Simulation model for the dynamics of dengue with asymptomatic transmission and the effect of temperature

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Abstract

Background: One of the fastest spreading vector-borne diseases in tropical and subtropical regions is dengue, which generates cost overruns for public health entities. Several factors can influence the dynamics of dengue virus transmission: environmental and climatic (abundance of vectors), interactions between hosts (infections by asymptomatic individuals), and population immunological factors. Given these conditions, it is necessary to carry out theoretical studies based on meteorological factors and asymptomatic transmission that are associated with both the existence of the vector and its incidence, in order to provide a scientific basis for health entities in decision-making.

Methods: A mathematical model based on nonlinear ordinary differential equations is proposed to interpret the dynamics of dengue transmission in humans coupled to the dynamics of the Aedes aegypti species, considering the population of symptomatic and asymptomatic infected humans and the effect of temperature variability. The basic reproduction number was found and some simulation results based on the Runge-Kutta numerical method were obtained.

Results: The simulations showed that the temperature had a directly proportional relationship with the basic reproduction number. The cases of infected people and carrier mosquitoes increased when the temperature peaks increased drastically; in low temperatures the infection persisted with low morbidity due to the survival of asymptomatic people.

Conclusions: High temperatures tolerable by mosquitoes increase their life expectancy and their numbers in the environment which, together with a reservoir of asymptomatic infected people, leads to a
higher incidence of the dengue virus in certain seasons or maintains its circulation in seasons of low temperatures, despite lower vector survival rates.

**Keywords**
Dengue, temperature, Aedes aegypti, asymptomatic, basic reproduction number, simulation model

This article is included in the Emerging Diseases and Outbreaks gateway.
Introduction
Dengue is a viral disease transmitted by mosquitoes of the *Aedes* genus, mainly by the *Aedes aegypti* species, characterized by biphasic fever, myalgia, skin rash, among other symptoms, and can evolve into a clinical condition called severe dengue that can lead to death; this disease is a public health problem worldwide, since it is estimated that about 390 million people are infected annually, and no effective vaccine is available to reduce its incidence. As a consequence, the approaches to reduce its transmission are directed towards control of vector transport by humans through land, air and sea transportation, which has caused its successful colonization around the world. For this reason, and due to the introduction of infectious people into new territories, the dengue virus has spread to more than 100 countries.

Scientifically, it is known that some people infected with dengue are asymptomatic, defined as those infected who do not present clinical symptoms detectable by public health systems; asymptomatic people were considered dead points in the transmission of the dengue virus, since it was believed that their average level of viremia was not high enough to transmit the virus to the mosquito vector, however, recent studies have shown that asymptomatic people, despite their low average level of viremia, are potentially infectious for mosquitoes. It is estimated that of the nearly 390 million cases of dengue infections per year, around 300 million are asymptomatic, that is, no apparent disease interrupts the daily routine of these individuals.

This article is organized as follows: the mathematical model that interprets the dynamics of dengue transmission including the asymptomatic human population coupled to the life cycle of *Aedes aegypti* and temperature variability is formulated in the subsequent sections Methods and Mathematical model formulation; the basic reproduction number of the infection is determined and interpreted in the Basic reproduction number section; the Results and discussion section presents facts from numerical simulations based on the Runge-Kutta approximation method. Finally, the turn of this research considering other factors that affect the transmission dynamics of the dengue virus is discussed in the Conclusions section.

Methods
A mathematical model based on nonlinear ordinary differential equations was formulated to describe the dynamics of dengue virus transmission through the interaction of human populations and female *Aedes aegypti* mosquitoes. This is an extension of the susceptible-infected-recovered dynamic for the human population and a susceptible-infected type dynamic for the mosquito population. Some parameters sensitive to temperature depend on it and, in turn, the daily temperature varied over time, in order to delimit the effect of temperature changes on the behavior of populations. The system simulations were carried out in Matlab R2020b software, implementing an algorithm of the fourth order using the Runge-Kutta numerical method with values for the constant parameters extracted from the literature.

Mathematical model formulation
The formulated mathematical model is an extension of the susceptible-infected-recovered dynamic (SIR) for the human population and a susceptible-infected (SI)-type dynamic for the mosquito population; a single dengue serotype is assumed in the transmission dynamics; the infected persons capable of transmitting the dengue virus are divided into two states, symptomatic and asymptomatic, and only the population of female mosquitoes is considered; once a mosquito has become a carrier of a dengue virus serotype, it never ceases to be so.

