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Review - Human and Animal Health

How Have Particulate Matter, Weather Conditions and Smoking Contributed to the Transmission and Aggravation of the COVID-19 Pandemic?

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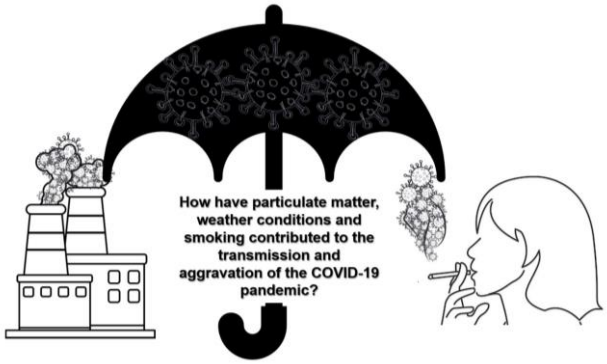
HIGHLIGHTS

- Understanding the risk factors for the severity of COVID-19.
- Association between SARS-CoV-2 contagion and weather.
- Particulate matter levels have exacerbated the pandemic.
- Is smoking a risk factor for COVID-19?

Abstract: One of the most important issues, according to the World Health Organization, to be addressed during the COVID-19 pandemic is understanding the risk factors for the severity of the disease. Some studies show a possible association of SARS-CoV-2 with risk factors such as particulate matter and some weather conditions, in addition to behavioral factors such as smoking. The present review aimed to evaluate the correlation between COVID-19 and these potential risk factors. The Web of Science database searched for eligible studies covering experimental and epidemiological studies from March 2020 to March 2022. The recognized risk groups for an unfavorable evolution are the elderly, those with chronic diseases (such as diabetes, hypertension, and pulmonary diseases), and those who use immunobiological or chemotherapy drugs. But some environmental factors may come to transmit the severity of COVID-19 cases. Lifestyle may be responsible for the variability in the severity of COVID-19, with smoking being one of the main factors, yet environmental factors such as particulate matter levels, humidity, and temperature have been shown to affect the transmissibility of SARS-CoV-2.

Keywords: Atmospheric pollution; contagion; Coronavirus infections; particulate matter; SARS-CoV-2.

GRAPHICAL ABSTRACT



INTRODUCTION

Novel coronavirus disease (COVID-19), an acute respiratory illness caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), has quickly become a worldwide pandemic. This virus predominantly affects the respiratory system, causing pneumonia [1,2], although other systems are also involved, especially in severe cases due to vascular dysfunction and cytokine storm [3], resulting in systemic inflammation [4]. Multiple conditions such as chronic diseases, lifestyle, and environmental factors have been considered risk factors for the susceptibility and severity of COVID-19 [5]. As a result, studies of risk factors for both the incidence and severity of SARS-CoV-2 have gained great interest.

A recent study demonstrated that lifestyle might be responsible for the variability in the severity of COVID-19, with smoking being one of the main factors [6]. Yet, environmental factors such as humidity and temperature have been shown to affect virus transmissibility [7], in addition to environmental pollution that has also been shown to affect the epidemiological parameters of the infection [8]. Air pollution and smoke are the main causes of human morbidity and mortality worldwide and can increase the risk of many diseases, including respiratory diseases such as COVID-19 [9,10].

The role of smoking in the current public health situation has been little remembered and even less discussed, yet other factors, such as climatic conditions and environmental pollution, also need to have their role better understood. According to the World Health Organization (WHO), one of the most important issues to be addressed during the COVID-19 pandemic is understanding the risk factors for the severity of the disease [9]. The question that guided this Literature Review was "How particulate matter, climatic conditions and the habit of smoking have contributed to the transmission and aggravation of the COVID-19 pandemic?" The objectives were to assess how much the smoking habit, the levels of particulate matter, and the climatic variations contributed to COVID-19 transmission worldwide.

MATERIAL AND METHODS

The Web of Science database searched for eligible studies covering experimental and epidemiological studies from March 2020 to March 2022. The following descriptors were used: "weather conditions and COVID-19 or Sars-CoV-2"; "Temperature and COVID-19 or Sars-CoV-2"; "Smoking and COVID-19 or Sars-CoV-2"; "Tobacco and COVID-19 or Sars-CoV-2"; "Air pollution and COVID-19 or Sars-CoV-2";"Fine particulate and COVID-19 or Sars-CoV-2"; "particulate matter and COVID-19 or Sars-CoV-2".

As inclusion criteria, we defined: original articles published in Portuguese, English and Spanish that answer the guiding question of the review. The exclusion criteria established were: theses, dissertations, editorials, book chapters, letters to the reader, literature reviews, commentary, free communication, duplicate articles, perspective studies, guidelines, experience reports and those that did not answer the guiding question of the review. The articles obtained with the research carried out through the descriptors had their titles, abstracts, and full texts independently evaluated by two authors to assess the inclusion or exclusion of the study in the review. From the search for studies through double crossings, 1528 articles were found in the database used. According to the follow-up of the development stages of this review, 984 articles were excluded according to the reading of the titles and 389 articles were excluded after reading the abstracts for not being in line with the theme or for not answering the guiding question. Of the 155 remaining articles, the studies were read in full, leaving 29 articles that demonstrated affinity with the theme proposed in the present study.

