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The Potential role of Particulate Matter in the Spreading of COVID-19 in Northern Italy: First Evidence-based Research Hypotheses

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Abstract

Background: Exposures to $PM_{2.5}$ and PM_{10} such as those usually recorded in the Po Vally (Northern Italy) are notoriously associated with a number of adverse health effects or premature death. At the same time, a number of studies have shown that airborne transmission route could spread viruses even further the close contact with infected people. An epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spread of the recent severe acute respiratory syndrome COVID-19 in Italy, which was fast and dramatic only in Lombardy and Po Valley. On March 16th 2020, we presented a Position Paper proposing a research hypothesis concerning the association between higher mortality rates due to COVID-19 observed in Northern Italy and the peaks of particulate matter concentrations, frequently exceeding the legal limit of 50 $\mu g/m^3$ as PM_{10} daily average **Methods**: To assess environmental factors related to the spread of the COVID-19 in Italy from February 24th to March 13th (the date when the lockdown has been imposed over Italy), official daily data relevant to ambient PM_{10} levels were collected from all Italian Provinces between February 9th and February 29th , taking into account the average time (estimated in 17 days) elapsed between the initial infection and the recorded COVID positivity. In addition to the number of exceedances of PM_{10} daily limit value, we considered also population data and daily travelling information per each Province. **Results**. PM_{10} daily limit value exceedances appear to be a significant predictor ($p < .001$) of infection in univariate analyses. Less polluted Provinces had a median of 0.03 infection cases over 1000 residents, while most polluted Provinces had a median of 0.26 cases over 1000 residents. Thirty-nine out of 41 Northern Italian Provinces resulted in the category with highest PM_{10} levels, while 62 out of 66 Southern Provinces presented low PM_{10} concentrations ($p< 0.001$). In Milan, the average growth rate before the lockdown was significantly higher than Rome (0.34 vs. 0.27 per day, with a doubling time of 2.0 days vs. 2.6, respectively), suggesting a basic reproductive number R_0 >6.0, comparable with the highest values estimated for China. **Conclusion:** A significant association has been found between the geographical distribution of daily PM_{10} exceedances and the spread of COVID-19 in the110 Italian Provinces.

Keywords: COVID-19; Air Pollution; Particulate Matter; super-spread event; Italy.

Introduction

Article Summary – "Strengths and limitations of this study"

- This is the first study confirming that PM10 appears to be a predictor ($p < .001$) of COVID-19;
- Most polluted areas in Italy had a higher spread of COVID-19 compared to less polluted ones;
- Despite these observations, no assumptions can be made about presence of SARS-COV-2 virus on particulate matter and COVID-19 outbreak progression in the Italian provinces which are experiencing the highest burden of the disease.

Severe acute respiratory syndrome known as COVID-19 disease (due to SARS-CoV-2 virus), is recognized to spread via respiratory droplets and close contacts [1]. However, this unique transmission model does not seem to explain properly the different spread observed in Italy from February 24th, 2020 to March 13rd, 2020. The huge virulence of COVID19 in the Po Valley is not comparable to the milder contagiousness observed in the central-southern regions. Demographic factors related to the ageing of the population and the possibility of infection without clinical symptoms for a quite long time - associated with the high rate of asymptomatic people that characterize COVID-19, estimated in 50-75% of infections - may only partially explain the fast spreading of the virus in Lombardy and Northern Italy [2,3]. Cai et al (2020) reported different incubation periods in patient(s) infected in Wuhan [4], but an epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spreading of the recent severe acute respiratory syndrome COVID-19 in Italy, which was fast and dramatic only in Lombardy and Po Valley. At the same time, a number of studies have shown that airborne transmission route could spread viruses even further the close contact with infected people [5-19]. Paules et al. (2020) highlighted that - besides close distance contacts - airborne transmission of SARS-CoV can also occur [5]. It has also been reported how for some pathogens the airborne transport can reach long distances [6-8]. Reche et al. (2018) described the aerosolization of soil-dust and organic aggregates in sea spray that facilitates the long-range transport of bacteria, and likely of viruses free in the atmosphere. In particular, virus deposition rates were positively correlated with organic aerosol <0.7 µm, implying that viruses could have longer persistence times in the atmosphere and, consequently, will be dispersed further [9]. Moreover Qin et al. (2020) analyzed the microbiome of the airborne particulate matter ($PM_{2.5}$ and PM_{10}) in Beijing over a period of 6 months in 2012 and 2013, putting in evidence a variability of the composition that depended on the months [10]. Temporal distribution of the relative abundance of the microbiome on the particulate matter (PM) showed the highest presence of viruses in January and February, just in coincidence with most severe PM pollution. Chen. et al (2017) demonstrated the relationship between short-term exposure $PM_{2.5}$ concentration and measles incidence in 21 cities in China [11]. Their meta-analyses showed that the nationwide measles incidence was significantly associated with an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ levels.

Other recent studies have also reported associations between PM and infectious diseases (e.g., influenza, hemorrhagic fever with renal syndrome): inhalation could bring PM deep into the lung and virus attached to particles may invade the lower part of respiratory tract directly, thus enhancing the induction of infections, as demonstrated by Sedlmaier et al (2009) [12]. Zhao et al. (2018) showed that the majority of the positive cases of highly pathogenic avian influenza (HPAI) H5N2 in Iowa (USA) in 2015 might have received airborne virus, carried by fine PM, from infected farms both within the same State and from neighboring States [13]. The condensation and stabilization of the bioaerosol, generating aggregates with atmospheric particles from primary (i.e. dust) and secondary particulate, has been indicated as mechanisms able to transport airborne bacteria and viruses to distant regions, even by the inter-continent-transported dust: Ma et al. (2017) observed a positive correlation of the measles incidence with PM_{10} in western China during the period 1986-2005 [14]; Ferrari et al. (2008) showed measles outbreaks occurring in dry seasons and disappearing at the onset of rainy seasons in Niger [15]; Brown et al (1935) found that the most severe measles epidemic in the United States occurred in Kansas in 1935 during the Dust Bowl period [16].

Coming to recent specific studies, laboratory experiments of Van Doremalen et al. (2020) indicated that airborne and fomite transmission of SARS-Cov-2 is plausible, since the virus can remain viable and infectious in aerosol for hours [17]. Field measurement by Liu et al. (2020) showed evidence of coronavirus RNA in air sampled in Wuhan Hospitals and even in ambient air in close proximity during COVID-19 outbreak, pointing at the airborne route as a possible important pathway for contamination, that should have a further confirmation [18]. Santarpia et. al. reported the presence of airborne SARS-Cov-2 in air sampled at the Nebraska University Hospital [19], while - at the opposite - some negative evidence of virus presence in air reported by Ong et al. (2020) come from explicitly poor sampling scheme [20]. A research carried out by the Harvard School of Public Health seems to confirm an association between increases in particulate matter concentration and mortality rates due to COVID-19 [21]. On March 16th 2020, we have released an official Position Paper highlighting that there are enough evidence to consider airborne route as a possible additional factor for interpreting the anomalous COVID-19 outbreaks notified in the Northern Italy, known to be one of the European areas characterized by highest PM concentration [22,23]. Data that led to the publication of the Position Paper are presented in this article, and are expected to trigger the interest of the research community at working on this topic.

Methods

We have analyzed daily data relevant to ambient PM_{10} levels, urban conditions and virus incidence from all Italian Provinces, in order to reliably determine the association between PM pollution level and the initial spread of COVID-19. PM_{10} daily concentration levels were collected by the official air quality monitoring stations of the Regional Environmental Protection Agencies, ARPA), publicly available on their websites. The number of PM_{10} daily limit value exceedances (50 $\mu g/m^3$) detected in the different Provinces, divided by the total number of PM_{10} monitoring stations for each selected Province was taken into account. Population data, population density and number of commuters related to each Italian Province were collected from ISTAT database for the 110 Provinces [3]. The number of COVID-19 infected people for each Province from February 24th to March 13th (the date when the lockdown was decided) was that reported on the official Government website, updated with daily frequency [24]. PM_{10} exceedances were collected between February 9th and February 29th, taking into account the *lag period*, which is the average time elapsed between the initial infection and the diagnosis. To investigate how high PM_{10} concentrations (above the daily limit value) might relate to infection diffusion, we performed an exploratory analysis considering the recursive binary partitioning tree approach, as implemented into the party package [25] of R [26].

Besides PM_{10} daily limit value exceedances we considered several further covariates related to the different Provinces: population absolute frequencies; population densities (n° inhabitants/km^2); the absolute frequencies of people daily travelling as estimated by the Italian National Institute of Statistics [3], and its proportion with respect to the overall Province population. As response variable we considered the infection rate of the disease, expressed as a proportion obtained binding together into a single two-dimensional vector both the number of COVID-19 cases and the rest of the Province population. We have performed statistical inferences analyses on Milan and Rome data, in order to observe the potential association between PM levels and COVID-19 spreading in big cities located in different geographic areas and with remarkable differences in PM_{10} exceedances, presenting at the same time quite similar urbanization, life style, population, ageing index, and number of commuters.

Results

The spatial distribution of ambient PM_{10} exceedances between Italian cities was geographically heterogeneous and it is presented in Fig. 1a. The highest numbers of exceedances were generally located in Northern Italian Regions, while zones with a lower contagion were sited in Central and Southern Regions. The maps in Fig 1 illustrate the mean of PM_{10} exceedances on the number of PM_{10} stations in all Italian Provinces in the period February 9th-29th 2020 (Fig. 1a), compared with the total COVID-19 infection per Province observed in the period March 4th-13th (Fig. 1b-e). Overall, there were 17,660 infected people during the time lapse of the study. The highest incidences of COVID-19 occurred in cities located in Northern Italy, and in particular in Lombardy Region, including its capital Milan. The lowest incidences of COVID-19 were observed in Southern Italy, as in Lazio Region, which includes Rome.

Figure 1. ***(a)*** *Average daily PM_{10} exceedances vs. number of monitoring stations in different Italian Provinces from February 9th to 29th 2020;* ***(b-e)*** *Spreading of COVID-19 infected people during the period March 3th – 13th 2020*

If continuing the observations beyond the date of the shutdown (March 13th), it was possible - by analyzing the trend of new daily COVID-19 infections - to observe a first reduction of the spreading rate of contagion around March 22nd (reflecting the school closure ordered on March 5th) and a second one around March 28th (reflecting the lockdown ordered on March 11th-13th) (Figure 2).

Figure 2*. New daily COVID-19 infections in Italy from February 24th to April 4th 2020*

On the basis, the *lag period* can be estimated in 17 days. In the univariate analysis, the PM_{10} daily limit value exceedances appear to be a significant predictor ($p < .001$) of infection (Fig. 3b) with a 1.29 cut-off value. The cut-off divides the Provinces into two classes, respectively with higher ($n = 43$) and lower ($n = 67$) PM_{10} concentrations. The boxplots depict the log-transformed infection rate of the disease: the less polluted Provinces had a median 0.03 infection case over 1000 residents (first – third quartile 0.01 – 0.09, range 0.00 – 0.56), while most polluted Provinces had a median 0.26 infection cases over 1000 Province residents (first – third quartile 0.14 – 0.51, range 0.00 – 4.92).

Dividing the Italian peninsula into two areas, the Northern and Southern part along the Tuscan-Emilian Apennines watershed, the exceedances results as follows: 39 of the 41 Northern Provinces falls in the higher PM_{10} category, while on the Southern Provinces the ratio is reversed: 62 over 66 have lower PM_{10} (odds ratio .00, Fisher exact test $p < .001$).

Figure 3. *Relationship between the PM_{10} daily limit value exceedances and the COVID-19 cases ratios over Italian Provinces population.* ***(a)*** *Scatterplot on semi-logarithmic scale relating the proportion of COVID-19 cases of Northern (gray squares) and Southern (black bullets) Italian Provinces population versus the average of PM_{10} daily limit value exceedances. The dashed binomial (logistic) regression is characterized by an increasing slope of 0.25 ($p < 0.001$).* ***(b)*** *Boxplots showing that - with a 1.29 cut-off value of exceedance - the proportion of COVID-19 cases is greater ($p < .001$) in most polluted Provinces (39 out of 41 located in Northern Italy) than less polluted Provinces, mainly located in Southern Italy (62 out of 66).*

Also the proportion of commuters over the Province population has a significant ($p = 0.01$, not depicted) role in predicting the infection rates according to the univariate binary partitioning tree analysis: after setting a cut-off of 47% people daily moving in Provinces, in the Provinces with a lower number of commuters (n = 51) the median infection case over 1000 Province residents is 0.03 (first – third quartile 0.01 – 0.05, range 0.00 – 0.33), while in the other Provinces the median infection cases over 1000 residents is 0.18 (first – third quartile 0.13 – 0.36, range 0.00 – 4.92).

Notably, when performing a bivariate conditional regression exploratory analysis joining both the pollution and the proportion of commuters as possible predictors of the infection rates, one obtains exactly the same tree depicted in Fig. 3b: the commuters proportion loose its effect, suggesting a strong correlation of air quality to the COVID-19 cases percentages breakout.

The logistic regression depicted in Fig. 3a (semi-logarithmic scales) confirms the exploratory analysis: a binomial distributed generalized linear model, corrected for overdispersion, reveals an increasing slope of 0.25 (s.e. 0.04, $p < 0.001$) of the linear predictor.

In order to observe the effect of the particulate matter in big cities having quite similar urbanization, life style, population and number of commuters, Milan and Rome were chosen, finding out that the presence of the first infected people was similar on February 25th: 8 and 3 infected persons in Milan and Rome, respectively. However, we considered as the first day of spread for both cities when in Rome the infected persons was about 6 on March 1st (Figure 4).

Figure 4. (a) *Trends of spread in Milan and Rome in the first 14 days of infection; the starting date in Milan is February 25th and could correspond to infections acquired by February 8th that become clinically evident or detectable within 17 days (interval between the infection and diagnosis);*

(b) *Distribution of the average daily PM_{10} exceedances in Rome and Milan on February 2020.*

The comparison of the COVID-19 spreads between Milan and Rome showed a higher exponential phase for the former than the latter. However, the trends presented a similar behavior up to 8 days; after the 9 days, the increase of the COVID-19 incidences showed a sudden acceleration of the viral infectivity in Milan. Besides the transmission of SARS-CoV-2 occurring via a close contact with infected people through the direct inhalation of liquid droplets emitted by coughs or exhalations and/or by the contact with surfaces contaminated by the virus, the dynamic of COVID-19 incidence observed in Milan with – if compared to that of Rome – suggested also to consider possible route of transmission by airborne route at longer distance. Considering 17 days as average of lag phase, the first day of the infection in Milan that we monitored in February 25th should be referred at the real contamination in February 8th. According to this, the acceleration of the COVID-19 incidences in Milan started close to February 14th (Figure 4a) in correspondence to the presence of a large peak of PM_{10} exceedances (Figure 4b) that in Rome was not observed because the start of the incidences was closed to February 13th in a period with the absence of PM_{10} exceedances.