To interpret the dynamics of dengue transmission, it is assumed that the average number of susceptible people \( S(t) \) increases constantly at the rate \( \mu N \) and decreases proportionally to the human mortality rate \( \mu \); at time \( t \), susceptible persons can become an average number \( I(t) \) of infected or an average number \( A(t) \) of asymptomatic by having effective contact with the population of carrier mosquitoes at rates \( \lambda_1 \) and \( \lambda_2 \), which represent the incidence of the population of symptomatic people and the population of asymptomatic people, respectively. The rate of change of susceptible persons with respect to time is given by:

\[
\frac{dS}{dt} = \mu N - \lambda_1 S - \lambda_2 S - \mu S. \tag{1}
\]

Populations of symptomatic and asymptomatic infected persons increase at incidence rates \( \lambda_1 \) and \( \lambda_2 \), respectively, and decrease proportionally to the natural death rate \( \mu \), as well as by the rate of persons recovering from a dengue virus serotype and who acquire immunity proportionally to the recovery rate \( \theta \); the population of recovered people \( R(t) \) decreases proportionally to the natural death rate \( \mu \) and increases according to the recovery rate \( \theta \) of the infected populations. The equations that represent the change of the infected asymptomatic, symptomatic people and the recovered population over time are given by:
\[
\frac{dA}{dt} = \lambda_2 S - \theta A - \mu A, \quad (2)
\]

\[
\frac{dI}{dt} = \lambda_1 S - \theta I - \mu I, \quad (3)
\]

\[
\frac{dR}{dt} = \theta I + \theta A - \mu R. \quad (4)
\]

To describe the dynamics of the female mosquito population, an intrinsic growth rate \( \phi \) in the population of non-dengue virus-carrying mosquitoes is considered, and the variable \( U(t) \) denotes the average number of non-carrier mosquitoes; denoting the average number of dengue virus-carrying mosquitoes by \( V(t) \), the rate of change of this variable depends on the proportion of non-carrier mosquitoes that come into effective contact with the population of infected people and become carrier mosquitoes, proportional to the incidence rates \( \lambda_I \) and \( \lambda_A \), which represent the population incidence of carrier and non-carrier mosquitoes, respectively. Both virus carrier and non-carrier mosquito populations decrease proportionally to the natural death rate of mosquitoes \( \epsilon(T) \) which depends on temperature. Therefore, the equations that describe the change in the population of female mosquitoes over time are given by:

\[
\frac{dU}{dt} = \phi - (\lambda_I + \lambda_A)U - \epsilon U, \quad (5)
\]

\[
\frac{dV}{dt} = (\lambda_I + \lambda_A)U - \epsilon V. \quad (6)
\]

From the equations described above, the system of nonlinear ordinary differential equations (7)-(12) emerges to interpret the dynamics of the dengue virus, including the population of the *Aedes aegypti* vector and the human population.

\[
\frac{dS}{dt} = \mu N - \lambda_3 S - \lambda_2 S - \mu S \equiv f_1(t), \quad (7)
\]

\[
\frac{dA}{dt} = \lambda_2 S - \theta A - \mu A \equiv f_2(t), \quad (8)
\]

\[
\frac{dI}{dt} = \lambda_1 S - \theta I - \mu I \equiv f_3(t), \quad (9)
\]

\[
\frac{dR}{dt} = \theta I + \theta A - \mu R \equiv f_4(t), \quad (10)
\]

\[
\frac{dU}{dt} = \phi - (\lambda_I + \lambda_A)U - \epsilon U \equiv f_5(t), \quad (11)
\]

\[
\frac{dV}{dt} = (\lambda_I + \lambda_A)U - \epsilon V \equiv f_6(t). \quad (12)
\]

The terms \( \lambda_1 \) and \( \lambda_2 \) are governed by a standard incidence, where the rate of newly infected people passing from the susceptible state to the symptomatic or asymptomatic infected state is proportional to the total number of effective contacts between susceptible individuals and the proportion of mosquitoes carrying a dengue virus serotype; these terms are described by:

\[
\lambda_I = f a \frac{\beta V}{M}; \quad \lambda_2 = (1-f) a \frac{\beta V}{M}.
\]

