Altitude and SARS-CoV-2 Infection in the First Pandemic Wave in Spain: An Ecological Study

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Research

Abstract

Background

After the first pandemic wave, a nationwide seroepidemiological survey assessed the seroprevalence of SARS-CoV-2 antibodies in the population of Spain and found notable differences among provinces whose causes remain unclear. The present study aimed to examine the influence of environmental factors on SARS-CoV-2 infection.

Methods

This ecological study analyzed the association between environmental and demographic factors and SARS-CoV-2 infection by province. Environmental temperature and humidity were obtained from the Spanish Meteorological Agency and province extension, and latitude and altitude above sea level of their capital cities from the Geographical Institute. The seroprevalence SARS-CoV-2 antibodies by province was obtained from a nationwide representative survey performed in June 2020, after the first pandemic wave in Spain. Linear regression was used in the analysis.

Results

The seroprevalence of SARS-CoV-2 antibodies of the 50 provinces ranged from 0.2% to 13.6%. Altitude explained nearly half of differences in seroprevalence (determination coefficient [R^2]=0.46, p<0.0001). Seroprevalence in people residing in provinces above the median altitude (215 meters) was threefold higher (6.5% vs 2.1%, p<0.0001). In the multivariate linear regression, the addition of population density significantly improved the predictive value of the altitude (R^2=0.55, p<0.0001). Every 100 meters of altitude increase and 100 inhabitants/km^2 of increase in population density, the seroprevalence increased by 0.84 and 0.63 percentage points, respectively.

Conclusions

Environmental conditions related to higher altitude in winter-spring, as lower temperature and absolute humidity, may be relevant to SARS-CoV-2 transmission. Places with such adverse conditions may require additional efforts for pandemic control.

Introduction

The first wave of the SARS-CoV-2 pandemic spread in Europe in March and April 2020, showing important geographical differences whose causes remain unclear [1]. The role of environmental and demographic conditions on SARS-CoV-2 transmission is not well known. Geographical comparisons have associated higher atmospheric temperature and humidity with lower SARS-CoV-2 transmission [2–5]. However, these studies may be affected by differences in the completeness of COVID-19 reporting in the first wave, since a high and variable percentage of cases were not confirmed [5]. Furthermore, those

studies that compare countries may be also affected by the differences in the introduction of preventive interventions [6, 7].

Spain is a mountainous and climatically diverse territory that was one of the first and most severely affected countries in Europe [1, 8]. Transmission increased steeply during the first half of March, and the main intervention was a lockdown implemented simultaneously in all Spanish regions on March 15 [9]. As no other relevant intervention was introduced, the important geographical differences observed in COVID-19 cumulative incidence in the first pandemic wave were probably related to case reporting, and to environmental and socio-demographical factors [2–6].

This study aimed to assess the possible influence of several environmental and demographic factors on the differences in the transmission of SARS-CoV-2 among province in Spain.

Material And Methods

This ecological study analyzed environmental and demographic factors to explain the geographical differences among provinces in the seroprevalence of SARS-CoV-2 antibodies after the first pandemic wave in Spain.

Data collection

Spain is divided into 50 provinces whose capital city is usually the most populated municipality. A nationwide Seroepidemiological Survey of SARS-CoV-2 Infection was performed in a representative sample of the population [10]. The first round of this survey included a representative sample of persons of each province who were recruited from April 27 to May 11, 2020. Immunoassay was performed for detection of IgG against SARS-CoV-2 in 51,958 persons. The seroprevalence of IgG antibodies was estimated by province [10].

Population data by January 2020 were obtained from the National Institute for Statistics. The Geographical Institute was consulted to obtain the province extension, as well as the latitude and altitude above sea level of their respective capital city (https://www.ign.es/web/ign/portal/ane-datos-geograficos/-/datos-geograficos/datosPoblacion?tipoBusqueda=capitales). Population density was calculated as inhabitants per km^2.

Since the increasing part and the peak of the pandemic wave took place in March 2020, and the lockdown started on March 15 and continued up to May, the meteorological conditions in March were considered relevant to evaluate their potential effect on SARS-CoV-2 transmission. From the National Meteorological Agency, we obtained the monthly mean of each capital city for relative humidity, as well as, daily maximum, minimum and mean temperatures in Celsius degrees (ºC) (https://opendata.aemet.es/centrodedescargas/productosAEMET?). Absolute humidity was calculated as a function of relative humidity, mean temperature, and atmospheric pressure.

