

MEDICC Review

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April–July 2019

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Dengue Cases in Colombia: Mathematical Forecasts for 2018–2022

Luis Eduardo López-Montenegro MS PhD, Ana María Pulecio-Montoya MS PhD, Germán Arturo Marcillo-Hernández MS

ABSTRACT

INTRODUCTION Dengue is a disease caused by any one of five virus serotypes and transmitted to humans by the *Aedes aegypti* mosquito. Climate change and health conditions have combined to make dengue a global public health problem. The situation is especially serious in Colombia, where by week 36 of 2018, dengue incidence was 96 cases per 100,000 population, with a total of 111 deaths. Different mathematical and statistical models have been proposed to understand the dynamics of transmission and consequently to apply control strategies to reduce the number of dengue cases.

OBJECTIVE Forecast the number of dengue cases expected in Colombia from 2018 through 2022 with the stochastic Auto-Regressive Integrated Moving Average (ARIMA) model and use the results to adjust the parameters of an ordinary differential equations model in order to determine the disease's basic reproduction number in the year presenting the highest number of dengue cases.

METHODS An ecological time series study was conducted to forecast dengue incidence in Colombia from 2018 through 2022. The data were compiled from Colombia's National Health Institute series on dengue cases reported by epidemiological week from 2009 to 2017. The stochastic ARIMA time series model was applied. Forecasts were then analyzed, and the year with the highest number of predicted cases was used to adjust the parameters of an ordinary differential

equations model (ODE) through nonlinear least squares regression to calculate the vectorial capacity of the transmitting mosquito.

RESULTS Forecasts of the total number of dengue cases per year in Colombia for the following five years were: 32,411 (2018); 88,221 (2019); 56,392 (2020); 47,940 (2021); and 77,344 (2022). The highest number of cases was forecast for 2019. Values for the parameters affecting dengue transmission that year (by the year's four quarters), such as recovery rate (0.0992, 0.0838, 0.1177, and 0.1535, respectively), vectorial capacity of the transmitting mosquito (0.1720, 0.1705, 0.1204, and 0.2147, respectively) and the basic dengue reproduction number (1.73, 2.03, 1.02, and 1.40, respectively) were estimated, indicating that most cases would occur in the second quarter and, since the basic reproduction number values were >1 , the disease would persist in the country throughout the entire year.

CONCLUSIONS ARIMA model forecasts for 2018 through 2022 predicted the highest incidence of dengue cases in Colombia would occur in 2019. Comparison of ARIMA model forecasts and the ODE model allowed projections of possible variations in dengue cases reported, and the basic reproduction number predicted that dengue would persist throughout 2019.

KEYWORDS Arboviruses, climate, dengue, models, theoretical, basic reproduction number, prognosis, Colombia

INTRODUCTION

Arboviral diseases have become a global public health problem due to factors such as climate change, population growth, waste accumulation, pollution, inadequate recycling, and insufficient vector control.[1] Dengue is an acute viral disease transmitted to humans by its principal vector, the *Aedes aegypti* mosquito. Dengue virus (DENV) comprises five serotypes (DENV1, DENV2, DENV3, DENV4, DENV5);[2] the first four circulate simultaneously in Colombia.[3] The different serotypes do not confer cross immunity; an individual who recovers from one acquires permanent immunity against that serotype but only partial and temporary immunity against the other four types.[4]

Several studies have shown that one of dengue's greatest dangers is the increased severity of the infection when multiple serotypes are simultaneously present. That is, a secondary infection with another dengue serotype has a greater probability of causing severe acute infections than the primary disease, due to formation of autoimmune complexes that can attack the body.[5,6]

IMPORTANCE Forecasts of dengue cases in Colombia from 2018 through 2022 based on a time-series study design, combined with an ordinary differential equations model, can help health systems and institutions take more effective, precise preventive and control measures to reduce dengue infection, a serious health problem in the country.

Application of different theoretical and mathematical models has helped us understand the epidemiological dynamics of dengue. Nonlinear models based on systems of ordinary differential equations (ODE) describe variations in numbers of cases in a specific population. However, many factors and conditions are involved in dengue transmission dynamics, and any variation in one of them can lead to significant changes in the shape of the curves that describe growth of the infected population. For example, the model proposed by López[7] contains the following variables: average numbers of healthy, infected, and recovered individuals and average number of mosquitos in the environment; classified as larval (aquatic) or aerial (adult) phase, with adults also classified as female or male.

Through a series of calculations, this model was simplified to include only two variables (proportion of healthy individuals and proportion of infected individuals), thus making it easier to analyze while preserving the hypothetical viral transmission factors of the original version.

Amaku's model considers the virus's state of latency in the mosquito population, its vertical transmission, and how variations in climate factors can influence transmission dynamics.[8] Koiller proposes a population growth model for the *Aedes aegypti* mosquito that considers all phases and states in its life cycle.[9] The model then incorporates a biological control measure through use of *Wolbachia* bacterium. This mosquito-growth dynamic is included in a model to determine the dynamics of transmission to humans under these assumptions, considering the number of individuals exposed.