DISCUSSION

Smoking habit and COVID-19

The World Health Organization has already warned that smoking can increase the risk of contracting COVID-19, as the behavior involves finger-to-lip contact and the removal of protective smoking face masks [9]. Furthermore, smoking is known to be a causative agent of cardiovascular and pulmonary diseases through its direct actions on various nicotinic receptors expressed in heart tissue, lungs, and blood vessels [11,12]. Cigarette smoking [13,14], including e-cigarette use [15], also increases the risk and severity of lung infections due to the damage they cause to the upper airways and decreased lung immune function. Thus, smokers have a higher risk of infection and mortality from COVID-19 [16].

Smokers are considered vulnerable groups as well to health complications from COVID-19. A meta-analysis of studies in China found that smokers were at increased risk of progression of COVID-19 compared to non-smokers [17]. Another recent analysis revealed an almost twice as high risk of COVID-19 severity in smokers (odds ratio = 1.98; confidence interval 95 %: 1.29–3.05) [18]. Other works state that tobacco smokers have a greater predisposition (1.4 times) to develop severe symptoms of COVID-19. This usually includes their entry into intensive care units and mechanical ventilation. In addition, their mortality rate is approximately 2.4 times higher than non-smokers [17, 19, 20].

However, another study found contradictions, indicating the lack of association between smoking and the worsening of COVID-19 [21]. But a systematic review and meta-analysis dated June 2020 showed that current smokers are more likely to experience complications during the COVID-19 illness than non-smokers but still have a lower risk than former smokers [22, 23]. Another study found a positive relationship between the continuation of the smoking habit and the progression of COVID-19 disease [24].

An explanation for the positive association between the habit of smoking and the greater chances of aggravation in COVID-19 must be associated with the fact that smoking increases the expression of angiotensin-converting enzyme 2 (ACE2), a known SARS-CoV-2 receptor. The ACE2 protein provides the host cell entry point for SARS-CoV-2 [25]. Thus, the relationship between ACE2 and SARS-CoV-2 is critical in the infection process [26, 27], upregulation of the ACE2 gene, which occurs in smokers, can increase susceptibility to SARS-CoV-2 infection and the severity of COVID-19 disease [20]. Although some studies have proposed increased ACE2 expression in smokers as a possible link between smoking and COVID-19, these mechanisms still need to be fully elucidated [20, 28]. It has also been suggested that ACE2 expression is upregulated in the small airway epithelium in patients with smoking-associated pathologies [29, 30]. Nevertheless, another study indicates that smoking treatment did not affect ACE2 levels but strongly inhibited SARS-CoV-2 replication in cells in vitro [31].

Smoking promotes lung inflammation, thus increasing inflammatory cytokine production and tumor necrosis factor expression. It also impairs mucociliary clearance [32]. Pro-interleukin (IL)-1β, which in turn is cleaved by caspase-1 followed by the formation of mature IL-1β; this is itself an important promoter of inflammatory processes in the lung, as well as fever and fibrosis [33]. For these reasons, we can suggest that smoking may increase the severity of the inflammatory response associated with COVID-19. In addition, this habit also affects the barrier junction in lung cells, leading to increased epithelial permeability, including increased mucosal permeability and decreased mucociliary clearance. All these modifications end up facilitating viral entry [13].

Oxidative stress may also be involved in the greater number of cases of COVID-19 aggravation in smokers since smoking causes oxidative stress and inflammation in the lung, and these two factors alter epithelial permeability and ACE2 expression [34]. In addition, tobacco smoke significantly suppresses the immune system, reducing antibody responses and T-cell proliferation, thus increasing the susceptibility of tobacco users to acute viral infections such as COVID-19 [35].

Some demographic data have shown an increased risk of severe COVID-19 associated with exposure to cigarette smoke [18, 36]. A laboratory study demonstrated that exposure to cigarette smoke in human mucociliary cultures increases the number of cells infected by SARS-CoV-2 and prevents the stem cell-mediated repair response [37]. Acute exposure to smoke can worsen COVID-19 cases by reducing the innate mucosal immune response, which has implications for the spread and severity of the disease in people exposed to cigarette smoke [37].

It has been proposed that smoking could protect individuals from worsening COVID-19 [22, 23, 38]. The biological mechanisms for this hypothesis include an effect of anti-inflammatory nicotine, generating a more attenuated immune response among smokers (thus reducing the risk of a cytokine storm during COVID-19) and increased nitric oxide in the respiratory tract (which can inhibit SARS-CoV-2) [38]. It has also been proposed that nicotine reduces inflammation through the α7 subunit of the nicotinic acetylcholine receptor

(nAChR) in macrophages [22, 23]. However, data supporting the "protection" of smoking are limited, and even if smoking does not necessarily increase the risk of contracting COVID-19, the biological and inflammatory cascade that occurs in SARS infection -CoV-2 can be serious for a smoker [39]. Furthermore, smoking is an independent risk associated with severe progression of COVID-19, including mortality.

