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# Role of atmospheric particulate matter exposure in COVID-19 and other health risks in human: A review

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## ABSTRACT

Due to intense industrialization and urbanization, air pollution has become a serious global concern as a hazard to human health. Epidemiological studies found that exposure to atmospheric particulate matter (PM) causes severe health problems in human and significant damage to the physiological systems. In recent days, PM exposure could be related as a carrier for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus transmission and Coronavirus disease 2019 (COVID-19) infection. Hence, it is important to understand the adverse effects of PM in human health. This review aims to provide insights on the detrimental effects of PM in various human health problems including respiratory, circulatory, nervous, and immune system along with their possible toxicity mechanisms. Overall, this review highlights the potential relationship of PM with several life-limiting human diseases and their significance for better management strategies.

## 1. Introduction

In the transitional stages of industrialization and urbanization, the world faces serious problems caused by air pollution. Particularly, atmospheric particulate matter (PM) is extremely harmful to the human health and environment. Epidemiological studies have revealed that exposure to PM pollution can adversely affect the human, while their higher concentrations cause more significant harms (Sanchez et al., 2020). Further, there is a strong relationship between PM and Coronavirus disease 2019 (COVID-19) infection (Amoatey et al., 2020; Setti et al., 2020). PM enters the human body through respiration and the large particulates are filtered by the nose and upper respiratory tract. But most small particulates are deposited in the lungs and some of which can be transferred into the blood and enters different organs, thereby causing damage to multiple physiological systems, especially the respiratory, cardiovascular and nervous systems (Forman and Finch, 2018).

## 2. Atmospheric particulate matter

Atmospheric particulate matter refers to the sum of all liquid or solid particles present in the atmospheric environment with a wide range of unit particle sizes and different physical and chemical properties. A

variety of PM is evenly distributed in the atmosphere, forming a relatively stable and complex suspension called the aerosol. Hence, PM is also called atmospheric aerosol (Pan et al., 2019). Based on the particle size, PM can be divided into following types such as total suspended particles (TSP), coarse particulate matter (PM<sub>10</sub>), fine particulate matter (PM<sub>2.5</sub>), and ultrafine particulate matter (PM<sub>1</sub>). TSP, PM<sub>10</sub>, PM<sub>2.5</sub>, and PM<sub>1</sub> are referred to suspended atmospheric particles with an aerodynamic equivalent diameter of  $\leq 100 \mu\text{m}$ ,  $\leq 10 \mu\text{m}$ ,  $\leq 2.5 \mu\text{m}$ , and  $\leq 1.0 \mu\text{m}$ , respectively. The chemical composition of PM constantly changes with space and time (Fang et al., 2019). It mainly consists of heterogeneous mixtures, which includes, i) carbonaceous components such as organic carbon, elemental carbon, and a small amount of carbonates and carbonic acid; ii) inorganic ions; iii) polycyclic aromatic hydrocarbons (PAHs) and iv) metals like, Cd, Cu, Zn, V and Ni (Kim et al., 2015; Sun et al., 2018).

### 2.1. Sources of PM

The PM enter into the atmosphere from natural and anthropogenic sources. Primarily, the solid or liquid particles that are directly entered into the atmosphere during daily activities contribute to the major part. For instance, industrial activities, combustion of coal, vehicle exhaust

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emissions, mining, biomass burning, construction-generated dust and abrasion of brakes and tires (Kim et al., 2015; Chowdhury et al., 2018). In developing countries, traffic-related air pollution (TRAP) and solid fuel used for cooking and heating are the major sources of PM<sub>2.5</sub> (Gautam et al., 2016; Morishita et al., 2019). The natural sources of PM are volcanoes, forest fires, dust storms, sea spray and vegetation (Kim et al., 2015). The photochemical reactions of gaseous contaminants in the atmosphere contribute to the secondary sources of PM (Xia et al., 2019). For example, nitrogen oxides, including nitric oxide and nitrous oxide, sulfur dioxide, and some organic gases, can produce nitrates, sulfates, and organic PM after a series of reactions in the atmosphere.

## 2.2. Health effects of PM in human

PM is one of the crucial air pollutants and found to cause a wide range of health effects in human (Manojkumar and Srimuruganandam, 2021). Epidemiological studies have revealed a strong association between PM and diseases involving multiple organ system (Cowell et al., 2019; Gu et al., 2020). For instance, the link between PM and the aggravation of respiratory illness such as, allergy and asthma has been well documented (Chowdhury et al., 2018). Besides, International Agency for Research on Cancer (IARC) has reported that PM in outdoor air pollution is a human carcinogen (IARC, 2016; Sun et al., 2018). Short term exposure to PM was significantly associated with acute cardiovascular risks like, myocardial infarction, arrhythmias, hypertension and metabolic syndrome (Chen et al., 2020a; Cowell et al., 2019). Furthermore, PM could also accelerate the risk of neurological effects, including Alzheimer's disease and dementia (Younan et al., 2020). It is apparent that the PM causes significant damage to various organ systems. Hence, this review highlights the health effects of PM along with underlying molecular mechanism in physiological systems such as respiratory, cardiovascular, nervous, and immune systems. In addition, the relationship between PM, SARS-CoV-2 transmission and COVID-19 infection was also reviewed.

## 3. Impact of PM on the respiratory system

### 3.1. Health effects

PM enters the human primarily through respiration and causes damage to the respiratory system. According to World Health

Organization (WHO), an estimated more than 2 million deaths worldwide every year results from air pollution-caused injuries to the respiratory system (WHO, 2018a). Long-term exposure to PM can trigger various respiratory diseases including asthma, respiratory tract inflammation, and even lung cancer. Elevated TSP level is positively correlated with the incidence of respiratory diseases in children (Pan et al., 2010). Exposure to PM<sub>10</sub> and PM<sub>2.5</sub> have been reported to increase the risk of asthmatic children in Guadeloupe (Cadelis et al., 2014). Therefore, PM is a significant cause for the development of respiratory diseases such as asthma and lung cancer. The impact of PM in the respiratory system was summarized in Table 1 and Fig. 1.

### 3.2. Toxicity mechanisms

Experimental evidences showed that exposure to PM can cause inflammation in lung tissues of rats, and the severity of inflammation tends to worsen as the dose increases (Xiao et al., 2007). The PM exposure causes various respiratory diseases mainly through the following mechanisms.

#### 3.2.1. Free radical peroxidation damage

Heavy metal components and organic substances in PM<sub>2.5</sub> can increase the free radical production and subsequent decrease of antioxidants level, which lead to lipid peroxidation in lung tissues (Pardo et al., 2019). The water-insoluble fraction of PM<sub>10</sub> may induce the production of hydrogen peroxide and weaken the enzymatic antioxidant defense, thereby inducing oxidative damage in human lung epithelial A549 cells (Yi et al., 2014). The oxidative damage might be the leading cause of impairment to the respiratory system (Wu et al., 2019; Sun et al., 2020).

#### 3.2.2. Inflammatory response

The inflammatory response is due to immune mechanism of the body in response to noxious stimuli. Long-term exposure of human lung epithelial cells to ambient PM<sub>10</sub> can reduce the anti-inflammatory proteins and leads to the excessive release of inflammatory cytokines (Jeon et al., 2011). PM<sub>2.5</sub> can stimulate the overexpression of multiple inflammatory cytokine-related genes (He et al., 2019; Zhao et al., 2019a). Excessive release of inflammatory cytokines can affect the pulmonary microenvironment, damage the lung tissues and reduce the lungs repair ability.

