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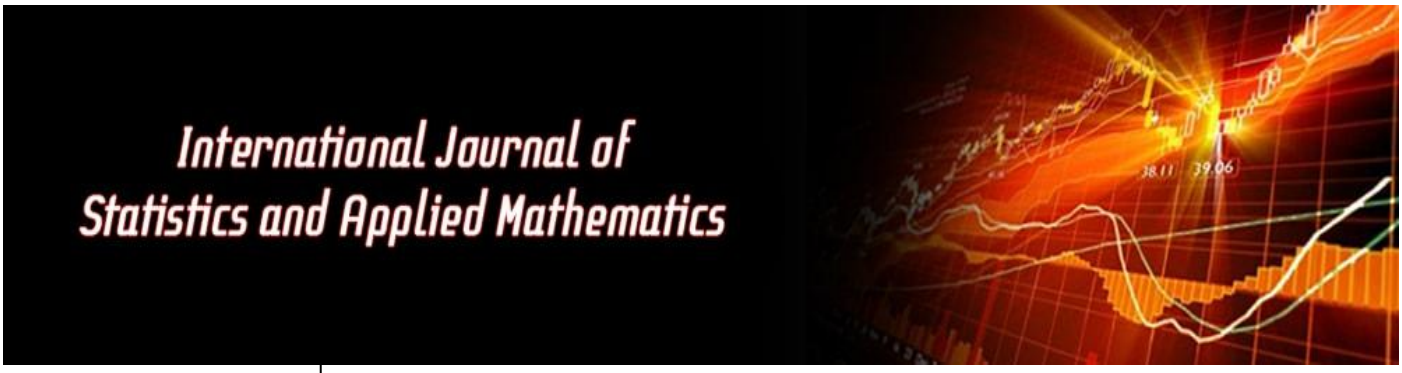

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Analysis of dengue disease by mathematical Model

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Abstract
In this paper the main purpose was to study the dynamics of dengue fever and its progression to the dengue haemorrhagic fever in order to understand the epidemic phenomenon and to suggest strategies for the control of the disease in general and the haemorrhagic form in particular. The nature of dengue epidemics is complex since it conjugates human, environmental, biological, geographical and socio-economic factors. Our model and simulations show that the strategy based on the prevention of dengue epidemic using vector control through environmental management or chemical methods remains insufficient since it only permits to delay the outbreak of the epidemic.

Keywords: Dengue disease, mathematical Model, haemorrhagic

Introduction
With medical research achievements in terms of vaccination, antibiotics and improvement of life conditions from the second half of the 20th century, it was expected that infectious diseases were going to disappear. Consequently, in developed countries the efforts have been concentrated on illnesses as cancer. However, at the dawn of the new century, infectious diseases are still causing suffering and mortality in developing countries. Malaria, yellow fever, AIDS, Ebola and other names will have marked the memory of humanity forever.
So far, the strategies of mosquito control by insecticides or similar techniques proved to be inefficient. Moreover, the deterioration of the environment, the climatic changes, the unsanitary habitat, the poverty and the uncontrolled urbanization are as many favorable factors to the infectious illness propagation in general and dengue fever in particular. During the last decades the global prevalence of the dengue progressed dramatically. The disease is now endemic in more than 100 countries of Africa and America. The Southeast of Asia and the Western Pacific are seriously affected by the illness.
Before 1970, only nine countries had known epidemics of dengue haemorrhagic fever, but this number had increased more than fourfold in 1995 and about 2500 million of people are now exposed to the risk of the dengue fever. According to the present evaluations of the World Health Organization (WHO), about 50 million cases of dengue occur in the world every year, with an increasing tendency. In 1998, there were more than 616, 000 cases of dengue in America, of which 11, 000 cases of dengue haemorrhagic fever, that's twice the number of cases recorded in the same region during the year 1995. In 2001 there were 400, 000 cases of haemorrhagic fever in Southeast Asia, whereas, in Rio de Janeiro alone, 500, 000 people were struck by a dengue outbreak in 2002. The epidemic effect reached Florida and southern Texas [1-3].
During epidemics of the dengue fever the rate of the infectious among the susceptibles is often between 40 and 50% but it may reach 80-90% in favorable geographic and environmental conditions. Every year more then 500, 000 cases of dengue haemorrhagic require an hospitalization.
Mathematical modelling became an interesting tool for the understanding of these illnesses and for the proposition of strategies. The formulation of the model and the possibility of a simulation with parameter estimation, allow tests for sensitivity and comparison of conjunctures [4].

