REVIEW

Mathematical model and COVID-19
Modelos matemáticos y el COVID-19

Elvia Karina Grillo Ardila[1] **, Julián Santaella-Tenorio**[2,3] **, Rodrigo Guerrero**[2] **, Luis Eduardo Bravo**[4,5]

elvia.grillo@correounivalle.edu.co

1 Universidad del Valle, Facultad de Salud, Doctorado en Salud. Estudiente de Doctorado, Cali, Colombia. **2** Universidad del Valle, Facultad de Salud, Escuela de Salud Pública, Cali, Colombia, **3.** Pontificia Universidad Javeriana, Maestría en Epidemiología Clínica Cali, Colombia, **4.** Registro Poblacional de Cáncer de Cali. Cali, Colombia. **6.** Universidad del Valle, Facultad de Salud, Departamento de Patología, Cali, Colombia.

Abstract

Currently, there are several mathematical models that have been developed to understand the dynamics of COVID-19 infection. However, the difference in the sociocultural contexts between countries requires the specific adjustment of these estimates to each scenario. This article analyses the main elements used for the construction of models from epidemiological patterns, to describe the interaction, explain the dynamics of infection and recovery, and to predict possible scenarios that may arise with the introduction of public health measures such as social distancing and quarantines, specifically in the case of the pandemic unleashed by the new SARS-CoV-2/COVID-19 virus.

Comment:

Mathematical models are highly relevant for making objective and effective decisions to control and eradicate the disease. These models used for COVID-19 have supported and will continue to provide information for the selection and implementation of programs and public policies that prevent associated complications, reduce the speed of the virus spread and minimize the occurrence of severe cases of the disease that may collapse health systems.

Conflict of Interest:

None declared

Corresponding author:

Elvia Karina Grillo Ardila, Registro Poblacional de Cáncer de Cali. Calle 4B 36-00 Edificio 116 Oficina 4009, Cali, Colombia. e-mail: elvia.grillo@ correounivalle.edu.co

Remark

1)Why was this study conducted?

This study was conducted to provide an overview of the design, approach and use of mathematical models, a useful analytic tool to guide the planning of health strategies; in this case, strategies for the SARS-CoV-2/COVID-19 pandemic.

2) What were the most relevant results of the study?

This study highlights the main elements used in mathematical models to predict patterns of infectious disease epidemics, with a focus on SARS-CoV-2/COVID-19; the review includes a description of epidemiological variables, population factors and public health interventions that can influence infection rates .

3) What do these results contribute?

This study provides information about the main components of mathematical models their characteristics and factors influencing the model components, and how they can be used to estimate possible future scenarios of the epidemic.

Resumen

En la actualidad existen varios modelos matemáticos que han sido desarrollados para entender la dinámica de la infección por COVID-19. Sin embargo, la diferencia en los contextos socioculturales entre países hace necesario el ajuste específico de estas estimaciones a cada escenario. Este artículo analiza los principales elementos usados para la construcción de los modelos a partir de patrones epidemiológicos, para lograr describir la interacción, explicar la dinámica de infección y recuperación, así como para predecir posibles escenarios que pueden presentarse con la introducción de medidas en salud pública como el distanciamiento social y cuarentenas, específicamente para el caso de la pandemia desatada por el nuevo virus SARS-CoV-2/COVID-19.

Comentario:

