Mathematical Analysis of Epidemiological Model of Virus Transmission Dynamics in Perspective of Bangladesh

by

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Declaration

This is to certify that the thesis work entitled "**Mathematical Analysis of Epidemiological Model of Virus Transmission Dynamics in Perspective of Bangladesh**" has been carried out by Rafiqul Islam in the Department of Mathematics, Khulna University of Engineering & Technology, Khulna, Bangladesh. The above thesis work or any part of this work has not been submitted anywhere for the award of any degree or diploma.

Signature of Supervisor

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Approval

This is to certify that the thesis work submitted by **Rafiqul Islam** entitled " **Mathematical Analysis of Epidemiological Model of Virus Transmission Dynamics in Perspective of Bangladesh** " has been approved by the board of examiners for the partial fulfillment of the requirements for the degree of **Master of Philosophy** in the Department of Mathematics, Khulna University of Engineering & Technology, Khulna, Bangladesh in June 2018.

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Dedication

To

My Parents

Acknowledgment

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Abstract

Infectious diseases cause great suffering all over the world like Japan, USA, India, China, Ghana, Bangladesh etc. every year. The cause of infectious diseases are mainly virus and bacteria, they are becoming resistant against existing drugs. Therefore, infectious diseases become great concern in public health. But the spread of infectious disease can be controlled by some preventive steps. To get the control strategy, we have to know the transmission dynamics of the viruses. Mathematical modeling plays a vital role in understanding the transmission dynamics of the virus. In order to find out the control strategy of the infectious diseases, several mathematical models are available in the literatures. SIR and SEIR are the most well-known models regarding the transmission dynamics of the infectious diseases. In this thesis we have applied mathematical model namely SEIR model to realize the dynamics of Influenza A (H1N1) virus and Nipah Virus. By analyzing sensitivity of their disease free equilibrium and endemic equilibrium we have got two controlling strategies –decrease of contact rate and/or increase of recovery rate. Moreover, we have got herd immunity threshold for them by basic reproduction number regarding data of Bangladesh. Our result suggests that vaccinating 15.31% population could be controlled spread out of Influenza A (H1N1) virus and keeping away 77.25% (susceptible) population from close contact with infected people could be controlled outbreak of Nipah virus in Bangladesh at their initial outbreak respectively. Using the above control strategy we have proposed vaccine induced SEIR model for Influenza A (H1N1) virus and controlled induced SEIR model for Nipah virus. For Influenza A (H1N1) virus, we considered 15.31% of the susceptible population will be vaccinated whereas for Nipah virus, 77.25% of the susceptible population will not be in close contact (by awareness) with infected population. Numerical solutions of the proposed vaccine induced SEIR model as well as control induced SEIR model regarding data of Bangladesh reveal the control of the outbreak of both diseases respectively. Moreover numerical simulation have been performed to analyze the performance of SEIR models and proposed control induced SEIR models for both the viruses.

Publications

The following articles have been extracted from this thesis work:

1. **Rafiqul Islam**, Md. Haider Ali Biswas, A. R. M Jala Uddin Jamali, (2017), "Mathematical Analysis of Epidemiological Model of Influenza A (H1N1) Virus Transmission Dynamics in Perspective of Bangladesh", Journal of Bangladesh mathematical society. Vol.37, pp.39-50.
2. **Rafiqul Islam**, Md. Haider Ali Biswas, A. R. M Jala Uddin Jamali (2015) "Mathematical analysis and control of the transmission dynamics of H1N1 virus in perspective of Bangladesh", Proceedings of the 1st International Conference of Mathematics and its Application, December 23, 2015, Khulna University, Khulna, Bangladesh, pp.94-98.
3. **Rafiqul Islam**, Md. Haider Ali Biswas, A .R. M Jala Uddin Jamali (2015) ," Stability analysis of the transmission dynamics of H1N1 virus in perspective of Bangladesh", abstract proceedings of the 19th International conference of Mathematics, 18-20 December, 2015, BRAC University & Bangladesh Mathematical Society, Dhaka, Bangladesh.

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CHAPTER I

Introduction

1.1 Background

Chronic diseases, such as cancer and heart diseases have been receiving more attention in developed countries whereas, infectious diseases are still important and cause of great suffering and mortality in developing countries. These, remain a serious medical burden all around the world with 15 million deaths per year estimated to be directly related to infectious diseases (Jones et al., 2008). The successful control of the emerging diseases is not just linked to medical infrastructure but also on the capacity to recognize its transmission characteristics and apply optimal medical and logistic policies. Public health often asks information such as (Hethcote, 2000): how many people will be infected, how many require hospitalization, what is the maximum number of people ill at a given time and how long will the epidemic last. As a result, it is necessary an ever-increasing capacity for a rapid response**.** This information can be found by mathematical analysis of epidemiological model of transmission dynamics of infectious disease.

