

Monitoring COVID-19 in Colombia during the first year of the pandemic

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Abstract

Background: COVID-19 cases in Medellín, the second largest city in Colombia, were monitored during the first year of the pandemic using both mathematical models based on transmission theory and surveillance from each observed epidemic phase.

Design and Methods: Expected cases were estimated using mandatory reporting data from Colombia's national epidemiological surveillance system from March 7, 2020 to March 7, 2021. Initially, the range of daily expected cases was estimated using a Borel-Tanner stochastic model and a deterministic Susceptible-Infected-Removed (SIR) model. A subsequent expanded version of the SIR model was used to include asymptomatic cases, severe cases and deaths. The moving average, standard deviation, and goodness of fit of estimated cases relative to confirmed reported cases were assessed, and local transmission in Medellín was contrasted with national transmission in Colombia.

Results: The initial phase was characterized by imported case detection and the later phase by community transmission and increases in case magnitude and severity. In the initial phase, a maximum range of expected cases was obtained based on the stochastic model, which even accounted for the reduction of new imported cases following the closure of international airports. The deterministic estimate achieved an adequate fit with respect to accumulated cases until the conclusion of the mandatory national quarantine and gradual reopening, when reported cases increased. The estimated new cases were reasonably fit with the maximum reported incidence.

Conclusion: Adequate model fit was obtained with the reported data. This experience of monitoring epidemic trajectory can be extended using models adapted to local conditions.

Keywords

COVID-19, theoretical model, epidemiological monitoring, Colombia

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Introduction

In December 2019, four cases of pneumonia of unknown cause were registered in the city of Wuhan (Hubei province in China) which were epidemiologically linked with a seafood market (Huanan Seafood Wholesale) where live animals were also sold.^{1,2} This cluster of cases activated the Chinese epidemiological surveillance protocol and the Chinese authorities notified to the World Health Organization (WHO) of pneumonia cases of unknown cause in 2019.²

The first WHO report, consolidated in January 2020, registered 41 new cases of pneumonia of unknown etiology.³

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Subsequently and quickly, a new type of coronavirus (Novel Coronavirus—2019-nCoV) and the genetic sequence was isolated from bronchoalveolar lavage samples from hospitalized patients.⁴ In February 2020, the WHO decided to designate this coronavirus disease as “COVID-19,” taking international recommendations to minimize unnecessary negative impact of disease names.⁵ Due to the international spread of the epidemic, the WHO declared a global health emergency on January 31, 2020 and declared the pandemic on March 11.⁶

As of March 31, 2021, this organization registered about 128 million accumulated cases and three million deaths worldwide, after a consecutive increase in cases during the first quarter of 2021. The report of cases and deaths has been higher in the Americas (43.58% and 48.02%) and in Europe (35.05% and 34.58%).⁷ Colombia reported more than two million cases from the beginning of the pandemic until March 31, 2021, with 4652.5 accumulated cases and 123.1 deaths per million inhabitants, placing among the top five most affected countries in the region.⁸ Disease behavior and mortality have varied across the country’s geographical regions, due to diverse socioeconomic conditions and health system response capacity.⁹

This work reports the experience of monitoring the COVID-19 pandemic during the first year of the epidemic in Medellín, the second largest city in Colombia, and compared with the national situation, guided by mathematical theory and epidemiological surveillance data analysis conducted in close and continuous communication with the epidemiological surveillance and academic teams.¹⁰

In the European guidelines for preparing the emergency response,¹¹ scenarios were established that took into account the onset of transmission derived from imported cases, increased community transmission, and increased pressure on health services to attend to cases. These phases were anticipated with the perspective of guiding the control measures, but a theoretical explanation was necessary through the use of mathematical models that would guide the understanding of the particularities of each phase and adjust the guidelines to local conditions, instead of assuming that the pandemic would follow the same evolution in all countries, based on a single explanation of the dynamics of disease transmission and therefore, on a single mathematical model.

We use successive models to explain the epidemic which originated in imported cases in a first phase, describe the occurrence of community transmission in a second phase, and an increase in severe cases in a third phase, with discussing the epidemiological team in real-time.^{11,12}

In Colombia, the first COVID-19 case was confirmed in Bogotá in a passenger from Italy on March 6, 2020.¹³ The first case from Medellín was confirmed on March 9, 2020, corresponding to an imported case from Spain.

During the first phase of the epidemic (March to April 2020), most of the detected cases were imported, which

gradually decreased after the closure of national and international airports on March 23, 2020. In the second phase (May to September 2020) community transmission was evidenced from the occurrence of localized outbreaks and the increase in detected cases. The country’s mandatory quarantine was officially extended from March 25 to August 30. As of September 1, 2020, national and international flights and various economic and social activities gradually resumed. The third phase of the epidemic was analyzed from the last quarter of 2020 and the first quarter of 2021 with notification data from Medellín, when severe cases and the demand for ICU beds increased.