Statistical analysis

Quantitative variables were presented as mean, standard deviation, median and range. Means were compared by the student t-test. Categorical variables were presented as percentages and compared by χ^2. Linear regression analysis was used to test the predictive value of each variable on the seroprevalence by province. The determination coefficient (R^2) was calculated as indicator of the proportion of the seroprevalence variability that was explained by the model.

Results

The seroprevalence of SARS-CoV-2 IgG antibodies of the 50 Spanish provinces ranged from 0.2–13.6%. Variability among capital cities was considerable in altitude (range from 5 to 1131 meters) and population density (range from 9 to 840 inhabitants/km^2). Very important differences were also observed in the average maximum, minimum, and mean temperatures in March 2020, as well as in average atmospheric absolute humidity (Table 1).

Table 1
Descriptive analysis of the variables considered for the 50 provinces, Spain.*

	Mean	SD	Range	Median
Seroprevalence of SARS-CoV-2 IgG, %	4.3	3.8	0.2–13.6	2.8
Altitude above sea level, m	370	362	5-1131	215
Latitude in degrees	39.9	3.2	28.1–43.3	40.5
Average absolute humidity (g/m^3)	7.3	1.3	4.9–10.6	7.3
Average of daily maximum temperatures	17.0	2.5	12.7–22.3	16.5
Average of daily minimum temperatures	7.0	3.6	1.0-16.1	6.6
Average of daily mean temperatures	11.9	3.0	6.2–19.2	11.7
Population (in thousands)	943	1208	90-6747	643
Extension (km^2)	9921	4805	1980–21766	9992
Density of population (inhabitants per km^2)	132	174	9-840	63

*Seroprevalence of SARS-CoV-2 IgG antibodies obtained by immunoassay test from April 27 to May 11, 2020. Meteorological variables were average variables of March 2020 referred to the province capital cit. Temperature in Celsius degrees. Altitude and latitude were referred to the province capital city.

In bivariate analyses, a higher altitude, a lower absolute humidity, and lower averages of daily maximum, minimum and mean temperatures were statistically significantly associated with a higher seroprevalence in the province. Altitude was the strongest predictive variable for the seroprevalence (R^2 = 0.46) (Table 2 and Figure).

Table 2
Results of linear regression at the province level (n = 50) between environmental and demographic variables and the seroprevalence of IgG antibodies against SARS-CoV-2 obtained by immunoassay test from April 27 to May 11, 2020, Spain.

	Beta	SE	p value	R^2
Bivariate analyses				
Altitude above sea level (per 100 m) *	0.71	0.11	< 0.001	0.47
Latitude in degrees *	0.19	0.17	0.261	0.03
Average absolute humidity (g/m^3) *	-1.40	0.35	< 0.001	0.25
Average of daily maximum temperatures, ºC *	-0.70	0.19	< 0.001	0.21
Average of daily minimum temperatures, ºC *	-0.47	0.13	0.001	0.20
Average of daily mean temperature, ºC *	-0.55	0.16	0.001	0.19
Province with coast	-4.10	0.90	< 0.001	0.30
Density of population (inhabitants per km^2)	-0.07	0.31	0.821	0.001
Multivariable analysis				0.55
Intercept	0.36	0.71	0.615	
Altitude above sea level (per 100 m) *	0.84	0.11	< 0.001	
Density of population (inhabitants per km^2)	0.63	0.23	0.009	
* Data referred to the capital city of the province.				
R^2 is the determination coefficient.				

In the multivariate linear regression model, population density was the only variable that significantly improved the predictive value of the altitude (R^2 = 0.55). Each 100 meters increase in altitude and 100 inhabitants/km^2 of increase in density the seroprevalence increased by 0.84 and 0.63 percentage points, respectively (Table 2).

The 25 provinces with altitude above the median (215 meters) showed a threefold higher seroprevalence (6.5% vs. 2.1%, p < 0.001), lower absolute humidity (6.4 vs. 8.3 g/m^3, p < 0.001), and lower averages of the daily maximum, minimum and mean temperatures than the others (15.5 vs. 18.6, 4.3 vs. 9.6, 9.9 vs. 13.8 ºC, respectively, p < 0.001) (Table 3).