Each factor involved in the complex dynamics of the disease (presence of asymptomatic individuals and infected individuals, dispersion of the vector and infected individuals, application of one vector control or another, resistance to controls, reinfection by a different serotype, etc.) opens new modeling options. No single model can include all the real factors involved in dengue transmission, so selection of a forecasting model often depends on availability of reliable information on the variables and parameters involved, and on the specific objective of the projection.

Time-series modeling, particularly with ARIMA models[10]—which benefit from repeated autocorrelations to make extrapolations—allows reasonable estimates of future effects of an infectious outbreak on a specific population. In combination with other predictive nonlinear models, ARIMA models have been extremely useful in epidemiological investigations to prevent and control infectious diseases.[11–14]

In Colombia, temperature changes caused by climate phenomena and the growing population living in unhealthy conditions have caused intense propagation of dengue virus and the appearance of new viruses in different regions.[15–17] The community epidemiological bulletin published by the National Epidemiological Surveillance System (SIVIGILA) reported a total of 13,427 confirmed dengue cases at the national level by week 23 of 2018,[15] and by week 36, an incidence rate of 96 cases per 100,000 population, with 111 deaths.[16] The Ministry of Health and Social Protection advised health sector units to monitor and control virus transmission and its effects on the population, which reconfirms the importance of projections to support decision-making and financial resources for preventive actions in the face of such a serious health problem.

The purpose of this study was to apply mathematical models to forecast the average number of dengue cases per year from 2018 through 2022 in Colombia, and to determine dengue's basic reproduction number (BRN) in the year with the highest number of predicted cases in order to identify possible outbreaks.

METHODS

Type of study A time-series study was conducted using Colombia's National Institute of Health routine surveillance system database. The study was conducted from February 2017 through March 2018 by researchers in San Juan de Pasto, Nariño Department, Colombia.

Data sources The database from which the reports on incidence of dengue were taken as time series from 2009 to 2017 was obtained from the National Health Institute's SIVIGILA web portal.[15] Specifically, the data correspond to dengue cases reported by the country's departments (principal administrative divisions) and municipalities as "confirmed" cases of dengue or severe dengue. Data were compiled in XLS-formatted files and included records of dengue cases for each epidemiological week of the respective year.

Variables The study considered two variables: 1) number of dengue cases in Colombia and 2) number of epidemiological weeks.

Mathematical models

ARIMA model This model effectively combines three components: autoregressive (AR), integrated (I) and moving average (MA). It is used to analyze stochastic time series and takes into consideration the correlation between the data and the errors

corresponding to the preceding periods.[10] It is generally represented as $ARIMA(a, d, b)$, where a is the number of autoregressive terms, d is the number of differences, and b is the number of moving average terms. Mathematically it is expressed as:

$$y_t^d = c + \alpha_1 y_{t-1}^d + \dots + \alpha_a y_{t-a}^d + \vartheta_1 \varepsilon_{t-1}^d + \dots + \vartheta_b \varepsilon_{t-b}^d + \varepsilon_t^d$$

where $\alpha_i, i = 1, \dots, a$ and $\vartheta_j, j = 1, \dots, b$ are the parameters to estimate and ε_t^d is a white-noise process.

The mathematical processes and algorithms to analyze time series and their respective predictive process with ARIMA follow four steps:[18]

- 1) Definition of the model, which includes the assumption that forecast errors will be distributed normally around the mean and time-independent variance (white noise) and application of simple and partial autocorrelation functions (ACF and PACF, respectively).
- 2) Estimation of parameters with the orders of the fitting process, according to ACF and PACF functions.
- 3) Evaluation and validation of the tentative ARIMA model.
- 4) Forecasting of time series.

To carry out these four steps, researchers used R software,[19] a free programming language and statistical computing and graphics tool, together with a series of algorithms and packages related to the models under consideration.

Step 1: The time series was generated from the data to be analyzed. Trend and seasonality could be identified and removed through differentiation. A density histogram was also constructed to determine whether the series is stationary, which means forecast errors normally distributed, with zero mean and constant variance.

Step 2: ACF and PACF analyses were performed along with the application of several functions related to ARIMA in the R statistical package; respective graphics were plotted indicating the appropriate order of the lag in the linear $ARIMA(a, d, b)$ model, and respective parameters of the polynomial coefficients were estimated for the tentative model.

Step 3: The Ljung-Box[20] contrast was used to determine the dependency relation among residuals, enabling validation of the model's forecasting capacity.

Step 4: The previously validated $ARIMA(a, d, b)$ model and periodogram were used to forecast future incidence of dengue.

ODE model These equations relate a dependent variable with one or more of its derivatives with respect to an independent variable.[21] In infectious diseases such as dengue, ODEs are generally used to represent variations in time of average numbers of susceptible individuals, infected individuals and recovered individuals, providing a basis for fitting models with parameters that weight features associated with disease transmission. These models are used to estimate the disease prevalence or to predict its disappearance in a particular setting.[22,23]

This study is based on a system formulated by López[7] presented below and adjusted to fit the reported data on dengue in Colombia. The authors have shown that the new model, a simplified version of a more complex one that includes a larger number of variables and parameters, nevertheless preserves the properties of the original model. The rationale for the use of this simplified system