We consider that this work, of construction of the models, in an iterative and continuous process and in close collaboration with those in charge of epidemiological surveillance, can be valuable, as it enables other countries in similar circumstances to adapt these models to their local conditions.^{12,14,15}

Design and methods

The COVID-19 epidemic was monitored in Medellín, Colombia, using different mathematical models that made it possible to understand the behavior of confirmed cases in each observed epidemic phase.

The design and execution of the models followed a systematic and iterative process,¹⁴ summarized in Table 1: (a) description of the temporal behavior, empirical and theoretical explanation of the problem and formulation of the question to be modeled in collaborative work with the interested parties. For the description of temporal behavior, we obtained reported case data according to the date of symptom onset, notification, and diagnosis. Data were disaggregated according to source of origin (imported, related or relatives/close contacts, and under study or testing) and severity (mild, moderate, severe, asymptomatic, fatal). Information was obtained from individual reports of laboratory-confirmed cases (March 2020 through April 11, 2021) published openly by the National Institute of Health of Colombia (Instituto Nacional de Salud, in Spanish), following case definition, diagnostic procedures and mandatory notification protocols.¹⁶ At the beginning of the epidemic, the case definition included: fever measured greater than or equal to 38°C and cough, with mild, moderate or severe acute respiratory infection, and at least one of the following conditions: recent travel to China or other areas with confirmed viral circulation of the novel coronavirus during the 14 days prior to the onset of symptoms, health worker or other hospital personnel with close contact with a probable or confirmed case, or a history of close contact with a probable or confirmed case in the last 14 days.¹⁶ The need to estimate the expected cases was identified, as a question to be modeled, from the analysis of the empirical behavior and the theoretical explanation of each phase observed in the epidemic.

Table 1. Reference framework for the description and theoretical explanation of the phases of the Covid-19 epidemic in Medellín and Colombia.

Steps	First phase March–April 2020	Second phase May–Sept. 2020	Third phase Oct. 2020–March 2021
Description of the behavior of the epidemic: Main findings	At the beginning of the pandemic, mainly imported cases were reported.	Community transmission was postulated when the number of cases under study whose epidemiological link could not be established in contact tracing and outbreaks research.	An increase in cases and deaths was reported. The need to estimate the ICU beds required to attend severe cases was identified.
Empirical and theoretical explanation of the problem	Transmission limited to local clusters generated by imported cases	Sustained community transmission	Sustained community transmission with increasing pressure on health care system
Formulation of the question	What is the number of cases expected at the beginning of the epidemic?	What is the number of cases expected according to the trajectory of the epidemic?	What is the expected number of cases that require hospitalization in intensive care unit (ICU)?
Selection and construction of the model	Stochastic branching process following a Borel-Tanner distribution	Deterministic Susceptible-Infected-Removed (SIR) model	Deterministic Extended SIR model (Susceptible, Symptomatic Infected, Asymptomatic Infected, Severe - hospitalized in ICU, Recovered, Deceased)
Verification and adjustment of the model: critical analysis of the results	Estimation of expected cases, mean and standard deviation using accumulated imported cases (Supplemental equations 1–4)	Model: classical deterministic Approximate solution of removals $R(t)$ (Supplemental equation 10), Estimation of new cases detected per unit of time (Supplemental equation 12)	Model: extended deterministic Numerical solution (Supplemental equations 23–30)
Decision of the course to follow: main measures taken	Follow-up of contacts, home isolation of cases	Outbreak investigation, increased capacity for diagnosis and case management	Increase in hospital care capacity - ICU beds

(b) Selection, construction, and verification of the model according to the empirical and theoretical explanation of the problem: in the first phase of the epidemic (March–April 2020), expected cases were estimated using a stochastic branching model following the Borel-Tanner distribution.^{17,18} The Borel Tanner distribution describes the size of the outbreak up to a certain period of time, assuming that imported cases generate secondary cases (or offspring in the language of branching processes) with a certain mean and variance. Given that after the closure of the airports the arrival of new imported cases would not be expected, the secondary cases cause a minor outbreak of a stochastic nature. The size of the outbreak until a given time, was estimated based on data from imported cases and their relatives or close contacts. Imported case data were recorded for each notification date, to estimate the mean and variance of the accumulated number of cases estimated each day whose expressions are shown in the Supplemental material.

