An Epidemic Model for the Propagation of Leptospirosis Outbreaks

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Abstract: Leptospirosis is a disease of worldwide distribution caused by spirochetes of the genus *Leptospira*. Rodents have been recognized as the most important and most widely distributed reservoirs of leptospirosis. In different regions of the world, there are outbreaks of leptospirosis that have a seasonal distribution and coincide with the rainy months. One way to study the spread of epidemics is through mathematical models. In the present work, the objective of the authors was to develop and explore a model of leptospirosis outbreak, combining the dynamics of propagation in human population with the dynamics of transmission from rodent reservoirs to humans. The authors designed a deterministic model based on differential equations. The dynamics of the model were explored through computational simulations. The typical evolution of prevalence observed in the model, qualitatively coincides with the dynamics of actual leptospirosis outbreaks. In the model, the peak prevalence was reduced when the transmission parameter and the number of rodents decreased, and when the leptospira decay rate increased. These results coincide with what was expected. The present development could be considered as a starting point for the generation of a more complex design.

Key words: Leptospirosis, epidemic model, simulation, public health.

1. Introduction

Epidemic models are formal designs that allow capturing the behavior of the propagation of infectious diseases. They achieve this goal through the mathematical representation of processes that regulate the dynamics of outbreaks. In this way, they can provide trends regarding the results of different health interventions and the influence of certain factors of interest on the problem addressed [1-4].

The theoretical approach of the epidemiological models is based on the two elements mentioned below: (1) the population is divided into categories according to the different stages considered within the disease under study and (2) the temporal evolution of the number of individuals in each of these categories is formulated mathematically. For example, in the classic SIR (susceptible-infected-recovered) scheme,

the population is divided into three successive categories: susceptible (S), infected (I) and recovered with immunity (R). According to this grouping, transitions S-I (infection) and I-R (recovery) are defined mathematically as a function of time [5, 6].

At present, epidemiological models based on approaches of different complexity coexist. In the literature can be found from classic designs represented by systems of differential equations [7-9], to the most advanced computational simulation developments [10-12]. Differential equations models, such as the one developed in the present paper, have a simple construction and can be explored by unsophisticated computational means. The purposes for which the epidemiological mathematical models are developed are many and varied [1]. There are models that are developed to be used in real time during a particular epidemic. Others, such as the one presented in the present work, are developed for the general understanding of the dynamics of transmission through a qualitative analysis.

Despite the continuous and growing development

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of research in epidemiological models, not all diseases have had the same level of attention. Lloyd-Smith et al. [13], in their review of models of zoonotic diseases, show a remarkable imbalance. Among the diseases that may involve some step of transmission from species of vertebrate reservoirs to man, more than half of the studies collected by these authors correspond to rabies, influenza or severe acute respiratory syndrome. Some diseases of important sanitary interest have been relegated. Leptospirosis is one of them.

Leptospirosis is a disease of worldwide distribution caused by spirochetes of the genus *Leptospira* [14, 15]. It is an important emerging public health problem [16-18]. The disease affects several animals, including rats and other rodents, cattle and dogs [19, 20]. The man acquires the disease by exposure to urine from infected animal reservoirs, which eliminate spirochetes through urinary pathway [21]. Exposure can be direct, or indirect, by contamination of soil and water [14, 16]. Transmission between humans is considered unimportant [14, 22]. The disease produces in man various symptoms, which may include fever, headache, myalgia, jaundice, acute renal failure and conjunctival disease [23, 24]. On average, the case-fatality rate would be around 7% [25].

