Multibacillary and Paucibacillary Leprosy Dynamics: A Simulation Model Including a Delay

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Abstract

A mathematical simulation model based on nonlinear ordinary differential equations is proposed, which interprets the transmission dynamics of the multibacillary leprosy (MB) and paucibacillary leprosy (PB), including an asymptomatic stage where a delay time is taken into account in the development of the disease. Simulations of the model are carried out, considering parameter values taken from the literature to interpret the behavior of different stages of the illness. It was deduced to reduce the epidemic impact it is necessary to apply a treatment to the population density who develops multibacillary leprosy disease.

Keywords: Multibacillary leprosy, paucibacillary leprosy, asymptomatic, delay time
1 Introduction

Leprosy or Hansen’s disease, was first described by Armauer Hansen in 1873, is a granulomatous bacterial chronic disease, caused by the bacillus *Mycobacterium leprae*, which mainly affects the skin, presenting dysesthetic hypochronic stains, peripheral nerves, mucosa of the upper respiratory tract and the eyes. These signs depend on the immunological response that each patient may have, although it is not a highly contagious disease, it is transmitted by means of nasal droplets and orally when there is frequent contact with untreated infected people. According to the bacterial load and the number of patches, it can be classified in paucibacillary leprosy (PB) or multibacillary leprosy (MB), for terms of treatment [1, 2].

Throughout the history of mankind, the existence of leprosy in almost all civilizations has been documented, although governmental entities of health have been proposed to control it by devising strategies of prevention and control. This disease is still a public health problem. According to global statistics reported by the WHO 96% of reported cases with leprosy disease they are located in 22 priority countries, of which five countries with the highest incidence are currently reported, India, Brazil, Indonesia, Bangladesh and Ethiopia [1, 2, 3, 4].

This disease can be curable by means of a multidrug treatment (MDT) or polychemotherapy (PQT), which consists of a combination therapy of different antibiotics, rifampicin, clofazimine and dapsone, the combination between them is determined according to the leprosy classification. The eradication of this disease is possible, since there is only one effective transmission way through infected people who do not receive treatment [1, 3, 12].

Mathematical models throughout history aim to represent in a simplified way a situation or natural phenomenon. According to the literature, Lechat *et al.* in 1970 and 1980 were one of the first to implement a mathematical model that studies the dynamics of leprosy disease, which led to the research on the evolution of leprosy taking different assumptions and the effect of the control strategy [4, 5, 6, 7, 8]. Lietman *et al.* in 1997 propose a model based on ordinary differential equations to interpret the dynamics of leprosy disease in the absence of tuberculosis disease and the tuberculosis in absence of leprosy, then combine them and investigate the importance of cross immunity [13]. In 1999, Meima *et al.* proposed a model type SIMLEP to study the epidemiology of leprosy disease, taking account for variations respect to people’s natural immunity, the incubation period and a delay in the treatment of leprosy [4, 9]. Fischer *et al.* (2010) propose a SIMCOLEP stochastic model based on each
individual, that models the leprosy transmission in a population [4, 10]. In 2013 Nohman and Vos-Böhmen pose a model of ordinary differential equations that interprets the epidemiological consequences of co-infection between leprosy and tubercolusis disease [11].

This writing is structured as follows. Firstly it is carried out adaptation to the model proposed by Lietman, taking into account a delay time in the development of multibacillary and paucibacillary leprosy disease in the latency stage. Some simulations with random initial conditions considering parameters taken from the literature, are carried out. Finally, several conclusions to the considered populations (susceptible, latent, infected by multibacillary and paucibacillary forms), are deduced from.

2 The Model

In the approach of the model, the following considerations are made: (i) the population has the same probability of being infected, (ii) the death rate of multibacillary leprosy is higher than the natural death rate, (iii) the paucibacillary leprosy death rate does not consider, (iv) the rates considered are annual and (v) it is considered a latency stage.

The following variables and parameters are considered in the model: $x(t)$ is the susceptible population, $y(t)$ is the population of asymptomatic infected people, $z(t)$ is the infected population by multibacillary leprosy, $w(t)$ is the infected population by paucibacillary leprosy in a time $t$, $n(t)$ is the total population over time, $\rho$ is the annual net growth rate, $\beta_p$ is the effective contact rate for the paucibacillary leprosy transmission, $\beta_m$ is the effective contact rate for multibacillary leprosy transmission, $\theta$ is the rate of progress of an asymptomatic to the leprosy symptomatic stage, $f$ is a fraction of people who developed multibacillary leprosy, $(1 - f)$ is a fraction of people who developed paucibacillary leprosy, $\tau$ is the delay time, $\mu_m$ is the death rate of the infected population by multibacillary leprosy and $\mu$ is the natural death rate.

