Tehreem umar Analysis of the transmission of NEU Dengue fever disease 2021

ANALYSIS OF THE TRANSMISSION OF DENGUE FEVER DISEASE

A THESIS SUBMITTED TO THE INSTITUTE OF GRADUATE STUDIES

OF

NEAR EAST UNIVERSITY

By

TEHREEM UMAR

In Partial Fulfillment of the Requirements for the Degree of Master of Science in Mathematics

NICOSIA, 2021

SENSITIVITY ANALYSIS IN COVID-19 EPIDEMIC MODEL

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Approval of Director of Instıtute of Graduate Studies

Prof. Dr. K. Hüsnü Can BAŞER

We certify this thesis is satisfactory for the award of the degree of Masters of Science in Mathematics

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I declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

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To my parents…

ABSTRACT

This thesis is about the analysis of the transmission of dengue fever disease, using SIR model. Dengue virus is the connection between human and mosquito named aedes aegypti. Dengue virus speared because of mosquito bite.

To analysis the transmission of dengue virus from mosquito to human and human to mosquito we used SIR models. Whole population divided into two parts, human and mosquito. Further human population is divided into three parts, susceptible, infected and recovered(immune), and the vector(mosquito) population divided into two parts that is susceptible and infected. The change in these five classes is defined through Five nonlinear differential equations. For the solution of this model, we find equilibrium point (disease-free equilibrium, Endemic Equilibrium) and basic reproduction ratio, by next generation matrix method. Then stability analysis discus for all possible equilibrium points. numerical analysis of dengue transmission is studied and on the basis of basic reproduction ratio R_o we come to our conclusion about transmission of dengue fever disease.

Keywords: SIR model; dengue transmission; differential equations; equilibrium points; stability analysis

OZET

Bu tez, SIR modeli kullanılarak dang humması hastalığının bulaşmasının analizi ile ilgilidir. Dang virüsü, insan ile aedes aegypti adlı sivrisinek arasındaki bağlantıdır. dang virüsü sivrisinek ısırığı nedeniyle mızrakladı.

Dang virüsünün sivrisinekten bulaşmasını analiz etmek İnsana ve insandan sivrisinek için SIR modellerini kullandık. Tüm nüfus, insan ve sivrisinek olmak üzere iki kısma ayrılmıştır. Daha fazla insan popülasyonu, duyarlı, enfekte ve iyileşmiş (bağışık) olmak üzere üç kısma ayrılır ve vektör (sivrisinek) popülasyonu, duyarlı ve enfekte olan iki kısma ayrılır. bu beş sınıftaki değişim, Beş doğrusal olmayan diferansiyel denklemle tanımlanır.

Bu modelin çözümü için yeni nesil matris yöntemi ile denge noktası (hastalıksız denge, Endemik Denge) ve temel üreme oranı bulunur. Ardından, olası tüm denge noktaları için stabilite analizi yapılır. Dang humması bulaşmasının sayısal analizi incelenir ve temel üreme oranı $R_\circ$ temelinde dang humması hastalığının bulaşmasına ilişkin sonuca varırız.

Anahtar Kelimeler: dang humması bulaşması; diferensiyel denklemler; denge noktaları; kararlılık analizi

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1
INTRODUCTION

Infectious diseases are disordered caused by organism, such as bacteria, viruses, fungi and parasites. Some infectious diseases can be passed from person to person but dengue fever disease is the link between human and mosquitos.

1.1 Infectious Disease

Infectious disease can be passed through human, insects, animals and some time through contaminated food and water. Mostly infectious diseases have same symptoms like fever, coughing and body aches. Most infectious diseases have only minor complications. But some infections — such as pneumonia, AIDS and meningitis — can become life-threatening. A few types of infections have been linked to a long-term increased risk of cancer. In addition, some infectious diseases may become silent, only to appear again in the future — sometimes even decades later. For example, someone who's had chickenpox may develop shingles much later in life. (Mayo foundation, 2021).

1.2 Dengue Disease

As medical research advancement grew at the end year's 20th century and vaccinations, antibiotics, and improvement of life conditions became top priorities, it was expected that the spread of infectious diseases was going to be overcome (Khalid et al.,2015). However, in fact, in the beginning of 21st century, infectious diseases still caused sorrow in the developing countries Malaria, jaundice, AIDS, and Ebola are some of the culprits (Nur et al.,2018).

Dengue fever disease is one of these which spread in the southeast Asia and all over the world, particularly in the tropical climate countries (Murray and Lopez, 1996). Dengue is produced by viruses of the genus ogaviridae, subgenus Flavivirus., Three of the vectors are Aedes aegypti Linnaeus, Aedes albopictus Skuse, and Aedes scutellaris Walk (Feng and Velasco-Hernández, 1997). Globally, dengue viruses currently considered be the most important arthropod-borne viruses transmitted to humans, whether measured in of the number of human infections the number of deaths (focks ed al., 1995). It is estimated that more than 50 million infections occur each year, where 500,000 for dengue haemorrhagic fever (Gubler, 2004). In 2009 the World Health Organization (WHO) estimated 50 to 100 million reported cases worldwide (WHO fact sheets, 2009). Dengue has been recognized in over 100 countries and 2.5 billion people live in areas, where the dengue is endemic (Geneva, 1997). The number of dengue cases reported to WHO increased over 8-fold over the last two decades, from 505,430 cases in 2000, to over 2.4 million in 2010, and 5.2 million in 2014. Reported deaths between the year 2000 and 2015 increased from 960 to 4032. (Who fact sheet.2014)

