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Could the COVID-19 Positive Asymptomatic Tobacco Smoker be a Silent Superspeader?

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Abstract. There appears to be a connection between COVID-19 infection and an airborne microscopic pollutant called particulate matter which has been suggested to act as vector for viral transmission. The highest human exposure to particulate matter occurs during smoking and to a lesser extent to 2nd hand smoking. This article offers a hypothetical proposition that particulate matter derived from tobacco smoking may act as COVID-19's vector for infection transmission. With a background smoking Chinese male population of more than 66% and more than 70% of Chinese nonsmokers exposed to 2nd hand smoke, the potential of exhaled smoke acting as a viral vector is significant. If this hypothesis is proven, measures such as face protection to reduce coronavirus-laden particulate matter transmission, measures of social distancing and legislation to protect nonsmokers from contracting the infection through 2nd hand smoking should be implemented. (www.actabiomedica.it)

Key words:

Introduction

The COVID-19 pandemic appears to have initiated in the Chinese province of Hubei, the index case diagnosed in early December 2019. The index case appears to have transmitted the infection at a Wuhan animal market where the outbreak rapidly spread. Soon after, following arrivals from China, COVID-19 spread to Qoms in Iran and Bergamo in Italy. A characteristic common to all three cities was the presence of very high levels of the particulate matter component of atmospheric pollution at the time of the outbreak (1).

Following the January 2020 lockdown in China, the atmospheric particulate matter levels decreased as did most the components of airborne pollution (2). The main cause for the reduction in atmospheric pollution was the reduction in coal combustion in China decreasing from 80,000 tonnes per day to 40,000 tonnes daily subsequent to the lockdown in China (2). Sporadic outbreaks in China still persisted suggesting that besides atmospheric origination, particulate matter from other sources may have been responsible for COVID-19 spread in China. Particulate matter eminently present in tobacco smoke may have spread the epidemic, taking into consideration the background smoking population with more than 66% of Chinese males being smokers and more than 70% of Chinese nonsmokers exposed to 2nd hand smoke (3).

COVID-19 Evolution and Tobacco Smoking following lockdown in China

The epidemic in China decreased after lockdown, however sporadic outbreaks still persisted. Coinciding with the reduction in COVID-19 infection in mid-February, promulgated by the original viral Clade D (Wuhan 1), was the appearance of a mutant delineated as Clade G. The mutation involved the replacement of aspartic acid with glycine at the D614 position of the gene coding for COVID-19 spike protein (4).

From mid-February onwards Clade G slowly gained predominance despite the persisting reduction in atmospheric particulate matter (4).

Particulate matter derived from smoking is a common occurrence in China with more than 66% of Chinese males being smokers (3). Accelerating COVID-19 transmission is the obvious necessity whereby the act of smoking requires the removal of face protection. Face protection has been shown to significantly reduce COVID-19 spread (5). The removal of face protection not only exposed the smoker to infection but also nearby smokers and non-smoking individuals. Moreover the lockdown itself enforced smokers indoors, reducing the dispersal effect of outdoors' natural ventilatory attributes. The World Health Organization indicates that safe limits of ambient PM2.5 should not exceed 25μg/m3. Exceedingly high PM2.5 levels of 1,000μg/m3 have been shown in some smoking venues. These elevated levels of PM2.5 are more likely in densely populated areas with poor ventilation, in the presence of smokers (6).

The evolution in viral clade may have also arisen due to the change in particulate matter, the proposed viral vector. The water content in particulate matter derived from smoking is significantly higher than that from the atmosphere. The volume of particulate matter originating from the respiratory tract increases 1.5 times due to the adherence of water molecules to particulate matter travelling through the humidified bronchial tree (7).

The spike protein of COVID-19 differs between both clades in the configuration of its constituent three peptides. The original Clade D has a "closed" configuration of its spike protein three peptides, while Clade G has an "open" configuration (8). Adherence to the angiotensin II converting enzyme receptor on the goblet cells requires that at least two peptides are in an "open" configuration (9). Hidden deep in the spike protein are hydrophobic sites on the N-terminal portion of the constituent peptides (10,11). The change in the trimeric peptide configuration may suggest a reduction in the hydrophobic properties in the spike protein of the mutant making it more amenable to carriage on particulate matter originating from the respiratory tract.

Following the appearance of COVID-19 in the city of Bergamo, COVID-19 infection spread throughout the Lombardy region which has one of the highest proportion of smokers in Italy. The Lombardy region had the first lockdown due to the exponential mortality rate it experienced. A fortnight later the cities of Madrid, Paris, London and New York followed suite and a month later, cities in Mexico, Brazil and India were also affected.

COVID-19 transmission and Particulate Matter

The index of COVID-19 transmissibility (Ro) was at its peak estimated to be as high as 5.7, 4.5, and later settled at 3.28 (12,13,14). At its height the Ro of the seasonal influenza is estimated at 1 to 1.1. This may suggest that besides human to human transmission there may be other variables accelerating the transmission of COVID-19. The presence of an airborne vector in the form of particulate matter may have augmented the viral transmission and may also have had a hand in COVID-19 clade evolution.