Particulate matter and COVID-19

As for pollution, there is a linear relationship between exposure to air pollutants and the spread of the Sars-Cov2 virus: however, this correlation is not established as a cause-effect relationship. Atmospheric particulate matter (PM) would function as a carrier, or transport vector, for many viruses. Thus, PM may have increased the effectiveness of the spread of Sars-Cov2, as it creates a suitable microenvironment for its persistence [40].

PM is characterized as a mixture of several chemical compounds, and they are divided by their origin into primary and secondary. Primary PM is emitted directly from its source, while secondary PM originates from chemical reactions and physical processes involving emissions of precursor gases [41]. In urban areas, several anthropogenic sources contribute to PM generation [42]. Some studies have also demonstrated that natural sources can make a significant contribution to PM formation, such as desert dust [43].

Some laboratory experiments performed by Van Doremalen and coauthors [44] indicated that airborne and fomite transmission of SARS-Cov-2 is plausible since the virus can remain viable and infectious in aerosol for several hours. In addition, another study has already identified the presence of viruses in marine aerosols and dust from the Sahara [45]. Besides, breathing can take PM deep into the lungs so that PM-bound viral particles can directly invade the lower respiratory tract, as demonstrated by Sedlmaier and coauthors [46]. Further, Setti and coauthors [47] suggested that the air route would be a possible hypothesis to interpret the anomalous outbreaks of COVID-19 in northern Italy, which is characterized by high PM concentrations.

During the 2003 severe acute respiratory syndrome epidemic, the air pollution index showed a correlation with death rates. Chinese cities with high air pollution had twice the death rates compared to cities with low air pollution [48]. Currently, the increase in $PM_{2.5}$, PM_{10}, NO_2, and O_3 concentrations in 120 cities in China has been associated with an increase in COVID-19 cases [8]. Besides, an increase in 1 $\mu g\ m^{-3}$ in $PM_{2.5}$ results in an 8 % increase in the COVID-19 mortality rate [49]. Pozzer and coauthors [50] verified air pollution through satellite data worldwide as an aggravating factor for COVID-19 lethality and mortality. Data were obtained from epidemiological data concerning China and the USA. According to this article, about 15 % of COVID-19 mortality globally can be attributed to general air pollution, including PM. Another study analyzed the relationship between air pollution in England and COVID-19 cases and deaths, and they found evidence of a correlation between poor air quality and COVID-19 case and death rates, adjusted for population density and especially PM was associated with increased infectivity [51].

Frontera and coauthors [52], analyzing air quality in Italy and China during the period of maximum virulence of COVID-19, found that levels of $PM_{2.5}$ were particularly high, and Marteletti and Marteletti [53] reached the same conclusions. These authors speculate that the atmosphere, rich in atmospheric pollutants, may promote greater permanence of viral particles in the air. Further, different authors have also found a statistically significant relationship between PM levels and SARS-CoV-2 infection in certain geographic areas [51, 54, 55]. In addition to these findings, some studies focus on long-term effects, such as Coccia and coauthors [56], using data from 55 Italian capitals, found an association between exceeding the limits established for PM in previous years and the detected cases of COVID-19. Corroborating this, another study using data from 9 Asian cities shows that previous year exposures to high levels of $PM_{2.5}$ over a prolonged period are significantly correlated with mortality rates caused by COVID-19 [57]. It is already clear in the literature that prolonged exposure to air pollution can induce persistent modifications of the immune system, and this will increase COVID-19 infections and the worsening of this disease, mainly causing severe respiratory and cardiovascular problems [58].

Even though many studies have suggested an association between exposure to air pollutants and increased risk of respiratory virus infection, the potential mechanisms behind this are largely unexplored, and different scientific hypotheses have been put forward. Some hypotheses suggest that polluting agents such as PM, as they induce oxidative stress, may injure the respiratory system by producing free radicals [59]. In addition, exposure to air pollutants has also been shown to alter the function of hydrophilic surfactant proteins, resulting in increased susceptibility to respiratory virus infections [60]. Another report showed that pollutants could modulate the host's antiviral defenses, reducing, for example, the ability of macrophages to phagocytose [61].

Further to the epidemiological studies presented above, experimental studies show that after exposure for three months to $PM_{2.5,}$ mice showed an increase in Interleukin-4, tumor necrosis factor-alpha (TNF-α), and TGF beta in both serum and lung cells, in addition to leukocytes and increased macrophages [62]. A separate human study related that both PM2.5 and PM10 cause systemic inflammation and increase in platelet-derived growth factor, vasoendothelial growth factor, TNFα, Interleukin 1, and Interleukin 6. From the results, it seems to have a direct relationship with the time of pollutant exposure [62]. Likewise, an already present baseline inflammatory condition, exacerbated by pollution, can easily contribute to better explaining why individuals exposed to pollution appear to be at greater risk of developing severe cases of COVID-19, for example [63, 64].

Weather conditions and COVID-19

The correlation between meteorological variables and the spread of SARS-CoV-2 gained considerable attention after some studies carried out an association between meteorological variables, mainly temperature and humidity, in regions that were experiencing high rates of COVID-19 [65, 66, 67,68]. A study conducted in China, based on case studies in Hong Kong, Guangzhou, Beijing, and Taiyuan, indicated that SARS outbreaks were significantly associated with temperature variations [69].