1.3 Dengue Virus Transmission

Dengue virus transmission due to a mosquito belonging to the Genus Aedes, this type of mosquitos has black and white strips on their body. The main cause of dengue virus and dengue mosquito's transmission for one part of the globe to other is international and national travel and trade (Ali ed al, 2013). virus is transmitted to human beings by the mosquito bite and dengue viruses infect immature dendritic cells in the skin through the non-specific receptor dendritic cell-specific ICAM3-grabbing non-integrin (DC-SIGN). (Guzman ed al., 2010). Dengue virus exists in human body in two forms: the Dengue Fever (DF) or classic dengue and Dengue Hemorrhagic Fever (DHF), In this type blood comes different parts of body like (Nose, Ear, Teeth). The classical Dengue fever is a disease of older children and adults. DHF on the other hand is primarily a disease of children under the age of 15 (Pongsumpun and Tang, 2003). Important risk factors for DHF include the strain and serotype of the virus involved, as well as the age, immune status, and genetic predisposition of the

patient (Gubler and Clark, 1995). It's a mosquito-borne infection caused by 4 serotypes of dengue virus, DEN-1, DEN-2, DEN-3, and DEN-4. When a person gets infected by one of the four, will never be infected by the same once again, which is a phenomena homologous immunity, However, once the human subject is attacked by either of the four, he loses immunity to the other three in about 12 weeks; this is known as heterologous immunity. This makes the patient more susceptible to cave into Dengue Hemorrhagic Fever (DHF) (Khalid ed al.,2015). When mosquito bite a person, virus goes their body and between 4 to 7 days infections expose and some symptoms appear like temperature, headache, pain in body and joints, some red sports in skin and vomiting, after that the person enters the acute phase of infection. If other mosquitoes bite the infective person during this acute phase these mosquitos become the infective and subsequently begin the transmission cycle anew (Pandey ed al, 2013). During epidemics of dengue, attack rates may be 80%–90% in susceptible persons. Although, it is not usually recognized, more than half the people who are infected with a dengue virus may be asymptomatic, which would indicate a substantial underreporting of infections (Calisher, 2005). Dengue virus speared in uncover clean accumulated water. The most likely place, were dengue's mosquito gives their eggs is open water tanks, or where the rain water stand or open bucket of clean water. Ae. aegypti is a daytime feeder, its peak biting periods are early in the morning and in the evening before dusk (Who dengue and severe dengue, 2014).

1.4 Symptoms of Dengue Virus

The symptoms of dengue infection appear in the form of fever and frontal headache, body aches, nausea and vomiting (Gubler, 1998). Dengue fever is a non-fatal illness characterized by a sudden onset of a headache, retro-orbital pain, joint pain and a high fever (Sriprom ed al.,2007). some time because of dengue infection there is high fever with severe headache and joint pain, and even to internal hemorrhaging, circulatory failure and death. Two severe type of dengue fever are, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). (Medlock ed al., 2009).

1.5 Dengue in Pakistan

In Pakistan Dengue fever first time reported in 1982 in which out of 174 patients, 12 were the affected patients (Qamash ed al. ,2020). Pakistan first reported an epidemic of dengue fever in 1994(Jahan, 2011). In 2005, serotype-3 was reported in Pakistan after a break of ten years (Haider and Iqbal, 2016). Pakistan experienced large epidemics of dengue fever during 2008, 2010 and 2011 affecting thousands of people and claiming hundreds of deaths (Haider ed al., 2015). In 2011, Pakistan had the worst strike of dengue in which more than 20,000 cases and 300 deaths were reported officially which according to experts reflect under reporting (khanani ed al., 2011). Another dengue epidemic occurred in Pakistan from July to December of 2013. In this epidemic, 1175 patients suffering from dengue infections in only one city, Rawalpindi, of Pakistan (Khurram ed al., 2014). In 2017 a huge dengue outbreak happens in Peshawar city of Pakistan with 69 deaths and 24,807 laboratory-confirmed cases (Ali ed al., 2019). From 1995 to 2019, there were around 147,200 cases of dengue infection and over 800 deaths (Fatima, 2019). more than 50,000 dengue cases and 90 deaths due to dengue reported in 2019 (WHO dengue in Pakistan, 2019). dengue history in Pakistan shown in Table 1.1.

Table 1.1: Dengue history in Pakistan from 2006 to 2013. (Ahmed, 2016).

Year	Suspected cases	Deaths
2006	4961	41
2007	2304	18
2008	2792	17
2009	1940	13

2010	15,901	40
2011	252,935	219
2012	3913	33
2013	9037	6

Dengue infection rate is high in Pakistan due to many reasons, lack of public awareness, lake of health care facilities and especially the intense floods and storms which come every year after, increase the rate of infection.

1.6 Mathematical Model

İn this thesis we are analysis the transmission of dengue virus for this porpose the Mathematical model help us, for describing and analyzing the behavior of disease. With the help of SIR model we describe the transmission of disease.Mathematical models are highly used for the transmission of several diseases, First SIR model costructed by Kermak and McKendrick in 1927. After these model most of mathematicians construct the models depand on the dynamics of the disease.Recent years have seen an increasing trend in the representation of mathematical models in publications in the epidemiological literature, from specialist journals of medicine, biology and mathematics to the highest impact generalist journals (Ferguson, 2006), showing the importance of interdisciplinary.

Mathematical models for dengue fever have investigated compartment dynamics using susceptible, infected and recovered (SIR) models (Derouich and Boutayeb, 2006). SIR (susceptible-infected-recovery) model is used to describe the transmission of dengue disease with constant human and vector populations (Esteva and Vargas, 1998). some articles have discussed the dengue fever transmission model, SIR model, and looked for disease-free

equilibrium and the three endemics equilibriums to reduce the sufferers of dengue fever (Noraini ed al., 2007).