In the case of dengue fever, the mathematical models we have found in the literature propose compartmental dynamics with Susceptible, Exposed, Infective and Removed (immunised). In particular, SEIRS models [5] and SIR models [6] with only one virus or two viruses acting simultaneously [7] were considered.

In the present paper, while pointing out that the idea of two viruses coexisting in the same epidemic is controversial [7], a model with two different viruses acting at separated intervals of time is proposed. Our main purpose is to study the dynamics of dengue fever, while concentrating on its progression to the haemorrhagic form, in order to understand the epidemic phenomenon and to suggest strategies for the control of the disease. In search of clarity and simplicity, we assume that the latent period is not crucial for the susceptible-infective interaction, hence we omit the compartment of exposed and consider a SIR model.

Parameters of the Model

We suppose that we dispose of a human population (respectively of mosquito population) of size N_h (resp. N_v) formed of Susceptibles S_h, of Infective I_h and of Removed R_h (resp. S_v and I_v).

The model supposes a homogeneous mixing of human and mosquito population so that each bite has an equal probability of being taken from any particular human. While noting b_s the average biting rate of susceptible vectors, p_{hv} the average transmission probability of an infectious human to a susceptible vector, the rate of exposure for vectors is given by: $(p_{hv}I_hb_s)/N_h$. It is admitted [6] that some infections increase the number of bites by the infected mosquitos in relation to the susceptible, therefore, we will assume that the rate of infected mosquito bites b_i is greater than the one of the susceptible mosquitos b_s.

Noting p_{vh} the average transmission probability of an infectious vector to human and I_v the infectious vector number, the rate of exposure for humans is given by: $(p_{vh}I_vb_i)/N_h$ so:

- The adequate contact rate of human to vectors is given by: $C_{hv} = P_{hv}b_s$
- The adequate contact rate of vectors to human is given by: $C_{vh} = p_{vh}b_i$.

The man life span is taken equal to 25 000 days (68.5 years), and the one of the vector is of 4 days. Other parameters values are given in the following section.

Table 1: Basis parameters

Name of the parameter	Notation	Base value
transmission probability of vector to human	p_{hv}	0.75
transmission probability of human to vector	p_{vh}	0.75
Bites per susceptible mosquito per day	b_s	0.5
Bites per infectious mosquito per day	b_i	1.0
Effective contact rate, human to vector	C_{hv}	0.375
Effective contact rate, vector to human	C_{vh}	0.75
Human life span	$\frac{1}{\mu_h}$	25000 days
Vector life span	$\frac{1}{\mu_v}$	4 days
Host infection duration	$\frac{1}{\mu_h + \gamma_h}$	3 days

Up to now there is no vaccine against dengue viruses but research is going on and the eventuality of an immunization program is not excluded in the medium term. In this study we investigate the effect of such an immunization option and we also discuss the possibility of a partial vaccination against each serotype that will enable the control of the second epidemic and the evolution of dengue to dengue haemorrhagic fever.

In the case of first epidemic, the simplest assumption is that a random fraction, p, of susceptible humans can permanently be immunized against all the four serotypes. While for the second epidemic, a partial immunization is applied to the removed from the first epidemic. The dynamics of this disease in the host and vector populations is given by the following equations:

First epidemic

The model is governed by the following equations:

Human population

$$\begin{cases} \frac{dS_h}{dt} = \mu_h N_h - (\mu_h + p + C_{vh}I_v / N_h) S_h \\ \frac{dI_h}{dt} = (C_{vh}I_v / N_h) S_h - (\mu_h + \gamma_h) I_h \\ \frac{dR_h}{dt} = pS_h + \gamma_h I_h - \mu_h R_h \end{cases}$$

Vector population

$$\begin{cases} \frac{dS_v}{dt} = \mu_v N_v - (\mu_v + C_{hv}I_h / N_h) S_v \\ \frac{dI_v}{dt} = (C_{hv}I_h / N_h) S_v - \mu_v I_v \end{cases}$$

With the conditions $S_h + I_h + R_h = N_h$ and $S_v + I_v = N_v$, so: $R_h = N_h - S_h - I_h$ and $S_v = N_v - I_v$ then the two previous systems become:

$$\begin{cases} \frac{dS_h}{dt} = \mu_h N_h - (\mu_h + p + C_{vh}I_v / N_h) S_h \\ \frac{dI_h}{dt} = (C_{vh}I_v / N_h) S_h - (\mu_h + \gamma_h) I_h \\ \frac{dI_v}{dt} = C_{hv}I_h / N_h (N_v - I_v) - \mu_v I_v \end{cases}$$