Los modelos matemáticos son de gran relevancia para la toma de decisiones objetivas y eficaces para controlar y erradicar la enfermedad. Estos modelos usados para el COVID-19, han apoyado y seguirán aportando información para la selección e implementación de programas y políticas públicas que prevengan complicaciones asociadas, disminuyan la velocidad de propagación del virus y minimicen la aparición de casos severos de enfermedad que puedan colapsar los sistemas de salud.
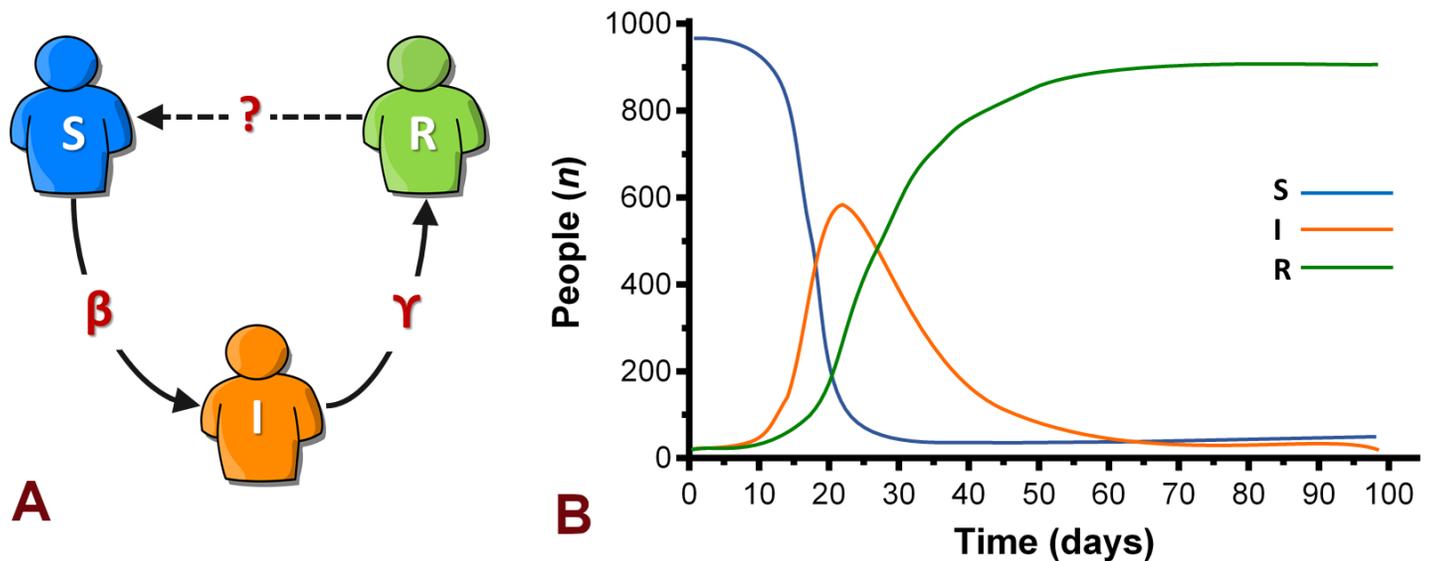
Figure 1. Dynamic model of the COVID-19 pandemic. The model has three dependent variables: the number of susceptible (S), infected (I), and recovered (R) people, which are influenced by the infection rate (β) and the recovery rate (Ƴ). The variation over time in the number of people who are susceptible (S) decreases with time and depends on the infection rate (β). The variation over time of the number of infected depends on the infection rate (β) and the recovery rate of the infected (Ƴ). The variation over time in the number of recovered (R) depends on the recovery rate (Ƴ) of those infected.

The effort to decipher the behavior of diseases through mathematical formulas, the so-called "models", has recently had a great resurgence, especially regarding infectious diseases [1], but this interest is not new. In 1760, Daniel Bernoulli proposed several mathematical models for some infectious diseases, especially smallpox, which at that time affected the English population [2,3]. Moreover, Ronald Ross explained the model of human malaria, with the complete cycle and the inclusion of the mosquito as a vector and the Plasmodium parasite, which is why he won the Nobel Prize in 1902 [2]. Below we will mention some of the recent publications on modelling [4-7].

The SIR model for Spread of Disease

Although there are currently several models for COVID-19 [4], the differences in the sociocultural contexts between countries require the specific adjustment of these estimates to each scenario. Since COVID-19 is a disease caused by a new virus, it requires modelling of new factors that help in the development and evaluation of disposals such as confinement and other proposed social measures [8].

In its simplest form, a global model to predict the dynamics of COVID-19 considers the behavior of the virus in the population and takes into account three groups: Susceptible, Infected and Recovered, which is known as the SIR model. For this model, it is important to know the rates of infection (β) (% of infected among those exposed) and recovery (Ƴ) (% of recovered among those infected). Figure 1 shows the variation over time in the size of each SIR population and how it depends on the infection (β) and recovery (Ƴ) rates.

Although this model is very useful for studying the dynamics of the population as a whole, it does not take into account the local interactions between individuals beyond what is reflected in the parameters, nor does it take into account the number of infected people who die, or whether the immunity induced by the infection is permanent.