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CHAPTER 2

ANALYSIS OF DENGUE MODEL

In this chapter we have analysis the transmission of dengue virus using SIR model.
We have found the basic reproduction ratio by next generation matrix method and equilibriums point (disease free equilibrium point and endemic equilibrium point).
We have discussed the stability analysis using Jacobian matrix method and find the eigenvalue for equilibrium points.

2.1 model for dengue virus transmission

This model is based on Susceptible, Infected, and Removed (SIR) model, adopted by (Side and Noorani, 2013). We divide our population into two parts a human population (N_H) and a vector population (N_V). Further the human population (N_H) is divided into three groups:

(i) people who may potentially get infected with dengue virus (susceptible; S_H),
(ii) people who are infected with dengue (infected; I_H), and
(iii) people who have recovered (removed; R_H).

The vector population of mosquitoes (N_V) is divided into two groups

(i) mosquitoes that may potentially become infected with dengue virus (susceptible; S_V).
(ii) mosquitoes that are infected with dengue virus (infected; I_V).

No immune or recovery class exists in vector population, since the mosquito dies before it can recover from the disease.

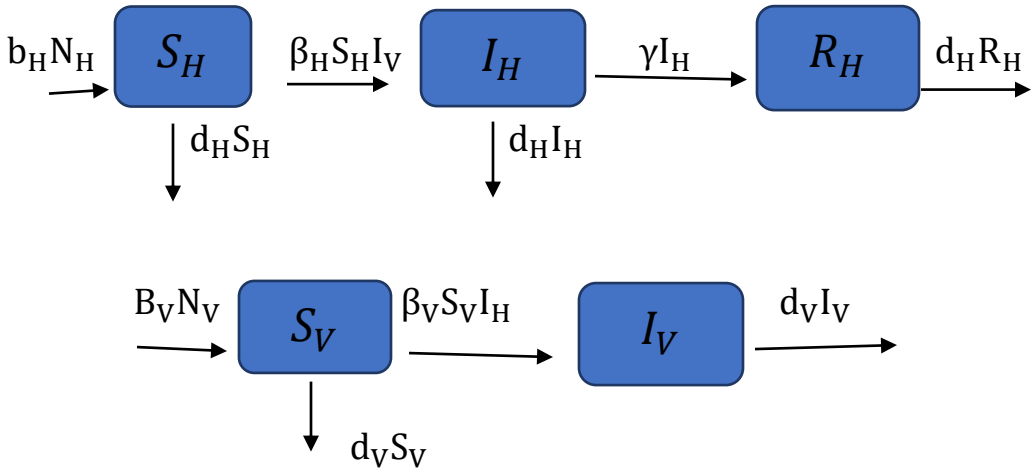

Figure 2.1: Transfer diagram of the model.

With using Figure (2.1) and with the following assumptions,

1. number of people in the population have already been infected by the virus while others have not.
2. transmission of the virus continues in the population, but the number of mosquitoes is constant.
3. The natural birth and death rate are included in the model.
4. Both people and mosquitoes are categorized in one group at a time.

We obtain the Changes that occur in all groups of people and of mosquitoes, as nonlinear differential equations.

$$\frac{dS_H}{dt} = b_H N_H - \beta_H S_H I_V - d_H S_H,$$

$$\frac{dI_H}{dt} = \beta_H S_H I_V - \gamma I_H - d_H I_H,$$

$$\frac{dR_H}{dt} = \gamma I_H - d_H R_{H,} \qquad (2.1)$$

$$\frac{dS_V}{dt} = b_V N_V - \beta_V S_V I_H - d_V S_V,$$

$$\frac{dI_V}{dt} = \beta_V S_V I_H - d_V I_V,$$

Table 2.1: Describes the variable and the parameter of the model (2.1).

Parameters	**Descriptions**
b_H , b_V	The birth rates for human and vector respectively
β_H, β_v	The transmission rate of dengue virus from vector to human, from human to vector respectively
d_H , d_V	The death rate of human population and vector population respectively
N_H , N_V	total human and vector population
γ,	recovery rate

2.2 Equilibrium points

An equilibrium point is the constant soulation to a differential equations, so we equlizing the equations to zero. Then find the disease free equlibrium and endemic equlibrium.

$$b_H N_H - \beta_H S_H I_V - d_H S_H = 0 \qquad (2.2)$$

$$b_V N_V - \beta_V S_V I_H - d_V S_V = 0 \qquad (2.3)$$

2.2.1, Disease- free Equilibrium

disease free equilibrium means there is no infection of dengue virus so I_H , I_V =0

put in equations 2.2 and 2.3,

we get,

$$b_H N_H - 0 - d_H S_H = 0$$

and

$$b_V N_V - 0 - d_V S_V = 0$$

Thus,

$$S_H = \frac{b_H N_H}{d_H} \quad \text{and} \quad S_V = \frac{b_V N_V}{d_V} \ ,$$

Hence disease-free equilibrium points are,

$$E_o = (\frac{b_H N_H}{d_H} , 0, \frac{b_V N_V}{d_V} , 0).$$

2.2.2, Endemic Equilibrium

Endemic equilibrium, we have three categories

(a), Human Infected Equilibrium

İn this category we assume there is no vector born infected so I_H=0, $I_V \neq 0$

Put in equation 2.2 and 2.3

we get,

$$S_H = \frac{b_H N_H}{\beta_H I_V + d_H} \ ,$$

And

$$S_V = \frac{b_V N_V}{d_V} \ ,$$

And

$$I_V = \frac{\beta_V S_V I_H}{d_V} \ ,$$

Thus, human infected equilibrium points are,

$$E_1 = \left(\frac{b_H N_H}{\beta_H I_V + d_H}, 0, \frac{b_V N_V}{d_V}, \frac{\beta_V S_V I_H}{d_V}\right),$$

