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# Assessing the relationship between ground levels of ozone ($O_3$) and nitrogen dioxide ($NO_2$) with coronavirus (COVID-19) in Milan, Italy

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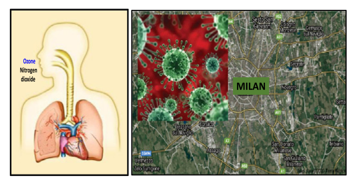
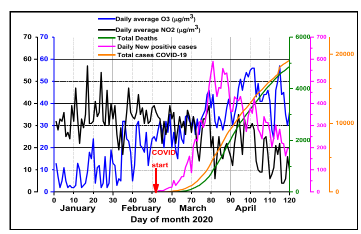
## HIGHLIGHTS

- COVID-19 viral infections are positively correlated with ground level ozone.
- Ground level nitrogen dioxide is inversely correlated with COVID-19 infections.
- Dry air, low winds and precipitation rates supports COVID-19 virus diffusion.
- Warm season will not stop COVID-19 spreading.
- Outdoor airborne aerosols might be possible carriers of COVID-19.

## GRAPHICAL ABSTRACT

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## ABSTRACT

This paper investigates the correlation between the high level of coronavirus SARS-CoV-2 infection accelerated transmission and lethality, and surface air pollution in Milan metropolitan area, Lombardy region in Italy. For January–April 2020 period, time series of daily average inhalable gaseous pollutants ozone ($O_3$) and nitrogen dioxide ($NO_2$), together climate variables (air temperature, relative humidity, wind speed, precipitation rate, atmospheric pressure field and Planetary Boundary Layer) were analyzed. In spite of being considered primarily transmitted by indoor bioaerosols droplets and infected surfaces or direct human-to-human personal contacts, it seems that high levels of urban air pollution, and climate conditions have a significant impact on SARS-CoV-2 diffusion. Exhibited positive correlations of ambient ozone levels and negative correlations of $NO_2$ with the increased rates of COVID-19 infections (Total number, Daily New positive and Total Deaths cases), can be attributed to airborne bioaerosols distribution. The results show positive correlation of daily averaged $O_3$ with air temperature and inversely correlations with relative humidity and precipitation rates. Viral genome contains distinctive features, including a unique N-terminal fragment within the spike protein, which allows coronavirus attachment on ambient air pollutants. At this moment it is not clear if through airborne diffusion, in the presence of outdoor and indoor aerosols, this protein "spike" of the new COVID-19 is involved in the infectious agent transmission from a reservoir to a susceptible host during the highest nosocomial outbreak in some agglomerated industrialized urban areas like Milan is. Also, in spite of collected data for cold season (winter-early spring) period, when usually ozone levels have lower values than in summer, the findings of this study support possibility as $O_3$ can acts as a COVID-19 virus incubator. Being a novel pandemic coronavirus version, it might be ongoing during summer conditions associated with higher air temperatures, low relative humidity and precipitation levels.



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## 1. Introduction

The ongoing worldwide outbreak of the novel coronavirus SARS-CoV-2 (COVID-19) started as an epidemic event in the city of Wuhan, China in late December 2019 and evolved as a pandemic declared by March 2020 (World Health Organization, 2020, L. Wang et al., 2020). According to the report of the World Health Organization as of 29 April 2020, the current outbreak of COVID-19, has affected over 3,160,540 people and killed >219,253 people in >200 countries throughout the world, and only few countries appear to have passed the peak. In Italy have been recorded 201,505 confirmed COVID-19 cases and 27,359 fatalities. Total number of confirmed cases in Milan metropolitan area (Lombardy), representing 9.4% of Italy counts was of 18,837. In Italy outbreak of COVID-19 started in Lombardy county, first 3 COVID-19 cases have been reported on 15 February 2020.

Early studies estimated the risk of COVID-19 cases importation to Europe by air travel from infected areas in China (Pullano et al., 2020). Also, was recognized that air pollution can act as coronavirus carrier, promoting its spreading together the air associated risk factors of the disease development at older age people (Wu et al., 2020; Bontempi, 2020), with history of smoking (Liu et al., 2020; Y. Chen et al., 2020), hypertension and heart disease (M. Chen et al., 2020), with chronic lung disease or moderate to severe asthma.

Within Milan and enclosed Po Valley topography, concentrations of $O_3$, $NO_2$ and other air pollutants are enhanced by fog and low-level clouds, which are transient phenomena in the atmosphere during the winter-time fog season and also subject to the formation of inversion layers, stagnant air conditions and accumulation of higher pollutant concentrations at the ground level.

It was demonstrated that exposure to air pollutants like as ozone ($O_3$), nitrogen dioxide ($NO_2$), carbon monoxide (CO), particulate matter (PM) in different size fractions (PM0.1 μm, PM2.5 μm and PM10 μm), volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), etc. may induce oxidative stress, responsible of the free radicals production, which can damage the cardio-respiratory and immune systems, by altering the host resistance to viral and bacterial infections (Ciencewick, Jaspers, 2007; Lee et al., 2007; Martelletti and Martelletti, 2020; Yin and Wunderink, 2018; Alghamdi et al., 2014; Carugno et al., 2016).

This study considered the impact of the most abundant gaseous air pollutants O3 & NO2 in some relations with particulate matter and climate factors on SARS-CoV-2 spreading in densely metropolitan area of Milan. Previous (Mudway and Kelly, 2004; Nuvolone et al., 2018; Arjomandi et al., 2018; Kesic et al., 2012; Yan et al., 2016) and currently epidemiological studies (Conticini et al., 2020; Ogen, 2020; Travaglio et al., 2020; Lippi et al., 2020) have suggested that long-term and short-term exposure to ambient ground level $O_3$ & $NO_2$ can play an important role in the phenotypes of cardio-respiratory diseases, including influenza, asthma and severe acute respiratory syndrome. Outdoor and indoor high exposure to pulmonary irritant gaseous gases $O_3$ and $NO_2$ is responsible for inflammatory process in the lungs as well as a cascade of subsequent responses (Fuller et al., 2020; Arjomandi et al., 2018; Tager et al., 2005; Wilson et al., 2017). Also, air pollution is exacerbating the susceptibility and severity of respiratory viral infections like as coronaviruses (SARS, MARS and COVID-19), with a high impact on host morbidity and mortality and public health all over the world (Manisalidis et al., 2020; Pothirat et al., 2019).

