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MATHEMATICAL MODELS OF BIOLOGICAL CONTROL OF DENGUE

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Abstract

Dengue fever, transmitted by Aedes mosquitoes, poses a significant public health threat in tropical and subtropical regions worldwide. Despite efforts to control its spread through various means, including vector control strategies and vaccine development, dengue remains a formidable challenge. Mathematical modeling has emerged as a valuable tool in understanding the complex dynamics of dengue transmission and evaluating control strategies, particularly those involving biological control methods.

Keywords: Dengue fever, Aedes mosquitoes, Vector control, strategies, Biological control methods

Introduction

Dengue is a viral endemic infection transmitted to humans through the bite of infected mosquitoes and is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. Primary vectors which transmit dengue fever are Aedes

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aegypti mosquitoes and, to a lesser extent, Aedes albopictus [1]. Dengue virus (in short, DENV) has four related serotypes of the genus which is called Flavivirus and consists: DENV-1; DENV-2; DENV-3; and DENV-4. The recovery from one of these serotypes, gives lifelong immunity against that serotype. But the cross-reactive immunity of the other serotypes is only temporary [2].

Dengue is endemic in Nepal and is experiencing a surge in cases that started from the week commencing 8, August to 26 August, 2022. In 2022, a total of 28,108 conformed and suspected dengue cases and 38 conformed deaths due to dengue have been recorded, affecting all province of Nepal. This shows the largest dengue outbreak in Nepal with regard to commutative number of cases recorded countrywide per year [1].

In the last few years, the incidence of dengue epidemics has increased dangerously, evolving from being reported in only 9 countries in the seventies, and now currently being in more than 100 countries. So, the risk of an outbreak of dengue is now latent [3]. The extent and intensity of the trouble forced by dengue infection and disease have transformed calls for immediate interference and control [4,5,6,7].

Mathematical model has a long history in biological research. Study of model describing dengue fever epidemiological dynamics is found back from 1970. It is a viral mosquito borne infection, a major international public health concern [3].

Biological methods depend on the application of biological control agents (lavivorous fish, copepods, genetically modified mosquitoes, and wolbachia-infected mosquitoes), that are unable to transform arboviral pathogens. In biological control method, wolbachia control technique is famous for controlling viral disease (dengue). This technique is self-sustaining [8,9,10].

Vector control technique is also most applicable technique to suppress the transmission of dengue. It is primary technique and performed through use of chemicals [11,12]. Besides the understandings of the life cycles of the vectors for the dengue and the methods of treatments for the dengue patients, if is equally necessary to understand the dengue spreading dynamics, where can contribute.

Among the various existing models, the reaction- diffusion equation model will be used to study in biological control of dengue. Reaction diffusion equations modeling are physical, chemical and biological phenomena. These equations will explain how the concentration distributed in space varies under the influence of two processes: reaction and diffusion.

Reaction is local interactions of species, and diffusion is the spread of species in space. In population biology, diffusion represents a random motion of individuals and reaction terms describe their reproduction [13].

The population is modeled as having a growth rate that is proportional to the population, for single with unlimited resources. The reaction –diffusion equations can be used to model infectious outbreak over times as individual are susceptible, exposed, infected, and then either recover or die. These equations are used to model any biological system that changes over time [13].

Rationale of the Study

Dengue is one of the most significant arboviral infections in present world. Its burden has grown dramatically. Research on dengue is necessary to gain adequate knowledge, positive attitude, correct practice for its prevention, knowledge of its mutation and new variants to make medicine. As mathematical models are storytellers and they do as guiding tools to predict the future stages of epidemics, the outcomes of the study will help public health officers on decision making for dengue control.

Preliminary Definitions

Wolbachia

Wolbachia is a newly formed technique applied in several countries as a way to kill mosquito borne diseases. It is mainly based on the effect of a bacterium that blocks the transmission of arboviruses from a carrying mosquito to humans [13].

If the frequency or density is $u(t,x)$of Wolbachia- carrying mosquitoes with respect to the total mosquito population is defined by

$$U = \frac{\text{Wolbachia carrying individuals}}{\text{Total mosquito population}} \qquad (1)$$

Vector Control Techniques

Since there is no accepted vaccine for the treatment of dengue,the prevention and control mainly depend on vector control measures. There are number of techniques for controlling dengue, as for insecticide spraying, sterile insect, and genetic modifications [13].

