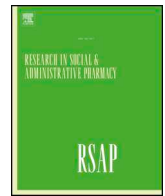




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



COVID-19 in Colombia endpoints. Are we different, like Europe?

Pedro Amariles^{a,b,*}, Johan Granados^{a,b}, Mauricio Ceballos^{a,b}, Carlos Julio Montoya^a

^a Universidad de Antioquia, Medellín, Colombia

^b Research Group on Pharmaceutical Promotion and Prevention, Universidad de Antioquia, Medellín, Colombia

ABSTRACT

The infection by the new coronavirus (SARS-CoV-2) has taken the dimension of a pandemic, affecting more than 160 countries in a few weeks. In Colombia, despite the implementation of the rules established by the national government, exists an elevate concern both for mortality and for the limited capacity of the health system to respond effectively to the needs of patients infected. For Colombia, assuming a case fatality rate among people infected with SARS-CoV-2 of 0.6% (average data from the information reported for Latin American countries for March 18) (Table 1), the number of deaths, in one or two weeks, could be 16 and 243, respectively. These estimates differ markedly from those documented in countries such as Spain and Italy, in which COVID-19 case fatality rates exceed 8% (case of Italy) and from the percentage of patients who have required intensive care, which has ranged from 9% to 11% of patients in Mediterranean European countries. These differences could be explained due to: a) the percentage of the population at risk (individuals older than 60 years); b) a higher epidemiological exposure to viral respiratory infections associated with more frequent exposure to them, due to geographic and climatic conditions; c) less spread of the virus by location in the tropical zone; and d) earlier preventive measures to contain the spread of SARS-CoV-2 infection. Therefore, it is possible to establish that the situation in this country will be different from in European Mediterranean and that Colombia could have different endpoints from Spain and Italy.

Introduction

The infection by the new coronavirus (SARS-CoV-2) has taken the dimension of a pandemic, affecting more than 160 countries in a few weeks. In China, although containment measures have significantly reduced new cases of COVID-19, in other countries, this reduction has not been similar. In Colombia, despite the implementation of the rules established by the national government, exists an elevate concern both for mortality and for the limited capacity of the health system to respond effectively to the needs of patients infected and requiring intensive care by the respiratory complications associated with this infection.¹

The data collected so far on the number of infected people and the evolution of the epidemic are imprecise. Even though to date in Colombia (March 19, 2020) there are no deaths yet, nor patients in intensive care by COVID-19, the diagnoses of infection by SARS-CoV-2 have increased (Fig. 1). In this country, since the first case was reported (March 6, 2020), the number of infected patients follows an exponential trend, like other countries in the region, except Ecuador, with a lower incidence. If this trend continues, in a week (until March 26, 2020) or two (April 2, 2020), there will be 2581 and 40,535 infected patients, respectively, as shown in Fig. 2.^{1,2}

According with the Knowledge of this infection so far, the high-risk age groups are among the people over 60 years of age, primarily due to the burden of disease and the complications that this infection

generates in them. Regarding to the current COVID-19 data available from Colombia, the proportion of patients in that age group is 15%, and of them, 4.7% needing hospitalizing, proportion which is lower than in other age groups. Additionally, as of March 19, most cases are imported (64%).³

On the other hand, according to the official reports of the World Health Organization (updated to March 19, 2020), in Latin American countries the first cases of mortality by COVID-19 occurred in Argentina after the 12th day of the first case was diagnosed, and in Panama was the first death was reported after the sixth day. This situation differs from European countries, where COVID-19 associated deaths started until after the 23rd of the first diagnosis (France). Additionally, the reports curve of some European countries has a slower start compared to Latin American countries. This situation may be due to a higher degree of alertness in this region, motivated by the experiences of European and Asian countries, leading to earlier diagnostic tests (early detection). Additionally, in Europe, at the beginning of the infection, the diagnoses were oriented to people with symptoms.