Besides environmental pollution, climate change and increased frequency of extreme events as a recorded feedback of anthropogenic pollution can also affect the geographical distribution of several infectious diseases including COVID-19 (Kawasaki et al., 2019; Linares et al., 2020).

The aim of this paper is to investigate the effects played by air pollution and climatic factors on COVID-19 outbreak in Milan metropolitan area, Italy. In order to assess the effects of these variables on COVID-19 fast diffusion and fatality, time series data of the main surface gaseous pollutants ($O_3$ & $NO_2$), Planetary Boundary Layer (PBL) characteristics and meteorological variables over the study period January–April 2020, together with COVID-19 confirmed total cases, daily new positive cases and total deaths have been examined.

## 2. Materials and methods

### 2.1. COVID-19 and air pollution with gaseous pollutants

#### 2.1.1. COVID-19

The atypical pneumonia caused by novel coronavirus (SARS-CoV-2) in Wuhan, China in December 2019 is a highly contagious disease (Zhu et al., 2020; L. Wang et al., 2020; Zu et al., 2020; C. Huang et al., 2020). As an infectious viral disease SARS-CoV-2 (COVID-2019) arised from viruses, like previous outbreaks: 2002–2003 Severe Acute Respiratory Syndrome (SARS-CoV) viruses and 2012–2015 Middle East Respiratory Syndrome (MERS-CoV), belongs to human Beta coronaviruses category. This new coronavirus responsible of an invasive pneumococcal disease has some similarities with the previous versions, but also has differences in its genomic and phenotypic structure that can influence their pathogenesis (X. Huang et al., 2020; Y. Wang et al., 2020; Mehta et al., 2020; Perlman, 2020). COVID-19 is a spherical or pleomorphic enveloped particle with an average diameter size of 0.1 μm in the range of 0.06–0.14 μm, and contains single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein (Mousavizadeh and Ghasemi, 2020; Y. Chen et al., 2020; Lu et al., 2020; Bosch et al., 2003). The viral genome contains distinctive features, including a unique N-terminal fragment within the spike protein. This peculiar configuration allows coronavirus attachment to ambient air pollutants. It seems that the novel coronavirus SARS-CoV-2 is aerosolized through talking or exhalation. Is not very clear if one inherent molecular or biological characteristic of bioaerosols determines whether a protein is destined to be toxic (Bowers et al., 2013; Zowalaty and Järhult, 2020). These viral or bacterial bioaerosols can act on the human immune system through damage of innate immune recognition receptors that respond to unique pathogen-associated molecular patterns. Bioaerosols are present in most of the enclosed environments due to its ubiquitous nature, but can be found and outdoor (Ariya and Amyot, 2004; Jones and Harrison, 2004; Gong et al., 2020). Advanced new studies attribute the fatalities of COVID-19 to cytokine storm syndrome (Guo et al., 2020; Mehta et al., 2020), also known as hypercytokinemia, which is characterized by an uncontrolled release of pro-inflammatory cytokines (Tisoncik et al., 2012), being a severe reaction of the immunity system, leading to death. Both indoors ~~or~~ and outdoors, the air we breathe, is universally contaminated by particles, gases, bacteria and viruses originating from both natural and anthropogenic sources that can reach the eyes, the nose, the upper and lower airways, and the lung parenchyma (Smets et al., 2016).

#### 2.1.2. $O_3$ & $NO_2$

Ozone is a gas that occurs both in the Earth's upper atmosphere (stratosphere) and at ground level. While stratospheric ozone is considered to be "good" acting as a barrier for ultraviolet rays, in the troposphere and at the ground level it is a secondary air pollutant generated through a series of complex photochemical reactions involving solar radiation and ozone-precursors. As an important greenhouse gas, O3 is making significant contributions to the climate change (Monks et al., 2015). The formation of ground level O3 is determined by the relative concentrations of its precursors in the atmosphere, as well as by local and regional meteorological conditions. Variability of ground air temperature, wind speed and direction, relative humidity, and precipitation associated with climate change have the potential to affect the generation, distribution, and deposition of O3.

Ozone is a natural compound of the troposphere that has an important role in the cleansing capacity of the atmosphere. During the past centuries ozone levels have increased as a result of human activities such as transportation, industrial processing and energy production.

Photochemical processes influenced by anthropogenic emissions of nitrogen oxides (NOx) and Volatile Organic Compounds (VOCs) cause current tropospheric ozone levels to be substantially increased compared to its natural background.