(b) Vector born infected Equilibrium,

İn vector born infected equlibrium we assume there is no human infected,

So $I_H \neq 0$, I_V=0

Put in equation 2.2and 2.3,

we get,

$$S_H = \frac{b_H N_H}{d_H},$$

and,

$$I_H = \frac{\beta_H S_H I_V}{\gamma + d_H},$$

and,

$$S_V = \frac{b_V N_V}{\beta_V I_H + d_V},$$

so, vector born equilibrium points are,

$$E_2 = \left(\frac{b_H N_H}{d_H}, \frac{\beta_H S_H I_V}{\gamma + d_H}, S_V = \frac{b_V N_V}{\beta_V I_H + d_V}, 0\right),$$

(c) Both endemic Equilibrium

in this catogory both endemic are ther, so $I_H \neq 0$, $I_V \neq 0$,

put in equation 2.2 and 2.3,

we get,

$$S_H = \frac{b_H N_H}{\beta_H I_V + d_H},$$

and,

$$I_H = \frac{\beta_H S_H I_V}{\gamma + d_H}, \quad S_V = \frac{b_V N_V}{\beta_V I_H + d_V}, \quad I_V = \frac{\beta_V S_V I_H}{d_V},$$

so, both endemic equilibrium points are,

$$E_3 = \left(\frac{b_H N_H}{\beta_H I_V + d_H}, \frac{\beta_H S_H I_V}{\gamma + d_H}, \frac{b_V N_V}{\beta_V I_H + d_V}, \frac{\beta_V S_V I_H}{d_V}\right).$$

Thus,

E_o, E_1,E_2,E_2 are the equilibriums points.

2.3 BASIC REPRODUCTION RATIO

The basic reproductive ratio, R_0, is defined as the expected number of secondary infections arising from a single individual during his or her entire infectious period, in a population of susceptible. R_0 developed for the study of demographics (Sharpe and Lotka, 1977) and (Kuczynski, 1928) it was independently studied for vector-borne diseases such as malaria (Ross, 1911) and directly transmitted human infections (Kermack and McKendrick, 1927). It is now widely used in the study of infectious disease, and more recently, in models of in-host population dynamics. (Dietz, 1993). R_0 Value show how much infection will occur to individuals as a result of infection. If a patient is free from dengue fever, $R_0 \leq 1$ value. If the patient can transmit to other individuals and more than one, the value $R_0 \geq 1$.

The method to compute the basic reproduction ratio using the next-generation matrix is given By (Diekmann *et al.*, 1990) and (Watmough, 2002).

The matrix FV^{-1} is know as next generation matrix, the eigenvalue is the basic reproduction value of the model. Where (F) is represents the rate of appearance of new infections, V represent the rate of transfer from the infections class.

$$F = \begin{bmatrix} 0 & \beta_H S_H \\ \beta_V S_V & 0 \end{bmatrix}$$

and,

$$V = \begin{bmatrix} \gamma + d_H & 0 \\ 0 & d_V \end{bmatrix}.$$

Then,

$$V^{-1} = \frac{1}{\det V} \times adj\, V\,, \tag{2.4}$$

and,

$$|V| = \begin{vmatrix} \gamma + d_H & 0 \\ 0 & d_V \end{vmatrix}$$

$$= (\gamma + d_H \times d_V) + (0 \times 0)$$

$$= (\gamma + d_H) d_V \tag{2.5}$$

and

$$adj\, V = \begin{bmatrix} d_V & 0 \\ 0 & \gamma + d_H \end{bmatrix} \tag{2.6}$$

Put value of (2.5) and (2.6) in (2.4), we get

$$V^{-1} = \begin{bmatrix} \frac{1}{\gamma + d_H} & 0 \\ 0 & \frac{1}{d_V} \end{bmatrix}.$$

Thus,

$$FV^{-1} = \begin{bmatrix} 0 & \beta_H S_H \\ \beta_V S_V & 0 \end{bmatrix} \times \begin{bmatrix} \frac{1}{\gamma + d_H} & 0 \\ 0 & \frac{1}{d_V} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} (0 \times \frac{1}{\gamma + d_H}) + (\beta_H S_H \times 0) & (0 \times 0) + (\beta_H S_H \times \frac{1}{d_V}) \\ \left(\beta_V S_V \times \frac{1}{\gamma + d_H}\right) + (0 \times 0) & (\beta_V S_V \times 0) + (0 \times \frac{1}{d_V}) \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 + 0 & 0 + \frac{\beta_H S_H}{d_V} \\ \frac{\beta_V S_V}{\gamma + d_H} + 0 & 0 + 0 \end{bmatrix}.$$

Thus,

$$FV^{-1} = \begin{bmatrix} 0 & \frac{\beta_H S_H}{d_V} \\ \frac{\beta_V S_V}{\gamma + d_H} & 0 \end{bmatrix},$$

then,

$$FV^{-1} - \lambda I = \begin{bmatrix} -\lambda & \frac{\beta_H S_H}{d_V} \\ \frac{\beta_V S_V}{\gamma + d_H} & -\lambda \end{bmatrix}.$$

For finding value of λ put $|FV^{-1} - \lambda I| = 0$

$$\begin{vmatrix} -\lambda & \frac{\beta_H S_H}{d_V} \\ \frac{\beta_V S_V}{\gamma + d_H} & -\lambda \end{vmatrix} = 0$$

By solving Determinate, we have

$$\lambda^2 - \left(\frac{\beta_H S_H}{d_V}\right)\left(\frac{\beta_V S_V}{\gamma + d_H}\right) = 0,$$

Then,

$$\lambda^2 = \frac{(\beta_H S_H)(\beta_V S_V)}{d_V(\gamma + d_H)}$$

and,

$$\lambda = \sqrt{\frac{(\beta_H S_H)(\beta_V S_V)}{d_V(\gamma + d_H)}}.$$

Then R_0 can be obtained as

$$R_0 = \lambda(E_o) = \frac{b_H N_H}{\beta_H + d_H} \sqrt{\frac{(\beta_H S_H)(\beta_V S_V)}{d_V(\gamma + d_H)}}$$

2.4 STABILITY ANALYSIS

Theorem 2.1. disease free equilibrium is stable when $R_o < 1$.