The incidence growth rate in Italy was 0,19 per day with a doubling time close to 3.6 days in according with Sanche et al. (2020) who showed a growth rate of infection of COVID-19 in Wuhan, Hubei Province (China) on January 2020 close to 0.21-0.30 per day with a doubling time of 2.3-3.3 [27]. The basic reproductive number (R_0), estimated by the researchers, was 5.7 consistently with a “super-spread event” by an airborne droplet transmission as described by Wellings and Teunis (2004) for the epidemic curves for Sever Acute Respiratory Sindrome (SARS) during the outbreak on February-June 2003 in Hong Kong, Vietnam, Singapore and Canada [28]. In Rome the growth rate before the lockdown measures (March 13th) was 0,27 per day with a doubling time of 2.6 days that were comparable with a “super-spread event” as described for SARS. In Milan the growth rate was significantly higher, close to 0.34 per day with a doubling time of 2.0 days, and suggests a R_0 value higher than 6.0 quite similar to the epidemic transmission by airborne droplets observed for measles (known to be around 12-18) [29] and to the highest R_0 estimates documented for China, ranging from 1.4 to 6.49 with a mean of 3.28 and a median of 2.79 (Wuhan: 2.55-2.68; Hubei Province: 6.49; China: 2.2-6.47) [30].

Discussion

Based on the available literature [2-19], there is enough evidence to consider the airborne route, ant specifically the role of particulate matter, as a possible additional infection "boosting" factor for interpreting the anomalous COVID-19 outbreaks observed in the Northern Italy – known to be one of the European areas characterized by the highest PM concentration [1]. Airborne transmission is certainly more effective in indoor environments, with little ventilation, but it must be considered that the Po Valley, by its atmospheric stability, closely resembles a confined environment and that long-distance virus transport is favored by high concentration of dusts. However, the highly diluted nature of viral bioaerosol in ambient air has been considered a major impediment to viral aerobiological detection –including the investigation of viral interactions with other airborne particles – despite bioaerosol is a well-known factor for the virus transmission via airborne. Recently, Groulx et al. (2018), using an in vitro PM concentrator, suggested that the interaction between airborne viruses and airborne fine particulate matter influence viral stability and infectivity [31]. The stability of aerosol and condensation reactions occur frequently in atmosphere, as organic aerosol change the properties (hygroscopicity, toxicity, optical properties) of other aerosol [32].

Cruz-Sanchez et al. (2013) demonstrated that Respiratory Syncytial virus (RSV) exposed to black carbon, in the form of India ink, prior to co-aerosolization in vitro, and then deposited on a cell substrate, increased viral infectivity [33]. In areas of high vehicle traffic, many different pollutants arising from a variety of sources coexist (car or truck exhausts, emissions from heating installations, etc.) [34], which present a particulate matter emissions containing carbon, ammonium, nitrate and sulfate.

Our findings showed that high frequency of PM_{10} concentration peaks (exceeding 50 $\mu g/m^3$) result in a spread acceleration of COVID-19, suggesting a "boost effect" for the viral infectivity. We found significance differences both in PM_{10} exceedances and COVID-19 spreading between Northern and Southern Italian regions, and we made a focus on Milan and Rome. The infection rate of disease has been higher in Milan, (1.35 million inhabitants, Northern Italy) than in Rome (2.87 million inhabitants, Southern Italy), even if there has not been a substantial difference in urban management and social confinement as well as in ageing index of the two populations. Our research hypothesis is that the acceleration of the growth rate observed in Milan could be attributed to a "boost effect" (a kind of exceptional "super-spread event") on the viral infectivity of COVID-19, corresponding to the peaks of particulate matter.

These first observations suggest that particulate matter could be regarded as an indicator of the severity of COVID-19 infection in terms of diffusion and health outcomes. The other hypothesis is that PM could act as a carrier for droplet nuclei, triggering a boost effect on the spread of the virus (Figure 5). It could be possible to look at the airborne route of transmission, and specifically to particulate matter, as a "highway " for the viral diffusion, in which the droplet nuclei emitted by the exhalations are stabilized in the air through the coalescence of aerosol with the PM at high concentrations in stability conditions. In fact, the fate of a small droplet of a virus, under normal conditions of clean air and atmospheric turbulence, evaporates and /or disperses quickly in atmosphere. On the contrary in conditions of atmospheric stability and high concentrations of PM, viruses have a high probability of creating clusters with the particles and, by reducing their diffusion coefficient, enhancing their residence time and amount in atmosphere and promoting contagion.

Figure 5. Scheme of possible enhancement of viral transmission through stabilized human exhalation on PM

Nevertheless, coalescence phenomena require optimal conditions of temperature and humidity to stabilize the aerosols in airborne, around 0-5 °C and 90-100% relative humidity. Recently, Ficetola et al. (2020) showed that the spread of COVID-19 peaked in temperate regions of the Northern Hemisphere with mean temperature of 5°C and humidity of 0.6-1.0 kPa, while decreased in warmer and colder regions [35]. These climatic variables could have a role, together with the presence of high concentrations of particulate matter in the air, in favoring the stabilization of the aerosol in airborne, in line with the model proposed in Fig. 5. Further experimental studies could confirm the possibility that particulate matter may act as a “carrier” for the viral droplet nuclei, impressing a boost effect for the spreading of the viral infection, as it has been shown for other viruses. Recent studies [36] and recommendation [37] about increased social distancing indicate that a recommended interpersonal distance of significantly more than one meter and usage of personal masks [38] are advisable prevention measures.

It must also be pointed out that long term exposures to high levels of particulate matter itself chronically impair human health and possibly influence clinical course of infections acquired by already debilitated individuals, especially in most vulnerable age groups. Indeed, according to 2005 WHO guidelines, annual average concentrations of PM10 should not exceed 20 μg/m3 (compared to current EU legal limits of 40 μg/m3) and PM2.5 should not exceed 10μg/m3 (compared to current EU legal limits of 25 μg/m3) [39].

Moreover, the exposure-effect relationship between fine particulate matter and health damages is not of linear type, so that it is not really possible to set a threshold below which is foreseeable a complete absence of damage to human health [39].

Conclusion

The available literature on the role of airborne transmission, and this first preliminary observation of consistent association between the number of COVID-19 infected people and PM_{10} peaks, points out the opportunity of a further computational and experimental research on this route of transmission, and the potential role of PM on viral spread and infectivity (in addition to the possibility of regarding PM levels as an "indicator" of the expected impact of COVID-19 in most polluted areas). There is the rational for carrying out experimental studies specifically aimed at confirming or excluding the presence of the SARS-CoV-2 and its potential virulence on particulate matter of Italian cities as well as at European and international level. Urgent actions must be adopted to counteract climate changes and the alteration of ecosystems that might trigger new and unexpected threats to human health such as that of COVID-19, which we are so dramatically experiencing worldwide.

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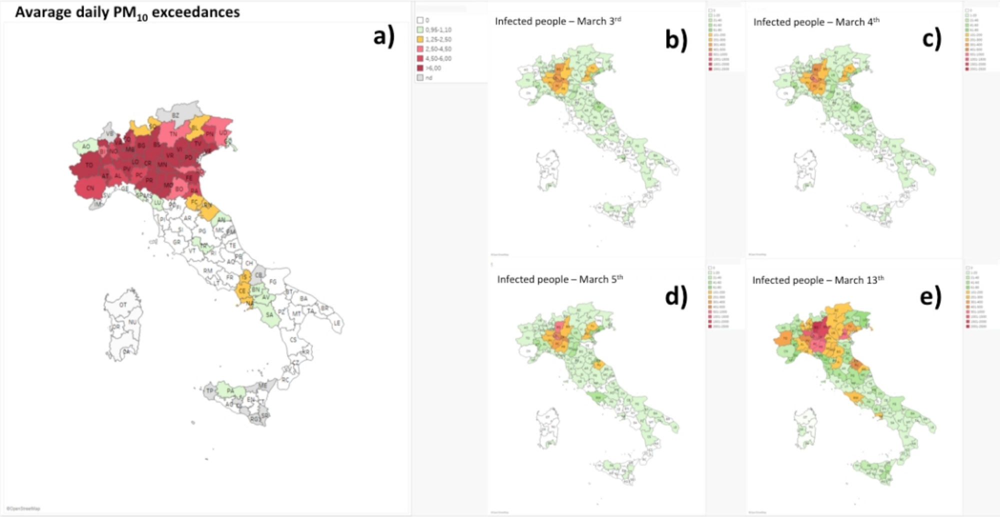
Avarage daily PM10 exceedances
a)
0
0,95-1,10
1,25-2,50
2,50-4,50
4,50-6,00
>6,00
nd
Infected people – March 3rd
b)
Infected people – March 4th
c)
Infected people – March 5th
d)
Infected people – March 13th
e)

FIG1

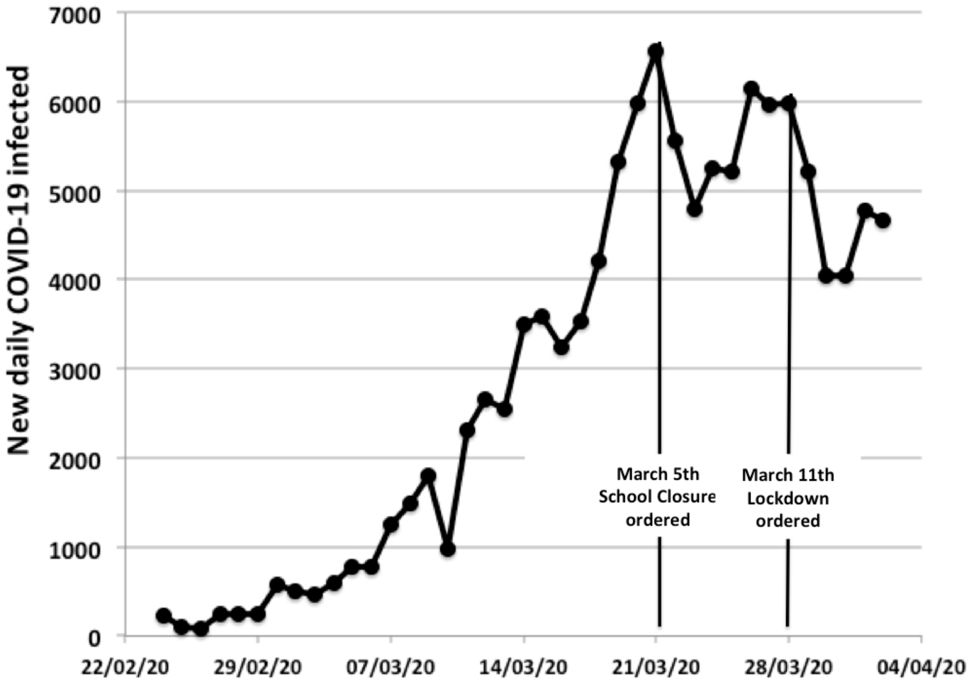
New daily COVID-19 infected
7000
6000
5000
4000
3000
2000
1000
0
22/02/20
29/02/20
07/03/20
14/03/20
21/03/20
28/03/20
04/04/20
March 5th
School Closure
ordered
March 11th
Lockdown
ordered

FIG2

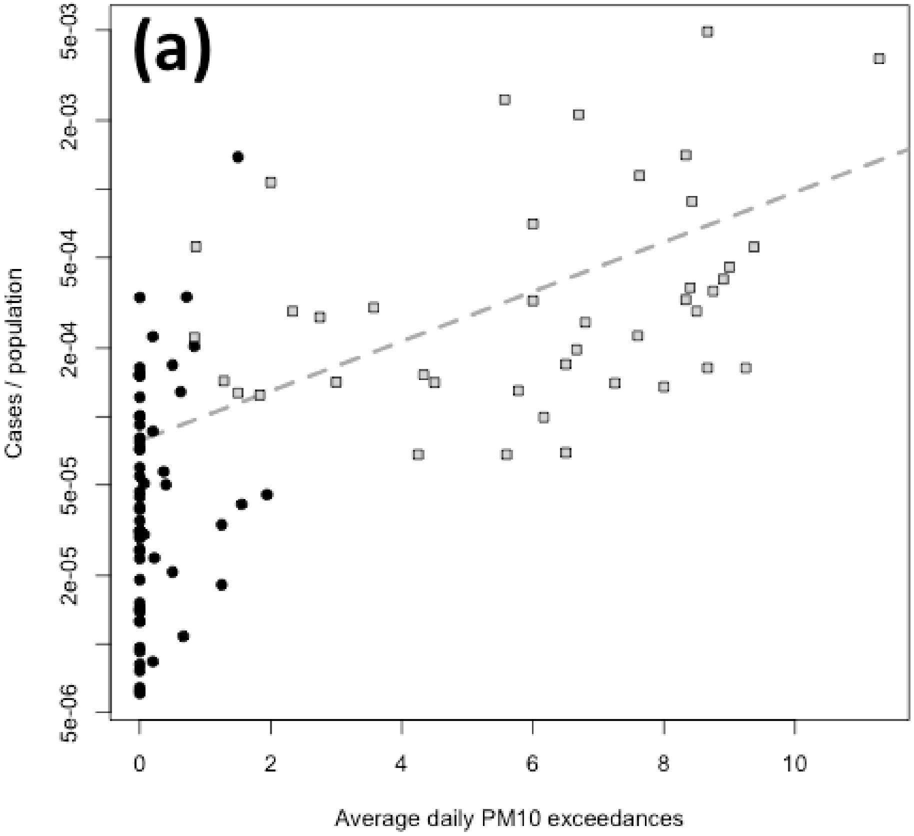

FIG3a

187x165mm (72 x 72 DPI)

