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Role of meteorological factors on SARS-CoV-2 infection incidence in Italy and Spain before the vaccination campaign. A multi-city time series study

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ABSTRACT

Numerous studies have been conducted worldwide to investigate if an association exists between meteorological factors and the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection incidence. Although research studies provide conflicting results, which can be partially explained by different methods used, some clear trends emerge on the role of weather conditions and SARS-CoV-2 infection, especially for temperature and humidity. This study sheds more light on the relationship between meteorological factors and SARS-CoV-2 infection incidence in 23 Italian and 52 Spanish cities. For the purposes of this study, daily air temperature, absolute and relative humidity, wind speed, ultraviolet radiation, and rainfall are considered exposure variables. We conducted a two-stage meta-regression. In the first stage, we estimated the exposure-response association through time series regression analysis at the municipal level. In the second stage, we pooled the association parameters using a meta-analytic model. The study demonstrates an association between meteorological factors and SARS-CoV-2 infection incidence. Specifically, low levels of ambient temperatures and absolute humidity were associated with an increased relative risk. On the other hand, low and high levels of relative humidity and ultraviolet radiation were associated with a decreased relative risk. Concerning wind speed and rainfall, higher values contributed to the reduction of the risk of infection. Overall, our results contribute to a better understanding of how the meteorological factors influence the spread of the SARS-CoV-2 and should be considered in a wider context of existing robust literature that highlight the importance of measures such as social distancing, improved hygiene, face masks and vaccination campaign.

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic arose in late December 2019 in Wuhan, China. From then, sustained local transmission has occurred in most countries, leading to political, social, and economic challenges and devastating loss of life. According to data reported on February 04, 2022, by Johns Hopkins University Coronavirus Resource Center, more than 5 million people have died from COVID-19 worldwide. The first cases of COVID-19 in Italy and Spain were reported on January 31, 2020, and February 01, 2020, respectively. From then to February 04, 2022, these countries have reported 11,235,745 and 10,125,348 cases, and 147,320 and 93,857 deaths, respectively (Johns Hopkins Coronavirus Resource Center, 2021).

Since the beginning of the pandemic, there was a great interest in investigating the role of environmental exposures on the incidence of SARS-CoV-2 infection. Regarding the role of meteorological factors, there are many mechanisms that can influence the survival and transmission of SARS-CoV-2. Lower temperature enhances the lipid order of the virus envelope improving stability (Ma et al., 2020) and lower humidity favour droplet nuclei formation which prolong the viability and transmissibility of SARS-CoV-2 (Lowen et al., 2007). Moreover, cold and
dry conditions can impair the human system responses reducing the body’s ability to fight infections (WMO, 2021). Also, unfavourable climate conditions (extreme cold and heat) can shift people’s behaviour into meeting in closed spaces increasing the transmission of SARS-CoV-2 (Moriyama et al., 2020). The role of outdoor air pollution has also been extensively investigated, and the results of most of the published studies showed a significant association between exposure to various pollutants and the incidence and severity of COVID-19 (Marques and Domingo, 2022). With regards to particulate matter (PM) exposure, one of the most plausible mechanisms that explain this association is the bind of the virus droplets and PM which promotes viral diffusion in the air (Morawska and Milton, 2020).

Numerous studies have been conducted worldwide to investigate if an association exists between meteorological factors and the incidence of SARS-CoV-2 infection. Although research studies provide conflicting results, some clear trends emerge on the role of weather conditions and SARS-CoV-2 infection, especially for temperature and humidity. Most of the studies included in one of the first systematic reviews showed that cool and dry conditions favour transmission of SARS-CoV-2 (Mecenas et al., 2020). Similarly, another systematic review showed a negative correlation between SARS-CoV-2 infection incidence and temperature and humidity in most studies (Briz-Redón and Serrano-Aroca, 2020). The first meta-analysis on this topic found significant correlations between temperature, humidity and wind speed with SARS-CoV-2 infection incidence (Majumder and Ray, 2021). A more recent systematic review found a negative association between temperature and humidity with SARS-CoV-2 mortality in the majority of studies (Romero Starke et al., 2021). A more extensive systematic review, which includes 62 ecological studies, found a negative association between temperature and SARS-CoV-2 infection incidence, while conflicting results were found for humidity (Zheng et al., 2021). The authors of these systematic reviews state that findings should be interpreted with caution due to the presence of a high-risk bias and low level of evidence in most of the studies, mainly due to inadequate statistical analysis and control of confounding. Moreover, no conclusions can be drawn for wind speed, rainfall, pressure, and sunlight.

