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The relationship between PM2.5 and incidence and severity of Covid-19

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Abstract: *Covid-19 viral pandemic enforced restrictions and consequent short term reduction in anthropogenic emissions were reported to bear a positive impact on air quality in many parts of the world. At the same time numerous reports indicated a positive correlation between exposure to certain types of air pollutants especially fine particulate matter and incidence and severity of Covid-19. Several research studies have suggested an increment of Particulate Matter (PM2.5 and PM10) with an associated increase of Covid-19 mortality. Studies have established that aerosols generated from SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infected patients serve as a highly virulent direct transmission route while ambient aerosols can act as cargo helping indirect transmission of the virus though viability and virulence of the virus stuck on the surface of particulate matter is not confirmed yet.PM induces lung cells inflammation and exposure to PM could enhance the susceptibility and severity of the Covid-19 patients. This review study was conducted to comprehend the intricate relationship between PM2.5 and incidence and severity of Covid-19. An extensive search was carried out to gather published literature related to the review topic using online PubMed and Science direct databases. Articles focusing on relationship between Covid-19 and air pollutant PM2.5 were selected and analysed, based on their relevance with the current review topic. In conclusion, PM2.5 have a positive correlation with spread and severity of Covid-19. The study has implications for environmental intervention in regions with unusually high number of Covid-19 cases and framing stringent air quality policies to reduce the risk of other fatal outbreaks in future.*

Keywords: *Air pollutants; Covid-19; Particulate matter; PM2.5; SARS-CoV-2.*

1. INTRODUCTION:

It has been two years, world is struggling with Covid-19 a highly infectious and invasive pneumococcal disease caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) first reported in December 2019 in Wuhan, China. By March 2020 the disease transformed from epidemic to pandemic [1] as the virus spread globally, owing to its highly contagious and aggressive nature. The virus affected all sections of society across the globe and a substantially high proportion of global population was infected. As per World Health Organization (data accessed as on 17 December 2021) there have been 271,963,258 confirmed cases of Covid-19 out of which 5,331,019 individuals have lost their lives, due to the disease [2]. SARS-CoV-2 primarily causes respiratory disease as it attacks the lungs but is reported to impact other vital body organs such as brain, heart and kidney too, causing various clinical symptoms [3]. Multiple transmission modes of SARS-CoV-2 [4] enhances the chances of its spread. Though the disease is a serious global health issue but the effects are not homogenous across the globe; few parts of the world affected more severely in terms of its incidence and severity as compared to others. The factors behind the variability could be numerous and we are yet to understand them completely. However, studies have suggested air pollution as a plausible player transmitting and aggravating this novel Corona virus and indicated a positive correlation between higher air pollution levels and Covid-19 [5-11] although some indicated a negative correlation [12]. Higher levels of particulate matter (PM2.5 and PM10) and increased Covid-19 infections and mortality are reported in many cases [13-19] indicating a link between exposure to PM levels and Covid-19 (Table1). In this review study an attempt has been made to understand the impact of PM2.5, a ubiquitous air pollutant on the spread and severity of SARS-CoV-2.

2. MATERIAL AND METHODS:

An extensive search was carried out to gather published literature related to the review topic using online PubMed and Science direct databases. Articles focusing on relationship between Covid-19 and air pollutant PM2.5 were selected and analysed, based on their relevance with the current review topic. Keywords used included: Covid-19, air pollution

and PM2.5. Further, backward references were also searched from the selected articles. The information gathered is presented under the following subheadings, namely: Air pollution and Covid-19, PM2.5 and Covid-19, PM2.5 and incidence of Covid-19 and PM2.5 and severity of Covid-19.

3. AIR POLLUTION AND COVID-19 :

Air pollution has been considered as a major environmental health issue. Studies have underpinned long- term exposure to air pollution responsible for increased load of respiratory and cardiovascular diseases and premature mortality [20,21,22] while short term exposure to augmented levels reduce life expectancy by exacerbating pre-existing respiratory and cardiovascular problems [23]. Exposure to air pollutants can increase probability of viral infections by inducing oxidative stress, leading to generation of free radicals, that can adversely affect respiratory system and lower resistance to infections caused by viruses and bacteria [24]. Airborne particulate matter (PM) also known as atmospheric aerosols or Suspended Particulate Matter (SPM) is highly detrimental to human health due to complexity of nature and long persistence in air. The size of these particles varies widely and has a direct bearing on their ability to cause health issues. Particulate Matter, based on the diameter can be divided into coarse (≤ 10 μm) and fine particulate matter (≤ 2.5 μm). Studies have linked PM with cardiovascular [25] and respiratory diseases [26]. During Covid-19 induced lockdown, PM level was drastically reduced in different parts of the world [27] that indicates PM level was high during pre Covid-19 period. Air is the dominant route of transmission for SARS-CoV-2 [9,28] and ambient aerosols can serve as source of Covid-19 transmission [29]. PM has been shown to facilitate respiratory viral transmissions in various respiratory diseases. In addition, PM2.5 has been shown to disrupt integrity of nasal epithelial barrier, thus enhancing the viral replication [30,31]. During Covid-19, a close association between air pollution and Coronavirus was established as the two exhibited an interdependent relationship in various parts of the world as evidenced from several reports documenting high air pollution levels and high number of Covid-19 cases and deaths [5-11,32-37]. Another observation was association of severity and mortality of Covid-19 cases with cardiovascular [38] and respiratory diseases [39] and certain comorbid conditions like hypertension [40] and interestingly exposure to PM2.5 is known to exacerbate these disease conditions [41,42,43]. Several possible linkages such as - extended stay of the virus in aerosols, reduced immunity, advancement of pro-inflammatory state and elevated Angiotensin-converting enzyme 2 (ACE-2) receptor expression have been suggested, between air pollution and Covid-19 [44].