The ability of the health system to detect the SARS-CoV-2 infection is a factor that can influence the diagnosis and reporting of cases. By March 18, 2020, Italy had already carried out 148,657 tests (31,506–21.2% -positive), South Korea: 286,716 (8320–2.9% - positive), and Colombia: 2571 tests (93–3.6% - positive). Although the number of SARS-CoV-2 tests performed should be like the number of people tested, the values may differ because some people need a

* Corresponding author. Street 67 # 53 -108 Office 2-118, University of Antioquia, Medellin- Antioquia, Colombia.

E-mail address: pedro.amariles@udea.edu.co (P. Amariles).

<https://doi.org/10.1016/j.sapharm.2020.03.013>

Received 22 March 2020; Accepted 23 March 2020

1551-7411/ © 2020 Published by Elsevier Inc.

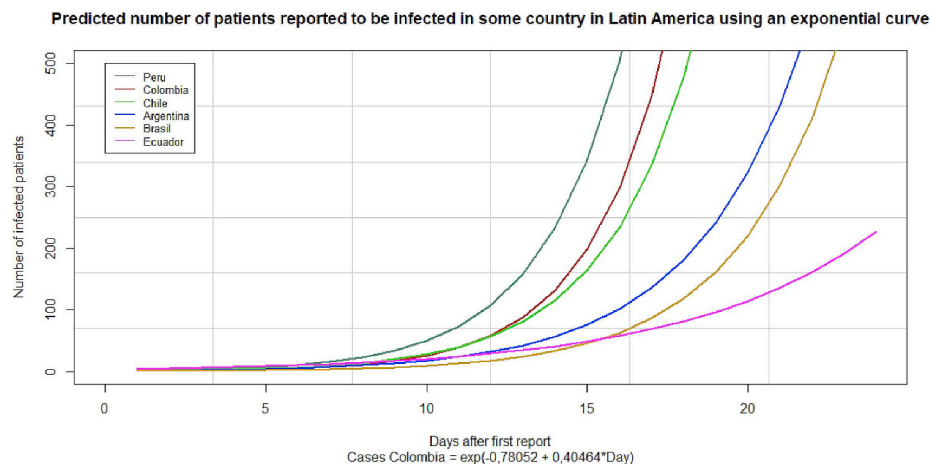


Fig. 1. Exponential regression models in some countries of South America until 19 to March 2020.

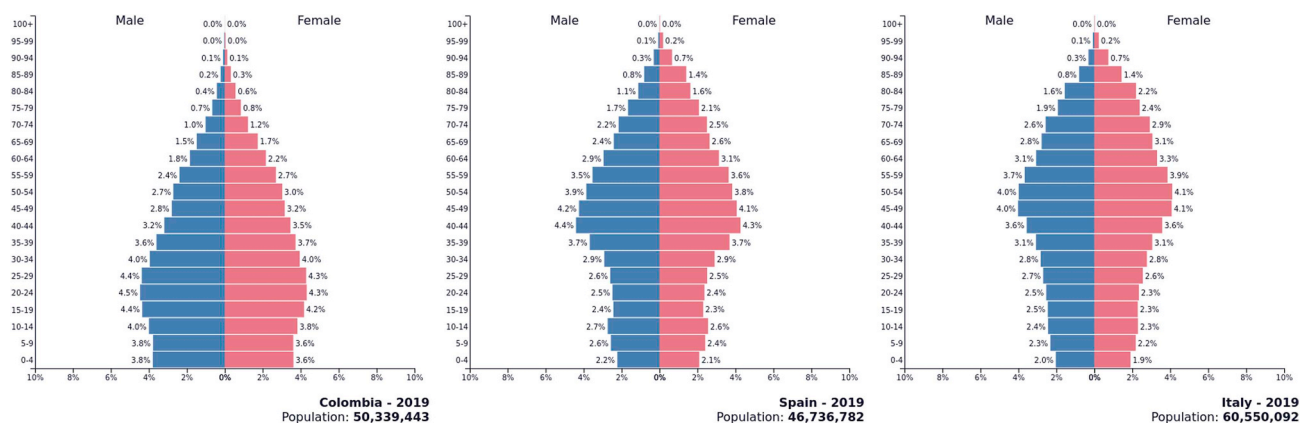


Fig. 2. Population distribution of Colombia, Spain and Italy 2019.⁶

duplicate of the test. The reason for this is that there are “false negative” results.⁴ However, the ability of a health system to perform these tests greatly influences the case fatality rate, as the denominator determines its value. Therefore, conducting random tests in the people infected with symptoms or disease decrease in the case fatality rate. In China, where they have done a random SARS-CoV-2 screening, the severity of the infection has shown that: 80% of the cases present mild symptoms, 15% severe, and 5% critical. For its part, in Spain, the behavior is more worrying (60% mild, 30% will require hospitalization, and 10% intensive care).⁵