Proof. We proof this theorem by Jacobian matrix method

$$J = \begin{bmatrix} -\beta_H I_V - d_H & 0 & 0 & 0 & -\beta_H S_H \\ \beta_H I_V & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & -\beta_V I_H - d_V & 0 \\ 0 & \beta_V S_V & 0 & \beta_V I_H & -d_V \end{bmatrix}.$$

Since its disease free so there is no human and vector infected, I_H, I_V =0

$$J = \begin{bmatrix} - d_H & 0 & 0 & 0 & -\beta_H S_H \\ 0 & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & - d_V & 0 \\ 0 & \beta_V S_V & 0 & 0 & -d_V \end{bmatrix}.$$

Eigenvalues obtained if and only if $|J - \lambda I|$=0 with J is the Jacobian matrix, λ is eigenvalues and I is the identity matrix. Then the eigenvalue for disease free equilibrium point as follows.

$$(-d_H - \lambda)(-d_V - \lambda)\{(-\gamma - d_H - \lambda)(-d_V - \lambda) - (\beta_H S_H)(\beta_V S_V)\} = 0.$$

Therefore,

$$(-d_H - \lambda) = 0, \qquad (2.7)$$

$(-d_V - \lambda)$=0 (2.8)

and

$(-\gamma - d_H - \lambda)(-d_V - \lambda) - (\beta_H S_H)(\beta_V S_V) = 0$. (2.9)

Thus,

From equation (2.7), (2.8) and (2.9) the eigenvalues are

$$\lambda_1 = -d_V, \quad \lambda_2 = -d_H \text{ and}$$

$$\lambda_3 = \frac{-(\gamma + d_V) \pm \sqrt{(\gamma - d_V)^2 - 4(\gamma d_V + d_H d_V - \beta_H S_H)(\beta_V S_V)}}{2}$$

All value of λ is < 0 . Hence by the Jacobian matrix method, the disease-free equilibrium point is asymptotically stable.

Theorem 2.2. Endemic Human Infected Equilibrium point is stable whenever R_o>1.

Proof. We proof this theorem by Jacobian matrix method.

$$J = \begin{bmatrix} -\beta_H I_V - d_H & 0 & 0 & 0 & -\beta_H S_H \\ \beta_H I_V & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & -\beta_V I_H - d_V & 0 \\ 0 & \beta_V S_V & 0 & \beta_V I_H & 0 \end{bmatrix}$$

we suppose that there is no human infective so I_H=0,

But there is vector infective, $I_V \neq 0$

$$J = \begin{bmatrix} -\beta_V I_V - d_H & 0 & 0 & 0 & -\beta_H S_H \\ \beta_H I_V & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & -d_V & 0 \\ 0 & \beta_V S_V & 0 & 0 & -d_V \end{bmatrix}$$

Eigenvalues obtained if and only if $|J - \lambda I|$=0 with J is the Jacobian matrix, λ is eigenvalues and I is the identity matrix.

Thus,

$$(-d_V - \lambda)(-d_H - \lambda)\{(-\beta_H I_V - d_H - \lambda)(-\gamma - d_H - \lambda)(-d_V - \lambda) - (-\beta_H I_V - d_V - \lambda)(\beta_H S_H)(\beta_V S_V) + (\beta_H I_V)(\beta_V S_V)(-\beta_H S_H)\} = 0$$

eigenvalue equations for the endemic state E_1.

$$(-d_V - \lambda) = 0 \qquad (2.10)$$

$$(-d_H - \lambda) = 0 \qquad (2.11)$$

and,

$$(-\beta_H I_V - d_H - \lambda)(-\gamma - d_H - \lambda)(-d_V - \lambda) - (-\beta_H I_V - d_V - \lambda)(\beta_H S_H)(\beta_V S_V) + (\beta_H I_V)(\beta_V S_V)(-\beta_H S_H)\} = 0.. \qquad (2.12)$$

Therefore, from these equations' eigenvalues are,

$$\lambda_1 = -d_H$$

$$\lambda_2 = -d_V$$

and,

$$\lambda_3 = \frac{-(\gamma + \beta_H I_V + 2d_H) \pm \sqrt{(\gamma + \beta_H I_V + d_V)^2 - 4(\gamma\beta_H I_V + \beta_H I_H d_H + \gamma d_H - \beta_H S_H)(\beta_V S_V)}}{2}$$

All values of λ are negative,

Hence by the Jacobian matrix method, Endemic Human Infected Equilibrium point is stable.

Theorem 2.3. Endemic Vector born infected Equilibrium, is stable whenever R_o>1.