Literature Review

Recently, reaction-diffusion equations have been used by many scholars in epidemiology as well as in virology. Wang and Wang [14] projected a model to simulate the hepatitis B virus (HBV) infection with spatial dependence. They introduced the random mobility of viruses into the basic model proposed by Nowak et al. [15]. They assume that the motion of virus follows a Fickian diffusion which is the population flux of the virus that is proportional to the concentration gradient. The proportionality constant is taken to be negative. They have neglected the mobility of susceptible cells and infected cells. They assumed that the domain is the whole real line and established the existence of traveling waves via the geometric singular perturbation method [15]. Wang et al. [22] introduced into an intracellular time delay between the infection of a cell and the production of new virus particles. They have taken the initial conditions in a one-dimensional interval with Neumann boundary conditions. The authors ignored the diffusion by assuming that the space is homogeneous in order to set up the global stability of equilibrium solutions. When the space is inhomogeneous, the effects of diffusion and intracellular time delay can be obtained by computer simulations [16]. Xu and Ma [17] discovered the saturation response to the model and obtained sufficient conditions for the global stability of the infected steady state. In epidemiology, Yang et al. [18] considered the SIR epidemic model with time delay and nonlinear the incidence rate was presented and studied by Xu and Ma [17]. They introduced special diffusion model and assumed that three diffusion coefficients are equal in order to prove the existence of traveling waves solutions for the model. They discussed the local stability of a disease-free steady state and an endemic steady state to this model under homogeneous Neumann boundary conditions. Wang and Li [19] explained the local stability of constant steady-state solutions to reaction–diffusion systems with Neumann boundary conditions. They derived a set of conditions, which they called the minor condition. In addition, they applied their results on an example in epidemiology. Hattak and Yousfi[20] studied the global stability for some diffusion equations in biology by constructing Lyapunov equations functional. Their Lyapunov functionals are obtained from those for ordinary differential equations. They gave several examples from virology and epidemiology to illustrate their model.

Shrestha et al. [21] studied the Serological and Entomological study of dengue in Dang and Chitwan Districts of Nepal and concluded that the first case of dengue in Nepal was recorded in a foreigner in Chitwan in 2004 and subsequently the larger outbreak occurred

in 9 districts of Terai region in 2006 with 23 confirmed dengue cases following the Indian epidemic of DF/DHF in September-October 2006. After four years, another significant outbreak occurred in 2010 in Chitwan with at least 359 confirmed dengue cases. So it can be concluded that dengue is a significant problem in the districts of Terai region of Nepal including Chitwan and Dang.

Several workers like Wang et al. [22], Wang and Wu [23], Mottoni et al. [24], LI et al. [25], Li et al. [26] etc. have made their contributions and enriched the theory of virology and epidemiology and their applications. Literature concerning this theory can be found in any standard text books and monographs of epidemiology, for instance: Dunn [27], Bang [28],Rozendaal [29],Sharma et al. [30], Christopher,[31],Gubler [32] , to name a few.

Mathematical Model of Dengue

It is not easy to model a tool to guide public health strategies to control the transmission of dengue. A lot of complicated models will use to understand the dynamics of transmission of dengue. This present work will use reaction- diffusion model equation to study its transmission and control measures. Let the ordinary differential equation to model the population growth of vectors to be following initial value problem:

$$u'(t) = a(u(t))\,u(t), \quad u(0) = u_0 \qquad \text{(ii)}$$

where $u_t =$ The population size at time t,

$a(u)$ = Population dependent growth rate

This model assumes that the rate of population changes is proportional to the population size. If we take,

$$a(u) = a\left(1 - \frac{u(t)}{u_\infty}\right) \qquad \text{(iii)}$$

for constant positive parameters, then population grows when the population is smaller than the limiting value u_∞ and size decreases if u exceeds this value. The equation (ii) is autonomous differential equation that has critical points at u = 0, and u = u_∞ .The critical point is unstable for zero and stable for other values. Now, equation (ii) takes the form

$$u'(t) = F(u(t)) \qquad \text{(iv)}$$

is the special case of general autonomous equation. The partial differential equation of the form

$\partial_t u(x,t)$ - $\nabla^2 u(x,t)$ = *F(u(x, t)),* $x \in R^n$, $t > 0$

(v)represent the mechanism of diffusion into population model. When n =1, the equation (iv) takes form

$\partial_1 u(x,t)$ - $\partial_{xx} b(u(x,t)$ = *F(u(x, t))*, b(u)> 0 (vi)

where b is biting rate and equation (v) arises in a variety of biological applications and in modeling certain chemical reaction and are called reaction-diffusion equations. This equation (v) can be written as in (ii) equation as

$\partial_1 u(x,t)$ - *D* $\partial_{xx}\ u(x,t) = \alpha$ *u(x, t)* $\left(1 - \frac{u(t)}{u_\infty}\right)$ (vii)

is Fisher's equation and is also a population growth model [3].