PM2.5 and Covid-19: PM2.5, owing to its small size, is highly injurious as it can easily penetrate the respiratory tract and reach the alveoli [45] and can translocate to extra-pulmonary sites via blood circulation. Augmentation of PM2.5 has been linked with increased all-cause mortality [44] lung cancer deaths [46] and deaths resulting from respiratory disease [47]. During Covid-19, as the research studies progressed, PM2.5 emerged as a potential culprit closely associated with the incidence and severity of Covid-19 as several studies found a positive correlation between the two (Table1.), thus generating interest of researchers to investigate the role of PM2.5 in promoting Covid-19.

Study area	PM2.5	PM10	Author
Asia (9 cities)	+	*	Gupta et al., 2021
California, USA	+		Meo et al., 2021
Chile (188 communes)	+	+	Valdes et al. (2020)
England	+	+	Konstantinoudis et al.,2020
Germany	+		Bilal Bashir et al., 2020
Italy	+	+	Daniele and Francesco,2020
Milan, Italy	+	+	Zoran et al., 2020
Wuhan, China	+	-	Jiang and Xu, 2020

Note: '+' stands for positive correlation, '-' stands for negative correlation, '*' stands for not significant and blank space represents no research

Table-1 Studies showing associations of PM2.5 and PM10 with the COVID-19 in different regions of the world

Several mechanisms need to be taken into account to understand the possible role of PM2.5 in the transmission of SARS-Co-V-2, impacting the spread and severity of Covid-19. PM2.5 can act as virus carrier indirectly by providing a suitable environment for transportation to greater distances [28,29,47,48,49]. PM2.5 is also known to disrupt the integrity of respiratory barrier and remodelling of nasal mucosa that might facilitate virus entry [30,31]. Another mechanism highlights the association of chronic exposure to PM2.5 with various cardiovascular and especially respiratory diseases.

Patients exposed to high PM2.5 levels for long term exhibit enhanced Angiotensin-converting enzyme 2 (ACE-2) and transmembrane serine protease 2 (TMPRESS2) expression [50] and depletion of ACE-2 due to binding with SARS-CoV-2, exacerbates the disease conditions, thus adding to the severity and mortality of Covid-19 cases. Long term PM2.5 exposures induced damage to lungs, leads to increased inflammation. This increased inflammation stimulates enhanced expression of ACE-2, a protective mechanism, to prevent acute injury to lungs by generation of an anti-inflammatory peptide [51]. This acts like a double hit as increased expression of ACE-2 not only provides more binding sites for SARS-Cov-2, thus increasing the susceptibility of the host to the virus but might also elicit deficient anti-inflammatory response leading to acute lung injury and aggravate the inflammation and thus adding to increased mortality and severity in Covid-19 cases.