**Table 1**  
Health effects of PM on the respiratory system.

S. No.	PM type	Country/Location	Period	Patients/Subject	Health effects	Reference
1.	PM <sub>10</sub> , PM <sub>2.5</sub> and PM <sub>1</sub>	Oporto, Portugal	2018–2019	65 mothers and their newborns	PM <sub>10</sub> deposited in the head region, while PM <sub>2.5</sub> and PM <sub>1</sub> deposited in the pulmonary area	Madureira et al. (2020)
2.	PM <sub>10</sub> , PM <sub>2.5</sub> and PM <sub>1</sub>	7 Northeastern Chinese cities	2012–2013	6740 children	Impaired lung function with significant impact on body mass index (BMI)	Xing et al. (2020)
3.	PM <sub>10</sub> and PM <sub>2.5</sub>	96 cities of China	2013–2016	Meteorological and hospital data	Increases the risk of COPD	Tian et al. (2020)
4.	PM <sub>10</sub> and PM <sub>2.5</sub>	China	2013–2018	69,491 patients	Increases the risk of respiratory system related diseases	Chang et al. (2020)
5.	PM <sub>10</sub> and PM <sub>2.5</sub>	4 Brazilian Southeast capitals	2015–2018	Meteorological and hospital data	Causes respiratory diseases	de Oliveira Fernandes et al. (2020)
6.	PM <sub>10</sub>	Taiwan	2010–2012	120 children	Adverse effects on lung function	Yen et al. (2020)
7.	PM <sub>10</sub>	Bangkok, Thailand	2013–2018	Meteorological and hospital data	Respiratory diseases are associated with air pollution	Thongkum et al. (2020)
8.	PM <sub>10</sub>	England	1991–1992	14,541 pregnant women with 13,963 children	Reductions in lung function in mid-childhood	Cai et al. (2020)
9.	PM <sub>2.5</sub>	Shanghai, China	2012–2014	5281 participants	Decreases forced vital capacity (FVC), inspiration capacity (IC), and vital capacity (VC) with impaired lung function	Hou et al. (2020)
10.	PM <sub>2.5</sub>	Shenyang, China	2015–2016	114 healthy volunteers	Causes imbalance in the oropharyngeal microbiota and impaired lung function in young people	Li et al. (2019a)
11.	PM <sub>2.5</sub>	United States	2000–2018	7071 participants	Associated with increased emphysema	Wang et al. (2019a)
12.	PM	Eastern Massachusetts	2012–2014	81 COPD patients	Promotes systemic oxidative stress	Huang et al. (2020)

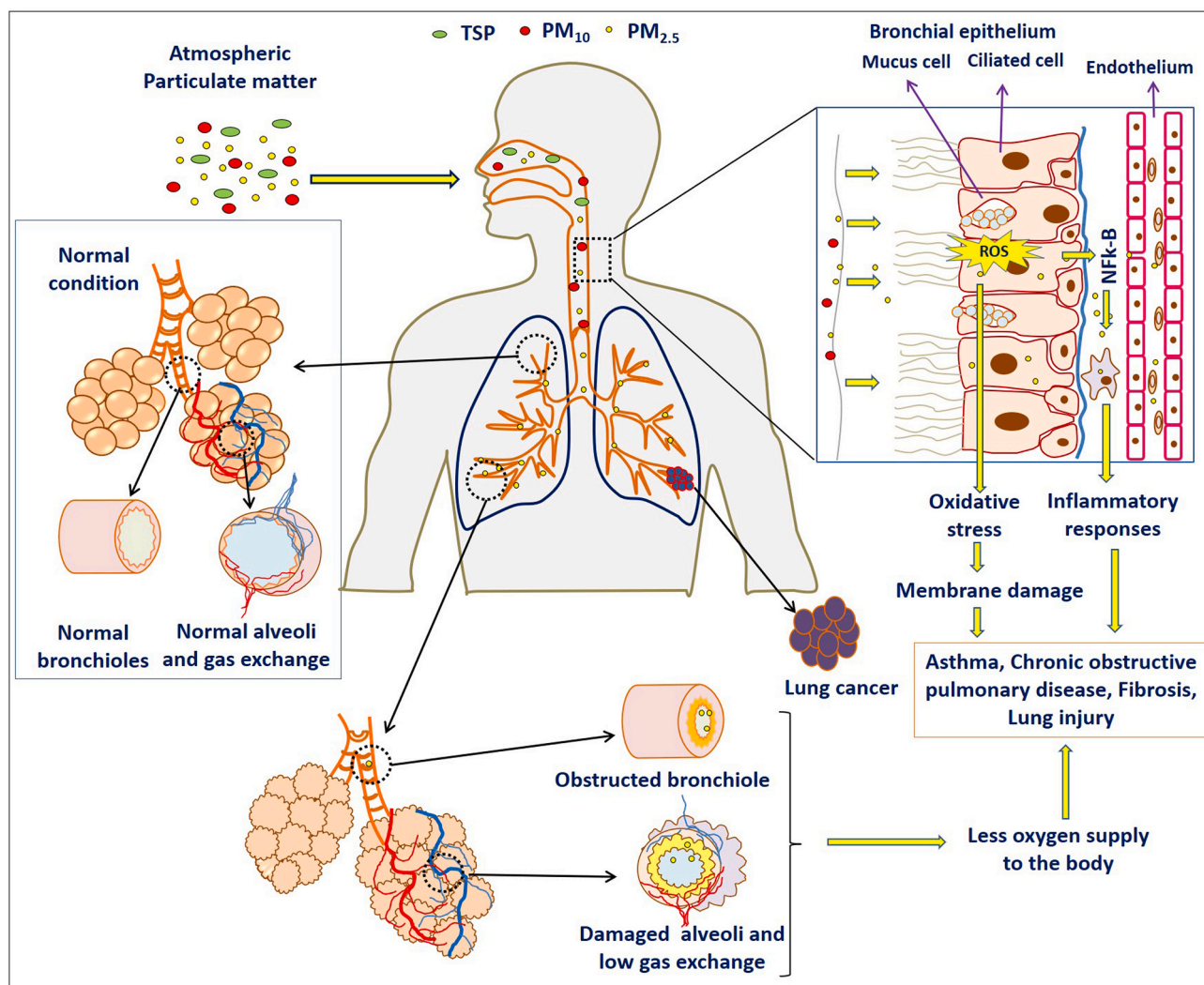


Fig. 1. Health effects of PM in respiratory system.

### 3.2.3. Imbalance of intracellular calcium homeostasis

Calcium (Ca) is an important second messenger that regulates the physiological functions of the body. Ca<sup>2+</sup> plays a vital regulatory function after tissue injury in the respiratory system. PM<sub>2.5</sub> disrupts the calcium ion homeostasis in the body, causing cell damage and apoptosis (Geng et al., 2006). PM<sub>2.5</sub> increases the intracellular Ca<sup>2+</sup> concentration in lymphocytes by regulating Ca<sup>2+</sup>-Mg<sup>2+</sup>-ATPase enzyme activities, resulting in imbalanced Ca<sup>2+</sup> homeostasis and leads to an inflammatory response (Zhao et al., 2019b). In addition, the massive production of Ca<sup>2+</sup> can cause a variety of subcellular damages, such as endoplasmic reticulum swelling, mitochondrial fission, and mitochondrial crista degeneration, eventually leading to cell death and affect the normal functioning of lung tissues (Guo et al., 2017).