Proof. we Proof this theorem by Jacobian matrix method

$$J = \begin{bmatrix} -\beta_H I_V - d_H & 0 & 0 & 0 & -\beta_H S_H \\ \beta_H I_V & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & -\beta_V I_H - d_V & 0 \\ 0 & \beta_V S_V & 0 & \beta_V I_H & -d_V \end{bmatrix}$$

We suppose that there is no human infective so $I_H \neq 0$

But there is vector infective, $I_V = 0$

$$J = \begin{bmatrix} -d_H & 0 & 0 & 0 & -\beta_H S_H \\ 0 & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & -\beta_V I_H - d_V & 0 \\ 0 & \beta_V S_V & 0 & \beta_V I_H & -d_V \end{bmatrix}$$

Eigenvalues obtained if and only if $|J - \lambda I|$=0 with J is the Jacobian matrix, λ is eigenvalues and I is the identity matrix.

$$(-d_H-\lambda)\{(-\beta_V\ I_H\ -d_V-\lambda)(-\gamma-d_H\ -\lambda)\ (-d_V\ -\lambda)+(-\beta_V\ S_V)\ (\beta_H\ S_H)(\beta_V\ I_H)$$
$$-(\beta_H\ S_H)(\beta_V\ S_V)\ \ (-\beta_V\ I_H\ -d_V-\lambda)\}\ =0$$

Then,

$$(-d_H-\lambda)\ (-d_V-\lambda)\{\lambda^2+\lambda(\beta_V\ I_H\ +d_V+\gamma+d_H)-(\beta_H\ S_H)(\beta_V\ S_V)+\beta_H I_H\gamma\ +d_V d_H+$$
$$\gamma d_V+\beta_H I_H d_H\}=0$$

The eigenvalue equations for the endemic state E_2,

$$(-d_H-\lambda)=0$$

$$(-d_V-\lambda)=0$$

$$\{\lambda^2+\lambda(\beta_V\ I_H\ +d_V+\gamma+d_H)-(\beta_H\ S_H)(\beta_V\ S_V)+\beta_H I_H\gamma\ +d_V d_H+\ \gamma d_V+\beta_H I_H d_H\}=0$$

Thus,

From these equations,

$$\lambda_1=\ -d_H$$

$$\lambda_2=\ -d_V\ ,$$

And,

$$\lambda_3=\frac{-(\gamma+\beta_V I_H+d_V+d_H)\pm\sqrt{(\gamma+\beta_V I_H+d_V+d_H)^2-4(\gamma\beta_H I_H+\beta_V I_H d_H+\gamma d_V+d_V d_H-\beta_H S_H\beta_V S_V)}}{2},$$

All value of $\lambda<0$,

Hence equilibrium points are stable by Jacobian matric methods.

Theorem 2.4. Endemic Equilibrium point is stable whenever R_o>1.

Proof. we Proof this theorem by Jacobian matrix method.

In endemic equilibrium, both $I_V,\ I_H\neq 0$.

$$J = \begin{bmatrix} -\beta_H I_V - d_H & 0 & 0 & 0 & -\beta_H S_H \\ \beta_H I_V & -\gamma - d_H & 0 & 0 & \beta_H S_H \\ 0 & \gamma & -d_H & 0 & 0 \\ 0 & -\beta_V S_V & 0 & -\beta_V I_H - d_V & 0 \\ 0 & \beta_V S_V & 0 & \beta_V I_H & -d_V \end{bmatrix}$$

Eigenvalues obtained if and only if $|J - \lambda I|$=0 with J is the Jacobian matrix, λ is eigenvalues and I is the identity matrix.

$$(-d_H - \lambda)[(-\beta_V I_H - d_V - \lambda)(-\gamma - d_H - \lambda)(-\beta_H I_V - d_H - \lambda)(-d_V - \lambda) +$$

$$(-\beta_H I_V - d_H - \lambda)(\beta_H S_H)\{(-\beta_V S_V)(\beta_V I_H) - (-\beta_V I_H - d_V - \lambda)(\beta_V S_V)\} +$$

$$(-\beta_H S_H)(\beta_H I_V)\{(-\beta_V S_V)(-\beta_V I_H) - (\beta_V S_V)(-\beta_V I_H - d_V - \lambda)\}] = 0$$

This gives,

$$(-d_H - \lambda)\{\lambda^4 + \lambda^3(\beta_H I_V + 2d_V + 2d_H + \gamma + \beta_V I_H) + \lambda^2(2\beta_H I_V d_V + \beta_H I_V \beta_V I_H + \gamma\beta_H I_V$$

$$+ \beta_H I_V d_H + 4d_H d_V + 2\beta_V I_V d_H + \gamma d_H + {d_H}^2 + \beta_V I_H d_V + 2d_V\gamma + {d_V}^2 + \gamma\beta_V I_H -$$

$$\beta_H S_H \beta_V S_V) + \lambda(\beta_H I_V d_V \beta_V I_H + \beta_H I_V {d_V}^2 + \gamma\beta_H I_H d_V + \beta_H I_V d_H d_V + \gamma\beta_H\beta_V I_H I_V +$$

$$\beta_H\beta_V I_H I_V d_H + 2\gamma d_V \beta_H I_H + \beta_H I_V d_H d_V + 2\beta_V I_H d_V d_H + 2d_H {d_V}^2 + 2\gamma d_H d_V + 2d_V {d_H}^2 +$$

$$\gamma\beta_V I_H d_H + {d_H}^2 \beta_V I_H + \gamma {d_V}^2 - \beta_H S_H \beta_V S_V d_V - 2\beta_H S_H \beta_V S_V \beta_H I_V + \beta_H S_H \beta_V S_V \beta_V I_V +$$

$$\beta_H S_H \beta_V S_V \beta_V I_H - \beta_H S_H \beta_V S_V d_H) + \gamma\beta_H I_V d_V \beta_V I_H + \gamma\beta_H I_V {d_V}^2 + \beta_H I_V \beta_V I_H d_H d_V +$$

$$\gamma\beta_H d_V I_H d_H + d_H {d_V}^2 \beta_H I_V + d_V {d_H}^2 \beta_V I_H + {d_H}^2 {d_V}^2 + \gamma d_H {d_V}^2 - \beta_H S_H \beta_V S_V \beta_V I_H \beta_H I_V -$$

$$2\beta_H S_H \beta_V S_V \beta_H I_V d_V - \beta_H S_H \beta_V S_V d_V d_H - \beta_H S_H \beta_V S_V \beta_H I_H \beta_V I_H)\} = 0$$