Similarly, the terms \( \lambda_I \) and \( \lambda_A \) are also governed by a standard incidence. Here the rate of new cases of carrier mosquitoes is proportional to the total number of effective contacts between non-carrier mosquitoes and infected symptomatic or asymptomatic persons, respectively, these terms are described for:

\[
\lambda_I = a \sigma \frac{I}{N}; \quad \lambda_A = a \sigma \frac{A}{N}.
\]
The total population of humans and female mosquitoes, described by \( N = S + A + I + R \) and \( M = U + V \) respectively, grow at rates:

\[
\frac{dN}{dt} = \frac{dS}{dt} + \frac{dA}{dt} + \frac{dI}{dt} + \frac{dR}{dt}; \quad \frac{dM}{dt} = \frac{dU}{dt} + \frac{dV}{dt}.
\]

These rates are such that:

\[
\frac{dN}{dt} = 0; \quad \frac{dM}{dt} = \phi - \epsilon M.
\]  

From the equations (13) it can be deduced that the total population of humans \( N \) is constant over time, in addition to the fact that asymptotically, the total population of female mosquitoes tends to \( \phi / \epsilon \).

For the system of equations (7) - (12), the following initial conditions were considered: \( S(0) = S_0, A(0) = A_0, I(0) = I_0, R(0) = R_0, U(0) = U_0, V(0) = V_0 \), as well as the following restrictions for the parameters: \( 0 < \alpha, 0 < \theta, 0 < \epsilon, 0 < \mu, 0 < \phi, 0 < f < 1, 0 < \beta < 1, 0 < \sigma < 1 \). The region of epidemiological sense is given by:

\[
\Omega = \left\{ (S,A,I,R,U,V) \in \mathbb{R}^6_+ | 0 < S + A + I + R \leq N, 0 \leq U + V \leq \frac{\phi}{\epsilon} \right\}.
\]

The temperature-dependent parameters are represented by the following functional expressions described and compiled by authors such as Hyojong Lee et al. in Ref. 9, Liu-Helmersson et al. in Ref. 10 and Polwiang in Ref. 11:

**Daily biting rate:**

\[
\alpha(T) = \begin{cases} 
0.000202T(T - 13.35)\sqrt{40.08 - T} & \text{if } 13.35^\circ C < T < 40.08^\circ C \\
0 & \text{otherwise}
\end{cases}
\]  

**Probability of mosquito-to-human transmission:**

\[
\beta(T) = \begin{cases} 
0.001044T(T - 12.286)\sqrt{32.461 - T} & \text{if } 12.26^\circ C < T < 32.46^\circ C \\
0 & \text{otherwise}
\end{cases}
\]

**Probability of human-to-mosquito transmission:**

\[
\beta(T) = \begin{cases} 
-0.9037 + 0.0729T & \text{if } 12.4^\circ C < T < 26.1^\circ C \\
1 & \text{if } 26.1^\circ C < T < 32.5^\circ C \\
0 & \text{otherwise}
\end{cases}
\]

**Natural death rate of the mosquito:**

\[
\epsilon(T) = 8.692 \times 10^{-1} - 1.590 \times 10^{-1}T + 1.116 \times 10^{-2}T^2 - 3.408 \times 10^{-4}T^3 + 3.809 \times 10^{-6}T^4
\]

The description and the value of the parameters used for the construction of the model are shown in the Table 1.

**Basic reproduction number**

In the epidemiology of infectious diseases, the basic reproduction number \( R_0 \) is one of the most relevant quantitative parameters in situations of epidemic outbreaks. As a biological definition, the basic reproduction number \( R_0 \) is said to be the number of secondary cases produced by an infected individual introduced into a fully susceptible population during its entire infectious period. Mathematically, the \( R_0 \) is characterized by considering the infectious process as a demographic process in which the increase in offspring is not considered as a birth, but rather as the introduction of new cases of infected through transmission, which entails to look at transmission in terms of consecutive generations of infected individuals.\(^{12,13}\)

Since \( R_0 \) is considered a disease threshold, its value determines whether or not an epidemic exists: if \( R_0 > 1 \), an infected person will infect more than one susceptible person during their infectious period and the disease will spread, generating an epidemic; otherwise, if \( R_0 < 1 \) the disease will tend to disappear, as this indicates that an infected person introduced into
a totally susceptible population transmits the disease on average to less than one person, so the disease will tend to become extinct over time.\textsuperscript{13,14}

Considering the methodology of the spectral radius of the matrix of the next generation,\textsuperscript{19} the equilibrium point without the presence of the disease $E_0 = (N, 0, 0, 0, 0, 0, 0)$ and the asymptotic behavior of the total population of mosquitoes $M$, we proceeded to calculate the basic reproduction number $R_0$, which is determined by the following expression:

$$R_0 = \frac{(1 - f)\alpha^2 \sigma \beta}{\epsilon (\theta + \mu)} + \frac{f \alpha^2 \sigma \beta}{\epsilon (\theta + \mu)}$$ \hspace{1cm} (18)

