

**DYNAMICS OF DENGUE FEVER:
DETERMINISM AND PREDICTABILITY
WITH THE SIHR MODEL**

By

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The work described in this thesis was carried out by me under the supervision of Dr. N.G.A. Karunathilake and Dr. (Ms) R.P.K.C.M. Ranasinghe a report on this has not been submitted in whole or in part to any university or any other institution for another Degree/Diploma.

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ABSTRACT

A deterministic compartment model is derived with the aim of studying the dynamics of the Dengue virus fever which emerged as an epidemic in Sri Lanka for the past few decades. The model is based on the epidemiological behavior of the dengue virus in the human body. The host population is subdivided into a set of distinct compartments, namely, Susceptible (S), Dengue fever infected (I), Dengue hemorrhagic fever infected (H) and recovered(R).

Considering the rate of flux of individuals between compartments a system of ordinary differential equations is derived for the description of the dynamic of S , I , H and R , respectively. Taking the total population as the characteristic scale, the dimensionless form of the system is obtained. Then the existence and uniqueness of the solution of the system is established examine the conditions of Picard-Lindelof theorem. The stability analysis reveals that the system contains two equilibrium points namely disease free sate and endemic state. And also the system stability at these equilibrium points can be justified by observing the behavior of the reproduction number.

The model parameters involved in the system are estimated by approaching different statistical techniques depending on their nature. Details of Dengue virus fever in Gampaha district for past few years are used for the determination of parameters.

We numerically simulate the solution of SIHR model, with respect to the global error, by means of the fourth order Runge-Kutta method. The numerical solution of SIHR model shows that it takes nearly five or six months to spread dengue fever all over the area. Between ninth and eleventh month the maximum number of patients are infected and after eighteen or nineteen months the disease disappear.

Chapter One

1 INTRODUCTION

Dengue is an African word meaning *bone breaking*. The dengue which is a member of the virus family Flaviviridae was first reported as an epidemics fever in 1779-1780 in Asia, Africa, and North America with the simultaneous outbreaks. The dengue viruses and their mosquito vector have had a worldwide distribution in the tropics for more than 200 years. The dengue fever is a mosquito borne disease caused by dengue virus. It is rapidly expanding in most tropical and subtropical region in the world. Dengue fever may occur in people of all ages who are exposed to infected mosquitoes during the rainy seasons.

Dengue Fever, the member of virus family Flaviviridae has been one of the most important resurgent diseases in the tropical and sub tropical countries in the world. Since the distribution of both viruses and mosquitoes are occurred in the urban and suburban regions around the country the dengue fever outbreaks rapidly affecting the young and the old, the rich and the poor in highly densely populated areas.

The prime aim of the paper is to develop a mathematical model to describe the dynamic of the dengue fever and predict future situation as the measures of approximated numerical representation.

The dengue infected individuals in the model are identified as Dengue Fever or Dengue Hemorrhagic Fever patients. With respect to the factors that influence the affect of the virus, it behaves at different levels in a human body. Thus the symptoms and disease characteristics of an infected body may differ accordingly. The individuals at a certain level of virus affection with similar symptoms are considered to be a compartment.

With the idea of developing a compartmental model for the dengue epidemiological disease, the host population is initially divided into distinct compartments according to the epidemiological status of the dengue fever. The number of compartments in the model is determined by the environmental factors and other biological views of the virus along with the symptoms of the infected human body. The SIHR model consists of four distinct epidemiological compartments for the individuals in susceptible, Dengue Fever, Dengue Hemorrhagic Fever, and Recovery states. At the model inception all individuals in the system are assigned to one of these compartments according to their symptoms on the infected body. By the time passing if the symptoms are differed they will be moved to the next respective compartment of the model. The flux of these individuals between model compartments is interpreted by the model parameters. The dynamics of the population size is another important factor in epidemiological models. In the cases of dengue fever the population size is assumed to be at a constant level because the model is employed for the short period of time. And then the birth and death rates are adjusted accordingly. Under this phenomenon the behavior of these compartments is interpreted by the system of differential equations. The parameters are estimated by the data collected from the real world cases such that the model can describe the dynamics of the physical phenomenon and to make a prediction of future situation of the fever. At last the model validity is checked over the medical data gathered from MOH offices in the district since there may be discrepancies between model solutions and physical observations.

The chapter one describes the overview of developing a compartmental model for the dengue epidemic disease.

The chapter two describes Hierarchical Epidemiological Models

The chapter three describes the basics of the dengue fever and the symptoms to distinguish the level of Dengue Fever individuals. Furthermore the methods of controlling the virus transmission and methods of prevention to reduce the infectious individuals will be discussed.

The chapter four describes the dynamics of the epidemiological model SIHR and its stability. The infectious period of an individual in a compartment is identified as to follow an exponential distribution. And also the concept reproduction ratio of epidemiological model is observed as a threshold value in the endemic diseases.

The chapter five describes the new model SIHR by dividing the host population in to four compartments according to the epidemiological states of the dengue virus.

The chapter six describes the existence and the uniqueness of the solutions at the equilibrium points. A reproduction ratio which is a threshold value of the SIHR model is defined as a combination of model parameters.