Climate change is expected to increase $O_3$ and $NO_2$ concentrations as well as the number of high ozone days in urban areas around the globe, potentially heightening adverse impacts on respiratory health (Wilson et al., 2017; Zoran et al., 2013; L. He et al., 2020; Fattorini and Regoli, 2020). Epidemiological and toxicological research continues to support a link between urban air pollution and an increased incidence and/or severity of airway disease. Detrimental effects of ozone, nitrogen dioxide and particulate matter, as well as traffic-related pollution as a whole, on respiratory symptoms and function are well documented (Seposo et al., 2020; McDonnell et al., 1983; Kulle et al., 1985; Kinney et al., 1996; Peters et al., 1999; Tager et al., 2005). Besides local air pollution sources, meteorological factors, planetary (atmospheric) boundary layer processes and regional/long range transport play important roles in determining the $O_3$ and $NO_2$ concentrations function on the topography of the observational site. Several epidemiological and experimental researches suggested a strong correlation between exposure to $O_3$, $NO_2$, or other combustion traffic related products and increased susceptibility to and morbidity from respiratory infection (Bayram et al., 2001; L. He et al., 2020). New advances in mechanisms implicated in the association of air pollutants and airway disease considered epigenetic alteration of genes by combustion-related pollutants and how polymorphisms in genes involved in antioxidant pathways and airway inflammation could modify responses to air pollution exposures (Kelly and Fussell, 2011; Mudway and Kelly, 2004; Xie et al., 2018). Ozone is a potential oxidizer and pulmonary irritant causing an inflammatory response in the lungs as well as a cascade of subsequent responses (Arjomandi et al., 2018; Fuller et al., 2020). $NO_2$, as principally generated via different anthropogenic (traffic related combustion, industrial furnaces, and heating installations) as well as by natural processes (agriculture, forest fires, production of biogenic compounds, and photochemical destruction of nitrogen compounds in the upper atmosphere), has both long-term and short-term effects on chronic respiratory disease in adults and children, even in a region with overall low levels of air pollution. Nitrogen dioxide is exacerbating bronchitis symptoms, being responsible for decreased lung function development (Viegi et al., 2006; Kirby et al., 1998; Oftedal et al., 2008; Zhou and Levy, 2007). The trends between $O_3$ and $NO_x$ are strongly anti-correlated, indicating that the $O_3$ is strongly depressed by high $NO_x$ (W. Gao et al., 2017). It was demonstrated that exposure to $NO_2$ and particulate matter PM2.5 and PM10 is associated with increased mortality due to respiratory problems like as cellular inflammation, bronchial hyperresponsiveness, increased blood pressure and decreased lung function, as well as increased risk of respiratory infection (M.Z. He et al., 2020).

### *2.2. Investigation test site*

Milan (45° 28′N; 9° 13′E), test site (Fig. 1) is located in the Po Valley, Lombardy region, a high industrialized and agricultural large area in the Northern part of Italy. The Lombardy region is a major populated area, with a population density among the highest in Europe. Milan urban area has about 1,5 millions inhabitants, being the second largest town in Italy, after Rome, and considering the whole Milan metropolitan area the population is about 3.1 millions inhabitants.

The region is an air pollution hot spot in Europe, where the air quality standards indicated in the Directive 2008/50/EC are exceeded for $O_3$, $NO_2$ and particulate matter PM2.5 and PM10. $NO_2$ footprint and its contribution to local concentration are relevant especially during wintertime (Bigi et al., 2017; Innocente et al., 2017;Carnevale et al., 2010). The peculiar geomorphologic features of the Po river plain, surrounded on three sides by the Alps and Apennine Mountains, favor stagnant weather associated with haze and fog conditions and accumulation of high levels of air pollutants.

### *2.3. Data used*

Time series data of daily average air pollutants PM2.5, PM10, $O_3$ and $NO_2$ for Milan selected stations have been collected from https://aqicn.org. Almost real time data for coronavirus infections COVID-19 Total, Daily New and deaths recorded in Italy, Lombardy county and Milan have been provided by the following websites: https://www.worldometers.info and https://www.statista.com/statistics. It is known that the number of COVID-19 total confirmed positive infections cannot always correspond with real existing cases, for several reasons like as symptomless or non-tested people. Anyway, this is a certified parameter to be considered in the present analysis. Besides this variable the other two will be considered, namely: daily new and fatalities cases registered in Milan.

Time series meteorological data, including daily average temperature (T), relative humidity (RH), wind speed intensity and precipitation rate (R) for Milan metropolitan region were retrieved from Weather Underground (https://www.wunderground.com/). The Omega surface charts for Europe at 850 mb and 925 mb have been provided by NASA, NOAA/OAR/ESRL PSD, Boulder, Colorado, USA (http://www.esrl.noaa.gov/psd/). According to content of meteorological information, downwards airflows are given by positive values of omega (in Pa/s), while upwards airflow by negative values of omega surface charts. Planetary Boundary Layer PBL data were collected from the archived data of NOAA's Air Resources Laboratory (https://ready.arl.noaa.gov). In order to analyze Milan weather conditions in the lower atmosphere associated with people's exposure to air pollutants during 1 January- 25 April investigated period we used Omega surface charts provided by NASA satellites for vertical air masses motion assessment relative to Earth's surface at different levels: 825 hPa chart (at an altitude of 1.5 km), 925 hPa chart (at an altitude of 0.762 km) and 1000 hPa chart (at about sea level height). Information on surface precipitation rate (mm/day) for investigated period January–April 2020 was also provided by NASA NCEP/NCAR Reanalysis USA (http://www.esrl.noaa.gov/psd/). Origin 10 software was used for time series of data analysis.

## 3. Results and discussion

### *3.1. Descriptive analysis*

In this study, to assess the relationship between gaseous pollutants $O_3$ and $NO_{2,}$ climate variables data and COVID-19 infections and fatalities, Pearson correlation test was used. Pearson correlation coefficient is a measure of the strength of the linear relationship between pairs of two variables. To compare $O_3$ and $NO_2$ data with data of climate signals, all the data have been standardized. The value of Pearson coefficients varies from 1 - to 1. If the two variables are in perfect linear relationship, the correlation coefficient will be either 1 or −1. The sign depends on whether the variables are positively (directly) or negatively (inversely) related. The correlation coefficient is 0 if there is no linear relationship between the variables. Also, the *p*-values, with 0.05 significance level, were calculated to accept (reject) the statistical significance of the correlation between pairs of two variables. The null hypothesis was that the value of r in the population was zero. If the calculated p-value was $<0.05$, the null hypothesis No (no correlation) would be rejected and vice versa; if p-value $> 0.05$, it means the correlation would be statistically significant. Correlation coefficients and *P*-values were calculated using ORIGIN 10 software. Because Spearman and Kendall non-parametric correlation coefficients had almost similar values with Pearson correlation coefficients, in this paper have been used Pearson correlation. Also, because the dataset for the current research was not normally distributed, we have used Pearson and correlation tests as an empirical methodology to observe gaseous air pollutants $O_3$ and $NO_2$ and climate factors correlation with COVID-19 in Milan.