The emerging and reemerging diseases have led to a revived interest in infectious diseases. Mathematical models have become important tools in analyzing the spread and control of infectious diseases. The model formulation process clarifies assumptions, variables, and parameters; moreover, models provide conceptual results such as thresholds, basic reproduction numbers, contact numbers, and replacement numbers. Mathematical models and computer simulations are useful experimental tools for building and testing theories, assessing quantitative conjectures, answering specific questions, determining sensitivities to changes in parameter values, and estimating key parameters from data. Understanding the transmission characteristics of infectious diseases in communities, regions, and countries can lead to better approaches to decreasing the transmission of these diseases. Mathematical models are used in comparing, planning, implementing, evaluating, and optimizing various detection, prevention, therapy, and control programs. Epidemiology

modeling can contribute to the design and analysis of epidemiological surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecasts (Hethcote, 2000 and reference therein). Epidemiology is the study of the occurrence and distribution of health-related events, states, and processes in specified populations, including the study of the determinants influencing such processes, and the application of this knowledge to control relevant health problems (Heffernan, 2005). Epidemiology concerns itself with populations or groups of populations while clinical medicine deals with individuals (patients).Therefore epidemiology describes health and disease in terms of frequencies and distributions of determinants and conditions in a specific group of population.

1.2 Literature Review

Mathematical study of diseases and their spreading is at most just over three hundred years old. It all started in 1662 when John Graunt published his "Natural and Political Observations made upon the Bills of Mortality" (www.wikipedia / John_Graunt , 2014). In this book, he made observations on the death records and calculated risks of death concerning certain disease. A century later, in 1760, a smallpox model was proposed by Daniel Bernoulli and is considered as a first epidemiological mathematical model (Dietz and Heesterbeek, 2002). Modern mathematical biology begins with Hamer. He in 1906 first applied the Simple Mass Action Principle1for a deterministic epidemic model in discrete time. Ross's Simple Epidemic Model was published in 1911 (Bubniakov´a, 2007). Murray (2000) discussed that theoretical papers by Kermack and McKendrinck, between 1927 and 1933 about infectious disease models have a great influence in the development of mathematical epidemiology models. Most of the basic theory had been developed during that time, but the theoretical progress has been steady since then (Brauer and Castillo-Chavez, 2011). Mathematical models are being increasingly used to elucidate the transmission of several diseases. These models, are usually based on compartment models, studying them is crucial in gaining important knowledge of the underlying aspects of the infectious diseases spread out (Hethcote, 1994) and to evaluate the potential impact of control programs in reducing morbidity and mortality. After the Second World War, the strategy of public health has been focusing on the control and elimination of the organisms that cause the diseases. The appearance of new antibiotics and vaccines brought a positive

perspective of the diseases eradication. However, factors such as resistance to the medicine by the microorganisms, demographic evolution, accelerated urbanization, increased traveling and climate change, led to new diseases and the resurgence of old ones. In 1981, the human immunodeficiency virus (HIV) appears and since then, become as important sexually transmitted disease throughout the world (Hethcote, 2000). Furthermore, malaria, tuberculosis, dengue, yellow fever and influenza have re-emerged and, as a result of climate changes, have been spreading into new regions (Hethcote, 2000). Recent years, from specialist journals of medicine, biology and mathematics to the highest impact generalist journals, it has been seen an increasing trend in the representation of mathematical models in the epidemiological literature (Ferguson, 2006). The role of mathematical models in comparing, planning, implementing and evaluating various control programs has gained major importance to public health decision makers. This interest has been reinforced by the recent examples of Nipah Virus in 1998, SARS (Severe Acute Respiratory Syndrome) epidemic in 2003 and influenza A (H1N1) virus in 2009 etc. Lipsitch et al. (2003) analyzed the Transmission Dynamics and Control of SARS virus .In 2012, Yang and Hsu studied the Transmission Dynamics and Control of influenza A (H1N1) virus. They proposed a new SIR- based model for influenza epidemic (Yang and Hsu, 2012). Tan et al. (2013) modeled the initial transmission dynamics of influenza A (H1N1) in Gundong Providence, china in 2013. Okyere et al. (2013) reviewed epidemiological model of influenza A (H1N1) transmission in Ashanti region of Ghana, 2012. Satio et al. (2013) extended and verified SEIR model on the 2009 influenza pandemic in Japan. Islam et al. (2015) analyzed the stability of steady states for epidemiological model of Influenza A (H1N1) Virus transmission dynamics in perspective of Bangladesh. The readers are referred to (Nemarazhe, 2010) for nice review regarding mathematical model of epidemic diseases.

Though Mathematical models of biological phenomena especially epidemic diseases are amazing field of recent researches but very few research works have been carrying on in Bangladesh in this regards. The main obstacle is the lack of sufficient real data as well as information. The hospitals as well as related research institutes did not able to preserve all information regarding epidemic diseases. As far as well know two research institutes namely IEDCR and ICDDR, B is dedicated in public health especially IEDCR is concerned with infectious diseases. But their data bank regarding Influenza A (H1N1) and

Nipah virus is not sufficient. It is worthwhile to mention here that the international organization CDC, WHO etc. work with these two research institutes in collaboration.