According to previous systematic reviews, much of the methodological weakness could be attributed to inadequate study designs and statistical methods (Dong et al., 2021). For example, the studies did not consider the possibility of a non-linear relation and lagged effects of weather and incidence, or they did not account for time-varying confounders, and they did not consider location-specific confounders. The time series regression method, which is often used to quantify short-term associations of environmental exposures with health outcomes, for example infection diseases (Imai et al., 2015), would allow controlling for seasonality and long-term trends and other confounding factors, autocorrelation, and explore the association for delayed exposure effects (Bhaskaran et al., 2013). Despite the advantages of this method, its use has not been overly prevalent in research, and only a few studies used it (Fang et al., 2021; Fong et al., 2021; Nottmeyer and Sera, 2021).

Another factor that may have affected the study outcomes is the choice of the geographical unit as the basis of analysis. Most of the studies consisted of country or regional level analysis, but the city levels studies are more appropriate because they allow accounting for phenomena, like high levels of population density or human mobility, which are only observable on a small scale (Bhaskaran et al., 2013). The aim of this study was to shed more light on the relationship between temperature, humidity, wind speed, ultraviolet radiation and rainfall and SARS-CoV-2 infection incidence in Italy and Spain before the vaccination campaign, using a two-stage multicentric time-series design.

2. Methods

2.1. Study data

We considered 23 Italian and 52 Spanish cities for a total of 75 cities. More specifically, we included a no-systematic sample of Italian cities for which we had available some demographic and socio-economic indicators. Regarding Spain, we included all the capital cities of Spain’s provinces. For each city, we retrieve daily time series of SARS-CoV-2 infection cases from January 30 to October 31, 2020. We defined the outcome as the daily number of SARS-CoV-2 infection cases using the data provided by the Italian (https://dati-covid.italia.it/) and Spanish (https://ecocovid.isciii.es/covid19/) governments. The cases data included all positive lab-confirmed virus test results. Dates in the dataset refer to the date at which a positive COVID-19 test result was notified. The SARS-CoV-2 time series was aggregated at lower-tier local authority resolution (provinces) and linked to the capital city of the provinces.

To define the daily time series of the exposure, we used temperature and dew point temperature time series from the ERA5 dataset. These are published by Copernicus on a regular 0.25° × 0.25° latitude/longitude grid in NetCDF format (Hersbach et al., 2018). The bi-hourly mean temperatures and dew point temperatures 2 m above the surface were averaged for each day at the closest data point available to the centroid coordinate of every city. From the daily dew point temperature and the corresponding temperature, we obtained absolute and relative humidity (AH and RH) using the R “humidity” package (Cai, 2018).

Moreover, from the ERA5 dataset, we also derived daily average wind speed (m/s), ultraviolet (UV) radiation (J/m²) and total precipitation rate (mm) as meteorological exposure variables.

As an indicator for policy measures that governments have taken to tackle COVID-19, we extracted time-series of Stringency Index data for Italy and Spain, that is an index calculated by the Oxford SARS-CoV-2 Government Response Tracker project (OxCGRT, 2020) to record the strictness of government policies. Moreover, we extracted the Google Mobility index (residential mobility) (Google, 2020). This index represents the change in duration spent at home on a given day compared to that weekday’s median in the period from January 03 and February 06, 2020, before the pandemic reached Italy and Spain (according to reported cases) (Google, 2020).

For each city, demographic background information such as population size, population density, and age proportion above 65 years was retrieved from the OECD Regional and Metropolitan database (OECD, 2016).