Table 3
Comparison of average characteristics between provinces (n = 50) with altitude above and below the median (215 m). Spain, 2020.*

	Provinces with altitude > 215 m (n = 25)		Provinces with altitude < 215 m (n = 25)		p value
	Mean	SD	Mean	SD	
Seroprevalence of SARS-CoV-2 IgG, %	6.5	4.1	2.1	1.3	< 0.001
Latitude in degrees	40.8	1.7	39.0	4.0	0.043
Average absolute humidity (g/m^3)	6.4	0.7	8.3	1.2	< 0.001
Average of daily maximum temperatures, °C	15.5	1.7	18.6	2.3	< 0.001
Average of daily minimum temperatures, °C	4.3	1.9	9.6	2.8	< 0.001
Average of daily mean temperatures, °C	9.9	1.7	13.8	2.7	< 0.001
Density of population (inhabitants per km^2)	69	163	194	164	< 0.001

*Seroprevalence of SARS-CoV-2 IgG antibodies obtained by immunoassay test from April 27 to May 11, 2020. Meteorological variables were average variables of March 2020 referred to the province capital city.

Discussion

Nearly half (46%) of the important geographical differences in SARS-CoV-2 infection during the first pandemic wave in Spain may be explained by the altitude of the province of residence, and this proportion increased up to 55% when population density was also considered. The seroprevalence of SARS-CoV-2 antibodies was threefold higher in people living in provinces with altitude above the median.

It has been suggested that geographical differences in cumulative incidence of COVID-19 could be indicative of the success of preventive measures implemented [6, 7]. However, in the first wave in Spain, a decisive part of SARS-CoV-2 transmission happened before the relevant preventive measures had been introduced. Spain has coastline almost all around and many mountain ranges. Some nearby provinces have large altitude differences, while some distant provinces have similar altitude; this geographical pattern seems to have carried over to SARS-CoV-2 infection [10].

Other ecological studies have evaluated the relationship between environmental factors and SARS-CoV-2 infection [2, 11–14]; however, comparability among Spanish provinces was optimal in the present study

because seroprevalence was assessed with the same protocol, interventions were simultaneously introduced, and social differences within the same country are probably smaller.

Studies in Latin America have not found altitude associated with higher transmission [11–14]. but the wider altitude range and tropical latitude make difficult the comparison with our results. In the present study, altitude was more predictive than any meteorological parameter, suggesting a complex synergy of several parameters on SARS-CoV-2 transmission. In Spain, an increase in altitude in March was associated with lower absolute humidity and temperature, and both factors have been related to increases in respiratory virus transmission [2–4]. Places with such conditions may have additional difficulties for effective control of transmission and may need more strict preventive measures to achieve similar results. As the present study sugests, environmental factors may modify the efficiency of SARS-CoV-2 transmission, but they are not sufficient to stop the spread; therefore, preventive interventions are necessary for all regions [5, 7, 15].

Our results of the bivariate analysis were consistent with worldwide or large countries studies that did not find association between population density and SARS-CoV-2 spread [2, 14]. However, a higher population density in the province was an independent predictor of SARS-CoV-2 seroprevalence when altitude was adjusted for. Population density has been described as a relevant factor for SARS-CoV-2 transmission in other studies [16–18]; therefore, some effect of population density on transmission in the period before the lockdown seems plausible.

The main strength of this study is that Spain met special conditions in the first pandemic wave to evaluate this association, since it is an environmentally diverse territory, the lockdown was implemented simultaneously in all regions, and a nationwide survey has been performed to obtain comparable estimates of the seroprevalence of SARS-CoV-2 by provinces.

This study has limitations. The ecological analysis may suggest a hypothesis but cannot conclude causality. Parameters of the capital city were assigned to the whole province; however, parameters of the capital city are usually a good proxy of the average conditions to which the population of the province is exposed. These results may not predict infections in further waves because a part of the population may have acquire immunity, many preventive interventions have been introduced and the weather conditions in other months may be different.

Conclusions

In summary, important differences among Spanish provinces were observed in the seroprevalence of SARS-CoV-2 antibodies after the first pandemic wave. Nearly half of these differences may be explained by altitude. Environmental conditions related to higher altitude in winter-spring, as the combination of low temperature and humidity, may be relevant for SARS-CoV-2 transmission. A higher population density was also a predictive factor for transmission. Although spread of SARS-CoV-2 widely depends on social behaviors and preventive interventions, places with adverse environmental conditions may require additional efforts to achieve similar pandemic control.

Abbreviations

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe-acute-respiratory-syndrome coronavirus type 2; ºC: Celsius degrees; R^2: determination coefficient; SD: standard deviation.