Very few authors discussed mathematical model especially for Nipah virus in perspective of Bangladesh. Biswas first in 2012 and in 2014, considered SIR model for Nipah virus (NiV) (Biswas, 2012 and Biswas, 2014b). He discussed the model and control strategy of the deadly infections NiV regarding Bangladesh. Recently Sultana and Podder (2016) also considered SIR model for controlled strategy of NiV virus in which they considered variable size population and two control strategies: creating awareness and treatment are considered as controls. Mondal at el. (2017) considered SEIR model for Nipah virus too, to control the spread of NiV infection with vital dynamics (birth and death rates are not equal) by incorporating the quarantines of exposed individuals by availability of isolation centers and surveillance coverage.

1.3 Goal of the Thesis

The Influenza A (H1N1) virus and Nipah virus cause great suffering all over the world as well as in Bangladesh. To control or mitigate their sufferings, we need to understand their transmission dynamics as well as find out controlling strategies for them. By mathematical analysis of epidemiological model of infectious diseases their transmission dynamics can be understood and controlling strategies also can be found. The main objective of research works are pointed out bellow:

(i) The control strategy of transmission dynamics of Influenza A (H1N1) and Nipah virus in perspective of Bangladesh have been studied.

(ii) The sensitivity of Disease Free Equilibrium as well as Endemic Equilibrium for Influenza A (H1N1) virus and Nipah virus have been analyzed.

(iii) The numerical simulation of the control strategy for the transmission dynamic of Influenza A (H1N1) virus as well as Nipah virus in various compartments also have been studied.

(iv) By inducing control strategy into SEIR model, modified SEIR model have been reformulated for both Influenza A (H1N1) virus as well as Nipah virus. It is

worthwhile to mention here that our main attention to control the transmission dynamics of virus is into susceptible compartment only.

(v) Numerical experiments have been performed to justify and the validity of the proposed model and control strategy to prevent outbreak of Influenza A (H1N1) virus and Nipah virus.

1.4 Organization of the Thesis

In **chapter I,** the introduction of the study is presented which includes the background of the research, literature review and goal of the study and arrangement of the thesis as well**.** **Chapter II** covers some basic definitions and mathematical preliminaries which are related to this thesis**.** In **Chapter III,** SEIR epidemic model are discussed a bit elaborately. The Formulation of the model, stability of the disease free equilibrium and endemic equilibrium, estimation of basic reproduction number and herd immunity threshed, have been also discussed in this chapter. In **Chapter IV,** transmission dynamics of Influenza A (H1N1) virus are discussed according to the by SEIR model. After analyzing the, Sensitivity of disease free equilibrium and endemic equilibrium for Influenza A (H1N1) virus, herd immunity threshold for Influenza A (H1N1) virus, a modified vaccine induced SEIR model for Influenza A (H1N1) virus is proposed. Moreover, numerical simulations regarding data of Bangladesh have been carried out to justify the validity of the proposed model. Furthermore we have proposed control strategies to control outbreak of A (H1N1) virus. In **Chapter V,** transmission dynamics of Nipah virus are discussed by SEIR model too. Sensitivity of disease free equilibrium and endemic equilibrium for Nipah virus, herd immunity threshold of Nipah virus are discussed as well. The proposed control induced SEIR model for Nipah virus are presented in this chapter. Numerical simulation of the proposed control induced SEIR are presented. For the numerical simulation we have considered data of Bangladesh. Finally the concluding discussion has been presented in the Chapter VI.

CHAPTER II

Basics and Preliminaries

2.1 Introduction

This dissertation leads to a study of virus transmission dynamics by deterministic compartmental models in epidemiology. This chapter contains several necessary definitions and theorems regarding epidemiology. Moreover, some theorems and methods which are elementary prerequisites for epidemiological models are also elaborately discussed in this chapter.

2.2 Basic Reproduction Number

The basic reproduction number (ratio) R_0 is arguably the most important quantity in infectious disease epidemiology. It is among the quantities most urgently estimated for infectious diseases in outbreak situations and its value provide insight when designing control interventions for established infections. From a theoretical point of view R_0 plays a vital role in analysis of and consequent insight from, infectious disease models. There is hardly a paper on dynamic epidemiological models in the literature where R_0 does not play a role. R_0 is defined as the average number of new cases of an infection caused by one typical infected individual, in a population consisting of susceptible only. (Diekmann et al., 2013). R_0 is known as a threshold quantity (Driesschea and Watmough, 2002). The dynamics of Compartmental epidemiological models tend generally to be completely determined by threshold quantity R_0. There is a established basic property of R_0 (Driesschea and Watmough, 2002 and Hetecote, 2000 and the references therein) which is given below:

- There is a basic reproduction number R_0 such that
  (i) if $R_0 < 1$, the disease dies out.
  (ii) if $R_0 > 1$ there is an epidemic.