2.2. Statistical analysis

We investigate short-term associations between meteorological exposures and SARS-CoV-2 infection incidence using a two-stage design. In the first stage, we estimated the location-specific exposure-response association through time series regression (TSR) analysis adjusting for time-varying confounders. In the second stage, the association parameter, i.e. the model coefficients of the TSR, were pooled using a meta-analytic model. Meta-regression considers the precision of the estimate and can incorporate location-specific predictors (e.g. population density). The described two-stage statistical modelling approach was used for estimations of temperature, RH, AH, UV radiation, wind speed and total precipitation rate effects separately.

2.3. First stage analysis

In the first stage, we started the analysis 10 days before the day on which 10 confirmed cases were observed. The aim was to eliminate initial imported cases and only account for local transmission while having enough exposure data to consider a lagged effect of up to 10 days before the observed outcome. This was changed in the sensitivity analysis considering different lags.
For each location, a generalized linear model with a log link was used to model the observed SARS-CoV-2 cases assuming a quasi-Poisson distribution of case counts. The meteorological exposure variables ambient temperature, RH, AH, ultraviolet (UV) radiation, wind speed and total precipitation rate were modelled in turn using distributed lag non-linear model (DLNM) terms. In this way, possible non-linear exposure-outcome relationships were described together with non-linear delayed lag-response effects (Gasparrini, 2014).

The DLNM terms (crossbasis) act as basis function predictors in two dimensions: the exposure space and the lag space. For the exposure space, we chose as basis function the natural cubic spline function with 3 knots respectively corresponding to the 25th, the 50th, and the 75th percentile of the city-specific exposure distribution. As the current literature suggests, an approximate incubation period between 5 and 12 days for SARS-CoV-2, we considered 0–10 days as the default lag, accordingly (Lauer et al., 2020). In the lag dimension, we considered as basis function a natural spline with one internal knot.

The crossbasis terms were reduced by the lag or exposure dimensions to analyse the association on the exposure or lag dimension, respectively. The R package “dlnm” allowed to include the crossbasis-element and fit the generalized linear model of the TSR (Gasparrini, 2011). Confounding by season and long-term trends was modelled by a natural spline function of time in dates with 6 degrees of freedom (df) (Imai et al., 2015).

Lagged autocorrelation due to “true contagion” was incorporated for all days up to 5 days before. The logarithm of lagged outcome counts was used instead of past counts. (Imai et al., 2015). As time series contained days with no cases, these values were replaced by one.

Residential mobility was considered as a possible confounder as it is associated with the outcome of SARS-CoV-2 cases (via affecting population mixing) as well as the exposures (e.g. weather-dependent free time outdoor mobility), and is not on the causal pathway between the exposures and the outcome. The mobility term was modelled by a distributed linear term with a lag of 0–10 days, where the lag dimension was modelled with a natural cubic spline with one internal knot equally spaced on a log scale. We also included a week-end indicator variable as a possible confounder.

We fitted a series of first stage models considering each meteorological variable (outdoor temperature, absolute humidity, relative humidity, ultraviolet radiation, wind speed, and total precipitation rate) as main exposure (univariable models) adjusting by trend, residential mobility, and autocorrelation.

2.4. Second stage analysis

The obtained TSR coefficients and corresponding covariance matrices from the first-stage modelling at the city level were pooled via multivariate meta-regression models using a restricted maximum likelihood (REML) method for estimation (Sera et al., 2019). To consider the fact that there might be country differences between Italy and Spain the country variable was added into the meta-model at the innermost random effects level. The pooled set of spline coefficients was used to obtain the exposure-response function, which was expressed in terms of relative risk (RR) and confidence intervals (CIs). The exposure-response functions were centred to the median of the exposure distribution. For the lag-response plots, we used the 5th lag day as reference (i.e. the middle of the 10 lag days included). We used the I2-statistic which measures the relative excess in heterogeneity that cannot be explained by the sampling error (Gasparrini et al., 2012). For fitting the multivariate meta-analysis, we used the R package “mixmeta” (Sera et al., 2019).

