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Environmental and climatic impact on the infection and mortality of SARS-CoV-2 in Peru

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Abstract

Objectives: The role of the environment and climate in the transmission and case fatality rates of SARS-CoV-2 is still being investigated a year into the pandemic. Elevation and air quality are believed to be significant factors in the development of the pandemic, but the influence of additional environmental factors remains unclear.

Methods: We explored the relationship between the cumulative number of infections and mortality cases with climate (temperature, precipitation, solar radiation, water vapor pressure, wind), environmental data (elevation, normalized difference vegetation index or NDVI, particulate matter at 2.5 µm or $PM_{2.5}$ and NO_2 concentration), and population density in Peru. We use confirmed cases of infection from 1,287 districts and mortality in 479 districts, we used Spearman's correlations to assess the bivariate correlation between environmental and climatic factors with cumulative infection cases, cumulative mortality and case-fatality rate. We explored district cases within the ecozones of coast, sierra, high montane forest and lowland rainforest.

Results: Multiple linear regression models indicate elevation, mean solar radiation, air quality, population density and green vegetation cover, as a socioeconomic proxy, are influential factors in the distribution of infection and mortality of SARS-CoV-2 in Peru. Case-fatality rate was weakly associated with elevation.

Conclusions: Our results also strongly suggest that exposure to poor air quality is a significant factor in the mortality of individuals below the age of 30. We conclude that environmental and climatic factors do play a significant role in the transmission and case fatality rates in Peru, however further study is required to see if these relationships are maintained over time.

Keywords: age groups; air quality; COVID-19; elevation; gender; solar radiation.

Introduction

As SARS-CoV-2 spread around the world within a few months of detection, several groups of investigators are looking into the different factors that could be related to the distribution of the infection and the severity of the disease. The incidence of infection in different countries and cities suggests that several factors influence the rate of infection, which are not only related to the virus and the immune system. In the case of Peru, the cities that have the most cases are generally located near the coast and have poor air quality throughout the year (https://www.datosabiertos.gob.pe/). In addition, population density seems to be a key factor in the spread of the virus, where overcrowded cities increase the probability of contact with infected individuals, increasing the number of infection and mortality cases in a short amount of time. Therefore, population density has been taken into account as one of the cofactors in SARS-CoV-2 distribution.

Although more studies are necessary, the rate of infection and the severity of the diseases seems different for people living in cities at high altitudes, where not only hypoxia is a major factor, but other factors such as air quality, solar radiation, and population density, could play a role in SARS-CoV-2 person-to-person transmission. Arias-Reyes et al. [1] suggested that there exists less rate of infection at high altitude possibly due to a lower level of expression of ACE2 compared to sea level. This observation is important, particularly since SARS-CoV-2 uses ACE2 as a point of infection for the cells [2]. Yao et al. [3] explored the rate of SARS-CoV-2 infection across China, and concluded that there was no correlation between temperature, UV, and the rate of infection. However, they recommended future studies using more complex models and environmental factors. Finch et al. [4] explored the role of pollution exposure in the development of different diseases, where heart and respiratory diseases indicated a detrimental role of pollution on the endothelial integrity, and the changes

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in the levels of Endothelin I could be observed in people that were exposed to air pollution [5].

Environmentals factors related to mechanics of different viruses spread have been studied by several groups, before the pandemic. Pica et al. [6] studied the environmental factors related to the spread of seasonal influenza and concluded that some meteorological factors play a central role in the person-to-person transmission of the virus, besides the sociodemographic factors. It is well known that UV radiation can decontaminate surfaces and air, and UV incidence increases at higher elevations and cities will have different exposures depending on their location. Kowalski [7] demonstrated that the UV light can destroy a bacteria, many viruses, and fungi, but additional studies are necessary to understand the impact of UV on SARS-CoV-2 in the natural environment, since no amount of germicidal UV-C and only 5% of UV-B reaches below the Earth's surface [8].

A growing body of research indicate that environmental and climatic factors, specifically temperature and air pollution, may indeed be factors in the heterogeneous distribution and rate of infection and mortality of SARS-CoV-2 in many parts of the world. Lower average temperatures and relative humidity seem to contribute to the increase the number of total infections in various cities from a range of climates, such as the temperate to subtropical climates in China [9], Mediterranean climate of Italy [10] and tropical and subtropical climates in Brazil [11]. Similarly, increasing air pollution density, particularly with particulate matter at 2.5 μm ($PM_{2.5}$) and nitrogen dioxide (NO_2), has been associated with increasing SARS-CoV-2 infection and mortality in different parts of Europe [12–14], Asia [15–17], and the America [18, 19]. However, it is less clear which factors may be contributing to the lower rates of infection at high altitudes, principally due to confounding factors and lack of data [8].