Demongeot and coauthors [67] illustrated that the virulence of coronavirus diseases due to SARS-CoV and MERS-CoV decreases in hot and humid climatic conditions. Another work by Wang and coauthors [65] demonstrated similar data stating that high temperature and high humidity reduce the transmission of COVID-19, although the mechanisms linked to this are largely unknown. A possible process is that higher ambient temperatures lead to faster evaporation of droplets that transmit viruses and can thus prevent the spread [67]. Adding to these findings, Sobral and coauthors [70] showed that temperature was negatively correlated with the number of infections, and the significance of this relationship remained even after adding additional variables, such as maximum and minimum average temperatures and exposure time to the disease.

According to Marvi and coauthors [71] work, the relationship between average temperature and the rate of spread of COVID-19 in several regions of the world was investigated, and the authors inferred that the rate of spread of the virus is slower in regions with extreme temperatures. A laboratory study published by Chin and coauthors [72] reported that SARS-CoV-2 was highly stable at 4 °C but sensitive to heat; the virus survival time was reduced to 5 min as the incubation temperature increased to 70 °C. Several other studies also indicate that SARS-CoV-2 is sensitive to high temperatures and humidity [73, 74, 75].

The researchers of another study estimated that climatic variables explain 18 % of the variation in the doubling time of the disease, and the remaining 82 % may be related to containment measures, general health policies, population density, transport, or cultural aspects [76]. According to another study, the spread of the virus is associated with latitude and longitude as geographic indicators and seasonal dynamics [77]. As for humidity Bukhari and Jameel [78] showed that countries with high absolute humidity above 10 gm^{-3} saw a deceleration in COVID-19 transmissions in a short time. Ward and coauthors [79] in their work also reported that under high-temperature conditions in the southern hemisphere, summer relative humidity can affect the transmission of COVID-19.

Unlike the conclusions of previous studies, Yao and coauthors [80] reported no association between COVID-19 transmission and temperature in Chinese cities. However, Huang and coauthors [81], after analyzing data from 185 countries/regions between January 21 and May 6. It was illustrated that 60 % of COVID-19 cases were detected in a temperature range of 5 °C to 15 °C, peaking at 11 °C. In the same study, global COVID-19 cases increased by 27,536 per 1 °C below 10 °C, and COVID-19 cases peaked at 65 % of relative humidity. A possible explanation for this is that colder temperatures can impair the innate immunity of humans, reducing the number of immune cells in the nasal mucosa [68]. Also, low humidity reduces the ability of airway hair cells to remove viral particles, thereby exposing the host to the virus [82, 83]. Besides, another study suggested that the phagocytic function of pulmonary alveolar macrophages decreased under cold stress in an in vitro experiment [84]. It is well known that breathing in cold air can lead to bronchial constriction, promoting susceptibility to pulmonary infection [85].

We can also mention the beneficial behavioral factors for transmitting the virus at low temperatures, such as indoor crowding and poor ventilation on cold days [86]. Therefore, the human body is at a higher risk of virus infection in low-temperature and low-humidity environments. Other studies analyzing additional variables, such as sun duration [87], wind level [54], relative humidity [88], absolute humidity [89], and daytime temperature [89], were correlated with the number of COVID-19 cases; however, the effect of weather conditions on virus transmission is likely to be sensitive to other factors, where habits, culture, social and economic conditions, and government intervention dominate them.

CONCLUSION

The transmission of SARS-CoV-2 is still a crucial public health concern, given the new variants, and the aspects that contribute to the severity and spread of COVID-19 require additional studies. The increased susceptibility to SARS-CoV-2 infection due to smoking is still unclear but appears to be linked to increased ACE2 receptors in smokers. Although the relationship between smoking and COVID-19 needs to be clarified, there is no doubt that smoking and related diseases are among the main risk factors for severe forms of the disease. PM containing SARS-CoV-2 could be a direct transmission model in a highly polluted area; also, PM upregulates ACE2 expression, and SARS-CoV-2 has a high affinity for ACE2 receptors. This suggests that PM and smoking can increase the risk of SARS-CoV-2 in the same way through ACE2 expression. The results presented in this review still suggest that the climate is important for transmitting COVID-19, particularly temperature and humidity, but other factors, such as government interventions, can impact this variable.