In order to have a clearer conception of what the expression of (18) represents, the terms that compose it must be interpreted. First, the additive effect that represents one of the considerations of the model can be appreciated, since it takes into account two routes or sources of infection caused by the population of asymptomatic and symptomatic infected people: the expression $\frac{(1 - f)\alpha^2 \sigma \beta}{\epsilon (\theta + \mu)}$ in the first additive term represents the incidence of new cases of asymptomatic infections in the human population; on the other hand, the expression $\frac{f \alpha^2 \sigma \beta}{\epsilon (\theta + \mu)}$ in the second additive term represents the incidence of new cases of asymptomatic infections in the human population, and the expression $\frac{\sigma}{\epsilon}$ shared by the two additive terms represents the new cases of mosquitoes carrying the virus.

After having an expression for the basic reproduction number based on the parameters considered in the model, $R_0$ was simulated taking the values included in Table 1; for the temperature-dependent parameters, the daily temperature data collated by the meteorological forecasting company AccuWeather Inc.\textsuperscript{28} were used and the functions (14) - (17) were evaluated for the mean value between the minimum and the maximum daily temperatures of the city of Armenia - Quindío, Colombia, as shown in Figure 1.

Figure 1 shows the graphical representation of the basic reproduction number ($R_0$) throughout a year, compared with the daily temperature data for the year 2019. First, highlighting the biological definition of $R_0$, it can be seen that most of the time considered in the simulation, the value of the basic reproduction number exceeds the epidemic level 1, from which it can be deduced that throughout the year there was a continuous epidemic risk. Another result of importance observed is the effect produced by changes in temperature over time, since comparing the continuous red line that represents $R_0$ and the blue dotted line that represents daily temperature, the increase in temperature produces an increase in its value, from which it can be deduced that the increase in temperature increases the risk of producing an epidemic of dengue disease in the city of Armenia.

**Results and discussion**

The simulations of the system (7) - (12) are carried out in Matlab R2020b software, implementing an algorithm of the fourth order Runge Kutta numerical method\textsuperscript{15,16} with values for the parameters retrieved from the literature and described in Table 1. The following simulations show the variation over time of the populations considered and the variation over time of the daily temperature, in order to demarcate the effect of temperature changes on the behavior of the populations. Figure 2 shows the behavior of the symptomatic and asymptomatic infected population, considering that the fraction of people who acquire the virus and are symptomatic is $f = 0.75$, which means that a quarter of those infected have no symptoms.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Definition</th>
<th>Value</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\mu$</td>
<td>Mortality rate of the human population</td>
<td>0.000039</td>
<td>14,15</td>
</tr>
<tr>
<td>$\theta$</td>
<td>Recovery rate of a dengue virus serotype</td>
<td>0.14-0.33</td>
<td>16,17</td>
</tr>
<tr>
<td>$\phi$</td>
<td>Constant increase in the population of female mosquitoes</td>
<td>400-5000</td>
<td>16-18</td>
</tr>
<tr>
<td>$f$</td>
<td>Fraction of people who acquire the virus and are symptomatic</td>
<td>0-1</td>
<td>---</td>
</tr>
<tr>
<td>$\alpha(T)$</td>
<td>Daily biting rate</td>
<td>Variable</td>
<td>9-11</td>
</tr>
<tr>
<td>$\beta(T)$</td>
<td>Probability of transmission from mosquito to human by bite</td>
<td>Variable</td>
<td>9-11</td>
</tr>
<tr>
<td>$\sigma(T)$</td>
<td>Probability of transmission from human to mosquito by bite</td>
<td>Variable</td>
<td>9-11</td>
</tr>
<tr>
<td>$\epsilon(T)$</td>
<td>Natural death rate of mosquitoes</td>
<td>Variable</td>
<td>9-11</td>
</tr>
</tbody>
</table>
From Figure 2 it appears that when considering a lower fraction of asymptomatic infected than of symptomatic infected people, the population of symptomatic people is higher than that of asymptomatic people; however, the population of asymptomatic people permanently marked the evolution of the symptomatic class throughout the simulation, since asymptomatic people are those infected with the dengue virus with the ability to transmit it despite not presenting any type of clinical symptomatology. Other important characteristics that could be observed were the high and low peaks of the blue curve in the lower graph of Figure 2, which represents the daily temperature variability in Armenia (Quindío) in the year 2019, are reflected in the time-series of populations of symptomatic and asymptomatic people. From this, it can be deduced that the increase in temperature increases the cases of symptomatic and asymptomatic infected people, and more specifically, that sudden changes in temperature have a significant impact on the increase or decrease of these two populations.20–23

