Why does the COVID-19 outbreak in Mexico seem to be slower? Some hypotheses for testing

Manuel Elías-Gutiérrez
El Colegio de la Frontera Sur  https://orcid.org/0000-0003-2562-4584

Manuel Mendoza-Carranza (✉ mcarranza@ecosur.mx)
El Colegio de la Frontera Sur  https://orcid.org/0000-0001-8216-2115

Umon Takahashi-Aguilar
Martha Valdez-Moreno
El Colegio de la Frontera Sur

Jenny Alexandra Prado-Bernal
Clínica Carranza

Claudia Mora-Loya
Clínica Carranza

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Abstract

Aim: The current paper aims to present and discuss some hypothesis about why in Mexico and in particular the Mexico City the epidemic of COVID-19 seems to be slower than other countries.

Subject and methods: We compared daily UVI maximum and the reported COVID cases in Mexico City, New York, and Los Angeles and performed an ADONIS permutation test to look for significant differences between case numbers and its relationship with the UV index. We performed a quantile regression to explain the relation between UVI and daily COVID cases. We also investigated and analyzed other possible factors contributing to this slowdown because UVI cannot be the only explanation.

Results: Although Mexican authorities have applied one of the smaller numbers of tests in the world, it is possible to identify a slowdown in Mexico’s rate of infections. We found a negative and significant difference between the UV and registered cases among the three cities analyzed. However, this slowdown cannot be explained by a single factor. It is possible to hypothesize about the confluence of other factors as Vitamin D levels in Mexican population, lack of central air conditioning and the ventilation in houses and metropolitan transportation systems. Also, the Bacillus Calmette–Guérin vaccination could be part of the explanation of this phenomenon.

Conclusions: Single parameter models as solar irradiation can explain partially the complicated spread of COVID-19 in different parts of the world. However, it is necessary to extend our scientific understanding of environmental effects, city infrastructure, population age, vaccination schemes, socioeconomic conditions, social and political behavior on COVID-19 epidemic dynamics.

Introduction

The rate of infection of COVID-19, is accelerating in most countries, particularly in the United States. In contrast, the infection rate appears to be slower in Mexico, despite populated areas of the country being ripe for wide-spread infection. For example, the Mexico City Metropolitan Area hosts, together with the suburbs in the State of Mexico, more than 20 million people (CONAPO 2010) in about 7954 km$^2$, making human-to-human transmission highly favorable. The populace itself should also be highly susceptible to complications from COVID-19 due to limited sanitary services, poor air quality due to pollution, rampant diabetes, and obesity. Additionally, while the federal government initially explained that they were sampling accordingly with the Sentinel Surveillance model, developed by the World Health Organization (WHO) for other pandemics, it seems that strategy was abandoned following an intense polemic.

Mexico is one of the principal economies in Latin America and the tenth most populous in the world with 129 million people. However, COVID-19 studies are scarce and most of them are descriptions about the general situation and development of the pandemic (e.g. Centeno 2020; Ñamendys-Silva 2020; Ramos 2020). Consequently, possible causes of the growth epidemic rate of Mexico cases are unknown, being the lowest in the world for testing (Table 1). Taken together, one would expect this country to have a high number of COVID-19 cases, and the outbreak should certainly not be slowing for no reason this early in
the pandemic. In this article, we sought to understand the reasons for this phenomenon better. Our goal was to inquiry why the reported number of infections in Mexico is lower than expected based on population size and the aforementioned factors. We focused our discussion in a series of potential environmental factors that could be related with the lower rate of infections observed especially in Mexico City, as the solar UV irradiation (Sagripanti and Lyte 2007; Gunthe et al. 2020), the ventilation of houses and public transport, and Mexican vaccination scheme. It is important to highlight a possible gap in epidemic statistics based in the low number of COVID-19 tests in relation to population size in Mexico (Theodoros et al. 2020).

Materials And Methods

Checking if there is a slowdown

We determined the number of patients in hospitals in Mexico City, using COVID-19 tracking apps developed by the government (Gobierno de la Ciudad de México 2020a) and examined several institutions as the National Institute of Respiratory Diseases. Also, we examined the number of casualties in the whole country.

Comparisons

We focused on Mexico City and compared it with two cities in the United States (New York and Los Angeles). We compared the whole country with other Latin American countries. We concede that no country can know their correct number of cases, as that would require continuous testing of every individual in their population. However, the number of cases in Mexico is assumed to be much higher than reported because of Mexico’s below-average testing.

UV Irradiance

We inquiry, among other factors, that there might be a causal relationship between local UV index (UVI) and the number of COVID cases. To test this hypothesis, we used as model the maximum daily UVI and reported COVID positive cases in Mexico City (CDMX), New York (NY), and Los Angeles (LA) from March 12th to June 26th, 2020.