For Colombia, assuming a case fatality rate among people infected with SARS-CoV-2 of 0.6% (average data from the information reported for Latin American countries for March 18) (Table 1), the number of deaths, in one or two weeks, could be 16 and 243, respectively. These estimates differ markedly from those documented in countries such as Spain and Italy, in which COVID-19 case fatality rates exceed 8% (case of Italy) and from the percentage of patients who have required intensive care, which has ranged from 9% to 11% of patients in Mediterranean European countries. Differences could be explained due to: a) the percentage of the population at risk (individuals older than 60 years); b) a higher epidemiological exposure to viral respiratory infections associated with more frequent exposure to them, due to geographic and climatic conditions; c) less spread of the virus by location in the tropical zone; and d) earlier preventive measures to contain the spread of SARS-CoV-2 infection.

Differences in the percentage of the population at risk by age

In Colombia, the proportion of people aged 60 is 13%, while in Italy

Table 1

COVID-19 case fatality in different European and Latin American countries.

Country	Cases ^a	Day ^b	Deaths	Day of the first death	Lethality
Germany	15320	53	44	43	0.3
Australia	572	54	5	40	0.9
Finland	400	51	0	NA	NA
France	10871	56	243	2.3	2.2
Italy	41035	49	3405	24	8.3
United Kingdom	2689	49	137	36	5.1
Spain	17963	48	830	3.4	4.6
Ecuador	199	19	3	NA	1.5
Argentina	97	17	3	5	3.1
Brazil	621	2.3	6	21	1.0
Chile	238	17	0	NA	NA
Colombia	128	14	0	NA	NA
Mexico	118	21	1	NA	0.8
Panama	109	10	1	2	0.9
Peru	2.3.4	13	0	NA	NA

^a Cases reported (March 18, 2020).

^b Days elapsed since the first report.

29% and Spain 25% (Fig. 3). Therefore, it is plausible to think that, compared to Italy (the country with the highest fatality rate due to the coronavirus), the incidence of fatal cases in Colombia would be lower due to the lower proportion of high-risk people.

Epidemiological exposure to viral respiratory infections: more frequent viral infections by different viruses, due to geographic and climatic conditions

The known case-fatality data for COVID-19 in the European

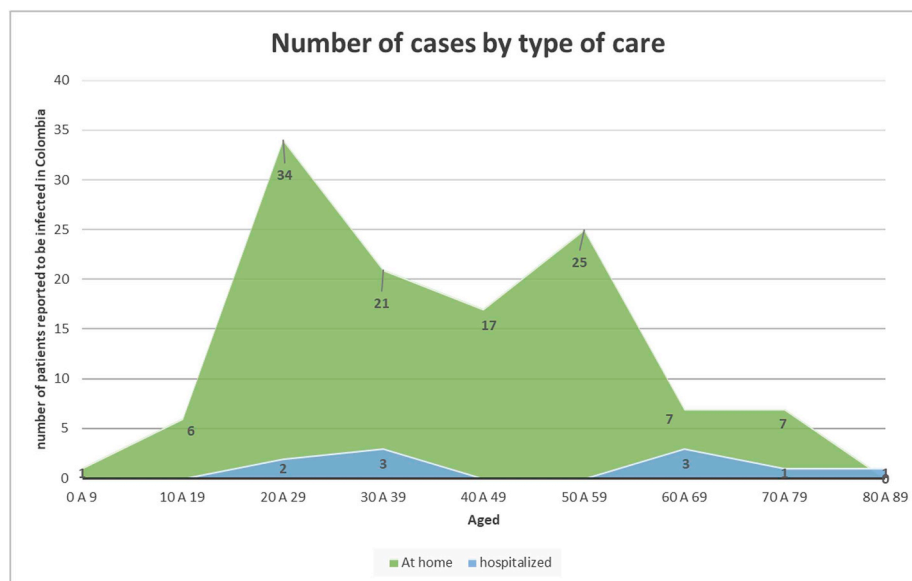


Fig. 3. Number of reported cases and type of care in Colombia. March 19, 2020 (n = 128).