Understanding all the factors that are related to the spread of SARS-CoV-2 will be an important part of public policy, particularly toward the implementation of focalized quarantines in cities and districts where the cases of infection are high and the implementation of effective vaccination distribution. Therefore, this study aims to explore the different cofactors that could increase or decrease the possibility of person-to-person transmission of SARS-CoV-2. The main objectives of this study was to explore the relationship between SARS-CoV-2 infection and mortality cases, case-fatality rates with a set of climate (temperature, precipitation, solar radiation, water vapor pressure, and wind), environmental data (elevation, normalized difference vegetation index or NDVI, particulate matter at 2.5 μm or $PM_{2.5}$ and NO_2 concentration), and population density in Peru. We also divide the distribution of infection, mortality, and case-fatality rates by four ecozones (coast, sierra, high montane forest, and lowland rainforest) and subset mortality cases by age groups and gender.

Materials and methods

We obtained SARS CoV two confirmed cases by district, of the 1873 districts in Peru, from official reports provided by the Peruvian Ministry of Health (MINSA), through an official government open data portal (https://www.datosabiertos.gob.pe/). We used the cumulative number of confirmed cases of infection from 1,287 districts and confirmed cases of mortality in 479 districts, where at least one confirmed case was registered as of June 27, 2020 (Figure 1a). The first case of SARS-CoV-2 was registered on March 5, 2020. Under this criteria, the number of positive SARS-CoV-2 cases analyzed were 263, 743 and 7,877 deaths by June 27, 2020. Available data of infection included date of confirmation, while data on mortality included age, sex, and date registered. The first confirmed case of SARS-CoV-2 in Peru was on March 6, 2020. Infection and mortality values were log-transformed to meet statistical assumptions in relation to residuals and added one to avoid taking the logarithm of 0 [9, 16, 17, 20].

We also assessed case-fatality rates, which implies the severity of the condition by estimating the proportion of cases that die of a given condition [21]. The case-fatality rate was estimated by dividing the number of cause-specific deaths among the incidence cases by the total number of incident cases*100 [22].

We labeled districts based on four ecozones, including coast, sierra, high montane forest, and lowland rainforest (Figure 1d), which was originally developed based on elevation and biogeography and used in national and international reporting, and have a significant effect on agricultural activity, population density, population connectivity, and other socioeconomic activities ([23]; see Supplementary Materials for more details).

Climate and environmental data

A set of climate metrics were obtained from WorldClim version 2.1 [24], which presents a historical baseline from the years 1979–2000 and includes monthly temperature, rainfall, wind speed, and solar radiation. Satellite-based environmental data was obtained from a variety of satellite sensors that detect environmental variables, including elevation, vegetation cover, and air quality. Vegetation cover was estimated through NDVI (Normalized Difference Vegetation Index), a commonly used spectral index used to quantify green cover, including agricultural extent, forest cover, and green cover in urban settings. We infer air quality through the metrics of two health-relevant air pollutants, which include particulate matter at 2.5 μm ($PM_{2.5}$) and nitrogen dioxide (NO_2; Figure 1c). Population density was obtained from the WorldPop model of population density (people km^{-2}) for Peru adjusted to match official United Nations population estimates for the year 2020 (www.worldpop.org; Figure 1b). Further details on climate data and satellite-based environmental data are provided in the online Supplementary Materials.