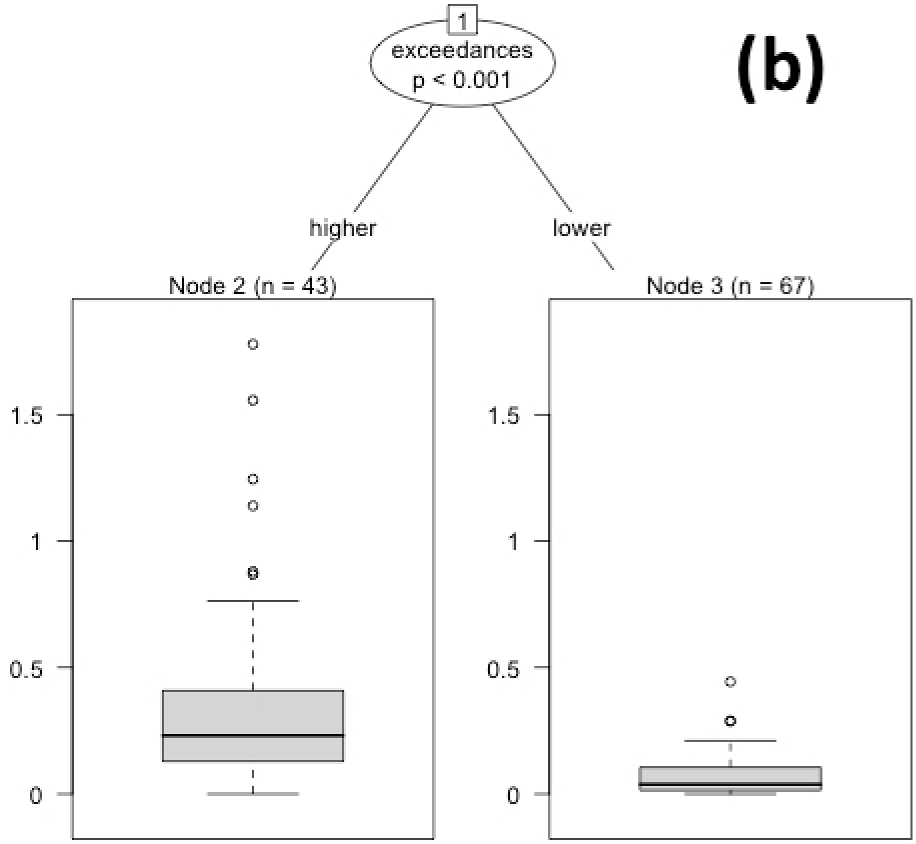

FIG3b

164x158mm (72 x 72 DPI)

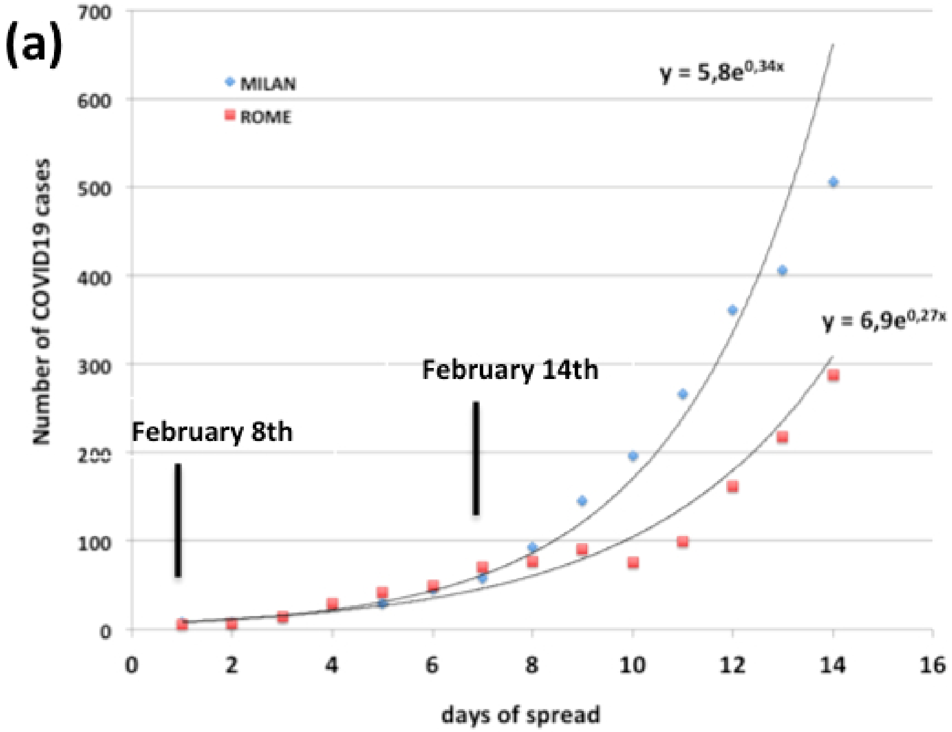

FIG4a

192x152mm (72 x 72 DPI)

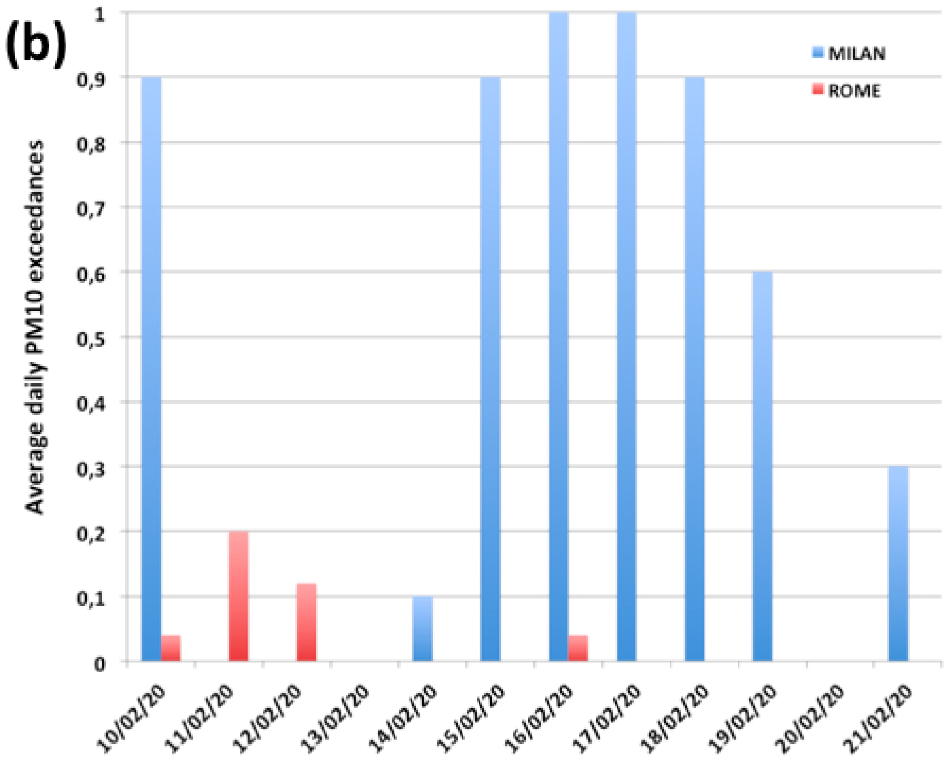

FIG4b

186x152mm (72 x 72 DPI)

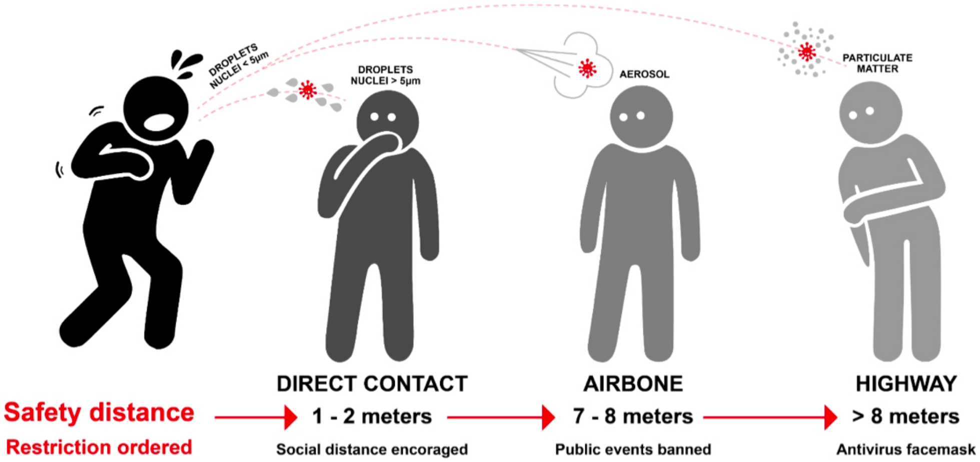
DROPLETS
NUCLEI < 5µm
DROPLETS
NUCLEI > 5µm
AEROSOL
PARTICULATE
MATTER
DIRECT CONTACT
AIRBONE
HIGHWAY
Safety distance
Restriction ordered
1 - 2 meters
7 - 8 meters
> 8 meters
Social distance encoraged
Public events banned
Antivirus facemask

FIG5

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The Potential role of Particulate Matter in the Spreading of COVID-19 in Northern Italy: First Observational Study based on Initial Epidemic Diffusion

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The Potential role of Particulate Matter in the Spreading of COVID-19 in Northern Italy: First Observational Study based on Initial Epidemic Diffusion

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Abstract

Background: Exposures to $PM_{2.5}$ and PM_{10} such as those usually recorded in the Po Valley (Northern Italy) are notoriously associated with a number of adverse health effects or premature deaths. At the same time, a number of studies have shown that airborne transmission route could spread many viruses even further the close contact with infected people. An epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spread of the recent severe acute respiratory syndrome COVID-19 in Italy, which was fast and dramatic only in Lombardy and Po Valley. On March 16th 2020, we presented a Position Paper proposing a research hypothesis concerning the association between higher mortality rates due to COVID-19 observed in Northern Italy and the peaks of particulate matter concentrations, frequently exceeding the legal limit of 50 $\mu g/m^3$as PM_{10} daily average. **Methods**: To assess environmental factors related to the spread of the COVID-19 in Italy from February 24th to March 13th (the date of the Italian lockdown), official daily data relevant to ambient PM_{10} levels were collected from all Italian Provinces between February 9th and February29th, taking into account the average time (estimated in 17 days) elapsed between the initial infection and the recorded COVID-19 positivity. In addition to the number of exceedances of PM_{10} daily limit value, we considered also population data and daily travelling information per each Province. **Results**: PM_{10} daily limit value exceedances appear to be a significant predictor ($p < .001$) of infection in univariate analyses. Less polluted Provinces had a median of 0.03 infections over 1000 residents, while most polluted Provinces had a median of 0.26 cases over 1000 residents. Thirty-nine out of 41 Northern Italian Provinces resulted in the category with highest PM_{10} levels, while 62 out of 66 Southern Provinces presented low PM_{10} concentrations ($p<0.001$). In Milan, the average growth rate before the lockdown was significantly higher than in Rome (0.34 vs. 0.27 per day, with a doubling time of 2.0 days vs. 2.6, respectively), thus suggesting a basic reproductive number $R_0>6.0$, comparable with the highest values estimated for China. **Conclusion:** A significant association has been found between the geographical distribution of daily PM_{10} exceedances and the initial spread of COVID-19 in the110 Italian Provinces.

Keywords: COVID-19; Air Pollution; Particulate Matter; Italy.

Strengths and limitations

- In the perspective of a mere observational study design, we have analyzed daily data relevant to ambient PM_{10} levels, urban conditions and COVID-19 incidence from all Italian Provinces, in order to reliably determine potential association between PM pollution level and the initial spread of COVID-19;
- We used PM_{10} daily concentration levels collected by the official air quality monitoring stations for each Italian province, but no information about the presence of the virus on PM and its vitality or infective potential was available;
- All the Provinces have been assigned to two geographical areas (Northern or Southern Italy);
- The number of PM_{10} daily limit value exceedances (50 $\mu g/m^3$) detected in the different Provinces and the number of PM_{10} monitoring stations for each Province were considered as well as the latitude and population data (number of inhabitants and density);
- The number of PM exceedances were computed between February 9th and February 29th in order to take into account the *lag period* of14-days, which is the average time elapsed between the contagion and the first weeks of the Italian epidemic (February 24th-March 13th);

Introduction

Severe acute respiratory syndrome known as COVID-19 disease (due to the new SARS-CoV-2 virus), is recognized to spread via respiratory droplets and close contact [1]. However, this unique transmission model does not seem to explain properly the initial different spreading of the virus observed in Italy from February 24th 2020 to March 13th 2020. The huge virulence of COVID19 in the Po Valley is not comparable to the milder contagiousness observed in the Central-Southern regions. Demographic factors related to the ageing of the population and the possibility of infection without clinical symptoms for a quite long time – associated with the high rate of asymptomatic people that characterizes COVID-19, estimated at 50-75% of infections – may only partially explain the fast spreading of the virus in Lombardy and Northern Italy [2,3]. Cai et al (2020) reported different incubation periods in patients infected in Wuhan [4], but an epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spreading of the recent severe acute respiratory syndrome COVID-19 in Italy, which was fast and dramatic only in Lombardy and Po Valley. At the same time, a number of studies have shown that airborne transmission route could spread viruses even further the close contacts with infected people [5-19]. Paules et al. (2020) highlighted that – besides close distance contacts – airborne transmission of SARS-CoV can also occur [5]. It has also been reported that for some pathogens the airborne transport can reach long distances [6-8]. Reche et al. (2018) described the aerosolization of soil-dust and organic aggregates in sea spray that facilitates the long-range transport of bacteria, and likely of viruses, free in the atmosphere; in particular, virus deposition rates were positively correlated with organic aerosol <0.7 µm, implying that viruses could have longer persistence time in the atmosphere and, consequently, can be dispersed further [8]. Moreover Qin et al. (2020) analyzed the microbiome of the airborne particulate matter ($PM_{2.5}$ and PM_{10}) in Beijing over a period of 6 months in 2012 and 2013, putting in evidence a variability of the composition that depended on the months analyzed [9]. Temporal distribution of the relative abundance of microbiome on particulate matter (PM) showed the highest presence of viruses in January and February, just in coincidence with most severe PM pollution. Chen. et al. (2017) demonstrated the relationship between short-term exposure to $PM_{2.5}$ concentration and measles incidence in 21 cities in China [10]. Their meta-analyses showed that the nationwide measles incidence was significantly associated with an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ levels.

Other recent studies have also reported associations between PM and infectious diseases (e.g., influenza, hemorrhagic fever with renal syndrome) as inhalation could bring PM deep into the lung, and viruses attached to particles may directly invade the lower part of respiratory tract, thus enhancing the induction of infections, as demonstrated by Sedlmaier et al. (2009) [11]. Zhao et al. (2018) showed that the majority of positive cases of highly pathogenic avian influenza (HPAI) H5N2 in Iowa (USA) in 2015 might have been infected by airborne viruses carried by fine PM from infected farms, both within the same State and from neighboring States [12]. Ma et al. (2017) observed a positive correlation of the measles incidence with PM_{10} in western China during the period 1986-2005; the condensation and stabilization of the bioaerosol, generating aggregates with atmospheric particles from primary (i.e. dust) and secondary particulate, have been indicated as mechanisms able to transport airborne bacteria and viruses to distant regions, even by the inter-continent-transported dust [13]. Ferrari et al. (2008) showed measles outbreaks occurring in dry seasons and disappearing at the onset of rainy seasons in Niger [14], while Brown et al (1935) found that the most severe measles epidemic in the United States occurred in Kansas in 1935 during the Dust Bowl period [15].