2.5. Sensitivity analysis

The main model was tested for sensitivity considering the following modelling alterations. Firstly, we changed the lagged effect of the crossbasis from 0–10 days to 0–7 days or 0–14 days. Secondly, we analyzed the influence of using other mobility indicators considering each indicator as an alternative confounding term in the first-stage models. Moreover, an alteration of the date-term from 6 df to 4 df natural spline function was conducted. Also, we included population statistics such as population density and proportion of above 65-years-olds, poverty levels, latitude, winter, summer, and general mean temperature as well as different pollution levels in the different cities during the study period at the second stage analysis as variables in the meta-regression.

3. Results

3.1. Descriptive analysis

Overall, 1,599,251 SARS-CoV-2 cases were confirmed during the 281-day study period in the 23 Italian cities and 52 Spanish cities considered (Fig. 1).

There were huge differences in cumulative cases spanning from 1218 cases in Rieti, Italy, up to 314,953 in Madrid, Spain (Table 1). The proportion of over 65-year-olds varied between approximately 8.7 to 27.2% and pollution levels (PM2.5) in the cities varied between 8.1 and 33.4 μg/m³.

Average temperature, RH and AH-levels, ultraviolet radiation, wind speed, and total precipitation rate varied between the different cities. The overall range of observed exposure values varied between approximately 0.3 and 34.2 °C for temperature, 17.3 and 97.7% for RH, 2.1 and 22.1 g/m³ for AH, 9.6 and 368.6 J/m² for ultraviolet radiation, 0.0 and 11.4 m/s for wind speed, and 0 and 82.2 mm for total precipitation rate. More details are displayed in Table 2.

3.2. Analysis of the association

The pooled overall cumulative relationships between SARS-CoV-2 infection and meteorological factors are illustrated in Fig. 2. As shown in Fig. 2a, low temperatures were associated with an increased risk of infection. For example, a temperature of 7.0 °C corresponds to 1.42-times the baseline risk ratio (95%-CI: 1.10; 1.82) with respect to the centring point of 18.3 °C (median value). Similarly, low levels of absolute humidity are associated with an increased risk (Fig. 2b). An absolute humidity of 7.0 g/m³ corresponds to 1.37-times the baseline risk ratio (95%-CI: 1.24; 1.51) with respect to the centring point of 10.3 g/m³. For relative humidity, low and high levels are associated with a decreased risk (Fig. 2c). A value of 85.9% corresponds to 0.76-times the baseline risk ratio (95%-CI: 0.63; 0.91) with respect to the centring point of 64.7%. Regarding ultraviolet radiation, a non-linear association was observed with low and high UV levels associated with a lower SARS-CoV-2 incidence (Fig. 2d). Concerning wind speed and total precipitation rates, high levels are associated with a decreased risk. For wind speed, a value of 6.0 m/s corresponds to 0.71-times the baseline risk ratio (95%-CI: 0.53; 0.94) respect to the centring point of 2.0 m/s (Fig. 2e), while a value of total precipitation rate of 10.4 mm/day corresponds to 0.84-times the baseline risk ratio (95%-CI: 0.61; 0.97) respect to the centring point of 0.2 mm/day (Fig. 2f).

3.3. Sensitivity analysis

For all meteorological factors, changing the incorporation of 0–10 lag days down to 0–7 lag days and up to 0–14 lag days, showed that the observed effect shape on the SARS-CoV-2 risk is generally robust over the different parametrisations. However, we observed lower risks when we incorporate 0–7 lag days and higher risks when we incorporate 0–14 lag days for temperature, relative and absolute humidity (Table A.1 Appendix A). Model uncertainties around the effect estimates rise the more days are included. Changing the Stringency index with the Google community mobility reports data, we observe similar exposure-response associations (Table A.2 Appendix A). Decreasing the degrees of freedoms.
in the natural spline for long-term trends from 6 to 4 df leads to more evident associations between temperature, RH and AH and SARS-CoV-2 incidence (Table A.3 Appendix A). Also, adding the population density, age proportion above 65 years, poverty levels, latitude, average daily mean temperature and the pollution levels of the cities into the meta-regression, produced similar exposure-response associations (Table A.4 Appendix A). Stratifying for the country, we observed more pronounced risk ratios in Italian cities than in Spanish ones, specifically for temperature, relative and absolute humidity (Table A.5 Appendix A).