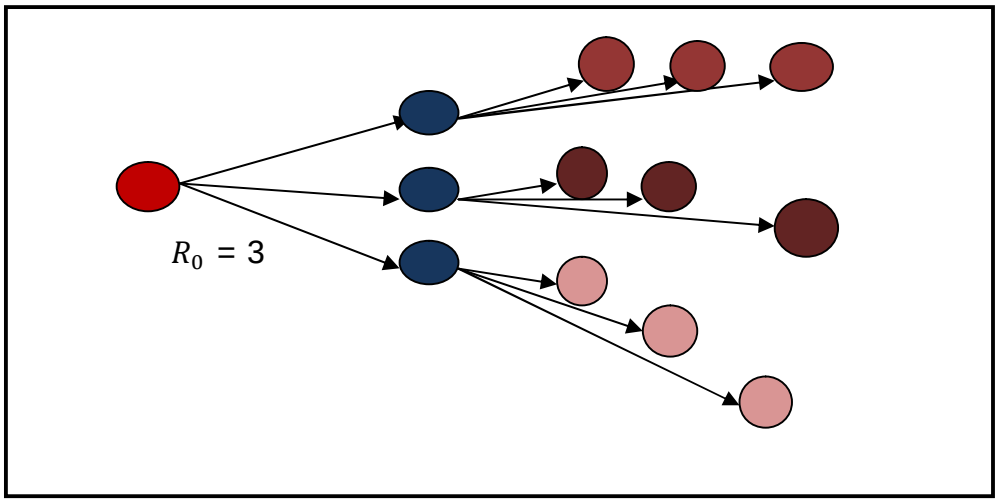

Figure 2.1: Schematic view of the transmission of an infection with $R_0 = 3$

The Figure 2.1 shows a pictorial view the transmission of an infection when basic reproduction number $R_0 = 3$ (Paul and Fine, 1993). The phenomenon, where the disease-free equilibrium (*DFE)* and an Endemic equilibrium (*EE)* exchange their stability at $R_0 = 1$, is known as *forward bifurcation* (or, transcritical bifurcation) A schematic description is given in Figure 2.2 (Islam, 2018 and Iannelli, 2005).

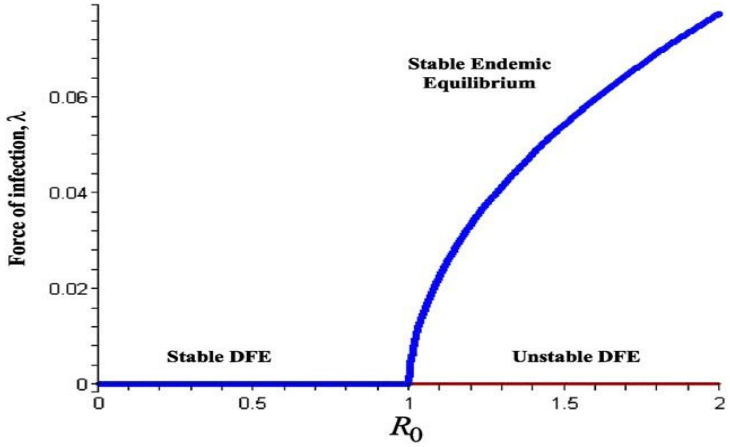

Figure 2.2: Forward bifurcation diagram

The forward bifurcation phenomenon was first noted by Kermack and Mc Kendrick (Kermack and McKendrick, 1927), and has been observed in many disease transmission models ever since (Heectcoke, 2000, and the references therein). In general, for models that exhibit forward bifurcation the requirement $R_0 < 1$ is necessary and sufficient for

disease elimination (i.e., the number of infective at steady state depends continuously on R_0). A number of studies have shown that while $R_0 < 1$ is necessary for disease elimination, but this requirement may not be sufficient.

2.3 Spectral Radius

The spectral radius $\rho(\mathrm{A})$ of a n-square matrix A is defined by $\rho(A) = max\{|\lambda_i| ; i = 1,2,\cdots,n\}$, where $\lambda_i , i = 1,2,\ldots n$ are the eigenvalue of A **(**Burden and Faires, 2002). For the complex eigen value (of the form $+i\beta$), we have $\lambda = \sqrt{(a^2 + \beta^2)}$. For the demonstration of the Spectral Radius the following Example 2.1 is considered.

Example 2.1: Find the Spectral Radius of the matrix $\mathrm{A} = \begin{vmatrix} 1 & 0 & 2 \\ 0 & 1 & -1 \\ -1 & 1 & 1 \end{vmatrix}$

The eigenvalues (λ) are the solutions of the characteristic equation of the matrix **A** i.e.

$$|A - \lambda I| = 0$$

$$\Rightarrow \quad \begin{vmatrix} 1-\lambda & 0 & 2 \\ 0 & 1-\lambda & -1 \\ -1 & 1 & 1-\lambda \end{vmatrix} = 0$$

$$\Rightarrow \quad (\lambda - 1)(\lambda^2 - 2\lambda + 4) = 0$$

$$\Rightarrow \quad \lambda = \{1, (1 + \sqrt{3}i)(1 - \sqrt{3}i)\}$$

Therefore, the spectral radius, $\rho(\mathbf{A}) = \max\{1, |1 + \sqrt{3}i|, |1 - \sqrt{3}i|\} = \max\{1, 2, 2\} = 2.$