### 3.2.4. Macrophage damage

After the PM entered into lungs, it stimulates alveolar macrophages to elicit a series of immune responses, which plays an important role in the induction of different diseases. PM<sub>10</sub> exposure in macrophages can result in cytoskeletal changes and impairs the phagocytic capacity and motility of macrophages (Brown et al., 2004). PM<sub>2.5</sub> can affect the cytoskeleton rearrangement by increasing the expression of PI3Kδ and inhibition of RhoA activity, thereby causing phagocytic dysfunction of macrophages in rats with chronic obstructive pulmonary disease (COPD) (Xia et al., 2017). Therefore, the damage to cytoskeletons may reduce the ability of macrophages to remove PM from the lungs, which

resulted in lung damage.

### 3.2.5. Cell cycle dysregulation

The PM has a dual role in regulating cell cycle, i.e., initiating or inhibiting cell cycle arrest. PM<sub>10</sub> can lead to abnormal cell death in lung tissues by inducing G0/G1 cell cycle arrest. PM<sub>2.5</sub> modulates the expression of the p21 protein through the long noncoding RNA (LINC0034) to block the bronchial epithelial cells at the G2/M phase (Xu et al., 2017). PM<sub>2.5</sub> can also arrest the G1 to S phase transition and the S phase checkpoint signaling pathway, which affects the cell survival. Furthermore, PM<sub>10</sub> exposure may induce apoptosis evasion in lung cells by activating STAT3 via PKCζ and Src kinases, leading to lung cancer (Reyes-Zárate et al., 2016; Abbas et al., 2019).

## 4. Impact of PM on the cardiovascular system

### 4.1. Health effects

The cardiovascular system is one of the main targets of air pollution-induced toxic effects (Brook et al., 2010). Exposure to ambient PM can lead to various cardiovascular diseases (CVD), such as myocardial infarction, coronary heart disease, stroke, and cardiac failure. Cao et al. found that for every rise of 10 μg/m<sup>3</sup> TSP, the risk of cardiovascular mortality increased by 0.9% (Cao et al., 2011). Other studies reported that the rise of 10 μg/m<sup>3</sup> PM<sub>10</sub> and PM<sub>2.5</sub> could increase the

cardiovascular and circulatory disease mortality by 0.55% and 1.22%, respectively (Guo et al., 2010; Yang et al., 2012). PM<sub>10</sub> and PM<sub>2.5</sub> can decrease the heart rate variability and increase blood pressure and thereby increases the risk of CVD in humans (Tofler and Muller, 2006). Table 2 and Fig. 2 showed the health impact of PM in the cardiovascular system.

#### 4.2. Toxicity mechanisms

##### 4.2.1. Inflammatory response

PM<sub>10</sub> exposure increased the expression of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin 6 (IL-6), and other inflammatory factors in rat myocardium, causing myocardial inflammatory responses and injuries to the cardiovascular system (Radan et al., 2019). Cui et al. have shown that PM<sub>2.5</sub> exposure could significantly reduce the number of circulating endothelial progenitor cells in mice, induce serum inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$ , thereby leading to the occurrence and progression of CVD (Cui et al., 2015).

##### 4.2.2. Oxidative stress

Cen et al. have found that PM<sub>10</sub> induced cardiovascular toxicity in zebrafish larvae by increasing oxidative stress (Cen et al., 2020). When the fine PM is phagocytosed by macrophages, the extracellular concentrations of reactive oxygen species (ROS) will be greatly increased (Long et al., 2020). PM<sub>2.5</sub> can also activate the Wnt/ $\beta$ -catenin signaling pathway (Zhou et al., 2010) and induces massive ROS production in the body. It leads to oxidative stress, cell membrane lipid peroxidation and subsequent damage to the cardiovascular system.

##### 4.2.3. Apoptosis

PM<sub>2.5</sub> can induce apoptosis in endothelial cells and cardiomyocytes and causing damage to the cardiovascular system. Endothelial cells are important interfaces in regulating the homeostasis of the cardiovascular system (Wang and Tang, 2020). An excessive increase in PM<sub>2.5</sub> concentration can enhance the expression of cytochrome c, thereby promoting the activation of apoptotic proteins such as caspase-9 and caspase-3 and leading to apoptosis of endothelial cells (Dong et al.,

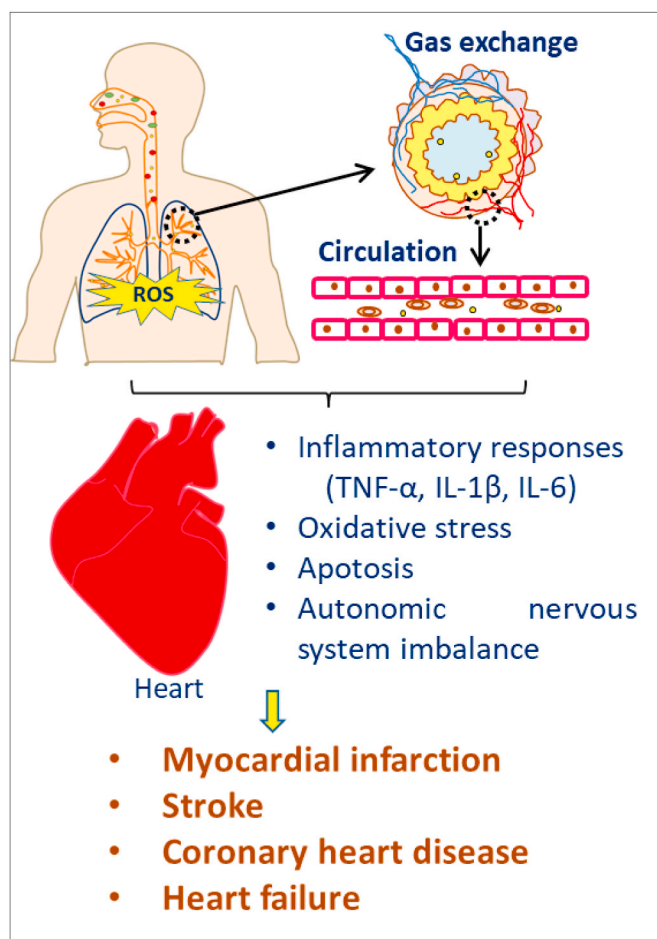


Fig. 2. Health effects of PM in cardiovascular system.

Table 2

Health effects of PM on the cardiovascular system.