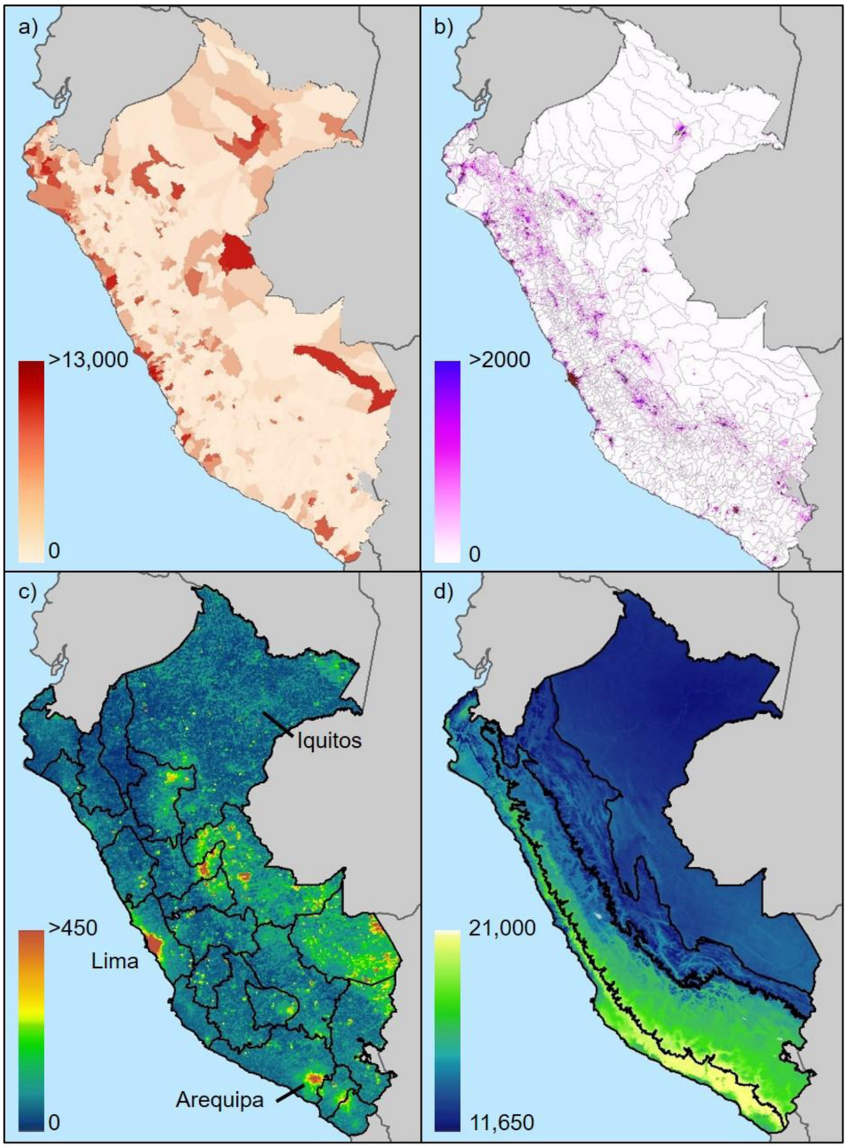

Figure 1: a) Cumulative number of confirmed infected cases per district, b) modeled population density (people km^{-2}) for the year 2020, c) maximum tropospheric NO_2 density (μmol m^{-2}) for 2019, and d) mean solar radiation (kJ m^{-2} day^{-1}). Outlines in panels a) and b) are district boundaries, while outlines in c) indicate departmental boundaries and d) (left to right) the coast, sierra, high montane forest and lowland rainforest ecozones.

Data analysis

We extracted the zonal statistics by district (i.e. average value per district polygon) of each of the climate, remotely sensed, and population density layers using ArcPro (verison 2.2). We used SPSS 25.0 (IBM, USA) for all statistical analysis of the extracted values. We used the one-sample Kolmogorov-Smirnov parametric test to evaluate the distribution of residuals obtained for each district from each of the original 36 data layers used. Bivariate covariance within the subsets of climate and environmental variables were estimated with Spearman's Rho correlation, (following [16, 17], where correlation of the order of 0.9 or larger were determined to have a high covariance. As a result, the final reduced data set used in this study were 21 data layers, including 14 climatic layers, six environmental layers and the population density model (Table S1). The climatic layers included four temperature, four rainfall, two solar radiation, two wind speed, and 2 water vapor metrics. All six environmental layers and the population density model had a relatively low level of covariance and were kept for further analysis. The climate and environmental data were also normalized (following [16, 17], due to the different units used in each variable, through the following method:

$$X = X_n - X_{an}/S_n \tag{1}$$

Where X is the normalized data, X_n is the raw data for the variable, X_{an} is the mean value of the raw data, and S_n is the standard deviation of X_n.