countries (mainly Mediterranean), which have four weather seasons per year, show a high case fatality in Italy (8.3%), Spain (4, 6%), France (2.2%) and Greece (1.3%). On the other hand, the Nordic countries, where the winter season is more extensive (up to 8 months of rain and snow), and the mortality rates are lower: Denmark (0.4%), Iceland (0.3), Norway (0.3%), Sweden (0.7%), and Finland (no deaths).

In Colombia, according to the National Institute of Health, consultations and hospitalizations for acute respiratory infections have at least two peaks during the year: the first between March to June, with May and June being the months with the highest number of cases; and the second between September and December. These peaks are associated with the rainy seasons that characterize those periods. From an *immunological perspective*, the Latin-American environmental condition characterized by a higher frequency of rains (like in Colombia and other tropical countries without the classic seasons), associated with a higher frequency of viral respiratory infections, caused by different types of viruses, could be related with a persistent exposition and training of the innate and adaptive immune responses, which allows an efficient response to respiratory viral infections, with better clinical evolution and, therefore, lower complications and mortality.⁷⁻¹⁰

Lower spread of virus in tropical countries

A study by Mohammad M. Sajadi et al., showed that the distribution of viral respiratory infection outbreaks depends on latitude, temperature, and humidity. As temperature and humidity are known factors that influence survival of SARS-CoV, MERS-CoV, and influenza viruses, it is plausible to consider that in tropical countries, like Colombia, the SARS-CoV-2 survival and spread could be lower.¹¹

Earlier preventive measures to contain the spread of the pandemic in Colombia

Within the actions taken to suppress transmission of SARS-CoV-2, Colombia closed universities and colleges to decrease the spread of this virus. Table 2 describes the time when this measures were taken in different countries, after the first case detected, as well as the number of people infected and deaths at the time of starting these actions. Additionally, from March 21 Colombia will be restricting the entry of foreigners, closing bars and clubs, and establishing quarantine for several days in the most populated cities as Medellin and Bogota.

Neil M Ferguson et al., conclude that the closure of schools and

Table 2

Closing day of colleges and universities for virus containment.

Country	Day ^a	Date	Cases ^b	Deaths
Colombia	10	03/16/2020	54	0
Argentina	14	03/16/2020	56	0
Panama	7	03/16/2020	55	1
Mexico	19	03/17/2020	82	0
Peru	7	03/12/2020	15	0
Brazil	20	03/16/2020	200	0
Chile	13	03/15/2020	74	0
Germany	15	03/16/2020	7272	0
France	53	03/16/2020	6650	448
Spain	42	03/13/2020	5232	133
Italy	35	03/05/2020	3858	148

^a Days elapsed since the first report.

^b Cases reported as of the closing date of colleges and universities.

universities will have a positive impact on containing the COVID-19 epidemic, under the assumption that children transmit viruses as much as adults do. Additionally, that strategy is more effective in supporting the suppression of epidemics when combined with the social distancing of the entire population; the effect of school closure is further to amplify the breakdown of social contacts between households, and thus suppress SARS-CoV-2 transmission. However, the closure of colleges and universities may be insufficient to mitigate an epidemic in isolation.¹²

Colombia is one of the countries that have reported the first case of SARS-CoV-2 infection in fewer days, compared to other countries in the region and Europe. Therefore, the predictions for COVID-19 in Colombia may be affected by the early and strong measures taken, and it is necessary to make a continuous analysis of the expansion and evolution SARS-CoV-2 infection and disease in this country, to evaluate the results of them. The WHO, with all the actions and data received at the global level, has begun to establish the strategies that must be structured to control the SARS-CoV-2 pandemic, such as: a) prepare and be ready, b) detect, protect and treat, c) reduce and suppress transmission, and d) learn, innovate, improve and improve.