S. No.	PM type	Country/Location	Period	Patients/Subject	Health effects	Reference
1.	PM <sub>2.5</sub> , PM <sub>2.5-10</sub> and PM <sub>10</sub>	United States	2007–2017	165,675 participants	PM <sub>2.5</sub> is associated with higher leukocyte count and reduced CD8 <sup>+</sup> T-cell proportions. Increased risk for CVD	Gondalia et al. (2020)
2.	PM <sub>2.5</sub> , PM <sub>2.5-10</sub> and PM <sub>10</sub>	Taiwan	2006–2011	90 Patients with prior myocardial infarction	Affects cardiac autonomic balance	Hung et al. (2020)
3.	PM <sub>10</sub> and PM <sub>2.5</sub>	Yichang, China	2015–2017	391,960 inpatient admissions	Increases respiratory disease and CVD hospital admissions	Yao et al. (2020a)
4.	PM <sub>10</sub> and PM <sub>2.5</sub>	9 cities in France, Iran and Italy	2015–2016	Meteorological and medical data	Increased risk of mortality for people with CVD and respiratory diseases	Sicard et al. (2019)
5.	PM <sub>2.5</sub>	Ann Arbor, Michigan	Two weeks	50 participants	Worsened aortic hemodynamics and increased the risk for CVD	Morishita et al. (2019)
6.	PM <sub>2.5</sub>	Seoul, Korea	2007	364 patients	Increased risk of rupture-prone coronary plaque	Yang et al. (2019)
7.	PM <sub>2.5</sub>	Allegheny County, Pennsylvania	2007–2015	31,414 individuals with atrial Fibrillation (AF)	Associated with high risk of ischemic stroke	Rhinehart et al. (2020)
8.	PM <sub>2.5</sub>	Shanghai, China	2014–2016	1,016,579 participants outpatients	Increased risk of cardiac arrhythmias	Yang et al. (2020)
9.	PM <sub>2.5</sub>	United States	2000	565,477 participants	Increased mortality due to ischemic heart disease and stroke	Hayes et al. (2019)
10.	PM <sub>2.5</sub>	Swedish	2018–2019	2927 participants	Increased dementia incidence via the heart failure and ischemic heart disease	Grande et al. (2020)
11.	PM <sub>2.5</sub>	China	2016–2017	2337 patients in intensive cardiac care unit	High risk of acute non-cardiovascular critical illnesses	Chen et al. (2020a)
12.	PM <sub>2.5</sub>	North Carolina	2004–2016	35,084 heart failure patients	Increased risk in individuals with cardiac failure	Ward-Caviness et al. (2020)
13.	PM <sub>2.5</sub>	Boston	2011–2012	237 maternal–infant pairs	Disrupt cardiac vagal tone during infancy, reduced autonomic flexibility	Cowell et al. (2019)
14.	PM <sub>2.5</sub>	China	2013–2016	Meteorological and medical data	Increased risks of CVD death	Xia et al. (2019)

2005). Moreover, PM<sub>2.5</sub> may facilitate autophagy and apoptosis in human endothelial cells by inducing excessive endoplasmic reticulum stress *in vivo* (Wang and Tang, 2020). Cardiomyocytes are the cells that constitute most of the heart tissue. PM<sub>2.5</sub> exposure can increase the phosphorylation levels of cardiac c-Jun NH2-terminal kinase (JNK) and p53, causing increased Bax (a downstream effector protein) and caspase-3 and decreased Bcl-2 levels to promote cardiomyocyte apoptosis (Wang et al., 2019b). Subsequently, the excessive activation of NF-κB by PM<sub>2.5</sub> damages the heart function and increases the risk of myocardial infarction (Li et al., 2017).

#### 4.2.4. Autonomic nervous system imbalance

The autonomic nervous system plays a vital role in regulating cardiac rate and its imbalance leads to heart rate variability which is considered as an important predictor of CVD. There is a correlation between PM exposure and reduction in heart rate variability (Mordukhovich et al., 2015). After PM<sub>2.5</sub> exposure, the imbalance in cardiac autonomic nerve regulation might be related to the potential occurrence of CVD such as arrhythmia and ischemic heart disease (Xie et al., 2016). PM<sub>2.5</sub> may change the autonomic tone and induce cardiac arrhythmia by activating the pulmonary reflex (Brook et al., 2004).

### 5. Impact of PM on the nervous system

#### 5.1. Health effects

PM causes a significant impact on the human central nervous system (CNS). PM damages the developing brain and causes neuronal disorders (Costa et al., 2020). Maher et al. reported that PM was found in the brain of some residents in the metropolitan area of Mexico City which indicates that PM can enter the CNS (Maher et al., 2016). PM<sub>10</sub> exposure affects the CNS that increases the risk of relapse in multiple sclerosis (a chronic neurological disease) (Roux et al., 2017). According to WHO, 93% of children are exposed to PM<sub>2.5</sub> above guideline level, among them, 630 million belong to under 5 years and 1.8 billion belong to under 15 years age group (WHO, 2018b). Long-term exposure to ambient PM<sub>10</sub> may increase the incidence of autism spectrum disorders in children (Yousefian et al., 2018). Many studies have shown that prenatal and early-childhood exposure to PM<sub>2.5</sub> will cause psychomotor retardation (Guxens et al., 2014) and mental retardation (Jedrychowski et al., 2015). The health effects of PM on the nervous system were shown

**Table 3**  
Health effects of PM on the nervous system.

S. No.	PM type	Country/Location	Period	Patients/Subject	Health effects	Reference
1.	PM <sub>10</sub> and PM <sub>2.5</sub>	Mexico	2016–2017	120 children	Diminished olfactory identification performance and affected CNS function	Guarneros et al. (2020)
2.	PM <sub>10</sub> and PM <sub>2.5</sub>	13 cities of China	2013–2015	111,842 hospital outpatients	Increases mental disorders exacerbations	Lu et al. (2020)
3.	PM <sub>10</sub> and PM <sub>2.5</sub>	China	2014–2015	16,601 anxiety hospital admissions	Worsens the risks of anxiety hospitalizations	Yue et al. (2019)
4.	PM <sub>10</sub>	Saxony, Germany	2005–2014	1,126,014 individuals	Increased risk of anxiety and depression	Zhao et al. (2020)
5.	PM <sub>2.5</sub>	United Kingdom	2006–2010	111,370 participants	Increases the risk of glaucoma via neurotoxic and/or vascular effects	Chua et al. (2019)
6.	PM <sub>2.5</sub>	Unites States	1999–2010	998 participants	Increased risk for Alzheimer's disease	Younan et al. (2020)
7.	PM <sub>2.5</sub>	Boston, New York, Shanghai or Changsha	2010–2014	135 first episode schizophrenia patients	Interacts with psychosis to reduce hippocampal volume	Worthington et al. (2020)
8.	PM <sub>2.5</sub>	Denmark	1989–2014	21,057 cases	Increased risk factor for CNS tumors	Poulsen et al. (2020)
9.	PM <sub>2.5</sub>	Mexico	2007–2011	509 mothers	Increased the risk of Postpartum depression and neuropsychological dysfunction in mothers	Niedzwiecki et al. (2020)
10.	PM <sub>2.5</sub>	Utah	1986–2015	2444 pediatric patients and 13,459 young adult patients with cancer	Increases cancer mortality in pediatric lymphomas and CNS tumors	Ou et al. (2020a)
11.	PM <sub>2.5</sub>	Barcelona	2012–2014	186 participants	Decreased corpus callosum volume in pre-adolescent children and behavior problems	Mortamais et al. (2019)
12.	PM	West Virginian counties, USA	2001–2005	Public Health and Socioeconomic Data	Increased dementia mortality	Salm and Benson (2019)

in Table 3 and Fig. 3.

#### 5.2. Toxicity mechanisms

Exposure to PM<sub>2.5</sub> can impair the cerebral cortex growth in pregnant mice, which lead to anxiety, depression, and changes social behavior in their progeny (Zhang et al., 2018). Neuroinflammation and oxidative stress are two hypothetical biological mechanisms by which air pollutants adversely affect the brain. Neuroinflammation and oxidative stress-related markers have been significantly increased in individuals exposed to high level of PM, suggesting the association of air pollution-induced neurotoxicity, such as neurodevelopmental disorders and neurodegenerative diseases (Heneka et al., 2018; Butterfield and Halliwell, 2019). Moreover, PM can increase the penetrability of the blood–brain barrier (BBB), allowing the noxious substances quickly into the CNS and produce adverse effects.

##### 5.2.1. Neuroinflammation

PM<sub>10</sub> can activate the molecular signaling cascades of tissue inflammation (Woodward et al., 2017), resulting in the production of massive amounts of proinflammatory and inflammatory cytokines. These cytokines might then be released into the blood which interacts and disrupts the normal functions of BBB. Many cytokines, monocytes, and macrophages can enter the brain through the damaged BBB system and causes brain inflammation (Farina et al., 2013). Ehsanifar et al. (2019) have found that PM<sub>2.5</sub> may increase inflammatory cytokines in the blood and thus cause the excessive activation of immune cells in the peripheral nervous system, resulting in inflammatory responses in the CNS and neurodegenerative disorders.