Zhu et al showed in a study of a large number of Chinese cities, an increase of 2% in COVID-19 new cases of with every 10μg/m3 increment in atmospheric PM2.5 (15).

This correlation between COVID-19 and levels of atmospheric particulate matter was also noted in studies undertaken in Northern Italy which was the first European country to be hard hit by COVID-19 (16,17).

Particulate matter also appears to influence the renin-angiotensin system which modulates pulmonary inflammatory response. Preclinical studies have demonstrated that the lack of angiotensin converting enzyme II was associated with delayed lung repair following PM2.5 induced injury (18). The pulmonary port of call for COVID-19 appears to be the angiotensin converting enzyme receptor on respiratory epithelial goblet cell (19). Tobacco smoke causes an increase in pulmonary goblet cells which in turn increase angiotensin converting enzyme II receptor sites (20).

The Air Quality Index (AQI), a real-time monitor of atmospheric pollution, consistently illustrates a concentration of unhealthy levels of PM2.5 conspicuously covering most cities in China. Following the Chinese lockdown the AQI confirmed the decrease in airborne pollution including particulate matter coinciding with the reduction of Clade D and the emergence of Clade G. With more than 66% of Chinese males indulging in cigarette smoking and the lockdown forcing smokers indoors, spread of Clade G utilizing smoke derived particulate matter acting as a viral vector was a distinct possibility (3). The Lombardy region hard hit with COVID-19 also has the highest percentage of smokers in Italy.

Carriage of COVID-19 by Particulate Matter

Following the exponential increase in deaths in Northern Italy, local lockdown was initiated in Lombardy in late February, with progressive extensions of this measure to the rest of the peninsula. Scientists in Milan confirmed that the genes appertaining to COVID-19 were detected on particulate matter. This raised the possibility that particulate matter including PM2.5 could have acted as a vector and co-factor for COVID-19 infection (16).

The implications of particulate matter acting as a vector suggest that viral carriage could go beyond the human to human transmission radius of 2 metres. Setti et al have postulated that with particulate matter acting as a vector, the transmission distance may be extended up to 10 metres (16). Another study in Northern Italy confirmed the elevated levels of particulate matter (both PM2.5 and PM10) correlated with the incidence of COVID-19 infection and similarly postulated that besides the deleterious influence particulate matter has on respiratory antimicrobial defences, this airborne pollutant could also act as a vector for COVID-19 (17).

Chronic exposure to PM2.5 has deleterious effects on health. The World Health Organization guideline recommends that PM2.5 levels should not exceed an average level of 25μg/m^3 24-hour. Several studies have shown adverse effects on respiratory defences against lung infection following exposure to particulate matter PM2.5 (21,22). In a study on a large American population of 65-year-olds by Wu et al, a small increment of 1 μg/m3 in long-term exposure to PM2.5 led to an increase of 0.73% in all-cause mortality. Consequently a recent study by the same authors showed that a similar increase of 1 μg/m3 in long-term PM2.5 exposure correlated with an 8% increase in the COVID-19 death rate. For the same 1μg/m3 increase in PM2.5, the magnitude of COVID related deaths increased eleven-fold (23).

Viral Infection and Air Pollution

There are reports indicating that there are other viral infections which have been associated with air pollution with particulate matter. Sedlmaier et al have shown a linkage between particulate matter and influenza and haemorrhagic fever with renal disease (24). During the 2003 Severe Acute Respiratory Syndrome (SARS) epidemic, the air pollution was shown to correlate with mortality rates. The mortality from SARS in Chinese regions with high air pollution index had doubled the death rates compared to provinces with low atmospheric pollution (RR =2.18, 95% CI: 1.31–3.65) (25). In 1997 high levels of particulate matter, both PM10 and PM2.5 components were implicated in the transmission of the Avian flu (26).

Measles known to have the highest transmissibility of all viruses with an Ro of 18 and has demonstrated outbreaks in the presence of elevated levels of particulate matter (PM10) in China (24). Dust events in the Gansu province in Western China between 1965 till 2005 evidenced a spike in measles outbreaks during this period (27). Dry seasons with greater atmospheric pollution coincide with measles outbreaks which disappear at the onset of rainy spells in the Niger (28). In 1935 the most severe measles epidemic in the USA occurred in Kansas in 1935 during the Dust Bowl period (29). In the absence of mass vaccination, rubella infection in the Pradesh region of India showed a greater incidence in adolescents who smoked tobacco products (30).

The COVID-19 Pandemic in the USA and Tobacco Smoking

A recent publication has indicated that COVID-19 infection rates were significantly higher in the States of the USA with higher percentages of the population with partial bans on tobacco smoking compared with highly regulated States (p<0.038) (31). The COVID-19 rates of infection in the States with partial bans was 2046/100,000 (sd+/-827), 23% higher the infection rates regulation (1660/100,000 (sd+/-686) in States with more severe smoking prohibitions (31).