Data Acquisition

All data used here are public. UV index (UVI) values were obtained for New York (NY) and Los Angeles (LA) from the UV-B Monitoring and Research Program of the Colorado State University (Colorado State University 2020). For Mexico City (CDMX), UVI values were obtained from two sources: 1) the solar radiation records of the CDMX Government (Gobierno de la Ciudad de México 2020b) for March data; and 2) the Weather online website (WeatherOnline Ltd 2020) for April and May data. Confirmed COVID cases for NY and LA data were obtained from the NYC Health Department (2020) and Department of Public
Health (2020) respectively. Mexico COVID data were obtained from the COVID-19 information site from Mexican Government (Gobierno de México 2020).

Statistical Analysis

Daily case numbers were standardized to cases per ten thousand inhabitants (=10ti). An ADONIS permutation (1000) test was performed to look for significant differences between the number of COVID cases and its relationship with the UV index. Finally, a quantile regression analysis was performed to explain the relation between maximum daily UVI and daily COVID cases per ten thousand inhabitants (Koenker and Hallock 2001; Koenker 2005), good of fit was measured using the pseudo $R^1$ calculation (Koenker and Machado 1999).

Source of Information for Hypotheses Proposed

Finally, we consulted the Web of Science (https://webofknowledge.com) to gather all COVID-19 updates until June 15th, 2020, mainly related to UV, BCG vaccination, and other themes that could help to explain the slowdown of the pandemics in Mexico.

Results

Slowdown of Infections in Mexico

From 78 hospitals designated as COVID-19 in CDMX (a low figure for the size of the city), 18 were still with places, according to the official site of the Mexican Government (Gobierno de la Ciudad de México 2020a). The average daily COVID cases for CDMX were 0.56 ± 0.41 cases per 10ti, while LA had 2.42 ± 1.33 cases per 10 ti, and NY had 2.35 ± 2.11 cases per 10 ti (Fig. 1A). Total number of deaths in Mexico by June 23th was 22,580, a higher number in proportion to detected cases than most countries (Roser et al. 2020).

UV index and COVID relation

Average UVI followed the opposite trend, with CDMX having the highest score (12.01 ± 0.47), followed by LA (8.26 ± 1.23) and NY (6.37 ± 2.6) (Fig. 1B). The Adonis permutation test indicates significant differences among positive COVID cases numbers between the three cities (p= 0.0009) and UVI scores (p=0.0009). In addition, we found an independent effect of the UVI on the number of COVID cases between each city (p=0.0009, Table 2) and the effect of City and UV (P=0.0009). Quantile regression analysis shows a negative relation between COVID case number and the increase of UVI. The pseudo $R^1$ value is increased in relation with quantile increase reaching a maximum $R^1$ of 0.36 for 90 and 95th quantiles (Table 3, Fig. 2).

Discussion
Gunthe et al. (2020) suggest a possible negative relationship between UV radiation, temperature, and COVID case numbers. However, their data are not conclusive because the adjusted curve diminishes on both sides around a peak, making it difficult to interpret. In China, Yao et al. (2020) found no relationship between average UVI and COVID case numbers, but in one region (Hubei), these authors show a possible negative correlation. Other unpublished studies have tried to resolve weather effects on a pandemic, with no conclusive results (Xu et al. 2020). Some possible bias in mentioned studies could be the use of daily UV averages. We used the maximum UVI per day (that goes from zero to maximum), producing a comprehensive relation between UVI and positive COVID-19 cases.

Despite the observed relation, it is important to remark that the UVI is only one part of the explanation to the low prevalence of COVID cases in CDMX compared to similar cities as NY and LA. Paradoxically, CDMX has ideal conditions for a rapid spread of any pandemic due to population density and other factors as high prevalence of chronic diseases and hotspots of people accumulation, as the subway system (Metro). In addition to the UV effect, it is necessary to consider other factors that can explain the behavior of the COVID epidemic in CDMX and most of the country. One factor related to high UVI, additional to latitude, is the altitude above sea level. In the case of the Mexican Plateau, where CDMX and other major cities such as Toluca, Puebla, Querétaro, and Morelia are found, the average elevation is ≥2000 masl. For example, the UVB levels in a station located about 60 km southeast of CDMX (Tlamacas, at 4000 masl) had a maximum average irradiance of 400 mW/m² of UVB in March, with a minimum near 250 mW/m² in January. Two other localities at the same latitude, but at sea level, have around 300 mW/m² (Manzanillo and Veracruz), with a minimum of about 150 mW/m² on the same dates (Valdes-Barron et al. 2013). In addition to the amount of UV reaching the surface, the type of it also affects its capacity to inactivate pathogens. UV is found in the environment in three forms: UVA, UVB, and UVC. Each of these will reach the surface in different quantities after atmospheric filtration, so the type of UV reaching the surface (and subsequent germicidal effect) is also affected by altitude over sea level (Dwivedi et al. 2018).