In the second phase of the epidemic (May–September 2020), when community transmission began, the expected cases were estimated using a classic deterministic Susceptible-Infected-Removed (SIR) model.¹⁹

The SIR model, represents the interaction process between infected individuals who were transmitting disease and susceptible individuals who acquired infection with an infection rate β , and the subsequent removal of those infected with a removal rate γ , due to isolation, diagnosis, and treatment which resulted in recovery or death. This model assumed a constant population, in which all susceptible individuals effectively had the same probability of infection, transmission occurred from person to person without intermediate hosts in the transmission chain or incubation period, and did not consider loss of immunity or reinfection. The model assumes that the actual number of infected individuals at every time was not observed, and confirmed cases belonged to the removed class, as they leave circulation through isolation as well as individual and community control measures prescribed by epidemiological surveillance. The expected cases accumulated up to a given date were estimated from the approximate solution of the model with respect to those removed.¹⁹ Additionally, the expected new cases per day were estimated, using analytical formulas derived from the model.¹⁹ The system of ordinary differential equations of the SIR model is shown in detail in the Supplemental material.

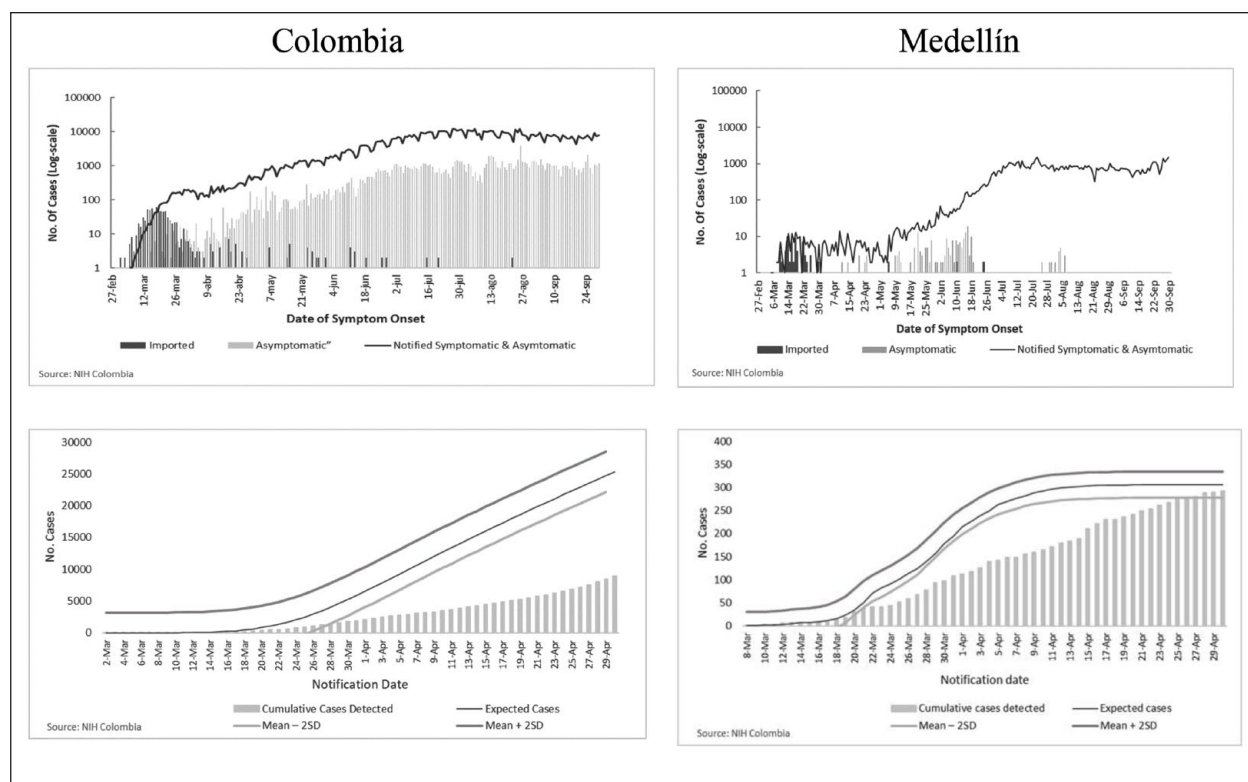


Figure 1. First phase of the epidemic from March to April 2020: Daily progression of confirmed COVID-19 cases and their close contacts (top) and stochastic estimation of expected cases from imported cases (bottom), Colombia and Medellín.

Later, in a third phase of the epidemic, from October 2020 to March 2021, cases were estimated according to severity, using an extended SIR model, including asymptomatic, serious, and deceased cases (Susceptible, Symptomatic Infected, Asymptomatic Infected, Severe-hospitalized in intensive care unit ICU, Recovered, Deceased).