2.4 Next Generation Matrix

A prosperous history in the literature addresses the derivation of R_0, or an equivalent threshold parameter, when more than one class of infective is involved **(**Heffernan et al., 2005 and reference therein). The next generation method, introduced by Diekmann et al. (1990) is a general method of deriving R_0, in such cases, encompassing any situation in which the population is divided into discrete, disjoint classes. The next generation operator can thus be used for models with underlying age structure or spatial structure, among other possibilities. For typical implementations, continuous variables within the population are approximated by a number of discrete classes. This approximation assumes that transmission probabilities between states are constant, or equivalently, that the distribution of residence times in each state is exponential. In the next generation method, R_0 is defined

as the spectral radius of the '*next generation matrix (operator*)'. The formation of the operator involves determining "*infected and non-infected*" compartments from the model. In the following subsection, we outline the steps needed to find the next generation operator in matrix notation (assuming only finitely many types), and then employ this method for a **susceptible–exposed– infectious–recovered (SEIR)** model and a model of malaria. For more details it is requested to see (Heffernan et al., 2005 and reference therein).

Let us assume that there are *n* compartments of which *m* are infected. We define the vector $\bar{x} = (x_i),\ i = 1, \ldots\ldots, n$, where x_i denotes the number or proportion of individuals in the compartment. Let $F_i(\bar{x})$ be the rate of appearance of new infections in compartment i and let $V_i(\bar{x}) = V_i^{-}(\bar{x}) - V_i^{+}(\bar{x})$, where V_i^{+} is the rate of transfer of individuals into compartment i by all other means and V_i^{-} is the rate of transfer of individuals out of the i^{th} compartment. The difference $F_i(\bar{x}) - V_i(\bar{x})$; gives the rate of change of x_i. It is noted that F_i should include only infections that are newly arising, but does not include terms which describe the transfer of infectious individuals from one infected compartment to another. Assuming that F_i and V_i meet the conditions outlined by (Diekmann et al., 1990 and Driessche and Watmough, 2002). Now we can form the next generation matrix (operator) FV^{-1} from matrices of partial derivatives of F_i and V_i. Specifically,

$$F = \frac{\partial F_i(x_0)}{\partial x_j}$$

and

$$V = \frac{\partial V_i(x_0)}{\partial x_j}$$

where $i, j = 1, , , m$ and where x_0 is the disease-free equilibrium. The entries of FV^{-1} give the rate at which infected individuals in x_j produce new infections in x_i, times the average length of time an individual spends in a single visit to compartment j. R_0 is given by the spectral radius (dominant eigenvalue) of the matrix FV^{-1} .

2.5 Herd Immunity Threshold

In order to prevent a disease from becoming endemic it is necessary to reduce the basic reproduction number R_0 (Brauer and Castillo-Chavez, 2011). It is noted that if immunity (i.e, successful vaccination) were delivered at random and if members of a population mixed at random, such that on average each individual contacted R_0 individuals in a manner sufficient to transmit the infection then rate of the infection would be reduced or increased will be depended upon the herd immunity threshold (H_T) values. The mathematical equation of HIT as follows (Paul et al., 2011):

$$H_T = 1\text{-}1/R_0$$

here R_0 is the basic reproduction number. That is the incidence of the infection would decline if the proportion immune exceeded H_T and the rate of the infection would not decline if the proportion immune does not exceeded H_T. The relation between herd immunity threshold and basic reproduction number is illustrated in Figure 2.3 (Paul and Fine, 1993).

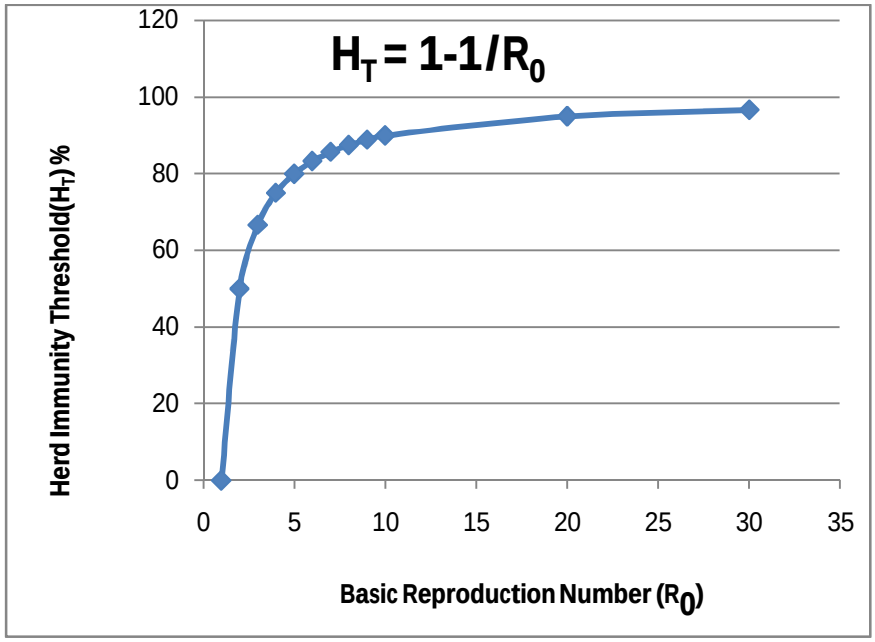

Figure 2.3: Relation between herd immunity threshold H_T and basic reproduction number R_0.