Average recorded during January–April 2020 time period daily average temperature, relative humidity, precipitation rate, Planetary


**Fig. 1.** Milan test site.

Boundary Layerand wind speed were $(8.3 \pm 4.54)°$ C, $(69.86 \pm 17.28)$%, $(797.53 \pm 568.36)$ m, and $(6.56 \pm 3.4)$ km/h, respectively. Average daily temperature had significantly positive correlations with daily average PBL height ($R^2 = 0.74$) and daily average wind speed ($R^2 = 0.25$) and negative correlations with daily average relative humidity ($R^2 = -0.61$). However, relative humidity had significant negative correlations with Planetary Boundary Layer ($R^2 = -0.61$) and wind speed ($R^2 = -0.31$). Table 1 summarizes the Pearson coefficients and *p*-values descriptive statistics of COVID-19 Milan cases (Total confirmed, Daily New positive and Total Deaths) and daily average ground level gaseous pollutants $O_3$ and $NO_2$ concentrations together daily average climate variables (Planetary Boundary Layer height, air temperature, relative humidity, wind speed intensity and precipitation rate).

Table 2 presents the Pearson coefficients and p-values descriptive statistics between daily average climate variables and daily average ground level gaseous pollutants $O_3$ and $NO_2$ concentrations.

The spatial analysis has been conducted on a regional scale for Milan large town, Lombardy county in Italy and combined with the recorded number of COVID-19 cases.

### *3.2. Impact of gaseous air pollutants $O_3$ and $NO_2$ on COVID-19 "hotspot" Milan area*

Time series analysis of ground level $O_3$ and $NO_2$ concentrations in Milan metropolitan region during January–April 2020 have shown an opposite correlation between daily average air surface concentrations of $O_3$ $(25.27 \pm 15.27)$ μg/m$^3$, placed in the range of (2–56) μg/m$^3$, and daily average air surface $NO_2$ values of $(28.97 \pm 9.66)$ μg/m$^3$, placed in the range of (6–57) μg/m$^3$, as can be seen in Fig. 2. Due to COVID-19 pandemic event, starting with the end of February 2020 lockdown (as can be seen on Fig. 2), where drastic measures for reduction of air pollution were adopted to limit the spread of the coronavirus, our study revealed different concentrations levels for $O_3$ and $NO_2$ corresponding to pre-pandemic period (January–February) and beyond lockdown (March–April) 2020, namely: $NO_2$ in Milan city has decreased by approximately 64.7%, while $O_3$ has increased by a factor of 2.25. The increase in $O_3$ concentrations is mainly correlated with $NO_x$ emissions reduction, leading to a lower $O_3$ titration by NO (Bauwens et al., 2020). These results are consistent with the recent findings for Milan in Italy (Collivignarelli et al., 2020) and for Wuhan area in China (Shi and Brasseur, 2020; Huang et al., 2020; P. Wang et al., 2020).

In good accordance with scientific literature (Yadav et al., 2016; Zoran et al., 2014; Penache and Zoran, 2019a; Zoran et al., 2019) daily average ozone concentrations at the ground level were negative correlated with both daily average particulate matterPM2.5 ($R^2 = -0.63$) and PM10 ($R^2 = -0.61$), as PM would significantly reflect the sunlight radiation and retard the photochemical reaction forming ozone. Analysis of the Pearson correlation coefficients show that daily average $O_3$ concentration in Milan was positive correlated with daily average temperature ($R^2 = 0.84$) and negative correlated with daily average relative humidity

**Table 1**
Pearson correlation coefficients and *p* values between COVID-19 Milan cases and daily average ground level gaseous pollutants concentrations and climate variables.

| Time period: January–April 2020 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| COVID-19 number cases | Air pollutant | | | | Climate parameter | | | | | | | | | |
| | Ozone $O_3$ (μg/m$^3$) | | Nitrogen dioxide $NO_2$ (μg/m$^3$) | | Planetary Boundary Layer (PBL) | | Air temperature T (°C) | | Relative Humidity RH % | | Wind speed intensity km/h | | Precipitation rate mm/day | |
| | Pearson | p value | Pearson | p value | Pearson | p value | Pearson | p value | Pearson | p value | Pearson | p value | Pearson | p value |
| Total cases | 0.64 | <0.01 | −0.55 | <0.01 | 0.79 | | 0.67 | <0.01 | −0.47 | <0.01 | −0.02 | 0.88 | −0.05 | 0.7 |
| Daily New cases | 0.50 | <0.01 | −0.35 | <0.01 | 0.36 | <0.01 | 0.24 | 0.065 | −0.32 | <0.01 | −0.14 | 0.269 | −0.21 | 0.09 |
| Total deaths | 0.69 | 0 | −0.58 | <0.01 | 0.82 | 0 | 0.73 | 0 | −0.53 | <0.01 | 0.15 | 0.122 | −0.04 | 0.78 |

($R^2 = -0.79$). The positive correlation between temperature and $O_3$ is attributed to the fact that solar radiation controls air temperature, which in turn increases the photolysis efficiency. So, the major photochemical paths for removal of $O_3$ are enhanced in presence of high humidity levels (Desideri et al., 2007; Akimoto et al., 2015; Steffens, 2020; Wang and Su, 2020). As higher relative humidity levels are associated with large cloud cover and atmospheric instability, the photochemical process slows down and surface $O_3$ is depleted by deposition on water droplets.