We used stepwise linear regression to explore the association of climatic and environmental variables with the log-transformed data of cumulative number of confirmed cases of infection and confirmed cases of mortality, across Peru and within ecozones. The numbers of cases were used as dependent variables, and the environmental and climatic were selected as independent variables. The resulting statistically significant predictive models use one or multiple variables that best explain the dependent variable. The adjusted R^2 from model fitting indicates the percentage of all factors that explain the distribution of cases and the magnitude of the standardized β reflects the influence of the corresponding variable in the predictive model.

Collinearity diagnostics, resulting from the regression, were also used to identify model variables that were highly correlated. Significant differences between means were evaluated using one-way ANOVA followed by a Tukey test.

Results

The district of San Juan de Lurigancho, of the department of Lima and in the coastal ecozone, had the most number of confirmed infected cases and case fatalities of SARS-CoV-2, with 13,724 total infections and 394 fatalities, up until the date of the data obtained for this study. The average number of confirmed cases of infection and fatalities was 205 (SD ± 938) and 16.4 (SD ± 42.2) per district, respectively. Across ecozones, the number of registered male fatalities was 5,601 (71.1%) and that of females were 2,276 (28.9%). The average age of total male fatalities was 64.2 (SD ± 15.6) and females was 66.3 (SD ± 15.9). There was also a significant difference between ecozones for mean age of fatalities and female only cases, but not in male only cases (see Table S2). We found no significant difference between the mean case-fatality rates by ecozones (F=0.34, p=0.80).

Correlation analysis indicated a positive correlation of total infections with $PM_{2.5}$ (ρ=0.449) and a negative correlation with elevation (ρ=–0.476), where the number of infections correlates with increased air pollution, while there are less number of infections with elevation Figure S1). Similarly, correlation analysis indicated a high positive correlation coefficient between mean tropospheric NO_2 (ρ=0.497, p<0.001), $PM_{2.5}$ (ρ=0.506; p<0.001) and registered mortality across sexes and in the male population with ρ=0.504 and ρ=0.486, respectively.

In stepwise linear regression model fitting, the three most important parameters that explain the distribution of cumulative number of infections across the country (R^2=0.46; p-value=0.038) were NDVI (β=–0.392), elevation (β=–0.311), and mean solar radiation (β=–0.244) (Table 1). The negative correlation indicates a decrease in the cumulative number of infections, with an increase in surrounding green cover (NDVI). In addition, the cumulative number of infections decreases with increasing elevation and increasing mean solar radiation. Within each ecozone, parameters importance change indicating the importance of population density (β=0.474) in the coast, NDVI (β=–0.359) in the sierra, maximum NO_2 (β=0.352) in high montane forest, and elevation (β=–0.441) in lowland rainforest.

Model fitting for cumulative mortality cases across the Peru indicated the negative correlation of NDVI (β=–0.299), elevation (β=–0.245), and mean solar radiation (β=–0.230), and the positive correlation with mean NO_2 (β=0.237) and population density (β=0.215) (Table 2). Population density was the most influential factor for mortality in the coastal ecozone, lowland rainforest, and male and female mortality across the country. It is worth noting that adjusted R^2 indicated that the models included at least 28% of the factors that affect the difference in mortality.

Regarding age groups, mean NO_2 was the most influential factor of difference of mortality for individuals with an age range of 0–17 (β=0.654) and 18–29 (β=0.422) (Table 3). Population density was the most influential factor for the remaining age ranges of 30–49 (β=0.306), 50–70 (β=0.483), and above 80 (β=0.309). However, it is worth noting that mean NO_2 was indicated as an influential factor for mortality for the age ranges of 30–49 (β=0.236) and above 80 (β=0.258).

Table 1: Predictive models of the relationship of cumulative case infection and environmental and climatic variables.

Dependent	Predictors	Standardized β	R^2	Adj. R^2	p-Value
Cumulative inf.	NDVI	−0.392	0.46	0.46	0.04
	Elevation	−0.311			
	Radiation mean	−0.244			
	NO_2 max	0.171			
	NO_2 mean	0.057			
	$PM_{2.5}$	0.129			
	Pop. density	0.150			
	Wind mean	−0.081			
	Radiation (SD)	−0.077			
Coast	Pop. density	0.474	0.35	0.34	0.03
	Elevation	−0.199			
	PM2.5	0.163			
Sierra	NDVI	−0.359	0.50	0.50	0.02
	Radiation mean	−0.272			
	Elevation	−0.244			
	NO_2 mean	0.191			
	$PM_{2.5}$	0.171			
	Pop. density	0.131			
	Wind SD	−0.077			
High montane rainforest	NO_2 max	0.325	0.40	0.39	<0.001
	$PM_{2.5}$	0.266			
	Elevation	−0.253			
Lowland rainforest	Elevation	−0.441	0.37	0.35	0.001
	Pop. density	0.327			

Table 2: Predictive models of the relationship of mortality across and within ecozones and environmental and climatic variables.