The chapter seven describes the estimation process of the identified parameters of the SIHR dengue epidemiological model. The parameter estimations are implemented over DF/DHF data collected from the office of Deputy Provincial director of Health Service-Gampaha District.

The chapter eight describes the numerical approximations of the SIHR system for the period of twelve months ahead. The fourth order Runge-Kutta method is employed as a tool of approximation method of the SIHR system. Move over in this chapter describes the variation of error in the model data derived by the Runge-Kutta method.

The chapter nine describes the dynamics of the dengue fever based on the characteristics of SIHR epidemiological model. And also this chapter remarks the

validity of predicting the future behavior of the dengue fever for the period of six months ahead.

Developing of such mathematical model it will be more important measurement to address disease patterns, evaluate and interpret data for critical decision-making and program customization to access infectious diseases. Since the mathematical models have become important tool in prediction as numerical measures of the spread, it is believed that the control program can anticipate the probable outcome in the implementation of pre-design action plans.

Chapter Two

2 HIERARCHICAL EPIDEMIOLOGICAL MODELS

Mathematical modeling is an essential tool in studying a diverse range of such diseases. Basic aims in studying Mathematical modeling of infectious disease can be dated back to 1760 when Daniel Bernoulli evaluated the effectiveness of variation of healthy people with smallpox virus. In 1960 Hamer formulated and analyzed a discrete time model in his attempt to understand the recurrence of measles epidemics. His model may have been the first to assume that the incidence (number of new cases per unit time) depend on the product of the densities of the susceptibles and infectives. Ross was interested in the incidence and control of malaria, so he developed differential equation models for malaria as a host vector disease in 1911. The other deterministic epidemiology models were then developed in papers by Ross and Hudson, Martin and Lotka. [24].

Starting in 1926 Kermack and McKendrick published papers on epidemic models and obtained the epidemic threshold result that the density of susceptibles must exceed a critical value in order for an epidemic outbreak to occur[8]. Mathematical epidemiology seems to have grown exponentially starting in the middle of the 20th century (the first edition in 1957 of Bailey's book [5] is an important landmark), so that a tremendous variety of models have now been formulated, mathematically analyzed, and applied to infectious diseases. The review of the literature shows rapid growth of epidemiological model. The recent models have involved aspects such as passive immunity, gradual loss of vaccine and disease-acquired immunity, stages of infection, vertical transmission, disease vectors, macro parasitic loads, age structure, social and sexual mixing groups,

spatial spread, vaccination, quarantine, and chemotherapy. Special models have been formulated for diseases such as measles, rubella, chickenpox, whooping cough, diphtheria, smallpox, malaria, onchocerciasis, filariasis, rabies, gonorrhoea, herpes, syphilis, and HIV/AIDS.

At the beginning of last century, a series of deterministic compartment models such as MSEIR, MSEIRS, SEIR, SEIRS, SIR, SIRS, SEI, SEIS, SI and SIS have been proposed based on the flow patterns between the compartments. However, there was a hiatus in epidemiological modeling until the beginning of the 20th century (1911), with the pioneers of Hamer[12] and Ross[24] on measles and malaria respectively. Most models developed later try to incorporate other factors into the models. These factors include variation of population size and age-structure. Two important developments recently are the discretization of the model so that statistical method can be applied directly in the estimation of the parameters.

Over the past century, there has been broadly studied of the epidemics modeling. One of the well-known mathematical models of epidemics is the susceptible- infectious-removed (SIR) model originally formulated by Kermack and McKendrick. In 1927, Kermack and McKendrick derived the celebrated threshold theorem, which is one of the key results in epidemiology[20]. It predicts, depending on the transmission potential of the infection the critical fraction of susceptibles in the population that must be exceeded if an epidemic is to occur. This was followed by the classic work of Bartlett[6], who examined models and data to expose the factors that determine disease persistence in large populations.

Arguably, the first landmark book on mathematical modeling of epidemiological systems was published by Bailey that led in part to the recognition of the importance of modeling in public health decision making.

In last two decades, infectious diseases have gained increasing recognition as a key component in the dynamics epidemic diseases prevailing in populations reviewed in Anderson and May 1991, Grenfell and Dobson in 1995[10].

A number of diseases are endemic in animal populations, that is, they are persistent and almost never go locally extinct. We can use the word endemic according to the epidemiological tradition, which is unrelated to the bio-geographic usage. The interaction between hosts and their endemic parasites has been modeled intensively. Both host-parasite and reduced host abundance can result from such interactions (Anderson 1978, May) Endemism (local persistence) depends on parasite vital rates, host abundance and host reproduction

Dana A. Focks, Eric Daniels, Dan G. Haile AND James E. Keesling have developed a pair of stochastic simulation models that describe the daily dynamics of dengue virus transmission in the urban environment. Their goal had been to construct comprehensive models that take into account the majority of factors known to influence dengue epidemiology. The models have an orientation toward site-specific data and are designed to be used by operational programs as well as researchers. The first model, the container-inhabiting mosquito simulation model (CIMSIM), a weather-driven dynamic life-table model of container-inhabiting mosquitoes such as *Aedes aegypti*, provides inputs to the transmission model and the dengue simulation model (DENSIM) is the second model to a description and validation of the entomology models.