Standard parameter estimation procedures and simulations of the estimated cases were carried out using an adaptive nonlinear least-squares algorithm implemented in the NLReg package[®] (version 6.5—P. Sherrod, TN, USA) including metrics for evaluating the quality of the fit of the model to the data by analyzing the variation of the residuals and performance metrics such as the adjusted coefficient of multiple determination, the root mean squared error, correlation, F-value test.²⁰ Maple's computer algebra package[®] (Maplesoft Inc, Ontario Canada) was used to solve the models both analytically and numerically. The variability of estimated cases was calculated using the centered and non-centered moving average and two standard deviations.²¹ The theory and results obtained were critically analyzed in conjunction with the local epidemiological surveillance team. Medellín has a health service network system and epidemiological surveillance that is coordinated by the regional and national health authority, in which daily data on cases reported and the availability of hospital

and ICU beds are centralized, facilitating the comparison of estimated and reported local and national transmission.

Ethical approval was not required for the use of anonymous data that were available on the internet and reported by the National Institute of Health of Colombia, as a health authority.

Results

The first phase of the epidemic (March–April 2020):

The majority of imported cases were detected through April 7, 2020 with 756 cases in Colombia and 72 imported cases in Medellín, which gradually declined following the closure of national and international airports (Figure 1).

During this phase, an adequate fit of the cases estimated with the stochastic model for Colombia and Medellín was observed (Figure 1).

The theoretical explanation of the occurrence of minor outbreaks caused by imported cases based on the descriptive analysis, allowed to plan slowly but quickly the control measures in this initial phase. Medellín's Secretary of Health promoted actions such as isolation of cases at home, neighborhood sample collection, daily telephone health status monitoring, and community contact tracing.

The second phase of the epidemic (May–September 2020):

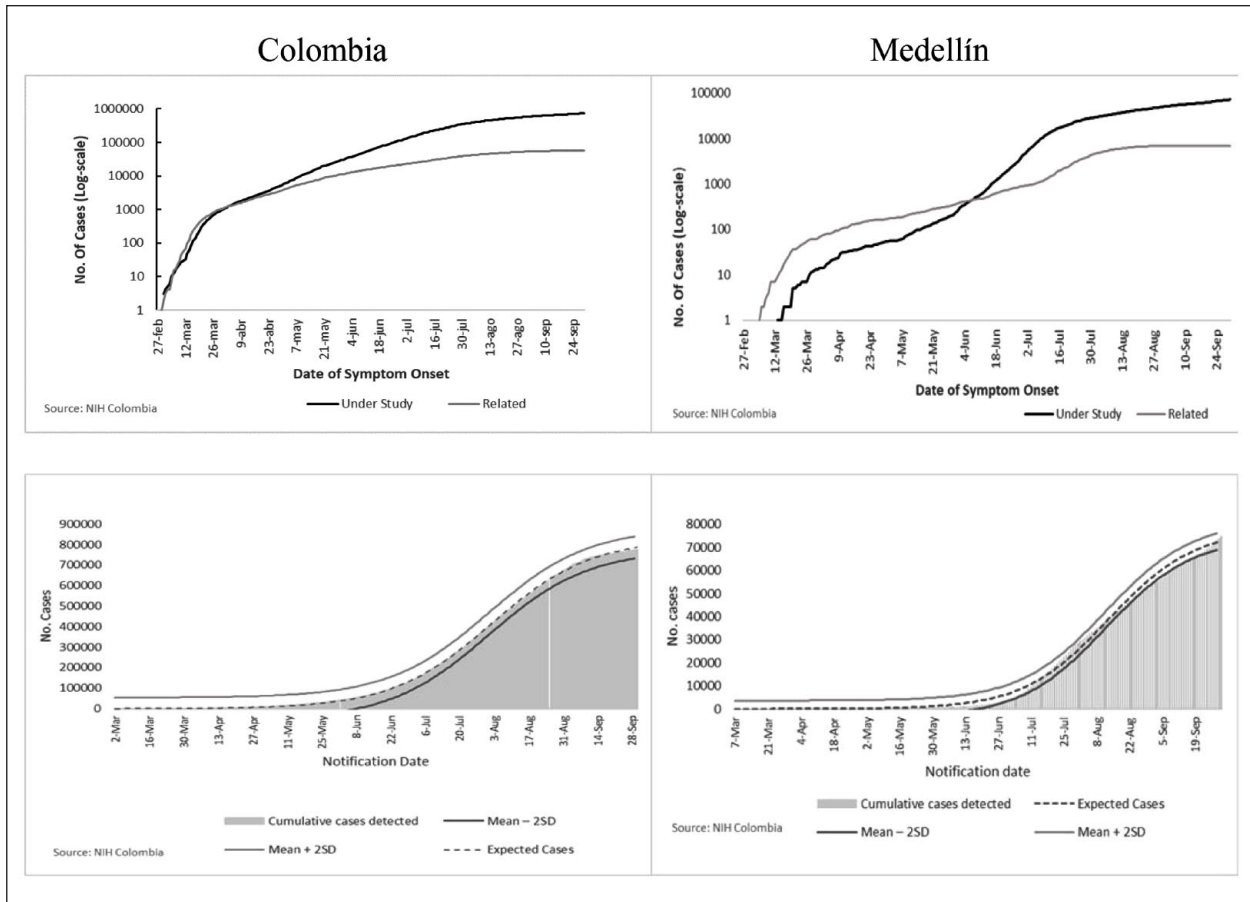


Figure 2. Second phase of the epidemic from May to September 2020: description of the evolution of COVID-19 cases according to type of epidemiological link (top) and deterministic estimation of expected cases according to the classic SIR model (bottom), Colombia and Medellín, 2020.