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REFERENCES

1. Li L, Huang T, Wang Y, Wang Z, Liang Y, Huang T, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J. Med. Virol. 2020 Mar 23;92(6):577–83.
2. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. J. Pharma. Anal. [Internet]. 2020 Mar 5;10(2):102–8. Available from: https://www.sciencedirect.com/science/article/pii/S2095177920302045#bib16
3. Shimabukuro-Vornhagen A, Gödel P, Subklewe M, Stemmler HJ, Schlößer HA, Schlaak M, et al. Cytokine release syndrome. J. ImmunoTher. of Cancer. 2018 Jun 15;6(1).
4. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clin. Immunol. 2020 Apr;215(1):108427.
5. Tsatsakis A, Petrakis D, Nikolouzakis TK, Docea AO, Calina D, Vinceti M, et al. COVID-19, an opportunity to reevaluate the correlation between long-term effects of anthropogenic pollutants on viral epidemic/pandemic events and prevalence. Food Chem. Toxicol. [Internet]. 2020 Jul 1;141:111418. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211730/
6. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. Brain, Behav., Immun. 2020 Jul; 87:184–7.
7. Ma Y, Zhao Y, Liu J, He X, Wang B, Fu S, et al. Effects of temperature variation and humidity on the death of COVID-19 in Wuhan, China. Sci. Total Environ. [Internet]. 2020 Mar 26;138226. Available from: https://www.sciencedirect.com/science/article/pii/S0048969720317393
8. Zhu Y, Xie J, Huang F, Cao L. Association between short-term exposure to air pollution and COVID-19 infection: Evidence from China. Sci. Total Environ 2020 Jul;727:138704.
9. World Health Organization W. Tobacco and waterpipe use increases the risk of suffering from COVID-19 | Know the truth | TFI [Internet]. www.emro.who.int. 2020. Available from: http://www.emro.who.int/tfi/know-the-truth/tobacco-and-waterpipe-users-are-at-increased-risk-of-covid-19-infection.html
10. 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.Pollution. 2020 Apr;261:114465.
11. Sailesh Harwani, Ratcliff JA, Sutterwala FS, Ballas ZK, Meyerholz DK, Chapleau MW, et al. Nicotine Mediates CD161a $^{+}$ Renal Macrophage Infiltration and Premature Hypertension in the Spontaneously Hypertensive Rat. 2016 Oct 28;119(10):1101–15.
12. Changeux JP. Nicotine addiction and nicotinic receptors: lessons from genetically modified mice. Nature Reviews Neuroscience [Internet]. 2010 Jun;11(6):389–401. Available from: https://www.nature.com/articles/nrn2849
13. Arcavi L, Benowitz NL. Cigarette smoking and infection. Archives of Internal Medicine [Internet]. 2004 Nov 8;164(20):2206–16. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15534156
14. Bauer CMT, Morissette MC, Stämpfli MR. The Influence of Cigarette Smoking on Viral Infections: Translating Bench Science to Impact COPD Pathogenesis and Acute Exacerbations of COPD Clinically. Chest [Internet]. 2013 Jan 1 [cited 2022 Jun 22];143(1):196–206. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0012369213600318
15. Gotts JE, Jordt SE, McConnell R, Tarran R. What are the respiratory effects of e-cigarettes? BMJ [Internet]. 2019 Sep 30;366:l5275. Available from: https://www.bmj.com/content/366/bmj.l5275
16. Park JE, Jung S, Kim A, Park JE. MERS transmission and risk factors: a systematic review. BMC Public Health [Internet]. 2018 May 2;18(1). Available from: https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-018-5484-8