Equilibrium points

Let the set Ω given by:

$\Omega = \{(S_h, I_h, I_v)/0 \leq I_v \leq N_v;\ 0 \leq I_h;\ 0 \leq S_h,\ (1 + p/\mu_h)S_h + I_h \leq N_h\}$

Second epidemic

In the same way as in the previous section we suppose the onset of a second epidemic with another virus. But in this case, we may assume that a proportion of the population of susceptibles is globally immunized against the four serotypes or partially immunized against one, two or tree viruses. Consequently, we may concentrate only on the removed from the first epidemic who are exposed to the DHF by taking the new population $N'_h = R^*_h$. Therefore the model is given by the following equations:

Human population

$$\begin{cases} \frac{dS'_h}{dt} = \mu_h N'_h - (\mu_h + p + C'_{vh}I_v / N_h) S'_h \\ \frac{dI'_h}{dt} = (C'_{vh}I_v / N_h) S'_h - (\mu_h + \gamma_h) I_h \\ \frac{d'R_h}{dt} = pS'_h + \gamma_h I'_h - \mu_h R'_h \end{cases}$$

Vector population

$$\begin{cases} \frac{dS_v}{dt} = \mu_v N_v - (\mu_v + C'_{hv} I'_h / N'_h) S_v \\ \frac{dI_v}{dt} = (C'_{hv} I'_h / N'_h) S_v - \mu_v I_v \end{cases}$$

With the conditions $S'_h + I'_h + R'_h = N'_h$ and $S_v + I_v = N_v$ so: $R'_h = N'_h - S'_h - I'_h$ et $S_v = N_v - I_v$ then the two previous systems become:

$$\begin{cases} \frac{dS'_h}{dt} = \mu_h N'_h - (\mu_h + p + C'_{vh} I_v / N_h) S'_h \\ \frac{dI'_h}{dt} = (C'_{vh} I_v / N_h) S'_h - (\mu_h + \gamma_h) I'_h \\ \frac{dI_v}{dt} = C'_{hv} I_h / N'_h (N_v - I_v) - \mu_v I_v \end{cases}$$

Equilibrium points

Let the set Ω given by:

$$\Omega = \{(S'_h, I'_h, I_v) / 0 \le I_v \le N_v; 0 \le I'_h; 0 \le S'_h, (1 + p') S'_h + I'_h \le N'_h\}$$

With $p' = p/\mu_h$

Results and Discussion

Assuming a vaccination program as an option that would enable a proportion p of susceptible humans to be globally immunized against the four serotypes, the stability analysis shows that the population may be protected from epidemics if p satisfies the principle of herd immunity: $\mu_h(R - 1) \le p$, where R is a function of the model parameters, defined as the number of new infected by an infective in interaction with susceptibles. Otherwise, there will be an endemic equilibrium and the disease will persist. But the problem is precisely in finding a vaccine against the four serotypes, which makes a strategy based on global immunization irrealistic in the short term. Meanwhile, a search leading to a partial vaccine against each serotype should be more feasible. In this direction, the proposed model shows that the evolution of dengue to dengue haemorrhagic fever can be controlled by a partial vaccine restricted to the people affected by the first epidemic.

In order to illustrate the dynamics of each epidemic and to study different strategies, a simulation was carried out using MATLAB routines with different values of the parameters implied in each model.

Mainly two directions can be envisaged to control the disease. The first may act on the number of mosquitoes and the second may consider the number of susceptible humans.

Conclusion

As mentioned in the introduction, Our main purpose was to study the dynamics of dengue disease and its progression to the dengue haemorrhagic fever in order to understand the epidemic phenomenon and to suggest strategies for the control of the disease in general and the haemorrhagic form in particular. This conclusion agrees with the experiences realized by EA. Newton and P. Reiter using insecticides [5].

On the other hand, although the model suggests the reduction of susceptibles via vaccination, such a strategy is unlikely to be applicable in the short term because it faces some hurdles due to the fact that a vaccine must protect against the four serotypes at the same time. However, we consider this option since its eventuality is not excluded in the medium and long term.

In the short term, an intermediate solution would be to combine as much as possible, the environmental prevention and a partial vaccination essentially to avoid the haemorrhagic form of the disease caused by different viruses. This suggestion may help health-care policy makers to tackle environment causes as preventive measures and researchers to investigate and concentrate on the search for a vaccine against each serotype rather than looking for a vaccine against the four serotypes at the same time.

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