In Colombia as a whole, it is possible that the rapid increase in symptomatic and asymptomatic cases reported in the first months delayed epidemiological surveillance activities such as the search and isolation of cases and contacts, leading to greater transmission (daily median of 211 cases in April, 980 in May, 2951 in June, 8708 in July, 9330 in August, and 7240 in September). The increase in related cases under study could mark the beginning of community transmission, when identification of asymptomatic cases during outbreaks and contact tracing visits increased at the end of April 2020 (Figure 2).

In Medellín, the increase in cases under study, with respect to those that were studied, was observed from June 2020, when the case report increased (daily median of six cases in April, 9 in May, 64 in June, 876 in July, 781 in August, and 723 in September) (Figure 2).

In this phase, an adequate fit of the classical deterministic SIR model was observed for Colombia and Medellín. In this city, greater oscillations were observed in the accumulated reported cases at the end of July and September 2020 (Figure 2).

Figure 3 shows that new confirmed symptomatic and asymptomatic cases in Colombia increased between the

last week of July and the first week of August, with a slight reduction through mid-September when the oscillation of cases stabilized (without differences in the data with respect to symptom onset and notification dates). This observed behavior coincided with the estimate using deterministic expression of the new cases and the estimated parameters (Figure 3). In Medellín, a reasonable fit with the estimated parameters was observed; however, a 1-week difference was observed between the dates corresponding to the reported and estimated maximum number of cases. After this maximum, the number of new reported cases oscillated and there was an increasing trend in new cases detected since mid-September (Figure 3).

The occurrence of outbreaks in confined populations (prisons, geriatric homes, marketplaces, hospitals, among others), indicated the need to implement other measures such as active search for cases, individual and community risk management and biosafety manuals. In particular, before the resumption of economic activities, the reporting of symptoms, hand disinfection, use of face masks, improvements in ventilation, and physical distancing were promoted. This was reinforced with the National Program for Testing, Tracking and Sustainable Selective Isolation