4. Discussion

4.1. Main findings

The analysis showed an association between meteorological factors and SARS-CoV-2 infection incidence. Specifically, low levels of ambient temperatures and absolute humidity were associated with an increased risk. Regarding relative humidity, low and high values were associated with lower risk. Low and high levels of ultraviolet radiation were associated with a decreased risk. Concerning wind speed and rainfall, high levels were associated with a decreased risk.

4.2. Possible mechanisms explaining the main results

The influence of low ambient temperature and absolute humidity on the number of SARS-CoV-2 cases could in part be attributed to the increase in the stability of SARS-CoV-2 in these environmental conditions (Christophi et al., 2021). The nonlinear relationship could be partially explained by the human behaviour change induced by climate conditions, with more time spent in closed spaces at high temperatures and humidity. For relative humidity, high values favour the increase and the fall of the droplet size reducing the risk of infection (Ahlawat et al., 2020). The results of UV radiation were unexpected under the hypothesis that UV light could cause the inactivation of viruses in the air and on surfaces (Nicastro et al., 2021, p. 2). The non-linear association in our study, with low and high levels of radiation associated with lower risk,
could be explained by the effects of weather-dependent human behaviour change and warrants further investigation.

The role of higher wind speed could be explained by the reduction of the levels of air pollutants, which increase the risk of adverse health effects to a broad population, especially for more vulnerable groups (Dettori et al., 2021). In addition, higher concentrations of PM promote a longer permanence of the viral particles in the air facilitating entry into the respiratory system (Solimini et al., 2021). Similarly, the washing effect of rainfall on particulate matter concentrations could explain the lower relative risk associated with the increase of the total precipitation rate (Liu et al., 2020).

4.3. Comparison with existing literature

To our knowledge, there has been little research that investigates the association between meteorological factors and SARS-CoV-2 infection incidence in Italy and Spain using time-series regression.

The relationship between temperature, absolute and relative humidity and COVID-19 mortality in Milan was investigated by Khursheed et al., 2021 (Khursheed et al., 2021). The authors used generalized additive models (GAMs) to model non-linear trends in time-series data from 23 February to 31 March 2020. The results showed a negative relationship between the three meteorological variables considered and COVID-19 death cases. Specifically, a decrease in COVID-19 mortality of 2.75% (95%-CI: 0.46%, 5.21%) was observed per unit increase in temperature. For absolute and relative humidity, a decrease in COVID-19 mortality of 3.54% (95%-CI: 0.65%, 5.81%) and 3.01% (95%-CI: 0.57%, 5.31%) was observed per unit increase, respectively.

Lolli et al. (2020) also considered wind speed as an explanatory variable to evaluate the impact of meteorological conditions on the number of hospitalized patients in Intensive or Sub-Intensive Care Unit in Milan, Florence, and the province of Trento over 103 days (March 08...
to June 19, 2020) (Lolli et al., 2020). The authors used non-linear Spearman and Kendall rank correlation tests to investigate the role of environmental conditions. Temperature, dew point temperature, absolute humidity, water vapour were negatively correlated with the virus transmission, while wind speed and atmospheric pressure show uncertain results.

Tobias et al. (2021) evaluated the influence of temperature, absolute humidity and solar radiation levels on the incidence of COVID-19 in Catalonia (Tobias et al., 2021). The authors used a Poisson regression model to evaluate the association for each county, then the county data were pooled to obtain the estimated effects as relative risks. A decrease of COVID-19 incidence of 6% (RR = 0.94, 95%-CI: 0.85, 1.04) was observed per unit increase in temperature. For absolute humidity and solar radiation, a decrease in COVID-19 incidence of 1.2% (RR = 0.99, 95%-CI: 0.85%, 1.04%) and 1.5% (RR = 0.98, 95%-CI: 0.97%, 1.02%) was observed per unit increase, respectively.