The effect of natural and artificial UV on virus inactivation has been extensively studied. For example, the influenza virus is inactivated by up to 99% if exposed to full sunlight during a single day in Mexico City, but this value lowers to 66% in the winter (Sagripanti and Lyte 2007; Sagripanti and Lytle 2020). Another study demonstrated that aerosolized MHV Coronavirus could be highly sensitive to 254 nm UV-C, but it is dependent on the culture medium (Walker and Ko 2007). The effect of the UV on viral inactivation is thought to be through uracil dimerization in the RNA (Woo et al. 2012). These authors also found that UVC inactivates a bacteriophage virus more efficiently in aerosols (with differences depending on the media) than droplets.

Other Factors Proposed to Explain the Slowdown

Differences in the behavior of COVID-19 development in Mexico (and possibly other countries at a similar latitude) compared to more northern countries can only be partially explained by the UV effect and altitude.
We suggest some other factors that need to be included in a more holistic model to explain the slowdown COVID-19 infection in Mexico and CDMX. A possible link between solar radiation-Vitamin-D production and the increase of immunological defenses against viruses (Grant 2008). Although controversial, the effect of vitamin D deserves further study because it seems to have a positive result against this type of infection (Kakodkar et al. 2020). Laird et al. (2020) suggest a positive relation between immune system and vitamin D regulating cytokine response to pathogens, fact confirmed by Daneshkhah et al. (2020)

Another factor influencing the COVID-19 epidemic behavior in Mexico could be the vaccination scheme. Recently, researchers have suggested that Bacillus Calmette-Guérin (BCG) vaccination against tuberculosis could diminish the spread of COVID-19 (Gupta 2020). This factor has three possible explanations: 1. The molecular similarity between BCG antigens and viral antigens. After vaccination, memory B and T cells recognize both BCG and respiratory pathogens; 2. BCG could lead to antigen-independent activation of bystander B and T cells; and 3. Long-term activation and reprogramming of innate immune cells called trained immunity. Monocytes undergo epigenetic histone modifications at promoter sites of genes encoding inflammatory cytokines, leading to long-term changes in their ability to respond to novel stimuli (Redelman-Sidi 2020). This effect leads the activation of Th1 immunity and downregulation of Th2, and the consequent reduction of local tissue destruction by SARS-Cov-2 (Gupta 2020). Indeed, there appears to be a significantly lower prevalence of COVID-19 in countries where it is mandatory for BCG vaccination. In Mexico, massive vaccination with BCG started in 1951 and continues up to the present (Hurtado-Ochoterena and Matías-Juan 2005).

It is also essential to notice that most houses in Mexico City have no central air conditioning or insulation system, unlike the northern temperate regions with severe weather. As a result, Mexican houses are sunny and well ventilated. Th air currents inside houses do not allow small particles to remain inside rooms or houses for a long time, diminishing the probability of infection. This hypothesis was analyzed, albeit only in a small number of studies (Hobday and Dancer 2013). Despite the effect of sunlight inside houses is not currently known it is possible that play a similar role as in the environment, neutralizing virus particles by UV radiation. Additionally, a sunny house represents a key element in preventing depression (An et al. 2016; Fleming et al. 2018) reinforcing the immune system (Szałach et al. 2019; Cruz-Pereira et al. 2020).

Similarly, the primary modes of metropolitan public transportation in Mexico also lack air conditioning, including the vast subway system (Metro) of CDMX used by hundreds of thousand people daily. These transportation systems always operate with the windows open and air circulation inside tunnels is enhanced using ventilation system. Overall, the citizens of Mexico live under conditions less favorable to virus survival on outdoor/public surfaces.

As we present along this paper, there are evidences that mentioned factors (UVI, vaccination scheme, airflow) could reduce the spread velocity of COVID-19 infection. However, no current models or data exist to explain how these factors affect the spread velocity of COVID-19 infection in large cities as CDMX. This city has a high density of population, with many people having pre-existing chronic diseases as
diabetes, high blood pressure and obesity making them more susceptible to viral diseases (Gnatiuc et al. 2019; Rodríguez-Torres and Casas-Patiño 2019)

We do not know precisely how each factor mentioned here contributes to lessening the spread of COVID-19. Nevertheless, the possible synergy of all of them appears to slower this pandemic. Currently, no model exists that can take all these factors into account. We, therefore, consider the aforementioned ideas as requiring rigorous testing.