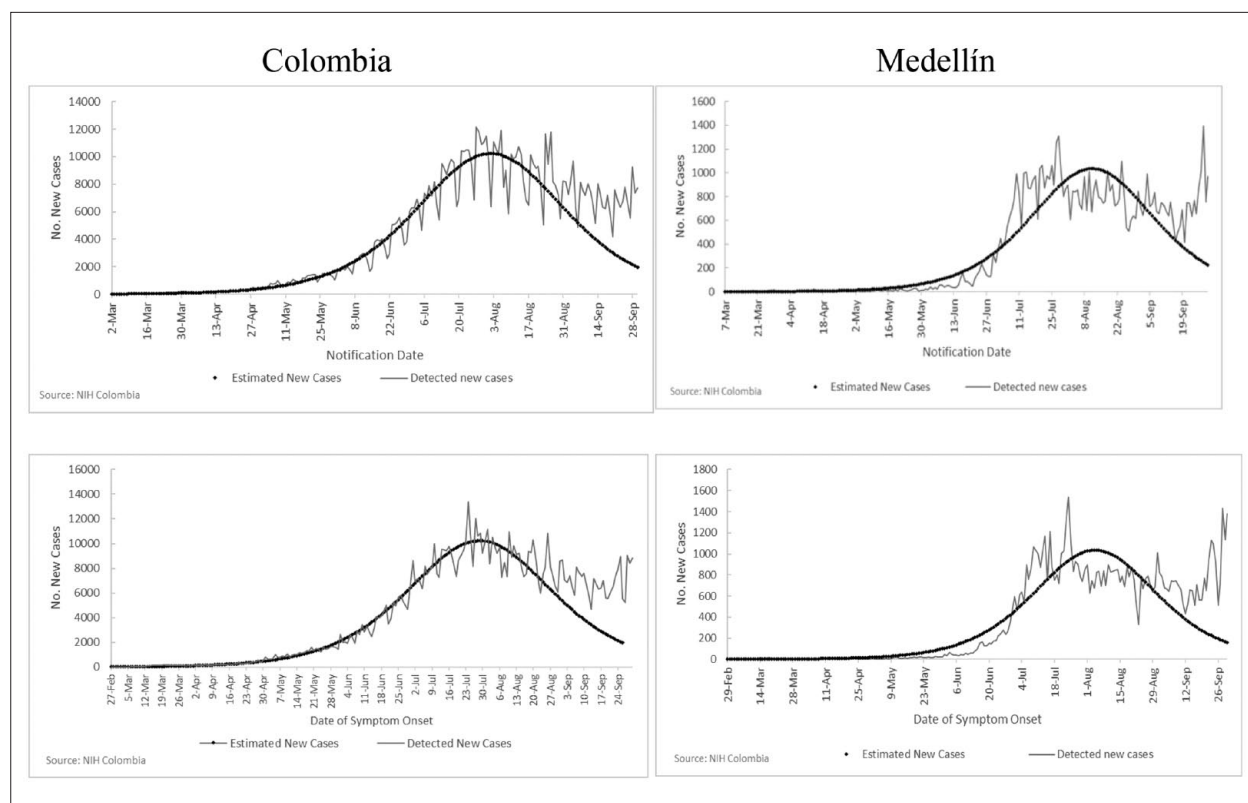


Figure 3. Deterministic estimate of expected new and detected COVID-19 cases, Colombia and Medellín, May–September 2020 (date of notification and onset of symptoms) according to the classic SIR model.

(PRASS—Programa nacional de Pruebas, Rastreo y Aislamiento Selectivo Sostenible in Spanish) (Decree 1109 of August 10, 2020) that gave guidance regarding collecting samples, conducting laboratory tests, and contact tracing.

The third phase of the epidemic (October 2020–March 2021):

It was characterized by an increase in cases, with maximum figures at October, the second half of December through January, and in March. Most of these cases were mild. The accelerated increase in case confirmation in March was accompanied by a higher frequency of severe cases and deaths (Figure 4). If this trend were to continue, the severe cases estimated according to the extended SIR model could triple through March 7 and April 7 2021 (Figure 4) and more intensive care unit (ICU) beds would be needed. During this phase, in addition to expanding intensive care unit beds, intermediate respiratory care units were implemented to handle moderate cases, thereby optimizing ICU occupancy.

Discussion

The course of the COVID-19 epidemic was monitored during its first year using models that made it possible to explain the dynamics of transmission in the different epidemic phases observed and from this, estimate the expected

cases daily, in an iterative process of case description reported, theoretical explanation and modeling.

Minor outbreaks that occur even with a basic reproductive number less than one have been reported in the stochastic modeling literature.²² This theory was used in the first phase of the epidemic to estimate the expected cases through a branching process in a subcritical regime under the Borel-Tanner distribution with basic reproductive number less than one.¹⁸ These new cases were propagated by importation, beginning with interactions with the closest contacts, without generating a reaction chain mediated by the βSI expression typical of community transmission. The Borel-Tanner model, assuming a minor outbreak, made it possible to explain the origin of the epidemic in accordance with what was observed in the first month of the epidemic. In contrast, if an SIR model were used, assuming a basic reproductive number of 2 or 3, for a population close to 50 million, as in the case of Colombia, the number of expected cases would be close to the size of the population, which it was not observed in the initial phase of the epidemic.

In the second phase, when considering community transmission, a deterministic SIR model was used, which reasonably described the number of cases removed per day through epidemiological surveillance, observing an adequate fit between what was reported and the model estimates. The early community transmission observed in this