Every model requires a precise knowledge of the population and of the infection and recovery rates. But in addition, the case fatality rate (% deaths among those infected) should be considered, which affects the number of people infected and recovered. In case of not knowing these rates and the case fatality rate, it is necessary to estimate them based on similar situations or simply to assume them. A model will be as accurate as the assumptions about susceptible population size, rates, and fatality rate are.

Next, the elements of the model for COVID-19 will be analyzed.

Susceptible population

The disease known as COVID-19 is a new, acute and severe respiratory syndrome caused by the novel coronavirus 2 (SARS-CoV-2). Because it is a virus that did not previously exist, it could be thought that the entire population is susceptible to becoming infected. And thus, for example we could assume that the entire population of Wuhan, a Chinese city of 11 million inhabitants was theoretically susceptible. But the risk of exposure varied widely as most of the initial cases were related to a local seafood and live animal market in Wuhan City [9,10]. Very soon it could be established that COVID-19 was more frequent and severe in people with certain lung diseases, hypertension and diabetes (comorbidities) [11,12]. From a practical point of view, it was impossible to determine exactly the population at risk and therefore impossible to accurately calculate the infection rate.

SARS-Cov-2 and infected population

SARS-CoV-2 is highly contagious, thus, it can be transmitted by direct skin-to-skin contact, by micro secretions of saliva or mucus when talking or coughing near another person, or by indirect contact with objects such as keys, infected packages, etc [13]. The virus is very sensitive to ultraviolet rays and is rapidly inactivated at cooking temperatures and in the presence of 95% ethanol or 0.1% sodium hypochlorite [14-16].

The average incubation period is 5-6 days and the duration of the disease is 14 days when the disease is mild and 3-6 weeks when it is severe. Hypoxemia is established in one week and death occurs between 2-8 weeks after the onset of symptoms. An estimated 60-80% of infections are asymptomatic and likely to produce long-lasting immunity, making it more difficult to estimate the population at risk [17,18].

COVID-19 Case Definition

Confirmatory laboratory diagnosis of SARS-CoV-2 infection is based on the identification of viral RNA by polymerase chain reaction (PCR) tests, in samples taken from nasopharyngeal secretions. In Colombia, according to the standards of the National Institute of Health, the case diagnosis of COVID-19 is made by detection of viral RNA using the RT-PCR technique (Reverse Transcriptase PCR).