Declarations

Authors' contributions

Jesús Castilla, Ujué Fresán, Camino Trobajo-Sanmartín and Marcela Guevara designed the study. Marcela Guevara and Jesús Castilla undertook the statistical analysis. JC and MG wrote the draft manuscript, and all authors revised and approved the final version.

Availability of data and materials

All data are available at Spanish Meteorological Agency (https://opendata.aemet.es/centrodedescargas/productosAEMET?),

Spanish Geographical Institute (https://www.ign.es/web/ign/portal/ane-datos-geograficos/-/datos-geograficos/datosPoblacion?tipoBusqueda=capitales), and Instituto de Salud Carlos III (https://portalcne.isciii.es/enecovid19/).

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

Not applicable.

References

1. European Centre for Disease Prevention and Control. Communicable Disease Threats Report. Week 20, 10-16 May 2020. https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-16-may-2020.pdf. Accessed 30 Dec 2020.

2. Tzampoglou P, Loukidis D. Investigation of the importance of climatic factors in COVID-19 worldwide intensity. Int J Environ Res Public Health. 2020;17(21):7730.

3. Sajadi MM, Habibzadeh P, Vintzileos A, Shokouhi S, Miralles-Wilhelm F, Amoroso A. Temperature, humidity, and latitude analysis to estimate potential spread and seasonality of coronavirus disease 2019 (COVID-19). JAMA Netw Open. 2020;3(6):e2011834.

4. Muñoz Cacho P, Hernández JL, López-Hoyos M, Martínez-Taboada VM. Can climatic factors explain the differences in COVID-19 incidence and severity across the Spanish regions?: An ecological study. Environ Health. 2020;19(1):106.

5. Merow C, Urban MC. Seasonality and uncertainty in global COVID-19 growth rates. PNAS. 2020;117(44):27456-27464.

6. Han E, Tan MMJ, Turk E, Sridhar D, Leung GM, Shibuya K, et al. Lessons learnt from easing COVID-19 restrictions: an analysis of countries and regions in Asia Pacific and Europe. Lancet. 2020;396(10261):1525-1534.

7. Jüni P, Rothenbühler M, Bobos P, Thorpe KE, da Costa BR, Fisman DN, et al. Impact of climate and public health interventions on the COVID-19 pandemic: a prospective cohort study. CMAJ. 2020;192(21):E566-E573.

8. Working group for the surveillance and control of COVID-19 in Spain. The first wave of COVID-19 pandemic in Spain: characterization of cases and risk factors for severe outcomes, as at 27 April 2020. Euro Surveill. 2020;25(50):pii=2001431.

9. Ministerio de Sanidad, Consumo y Bienestar Social. Plan para la transición hacia una nueva normalidad. https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov-China/planDesescalada.htm. Accessed 30 Dec 2020.

10. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet. 2020;396(10250):535-544.

11. Pun M, Turner R, Strapazzon G, Brugger H, Swenson ER. Lower incidence of COVID-19 at high altitude: facts and confounders. High Alt Med Biol. 2020;21(3):217-222.

12. Segovia-Juarez J, Castagnetto JM, Gonzales GF. High altitude reduces infection rate of COVID-19 but not case-fatality rate. Respir Physiol Neurobiol. 2020;281:103494.

13. Accinelli RA, Leon-Abarca JA. At high altitude COVID-19 is less frequent: The experience of Peru. [En la altura la COVID-19 es menos frecuente: la experiencia del Perú]. Arch Bronconeumol. 2020;56(11):760-761.

14. Hamidi S, Ewing R, Sabouri S. Longitudinal analyses of the relationship between development density and the COVID-19 morbidity and mortality rates: Early evidence from 1,165 metropolitan counties in the United States. Health Place. 2020;64:102378.

15. O'Reilly KM, Auzenbergs Mm Jafari Y, Liu Y, Flasche S, Lowe R. Effective transmission across the globe: the role of climate in COVID-19 mitigation strategies. Lancet Planetary Health. 2020;4(5):e172.

16. Wong DWS, Li Y. Spreading of COVID-19: Density matters. PLoS One. 2020;15(12):e0242398.

17. Coşkun H, Yıldırım N, Gündüz S. The spread of COVID-19 virus through population density and wind in Turkey cities. Sci Total Environ. 2021;751:141663.