17. Patanavanich R, Glantz SA. Smoking is Associated with COVID-19 Progression: A Meta-Analysis. Nicotine Toba. Res. 2020 May 13;22(9).
18. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Lian N, et al. The impact of COPD and smoking history on the severity of COVID-19: A systemic review and meta-analysis. J. Med. Virol. 2020 May 17;92(10).
19. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. New England J. Med. 2020 Feb 28;382(18).
20. Brake SJ, Barnsley K, Lu W, McAlinden KD, Eapen MS, Sohal SS. Smoking Upregulates Angiotensin-Converting Enzyme-2 Receptor: A Potential Adhesion Site for Novel Coronavirus SARS-CoV-2 (Covid-19). J. Clin. Med. 2020 Mar 20;9(3):841.
21. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). European J. Internal Med. 2020 Mar;
22. Farsalinos K, Niaura R, Le Houezec J, Barbouni A, Tsatsakis A, Kouretas D, et al. Editorial: Nicotine and SARS-CoV-2: COVID-19 may be a disease of the nicotinic cholinergic system. Toxicol. Rep. [Internet]. 2020 Apr 30; Available from: https://www.sciencedirect.com/science/article/pii/S2214750020302924
23. Farsalinos K, Barbouni A, Poulas K, Polosa R, Caponnetto P, Niaura R. Current smoking, former smoking, and adverse outcome among hospitalized COVID-19 patients: a systematic review and meta-analysis. Therap. Advan. in Chronic Disease. 2020 Jan;11:204062232093576.
24. Liu W, Tao ZW, Lei W, Ming-Li Y, Kui L, Ling Z, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chinese Med. J. 2020 Feb;133(9):1.
25. Battistoni A, Volpe M. Might renin–angiotensin system blockers play a role in the COVID-19 pandemic? Europ. Heart J. - Cardiovascular Pharm. 2020 Apr 14;6(4).
26. Gheblawi M, Wang K, Viveiros A, Nguyen Q, Zhong JC, Turner AJ, et al. Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System. Circ. Res. 2020 Apr 8;126(10).
27. Qiu Y, Zhao YB, Wang Q, Li JY, Zhou ZJ, Liao CH, et al. Predicting the angiotensin converting enzyme 2 (ACE2) utilizing capability as the receptor of SARS-CoV-2. Microbes and Infection. 2020 Mar;22(4-5).
28. Cai G. Bulk and single-cell transcriptomics identify tobacco-use disparity in lung gene expression of ACE2, the receptor of 2019-nCov. 2020 Feb 11 [cited 2021 Dec 7]; Available from: https://www.medrxiv.org/content/medrxiv/early/2020/02/17/2020.02.05.20020107.full.pdf
29. Leung JM, Yang CX, Tam A, Shaipanich T, Hackett TL, Singhera GK, et al. ACE-2 Expression in the Small Airway Epithelia of Smokers and COPD Patients: Implications for COVID-19. Europ. Resp. J. 2020 Apr 8;55:2000688.
30. Smith JC, Sausville EL, Girish V, Yuan ML, John KM, Sheltzer JM. Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract. 2020 Mar 31;
31. Tomchaney M, Contoli M, Mayo J, Baraldo S, Li S, Cabel CR, et al. Paradoxical effects of cigarette smoke and COPD on SARS-CoV-2 infection and disease. BMC Pulmonary Med. 2021 Aug 23;21(1).
32. Strzelak A, Ratajczak A, Adamiec A, Feleszko W. Tobacco Smoke Induces and Alters Immune Responses in the Lung Triggering Inflammation, Allergy, Asthma and Other Lung Diseases: A Mechanistic Review. International J. Enviro. Res. and Public Health [Internet]. 2018 May 21;15(5):1033. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5982072/
33. Conti P, Ronconi G, Caraffa A, Gallenga C, Ross R, Frydas I, et al. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. J. Bio. Regulators and Homeostatic Agents [Internet]. 2020;34(2):327–31. Available from: https://pubmed.ncbi.nlm.nih.gov/32171193/
34. Wiener RS, Cao YX, Hinds A, Ramirez MI, Williams MC. Angiotensin converting enzyme 2 is primarily epithelial and is developmentally regulated in the mouse lung. J. Cell. Biochemistry [Internet]. 2007 Aug 1 [cited 2020 Nov 15];101(5):1278–91. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7166549/
35. Wei Y, Shah R. Substance Use Disorder in the COVID-19 Pandemic: A Systematic Review of Vulnerabilities and Complications. Pharm. 2020 Jul 18;13(7):155.
36. Guo FR. Smoking links to the severity of COVID-19: An update of a meta-analysis. J.Med. Virol. 2020 Jul 11;92(11):2304–5.
37. Purkayastha A, Sen C, Garcia G, Langerman J, Shia DW, Meneses LK, et al. Direct Exposure to SARS-CoV-2 and Cigarette Smoke Increases Infection Severity and Alters the Stem Cell-Derived Airway Repair Response. Cell Stem Cell. 2020 Dec;27(6):869-875.e4.
38. Usman MS, Siddiqi TJ, Khan MS, Patel UK, Shahid I, Ahmed J, et al. Is there a smoker's paradox in COVID-19? BMJ Evidence-Based Med. [Internet]. 2020 Aug 11;26(6). Available from: https://ebm.bmj.com/content/early/2020/08/11/bmjebm-2020-111492
39. Leung JM, Sin DD. Smoking, ACE-2 and COVID-19: ongoing controversies. Europ. Resp. J. 2020 May 19;56(1):2001759.
40. Setti L. Evaluation of the potential relationship between Particulate Matter (PM) pollution and COVID-19 infection spread in Italy [Internet]. 2020. Available from: http://www.simaonlus.it/wpsima/wp-content/uploads/2020/03/COVID_19_position-paper_ENG.pdf
41. Zanoletti A, Bilo F, Federici S, Borgese L, Depero LE, Ponti J, et al. The first material made for air pollution control able to sequestrate fine and ultrafine air particulate matter. Sustainable Cities and Society. 2020 Feb;53(101961):101961.