Coming to recent specific studies, laboratory experiments of Van Doremalen et al. (2020) 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 [16]. On-field measurement carried out by Liu et al. (2020) showed evidence of coronavirus RNA in indoor air samples from Wuhan Hospitals and even in ambient air in close proximity, during COVID-19 outbreak, highlighting the airborne route as a possible important pathway for contamination that should undergo further confirmations [17]. Santarpia et. al. reported the presence of airborne SARS-Cov-2 in indoor air samples at the Nebraska University Hospital [18], while - at the opposite - some negative evidence of virus presence in air reported by Ong et al. (2020) come from explicitly poor sampling scheme [19]. Recently, we have published the first world evidence of the presence of COVID-19 on outdoor PM in samples collected between February 23th and March 9th in the province of Bergamo (Lombardy, Italy), which experienced the highest diffusion and mortality rates in Italy [20]. A research carried out by the Harvard School of Public Health seems to confirm an association between increases in particulate matter concentration and mortality rates due to COVID-19 [21]. On March 16th 2020, we have released an official Position Paper highlighting that there are enough evidence to consider airborne route as a possible additional factor for interpreting the anomalous COVID-19 outbreaks observed in Northern Italy, known to be one of the European areas characterized by highest PM concentration [22,23].

This article presents the data that led to the publication of our Position Paper and triggered high interest of the research community at working on the hypothesis of a further transmission possibility via airborne dust [24-26] taking into account that the potential survival of the virus could be influenced by climatic parameters such as humidity and temperature as well as by fine dust concentrations [27]. Other papers support the possible merging of contaminated aerosol with fine particulate in the atmosphere [28-30]. The concentration of fine particles has been also repeatedly recognized by other authors as an important co-factor in the mortality level in highly contaminated areas [31,32]. This study is aimed at searching for a possible association between the initial COVID-19 spreading in Italy from the end of February to the first weeks of March 2020 (February 24th-March 13th) and the frequency of high daily average concentrations of PM recorded before the lockdown, taking into account the lag period of the infection (February 9th-29th). The research hypotheses that we addressed is the possibility that air pollution could produce a "boost effect" of COVID 19 epidemic, thus resulting a kind of exceptional "super-spread event".

Methods

Data about daily PM10 exceedances and COVID-19 outbreak

In the frame of an observational design of the study, we have analyzed daily data relevant to ambient PM_{10} levels, urban conditions and COVID-19 incidence from all Italian Provinces, in order to reliably determine the association between PM pollution level and the initial spread of COVID-19. PM_{10} daily concentration levels were collected by the official air quality monitoring stations of the Regional Environmental Protection Agencies (ARPA), publicly available on their websites. The number of PM_{10} daily limit value exceedances (50 μg/m^3) detected in the different Provinces, divided by the total number of PM_{10}monitoring stations for each selected Province was computed.

Population data related to each Italian Province were collected from the National Institute for Statistics (ISTAT) for all the 110 Italian Provinces [33] paying specific attention to the absolute number of inhabitants and their density (n° inhabitants/km^{2}per each Province) as well as to the number of commuters and its proportion with respect to the Province population. We have computed the number of COVID-19 infected people for each Province and the infection rate based on the number of inhabitants from February 24th to March 13th (the date when the lockdown was decided), as reported by the official Government website, updated with daily frequency [34]. The number of PM exceedances were computed between February 9th and February 29th, as we had to take into account the *lag period* of 14 days, which is the average time elapsed between the contagion and the first weeks of the Italian epidemic (February 24th-March 13th). Further covariates related to the different Provinces have also been considered: the number of the air quality monitoring stations present in each Province, and the longitude and the latitude of the Province city center. All the Provinces have been assigned to two geographical areas (Northern or Southern Italy). The dataset is publicly available on a web page [35] along with statistical analyses reproducible code in R language [36].

Statistical analyses

To investigate how PM exceedances might relate to infection diffusion, we started performing an exploratory analysis on PM_{10} exceedances considering the recursive partitioning tree approach, as implemented into the party package [37]. Such implementation connects the exploratory techniques to the classical statistical test approach, with the advantage to exploit a motivated stopping criterion when pruning the tree – i.e. the p-value of a significance test on independence of any covariate and response [38]. Within recursive partitioning analyses, the response variable was represented by the proportion of COVID-19 cases over Province population; the log-transform of such proportion responses were reported into Figures, to improve graphical readability. Cut-offs identified by the recursive partitioning tree analysis were subsequently used into the binomial generalized linear models, both univariate and multivariable (i.e. logistic regression). The response of the binomial generalized linear models is expressed as a two-dimensional vector [39] obtained by binding the number of COVID-19 cases and the rest of the Province population. In presence of over-dispersion, quasi-binomial distributions were addressed. When suitable, association in contingency table has been expressed also in terms of odds ratios, and the Fisher exact test was issued to assess statistical significance. Exploratory analyses on $PM_{2.5}$ exceedances rates were held by recursive partitioning tree approach too. Correlation between $PM_{2.5}$ and PM_{10} exceedances rates per Province have been addressed by a linear model. Pearson coefficient was used to evaluate correlation and diagnostics plots were issued to assess model adequacy.

Sites description for the statistical analyses about Milan and Rome

We have performed statistical inferences analyses on Milan and Rome data, in order to observe the potential association between PM levels and COVID-19 spreading in big cities located in different geographical areas and with remarkable differences in PM_{10} exceedances, presenting at the same time quite similar urbanization, life style, population, ageing index, and number of commuters. The municipality of Rome is far more extensive, with 1,287 square kilometers of surface compared to just 182 in Milan. Talking about population, Rome has 2.87 million inhabitants compared to 1.35 million in Milan, but it is much less densely populated: 2,232 inhabitants per square kilometer and 7,439, while respectively (due to the huge extension of the city of Rome). However, an additional 1 million inhabitants live in Rome neighborhoods with an average density between 6,720 and 9,231 inhabitants/Km^2. The extension of Milan and Rome underground is currently about 98 and 54 km, respectively. Looking at the numbers of annual visitors, Rome has about 29.0 million tourists per year, compared to 12.1 million people visiting Milan. The number of daily commuters (people moving to Rome due to working reasons or similar) are higher in Rome (2.04 million trips) compared to Milan (1.66 million trips).

Results

COVID-19 diffusion in Italy and Particulate Matter exceedances

The spatial distribution of ambient PM_{10} exceedances between Italian cities was geographically heterogeneous and it is presented in Fig. 1a. The highest number of exceedances were generally located in Northern Italian Regions suffering from a rapid diffusion of COVID-19 epidemic, while zones with a lower contagion were sited in Central and Southern Regions. The maps in Fig. 1 illustrate the mean of PM_{10} exceedances on the number of PM_{10} stations in all Italian Provinces in the period February 9^{th}-29^{th} 2020 (Fig. 1a), compared with the total COVID-19 infection per Province observed in the period March 4^{th}-13^{th} (Fig. 1b-e). Overall, there were 17,660 infected people on 60,4 million inhabitants in Italy during the time of the study. The highest incidence rates of COVID-19 were recorded in cities located in Northern Italy, and in particularly in Lombardy Region, including Milan. The lowest incidence of COVID-19 was observed in Southern Italy, as in Lazio Region (which includes Rome).

Figure 1. (a) *Average daily PM10 exceedances vs. number of monitoring stations in different Italian Provinces from February 9th to 29th, 2020;* ***(b-e)*** *Spreading of COVID-19 infected people (officially confirmed cases) during the period March 3rd-13th, 2020*

SARS-Cov-2 is a highly contagious virus transmitted by airborne direct contact, showing super-spread event characteristics that has pushed governments to adopt extraordinary measures (namely total lockdown) to contain the outbreak [40]. In Figure 2(a), two main discontinuity trends are evident and can be attributed to the Italian lockdown. Continuing the observation beyond the date of the lockdown (March 11th-13th), it is possible – by analyzing the trend of new daily COVID-19 infections – to observe a first reduction of the spreading rate of the contagion around March 22nd (reflecting the school closure ordered on March 5th) and a second one around March 28th (reflecting the lockdown ordered between March 11th and 13th).

Figure 2(a) *New daily COVID-19 infections in Italy from February 24th to April 4th, 2020;* ***(b)*** *Trend of COVID-19 spreading in Italy during the first 15 days of the epidemic*

These observations confirm that the *lag period* for SARS-COV-2 infection can be estimated in 14-17 days, and thus our study analyzed the Italian outbreak before March 11th, when the incidence growth rate showed a typical exponential trend of the spread (Figure 2b).

In the univariate analysis, the PM_{10} daily limit value exceedances appear to be a significant predictor ($p < .001$) of infection with a 1.29 cut-off value (Fig. 3). The cut-off divides the Provinces into two classes, characterized by higher ($n = 43$) and lower ($n = 67$) PM_{10} concentrations, respectively: the less polluted Provinces had a median 0.03 infection cases over 1000 inhabitants (first – third quartile 0.01 – 0.09; range 0.00 – 0.56), while the most polluted Provinces had a median 0.26 infection cases over 1000 inhabitants (first – third quartile 0.14 – 0.51, range 0.00 – 4.92). The boxplots in Fig. 3b are log-transformed to enhance figure readability.

Dividing the Italian peninsula into two areas, the Northern and Southern part along the Tuscan-Emilian Apennines watershed, the exceedances results as follows: 39 out of 41 Northern Provinces falls in the higher

PM_{10} category, while for Southern Provinces the ratio is reverse: 62 out of 66 Provinces present lower PM_{10} (odds ratio .00, Fisher exact test $p < .001$).

Figure 3. *Relationship between the PM_{10} daily limit value exceedances and the COVID-19 cases ratios over Italian Provinces population.* ***(a)*** *Scatterplot on semi-logarithmic scale relating the proportion of COVID-19 cases of Northern (gray squares) and Southern (black bullets) Italian Provinces population versus the average of PM_{10} daily limit value exceedances. The dashed binomial (logistic) regression is characterized by an increasing slope of 0.25 ($p < 0.001$).* ***(b)*** *Boxplots showing that - with a 1.29 cut-off value of exceedance - the proportion of COVID-19 cases is greater ($p < .001$) in most polluted Provinces (39 out of 41located in Northern Italy) than less polluted Provinces, mainly located in Southern Italy (62 out of 66);* ***(c)*** *Boxplots suggest that considering also PM2.5 exceedances rates (despite the 39% presence of missing data) the proportion of COVID-19 in Po Valley might furtherly be stratified ($p < 0.001$) in agreement with previous Figures 1 (b-e).*

Also the proportion of commuters over the Province population (people coming to the examined city for job reasons on daily basis) seems to have a significant role ($p = 0.01$, not depicted) in predicting the infection rates according to the univariate binary partitioning tree analysis. We set a commuters cut-off at 47% describing the number of people travelling in the Provinces. In the 51 Provinces with a lower number of commuters (<47%), the median infection cases over 1000 inhabitants of the Province was 0.03 (first – third quartile 0.01 – 0.05; range 0.00 – 0.33), while in the other Provinces (commuters >47%) the median infection cases over 1000 inhabitants was 0.18 (first – third quartile 0.13 – 0.36; range 0.00 – 4.92).

Notably, when performing a bivariate conditional regression exploratory analysis combining both the pollution and the proportion of commuters as possible predictors of the infection rates, we obtained exactly the same tree depicted in Fig. 3b: the commuters proportion looses its effect, thus suggesting a strong association between air quality and COVID-19 infections.

The logistic regression depicted in Fig. 3 (semi-logarithmic scales) confirms the exploratory analysis: a binomial distributed generalized linear model, corrected for overdispersion, reveals an increasing slope of 0.25 (s.e. 0.04; $p < 0.001$) of the linear predictor. PM2.5 exceedances have been also explored: the possible association between PM2.5 and PM10 exceedances observed in each Province has been assessed by a linear model (intercept 1.06, slope 1.38), with satisfactory accuracy ($p < 0.001$; mild lack of normality into residuals according diagnostic plots, residual standard error: 1.82). PM2.5 exceedance rates appear to be very highly correlated to PM10 exceedance rates, showing a Pearson coefficient of 0.94 (IC95%: 0.90 – 0.96). When repeating exploratory analyses on PM2.5 exceedance rates by recursive partitioning tree analysis, a cutoff of 11 was identified, and an improved recursive partitioning tree was disclosed (Figure 3C). Despite the limitation of 39% missing values concerning PM2.5 data (no data available for 43 Provinces out of 110), it appears that, consistently with study outcome, the highest number of PM2.5 exceedances are mainly located in the Po Valley.

Understanding and Modeling the Super-spreading Events in Milan and Rome

In order to observe the effect of the particulate matter in big cities having quite similar urbanization, life style, population and number of commuters, Milan and Rome were chosen, finding out that the first infected people were identified on February 25th both in Milan and Rome (8 and 3 patients, respectively). However, we considered March 1st as the first day of COVID-19 outbreak for both cities, when in Rome there were at least 6 confirmed cases (Figure 4).

Figure 4.(a) *Trends of COVID-19 spread in Milan and Rome in the first 14 days of the infection; the starting date in Milan is February 25th and could correspond to infections acquired by February 8th that become clinically evident or detectable within the subsequent 17 days (interval between the infection and diagnosis);* ***(b)****Distribution of the average daily* PM_{10} *exceedances in Rome and Milan on February 2020.*

The comparison of the COVID-19 spreads between Milan and Rome showed a higher exponential phase for the former city compared to the latter one. However, the trends presented a similar behavior up to 8 days; after 9 days, the increase in COVID-19 incidence showed a sudden acceleration of the viral infectivity in Milan. Besides the transmission of SARS-CoV-2 occurring via close contacts with infected people through the direct inhalation of liquid droplets emitted by coughs or exhalations and/or by the contact with surfaces contaminated by the virus, the dynamic of COVID-19 diffusion observed in Milan – if compared to that observed in Rome – suggest to consider also other possible route of transmission including airborne route (with virus covering longer distances). Considering 14-17 days as the average value of the lag phase, the first day of the infection considered for Milan (February 25th) should be referred to contagion occurred by February 8th. According to this assumption, the acceleration of COVID-19 diffusion in Milan started on February 14th (Figure 4a), in correspondence to the presence of a relevant peak of PM_{10} exceedances (Figure 4b), that was not observed in Rome because the initial contagion started likely on February 13th in the absence of PM_{10} exceedances.

The incidence growth rate of COVID-19 infections in Italy was 0,19 per day with a doubling time close to 3.6 days, as showed by Sanche et al. (2020), who described in Wuhan (Hubei Province, China) a growth rate close to 0.21-0.30 per day with a doubling time of 2.3-3.3 on January 2020 [41]. The Italian basic reproductive number (R_0), estimated by the researchers was 5.7, [42] consistently with “super-spread event” characteristics possibly related to airborne droplets transmission, as described by Wellinga and Teunis (2004) for the epidemic curves for Sever Acute Respiratory Sindrome (SARS) during the outbreak occurred on February-June 2003 in Hong Kong, Vietnam, Singapore and Canada [43]. In Rome, the growth rate before the lockdown measures (March 13th) was 0,27 per day with a doubling time of 2.6 day, comparable with the “super-spread event” model described for SARS. In Milan, the growth rate was significantly higher, close to 0.34 per day with a doubling time of 2.0 days, suggesting a R_0 value higher than 6.0, quite similar to the epidemic transmission via airborne droplets observed for measles (known to be reach a value of 12-18) [44] and to the highest R_0 estimates documented for China, ranging from 1.4 to 6.49 with a mean of 3.28 and a median of 2.79 (Wuhan: 2.55-2.68; Hubei Province: 6.49; China: 2.2-6.47) [45].