PM2.5 and incidence of Covid-19: SARS-Cov-2 primarily gets transmitted via respiratory droplets of various sizes generated by infected patients. Ambient aerosols can act as carrier for SARS-CoV-2 as it can non-specifically get attached to various surfaces [52] and can remain viable upto 3h in aerosols under laboratory conditions, though the virulence gets reduced [29]. Ambient aerosols laden with virus can persist longer in air as compared to large respiratory droplets and can travel greater distances, thus facilitating the virus transmission as carriers. Together these factors make PM2.5 an ideal candidate to assist SARS-CoV-2. Viability of SARS-CoV-2 has been reported on different surfaces [29] so there is a possibility that virus laden on PM2.5 can be transported back into air. A recent study has suggested that PM2.5 can carry SARS-CoV-2 in the air during removal of Personal Protective Equipment (PPE) by health workers [49]. Together these factors indicate that PM2.5 can potentiate the viral transmission and accelerate the incidence of infection. Studies have shown that PM2.5 can also disrupt the integrity of nasal epithelial barrier by downregulating various tight junction (TJ) proteins and upregulating expression of proinflammatory cytokines, thus rendering the epithelial barriers dysfunctional due to oxidative stress leading to exposure of deeper respiratory tissue to foreign pathogens [30,31] resulting in increased susceptibility to viral infection. SARS-CoV-2 employs ACE-2 and TMPRSS2 as two keys to invade the lungs. The capsid spike protein (S) helps to bind the virus with the cell surface receptor ACE-2 of the target cells and the cellular protease TMPRSS2 brings out the S protein priming of virus, leading to fusion of virus and target cell membranes and virus entry into target cells [53]. As PM2.5 exposure enhances expression of ACE-2 and TMPRSS2 in human epithelial cell surfaces of respiratory tract [50], prolonged exposure to PM2.5 can translate into a predisposing factor for the virus entry, increasing susceptibility to Covid-19 and accelerating infection rate. This also explains susceptibility of people with certain comorbidities, to Coronavirus.

PM2.5 and severity of Covid-19: In one hand, PM2.5 mediated transmission of SARS-CoV-2 via aerosols is established accelerating the infection rate and on the other hand, PM2.5 induced respiratory and other diseases that potentiate the virus to enhance morbidity or severity in the patients have already been observed. Thus, another correlation among PM2.5 and Covid-19 could be via PM2.5 mediated complications. SARS-CoV-2 entry into the cells is mediated via binding of spike proteins on its crown with ACE-2 receptor expressed on the cellular surface. PM2.5 can induce inflammation of lung cells and stimulate over expression of ACE-2 in respiratory tract, thus adding to the severity of Covid-19 by providing increased ACE-2 binding sites for the virus resulting in increased viral load. Depletion of ACE-2 expression, a protective mechanism to prevent acute lung injury [54], due to binding of SARS-CoV-2 may ensue acute lung injury, resulting from depleted anti-inflammatory response and lead to impairment of local tissue repair mechanism. Apart from respiratory system which is the primary target of SARS-CoV-2, multiple organ dysfunction can occur in Covid-19 infections. It is also observed that medical conditions like hypertension [40], lung [39] and cardiovascular [38] diseases can increase the severity and mortally risk in patients with Covid-19 infection and PM2.5 is known to exacerbate these conditions [41,42,43]. Both ACE2 and TMPRSS2 are expressed in several other vital organs such as heart, liver, kidney, brain and digestive tract [55] that justifies extrapulmonory organ injury inflicted by Coronavirus in many patients. However, the expression level of ACE-2 varies in different human tissues, and explains the clinical symptoms of the disease [56]. Heart is another organ with high ACE-2 expression, highlighting its vulnerability to SARS-CoV-2. Higher mortality rate is observed in Covid-19 patients with cardiovascular issues resulting from long term PM2.5 exposures. This increased mortality can be explained as role of ACE-2 is not restricted to lungs and serving as SARS-CoV-2 receptor. It plays another important role in cardiovascular system as negative regulator of Renin-Angiotensin System (RAS) that maintains blood pressure homeostasis [38]. ACE-2 converts angiotensinogen II (Ang-II) to angiotensin (1-7) that acts as vasodilator and reduces blood pressure. In Covid-19 patients, downregulation of ACE-2 and upregulation of Ang- II could lead to over activation of RAS resulting into aggravation of cardiac injuries that probably explains the development of more complications and severity in case of Covid-19 patients with cardiac issues [51].

4. CONCLUSION:

The study concludes that PM2.5 plays a critical role in promoting incidence and severity of SARS-CoV-2, based on the several studies carried out across the globe. Long term as well as short term exposure to elevated PM2.5 levels can act as an additional epidemiological factor of Covid-19. PM2.5 serving as a carrier of the virus probably increases the incidence though research studies need to establish viability and virulence of the virus stuck on PM2.5. PM2.5 has a positive effect on severity of Covid-19. The mechanism can be attributed to PM2.5 mediated co-morbidities, PM2.5 induced respiratory disorders and enhanced expression of ACE-2 cellular surface receptor and TMPRSS2 serving as keys to entry for the virus. ACE-2 at one hand plays a protective role by turning off the RAS system at the other hand it is involved in increased susceptibility of population with Covid-9 to lung and cardiovascular diseases by serving as key to SARS-CoV-2 for cell entry. This review demonstrates the definite role of PM2.5 in the Covid-19 pandemic and has strong implications in the field of public health for designing prophylactic strategies as well as framing environmental policies for future, to avoid such pandemics. However, the author cautions there could be several other factors affecting the spread and severity of Covid-19, in different geographical regions, either enhancing or suppressing it. Further studies exploring the role of various environmental and socio-economic factors are needed in order to gain a comprehensive understanding of the issue.

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