42. Viana M, Reche C, Amato F, Andrés Alastuey, Querol X, Moreno T, et al. Evidence of biomass burning aerosols in the Barcelona urban environment during winter time. Atmospheric Environ. 2013 Jun 1;72:81–8.
43. Diapouli E, Manousakas MI, Vratolis S, Vasilatou V, Pateraki S, Bairachtari KA, et al. AIRUSE-LIFE +: estimation of natural source contributions to urban ambient air PM₁₀ and PM_{2. 5} concentrations in southern Europe – implications to compliance with limit values. Atmospheric Chem. and Physics. 2017 Mar 15;17(5):3673–85.
44. Van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. New England J. Med. 2020 Mar 17;382(16):1564–7.
45. Reche I, D'Orta G, Mladenov N, Winget DM, Suttle CA. Deposition rates of viruses and bacteria above the atmospheric boundary layer. The ISME J. 2018 Jan 29;12(4):1154–62.
46. Sedlmaier N, Hoppenheidt K, Krist H, Lehmann S, Lang H, Büttner M. Generation of avian influenza virus (AIV) contaminated fecal fine particulate matter (PM2.5): Genome and infectivity detection and calculation of immission. Vet. Microbiology. 2009 Oct;139(1-2):156–64.
47. Setti L, Passarini F, Gennaro GD, Barbieri P, Licen S, Perrone MG, et al. Potential role of particulate matter in the spreading of COVID-19 in Northern Italy: first observational study based on initial epidemic diffusion. BMJ Open [Internet]. 2020 Sep 1 [cited 2021 Feb 8];10(9):e039338. Available from: https://bmjopen.bmj.com/content/10/9/e039338
48. Cui Y, Zhang ZF, 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. 2003 Nov 20;2(1).
49. Wu X, Nethery RC, Sabath BM, Braun D, Dominici F. Exposure to air pollution and COVID-19 mortality in the United States: A Nationwide cross-sectional study. MedRxiv. 2020 Apr 27
50. Pozzer A, Dominici F, Haines A, Witt C, Münzel T, Lelieveld J. OUP accepted manuscript. Cardiov. Research 2020;116(14).
51. Travaglio M, Yu Y, Popovic R, Selley L, Leal NS, Martins LM. Links between air pollution and COVID-19 in England. Environ. Poll. 2020 Oct;268:115859.
52. Frontera A, Martin C, Vlachos K, Sgubin G. Regional air pollution persistence links to COVID-19 infection zoning. J.Infection. 2020 Apr;81(2).
53. Martelletti L, Martelletti P. Air Pollution and the Novel Covid-19 Disease: a Putative Disease Risk Factor. SN Comprehensive Clin. Med. 2020 Apr 15;2.
54. Jiang Y, Wu XJ, Guan YJ. Effect of ambient air pollutants and meteorological variables on COVID-19 incidence. Infect Control Hosp Epidemiol. 2020 May 11;41(9):1–11.
55. Fattorini D, Regoli F. Role of the chronic air pollution levels in the Covid-19 outbreak risk in Italy. Environ. Poll. 2020 Sep;264:114732.
56. Coccia M. High health expenditures and low exposure of population to air pollution as critical factors that can reduce fatality rate in COVID-19 pandemic crisis: a global analysis. Environ. Research. 2021 Aug;199:111339.
57. Gupta A, Bherwani H, Gautam S, Anjum S, Musugu K, Kumar N, et al. Air pollution aggravating COVID-19 lethality? Exploration in Asian cities using statistical models. Environ., Development and Sustainability. 2020 Jul 15;23.
58. Barcelo D. An environmental and health perspective for COVID-19 outbreak: Meteorology and air quality influence, sewage epidemiology indicator, hospitals disinfection, drug therapies and recommendations. J. Environ. Chem. Eng. 2020 Aug;8(4):104006.
59. Jaspers I, Ciencewicki JM, Zhang W, Brighton LE, Carson JL, Beck MA, et al. Diesel Exhaust Enhances Influenza Virus Infections in Respiratory Epithelial Cells. Toxicol. Sci. 2005 Mar 16;85(2):990–1002.
60. Silveyra P, Floros J. Air pollution and epigenetics: effects on SP-A and innate host defence in the lung. Swiss Med. Weekly. 2012 May 2;142.
61. Rylance J, Fullerton DG, Scriven J, Aljurayyan AN, Mzinza D, Barrett S, et al. Household Air Pollution Causes Dose-Dependent Inflammation and Altered Phagocytosis in Human Macrophages. American J. of Respiratory Cell and Mol. Biology [Internet]. 2015 May [cited 2021 May 1];52(5):584–93. Available from: https://dx.doi.org/10.1165%2Frcmb.2014-0188OC
62. Yang J, Chen Y, Yu Z, Ding H, Ma Z. The influence of PM2.5 on lung injury and cytokines in mice. Exp. Therapeutic Med. 2019 Aug 1;18(4).
63. Gao F, Zheng KI, Wang XB, Sun QF, Pan KH, Wang TY, et al. Obesity Is a Risk Factor for Greater COVID-19 Severity. Diabetes Care. 2020 May 14;43(7):e72–4.
64. Gao F, Zheng KI, Wang X, Yan H, Sun Q, Pan K, et al. Metabolic associated fatty liver disease increases coronavirus disease 2019 disease severity in nondiabetic patients. J. Gastroenterol Hepatol. 2020 Jun 5;36(1):204–7.
65. Wang J, Tang K, Feng K, Lin X, Lv W, Chen K, et al. Impact of temperature and relative humidity on the transmission of COVID-19: a modelling study in China and the United States. BMJ Open. 2021 Feb;11(2):e043863.
66. Wang M, Jiang A, Gong L, Luo L, Guo W, Li C, et al. Temperature significant change COVID-19 Transmission in 429 cities. medRxiv [Internet]. 2020 Feb 25; Available from: https://t.co/Wg5IEyrRtb
67. Demongeot J, Flet-Berliac Y, Seligmann H. Temperature Decreases Spread Parameters of the New Covid-19 Case Dynamics. Biol. 2020 May 3;9(5):94.