Discussion

Based on the available literature, and following our recent publication confirming the presence of SARS-COV-2 RNA on PM10 collected in Bergamo area (the epicenter of the Italian epidemic),[20] there is enough evidence to consider the airborne route, and specifically the role of particulate matter, as a possible additional infection “boosting” factor for interpreting the anomalous COVID-19 outbreaks observed in Northern Italy – known to be one of the European areas characterized by the highest PM concentration [1]. Airborne transmission is certainly more effective in indoor environments, with little ventilation, but it must be considered that the Po Valley – due to its atmospheric stability – closely resembles a confined environment, and that long-distance virus transport is favored by high concentration of dusts.

Despite bioaerosol is a well-known factor for the virus transmission via airborne, the highly diluted nature of viral bioaerosol in ambient air has been considered a major impediment to viral aerobiological detection, including the investigation of viral interactions with other airborne particles. Recently, Groulx et al. (2018), using an in vitro PM concentrator, suggested that the interaction between airborne viruses and airborne fine particulate matter is able to influence viral stability and infectious potential [46]. The stability of aerosol and condensation reactions occur frequently in atmosphere, as organic aerosol change the properties (hygroscopicity, toxicity, optical properties) of other aerosol [47].

Cruz-Sanchez et al. (2013) demonstrated that Respiratory Syncytial virus (RSV) exposed to black carbon, in the form of India ink, prior to co-aerosolization in vitro, and then deposited on a cell substrate, increased viral infectivity [48]. In areas of high vehicle traffic, many different pollutants arising from a variety of sources coexist (car or truck exhausts, emissions from heating installations etc.) [49], which present a particulate matter emissions containing carbon, ammonium, nitrate and sulfate.

Our findings showed that high frequency of PM_{10} concentration peaks (exceeding 50 $\mu g/m^3$) result in a spread acceleration of COVID-19, suggesting a possible "boost effect" for the viral infectivity. We found significance differences both in PM_{10} exceedances and COVID-19 spreading between Northern and Southern Italian regions, and we made a focus on Milan and Rome. The infection rate of disease has been higher in Milan, (1.35 million inhabitants, Northern Italy) than in Rome (2.87 million inhabitants, Southern Italy), even if there has not been a substantial difference in urban management and social confinement as well as in ageing index of the two populations. Our findings suggest that the acceleration of the growth rate observed in Milan could be attributed to a "boost effect" (a kind of exceptional "super-spread event") on the viral infectivity of COVID-19, corresponding to the peaks of particulate matter. According to this hypothesis, PM could then act as a potential "carrier" for droplet nuclei, triggering a boost effect on the spread of the virus (Figure 5). It could be possible to look at the airborne route of transmission, and specifically to particulate matter, as a "highway " for the viral diffusion, in which the droplet nuclei emitted by the exhalations are stabilized in the air through the coalescence of aerosol with the PM at high concentrations in stability conditions. In fact, the fate of a small droplet of a virus, under normal conditions of clean air and atmospheric turbulence, evaporates and /or disperses quickly in atmosphere. On the contrary in conditions of atmospheric stability and high concentrations of PM, viruses have a high probability of creating clusters with the particles and, by reducing their diffusion coefficient, enhancing their residence time and amount in atmosphere and promoting contagion. These first observations suggest that particulate matter could be regarded as a contributing factor to the severity of COVID-19 infection in terms of airborne diffusion and health outcomes, in accordance with the findings of Isaifan (2020) [50].

Figure 5. Scheme of possible enhancement of viral transmission through stabilized human exhalation on PM

Nevertheless, coalescence phenomena require optimal conditions of temperature and humidity to stabilize the aerosols in the air, namely around 0-5 °C and 90-100% relative humidity. Recently, Ficetola et al. (2020) showed that the spread of COVID-19 peaked in temperate regions of the Northern Hemisphere with mean temperature of 5°C and humidity of 0.6-1.0 kPa, while decreased in warmer and colder regions [51]. These climatic variables could have played a role, along with the presence of high concentrations of particulate matter in the air, in favoring the stabilization of the aerosol in airborne, in line with the model proposed in Figure 5.

Further experimental studies could confirm the possibility that particulate matter may act as a "carrier" for the viral droplet nuclei, impressing a boost effect for the spreading of the viral infection, as it has been shown for other viruses. Recent studies [52] and recommendations [53] about increased social distancing indicate that a recommended interpersonal distance of more than one meter and use of face masks [54] are useful prevention measures. It must also be pointed out that long term exposures to high levels of particulate matter itself chronically impair human health and possibly influence clinical course of infections acquired by already debilitated individuals, especially in most vulnerable age groups. Indeed, according to 2005 WHO guidelines, annual average concentrations of PM10 should not exceed 20 μg/m3 (compared to current EU legal limits of 40 μg/m3) and PM2.5 should not exceed 10μg/m3 (compared to current EU legal limits of 25 μg/m3). Moreover, the exposure-effect relationship between fine particulate matter and health damages is not of linear type, so that it is not really possible to set a threshold below which is foreseeable a complete absence of damage to human health [55].

Conclusion

The available literature on the role of airborne transmission, and this first preliminary observation of consistent association between the number of COVID-19 infected people andPM_{10}peaks, points out the opportunity of a further computational and experimental research on this route of transmission, and the potential role of PM on viral spread and infectivity(in addition to the possibility of regarding PM levels as an "indicator" of the expected impact of COVID-19 in most polluted areas). There is the rational for carrying out experimental studies specifically aimed at confirming or excluding the presence of the SARS-CoV-2 and its potential virulence on particulate matter of Italian cities as well as at European and international level.

Urgent actions must be adopted to counteract climate changes and the alteration of ecosystems that might trigger new and unexpected threats to human health such as that of COVID-19, which we are so dramatically experiencing worldwide.

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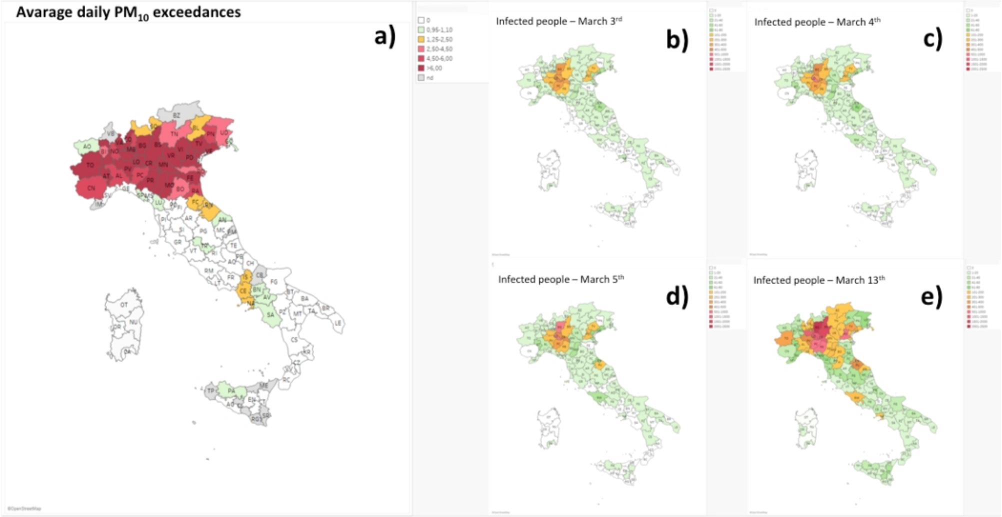
Avarage daily PM10 exceedances
a)
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1,25-2,50
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>6,00
nd
Infected people – March 3rd
b)
Infected people – March 4th
c)
Infected people – March 5th
d)
Infected people – March 13th
e)

FIG 1

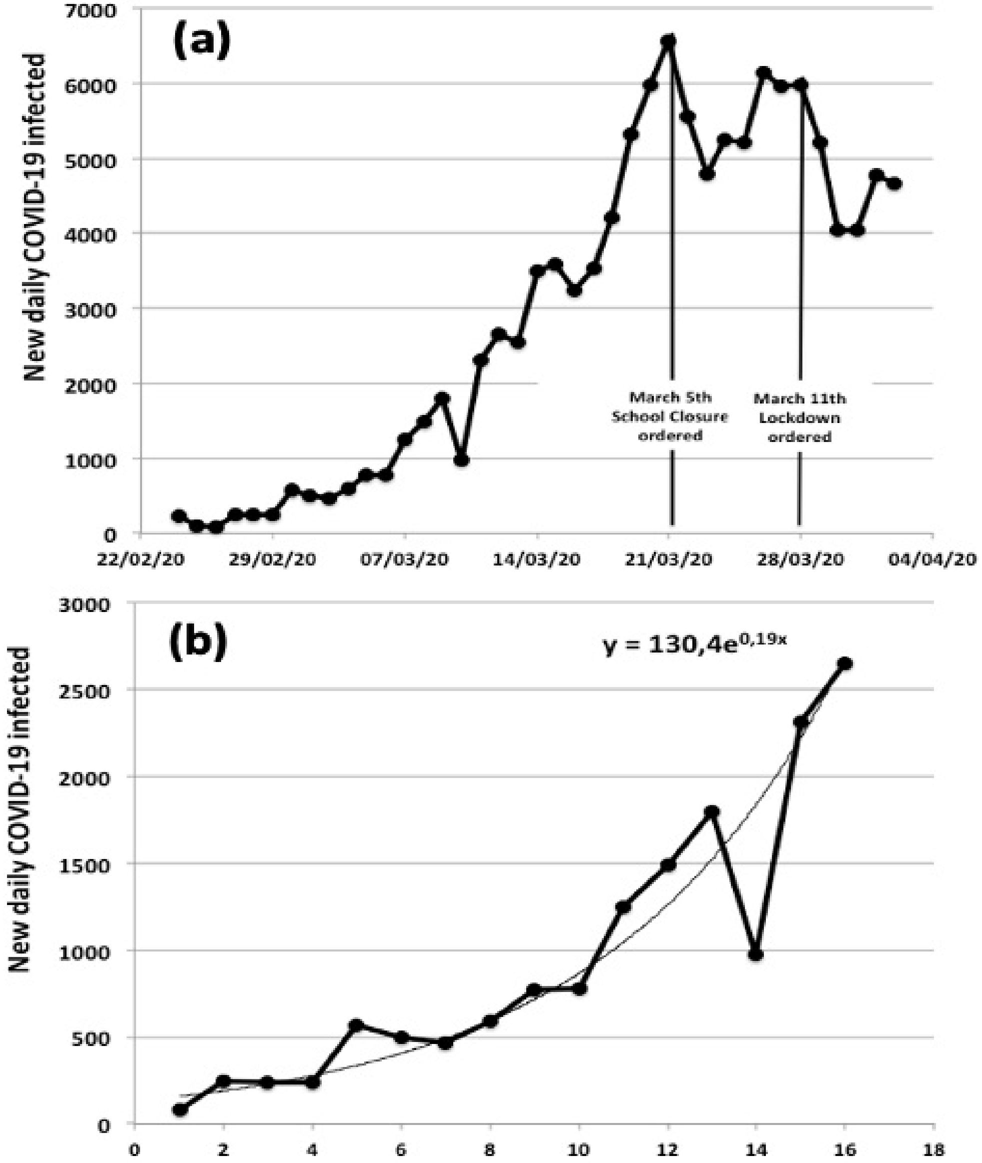

Fig. 2

137x162mm (96 x 96 DPI)

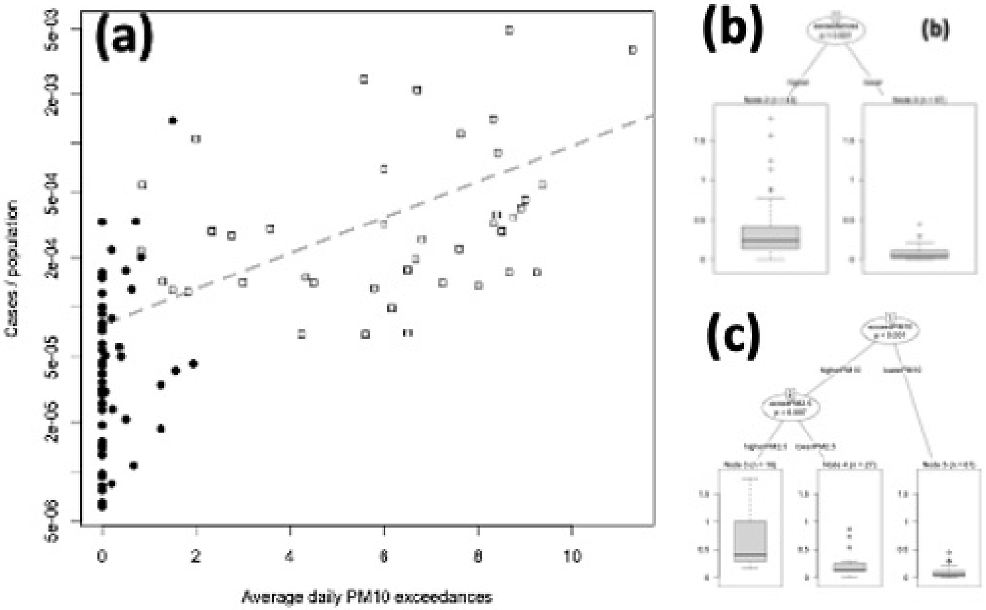

Fig. 3

134x94mm (96 x 96 DPI)