Rodents have been recognized as the most important and most widely distributed reservoirs of leptospirosis [26-28]. A known risk factor for outbreaks of leptospirosis includes the prevalence in communities of rodents neighboring human populations [21]. High percentages of leptospirosis prevalence in *Rattus norvegicus* have been found in several cities, such as Tokyo (17%) [29], Baltimore (90.4%) [30], Copenhagen (48-89%) [31] and Gran Buenos Aires (45.8%) [32]. The occurrence of *Leptospira* infection is more frequent in humid and warm climates [33]. The disease is mainly located in the Caribbean, Central and South America, the Indian subcontinent, Southeast Asia, Oceania and, to a lesser extent, in Eastern Europe [34]. Leptospirosis can have two conditions: endemic and epidemic [35, 36]. In

epidemic dynamics, which will be represented through the model developed in the present work, there are outbreaks that occur after the rains and floods, where water serves as a vehicle for infection [37-40].

Previously, leptospirosis propagation models have been developed (for example, Refs. [28, 41-46]). In the present work, the objective of the authors was to develop and explore a model of leptospirosis outbreak, combining the dynamics of propagation in human population with the dynamics of transmission from rodent reservoirs to humans.

2. Materials and Methods

2.1 The Model

A deterministic model based on differential equations was developed to simulate the propagation of a seasonal outbreak of leptospirosis. The model contemplates a community formed by humans and rodent reservoirs. Rodents release spirochetes that reach humans indirectly through flood waters. The model is represented by the following system of equations:

$$\begin{aligned}\frac{dS}{dt} &= -aSL, \\ \frac{dI}{dt} &= aSL - bI - cI, \\ \frac{dR}{dt} &= bI, \\ \frac{dL}{dt} &= eM - fL.\end{aligned}\tag{1}$$

A SIR scheme was considered for humans, so people were divided into susceptible (S), infected (I) and recovered (R) individuals. In this way, $S(t)$, $I(t)$ and $R(t)$ are the number of susceptible, infected and recovered individuals at time t , respectively. $L(t)$ is the number of spirochetes in flood waters at time t . Humans become infected when they come into contact with spirochetes in flood waters. It is assumed that the net rate at which infection occurs is proportional to the number of encounters between susceptible individuals

and spirochetes, aSL , where a is the transmission parameter. Infected individuals recover and die with rates b and c , respectively. The number of spirochetes released depends on the population size of the infected reservoirs, M . Spirochetes are released with an e rate and decay with a f rate, respectively.

2.2 Numerical Simulations

The dynamics of the model were explored through computational simulations. Specifically, the evolution of prevalence as a function of time was represented. The recovery rate b was based on Ref. [14], and the lethality rate c on Ref. [47]. The values of parameters e and f were in the order of the estimates mentioned in Ref. [28]. An arbitrary value of a was set because it was not found in the literature. In theoretical epidemiological models it is common to use arbitrary values, mainly when a qualitative analysis is intended (see, for example, Ref. [48]).

Arbitrary values of the initial conditions were set, but a human:infected rodent ratio of 1:3 was chosen, according to the information documented in several works [32, 49-51]. Time and parameters are expressed in day and 1/day, respectively. A benchmark case was established, where the following values were set for the initial conditions and parameters: $S(0) = 100$, $I(0) = 0$, $R(0) = 0$, $L(0) = 0$, $a = 10^{-8}$, $b = 0.14$, $c = 0.014$, $e = 10^3$, $f = 0.10$, $M = 300$, with the parameters a , b , c , e and f expressed in 1/day.

The influence of parameters a , M and f on the evolution of prevalence was explored. The simulations were implemented in the program Dynamics Solver 1.98 [52]. The numerical results obtained in the simulations were represented graphically using the program Infostat 2018 [53].

3. Results

The typical evolution of the prevalence predicted by the model, using the values of the benchmark case, is represented in Fig. 1. It is observed that the prevalence grows exponentially to a peak and then decreases.

Fig. 1 Evolution of the prevalence in the benchmark case. Initial conditions and parameters: $S(0) = 100$, $I(0) = 0$, $R(0) = 0$, $L(0) = 0$, $a = 10^{-8}$, $b = 0.14$, $c = 0.014$, $e = 10^3$, $f = 0.10$, $M = 300$ (a , b , c , e and f expressed in 1/day).