The percentage of the smokers in the States with partial bans was significantly higher that that of States with restrictive smoking legislation on tobacco smoking (p<0.0006). The percentage of smokers in States with minimal bans to smoking was 18.3% (sd+/-3.28) while States with greater smoking prohibitions had a smoking population percentage of 15.2% (sd+/-2.68). There was no significant difference between both groups of States as regards the state case-fatality ratio, population density, body mass index and the percentage of the state population aged 65years or above (31).

Significant correlations were borne out when comparing variables of all the USA States together and the two groups separately. The COVID-19 case-fatality ratio density correlated significantly with States' population (R=0.66 p<0.0001). The correlation of the population density/case fatality ratio still applied when the two groups of States were assessed separately, more significantly in the more regulated group R=0.74 (p<0.0001) than the less restrictive group R=0.58 (p<0.003) (31).

The COVID-19 case-fatality ratio correlated with advancing age in the 75 years and over age group (R=0.29 p<0.04). In the 75 years and over age group the proportion of foreign born population (0.7% sd+/-0.57) was significantly higher in the States with more prohibitive smoking regulations compared to the population of States with partial smoking bans (0.45% sd+/-0.45) (31).

The Evolution of the COVID-19 Pandemic in Utah

Utah is the state with the lowest percentage of smokers in the USA. It is interesting to note that at the time of the study (21st September 2020), Utah, the only US state with a single digit, 9% smoking population had a relatively elevated COVID-19 incidence but a low case-fatality ratio. Despite the low percentage smoking population in Utah, the COVID-19 infection rate was 1989/100,000 which was high for a State with a restrictive smoking regulation. The presence of bordering partial ban States such as Nevada, Idaho and Wyoming may explain Utah's COVID-19 incidence through cross-border infection transmission. Utah's case-fatality ratio was the lowest in the USA, possibly due to the combined factors of low smoking prevalence, low population density and low percentage cohorts in both the 65+ (11%) and 75+ (4.4%) age groups (31).

The situation in Utah has drastically changed since end of October after a number of Halloween parties were organized on the 30th October. The seven-day average positive rate was 18.2%, increasing to 23.6% a month later (32). The number of patients hospitalized increased by 33%. It was reported that hundreds of individuals attended these Halloween parties making the possibility of an asymptomatic COVID-19 smoking attendee acting as a superspreader more likely.

COVID-19 related mortality in the North-East USA Coast and Particulate Matter

A notable exception in the above trend was the high incidence of COVID-19 infection and case-fatality ratio in the North-East Coast of the USA. All the states except Connecticut have a restrictive regulation of smoking in public, in fact the percentage of these states' smoking population is low (12.8% -13.6% - USA National average 17%).[31] The reason that may explain the high incidence of COVID-19 infection and case-fatality ratio (32) in the North-East Coast of the USA may be due to the dense underground network connecting New York, Massachusetts, Rhode Island and Connecticut. Similarly affected was the nearby state New Jersey.

Besides the factor of commuter congestion increasing human to human transmission, particulate matter may also have had a hand in spreading the pandemic (33). The habitable site with the highest concentration of particulate matter is underground travel. Rail friction while trains travel through subways produces some of the highest concentrations of particulate matter which is trapped underground because of limited ventilation (33). Although smoke-free laws have been enacted to prevent smoking in underground networks, however on occasion these are not adhered (34).

A preprint has shown that in the presence of high levels of particulate matter the COVID-19 mortality rate was higher than in underground lines with lower concentration of this pollutant raising the possibility that particulate matter again acted as a vector (33). On a molecular level particulate matter in subways may be more sinister due to the haematite–rich component as opposed to the carbon-rich tobacco derived particulate matter. In the absence of carbon adsorbance properties, the haematite-rich particulate matter may be able to release any adherent COVID-19 in an easier manner. Moreover COVID-19 has been shown to survive on steel surfaces for 72 hours (35).

What Needs to be Done?

1. Experimental research needs to be undertaken to confirm or refute the vector effect of smoke-derived particulate matter for COVID-19 (36).
2. In venues where tobacco smoking is exercised,
3. effective indoor ventilation and measures to implement efficient social distancing need to be employed.
4. Legislation has to be implemented rigorously so that the general public is protected from 2nd hand smoking.
5. In the current and future pandemics widespread face protection has to be vigorously encouraged.

Conclusion

The ubiquitous spread of the COVID-19 Pandemic indicates that its transmission is likely to be multi-factorial in nature. The elevated Ro places COVID-19 closer to the measles league whereby besides human to human spread, environmental factors such as particular matter, dust pollution, dry seasons and tobacco smoking appear to play an important role in COVID-19's community transmission.

There are factors common to countries that controlled the COVID-19 pandemic. These factors include wearing of face protection, barring of mass events and extensive population testing, tracing and imposition of quarantine measures. These basic tenets of Public Health support social distancing impacting viral transmission as would measures to educate the populace regarding the adverse effects on health due to tobacco smoking and 2nd hand smoking.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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