Our results have shown that the severe reductions in $NO_2$ and other air pollution emissions during Milan's COVID-19 lockdown led to substantial increases in ground level $O_3$, which in turn increased atmospheric oxidizing capacity and enhanced formation of secondary aerosols, with subsequent negative impact on human respiratory health and increasing of COVID-19 confirmed and fatalities numbers. For this reason we considered $O_3$ as a COVID incubator. Also this study found that daily average ground level ozone concentrations values were positive correlated with all COVID-19 cases (confirmed Total, confirmed Daily New positive and Total Deaths) as can be seen in Table 1 and Fig. 2. A similar result was recently reported for COVID-19 infections and ozone in Italy (Pansini and Fornacca, 2020).

Because of the prominent contribution of traffic combustion sources in urban areas, local $NO_2$ is often used as a tracer of road traffic emissions (M.Z. He et al., 2020; Dutheil et al., 2020; Penache and Zoran, 2019b). The emitted NOx contributes to the formation of secondary airborne pollutants like $O_3$ and PM2.5. Temporal distribution of daily average air surface $NO_2$ concentrations during January –April 2020 in Milan shows a negative correlation with daily average ground level $O_3$, namely ($R^2 = -0.38$). Also, was found a negative correlation between average ground levels of $NO_2$ and COVID-19 cases (Total, confirmed Daily New positive cases and Total Deaths) as can be seen in Table 1 and Fig. 2.

### 3.3. Influences of planetary boundary layer on gaseous air pollutants and COVID-19 cases

Planetary (Atmospheric) Boundary Layer characteristics play a crucial role in the dispersion and dilution of air pollutants near the earth's surface. During days with higher average PBL height are recorded lower pollutant concentrations near the ground. Higher average PBL heights and enhanced convective activities allow the dilution of pollutants, followed by decreasing of their concentrations near the ground, while in days with lower PBL heights air pollutants get trapped near the ground (Zoran et al., 2014). Shallow PBL heights recoded during January–February months 2020 can be partially responsible for several pollution associated with haze episodes in urban metropolitan area of Milan and increase human respiratory vulnerability. Daily average values of PBL recorded in Milan large town during January–April 2020 were negative correlated with surface air concentrations of particulate matterPM2.5 ($R^2 = -0.57$) and PM10 ($R^2 = -0.56$) as well as with nitrogen dioxide $NO_2$ ($R^2 = -0.52$). A different situation was recorded for daily average values of PBL, which were positive correlated with ground level ozone $O_3$ concentrations, Pearson correlation coefficient being $R^2 = 0.74$, result which can be seen in Table 2. Based on our analysis was found that daily average PBL values were positive correlated with all COVID-19 cases (confirmed Total, confirmed Daily New positive and Total Deaths) as can be seen in Fig. 3.

**Table 2**
Pearson correlation coefficients and p values between climate variables and daily average ground level gaseous pollutants concentrations $O_3$ and $NO_2$.

| Time period: January–April 2020 | | | | |
|---|---|---|---|---|
| Daily average climate variable | Ozone $O_3$ (μg/m$^3$) | | Nitrogen dioxide $NO_2$ (μg/m$^3$) | |
| | $R^2$ | P-value | $R^2$ | p-value |
| Planetary Boundary Layer (PBL) | 0.74 | 0 | −0.52 | <0.01 |
| Air Temperature (T) | 0.84 | 0 | 0.46 | <0.01 |
| Relative Humidity (RH) | −0.79 | 0 | 0.19 | 0.05 |
| Wind speed | 0.26 | <0.01 | −0.50 | <0.01 |

### 3.4. Meteorological conditions in relation with COVID-19 cases

Statistical analysis shows that daily average ground level of $O_3$ concentrations in Milan was positive correlated with daily average temperature ($R^2 = 0.84$), in good accordance with other studies (Tosepu et al., 2020) and negative correlated with daily average relative humidity ($R^2 = -0.79$). Thus, in presence of high humidity and low temperature, $O_3$ production remains low (Xie and Zhu, 2020). Several studies confirmed that air low humidity levels might be an important risk factor

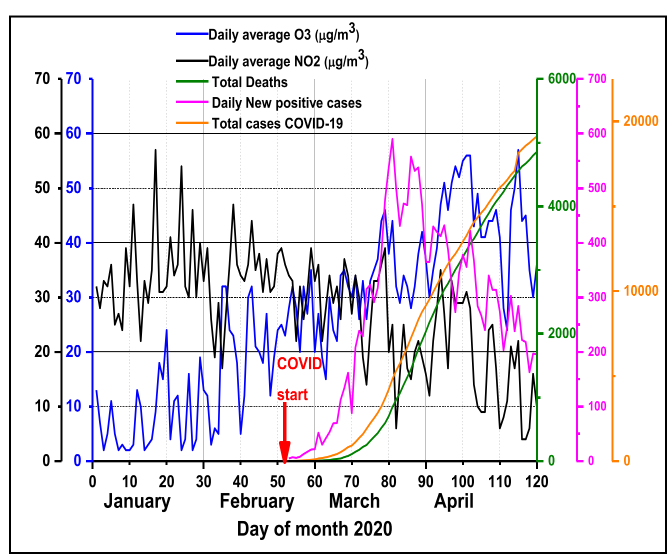


**Fig. 2.** Temporal variation of daily average ground levels $O_3$ and $NO_2$ in relation with COVID-19 infections in Milan during January–April 2020.

for respiratory infection diseases, low-humidity levels can cause a large increase in mortality rates (Barreca, 2012; Davis et al., 2016; Fallah and Mayvaneh, 2016; Tan et al., 2005; Dalziel et al., 2018; Sajadi et al., 2020). A possible explanation might be available for COVI-19, as breathing dry air could induce epithelial damage of respiratory tract or reduction of mucociliary clearance, and an increased susceptibility to respiratory virus infection. Also, the formation of small droplet nuclei is essential to viral infection transmission, while exhaled respiratory droplets settle very fast at air high humidity levels. Furthermore, air temperature also contributes towards the transmission of the virus (Chen et al., 2020; Ma et al., 2020; Shi et al., 2020) suggesting that humidity and temperature will play an important role in COVID-19 mortality rate. Climate indicators and air temperature are well correlated with the spread of COVID-19 (Poole, 2020; Ahmadi et al., 2020).