Figure 1 shows the compartment diagram that interprets the dynamics of leprosy disease.
According to the diagram in figure 1, the population of susceptible people is increased by an annual growth rate of people and is diminished by a density of people who die naturally or who are infected with leprosy by having an effective transmission contact with the population of people infected with paucibacillary and multibacillary leprosy. This population density passes to be in a latency stage \( y \), after being in this stage for a period of time, determined by the delay \( \tau \), some people leave the system by natural death and a fraction \( f \) of people develops the multibacillary leprosy disease, while the fraction \( (1 - f) \) develops paucibacillary leprosy. The population density that develops multibacillary leprosy is affected by a death rate \( \mu_m \) higher than the natural death rate, while the density of the infected population with paucibacillary leprosy is being decreased by a natural death rate. The nonlinear ordinary differential equation system that describes the behavior of the disease, is given by:

\[
\begin{align*}
\frac{dx}{dt} &= \rho - (\beta_m x \frac{z}{N} + \beta_p x \frac{w}{N}) - \mu x \\
\frac{dy}{dt} &= \beta_m x \frac{z}{N} + \beta_p x \frac{w}{N} - \theta y(t - \tau) - \mu y \\
\frac{dz}{dt} &= f \theta y(t - \tau) - \mu_m z \\
\frac{dw}{dt} &= \theta (1 - f) y(t - \tau) - \mu w \\
\frac{dN}{dt} &= \rho - \mu (x + w + y) - \mu_m z
\end{align*}
\]

(1)

Where \( \rho, \beta_m, \beta_p, \theta, f, \mu, \tau, \mu_m > 0 \) and with initial conditions \( x(0) = x_0, \ y(0) = y_0, \ z(0) = z_0, \ w(0) = w_0 \). The region where the system makes epidemiological sense is represented by:

\[
\Omega = \left\{ (x, y, z, w) \in \mathbb{R}_+^4 : 0 < x + y + z + w < \frac{\rho}{\mu} \right\}
\]
3 Simulations and results

The simulations of the system (1) were carried out in the Anaconda mathematical software Python 2.7 with the libraries numpy, matplotlib, scipy by means of the routine odeint. The values of the parameters were taken from the literature which are shown in table 1. In addition the time scale is annual and are taken different initial conditions for each population.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ρ</td>
<td>Annual net growth rate.</td>
<td>50</td>
</tr>
<tr>
<td>βp</td>
<td>Effective contact rate for paucibacillary leprosy transmission [17, 18].</td>
<td>0.3</td>
</tr>
<tr>
<td>βm</td>
<td>Effective contact rate for multibacillary leprosy transmission [17, 18].</td>
<td>0.5</td>
</tr>
<tr>
<td>θ</td>
<td>Rate of progress from an asymptomatic stage to the symptomatic stage of leprosy (average between the two rates of progress) [17, 20].</td>
<td>0.19</td>
</tr>
<tr>
<td>µm</td>
<td>Population death rate of infected individuals with multibacillary leprosy [?, 17].</td>
<td>0.045</td>
</tr>
<tr>
<td>µ</td>
<td>Natural death rate.</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Table 1: Values of the parameters

In figure 2 you can see four graphs representing the different stages, in which the dynamics of the disease transmission of leprosy, considering a delay time \( \tau = 5 \) that represents the average latency stage of the disease. The graphic in the lower right part are simulated all the stages considered in the system of equations (1). It is observed that the susceptible population grows quickly in the time interval where the delay is considered, while in this same interval time the infected populations and the population in latency stage grow gradually. The simulations show that around 20 years the infected population and the latency population stage behave inversely proportional to the susceptible population, meaning that these populations grow while the susceptible population decreases. It is also observed that infected with multibacillary leprosy are more infected than with paucibacillary leprosy, what was expected, due to the fraction taken from who developed multibacillary leprosy \( f = 0.7 \) was higher than the fraction of people who developed paucibacillary leprosy.
Figure 2: Graphs of the different stages of Leprosy disease $\tau = 5$, $t = 50$, $f = 0.7$ and with initial conditions $x_0 = 40, y_0 = 9, z_0 = 5, w_0 = 1, N_0 = x_0 + y_0 + z_0 + w_0$

Figure 3 shows that the infected population of paucibacillary leprosy grows rapidly after the interval of time in which the delay time $\tau$ is considered, while the infected population with multibacillary leprosy grows gradually and with a lower density respect to the other infected population. We assume this happens because when considering the fraction of people who develop multibacillary leprosy disease $f = 0.3$, is less than the fraction of people who develop paucibacillary leprosy.

The susceptible and latency population behave in a similar way as in the simulation results shown in Figure 2. However, the susceptible population has a higher density. This behavior could be due to the fact that according to the parameters considered in table 1, the effective contact rate for the transmission of multibacillary leprosy $\beta_m$ is higher than paucibacillary leprosy, so it is deduced that the density of the infected population with multibacillary leprosy has a greater impact on the susceptible population with respect to the other infectious stage.
According to the results of the simulations, it can be concluded that, although the two infected populations must be treated to reduce the epidemic impact, the treatment should be prioritized for the population that develops multibacillary leprosy, since it has more influence on the susceptible population.

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