054502v2>
- [38] World Health Organization (WHO). Global Health Observatory (GHO) data [cited Apr 19, 2020]. Available from: http://www.who.int/gho/phe/outdoor_airpollution/en/
- [39] Central Pollution Control Board (CPCB). National ambient air quality monitoring series. Ministry of environment and Forest, Government of India: Delhi, India.
- [40] Health Effects Institute. Outdoor air pollution and health in developing countries of Asia: a comprehensive review. [cited Nov 18, 2020]. Available from: <https://www.healtheffects.org/publication/outdoor-air-pollution-and-health-developing-countries-asia-comprehensive-review>
- [41] World Health Organization (WHO). Cumulative number of reported probable cases of SARS (From: Nov 1st, 2002 To: August 7th, 2003) World Health Organization, Communicable Disease Surveillance & Response (CSR) [cited Aug 15, 2003]. Available from: http://www.who.int/csr/sars/country/2003_08_15/en/.
- [42] Bates DV, Baker-Anderson M, Sizto R. Asthma attack periodicity: a study of hospital emergency visits in Vancouver. *Environ Res* 1990; 51,51-70.
- [43] Lebowitz MD. Epidemiological studies of the respiratory effects of air pollution. *Eur Respir J* 1996;9(5):029-1054
- [44] Arden Pope C, Burnett RT, Thun MJ. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002;287(9):1132-1141
- [45] Cui Y, Zhang Z, Froines J, Zhao J, Wang H, Yu SZ, et al. Air pollution and case fatality of SARS in the People's Republic of China: an ecologic study. *Environ Health Glob Access Sci Sour* 2003;2:15
- [46] 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;28:641–661.
- [47] Bell ML, Levy JK, Lin Z. The effect of sandstorms and air pollution on cause specific hospital admissions in Taipei. *Taiwan Occup Environ Med* 2008;65:104–111
- [48] National Institute of Health (NIH). COVID-19, MERS & SARS. [cited Mar 11, 2020]. Available from: <https://www.niaid.nih.gov/diseases-conditions/covid-19>.
- [49] World Health Organization (WHO) Ambient air pollution: health effect. [cited May 2, 2018]. Available from: [http://www.who.int/news-room/fact-sheets/detail/ambient-\(outdoor\)-air-quality-and-health](http://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health).