A large theoretical literature shows how to derive R_0 for different infections, often implying that the 1 - 1/ R_0 threshold be used as a target for immunization coverage and that

its achievement can lead to eradication of target infections (Anderson, 1991). A population is said to have herd immunity if a large enough fraction has been immunized to assure that the disease cannot become endemic. The only disease for which this has actually been achieved worldwide is smallpox for which R_0 is approximately 5, so that 80 percent immunization does provide herd immunity. For measles, epidemiological data in the United States indicate that R_0 for rural populations' ranges from 5.4 to 6.3, requiring vaccination of 81.5 percent to 84.1 percent of the population. In urban areas R_0 ranges from 8.3 to 13.0, requiring vaccination of 88.0 percent to 92.3 percent of the population. In Great Britain, R_0 ranges from 12.5 to 16.3, requiring vaccination of 92 percent to 94 percent of the population. The measles vaccine is not always effective, and vaccination campaigns are never able to reach everyone. As a result, herd immunity against measles has not been achieved (and probably never can be). Since smallpox is viewed as more serious and requires a lower percentage of the population be immunized, herd immunity was attainable for smallpox. In fact, smallpox has been eliminated; the last known case was in Somalia in 1977, and the virus is maintained now only in laboratories. The eradication of smallpox was actually more difficult than expected because high vaccination rates were achieved in some countries but not everywhere, and the disease persisted in some countries. The eradication of smallpox was possible only after an intensive campaign for worldwide vaccination (Brauer and Castillo-Chavez, 2011).

2.6 Equilibria of Linear and Non-linear Autonomous Systems

Consider the following equation

$$\dot{x} = f(x, t, \mu),\ x \in U \in R^n, t \in R^1, \mu \in V \in R^p \qquad (2.1)$$

where, U and V are open sets in R^n and R^p, respectively, and μ is a parameter. The over dot in (2.1) represents differentiation with respect to time (t). The equation (2.1) is an ordinary differential equation (ODE) and the right-hand side function, $f(x, t, \mu)$, is called a vector field. It is known that the ODEs which explicitly depend on time are called non-autonomous systems of differential equations, while those that are independent of time are called autonomous systems of differential equations (Niger, 2009). In this study we focus on autonomous system of differential equations. Consider the following general autonomous system

$$\dot{x} = f(x), x \in R^n \tag{2.2}$$

Definition: An equilibrium solution of Equation (2.2) is given by

$$\bar{x} = x \in R^n,$$

where $f(\bar{x}) = 0$ and $\bar{x}$ is called an equilibrium point (Niger, 2009).

Theorem 2.1 (Fundamental Existence-Uniqueness) (Niger, 2009 and there in) Let E be an open subset of R^n containing x_0 and assume that $f \in C^1(E)$. Then there exists an $a > 0$ such that the initial value problem (IVP)

$\dot{x} = f(x), x(0) = 0$

has a unique solution $x(t)$ on the interval $[-a, a]$.

2.7 Stability of Solutions

The following are standard definitions and theorems required to analyze the stability of equilibrium of an autonomous system. Let $\bar{x}(t)$ be any solution of Equation (2.2). Then, $\bar{x}(t)$ is *stable* if solutions starting "close" to $\bar{x}(t)$ at a given time remain close to $\bar{x}(t)$ for all later times. It is *asymptotically stable* if nearby solutions converge to $\bar{x}(t)$ as$t \to \infty$. These concepts are formally defined below:

Definition: The equilibriurn $\bar{x}(t)$ is said to be stable if given $\epsilon > 0$ there exists a $\delta(\epsilon) > 0$ such that, for any solution $y(t)$ of (2.2) satisfying $|\bar{x}(t_0) - \bar{y}(t_0)| < \delta$, $|\bar{x}(t) - \bar{y}(t)| < \epsilon$ for $t > t_0$ $t_0 \in R$ (Niger, 2009).

Definition: The equilibrium $\bar{x}(t)$ is said to be asymptotically stable if (i) it is stable and (ii) there exists a constant c > 0 such that, for any solution $y(t)$ of Equation (2.2) satisfying $|\bar{x}(t_0) - \bar{y}(t_0)| < c$, then $\lim_{t \to \infty} |\bar{x}(t) - \bar{y}(t)| = 0$ (Niger, 2009).