Is increasingly recognized that both indoor and outdoor relative humidity is an important factor associated with respiratory diseases severity. This study found that outdoor daily average relative humidity in Milan during January–April investigated period was positive correlated with particulate matter PM2.5 ($R^2 = 0.60$) and PM10 concentrations ($R^2 = 0.63$), which also had a strong negative impact on immunity and cardiorespiratory systems and the pathogenesis of severe respiratory infections. Daily average relative humidity was ($69.86 \pm 17.28$)% and its variation was in the range of (28.7–99.1)%. This can explain the high rate of total COVID-19 positive cases registered in the metropolitan area of Milan, possibly attributed to bronchial hyperreactivity and immune disorders through several pathways. Similar finding have been reported in the current literature (Ma et al., 2020; Poole, 2020; Domingo and Rovira, 2020; Yuen et al., 2020; Coccia, 2020). Among the climate variables, wind speed has a weakly inverse relationship with the recorded COVID-19 cases (Total confirmed, Daily New positive), as can be seen in Table 2. Temporal patterns of daily average temperature, relative humidity and wind speed in relation with dynamics of the coronavirus disease 2019 outbreak in Milan (Total confirmed, Daily New positive and Total Deaths) cases are presented in Fig. 4, which allows evaluating the data starting from first confirmed infections in Milan as a general comparison for 20 February–30 April 2020 analyzed period. Daily new confirmed cases reached the peak around 21 March 2020 as some models predicted (Fanelli and Piazza, 2020).

During analyzed period at the ground level have been registerd some episods of fog and haze, which favor the air pollutants including ambient bioaerosols accumulation at the surface, with negative impacts on respiratory system and human health (Wu et al., 2020; Wei et al., 2016; Ye et al., 2016). Another factor that possibly contributed at the recorded high levels of air pollution in Milan was the very low precipitation level, ranging from (0- few mm/day), and therefore low air washout processes.

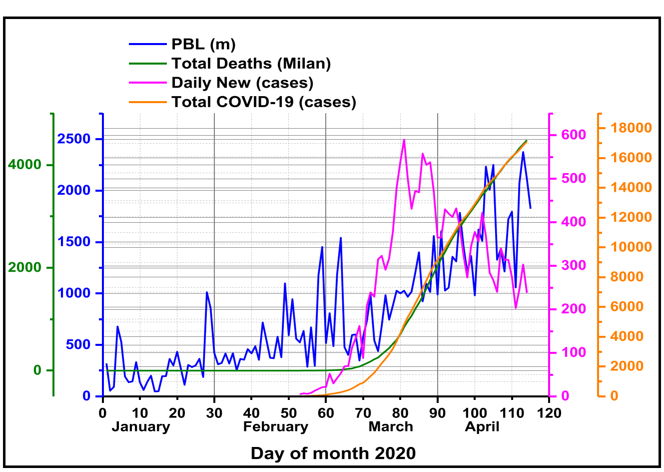


**Fig. 3.** Temporal distribution of daily average Planetary Boundary Layer during January–April 2020 and COVID-19 cases in Milan.

For January–April 2020 analyzed period, the daily mean precipitation rate was ($0.12 \pm 0.07$) mm/day in the range of (0–2.1) mm/day. Fig. 5 evidences the surface low precipitation rate (mm/day) levels recorded over Milan and Lombardy region in Italy by NASA NOAA satellites, NCEP/NCAR Reanalysis during January–April 2020, based on 1981–2010 clima data. Statistical Pearson correlation shows that precipitation rate recorded in Milan metropolitan region had important effects on the transmission and severity of respiratory viral infection COVID-19, being negatively correlated with Daily New positive cases ($R^2 = 0.21$ with significant $p$-value of $0.09 > 0.05$ and also low negatively correlations with Total COVID-19 and Total Deaths cases with significant $p$-values $> 0.05$, as can be seen in Table 1. Low levels of precipitation and air relative humidity are significant factors related to coronavirus infection transmission.

The removal efficiency of air pollutants can be triggered by the main two forcing: wind and precipitation. Based on historical climate data, wind speed measured in Milan and Po River plain is among the lowest in Europe, causing frequent phenomena of thermal inversion and trapping of smog and pollution close to the ground (Carugno et al., 2016). At lower daily average precipitation levels and wind speeds the diffusion of this invasive pneumococcal disease might have a high rate (Ahmadi et al., 2020). During January–April 2020 investigated period in Milan metropolitan area, the average daily wind speed had a low value, namely ($6.57 \pm 3.4$) km/h, in the range of (2.4–18.8) km/h, which means stability conditions, and air pollutants accumulation near the ground.