Based on these analyses and predictions, for now, Colombia could be in a better position regarding other countries for SARS-CoV-2 transmission and COVID-19 evolution, supported in early actions aimed to suppress virus transmission and the lower percentage of high-risk population for COVID-19 (older adults). The expansion, complications and mortality are highly variable, even in neighboring countries;

therefore, the data cannot be extrapolated, either to the worst-case like Italy or the best case like Finland (Table 2).

Colombia could have different endpoints from Spain and Italy

Predictions of COVID -19 evolution for Colombia, based on its behavior observed in Italy and Spain are very fearful, because they imply that this country lacks the response capability required for caring of all the patients who could become infected and, especially, for patients who will require admission to intensive care units. Therefore, there is a widespread fear of the high impact on morbidity, mortality and social costs due to the COVID-19 pandemic in Colombia. However, it is possible to establish that the situation in this country will be different from in European Mediterranean. Some differences support this hypothesis in favor of Colombia, such as: a) a lower percentage of the population at risk (by age); b) a possible better immunological capacity (due to the greater exposure to outbreaks of respiratory infections during the year); c) the characteristics of tropical regions that reduces the speed of virus transmission, and d) earlier implementation of preventive health policies. Finally, it is essential to highlight the difference between being infected with SARS-CoV-2 and presenting the COVID-19; in Colombia, as of March 19, 2020, only 8% of the patients positive for SARS-CoV-2 required hospitalization, and no patients have required intensive care unit (Fig. 1).

References

1. CSSEGISandData. CSSEGISandData/COVID-19 [Internet]. . [cited 2020 Mar 20]. Available from: <https://github.com/CSSEGISandData/COVID-19>; 2020.
2. Coronavirus en Colombia [Internet]. . [cited 2020 Mar 20]. Available from: <https://www.ins.gov.co/Noticias/Paginas/Coronavirus.aspx>.
3. Team TNCPERE. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China, 2020. *China CDC Wkly*. 2020 Feb 1;2(8):113–122.
4. Huang P, Liu T, Huang L, et al. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. *Radiology*. 2020 Feb 12;295:22–23.
5. SEMICYUC. Comunicado de las Juntas Directivas de la SEEIUC y la SEMICYUC ante el COVID-19 [Internet]. Semicyuc. [cited 2020 Mar 20]. Available from: <https://semicyuc.org/2020/03/comunicado-de-las-juntas-directivas-de-la-seeiuc-y-la-semicyuc-ante-el-covid-19/>.
6. Population Pyramids of the World from 1950 to 2100 [Internet]. PopulationPyramid.net. [cited 2020 Mar 20]. Available from: <https://www.populationpyramid.net/world/2019/>.
7. Annan A, Ebach F, Corman VM, et al. Similar virus spectra and seasonality in paediatric patients with acute respiratory disease, Ghana and Germany. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis*. 2016 April;22(4):340–346.
8. Couch RB, Kasel JA. Immunity to influenza in man. *Annu Rev Microbiol*. 1983;37:529–549.
9. Topham DJ, DeDiego ML, Nogales A, Sangster MY, Sant A. Immunity to influenza infection in humans. *Cold Spring Harb Perspect Med*. 2019 Dec 23:a038729.
10. Dong W, Bhide Y, Sicca F, et al. Cross-protective immune responses induced by sequential influenza virus infection and by sequential vaccination with inactivated influenza vaccines. *Front Immunol*. 2018;9:2312.
11. Sajadi MM, Habibzadeh P, Vintzileos A, Shokouhi S, Miralles-Wilhelm F, Amoroso A. *Temperature, Humidity and Latitude Analysis to Predict Potential Spread and Seasonality for COVID-19 [Internet]* Rochester, NY: Social Science Research Network; 2020. Mar [cited 2020 Mar 20]. Report No.: ID 3550308. Available from: <https://papers.ssrn.com/abstract=3550308>.
12. Ferguson NM, Laydon D, Nedjati-Gilani G, et al. *Impact of Non-pharmaceutical Interventions (NPIs) to Reduce COVID- 19 Mortality and Healthcare Demand*. vol. 20. 2020; 2020.