Definition: A solution which is not stable is said to be unstable.

Theorem 2.2 : Suppose all the eigenvalues of $Df(\bar{x})$ have negative real parts. Then the equilibrium solution $x = \bar{x}$ of the system (2.2) is locally asymptotically stable and unstable if at least one of the eigenvalues has positive real part (Niger, 2009).

2.8 Jacobian Matrix

A system of two (autonomous) differential equations has the form

$$\left.\begin{aligned}\frac{dx}{dt} &= f(x,y)\\ \frac{dy}{dt} &= g(x,y)\end{aligned}\right\} \tag{2.3}$$

The constant solutions to this system are called the equilibria. They satisfy the equation

$$f(x^*,y^*) = 0,\ g(x^*,y^*) = 0 \tag{2.4}$$

Recall from calculus that the linearization (or tangent plane approximation) of $f(x,y)$ at a point (x^*,y^*) is

$$f(x,y) \approx f(x^*,y^*) + f_x(x^*,y^*)(x-x^*) + f_y(x^*,y^*)(y-y^*) \tag{2.5}$$

where $f_x(x,y)$ is the partial derivative of f with respect to x This is also written $\frac{\partial f}{\partial x}$.

Linearization at an equilibrium point of a system of differential equations. By replacing in (2.3) with its linear approximations near(x^*,y^*), we obtain

$$\frac{dx}{dt} = f(x^*,y^*) + f_x(x^*,y^*)(x-x^*) + f_y(x^*,y^*)(y-y^*) \tag{2.6}$$

(x^*,y^*) is an equilibrium of (2.3), we have $f(x^*,y^*) = 0$, so we can drop that term on the right. The linear approximation of $g(x,y)$ near (x^*,y^*) gives a corresponding equation for $\frac{dy}{dt}$. Define new coordinates $u = x - x^*,\ v = y - y^*$. The (u,v) coordinates are coordinates measured relative to (x^*,y^*). In the (u,v) coordinates, the equilibrium is at the origin. Since x^* and y^* are constants, we have $\frac{du}{dt} = \frac{dx}{dt}$ and $\frac{dv}{dt} = \frac{dy}{dt}$.

Writing the linear approximations in terms of *u* and *v* we get

$$\left.\begin{aligned}\frac{du}{dt} &= f_x(x^*,y^*)u + f_y(x^*,y^*)v\\ \frac{dv}{dt} &= g_x(x^*,y^*)u + g_y(x^*,y^*)v\end{aligned}\right\} \tag{2.7}$$

This is the linearization of (2.3) at (x^*,y^*). By defining $\bar{u} = \begin{bmatrix}u\\v\end{bmatrix}$

we can write this in matrix form as follow:

$$\frac{d\bar{u}}{dt} = J\bar{u} \tag{2.8}$$

where

$$J = \begin{bmatrix} f_x(x^*, y^*) & f_y(x^*, y^*) \\ g_x(x^*, y^*) & g_y(x^*, y^*) \end{bmatrix} \tag{2.9}$$

and *J* is called *Jacobian Matrix*.

What does the linearization tell us about the original system? Equations (2.8) are the linear approximations to (2.3). But how good are the approximations? We have the following result:

- For differential equations: If the real parts of both eigenvalues are nonzero, then the behaviour of the system (2.3) near (x^*, y^*) is qualitatively the same as the behaviour of the linear approximation (2.8).
- The classification of the equilibrium in the nonlinear system is the same as the classification of the origin in the linearization **(**Weckesser, 2005).

To illustrate the concept of stability by Jacobian matrix we consider the following simple example:

Example 2.1: Consider the system of differential equations

$$\frac{dx}{dt} = 2x - y - x^2$$
$$\frac{dy}{dt} = x - 2y - y^2$$

So it has equilibria at (0, 0) and (1, 1) (set above equations to zero and solving it we get the equilibria points). Now we have the Jacobian Matrix

$$J = \begin{bmatrix} 2 - 2x & -1 \\ 1 & -2 - 2y \end{bmatrix}$$

So at (0,0) we get

$$J = \begin{bmatrix} 2 & -1 \\ 1 & -2 \end{bmatrix}$$

This matrix has eigenvalues: $\lambda_1 = -\sqrt{3}$ and $\lambda_2 = \sqrt{3}$, so the origin of the linearized system is a saddle point. Both eigenvalues are real and nonzero, so we conclude that the equilibrium $(0, 0)$, of the nonlinear system is also a saddle point.

Again at $(1, 1)$, by (2.9) we get

$$J = \begin{bmatrix} 0 & -1 \\ 1 & 0 \end{bmatrix}$$

This matrix has eigenvalues $\lambda = \pm i$, so the linearization results is a center. Because the real parts of the eigenvalues are zero, we cannot conclude that $(1,1)$, is actually a center in the nonlinear system. Trajectories near $(1,1)$, will rotate around $(1,1)$, but the linearization can not tell us if these trajectories actually form closed curves. The trajectories might, in fact, slowly spiral towards or away from $(1,1)$.