Model Formulation

Suppose T_H and T_V are human and vector population sizes respectively. Let human population have constant size with birth and death rate constant equal toμ_H. For the mosquito population, constant recruitment rate says A which is independent of the actual number of adult mosquitoes. Thin independency is justified by the fact that very few eggs and larva mature to adult, so this process does not depend on the size of the mosquito population [33].

The total death in the mosquito population = $\mu_v T_V$, (viii)

where $\mu_v$is the per capita mortality rate of mosquito. The ordinary differential equation which explains the population dynamics of vector population is

T'_V =A -$\mu_v T_v$ (ix)

Suppose, number of human susceptible = S'_H (t)

Infective = I'_H (t)

and similarly immunes in human population =R'_H (t)

Number of susceptible=S'_V (t)

Infective= I'_V (t) in the vector population.

Assume that the mosquitoes are always infected, never get recovered from infection. We exclude the vertical transmission in this model. The biting rate represented by b of mosquitoes is the average of number of bites per mosquito per day. In fact, the biting rate rely on a number of factors,e.g. climate, rainy season, but b is supposed to be constant throughout this model [32].Suppose m is the number of alternative hosts then probability of human as host is defined by

$$\frac{T_H}{(T_H+m)} \quad \text{(x)}$$

The number of bites per unit of time to human = $b\left(\frac{T_V}{T_H}\right)\frac{T_H}{(T_H+m)}$

The blood meals per unit of time taken to by mosquito = $b\,\frac{T_H}{(T_H+m)}$

The infection rates per susceptible human and susceptible vectors are defined by

$$\left.\begin{aligned} B_H\, b\frac{T_V}{T_H}\frac{T_H I'_v}{T_H+mT_V} &= \frac{B_H\, b}{T_H+m} I'_v \\ B_H\ b\ \frac{T_H I'H}{T_H+mT_H} &= \frac{B_v\, b}{T_H+m} I'_H \end{aligned}\right\} \quad \text{(xi)}$$

whereB_H represent the transmission probability from vectors to human and B_v is transmission probability from human to vector. So, the infection and recovery, both can be described by the reaction diffusion equation model, and the details of derivation will be discussing in the research report [33].

Expected Result

After this study, the in depth understanding of transmission of dengue is made mathematically and some effective way of its prevention is recommended. The sensitivity analysis will identify the significant and insignificant parameters in the model. Model effectiveness will be justified with available data.

Novelty/ Association to National Priority and Needs

Dengue is the mosquito borne disease has become a growing public health threat in Nepal due to its gradual increasing morbidity and mortality, since 2004. In 2022, the country

witnessed the worst ever dengue outbreak with 38 conform death [1]. Several works on dengue has been performed. But still many more study or research has to be done. As there is no specific treatment of dengue, it is necessary to gain information's regarding to dengue—including prevention measures. Researchers want to know how the dengue virus cause damage to the human body and how the immune system of human responds to make and develop new treatments [34]. Everyone has an important role to prevent dengue with programmatic preparation. So, the study of dengue should be in a high priority of the Nation.

May be due to the climate change and the global warming, the dengue infection is not now limited to the Terai region. As last years, the dengue disease might spread over almost all the districts of Nepal. Not only the policy, government and local authority should give priority and preparation for its control.

Future Prospect of Research

Due to increasing population, urbanization and climate factors, many experts forecast that dengue cases will increase in the future with new and new variants. So, it is very important to elaborating on some of the potential factors that derive dengue activity. There is also increasing need of regular research on new variants of dengue or mutations. So, the existing models and solutions techniques are needed to be improved.

Conclusion

Mathematical models serve as invaluable tools in the study of biological control strategies for dengue fever. By capturing the complex interactions between vectors, hosts, and environmental factors, these models enable researchers and policymakers to assess the impact of control measures and design effective interventions to mitigate the burden of dengue. As we continue to refine and validate these models, we move closer to achieving the ultimate goal of dengue eradication.

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