Remarks on Data Gathered

A common weakness of any model is the lack of data. In the case of COVID-19, we can be confident that this is the principal limitation in explaining the epidemic development in Mexico and elsewhere (Burdorf et al. 2020; Naudé 2020). If we add the asymptomatic people not reported but still contagious (Bai et al. 2020), the uncertainty may be higher. It is known that people's behavior is related to COVID-19 spread rates (Van Bavel et al. 2020). However, in certain conditions it is tough to calculate this relation, which is another source of uncertainly in the prediction models.

It has been suggested that the number of fatalities could be three times higher than it currently is in Mexico (Ahmed 2020). This figure would show 10-12,000 fatalities for the country and is currently not supported by hard data by May 8th. Except for Brazil, most Latin American countries are experiencing a slow spread of COVID-19. However, these data can be misleading due to a lack of testing, which is low in every Latin American country (Table 1). Despite a lack of testing, the pandemic's true extent will eventually become evident if COVID-19 cases overwhelm hospitals and funerary services, as they have in Ecuador (mainly in the city of Guayaquil).

We presume this slowdown will slow the rate of infection but also make it continuous throughout the summer complicating the function of sanitary services, including hospitals. Mexican authorities are working to solve the lack of services and resources needed to confront a massive infection of COVID-19, but already several hospitals have become a point of infection due to the lack of materials and poor installations (Kitroeff and Villegas 2020).

Conclusions

Single parameter models can explain partially the complicated spread patterns of COVID-19 in different parts of the world. We expect that the hypotheses presented here and other efforts will help to establish the causes of the differential epidemic spread observed. Other authors have marginally discussed part of the ideas exposed here (Zhang et al. 2020), although their work is controversial.

Finally, we need to extend our scientific understanding of environmental effects, city infrastructure, population age, vaccination schemes, socioeconomic conditions, social and political behavior on COVID-
19 epidemic dynamics. Otherwise, the decisions taken by the governments and people will be uninformed and potentially erroneous.

Declarations

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Competing Interests

The authors declare they have no competing interests

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TABLE 1 Total COVID-19 tests per thousand people by June 8\textsuperscript{th} or 9\textsuperscript{th} in some countries of the Americas.
*People tested; **Units unclear ***Samples tested +Tests performed.

| Country      | Total Tests/1,000 persons | Date of the last report (2020) |
|--------------|----------------------------|-------------------------------|
| Canada       | 75.43                      | Jul 2                         |
| United States| 101.09                     | Jul 2                         |
| Peru         | 7.76                       | Jul 3                         |
| Colombia     | 15.69                      | Jul 2                         |
| Ecuador      | 6.82                       | Jul 2                         |
| Mexico       | 4.04                       | Jun 26                        |
| Bolivia      | 6.63                       | Jul 1                         |

TABLE 2 ADONIS permutation test results for COVID cases number in New York, Los Angeles and Mexico Cities.

| Main effect         | d.f. | SS  | MS  | F.model | R2    | Pr(>F)  |
|---------------------|------|-----|-----|---------|-------|---------|
| City                | 2    | 11.61 | 5.80 | 58.19   | 0.221 | 0.0009  |
| UV index            | 1    | 3.15  | 3.15 | 31.62   | 0.060 | 0.0009  |
| City*UV index       | 2    | 7.59  | 3.79 | 38.03   | 0.144 | 0.0009  |
| Residuals           | 183  | 30.13 | 0.09 | 0.574   |       |         |
| Error               | 188  | 52.48 | 1.0  |         |       |         |

TABLE 3 Quantile regression estimates of B0 and B1, 95% confidence intervals for B1, pseudo R\textsuperscript{1} and P for Ho: B1 = 0 for four regression quantiles between UVI and COVID positive cases per 10 thousand inhabitants in New York, Los Angeles and Mexico City.
| T (quantile) | Bo  | B₁   | 95% CI for B₁ | R₁   | p          |
|-------------|-----|------|---------------|------|------------|
| 20<sup>th</sup> | 1.82 | -0.13 | -0.16 - 0.12 | 0.19 | P < 0.001  |
| 50<sup>th</sup> | 4.13 | -0.30 | -0.35 - 0.23 | 0.23 | P < 0.001  |
| 90<sup>th</sup> | 9.33 | -0.66 | -0.83 - 0.53 | 0.36 | P < 0.001  |
| 95<sup>th</sup> | 11.18 | -0.79 | -0.87 - 0.34 | 0.36 | P < 0.001  |

**Figures**
Figure 1

Daily confirmed cases/10,000 inhabitants in NY (magenta), LA (blue), and CDMX (green) from March 9th to June 26th and maximum daily in the same dates for UV index. Number of cases of cities are located in axis x at the average UVI index for each.
Figure 2

UVI index versus positive COVID cases by 10 thousand inhabitants. Red lines are the 20th, 50th, 90th and 95th quantile regressions.