	Predictors	Standardized β	R^2	Adj. R^2	p-Value
Cumulative mortality	NDVI	−0.299	0.48	0.48	<0.001
	Elevation	−0.245			
	NO_2 mean	0.237			
	Radiation mean	−0.230			
	Pop. density	0.215			
Male	Pop. density	0.250	0.46	0.45	<0.001
	NDVI	−0.245			
	NO_2 mean	0.229			
	Elevation	−0.223			
	Radiation mean	−0.200			
Female	Pop. density	0.379	0.33	0.33	0.015
	NO_2 mean	0.191			
	Elevation	−0.136			
Coast	Pop. density	0.502	0.37	0.36	<0.001
	$PM_{2.5}$	0.335			
Sierra	Elevation	−0.274	0.51	0.50	0.005
	NDVI	−0.273			
	Pop. density	0.253			
	NO_2 mean	0.193			
	Radiation mean	−0.162			
High montane rainforest	NO_2 max	0.576	0.55	0.53	0.003
	$PM_{2.5}$	0.139			
Lowland rainforest	Pop. density	0.548	0.30	0.28	<0.001

Table 3: Predictive models of the relationship of age of mortality and environmental and climatic variables.

Age range	Predictors	Standardized β	R^2	Adj. R^2	p-Value
0 to 17	NO_2 mean	0.654	0.43	0.40	<0.001
18 to 29	NO_2 mean	0.422	0.18	0.16	0.001
30 to 49	Pop. density	0.306	0.28	0.27	0.004
	NO_2 mean	0.236			
	Elevation	−0.14			
50 to 79	Pop. density	0.483	0.28	0.27	0.034
	Elevation	−0.14			
≥80	Pop. density	0.309	0.36	0.35	0.046
	NO_2 mean	0.258			
	$PM_{2.5}$	0.164			
	Solar radiation mean	−0.113			

A positive correlation from model fitting was found between case fatality rates and elevation (β=0.318), although a relatively low explanatory factor (R^2=0.12; p-value=0.015) compared to most predictive models performed in this study (Table 4). Indeed, case fatality rate models had the lowest R^2, although statistically significant ($p<0.05$), compared to models for infection and mortality. Elevation was the most influential factor for the coast (β=0.281), sierra (β=0.303), and high montane forest (β=0.466). Mean diurnal range was the main factor for case fatality rates in high montane forests (β=0.466) and the only climate variable to appear as a factor for model fitting in this study.

Discussion

Our study found that several environmental factors are influential in the cumulative number of SARS-CoV-2 infection and mortality, with particular factors having apparently significant roles in specific scenarios. Generally, the cumulative number of infections is reduced with increased elevation and solar radiation, but other factors such as poor air quality and population density have significant roles. Surprisingly, NDVI, as a measure of green vegetation cover and socioeconomic level in urban settings [25], was a strong predictive factor of SARS-CoV-2 infection (see Table 1). Previous studies have found that more affluent suburbs in Peru tend to be less populated, have more green space that reflects higher property values [25], and therefore, residents may be more likely to have access to private health measures and are physically distant, which could decrease rates of infection in the longer term.

Table 4: Predictive models of the relationship of case fatality rates and environmental and climatic variables.