Thus,

The eigenvalue equation for the endemic state E_3,

$(-d_H - \lambda) = 0$

And,

$$\{\lambda^4 + \lambda^3(\beta_H I_V + 2d_V + 2d_H + \gamma + \beta_V I_H) + \lambda^2(2\beta_H I_V d_V + \beta_H I_V \beta_V I_H + \gamma\beta_H I_V + \beta_H I_V d_H + 4d_H d_V + 2\beta_V I_V d_H + \gamma d_H + {d_H}^2 + \beta_V I_H d_V + 2d_V\gamma + {d_V}^2 + \gamma\beta_V I_H - \beta_H S_H \beta_V S_V) + \lambda(\beta_H I_V d_V \beta_V I_H + \beta_H I_V {d_V}^2 + \gamma\beta_H I_H d_V + \beta_H I_V d_H d_V + \gamma\beta_H\beta_V I_H I_V + \beta_H\beta_V I_H I_V d_H + 2\gamma d_V \beta_H I_H + \beta_H I_V d_H d_V + 2\beta_V I_H d_V d_H + 2d_H {d_V}^2 + 2\gamma d_H d_V + 2d_V {d_H}^2 + \gamma\beta_V I_H d_H + {d_H}^2 \beta_V I_H + \gamma {d_V}^2 - \beta_H S_H \beta_V S_V d_V - 2\beta_H S_H \beta_V S_V \beta_H I_V + \beta_H S_H \beta_V S_V \beta_V I_V + \beta_H S_H \beta_V S_V \beta_V I_H - \beta_H S_H \beta_V S_V d_H) + \gamma\beta_H I_V d_V \beta_V I_H + \gamma\beta_H I_V {d_V}^2 + \beta_H I_V \beta_V I_H d_H d_V + \gamma\beta_H d_V I_H d_H + d_H {d_V}^2 \beta_H I_V + d_V {d_H}^2 \beta_V I_H + {d_H}^2 {d_V}^2 + \gamma d_H {d_V}^2 - \beta_H S_H \beta_V S_V \beta_V I_H \beta_H I_V - 2\beta_H S_H \beta_V S_V \beta_H I_V d_V - \beta_H S_H \beta_V S_V d_V d_H - \beta_H S_H \beta_V S_V \beta_H I_H \beta_V I_H)\} = 0$$

Further,

$$(-\lambda - d_H)(-\lambda - d_V)(\lambda - d_V - \gamma)\{\lambda^2 + \lambda(\beta_H I_V + 2d_H + \beta_V I_H) + (\beta_V I_H d_V - \gamma d_H + \beta_H\beta_V I_V I_H + \beta_H I_V d_H + 2\beta_V I_H d_H + {d_H}^2 + \gamma d_V + \beta_H S_H \beta_V S_V)\} = 0$$

And,

$(-\lambda - d_H) = 0$

$(-\lambda - d_V) = 0$

$(\lambda - d_V - \gamma) = 0$

$\{\lambda^2 + \lambda(\beta_H I_V + 2d_H + \beta_V I_H) + (\beta_V I_H d_V - \gamma d_H + \beta_H \beta_V I_V I_H + \beta_H I_V d_H + 2\beta_V I_H d_H + {d_H}^2 + \gamma d_V + \beta_H S_H \beta_V S_V)\} = 0$

This gives,

$\lambda_1 = -d_H$,

$\lambda_2 = -d_V$

$\lambda_3 = -d_V - \gamma$,

And,

$$\lambda_4 = \frac{-(\beta_H I_V + 2d_H + \beta_V I_H) \pm \sqrt{(\beta_H I_V + 2d_H + \beta_V I_H)^2 - 4(\beta_V I_H d_V - \gamma d_H + \beta_H \beta_V I_V I_H + \beta_H I_V} d_H + 2\beta_V I_H d_H + {d_H}^2 + \gamma d_V + \beta_H S_H \beta_V S_V)}{2}$$

Thus, Endemic Equilibrium point is stable.

CHAPTER 3

NUMERICAL SIMULATION

We do our numerical simulation in this chapter for understanding the dynamics of our disease. First stability of model (2.1) for disease free equilibrium is investigated. Data of dengue virus collected from (Garda world,2021).

It is reported that an incubation period of the patients whose are infected from any of the four DENV serotypes ranging from 3 to 14 days (Rathore ed al., 2011). the clinical information says that all the infected patients were observed fever and body aches, some of them had skin rashes and hemorrhagic manifestations in the form of gum bleeding and bleeding from the nose. The patient recovered from fever in 2 to 3 days or maximum 4 to 5 days, while the death would be because of severe fever during 8 to 9 days.

The various clinical problems during the different phases of dengue can be summarized as in Table 3.1.(Who, 2009).

Table 3.1: Febrile, critical and recovery phases in dengue

Phase	**description**
Febrile phase	Dehydration; high fever may cause neurological disturbances and febrile seizures in young children
Critical phase	Shock from plasma leakage; severe haemorrhage; organ impairment

Recovery phase	Hypervolaemia (only if intravenous fluid therapy has been excessive and/or has extended into this period)

3.1 Numerical Data

Dengue virus is common in Asian countries, so the data are collected from Pakistan where dengue fever outbreaks every year, because of changing season of monsoon.