Additionally, the diagnosis of infection can be obtained by detecting antibodies resulting from the infection (serology) or by detecting antigens in blood. PCR requires infrastructure, qualified personnel, and results may be available from several hours to two days after sample collection [19]. Serological detection is rapid, the results are available in minutes and it allows to identify infected people who have developed IgM and IgG antibodies against the virus [13,20]. Antibodies are produced and detected serologically on average 5-7 days after the onset of
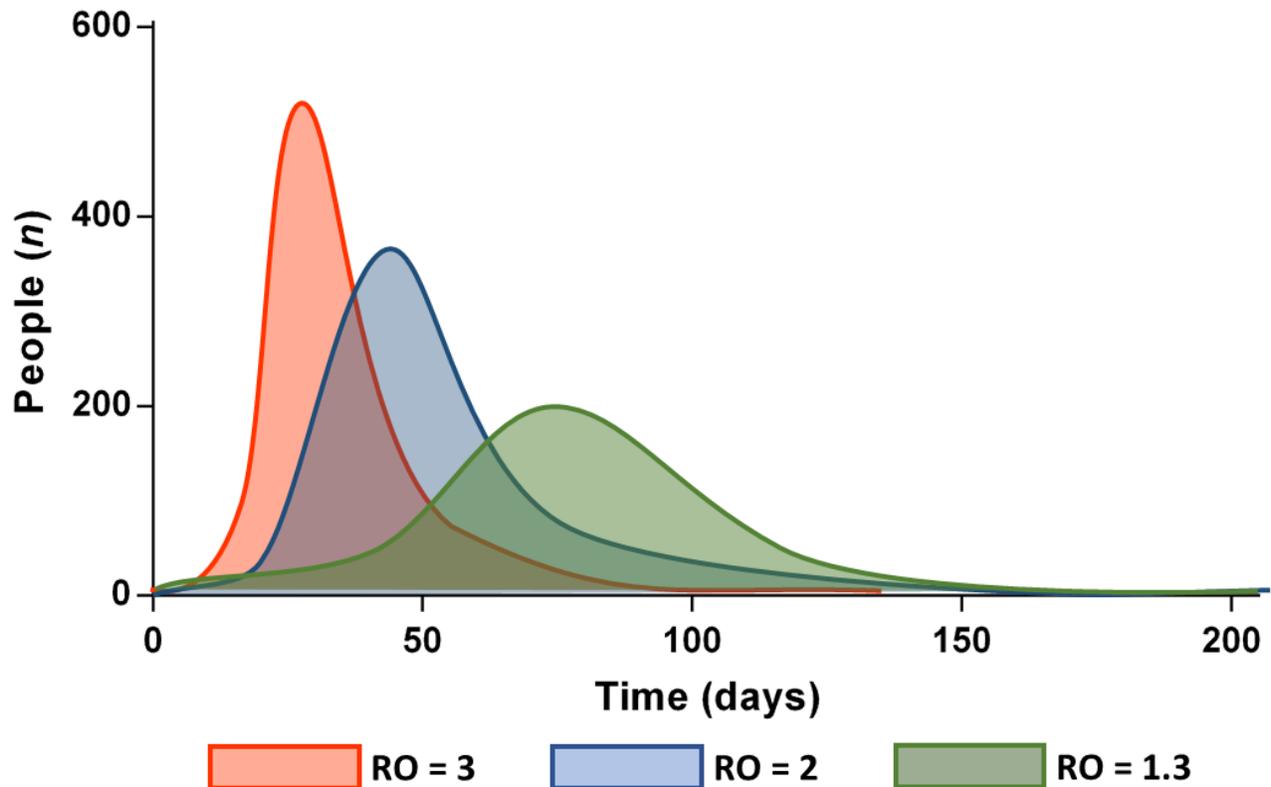
Figure 2. Dinámica del modelo SIR con diferentes valores del número reproductivo básico R 0. El comportamiento de la curva de infección varía de acuerdo al valor que asuma R0. Cuando el R0 es mayor la curva presenta un pico pronunciado de corta duración; mientras que cuando el R0 es más cercano a 1, la curva de infección es una pendiente más aplanada de mayor duración.

symptoms. People who have antibodies against the virus may be having symptoms, have been asymptomatic or have symptoms and be already in the recovery phase. The presence of antibodies shows that the person has immunity against the virus, although it is unknown for how long this immunity is conserved. From an epidemiological point of view, serological surveillance allows to know the prevalence and the herd immunity in a population [21].

Infection rates

It is important to know the probability of infection and its variability in a population, to understand its dynamics and the effects of the interventions. There are two important parameters to determine at the beginning of pandemics: The secondary attack rate and the reproductive number. Subsequent or post-pandemic investigations determine attack rate and prevalence.

Secondary attack rate

It is the probability of occurrence of SARS-CoV-2 virus infection among susceptible people who contacted the index case.

$$\text{Secondary attack rate: } \frac{\textit{Number of exposed people who end up infected}}{\textit{Number of susceptible people exposed}}$$

In the Guangdong and Sichuan provinces, the secondary intrafamilial rate of the SARS-CoV-2 virus was estimated to be between 3 and 10% [9].

Reproductive number

In the SIR model, the basic reproductive number (R_0), R0=β (infection rate)/γ(recovery rate), refers to the number of people who become infected from a case in a fully susceptible population [22]. R_0 is an indication of how and how fast the virus moves. For an epidemic to occur, R_0 must be > 1, because the infection rate is greater than the recovery rate and the infection spreads (Figure 2). In the Wuhan outbreak the R_0 was 2-2.5 [23,24].

Dynamics of the infected in an SIR model with N = 200 individuals and different values of R_0. Basic reproductive number. R = 0 = β⁄γ refers to the number of people who become infected from a case.

Because R_0 depends on the assumption that the population is completely susceptible, effective reproductive number (R_t) is used in mathematical models that analyse the evolution of transmission potential in a given period. R_t is defined as the number of infections caused by any case at a time t [25,26]. This term represents the effective version of R_0, the actual transmission rate of the virus at any given time. Its importance lies in that it provides great information by tracking the evolution of the transmission. Although its value is dynamic, which implies that it can change as control measures are implemented to prevent the spread of the disease (eg, quarantines, social distancing, mobility restriction, use of personal protection implements (face masks, protective suits, etc), it is possible to determine it with equations that take into account the temporal relationship between incident cases in different periods (25). Due to this, the effective reproductive number is of great importance in public health since it allows us to understand how effective infection control strategies have been in the population.