	Predictors	Standardized β	R^2	Adj. R^2	p-Value
Peru	Elevation	0.318	0.12	0.12	0.015
	NDVI	0.106			
Coast	Elevation	0.281	0.08	0.06	0.022
Sierra	Elevation	0.303	0.12	0.11	0.029
	NDVI	0.117			
High montane forest	Elevation	0.466	0.22	0.20	<0.001
Lowland rainforest	Mean diurnal range	0.460	0.21	0.19	0.002

Once we separate infection and mortality by ecozones, the influence of environmental factors is similar to looking at Peru as a whole, with a few notable exceptions. Solar radiation is a much more influential factor in the Sierra, where there are strong geographic and heterogeneous patterns particularly in the south, and UV radiation is known to be strong in these drier environments (see Figure 1d). If we take into account the UV radiation as a possible factor that could decrease the survival of the virus in the air, this could account for the decrease of infected people in the sierra and in the south of the country. However, we do acknowledge that further research is necessary to understand how the specific UV band is effecting SARS-CoV-2, as noted by Pun et al. [8]. Our study does provide the most numerous number of districts with infection and mortality data at high elevation and geospatial data on UV radiation to begin to understand that differences in UV-B concentration in different regions may be indicative of limiting conditions for infection other than temperature, which was not a significant factor in our study.

Mean NO_2 concentration is an overriding factor for the cumulative number of mortality for ages below 30. Higher mean NO_2 concentration is indicative of anthropogenic activity, such as fossil fuel consumption and biomass burning, which occur in more population dense districts, but it is only moderately correlated with population density in Peru. Mean NO_2 concentration in 2019 was highest in the metropolitan cities of Lima, Arequipa and the small southern city of Moquegua, where NO_2 density of above 250 µmol m^{-2} were found year round. Seasonal high concentrations, due to agricultural and other biomass burning, are found in cities in the Amazon basin during the dry season. The overall detrimental effects of air pollution on the health and mortality within populations, in accordance to type and length of exposure is known [26], along with other studies exploring its effects on the current pandemic [27].

Unlike male mortality, we found a significant difference in the mean age of women who died across ecozones in Peru, with a higher average age for women in the Sierra. To our knowledge, this is the first study to indicate the multiple environmental factors that seem to influence female mortality, including a negative correlation with elevation and mean solar radiation, but a larger positive correlation with population density, NDVI and mean NO_2 density. Female mortality from SARS-CoV-2 is lower than males in all the countries possibly due to the expression of the ACE2 (angiotensin-converting enzyme 2) receptor regulated by female hormones. However, protection is lost in older women, as the levels of hormones decrease. The probability of infection in older women becomes similar to their male counterpart, but there is still a higher rate of fatalities in men than women independent of age [28].

Our study also found elevation to be an influential factor in case fatality rate for the coast, sierra, high montane forest, lowland rainforest, and the country as a whole when looking at the data at the district level. This is contrary to the findings of [21]; which studied cases at the provincial level, instead of the district level, and found that the case fatality rate was not modified by elevation. Our analysis indicates a rather weak but statistically significant correlation. However, we acknowledge that further studies still need to be conducted to see if this relationship continues throughout the course of the pandemic.

Ultimately, our study provides a different perspective to understanding the factors effecting SARS-CoV-2 infection and mortality due to the greater number of environmental and climate variables available for analysis. Increasing elevation were found to be influential factors, as described in [1]. However, no temperature metric, including lower average temperature identified as important factors in refs. [9, 11]; were statistically significant contributors to the predictive models. When evaluating a larger set of factors, environmental variables, such as air quality, solar radiation, and elevation, appear to be more significant factors than either temperature or precipitation, which may reflect the more environmentally and climatically heterogeneous region. Notwithstanding, our research adds to the growing body of studies that strongly indicate that poor air quality is among the most significant factor of number of infection and mortality in any region of the world.

The limitations of this study are indicative of the asymptomatic nature of SARS-CoV-2 for many patients. It is currently unclear the magnitude of underestimation occurring at the present time and accurate numbers may not become available until widespread molecular testing is performed. As of December 2020, the Peruvian government continues to resist deploying a widespread molecular testing regime. Also, news reports indicate that the cumulative number of mortality may also be significantly underestimated due to the lack of testing and patient care in overwhelmed urban and rural hospitals, particularly during the peaks of SARS-CoV-2 infection.

Conclusion

Elevation is one of several factors that has determined the number of infections and mortality. Other significant factors include population density, air quality, solar radiation and NDVI, as a measure of both green vegetation cover and socioeconomic level. Poor air quality was the single most important factor to determine mortality below the age of 30. We also found that case fatality rate is modified, albeit weakly, by elevation, which is contrary to previously published findings. As more data becomes available, this study can be replicated to see if the relationship between SARS-CoV-2 and climatic and environmental factors are maintained over time.

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