There are confirmed 1,708 cases from February 18, 2021 till June 12, 2021.affected provinces are Sindh (926) cases and Baluchistan (772 cases).

Value of parameters in dengue transmission model (2.1) shown in Table 3.2.

Table 3.2: Value of parameters in dengue transmission system (2.1)

Parameters	**Description**	**values**
b_H	The birth rate	0.000351
d_H	The death rate	0.00031
β_H	The infection rate of human	0.22
γ	Recovery rate	0.32

to investigate the stability, we used MAPEL software.

Using the value of Table 3.1 the plot of infective individual related to our differential equations systems (2.1) is shown in below figure 3.1

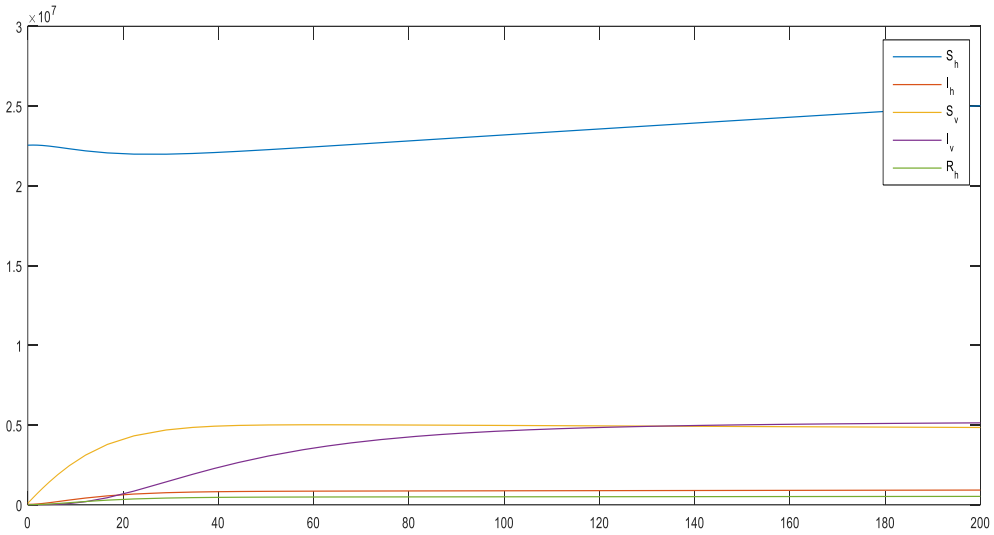

Figure 3.1: Dengue dynamic in Pakistan.

3.2 Numerical Simulation

With using Table 3.1, the basic reproduction value for dengue virus obtained as R_O=3.3563.

The reproduction ratio is more than one, which show that the endemic in future.to control this we need to control virus transmission by decreasing the rate of contact between suspectable and exposed classes.

At the present time, there is no special medication for dengue disease, but early detection and the appropriated medical care will decrease the fatality rates. A dengue vaccine would be another way to reduce the fatality rates. WHO reported the first dengue vaccine, called as

Dengvaxia (CYD-TDV). It was registered in several countries in late 2015 and early 2016 (Chanprasopchai ed al., 2018). Since dengue vaccine is not available in Pakistan yet so to control the transmission of this virus people must follow the precocious. Most important thing is, to gives awareness about dengue transmission and gives some instructions to peoples for improve the rate of recovery.

The ratio of dengue fever from male to female is 2:1, because in Pakistan most of woman stay at home and men goes for work so men are affected easily in day time.as dengue mosquitoes active in day time. Try to cover your body when goes out.

For recovery patients takes food in liquid form but it is not necessary to restrict fluids as the patient recovers. However, close monitoring is necessary to recognize heart failure or pulmonary edema during recovery especially in patients with comorbidities such as congenital heart disease, ischemic heart disease, hypertension, and diabetes (Rajapakse ed al., 2012).

CHAPTER 4

CONCLUSION

In this thesis, we analysis the transmission of dengue virus from human to mosquito and mosquito to human, for this purpose we use SIR model to understand the dynamic of dengue virus.

Firstly, we constructed the SIR model that showed in Figure 2.1, to show the transmission of dengue virus, which is very useful to understand the dynamic of inflectional disease, and then we find the equilibrium points, disease-free equilibrium and endemic equilibrium. And for endemic equilibrium we further find three more endemic equilibrium (human infected equilibrium, vector borne and both human and vector borne equilibrium) points.

Then we find the basic reproduction ratio $R0 = \frac{b_H N_H}{\beta_H + d_H} \sqrt{\frac{(\beta_H S_H)(\beta_V S_V)}{d_V(\gamma + d_H)}}$ for the model with use of next generation matrix method. And we found that if basic reproduction number is greater that one then disease will be outbreak and if basic reproduction number is less than one, the disease will die out.

For stability analysis, to show that each equilibrium points; disease-free and endemic equilibrium points are locally asymptotically stable we did theorems and used Jacobian matrix method.

In chapter 3 we did our numerical simulation to investigate the transmission of disease. We used the MAPLE software for numerical investigation of data which we take from Pakistan in June 2021.

To control the transmission of dengue virus in Pakistan government have to play a big rule, government arrange some survey in which they give the awareness about dengue virus, how its speared and what is first thing to do when people will be have dengue fever etc. because in

pandemic satiation there is no enough space in hospitals for patients. So, with these patients whose are not very much severe are able to cure their disease in home if they have proper knowledge and information. Always store clean water in cover buckets. Follow these precocious we will decrease the rate of infection. The future study will be base one the dengue virus transmission with more data and knowledge.

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