Fig. 2 Influence of the transmission parameter a on the evolution of the prevalence. Three values were evaluated (1/day): $a_1 = 10^{-8}$ (black), $a_2 = 8 \times 10^{-9}$ (dark grey), $a_3 = 6 \times 10^{-9}$ (light grey). The rest of the conditions were maintained as in the benchmark case.

Fig. 3 Influence of lespiral decay parameter f on the evolution of prevalence. Three values were evaluated (1/day): $f_1 = 0.10$ (black), $f_2 = 0.14$ (dark grey), $f_3 = 0.18$ (light grey). The rest of the conditions were maintained as in the benchmark case.

In order to study the influence of the transmission parameter a on the evolution of the system, three values (1/day) were compared: $a_1 = 10^{-8}$ (benchmark), $a_2 = 8 \times 10^{-9}$, $a_3 = 6 \times 10^{-9}$. The reduction of a caused a drop in peak prevalence (Fig. 2). With the purpose

Fig. 4 Influence of the population size of rodents M on the evolution of prevalence. Three values were evaluated: $M_1 = 300$ (black), $M_2 = 250$ (dark grey), $M_3 = 200$ (light grey). The rest of the conditions were maintained as in the reference case.

of evaluating the behavior of the system as a function of the leptospiral decay parameter f , the following values were compared (1/day): $f_1 = 0.10$ (benchmark), $f_2 = 0.14$, $f_3 = 0.18$. The increase in f produced a reduction in peak prevalence (Fig. 3). When different rodent population size values were compared ($M_1 = 300$, benchmark; $M_2 = 250$ and $M_3 = 200$), it was observed that the decrease in rodents led to a decline in peak prevalence (Fig. 4).

4. Discussion

In different regions of the world, there are outbreaks of leptospirosis that have a seasonal distribution and coincide with the rainy months [14, 21, 33, 54-56]. For example, in Argentina, a national study conducted between 1999 and 2005 found that the greatest incidence in humans occurs between mid-summer and late autumn, coinciding with hot and rainy weather [23]. In the present work, the authors have tried to simulate qualitatively the propagation of leptospirosis in such scenarios.

Holt et al. [28] developed a model for the spread of leptospirosis in one species of African rodent. Their model includes the release of leptospires into the environment and infection in reservoirs, but does not include humans. In the present paper, the authors relied on the development of Holt et al. [28] to model the release of leptospires into the environment, but represented the dynamics of infection in humans. The

model presented also includes elements from the works of Khan et al. [45] and Shukla et al. [57].

The typical evolution of prevalence observed in the model developed by the authors, qualitatively coincides with the dynamics of actual leptospirosis outbreaks (see, for example, Refs. [23] and [38]), where the number of cases increases to a peak and then drops to very low values.

When the evolution of the model as a function of the transmission parameter a was studied, the simulations showed that a reduction of a produced a reduction of the peak prevalence. Parameter a is related to the transmission probability when susceptible humans are exposed to leptospira in flood waters. The reduction of parameter a could represent an increase in the application of preventive measures, such as wearing appropriate protective clothing (waterproof boots, for example) when walking in a flooded area [17, 22]. In this way, the results observed in the simulations would coincide with what was expected.

During a flood, the concentration of leptospira in flooded areas may depend inversely on the distance to places where rodent droppings are highly concentrated, such as dumps [37]. Parameter f of the model developed in this paper, regulates the decay of leptospira in the environment. In this way, the increase of f could simulate the effect of an increase in the distance to a dump. In accordance with this approach, the simulations carried out show that an increase of f produces a reduction of the prevalence peak.

Reducing rodent populations is also an action that could be taken to control leptospirosis [22, 26, 55]. Congruently, when the model simulated a decrease in rodent numbers, a drop in human prevalence was observed.

5. Conclusion

The authors developed an original mathematical model that, through a relatively low number of parameters, qualitatively simulates the evolution of a

leptospirosis outbreak and also allows exploring some variables related to the behavior of this phenomenon. Future work could be oriented to formally verify the results provided by the model. Likewise, the present development could be considered as a starting point for the generation of a more complex design.

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