##### 5.2.2. Oxidative stress

The trace metals, endotoxins, and other soluble compounds present in the PM<sub>10</sub> can penetrate the fluid of the inner airway wall, interact with tissues, and induce ROS production through Fenton or Fenton-like reactions (Vidrio et al., 2008). Subsequently, ROS can react with lipids and proteins and alter their structures and functions. Since the brain is mainly composed of easily oxidizable lipids, PM can certainly cause brain damage. Long-term exposure to PM<sub>2.5</sub> can cause oxidative damage, lipid peroxidation, morphological disruptions of neurons, and neuronal apoptosis in brain tissues (Angoa-Pérez et al., 2006).

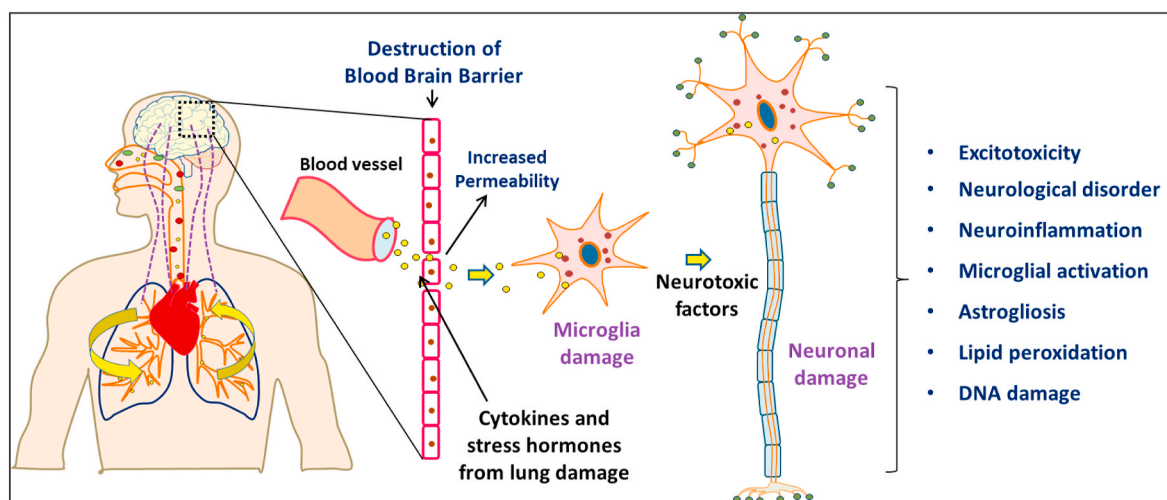


Fig. 3. Health effects of PM in nervous system.

5.2.3. Destruction of the blood–brain barrier

PM can break down the tight junctions between endothelial cells and increase the permeability of endothelial cell monolayers and the migration of monocytes. These effects indicate that exposure to PM compromises the integrity of the BBB which allows them to enter and damage the CNS (Shou et al., 2019). Biddlestone-Thorpe et al. has found that the PM<sub>2.5</sub> can disrupt the cellular ultrastructure underlying the BBB and cause local microhemorrhage and microdamage (Biddlestone-Thorpe et al., 2012). As a result, harmful substances in the blood can pass through the BBB and damage the neurons, destabilizing the CNS microenvironment.

6. Impact of PM on the immune system

6.1. Health effects

Exposure to PM can compromise immune function in humans, reducing immunity and thereby inducing or aggravating various diseases. PM<sub>2.5</sub> exposure may lead to disorders in T lymphocyte-mediated adaptive immune responses, causing injuries to the respiratory and cardiovascular systems (Zhao et al., 2013; Dobрева et al., 2015). A study assessed the relationship between PM and immune markers (CD4<sup>+</sup> T lymphocytes and CD8<sup>+</sup> T lymphocytes) has shown that chronic exposure

to PM leads to airway inflammation and activation of the cellular or humoral immune system (Leonardi et al., 2000). In the Czech Republic, the degree of air pollution in the urban area has been negatively correlated with the number of CD4<sup>+</sup> T lymphocytes and the low CD4<sup>+</sup>/CD8<sup>+</sup> ratio in the blood of newborn umbilical cords (Hertz-Picciotto et al., 2002). Health effects of PM in immune system were reviewed in Table 4.

6.2. Toxicity mechanism

Exposure to PM is closely related to the occurrence of immune system-related diseases. Xu et al. have reported that the severity of injury to the immune system in rats was positively correlated with the cumulative effect of the fine PM dose and exposure duration (Xu et al., 2008). Inflammation, oxidative damage, and apoptosis induced by PM exposure are the major mechanisms for the immune system damage.

6.2.1. Inflammatory response

PM directly enters the alveoli and interacts with the mucosal defense system. After, the alveolar macrophages identify the PM through the pattern recognition receptors and then a series of signal transduction mechanisms are activated to induce local or systemic inflammatory responses which leads to tissue damage (Sijan et al., 2015). Pope et al.

Table 4  
Health effects of PM in the immune system.

S. No.	PM type	Country/ Location	Period	Patients/Subject	Health effects	Reference
1.	PM <sub>10</sub> and PM <sub>2.5</sub>	Zhejiang and Shanxi, China	2012–2014	120 participants	Increased mtDNA copy number and IL-5 concentration	Wang et al. (2020a)
2.	PM <sub>10</sub> and PM <sub>2.5</sub>	Italy	2014–2015	50 healthy adult volunteers	Impaired the immune system	Dolci et al. (2018)
3.	PM <sub>10</sub> and PM <sub>2.5</sub>	Jinan, Shandong	2016	163 and 110 school children from the polluted and control areas, respectively	Decreased C3 and C4 levels, and B lymphocyte count	Li et al. (2019b)
4.	PM <sub>10</sub>	South Korea	2012–2013	100 participants	Impacts DNA methylation and immune responses	Lee et al. (2019)
5.	PM <sub>2.5</sub>	Mexico City	2013–2017	35 residents	Alters functional immune cell responses and increased risk for Tuberculosis development	Torres et al. (2019)
6.	PM <sub>2.5</sub>	Japan	2014–2015	Cell line study	Activated antigen presenting cells and T-cells led to respiratory diseases	Chowdhury et al. (2018)
7.	PM <sub>2.5</sub>	Shanghai, China	2016	43 volunteers	Saliva lysozyme (non-specific immune biomarker) was significantly inversely associated with indoor PM <sub>2.5</sub>	Gao et al. (2019a, b)
8.	PM <sub>2.5</sub>	United States	2012–2013	21 volunteers	Impairs critical antimycobacterial T cell immune functions	Ibronke et al. (2019)
9.	PM <sub>2.5</sub>	United States	2003–2011	774 participants	Impacts DNA methylation and the human immune system	Gao et al. (2019a, b)
10.	PM <sub>2.5</sub>	252 Chinese cities	2013–2017	117,338,867 hospital admissions	Increased risk of diseases in the digestive, musculoskeletal, and genitourinary systems	Gu et al. (2020)

(2016) has reported that PM<sub>2.5</sub> may increase the IL-6, IL-8, and TNF- $\alpha$  levels in the peripheral blood and lungs of nonsmoking adolescents and cause systemic inflammatory and immune disorders.