18. Jahangiri M, Jahangiri M, Najafgholipour M. The sensitivity and specificity analyses of ambient temperature and population size on the transmission rate of the novel coronavirus (COVID-19) in different provinces of Iran. Sci Total Environ. 2020;728:138872.
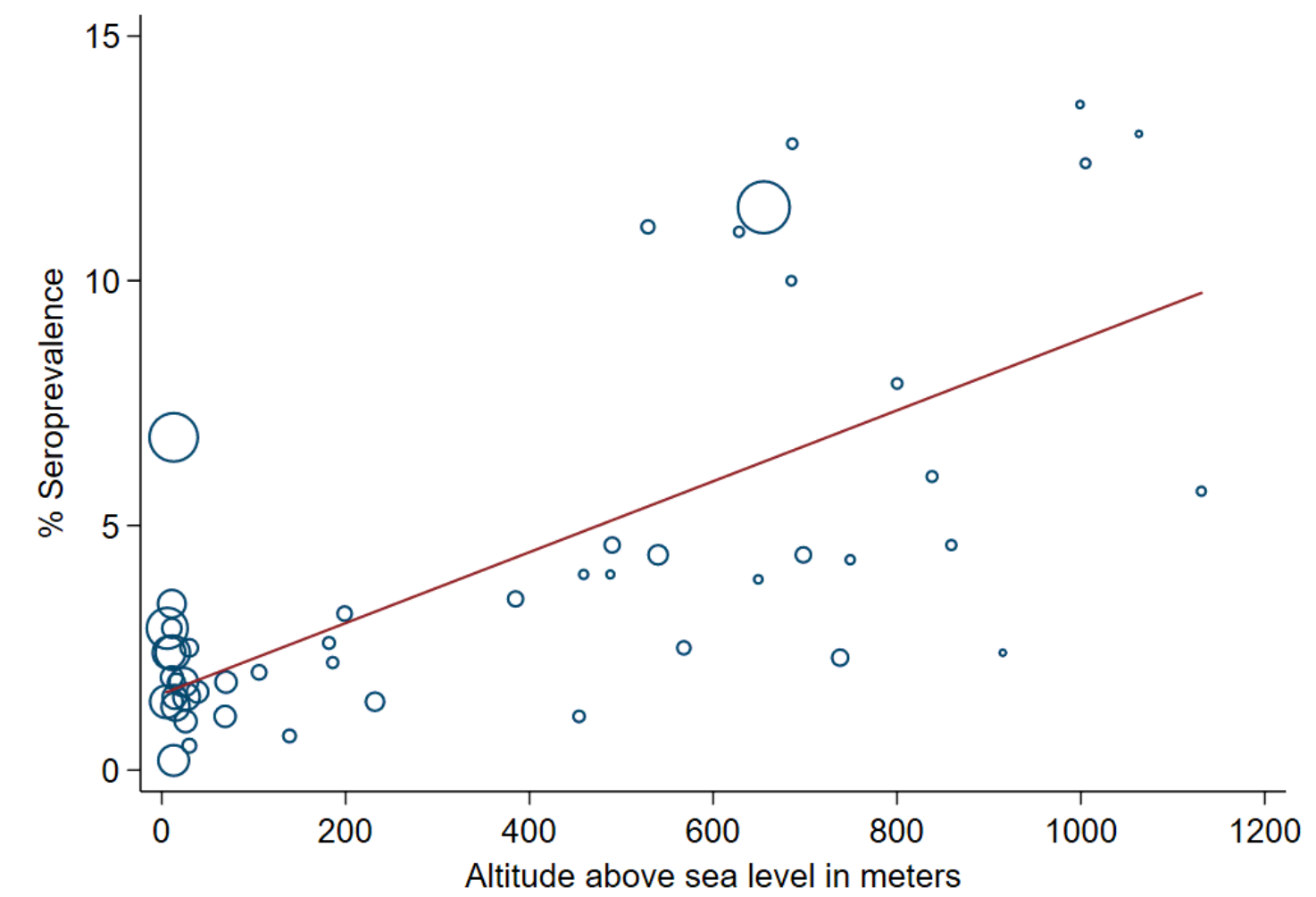
Figures

Figure 1

Linear regression analysis of the seroprevalence of IgG antibodies against SARS-CoV-2 as function of the altitude above sea level in meters by province. The diameter of the circles is proportional to the population density. The seroprevalence was obtained by immunoassay test in samples collected from April 27 to May 11, 2020, Spain.