68. Sun Z, Thilakavathy K, Kumar SS, He G, Liu SV. Potential Factors Influencing Repeated SARS Outbreaks in China. Int J Environ Res Public Health. 2020 Mar 3;17(5):1633.
69. Tan J. An initial investigation of the association between the SARS outbreak and weather: with the view of the environmental temperature and its variation. J Epidemiol Community Health [Internet]. 2005 Mar 1 [cited 2019 Dec 10];59(3):186–92. Available from: https://jech.bmj.com/content/59/3/186
70. Sobral MFF, Duarte GB, da Penha Sobral AIG, Marinho MLM, de Souza Melo A. Association between climate variables and global transmission oF SARS-CoV-2. The Sci. Total Environ.[Internet]. 2020 Aug 10;729:138997. Available from: https://pubmed.ncbi.nlm.nih.gov/32353724/
71. Marvi M, Arfeen A. Demystifying a Hidden Trend: Do Temperature Variations Affect COVID-19 Virus Spread? SSRN Electronic J. 2020;
72. Chin AW, Chu JT, Perera MR. Stability of SARS-CoV-2 in different environmental conditions. The Lancet Microbe [Internet]. 2020 Apr;01(01). Available from: https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30003-3/fulltext?tp=1
73. Chong KC, Lee TC, Bialasiewicz S, Chen J, Smith DW, Choy WSC, et al. Association between meteorological variations and activities of influenza A and B across different climate zones: a multi-region modelling analysis across the globe. J. Infection [Internet]. 2020 Jan 1 [cited 2022 Nov 3];80(1):84–98. Available from: https://pubmed.ncbi.nlm.nih.gov/31580867/
74. Chakraborty T, Ghosh I. Real-time forecasts and risk assessment of novel coronavirus (COVID-19) cases: A data-driven analysis. Chaos, Solit Fractals. 2020 Apr;135:109850.
75. Xie J, Zhu Y. Association between ambient temperature and COVID-19 infection in 122 cities from China. Sci. Total Environ.[Internet]. 2020 Jul 1;724(724):138201. Available from: https://www.sciencedirect.com/science/article/pii/S0048969720317149
76. Oliveiros B, Caramelo L, Ferreira NC, Caramelo F. Role of temperature and humidity in the modulation of the doubling time of COVID-19 cases. MedRxiv [Internet]. 2020 Mar 8 [cited 2020 Apr 9]; Available from: https://t.co/lH5Xff2CqY
77. Keshavarzi A. Coronavirus Infectious Disease (COVID-19) Modeling: Evidence of Geographical Signals. SSRN Electron J. 2020;
78. Bukhari Q, Jameel Y. Will Coronavirus Pandemic Diminish by Summer? SSRN Electron J. [Internet]. 2020; Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3556998
79. Ward MP, Xiao S, Zhang Z. The role of climate during the COVID-19 epidemic in New South Wales, Australia. Transbound Emerg Dis. 2020 Jun;67(6).
80. Yao Y, Pan J, Liu Z, Meng X, Wang W, Kan H, et al. No Association of COVID-19 transmission with temperature or UV radiation in Chinese cities. Eur. Resp. J. 2020 Apr 8;55(5):2000517.
81. Huang Z, Huang J, Gu Q, Du P, Liang H, Dong Q. Optimal temperature zone for the dispersal of COVID-19. Sci. Total Environ. 2020 Sep;736:139487.
82. Lowen AC, Mubareka S, Steel J, Palese P. Influenza Virus Transmission Is Dependent on Relative Humidity and Temperature. PLoS Pathogens. 2007;3(10):e151.
83. Kudo E, Song E, Yockey LJ, Rakib T, Wong PW, Homer RJ, et al. Low ambient humidity impairs barrier function and innate resistance against influenza infection. PNAS. 2019 May 13;116(22):10905–10.
84. Luo B, Liu J, Fei G, Han T, Zhang K, Wang L, et al. Impact of probable interaction of low temperature and ambient fine particulate matter on the function of rats alveolar macrophages. Environ Toxicol Pharm. 2017 Jan;49:172–8.
85. Martens WJM. Climate change, thermal stress and mortality changes. Social Sci. Med. 1998 Feb;46(3):331–44.
86. Bunker A, Wildenhain J, Vandenbergh A, Henschke N, Rocklöv J, Hajat S, et al. Effects of Air Temperature on Climate-Sensitive Mortality and Morbidity Outcomes in the Elderly; a Systematic Review and Meta-analysis of Epidemiological Evidence. EBioMedicine [Internet]. 2016;6:258–68. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27211569/
87. Li H, Xu XL, Dai DW, Huang ZY, Ma Z, Guan YJ. Air pollution and temperature are associated with increased COVID-19 incidence: A time series study. Int J Infect Dis [Internet]. 2020 Aug;97:278–82. Available from: https://www.ijidonline.com/article/S1201-9712%2820%2930383-0/pdf
88. Goswami K, Bharali S, Hazarika J. Projections for COVID-19 pandemic in India and effect of temperature and humidity. Diabetes & Metabolic Syndrome: Clin Res Rev. 2020 Sep;14(5):801–5.
89. Liu J, Zhou J, Yao J, Zhang X, Li L, Xu X, et al. Impact of meteorological factors on the COVID-19 transmission: A multi-city study in China. Sci. Total Environ. 2020 Jul;726:138513.