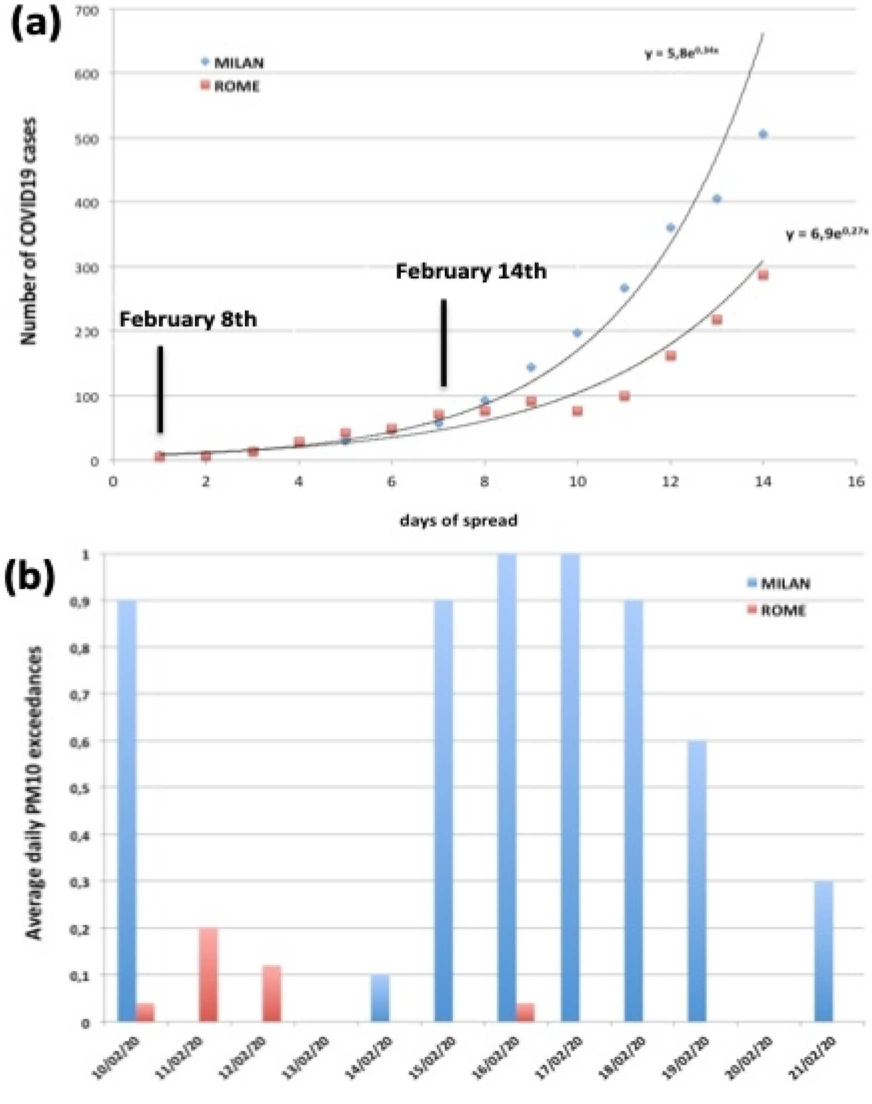

Fig. 4

121x148mm (96 x 96 DPI)

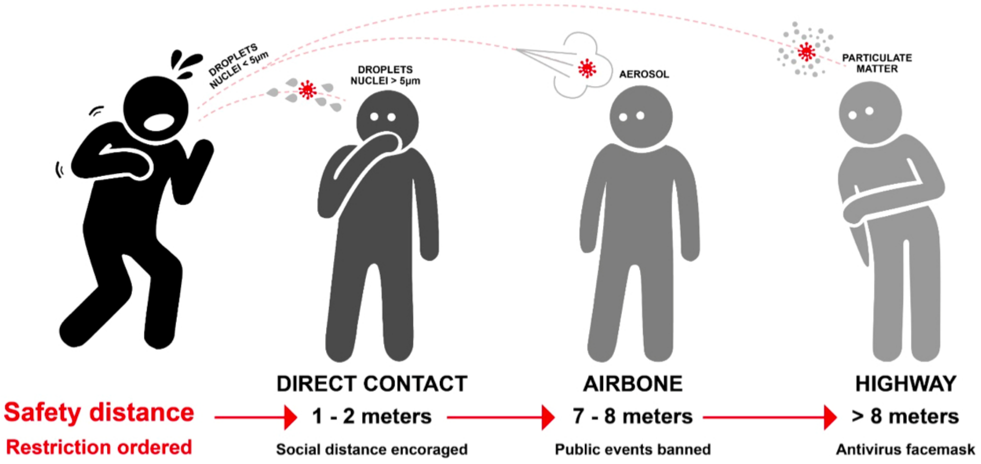
DROPLETS NUCLEI < 5μm
DROPLETS NUCLEI > 5μm
AEROSOL
PARTICULATE MATTER
Safety distance
Restriction ordered
DIRECT CONTACT
1 - 2 meters
Social distance encoraged
AIRBONE
7 - 8 meters
Public events banned
HIGHWAY
> 8 meters
Antivirus facemask

FIG 5

The Potential Role of Particulate Matter in the Spreading of COVID-19 in Northern Italy: First Observational Study based on Initial Epidemic Diffusion

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The Potential Role of Particulate Matter in the Spreading of COVID-19 in Northern Italy: First Observational Study based on Initial Epidemic Diffusion

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Abstract

Objectives: A number of studies have shown that airborne transmission route could spread many viruses even further the close contact with infected people. An epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spreading of COVID-19 in Italy. On March 16th 2020, we presented a Position Paper proposing a research hypothesis concerning the association between higher mortality rates due to COVID-19 observed in Northern Italy and PM$_{10}$ average concentrations exceeding daily limit of 50 $\mu g/m^3$. **Methods**: To monitor the spreading of COVID-19 in Italy from February 24th to March 13th (the date of the Italian lockdown), official daily data for PM$_{10}$ levels were collected from all Italian Provinces between February 9th and 29th, taking into account the maximum lag period (14 days) between the infection and diagnosis. In addition to the number of exceedances of PM$_{10}$ daily limit value, we considered also population data and daily travelling information per each Province. **Results**: PM$_{10}$ daily limit exceedances appear to be significant predictor of infection in univariate analyses ($p < .001$). Less polluted Provinces had a median of 0.03 infections over 1000 residents, while most polluted Provinces showed a median of 0.26 cases. Thirty-nine out of 41 Northern Italian Provinces resulted in the category with the highest PM$_{10}$ levels, while 62 out of 66 Southern Provinces presented low PM$_{10}$ concentrations ($p<0.001$). In Milan, the average growth rate before the lockdown was significantly higher than in Rome (0.34 vs. 0.27 per day, with a doubling time of 2.0 days vs. 2.6, respectively), thus suggesting a basic reproductive number $R_0>6.0$, comparable with the highest values estimated for China. **Conclusion:** A significant association has been found between the geographical distribution of daily PM$_{10}$ exceedances and the initial spreading of COVID-19 in the 110 Italian Provinces.

Keywords: COVID-19; Air Pollution; Particulate Matter; Italy.

Strengths and limitations

- In the perspective of observational study design, we have analyzed daily data relevant to ambient PM_{10} levels, urban conditions and COVID-19 incidence from all Italian Provinces, in order to assess potential association between particulate matter exceedances and the initial spread of COVID-19 in Italy;
- We used PM_{10} daily concentration levels collected by the official air quality monitoring stations for each Italian province, but no information about the presence of the virus on PM and its vitality or infective potential was available;
- All the Provinces have been assigned to two geographical areas (Northern or Southern Italy);
- The number of PM_{10} daily limit value exceedances (50 μg/m^3) detected in the different Provinces and the number of PM_{10} monitoring stations for each Province were considered in the analyses, as well as the latitude and population data (number of inhabitants and density);
- The number of PM exceedances were computed between February 9th and 29th in order to take into account the *lag period* of 14-days, which is the maximum average time elapsed between the contagion and the first weeks of the Italian epidemic (February 24th-March 13th);

Introduction

Severe acute respiratory syndrome known as COVID-19 disease (due to the new SARS-CoV-2 virus), is recognized to spread via respiratory droplets and close contact[1]. However, this unique transmission model does not seem to explain properly the different initial spreading of the virus observed in Italy from February 24th 2020 to March 13th 2020. The huge virulence of COVID19 in the Po Valley is not comparable to the milder contagiousness observed in the Central-Southern regions. Demographic factors related to the ageing of the population and the possibility of infection without clinical symptoms for a quite long time – together with the high rate of asymptomatic people that characterizes COVID-19 (estimated at 50-75% of infections) – may only partially explain the fast spreading of the virus in Lombardy and Northern Italy [2,3]. Cai et al (2020) reported different incubation periods in patients infected in Wuhan [4], but an epidemic model based only on respiratory droplets and close contact could not fully explain the regional differences in the spreading of COVID-19 in Italy, which was fast and dramatic only in Lombardy and Po Valley. At the same time, a number of studies have shown that airborne transmission route could spread viruses even further the close contacts with infected people [5-19]. Paules et al. (2020) highlighted that – besides close distance contacts – airborne transmission of SARS-CoV can also occur [5]. It has been reported that for some pathogens the airborne transport can reach long distances [6-8]. Reche et al. (2018) described the aerosolization of soil-dust and organic aggregates in sea spray that facilitates the long-range transport of bacteria, and likely of viruses, free in the atmosphere.

In particular, virus deposition rates were positively correlated with organic aerosol <0.7 µm, implying that viruses could have longer persistence time in the atmosphere and, consequently, can be dispersed further [8]. Moreover Qin et al. (2020) analyzed the microbiome of the airborne particulate matter ($PM_{2.5}$ and PM_{10}) in Beijing over a period of 6 months in 2012 and 2013, putting in evidence a variability of the composition that depended on the months analyzed [9]. Temporal distribution of the relative abundance of microbiome on particulate matter (PM) showed the highest presence of viruses in January and February, just in coincidence with most severe pollution due to PM. Chen. et al. (2017) demonstrated the relationship between short-term exposure to $PM_{2.5}$ concentrations and measles incidence in 21 cities in China [10]. Their meta-analyses showed that the nationwide measles incidence was significantly associated with an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ levels.

Other recent studies have also reported associations between PM and infectious diseases (e.g., influenza, hemorrhagic fever with renal syndrome) as inhalation could bring PM deep into the lungs, and viruses attached to particles may directly invade the lower part of respiratory tract, thus enhancing the induction of infections, as demonstrated by Sedlmaier et al. (2009) [11]. Zhao et al. (2018) showed that the majority of positive patients of highly pathogenic avian influenza (HPAI) H5N2 in Iowa (USA) in 2015 might have been infected by airborne viruses carried by fine PM from infected farms, both within the same State and from neighboring States [12]. Ma et al. (2017) observed a positive correlation of the measles incidence with PM_{10} in western China during the period 1986-2005; the condensation and stabilization of the bioaerosol, generating aggregates with atmospheric particles from primary (i.e. dust) and secondary particulate, have been indicated as mechanisms able to transport airborne bacteria and viruses to distant regions, even by the inter-continent-transported dust [13]. Ferrari et al. (2008) showed measles outbreaks occurring in dry seasons and disappearing at the onset of rainy seasons in Niger [14], while Brown et al (1935) found that the most severe measles epidemic in the United States occurred in Kansas in 1935 during the Dust Bowl period [15]. Coming to recent specific studies, laboratory experiments of Van Doremalen et al. (2020) 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 [16]. On-field measurement carried out by Liu et al. (2020) showed evidence of coronavirus RNA in indoor air samples from Wuhan Hospitals and even in ambient air in close proximity, during COVID-19 outbreak, highlighting the airborne route as a possible important pathway for contamination that should undergo further confirmations [17]. Santarpia et. al. reported the presence of airborne SARS-COV-2 in indoor air samples at the Nebraska University Hospital [18], while - at the opposite - some negative evidence of virus presence in air reported by Ong et al. (2020) come from explicitly poor sampling scheme [19]. Recently, we have published the first world evidence of the presence of COVID-19 on outdoor PM in samples collected between February 23th and March 9th in the province of Bergamo (Lombardy, Italy), which experienced the highest diffusion and mortality rates in Italy [20]. A research carried out by the Harvard School of Public Health seems to confirm an association between increases in particulate matter concentration and mortality rates due to COVID-19 [21]. On March 16th 2020, we have released an official Position Paper highlighting that there is enough evidence to consider airborne route as a possible additional factor for interpreting the anomalous COVID-19 outbreaks notified in the Northern Italy, known to be one of the European areas characterized by the highest PM concentrations [22,23].

This article presents the data that led to the publication of the Position Paper and triggered high interest of the research community at working on the hypothesis of a further transmission possibility via airborne dust [24-26], taking into account that the potential survival of the virus could be influenced by climatic parameters such as humidity and temperature as well as by fine dust concentrations [27]. Other papers support the possible merging of contaminated aerosol with fine particulate in the atmosphere [28-30]. The concentration of fine particles has been also repeatedly recognized by other authors as an important co-factor causing higher mortality rates in heavily contaminated areas [31,32]. This study is aimed at searching for a possible association between the initial COVID-19 spreading in Italy from the end of February to the first weeks of March 2020 (February 24th - March 13th) and the frequency of high daily average concentrations of PM recorded before the lockdown, taking into account the lag period of the infection (February 9th - 29th). The research hypotheses that we addressed is the possibility that air pollution could produce a “boost effect” of COVID-19 epidemic, thus representing a kind of exceptional “super-spread event”.

Methods

In the frame of an observational design of the study, we have analyzed daily data relevant to ambient PM_{10} levels, urban conditions and COVID-19 incidence from all Italian Provinces, in order to reliably determine the association between PM pollution levels and the initial spread of COVID-19 in Italy. PM_{10} daily concentrations were collected by the official air quality monitoring stations of the Regional Environmental Protection Agencies (ARPA), publicly available on their websites. The number of PM_{10} daily limit value exceedances (50 μg/m^3) detected in the different Provinces, divided by the total number of PM_{10} monitoring stations for each selected Province was computed.

Population data related to each Italian Province were collected from the National Institute for Statistics (ISTAT) for all the 110 Italian Provinces [33], paying specific attention to the absolute number of inhabitants and their density (number of inhabitants/km^2 per each Province) as well as to the number of commuters (people travelling from other Provinces for job reasons) and its proportion with respect to the Province population. We have computed the number of COVID-19 infected people for each Province and the infection rate based on the number of inhabitants from February 24th to March 13th (the date when the lockdown was decided), as reported by the official Government website, updated with daily frequency [34]. The number of PM exceedances were computed between February 9th and February 29th, as we had to take into account the maximum *lag period* of 14 days, which is the average time elapsed between the contagion and the first weeks of the Italian epidemic (February 24th-March 13th). Further covariates related to the different Provinces have also been considered: the number of air quality monitoring stations available in each Province, the longitude and the latitude of the Province city center. All the Provinces have been assigned to two geographical areas (Northern or Southern Italy). The dataset is publicly available on our web page [35] along with statistical analyses reproducible code in R language [36].