### 6.2.2. Oxidative damage

Oxidative stress induced by PM<sub>2.5</sub> causes significant increase in IL-4 and IL-13 (Th2-related cytokines) and a reduction in IFN- $\gamma$  (Th1-related cytokine) in the rat cardiac muscles, which enhanced the allergic inflammatory responses (Zhao et al., 2012). PM<sub>2.5</sub> damages the immune cells and alters cytokine secretion and causes disorders in the immune system (Kaur et al., 2011; Valavanidis et al., 2008).

### 6.2.3. Apoptosis

PM can upregulate pro-apoptotic genes, which controls the active cell death in tissues. For example, Reyes-Zárate et al. have found that PM<sub>10</sub> exposure can induce G1/G0 arrest and induce the apoptosis of immune cells (Reyes-Zárate et al., 2016). After exposure to PM, microglia can activate the MAPK pathway to induce apoptosis and alter the expression of Toll-like receptors, T lymphocyte receptors, and B lymphocyte receptors as well as various proinflammatory cytokines and their receptors (Sama et al., 2007).

## 7. Impact of PM in COVID-19 infection

The COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to WHO, a total of 130,422,190 confirmed cases with 2,842,135 deaths were reported worldwide by COVID-19 infection as of April 05, 2021 (WHO, 2021). It has been confirmed that respiratory droplets with an aerodynamic diameter of 5–10  $\mu\text{m}$  from the infected person could carry the virus and cause COVID-19 (WHO/Europe, 2020; WHO, 2020a; Amoatey et al., 2020). Many factors are associated with the spread of airborne COVID-19 infection (Srivastava, 2021). The potential transmission of SARS-CoV-2 through aerosols has confirmed the detection of viral RNA in a Wuhan hospital, China (Liu et al., 2020). It is well established that exposure to the PM could possibly carry different bacteria or viruses and pose harmful effects on human health (Zoran et al., 2020). PM could act as direct carrier and has prominent role in transmission of SARS-CoV-2 virus (Anand et al., 2021; Tung et al., 2021). For instance, Setti et al. (2020) have found the SARS-CoV-2 RNA on PM of Bergamo in Northern Italy. Further, PM<sub>2.5</sub> produced from healthcare facilities could influence the presence of SARS-CoV-2 RNA in indoor environments (Nor et al., 2021). The impact of PM in SARS-CoV-2 transmission and COVID-19 infection was shown in Table 5.

Several studies have suggested that SARS-CoV-2 can transmit through various indoor and outdoor aerosols, particularly by PM (Robotto et al., 2021; Senatore et al., 2021). Natural and anthropogenic sources such as industrial activities, domestic heating, and road transport in urban areas could contribute to PM production (Bontempi, 2020). In this context, Amoatey et al. (2020) have revealed that indoor burning could enable the possible transmission of SARS-CoV-2 virus droplets through PM. Recently, Wu et al. (2020) has demonstrated that an increase of PM<sub>2.5</sub> by 1  $\mu\text{g}/\text{m}^3$  could increase the COVID-19 mortality rate by 8%. Also, every rise of 10  $\mu\text{g}/\text{m}^3$  PM<sub>10</sub> and PM<sub>2.5</sub> was the strongly linked with increased COVID-19 fatality rate by 0.24% and 0.26%, respectively (Yao et al., 2020b). Overall, it is evident that PM contributes to the COVID-19 infection and highlights the need for preventive actions.

### 7.1. Role of face masks in preventing PM and COVID-19 infection

Airborne transmission of infectious respiratory diseases involves the emission of microorganism-containing aerosols and droplets nuclei ( $\leq 5$   $\mu\text{m}$  in diameter) resulted from the evaporation of droplets or aerosolization from various expiratory activities such as breathing, talking,

**Table 5**

Relationship between PM and COVID-19 infection.

S. No.	PM type	Country/ Location	Period	Observation	Reference
1.	PM <sub>10</sub> and PM <sub>2.5</sub>	China	January 26th - February 29th, 2020	PM <sub>2.5</sub> has the potential of COVID-19 transmission	Li et al. (2020)
2.	PM <sub>10</sub> and PM <sub>2.5</sub>	China	January 23rd - February 29th, 2020	Positively correlated with the risk of COVID-19 infection	Zhu et al. (2020)
3.	PM <sub>10</sub> and PM <sub>2.5</sub>	China	January 25th - February 29th, 2020	PM <sub>2.5</sub> increases the risk of COVID-19 infection	Jiang et al. (2020)
4.	PM <sub>10</sub> and PM <sub>2.5</sub>	China	Upto March 22nd, 2020	Rise of every 10 $\mu\text{g}/\text{m}^3$ of PM <sub>10</sub> and PM <sub>2.5</sub> was linked with increased COVID-19 mortality rate with 0.24% and 0.26%, respectively	Yao et al. (2020b)
5.	PM <sub>10</sub> and PM <sub>2.5</sub>	United States	March 4th - April 24th, 2020	Showed significant correlation between PM and COVID-19	Bashir et al. (2020)
6.	PM <sub>10</sub> and PM <sub>2.5</sub>	France	March 18th - April 27th, 2020	Direct association with COVID-19 mortality	Magazzino et al. (2020)
7.	PM <sub>10</sub> and PM <sub>2.5</sub>	Middle Eastern Countries	n.a.	Indoor burning could enable the possible spread of SARS-CoV-2 virus droplets	Amoatey et al. (2020)
8.	PM <sub>10</sub> and PM <sub>2.5</sub>	Italy	Upto March 31, 2020	Chronic exposure to PM <sub>2.5</sub> causes alveolar ACE-2 receptor overexpression that links to COVID-19 infection	Frontera et al. (2020)
9.	PM <sub>10</sub> and PM <sub>2.5</sub>	Italy	Upto April 27th, 2020	Favors the transmission of SARS-CoV-2 infection	Fattorini and Regoli (2020)
10.	PM <sub>10</sub>	Italy	February 10th - February 29th, 2020	Reported the presence of SARS-CoV-2 on PM	Setti et al. (2020)
11.	PM <sub>10</sub>	Italy	Upto April 7th, 2020	Transmission of COVID-19 is mainly by the air pollution	Coccia (2020)
12.	PM <sub>2.5</sub>	United States	Upto April 22nd, 2020	Increase of PM <sub>2.5</sub> by 1 $\mu\text{g}/\text{m}^3$ was connected with an 8% of increased COVID-19 fatality	Wu et al. (2020)
13.	PM <sub>2.5</sub>	New York	March 1st - April 20th, 2020	PM <sub>2.5</sub> was significantly associated COVID-19 infection, but not correlated with mortality	Adhikari and Yin (2020)

Note: n.a. – data not available.

coughing, and sneezing (WHO, 2020c; Chen et al., 2021). It is well documented that the relationship between PM and COVID-19 infection by the airborne transmission of SARS-CoV-2 from the infected person through small droplets and particles (Setti et al., 2020; CDC, 2020b). In this context, several precautionary measures are being advised to the public for preventing COVID-19 infection and mortality rate, for example, social distancing, hand wash with soap and water or use of sanitizer, use of masks, travel restrictions, etc., (CDC, 2020c). Since, many patients are asymptomatic and unaware of their infection, using a facemask is a well-established strategy to control respiratory infection



(Esposito et al., 2020).