The reproductive number is not an intrinsic variable of the infectious agent, since it is influenced by the duration of the contagion, the probability of infection between contacts, and by economic, social and environmental factors. Figure 2 shows the dynamics of those infected in an S.I.R. model with different R values.

For example, regarding COVID-19, the social practices of hugging and kissing each other to greet that Italians and Spaniards have, facilitate the transmission, in contrast to the respectful and distant bow of the Japanese. Likewise, environmental factors such as temperature (22-25° C) and relative humidity (40-50%) can favour the viability of the virus on surfaces [27], affecting the infection rate. Both wearing face masks and prompt and careful handwashing with soap is helpful in reducing the infection rate [28,29].

For the calculation of the infection rate, the models generally assume that contacts occur randomly, however, there are massive events classified as contagion epicentres or super-contagious events. An example of this was the football match played on February 19, 2020 attended by more than 40,000 Atalanta fans who travelled from Bergamo to Milan, which resulted in a large number of people infected with COVID-19 [30].

Case fatality rate

The Case Fatality Rate (CFR) gives an insight into the dangerousness of the virus and helps to better understand the COVID-19 pandemic and its risks. The proportion of hospital admissions requiring intensive care and/or mechanical ventilation and the death of people who had pre-existing medical conditions are also important indicators of severity. On the other hand, the CFR is different from the mortality rate. The CFR indicates the probability that a person has to die once they are infected by the virus, while the mortality rate indicates the probability of dying within a population.

It would be easy to calculate the CFR by dividing the total number of deaths with COVID-19 by the total number of those infected with SARS-CoV-2, but given that many infected

individuals spontaneously evolve towards cure, it is necessary to define precisely how to define being "infected": evidencing the infection through laboratory tests? With the appearance of symptoms? At the time of hospitalization? The CFR can vary considerably, according to these definitions and according to the strategies used to identify those infected in a country or region (eg, number of tests carried out to identify those infected).

Additionally, the CFR is significantly affected by factors associated with the quality of medical care, such as the presence of specialized personnel, Intensive Care Units, respirators, availability of treatments, etc. These factors can improve the survival of patients with severe symptoms. Likewise, the case fatality rate can be affected by previously mentioned conditions such as those related to the host: age, obesity and the presence of morbidity cofactors such as diabetes and lung and kidney diseases. The CFR has an important influence on the population of recovered patients in the SIR model.

Conclusions

Mathematical models are a useful instrument for addressing health problems. Given the current pandemic unleashed by the transmission of SARS-CoV-2, the construction of mathematical models based on epidemiological patterns has allowed to describe the interactions, explain the dynamics of infection and recovery, as well as predict possible scenarios that may arise with the introduction of measures such as social distancing and quarantines. However, there are important challenges in identifying positive cases and deaths related to infection, data that are key in estimating reproductive rates and numbers. Increasing efforts to identify the incidence of cases and deaths from the virus will help improve the prediction of potential infection scenarios in these models. Mathematical models are highly relevant for making objective and effective decisions to control and eradicate the disease. These models have supported and will continue to contribute in the selection and implementation of programs and public policies that prevent associated complications, slow down the spread of the virus and minimize the appearance of severe cases of disease that may collapse health systems.

An unexpected epidemiological aid: The Diamond Princess Cruise Case

The recent and interesting story of the passenger ship Diamond Princes has clarified some of the unknowns in the epidemiology of COVID-19. This ship set sail from Yokohama on February 4, 2020, carrying 2,666 passenger tourists and 1,045 crew. On the 7th, a passenger who had boarded in Yokohama disembarked in Hong Kong, with symptoms of COVID-19 that were confirmed by the health authority. The Diamond Princess and all its passengers were immediately quarantined. Diagnostic tests were carried out on more than 80% of the passengers and crew. 700 infected were found and 12 passengers died. The CFR was 2.3% considering those with symptoms and 1.2% when including also the asymptomatic. For the interpretation of the lethality, it must be taken into account that the average age of the passengers was 69 years old and that 55% of the passengers were women [31,32].

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