To investigate how PM exceedances might relate to infection diffusion, we started performing an exploratory analysis on PM_{10} exceedances considering the recursive partitioning tree approach, as implemented into the party package [37]. Such implementation connects the exploratory techniques to the classical statistical test approach, presenting the advantage to exploit a motivated stopping criterion when pruning the tree (i.e. the p-value of a significance test on independence of any covariate and response) [38]. Within recursive partitioning analyses, the response variable was represented by the proportion of COVID-

19 cases over Province population; the log-transform of such proportions response were reported into Figures. Cut-offs identified by the recursive partitioning tree analysis were subsequently used into binomial generalized linear models, both univariate and multivariable (i.e. logistic regression). The response of the binomial generalized linear models is expressed as a two-dimensional vector [39] obtained by binding the number of COVID-19 cases and the rest of the Province population. In presence of over-dispersion, quasi-binomial distributions were addressed. When suitable, association in contingency table has been expressed also in terms of odds ratios, and the Fisher exact test was issued to assess statistical significance. Exploratory analyses on $PM_{2.5}$ exceedances rates were held by recursive partitioning tree approach too. Correlation between $PM_{2.5}$ and PM_{10} exceedances rates per Province have been addressed by using a linear model. Pearson coefficient was applied to evaluate correlation; diagnostics plots were issued to assess model adequacy.

Similarly, we have performed statistical inferences analyses on Milan and Rome data, in order to observe the potential association between PM levels and COVID-19 spreading in big cities located in different geographical areas with remarkable differences in PM_{10} exceedances, but presenting at the same time quite similar urbanization, life style, population, ageing index, and number of commuters. The Roman municipality is far more extensive, with 1,287 square kilometers of surface compared to just 182 square kilometers of Milan. Talking about population, Rome has 2.87 million inhabitants compared to 1.35 million of Milan, but it is much less densely populated: 2,232 inhabitants per square kilometer vs. 7,439 (mainly due to the huge extension of the city of Rome). However, an additional 1 million inhabitants live in Rome neighborhoods with an average density between 6,720 and 9,231 inhabitants/Km^2. The extension of Milan and Rome underground is currently about 98 km and 54 km, respectively. Looking at the numbers of annual visitors, Rome has about 29.0 million tourists per year, compared to 12.1 million people visiting Milan. The number of daily commuters (people moving to Rome due to working reasons or similar) are higher in Rome (2.04 million trips) compared to Milan (1.66 million trips).

Results

The spatial distribution of ambient PM_{10} exceedances between Italian cities was geographically heterogeneous and it is presented in Figure 1a. The highest number of exceedances were generally located in Northern Italian Regions suffering from a rapid diffusion of COVID-19 epidemic, while zones with a lower contagion were located in Central and Southern Regions. The maps reported in Figure 1 illustrate the mean values of PM_{10} exceedances on the number of PM_{10} stations in all Italian Provinces during the period February 9th - 29th 2020 (Figure 1a), compared with the total COVID-19 infection per Province observed in the period March 4th - 13th (Figure 1b-e). Overall, there were 17,660 infected people on 60,4 million inhabitants in Italy at the time of the study. The highest incidence rates of COVID-19 were recorded in cities located in Northern Italy, and in particularly in Lombardy Region, including Milan. The lowest incidence of COVID-19 was observed in Southern Italy as well as in Lazio Region (which includes Rome).

Figure 1. (a) *Average daily PM10 exceedances vs. number of monitoring stations in different Italian Provinces from February 9th to 29th 2020;* ***(b-e)*** *Spreading of COVID-19 infections (officially confirmed cases) during the period March 4th-13th, 2020*

SARS-Cov-2 has been subsequently recognized as a high contagiously virus transmitted by airborne direct contact, showing super-spread event characteristics that has pushed the Italian Government to adopt extraordinary measures (namely total lockdown) to contain the outbreak [40]. In Figure 2a, two main discontinuity trends are evident and can be attributed to the Italian lockdown. If continuing the observation beyond the dates of the lockdown (March 11th-13th), it was possible – by analyzing the trend of new daily COVID-19 infections – to observe a first reduction in the spreading rate of the contagion around March 22nd (reflecting the school closure ordered on March 5th) and a second one around March 28th (reflecting the lockdown ordered between March 11th and 13th).

Figure 2.(a) *New daily COVID-19 infections in Italy from February 24th to April 4th 2020;* ***(b)*** *Trend of COVID-19 spreading in Italy during the first 15 days of the epidemic.*

As the *lag period* for SARS-COV-2 infection can be estimated in maximum 14 days, our study analyzed the Italian outbreak before March 11th, when the incidence growth rate was showing a typical exponential trend of the spreading (Figure 2b). In the univariate analysis, the PM_{10} daily limit value exceedances appear to be a significant predictor ($p < .001$) of infection with a 1.29 cut-off value (Figure 3). The cut-off divides the Provinces into two classes, characterized by higher ($n = 43$) and lower ($n = 67$) PM_{10} concentrations, respectively: the less polluted Provinces had a median 0.03 infection cases over 1000 inhabitants (first – third quartile 0.01 – 0.09; range 0.00 – 0.56), while the most polluted Provinces had a median 0.26 infection cases over 1000 inhabitants (first – third quartile 0.14 – 0.51, range 0.00 – 4.92). The boxplots in Figure 3 are log-transformed to enhance figure readability.

Dividing the Italian peninsula into two areas, the Northern and Southern part along the Tuscan-Emilian Apennines watershed, the PM_{10} exceedances results as follows: 39 out of 41 Northern Provinces falls in the higher PM_{10} category, while for Southern Provinces the ratio is reverse: 62 out of 66 Provinces present lower PM_{10} values (Odds ratio .00, Fisher exact test $p < .001$).

Figure 3. *Relationship between the PM_{10} daily limit value exceedances and the COVID-19 cases ratios over Italian Provinces population.* ***(a)*** *Scatterplot on semi-logarithmic scale relating the proportion of COVID-19 cases of Northern (gray squares) and Southern (black bullets) Italian Provinces population Vs. the average PM_{10} daily limit value exceedances. The dashed binomial (logistic) regression is characterized by an increasing slope of 0.25 ($p < 0.001$).* ***(b)*** *Boxplots showing that - with a 1.29 cut-off value of PM_{10} exceedance - the proportion of COVID-19 cases is greater ($p < .001$) in most polluted Provinces (39 out of 41located in Northern Italy) than less polluted Provinces, mainly located in Southern Italy (62 out of 66);* ***(c)*** *Boxplots showing that even considering $PM_{2.5}$ exceedances rates (despite a 39% missing data due to the absence of monitoring stations for $PM_{2.5}$) the proportion of COVID-19 in Po Valley might be stratified consistently ($p < 0.001$) with PM_{10} data presented in Figure 1 (b-e).*

Also the proportion of commuters over the Province population (people coming to the examined city for job reasons on daily basis) seems to have a significant role ($p = 0.01$, not depicted) in predicting the infection rates according to the univariate binary partitioning tree analysis. We set a commuters cut-off at 47% describing the number of job travellers. In the 51 Provinces with a lower number of commuters (<47%), the median infection cases over 1000 inhabitants of the Province was 0.03 (first – third quartile 0.01 – 0.05; range 0.00 – 0.33), while in the other Provinces (commuters >47%) the median infection cases over 1000 inhabitants was 0.18 (first – third quartile 0.13 – 0.36; range 0.00 – 4.92).

Notably, when performing a bivariate conditional regression exploratory analysis combining both the pollution and the proportion of commuters as possible predictors of the infection rates, we obtained exactly the same tree depicted in Figure 3: the commuters proportion loses its effect, thus suggesting a strong association between air quality and COVID-19 infections.

The logistic regression depicted in Figure 3 (on semi-logarithmic scales) confirms the exploratory analysis: a binomial distributed generalized linear model, corrected for overdispersion, reveals an increasing slope of 0.25 (s.e. 0.04; $p < 0.001$) of the linear predictor. $PM_{2.5}$ exceedances have been also explored: the possible association between $PM_{2.5}$ and PM_{10} exceedances observed in each Province has been assessed by a linear model (intercept 1.06, slope 1.38), with satisfactory accuracy ($p < 0.001$; mild lack of normality into residuals according diagnostic plots, residual standard error: 1.82). The $PM_{2.5}$ exceedance rates appear to be very highly correlated to PM_{10} exceedance rates, showing a Pearson coefficient of 0.94 (IC95%: 0.90 – 0.96). When repeating exploratory analyses on $PM_{2.5}$ exceedance rates by recursive partitioning tree analysis, a cutoff of 11 was identified, and an improved recursive partitioning tree was disclosed (Figure 3). Despite the limitation of 39% missing values concerning PM2.5 data (no data available for 43 Provinces out of 110), it appears that, consistently with main study outcome, the highest number of $PM_{2.5}$ exceedances are mainly located in Po Valley.

In order to observe the effect of the particulate matter in big cities presenting quite similar urbanization, life style, population and number of commuters, Milan and Rome were chosen, finding out that the first infected people were identified on February 25th both in Milan and Rome (8 and 3 patients, respectively). However, we considered March 1st as the first day of COVID-19 outbreak for both cities, when in Rome there were at least 6 confirmed cases (Figure 4).

Figure 4. ***(a)*** *Trends of COVID-19 spreading in Milan and Rome during the first 14 days of the epidemic; the starting date in Milan is February 25th and could correspond to infections acquired by February 8th that became clinically evident or detectable within the subsequent 17 days (lag period between the infection and diagnosis);* ***(b)*** *Distribution of the average daily* PM_{10} *exceedances in Rome and Milan on February 2020.*

The comparison of the COVID-19 outbreaks between Milan and Rome showed a higher exponential phase for the first city compared to the latter one. However, the trends presented a similar behavior up to 8 days; after 9 days, the increase in COVID-19 incidence showed a sudden acceleration of the viral infectivity only in Milan. Besides the transmission of SARS-CoV-2 occurring via close contacts with infected people through the direct inhalation of liquid droplets emitted by coughs or exhalations and/or by the contact with surfaces contaminated by the virus, the dynamic of COVID-19 diffusion observed in Milan – if compared to that observed in Rome – suggest to consider also other possible route of transmission including airborne route (with virus covering longer distances). If assuming 14-17 days as the average lenght of the lag phase, the first day of the infection considered for Milan (February 25th) should be referred to contagion occurred by February 8th. According to this assumption, the acceleration of COVID-19 diffusion in Milan started on February 14th (Figure 4a), in correspondence to the presence of a relevant peak of PM_{10} exceedances (Figure 4b), that was not observed in Rome, where the initial contagion started likely on February 13th in the absence of PM_{10} exceedances.

The incidence growth rate of COVID-19 infections in Italy was 0,19 per day with a doubling time close to 3.6 days, the same showed by Sanche et al. (2020) in Wuhan (Hubei Province, China), where a growth rate close to 0.21-0.30 per day with a doubling time of 2.3-3.3 was described on January 2020 [41]. The Italian basic reproductive number (R_0), estimated by the researchers was 5.7 [42], consistently with “super-spread event” characteristics possibly related to airborne droplets transmission, as described by Wellinga and Teunis (2004) for the epidemic curves of Sever Acute Respiratory Sindrome (SARS) during the outbreak occurred on February-June 2003 in Hong Kong, Vietnam, Singapore and Canada [43]. In Rome, the growth rate before the lockdown (March 13th) was 0,27 per day with a doubling time of 2.6 day, consistent with the “super-spread event” model described for SARS. In Milan, the growth rate was significantly higher, close to 0.34 per day, with a doubling time of 2.0 days, thus suggesting a R_0 value higher than 6.0, quite similar to the epidemic transmission via airborne droplets observed for measles (known to have reached a value of 12-18) [44] and to the highest R_0 estimates documented for China, ranging from 1.4 to 6.49 with a mean of 3.28 and a median of 2.79 (Wuhan: 2.55-2.68; Hubei Province: 6.49; China: 2.2-6.47) [45].

Discussion

Research Hypothesis. Based on the available literature, and following our recent publication confirming the presence of SARS-COV-2 RNA on PM10 collected in Bergamo area (the epicenter of the Italian epidemic) [20], there is enough evidence to consider the airborne route – and specifically the role of particulate matter – as a possible additional infection “boosting” factor for interpreting the anomalous COVID-19 outbreaks observed in Northern Italy, known to be one of the areas characterized by the highest PM concentrations in Europe [1]. Airborne transmission is certainly more effective in indoor environments, with little ventilation, but it must be considered that the Po Valley – due to its atmospheric stability – closely resembles a confined environment, and that long-distance virus transportation is favored by high concentration of dusts.

Current knowledge. Despite bio-aerosol is a well known factor for the virus transmission via airborne, the highly diluted nature of viral bioaerosol in ambient air has been considered a major impediment to viral aerobiological detection, including the investigation of viral interactions with other airborne particles. Recently, Groulx et al. (2018), using an in vitro PM concentrator, suggested that the interaction between airborne viruses and airborne fine particulate matter is able to influence viral stability and infectious potential [46]. The stability of aerosol and condensation reactions occur frequently in atmosphere, as organic aerosol change the properties (hygroscopicity, toxicity, optical properties) of other aerosol [47]. Cruz-Sanchez et al. (2013) demonstrated that Respiratory Syncytial virus (RSV) exposed to black carbon, in the form of India ink, prior to co-aerosolization in vitro, and then deposited on a cell substrate, increased viral infectivity [48]. Similarly, in areas of high vehicle traffic, many different pollutants arising from a variety of sources coexist (car or truck exhausts, emissions from heating installations etc.) [49], which present a particulate matter emissions containing carbon, ammonium, nitrate and sulfate.

Findings and research perspectives. Our observations showed that high frequency of PM_{10} concentration peaks (exceeding 50 μg/m^3) result in a spread acceleration of COVID-19, suggesting a possible “boost effect” for the viral infectivity. We found significance differences both in PM_{10} exceedances and COVID-19 spreading between Northern and Southern Italian regions, and we made a focus on Milan and Rome. The infection rate of disease has been higher in Milan, (1.35 million inhabitants, Northern Italy) than in Rome (2.87 million inhabitants, Southern Italy), even if there were no substantial difference in urban management and social confinement as well as in ageing index of the two populations. Our findings suggest that the acceleration of the growth rate observed in Milan could be attributed to a “boost effect” (a kind of exceptional “super-spread event”) on the viral infectivity of COVID-19, corresponding to the peaks of particulate matter. According to this hypothesis, PM could then act as a potential “carrier” for droplet nuclei, triggering a boost effect on the spread of the virus (Figure 5). It could be possible to look at the airborne route of transmission, and specifically to particulate matter, as a "highway " for the viral diffusion, in which the droplet nuclei emitted by the exhalations are stabilized in the air through the coalescence of aerosol with the PM at high concentrations in stability conditions. In fact, the fate of a small droplet of a virus, under normal conditions of clean air and atmospheric turbulence, evaporates and /or disperses quickly in atmosphere. On the contrary, in conditions of atmospheric stability and high concentrations of PM, viruses have a high probability of creating clusters with the particles and, by reducing their diffusion coefficient, enhancing their permanence time and amount in atmosphere and promoting contagion. These first observations suggest that particulate matter could be regarded as a contributing factor to the severity of COVID-19 infection in terms of airborne diffusion and health outcomes, in accordance with the findings published by Isaifan (2020) [50].