Masks and respirators act as a physical barrier to respiratory droplets that expelled from infected individual (Chua et al., 2020). The proper and early use of facemask could prevent the COVID-19 transmission and it serves as dual preventive purpose of protecting oneself from getting the viral infection and protecting others (Abboah-Offei et al., 2021). The quality of facemasks plays major role in COVID-19 prevention and it depends on the filtration efficiency of particulates, bacteria and virus (Dharmaraj et al., 2021). Currently, three types of masks are being used to prevent COVID-19 infection which includes surgical masks, respirators and cloth masks. Surgical masks are non-woven triple layered structure with a middle filter efficient to prevent the infectious droplets of larger than 5  $\mu\text{m}$  (Tcharkhtchi et al., 2021). Surgical masks are recommended to use not more than for 3–8 h. Respirators are one of the personal protective equipment (PPE) being in use among healthcare workers. N95 respirators filter about 0.3- $\mu\text{m}$  sized particles including bacteria and viruses. Its efficiency is about 95% and intended to use for 2 h (Dharmaraj et al., 2021). Cloth masks are breathable non-certified or home-made masks has been used to prevent community spread. The advantage of cloth masks is cheap, reusable and easy to handle. However, the filtration, effectiveness, fit, and performance of cloth masks are inferior to medical masks and respirators (Chughtai et al., 2020). Facemasks are made from non-renewable and non-biodegradable petroleum-based polymers (Dharmaraj et al., 2021). The increased production and widespread usage of face masks raises concern of microplastic pollution in the environment due to improper disposal.

## 7.2. Health effects of COVID-19

The clinical condition of COVID-19 infection is diverse, ranging from asymptomatic or severe with common symptoms like fever, cough, fatigue, diarrhea, sore throat, myalgia, loss of smell or taste and breathing difficulties (CDC, 2020a; WHO, 2020b). It can lead to life-threatening conditions in severe cases, including pneumonia, acute respiratory distress syndrome (ARDS), acute stroke, shock, myocardial infarction, kidney failure, and even death (Nalleballe et al., 2020). Fig. 4 shows the various health effects of COVID-19 infection in humans. SARS-CoV-2 infection primarily affects the pulmonary system. According to radiological examinations, symptoms like, pleural discharges, enlarged pulmonary vessels, lesions, lung opacities, and uncommon mediastinal lymphadenopathy can be used as the early indicator of lung injury (Albarelo et al., 2020). There is an increased risk for CVD such as,

myocarditis and myocardial injury as secondary consequences in infected patients (Deng et al. (2020)). Patients with severe infection showed neurologic disorders such as impaired consciousness, acute cerebrovascular diseases and skeletal muscle injuries (Mao et al., 2020). The death rate was higher in old age groups and the persons with co-morbidities such as hypertension, diabetes, and CVD (Zhou et al., 2020). COVID-19 is also linked with high prevalence of psychological distress and posed mental health problems (Xiong et al., 2020).

## 7.3. Mechanisms

It is possible that PM exposure may increase the COVID-19 infection by facilitating attachment of SARS-CoV-2 through angiotensin-converting enzyme 2 (ACE2) receptor overexpression (Tung et al., 2021). SARS-CoV-2 is a  $\beta$ -coronavirus that has shown a strong affinity towards the ACE2 membrane receptor. ACE2 is found throughout the body, including lungs, nasal and oral mucosa, brain, kidney, heart, intestine, liver, and blood vessels (Behl et al., 2020; Ciaglia et al., 2020). PM<sub>10</sub> exposure could upregulate the expression of ACE2 was reported in human respiratory epithelial and alveolar A549 cells (Miyashita et al., 2020). ACE2 is also expressed in myocytes and vascular endothelial cells and hence, there is a possibility of SARS-CoV-2 involvement in heart tissues, while interstitial mononuclear inflammatory infiltrates were found in cardiac tissues COVID-19 cases (Xu et al., 2020; Zhou et al., 2020). However, the relationship between the strong affinity of SARS-CoV-2 spike protein and ACE2 receptor towards infectivity is not well established (Chung et al., 2020). Whereas the binding of virus and ACE2 receptor lead to the entry of SARS-CoV-2 into the cell which in turn cause shedding and downregulation of ACE2 receptor (Verdecchia et al., 2020). The shedding of ACE2 is catalyzed by the action of a disintegrin and metalloproteinase (ADAM) 17 and ADAM 10, which releases the active form of soluble ACE2 into the plasma (Chung et al., 2020). ACE2 mediates the conversion of angiotensin II into angiotensin (1–7) through GPCR (G-protein coupled receptor) pathway. ACE2 and angiotensin (1–7) are involved in the protective functions of the body by anti-inflammatory and antioxidant actions (Behl et al., 2020). The downregulation of ACE2 reduces its protective action and worsening the angiotensin II effects. Hence, there is a strong relationship between SARS-CoV-2 and ACE2 in the COVID-19 disease severity. Angiotensin converting enzyme inhibitors (ACE inhibitors) are one of the current research area to find the potential therapeutic drug to control the infection (Ciaglia et al., 2020).

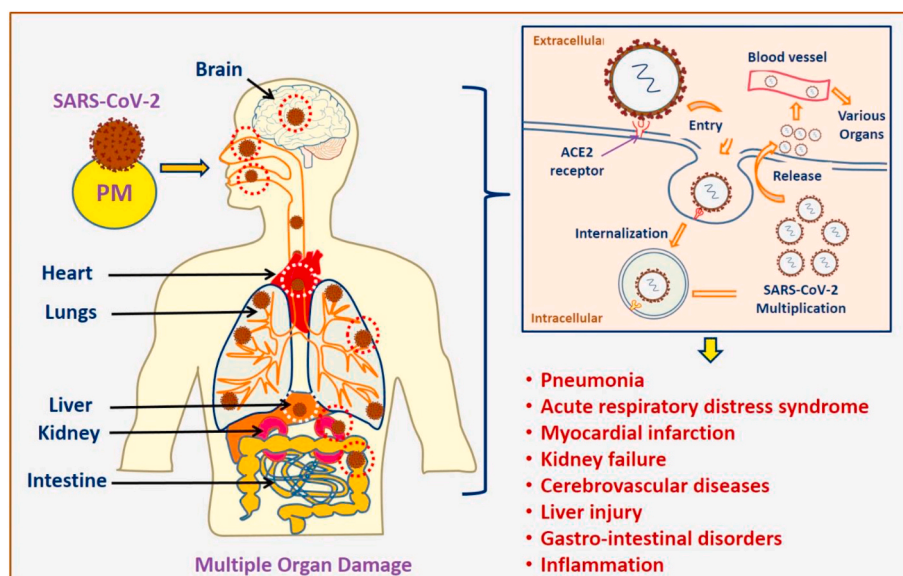


Fig. 4. Impact of PM on COVID-19 and its possible health effects.

## 8. Other health impacts of PM

The urinary, digestive and reproductive systems are affected by exposure to high level of atmospheric pollutants (Kampa and Castanas, 2008; Somers, 2011). Some studies suggest that people with prenatal exposure to PM<sub>2.5</sub> are susceptible to long-term metabolic syndrome (Wu et al., 2019). In addition, maternal exposure to PM<sub>2.5</sub> is closely correlated with premature birth, low birth weight, stillbirth, and poor postpartum health (Tan et al., 2017; Klepac et al., 2018; Melody et al., 2019). Air pollution is also associated with the prevalence, morbidity, and mortality of diabetes mellitus. It can affect skin condition, induce acne, and accelerate skin aging (Schraufnagel et al., 2019).