### 3.5. Atmospheric pressure field

During period of study, in order to define the atmospheric capability to disperse main pollutant gases (ozone and nitrogen dioxide), the NOAA satellite vertical airflows Omega surface charts at 850 mb

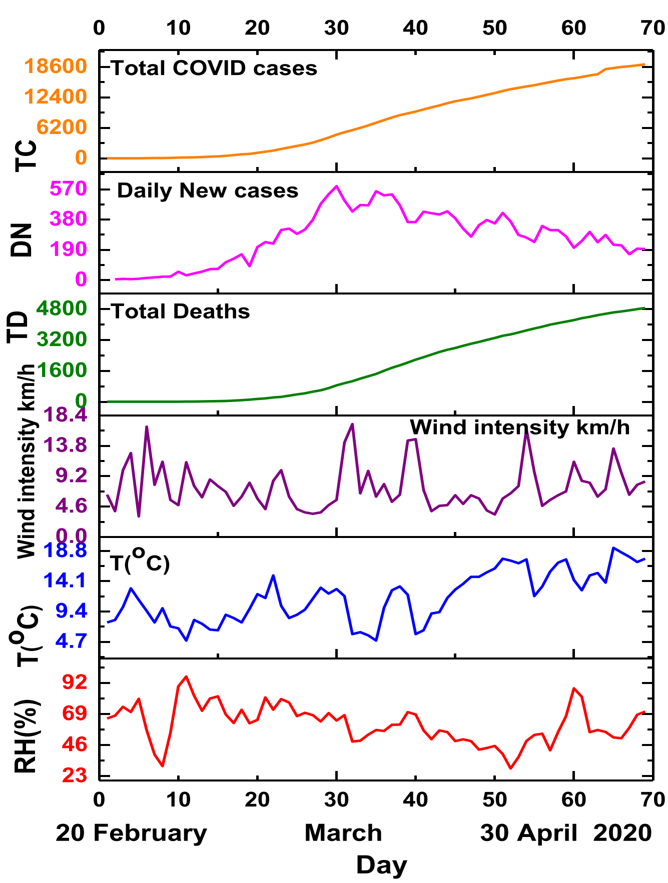


**Fig. 4.** Temporal pattern of daily average climate variables and COVID-19 cases in Milan.

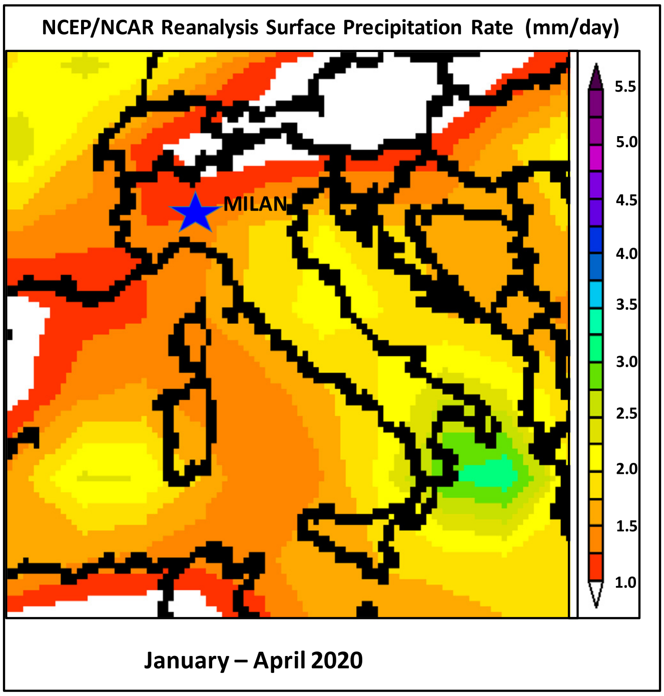


**Fig. 5.** NOAA surface precipitation rate chart over Milan, Italy in Europe during January–April 2020.

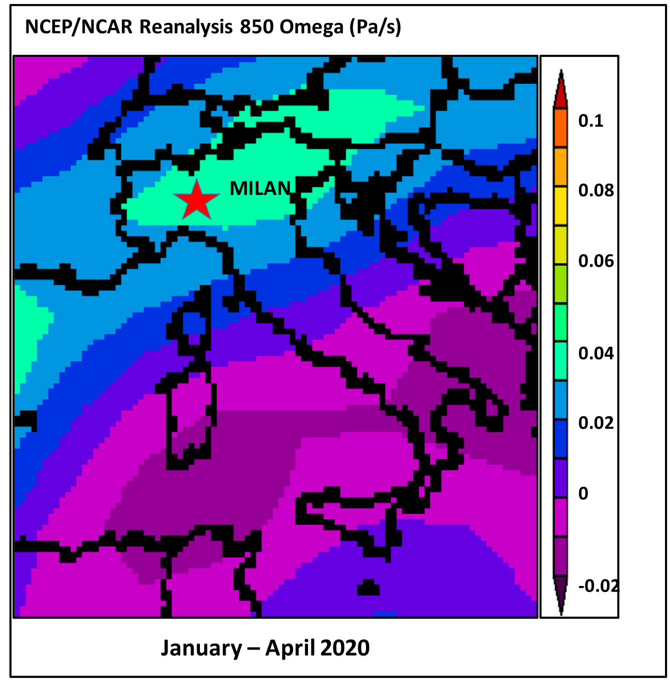


**Fig. 6.** NOAA satellite atmospheric pressure field Omega chart over Milan, Italy in Europe during January–April 2020 (inversion conditions).

(1.5 km above sea level) and 950 mb (0.762 km above sea level) have been used. According to these charts during investigated period over Northern part of Italy, whre Milan large area is located have been observed downwards airflows described by positive omega values, which averages atmospheric inversion, much intensely decribed by 850 mb map (0.03–0.05) Pa/s than 925 mb map (0.02–0.03) Pa/s during January–April period. Omega meteorological chart 950 mb (0.762 km above sea level) is a better choice for our analysis because daily average PBL value recorded for Milan area was (797.53 ± 568.35) m. NOAA satellite Omega image for Italy in Europe (Fig. 6) shows existing atmospheric thermal inversion conditions over Milan and Lombardy region, associated with accumulation near the ground of high air pollutants concentrations (non-viable aerosols and viable-bioaerosols including viruses like as coronaviruses, bacteria, fungi, etc.) leading to a higher risk of COVID-19 infections development (Ogen, 2020).