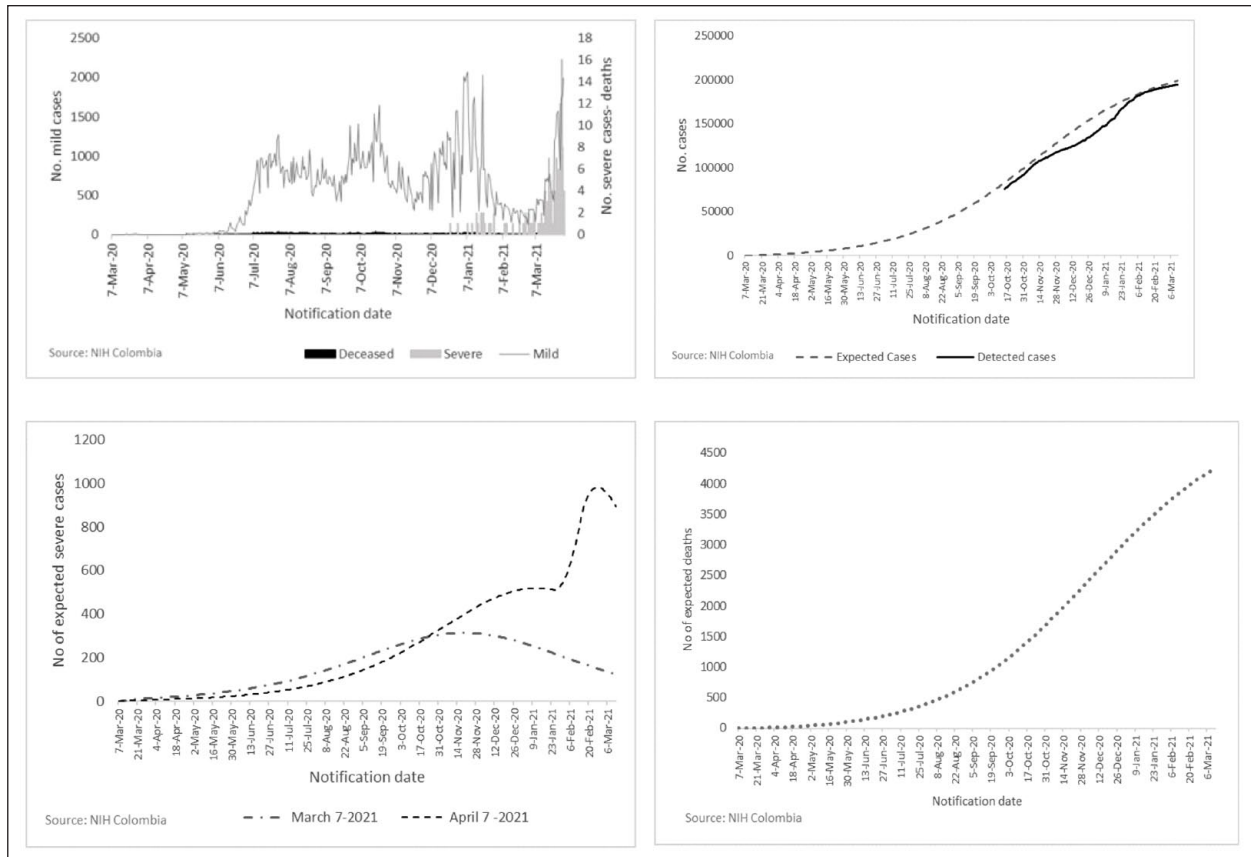


Figure 4. Third phase of the epidemic from October 2020 to March 2021: description of the evolution of COVID-19 cases according to severity level (top) and deterministic estimation of expected cases according to the extended SIR model (bottom), Medellín, October 2020–March 2021.

phase could be related to a greater arrival of cases imported to Bogotá DC, which is the capital district and headquarters of the main international airport.^{13,23} In contrast, the increase in cases under study in Medellín was only evidenced in June, possibly due to the gradual arrival of imported cases, which allowed the local surveillance team to prepare for contact tracing and case isolation, based on prior experience managing the H1N1 influenza pandemic and the reemergence of measles.

In the third phase of the epidemic, there was an observed need to develop a deterministic model that reflected the presence of asymptomatic cases and disease severity level. This model allowed for plausible estimation of severe case frequency, described short term future trajectory, and anticipated necessary hospital care resources, such as ICU beds. Close monitoring of protection measures in hospitals (ventilation in the emergency services, intensive care, and emergency room, and availability of isolation areas) required special attention given the transmission increases and emergence of viral variants.²⁴ Additionally, it was a need for reinforced respiratory control measures in hospitals, including individual rooms for suspected and confirmed cases, accompanied by compliance with respiratory protection measures for health personnel (administrative and clinical) and visitors.²⁵ A systematic

review²⁶ pointed out that specific exposures (intubation procedures, direct contact with the patient and/or with their secretions) are related to an increased risk of infection by SARS-CoV-2 in health workers. In the same review, the use of personal protective equipment and infection control training reduced the risk of infection in workers.

In this work, no “competition” was proposed between models that should be chosen and compared.¹⁵ Instead, models were used that sequentially, not simultaneously, helped to explain the observed behavior of the epidemic in its different phases. In this way, the selection of each model was based on the descriptive analysis of the epidemic’s behavior, the characteristics of the reported cases and the postulation of explanations about the central elements of the transmission dynamics that should be modeled.

In this work, observed cases were monitored daily and empirically contrasted estimates were obtained, rather than focus on reproductive number monitoring. The estimation of expected cases made it possible to directly estimate the resources required for individual care, community prevention and control as well as the protection of health personnel, as part of the emergency response preparedness plans.²⁷

The models used have several limitations: the SIR model assumed that all susceptible individuals had the

same probability of infection, ignoring the underlying structure of the social interactions and differences in exposure by occupation (e.g. health personnel), age, or socioeconomic stratum.²⁸ We assume that the susceptible population at the beginning of the epidemic was the closest contacts of imported cases, instead of considering that, with a homogeneous mixture, 100% of the population was susceptible. In this manner, we estimate the number of susceptible, the infection rate, and the removal rate from the reported cases (considered as “removed”) using the least squares method. This small number of estimated parameters is an advantage of this model, as it serves as a first approximation to understand the transmission dynamics of a little-known disease.²⁹

In estimating the expected cases, patients captured through surveillance were defined as “removed”; once notified, case confirmation and isolation of patients and their contacts begins. The consideration of incidence as an unobserved phenomenon has been proposed in classic models^{19,30,31} and applied to the follow-up of COVID-19 cases in Italy and Brazil.^{29,32} Still, other models assume that cases reported by health authorities in epidemiological surveillance refer to “infected” individuals,³³ which can generate differences in parameter estimation and in transmission process description.