Linares et al. (2021) analyzed the association between daily temperature and absolute humidity with the daily incidence, hospital and intensive care unit admissions, and death rates in the period from February 01 to May 31, 2020, for the City of Madrid (Linares et al., 2021). The authors showed that temperature and absolute humidity are negatively associated with all of the dependent variables considered, except in the case of deaths.

4.4. Strengths and limitations

This study has several strengths. The analysis was based on a large representative dataset which consist of daily values in 75 cities for 281 day-period allowing to obtain a higher statistical power. Also, we added to the models less-studied variables, which are wind speed and total precipitation rate, investigating their influence on SARS-CoV-2 infection incidence. Moreover, we used time-series models which allows to consider time varying confounders as seasonality, long-term trend and other factors (Imai et al., 2015). We also took into consideration the time lag between the moment a person becomes infected with the lab-confirmed virus test results.

A limitation of this study is that the number of SARS-CoV-2 infection cases is most likely lower than the true number of total cases. Another limitation of our analysis is that we considered the early pandemic phase, in which the role of meteorological factors could be less incisive than in the later stages of the pandemic, but this choice was made to limit the confounding role of vaccination campaign. Also, during observation period the surveillance system has improved, e.g. increasing the number of test performed on the population. This could lead to a spurious trend that could confound the association between meteorological variables and SARS-CoV-2 spread. In our analysis, we tried to mitigate this bias considering in the time-series models non-parametric function of time. An additional limitation is the potential role of socio-economic factors as possible confounders (Phorsri et al., 2021). In the sensitivity analysis, we adjusted the models for some demographic and socio-economics factors, and we did not observe relevant differences from the main model. We also adjusted the models for public holidays, and we did not notice any appreciable difference.

On reporting the results, we expressed the effects of meteorological variables relative to a reference level set to be the median of observation distribution. We obtained associations curves representing how the relative risk change by different levels of the meteorological variables, which can be compared with the results of previous studies (Guo et al., 2021; Nottmeyer and Sera, 2021; Yamasaki et al., 2021; Zhu et al., 2021). This representation underestimates uncertainty in the reference level and overestimates uncertainty in other exposure levels. Some authors have proposed different approaches, e.g. plotting the predicted incidence curve (Greenland et al., 1999), but these methods have not been applied yet in complex multi-city time-series studies with lagged effects and require further methodological developments.

Lastly, we only considered the number of confirmed cases, but further analysis could also investigate the role of meteorological factors on hospitalization and mortality due to COVID-19.

5. Conclusions

To our knowledge, this is the largest study that investigates the relationship between meteorological factors and SARS-CoV-2 infection incidence in Italy and Spain. The main strengths of this study are the large number of cities analyzed, the two-stage time-series design, and the inclusion of less studied variables, namely wind speed and rainfall. Our results show that low values of temperature and absolute humidity are associated with higher relative risks of infection. The nonlinear relationships observed could be explained by the change of human behaviours with the different climate conditions. On the other hand, low and high levels of relative humidity are associated with a decreased risk. Very high as well as low ultraviolet radiation was associated decreased risks. Regarding wind speed and rainfall, their role in reducing air pollution could explain the lower relative risks observed with the increase of them. To conclude, we believe that our results could contribute to a better understanding of how the meteorological factors influence the spread of the SARS-CoV-2. These results should be considered in a wider context of existing robust results which highlight the importance of measures such as social distancing, improved hygiene, face masks and vaccination campaign.

Credit author statement

Gabriele Donzelli: Formal analysis, Writing – original draft. Annibale Biggeri: Writing – review & editing. Aurelio Tobias: Writing – review & editing. Luise N. Nottmeyer: Writing – review & editing. Francesco Sera: Supervision, Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

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Declaration of competing interest

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

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Appendix A. Supplementary data

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