Local favorable stagnant atmospheric conditions due to local topography of Milan area, the preexisting high levels of air pollutants during January–February 2020 can explain the high incidence of people's respiratory diseases and increased susceptibility to new viral infections COVID-19. Long-term conditions of population exposure (several years before 2020) when the number of days in which the regulatory limits of $O_3$, $NO_2$, PM2.5 and PM10 have been exceeded (EEA, 2019, 2020; Remuzzi and Remuzzi, 2020) in Milan metropolitan region as well as short-term exposure to high ground levels of $O_3$, $NO_2$, PM2.5 and PM10 can be correlated with the decreased people's immunity and immunopathology to viruses, and high fatality COVID-19 rates observed in Milan and Lombardy region. Another possible contributor at atmospheric pollution in the area can be attributed to transborder air pollution from neibourghood regions and countries.

As an important result, our analysis show the direct correlation of daily averaged ground levels $O_3$ and $NO_2$, with meteorological factors on COVID-19 infections outbreak in Milan. In spite of cold season investigated period (winter-early spring) collected data, when usually recorded urban ozone levels have lower values than its summer peak concentrations, the findings of this study demonstrate that ground level ozone possible acts as a COVID-19 virus incubator, being positively correlated with COVID-19 infections and fatalities (Fig. 7). Being a novel pandemic coronavirus (SARS-CoV-2) version, it might be ongoing during summer conditions associated with higher temperatures and low humidity levels. Also, this paper supports the assumption that air pollutants can be responsible for both indoor and outdoor coronavirus airborne transmission.

It seems that under specific climate conditions (Bashir et al., 2020), air pollution acts as a carrier of the COVID-19 virus, facilitating its transmission and spreading, allowing its survival in active form with different residence times. Also, urban air pollution imposes an increased vulnerability of the population to respiratory syndromes, even in the absence of microbial causative agents (Wang and Su, 2020). Association between Milan, with several days of smog and haze, which favor air pollutants accumulation near the ground level in cold and dry winter to spring seasons and the highest number of COVID-19 infection cases (Total confirmed, Daily New positive and Total Deaths), thereby is supports the possibility as the degree of air pollution and local topography together climate conditions may contribute to accelerated diffusion

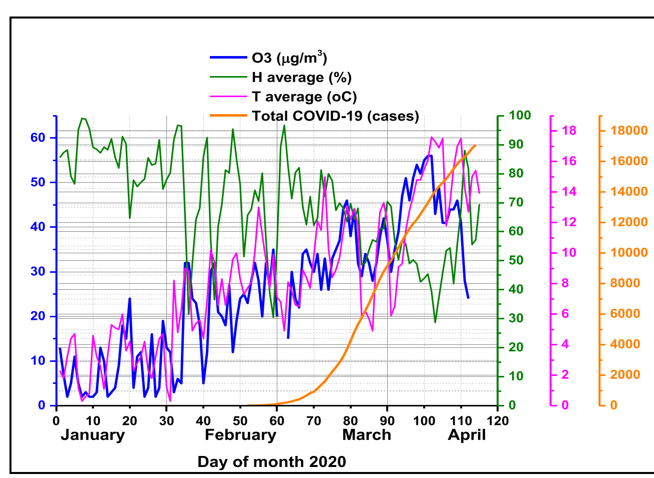


**Fig. 7.** Temporal pattern of daily average ground level $O_3$, air temperature and humidity in relation with COVID-19 Total confirmed cases in Milan over January–April 2020.

of COVID-19 cases. Results reveal that surface level O3 & NO2 concentrations in synergy with climatic and local geographic conditions, which cause the stagnation of pollutants near the ground can trigger human respiratory system damage.

## 4. Conclusion

In summary, we used a comprehensive time series analysis of the key air gaseous pollutants ozone and nitrogen dioxide, climate and coronavirus data for period January–April 2020 in order to provide additional evidence on the possible impacts of ground levels air pollution on fast diffusion effects of SARS-CoV-2, COVID-19 in Milan metropolitan city, Lombardy region in Italy. This study evidenced an inversely correlation of COVID-19 with daily average air relative humidity, and precipitation rate, showing that dry air supports viral ongoing diffusion, and positively correlation with air temperature, supporting the hypothesis that warm season will not stop COVID-19 spreading. Also, is known that chronic or short-term exposure to $O_3$, $NO_2$, particulate matter or other air pollutants, as possible carriers of viruses or bacteria has a significant negative impact of the human immune system and the pathogenesis of severe respiratory infections fast transmission in Milan, Italy. The COVID-19 lockdown in Milan led to a significant increase of ground level daily average $O_3$ concentrations by a factor of 2.25, while daily average $NO_2$ concentrations exhibited decreased levels by 64.7%. Our results have shown positive correlations between ambient ground ozone levels and negatively correlations of $NO_2$ with confirmed Total COVID-19 infections, Daily New positive and Total Deaths cases. Significant effects of $O_3$ and $NO_2$ on the transmission and severity of COVID-19 viral infections can be explained by adverse respiratory symptoms and decreasing of the immunity and respiratory systems, age or sex issues as well as specific climate and peculiar geomorphology of Milan city and Po-Valley conditions. At this moment is not clear if this protein "spike" of the new coronavirus COVID-19 is involved through mechanisms of attachment to outdoor and indoor aerosols transmission of the infectious agent from a reservoir to a susceptible host through airborne diffusion. A real understanding of the possible causes of coronavirus airborne transmission is crucial for development and selecting appropriate and effective control methods in hospitals, and the community in order to develop preventive strategies to handle the viral infection. The findings are particularly relevant to environments where coronavirus epidemics and air pollution, are currently both high, supporting the importance of sustainability and air quality improvement not only in a short-term but also in a long-term perspective.

## CRediT authorship contribution statement

**Maria A. Zoran:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Roxana S. Savastru:** Methodology, Validation, Visualization. **Dan M. Savastru:** Methodology, Validation, Visualization, Software. **Marina N. Tautan:** Methodology, Validation, Visualization, Software.

## Declaration of competing interest

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

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