The analysis considers reported cases as “removed” instead of population “disease incidence” following recognition of the insufficient coverage and representation of the surveillance system which precludes adequate detection of all suspected cases and confirmation of new cases. Although it was possible to increase consultation and case detection due to greater risk awareness compared to routine surveillance, other socioeconomic and cultural considerations such as fear, stigma, and lack of health services access could limit timely cases detection, thereby preventing transmission control and opportune case reporting. The non-existence of a single and integrated information system prevents monitoring of transmission heterogeneity according to population subgroup socioeconomic conditions such as care follow-up and clinical evolution, including mortality. In this work, we used openly published and daily updated data provided by the national health authority (Instituto Nacional de Salud), which encompassed indicators analyzed in this work. The limitations of the reported case profile data are known. Data on deaths obtained by epidemiological surveillance should be compared with death certificates. Asymptomatic cases are detected primarily in the contact tracing; the estimation of their population size requires additional studies. Severe cases detected by epidemiological surveillance can be compared with information from ICU admissions, but additional information on unmet demand is required.

The comparability of routine surveillance data between different countries may be limited by differences in cases confirmation criteria and diagnostic tests used, which

simultaneously limits the comparability of results obtained by this study and those reported in the literature. This work refers to laboratory-confirmed cases, in a stable surveillance system that has not had changes in criteria for case confirmation.

When an adequate fit between what is reported and what is expected is not observed, it will be necessary to adjust the model, since the approximate solution of the deterministic SIR model used in this work only applies if the total epidemic size is less than the ratio between the removal rate and the infection rate.¹⁹ The sequential increase in reported cases in each phase along with severity demonstrates the need to continue monitoring reported case occurrences and identify new theoretical and transmission control approaches, without exceeding health system capacity and exacerbating pauperization and socioeconomic inequality resulting from strict quarantines and other containment measures. It is necessary to develop other models that represent phenomena not observed or not studied in this work such as simultaneous outbreak occurrence, changes in biological and social susceptibility in population subgroups, the population effect of vaccination, temporal variation in infection and clearance rates, changes in virulence or viral variants, and the influence of gradual school, college, and university reopening on transmission.³⁴

The unprecedented social and public health emergency caused by the pandemic has stimulated the formation of working groups to try to understand disease behavior based on disease transmission dynamics theory and epidemiological surveillance experience, taking into account the lessons learned from the joint work.¹⁰ Although epidemiological surveillance data limitations have been recognized, the magnitude and trend of reported cases can be understood by decision makers, the public, and health personnel, who simultaneously need to apply them and work to improve data quality and disease control.

Conclusion

Adequate model fit was obtained with the reported data. The models used enabled proposal of theoretical explanations of different pandemic phases from the initial outbreaks driven by imported cases, through community transmission, and the subsequent continued spread, as well as estimation of the resources required for hospital care. This joint work, contrasting the empirical and theoretical, can be extended to other countries interested in understanding the local conditions of disease transmission.

Contribution

Acknowledgment that all authors have contributed significantly and that all authors agree with the content of the manuscript. Juan Ospina: Conceptualization, Investigation, Methodology, Formal analysis, Validation, Writing—Review & Editing.

Doracelly Hincapie-Palacio: Conceptualization, Investigation, Methodology, Software, Formal analysis, Validation, Writing—Original Draft, Writing - Review & Editing

Jesús Ochoa, Carlos Velasquez, Rita Almanza Payares: Conceptualization, Investigation, Methodology, Software, Formal analysis, Validation, Writing—Review & Editing

Declaration of conflicting interests

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Ethical approval and consent to participate

We used anonymous data from official sources. Ethical approval was not required for the use of anonymous data that were available on the internet and reported by the National Institute of Health of Colombia, as a health authority.

Patient consent for publication

This is not applicable

Informed consent

The manuscript does not contain any individual person’s data in any form

Significance for Public Health


This work reports COVID-19 epidemic monitoring during the first year of the pandemic in Medellín and compared with the national situation in Colombia, using epidemiological

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Availability of data and material

The data used to support the findings of this study are available from the corresponding author upon request

Supplemental material

Supplemental material for this article is available online.

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