Figure 5. *Scheme of possible enhancement of viral transmission through stabilized human exhalation on PM*

The potential role of climatic variables. Nevertheless, coalescence phenomena require optimal conditions of temperature and humidity to stabilize the aerosols in the air, namely around 0-5 °C and 90-100% relative humidity. Recently, Ficetola et al. (2020) showed that the spread of COVID-19 peaked in temperate regions of the Northern Hemisphere with mean temperature of 5°C and humidity of 0.6-1.0 kPa, while decreased in warmer and colder regions [51]. These climatic variables could have played a role, along with the presence of high concentrations of particulate matter in the air, in favoring the stabilization of the aerosol in airborne, in line with the model proposed in Figure 5.

Limitations and Practical Implications. This was an observational study and therefore further experimental are needed to confirm the possibility that particulate matter may act as a “carrier” for the viral droplet nuclei, impressing a boost effect for the spreading of the viral infection, as it has been shown for other viruses. Virological studies could be performed, specifically aimed at testing also the vitality and infectious potential of SARS-COV-2-contaminated particulate matter, if any. Recent studies [52] and recommendations [53] about increased social distancing indicate that a recommended interpersonal distance of more than one meter and use of face masks [54] are useful prevention measures. It must also be pointed out that long term exposures to high levels of particulate matter itself chronically impair human health and possibly influence clinical course of infections acquired by already debilitated individuals, especially in most vulnerable age groups. Indeed, according to 2005 WHO guidelines, annual average concentrations of PM10 should not exceed 20 µg/m3 (compared to current EU legal limits of 40 µg/m3) and PM2.5 should not exceed 10µg/m3 (compared to current EU legal limits of 25 µg/m3). Moreover, the exposure-effect relationship between fine particulate matter and health damages is not of linear type, so that it is not really possible to set a threshold below which is foreseeable a complete absence of damage to human health [55].

Conclusion

The available literature on the role of airborne transmission – as well as these first preliminary observations concerning the association between the number of COVID-19 infected people and PM_{10} peaks – points out the opportunity of performing further computational and experimental researches on airborne route of transmission, and the potential role of PM on viral spread and infectivity. There is the rational for carrying out experimental studies specifically aimed at confirming or excluding the presence of the SARS-CoV-2 and its potential virulence on particulate matter. Moreover, the possibility of looking at PM levels as an "indicator" of the expected impact of COVID-19 in most polluted areas should be considered. Urgent actions must be adopted to counteract climate changes and the alteration of ecosystems that might trigger new and unexpected threats to human health that we are so dramatically experiencing worldwide.

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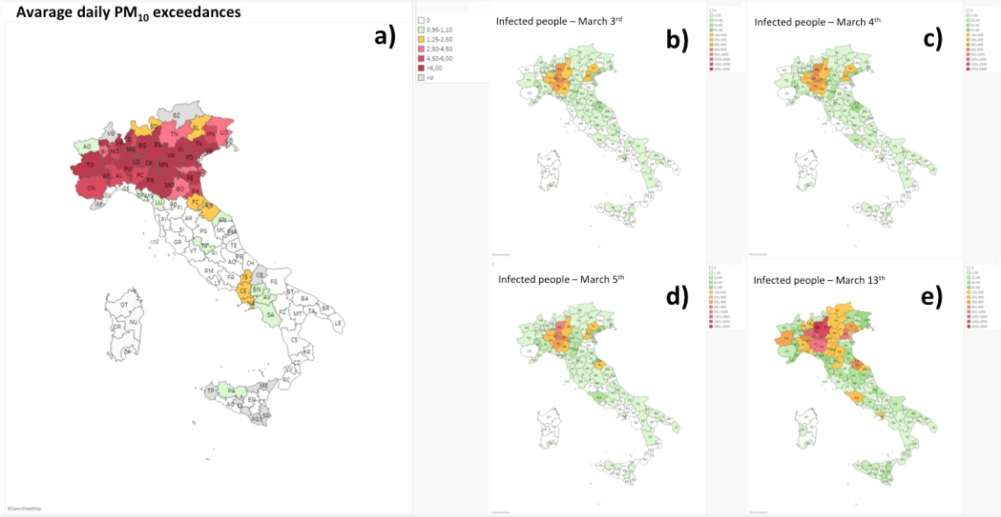
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1,25-2,50
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4,50-6,00
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nd
Infected people – March 3rd
b)
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c)
Infected people – March 5th
d)
Infected people – March 13th
e)

FIG 1

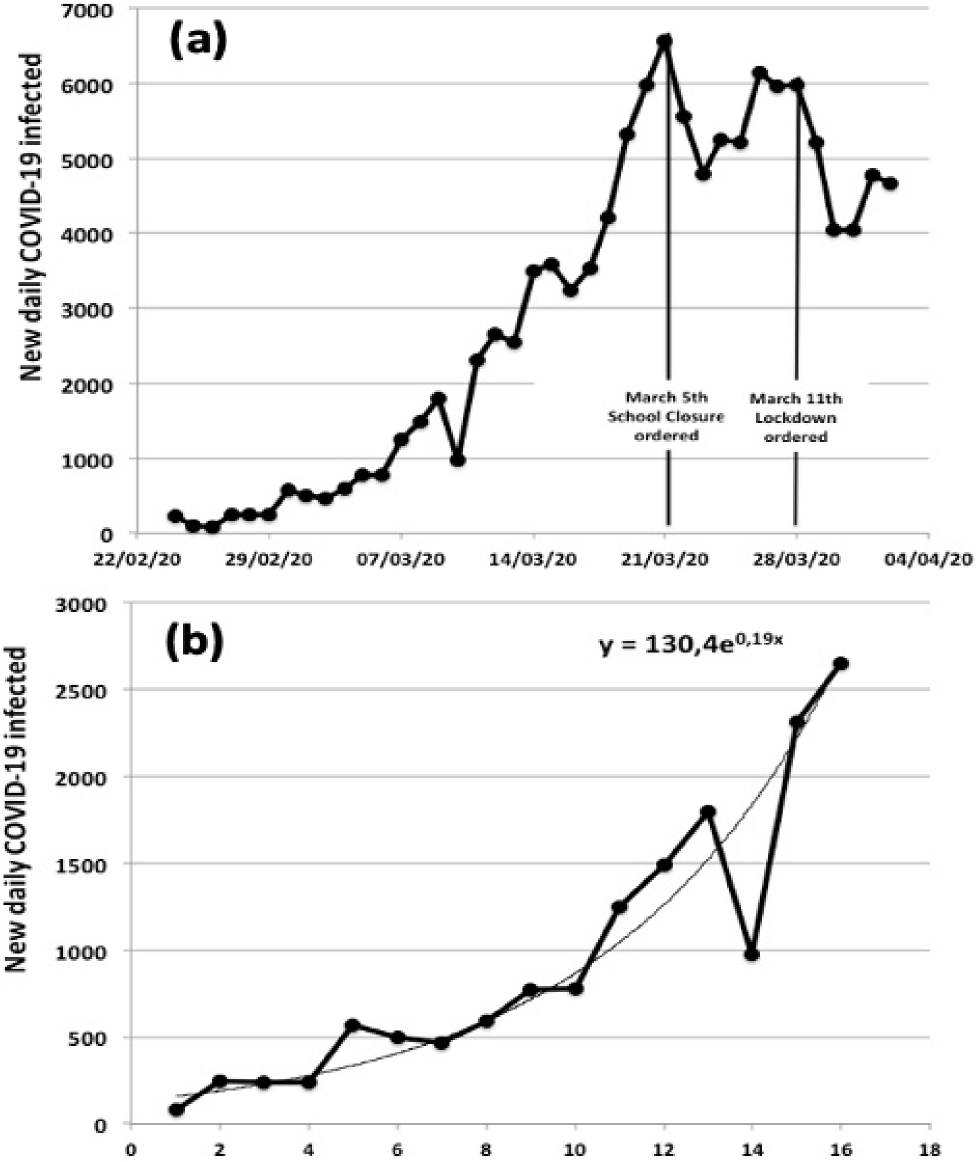

Fig. 2

137x162mm (96 x 96 DPI)

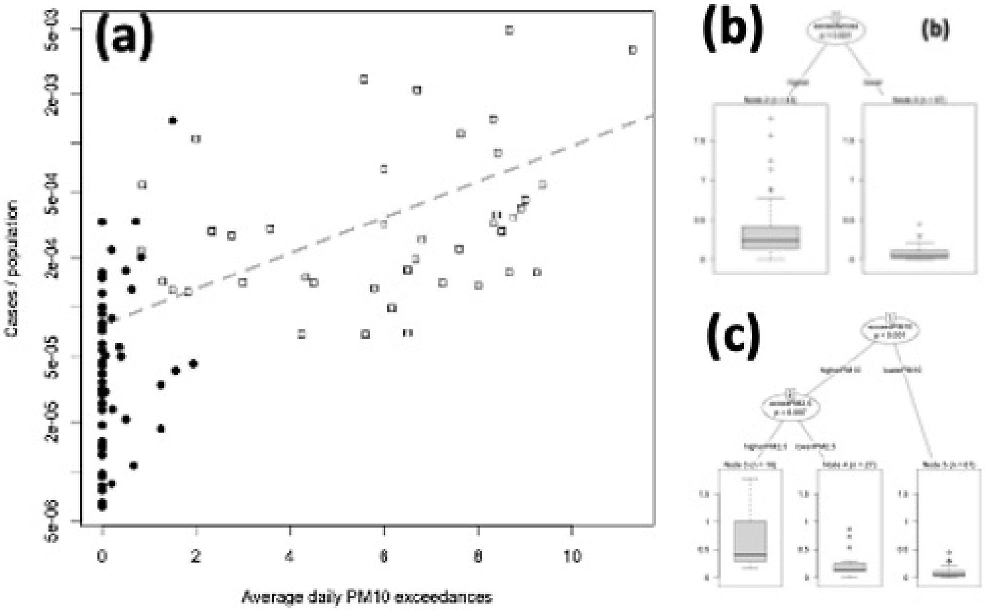

Fig. 3

134x94mm (96 x 96 DPI)

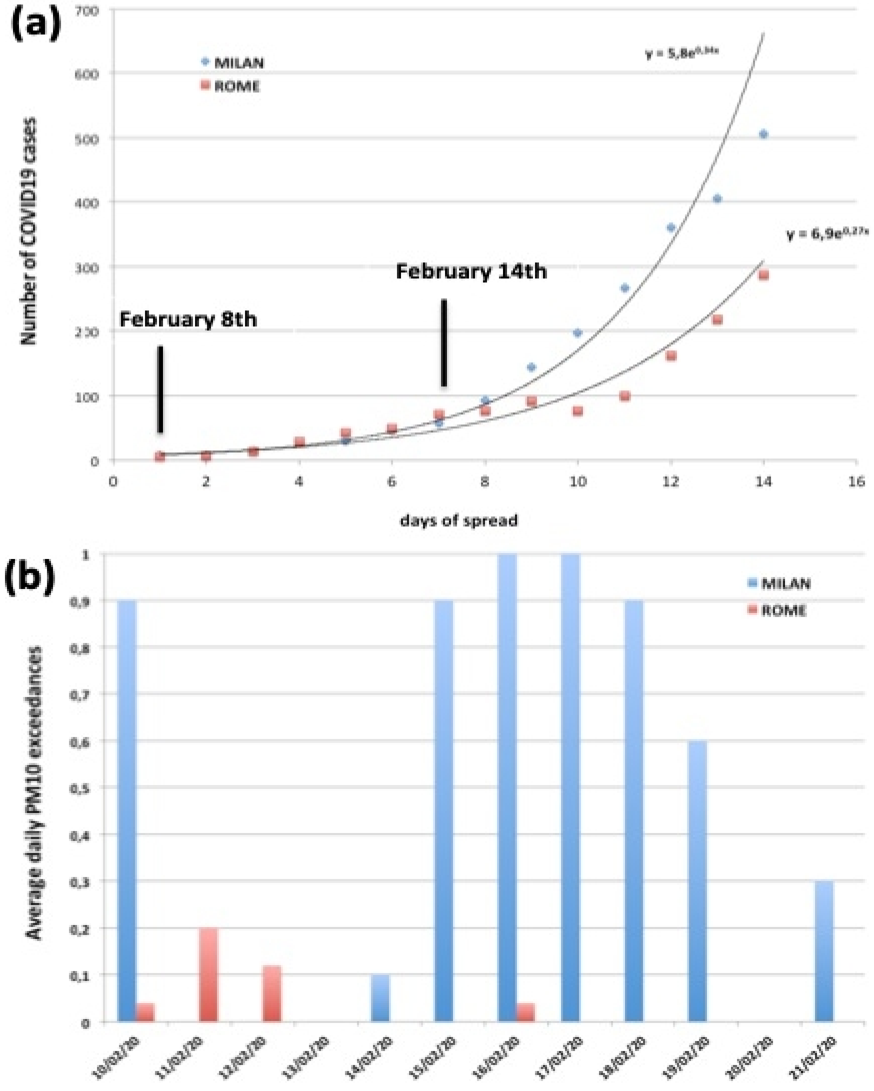

Fig. 4

121x148mm (96 x 96 DPI)

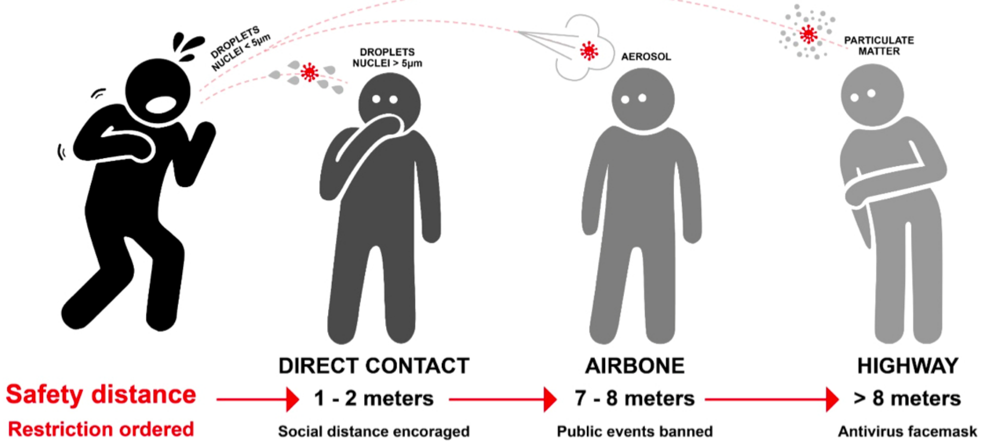
DROPLETS
NUCLEI < 5µm
DROPLETS
NUCLEI > 5µm
AEROSOL
PARTICULATE
MATTER
Safety distance
Restriction ordered
DIRECT CONTACT
1 - 2 meters
Social distance encoraged
AIRBONE
7 - 8 meters
Public events banned
HIGHWAY
> 8 meters
Antivirus facemask

FIG 5