The first graph in Figure 3 shows that the population of non-carrier female mosquitoes grew and quickly stabilized; the second graph of Figure 3 shows that the trend of the population of mosquitoes carrying the dengue virus reaches its maximum on day 50 and day 250. From this it can be deduced that a transmission pattern is present during most of the year and the variability of the temperature represented by the blue dotted curve is a significant determinant for the population of carrier mosquitoes, since the tendency of the mosquitoes to increase carriers coincided with temperature peaks.

**Figure 1.** Basic reproduction number.

**Figure 2.** Population of symptomatic and asymptomatic infected people with $f = 0.75$. 

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However, it is not as evident as in the behavior of the population of symptomatic and asymptomatic infected in Figure 2. When comparing both graphs, it can be said that the largest population of carrier female mosquitoes and of symptomatic and asymptomatic infected were found in between 50 to 250 days, which seems reasonable, since a greater number of carrier mosquitoes causes a greater number of new infection cases.

With the aim of determining the effect of the asymptomatic population on the dynamics of dengue transmission, in the following simulations the same parameters considered in previous simulations exposed in Table 1 were used, changing the value of the fraction of people who acquire the virus and are symptomatic to $f = 0.25$. In other words, it will be considered that the fraction of people who acquire the virus and are asymptomatic is equivalent to three quarters of the total number of people infected with a dengue virus serotype, which has been suggested in the literature. The graphs for the populations of symptomatic and asymptomatic infected people are shown below.

As expected, in Figure 4 the population size of asymptomatic infected people was greater than that of symptomatic people, which is due to a lower value of the fraction of people who acquire the virus and are symptomatic ($f = 0.25$) than for previous simulations; in this case, it could be interpreted that when considering the suggestions exposed in the
literature mentioned in the previous paragraph, most of the infected population are asymptomatic, which causes a great challenge for creating virus transmission control strategies; this population represents a constant reservoir of the virus that is not identified as an infected population in the clinical history (patients usually appear to health professionals after symptoms have already manifested) and interruption of the early cycle of transmission is difficult.25–27

Given that \( f \) and \( (1 - f) \) are fractions that complement each other and the population of mosquitoes carrying a dengue virus serotype considers both populations in its dynamics (observe equation (12)), the behavior of the population did not present any change with respect to Figure 3 and its inclusion in the simulations using \( f = 0.25 \) becomes unnecessary.

**Conclusions**

We presented a simulation model based on nonlinear ordinary differential equations describing the transmission dynamics of the dengue virus, considering the population of asymptomatic infected people and some entomological parameters that vary depending on the temperature of the city of Armenia (Quindío), Colombia. The basic reproduction number was determined and the simulations were carried out using a temporal window of one year; the graphs show that the \( R_0 \) exceeds the epidemic level 1, from which it is deduced that throughout the year there was a risk of continuous epidemic; in addition, the temperature had a directly proportional relationship with the basic reproduction number, and therefore climatic change increases the risk of a dengue epidemic.

The simulations of the proposed system of equations reveal that the population of asymptomatic people prevails over time, which can be considered as a constant reservoir of the dengue virus; in addition, the cases of infected people and carrier mosquitoes increased when the peaks of temperature increased drastically, a phenomenon which could be explained by the idea that the city of Armenia has a temperate climate, for which rain leads to a decrease in temperature, which results in clean water deposits; this in turn favors the reproduction of the vector as temperatures rise, increasing the average number of mosquitoes in the environment. Combined with a reservoir of asymptomatic infected people, this leads to a higher incidence of dengue virus.

In the future, the effect of human population movements will be determined considering that, as mentioned in this paper, the asymptomatic population has the capacity to transmit the dengue virus and its condition facilitates the transport of the virus to different areas of the city of Armenia (Quindío) Colombia. Since this population presents no symptoms, preventive measures are not taken to avoid the transmission of the virus.

**Data availability**

**Underlying data**


This project contains the following underlying data:

- Daily temperature data of the city of Armenia, Colombia year 2019.csv

**Extended data**


This project contains the following extended data:

- parametros1.m
- rk4modelo.m
- solverrk4modelo.m
- temperaturaaarmenia2019.xlsx

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Archived analysis code as at time of publication: https://doi.org/10.5281/zenodo.6328289

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