## 9. Discussion

PM comprises of a complex and heterogeneous mixtures of pollutants from natural and anthropogenic activities (Abbas et al., 2019). PM are associated with many diseases in human such as, COPD, lung cancer, asthma, premature death, multiple sclerosis and other respiratory and CVD (Roux et al., 2017; Wang et al., 2020b). In this review, the impact of PM induced adverse health effects in human physiological systems were described with underlying mechanism at cellular and molecular levels. The human body consists of highly organized and coordinated network of organ systems. Any changes or disruption in one organ functions will affect the homeostasis of the human body by interfering the molecular signaling pathways. The predominant route of human exposure to PM is through the inhalation that enables them to enter and deposit in the airways and centriacinar regions of the lungs (Leikauf et al., 2020). Fine and ultrafine particulates can escape into the blood stream and affect the cardiovascular system. The sensory receptors on the alveolar surface may activate the autonomic nervous system that can immediately affect cardiovascular functions.

In lungs, epithelial cells and alveolar macrophages are involved in the detoxification process and subsequent removal of toxics via the lymphatic system based on the antioxidant molecules ratio (Alemayehu et al., 2020). While PM are directly or indirectly involved in the induction of oxidative and pro-inflammatory response in human bronchial epithelial cells (Abbas et al., 2019). Under oxidative stress condition, macrophages produce cytokines that can enter into circulation and regulates the inflammatory reaction (Sijan et al., 2015). There is a growing evidence that oxidative stress and inflammatory responses are the major cause of PM induced adverse effects in respiratory, cardiovascular, nervous, and immune systems (Cui et al., 2015; Wei and Tang, 2018; Son et al., 2020).

The pathogenesis of many diseases is believed to be due to the oxidative damage of biomolecules. Generally, free radicals or ROS is formed in the mitochondria and peroxisomes during the reduction of oxygen in electron transport chain. The imbalance of antioxidant molecules causes the inability to neutralize or remove the free radicals formed that leads to oxidative stress. Exposure to PM promotes the radical formation that can quickly reacts with biomolecules, such as fatty acids, proteins and nucleic acids and results in oxidative damage (Leikauf et al., 2020). Besides, PM (PM SRM1648a) exposure also affects the cellular activity by the accumulation of intracellular calcium level that induce the inflammatory response and even cell death (Maher et al., 2018). Subsequently, other toxicity mechanisms are activated such as inflammatory responses, apoptosis, macrophage damage, cell cycle dysregulation, etc., which are associated with the detrimental health effects (Ehsanifar et al., 2019).

Antioxidant supplements have been suggested as a preventive method to attenuate the PM induced adverse health effects (Son et al., 2020). Antioxidant molecules play a major role in relieve oxidative damage or cell stress caused by PM through mitochondrial and endoplasmic reticulum (ER) stress-mediated pathways (Wang et al., 2020b). For instance, Glutathione-S-transferase, an antioxidant defense enzyme is involved in detoxification of diesel exhaust particles in the respiratory

tract (Meier-Girard et al., 2019). While the loss of GST protein increases the nasal allergic response in response to PM pollution (Schwartz et al., 2005). In this line, several studies have reported the preventive action of natural agents against oxidative damage. Recently, Radan et al. (2019) have reported the protective effect of gallic acid in PM induced cardiac dysfunction by lowering the oxidative stress and cytokine levels and improving the antioxidant enzymes. Nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor plays an important role in maintaining redox homeostasis and provide protective effects in PM induced toxicity (Pardo et al., 2019). Recently, Yang et al. (2021) has revealed the protective role of curcumin in PM<sub>2.5</sub> induced oxidative stress and inflammation by reducing the ROS levels and enhancing Nrf2 expression that in turn regulating the downstream antioxidant enzymes encoding genes. Hence, the natural compounds with antioxidant, anti-inflammatory and ROS inhibiting property can be exploited for mitigating PM induced health disorders.

## 10. Regulations and control strategies for mitigating PM impacts

It is well documented that the PM exposure could affect human health and environment. According to WHO air quality guideline, about 15% of air pollution-related deaths can be reduced by the decrease of PM<sub>10</sub> levels to 20 µg/m<sup>3</sup> and PM<sub>2.5</sub> levels to 10 µg/m<sup>3</sup> (WHO, 2018c). While many countries have set the guideline values for the regulation of PM concentrations to minimize the health impacts (Table 6). However, the emission of PM concentrations was found to be much higher in developing countries (Kim et al., 2015) and exceeding the guideline levels.

The primary step for reaching the regulatory standards can be the identification of emission-reduction targets and development of control strategies to achieve the targets (Ou et al., 2020b). Further, there is a correlation exists between the air pollutants and socio-economic factors (Chen et al., 2020b). The mitigation strategies that are advised to be technically and economically feasible to limit the negative impacts to air quality (Health Canada, 2016). Clean technologies that reduce the emission of air pollutants are being implemented in various industrial sectors, transport, urban planning, power generation and waste management, for instance, increased use of low-emission fuels and vehicles, combustion free power generations, making green cities, etc., (WHO, 2018c). Besides, the vehicular emissions can be controlled by decreasing the total number of old age vehicles. Furthermore, substantial health benefits can be attained by the substitution of high PM<sub>2.5</sub> emission sources such as industrial coal and industrial liquids with cost-effective electricity use from renewable energy (solar and wind power) (Ou et al., 2020b). In this context, Liang et al. (2019) have reported that fleet electrification in China can decrease the fine PM concentration and provide more health benefits. Hence, the combination of clean power

**Table 6**

Regulation guidelines for particulate matters (PM<sub>10</sub> and PM<sub>2.5</sub>) in different countries.

S. No.	Country	Daily (µg/m <sup>3</sup> )		Annual (µg/m <sup>3</sup> )		Reference
		PM <sub>10</sub>	PM <sub>2.5</sub>	PM <sub>10</sub>	PM <sub>2.5</sub>	
1.	China	150	75	70	35	Chen et al. (2020b)
2.	India	100	60	60	40	NAAQS (2019)
3.	United States	150	35	n.a.	12	EPA (2020)
4.	European Union	50	n.a.	40	25	EEA (2020)
5.	Australia	50	25	25	8	Air NEPM (2016)
6.	Canada	n.a.	27	n.a.	8.8	Health Canada (2016)
7.	Japan	n.a.	35	n.a.	15	Bota and Yamasaki (2020)
8.	WHO	50	25	20	10	WHO (2018c)

n.a. – data not available.

and electrified technologies are the key aspects to attain the PM reduction.

The important factors for mitigating PM pollution could be the investments in environmental protection and pollution control strategies. Moreover, the continuous monitoring of PM emission from various sources is essential for reviewing and updating the standards and regulations periodically, to ensure that they provide adequate health and environmental protection. Furthermore, the precautionary measures should be taken into consideration for the effective prevention and management of PM induced health issues in the highly polluted regions of the world.

## 11. Conclusion

The impact of atmospheric pollution on human health has become a hot topic in recent years including COVID-19. The negative impact of PM on human health is multifaceted. The PM first enters the human respiratory tract and triggers lung inflammation. Subsequently, it initiates systemic inflammatory responses, autonomic dysfunction, and a series of oxidative stress-induced injuries, which in turn causes severe damage to the human organ systems and functions. Oxidative stress and inflammatory responses are considered as the major mechanism involved in the PM induced adverse effects. A comprehensive understanding of the negative impact of PM on the human body and its associated mechanisms will help to develop a pollution control strategy to minimize the detrimental effects on public health.

## Credit author contribution statement

Chengyue Zhu: Conceptualization, Writing – original draft, Writing – review & editing, Validation, Methodology, Data curation. Kannan Maharajan: Conceptualization, Writing – original draft, Writing – review & editing, Validation, Methodology, Data curation. Kechun Liu: Conceptualization, Supervision, Funding acquisition, Data curation, Writing – review & editing. Yun Zhang: Conceptualization, Supervision, Funding acquisition, Data curation, Writing – review & editing

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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