2.9 Routh–Hurwitz Criterion

Linear Stability of the systems of ordinary differential equations such as arise in interacting population models and reaction kinetics system is determined by the roots of a polynomial. The stability analysis we are concerned with involves linear system of the vector form:

$$\frac{d\bar{X}}{dt} = A\bar{X} \tag{2.10}$$

Where A is the matrix of the linearised nonlinear interaction/reaction terms: it is the Jacobian matrix about the steady state – the community matrix in ecological terms. Solutions are obtained by setting

$$\bar{X} = \bar{X}_0 e^{\lambda t} \tag{2.11}$$

in Equation (2.10), where $\bar{X}_0$ is a constant vector and the eigenvalues λ are the roots of the characteristics polynomial

$$|A - \lambda I| = 0 \tag{2.12}$$

where I is the identity matrix. The solution x = 0 is stable if all the roots λ of the characteristic polynomial lie in the left-hand complex plane; that is, Re $\lambda < 0$ for all roots λ. If this holds then $x \to 0$ exponentially as $t \to \infty$ and hence **x** = 0 is stable to small (linear) perturbations. If the system is of *n*th order, the characteristic polynomial can be taken in the general form:

$$P(\lambda) = \lambda_n + a_1\lambda_{n-1} + \cdots + a_n = 0$$

where the coefficients $a_i, i = 0,1,\ldots,n$ are all real. We tacitly assume $a_n \neq 0$, since otherwise $\lambda = 0$ is a solution, and the polynomial is then of order n - 1 with the equivalent $a_n \neq 0$. We require conditions on the $a_i, i = 0,1,\ldots,n$ such that the zeros of $P(\lambda)$ have Re $\lambda < 0$. The necessary and sufficient conditions for this to hold are the

Routh–Hurwitz conditions (Murray, 2002). There are various equivalent forms of these, one of which is, together with $a_n > 0$,

$$D_1 = a_1 > 0,\ D_2 = \begin{vmatrix} a_1 & a_2 \\ 1 & a_1 \end{vmatrix} > 0,\ D_2 = \begin{vmatrix} a_1 & a_3 & a_5 \\ 1 & a_2 & a_4 \\ 0 & a_1 & a_3 \end{vmatrix} > 0$$

$$D_k = \begin{vmatrix} a_1 & a_3 & \cdot & \cdot & \cdot & \cdot \\ 1 & a_2 & a_4 & \cdot & \cdot & \cdot \\ 0 & a_1 & a_3 & \cdot & \cdot & \cdot \\ 0 & 1 & a_2 & \vdots & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ 0 & 0 & \cdot & \cdot & \cdot & a_k \end{vmatrix} > 0,\ k = 1,2, \ldots \ldots \ldots, n$$

These conditions are derived, using complex variable methods, in standard texts on the theory of dynamical systems (see, for example, (Willems, 1970)). As an example, for the cubic equation

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

the conditions for $Re\lambda < 0$ are as follow:

$a_1 > 0,\ \ a_3 > 0$; $a_1 a_2 - a_3 > 0$

2.10 Incidence

Definition: The horizontal incidence is the infection rate of susceptible individuals through their contacts with invectives (Hethcote, 2000).

Definition: Vertical incidence is the infection rate of newborns by their mothers. It is sometimes included in epidemiology models by assuming that a fixed fraction of the newborns is infected vertically (Hethcote, 2000).

CHAPTER III

SEIR Compartmental Model

3.1 Introduction

Mathematical models have become crucial tools in analyzing the dynamics and control of infectious diseases. Deterministic and stochastic are the general forms of mathematical models in epidemiology for infectious diseases. The deterministic models divide the total population of considered region into subclasses, and an ODE with independent variable time is formulated for each subclasses. The second ones employ randomness, with variables being described by probability distribution. The state variables are determined using parameters and initial conditions. The main focus in this chapter will be the deterministic SEIR model.

In this chapter, we present the formulation of an epidemiological model for Dynamics and Control of Virus by considering uniform mixing. We analyze various properties of the solutions of the model. We find the disease free equilibrium (DFE) and endemic equilibrium (EE) and stability of them, also control strategy of Virus spread out.

Epidemic models are based on splitting the whole population into a small number of compartments. In each compartment containing individuals have identical characteristic with respect to disease state. Here are some of the main compartments that a deterministic model contains.

■ **Passive Immune (M):** is composed by newborns that are temporary passively immune due to antibodies transferred by their mothers.

■ **Susceptible (S):** is the class of individuals who are the susceptible to infection; this can include the passively immune once they lose their immunity or, more many, any newborn infant whose mother has never been infected and therefore has not passed on any immunity.

■ **Exposed or Latent (E):** is a compartment whose individuals despite of infected do not show obvious sign of infection and do not transmit pathogen to others.

■ **Recovered or Resistant (R):** is a compartment whose individuals have been recovered from the disease.

According to the characteristics of the particular disease being modelled and the purpose of the model, the compartments are chose to include in the model. The exposed compartment is sometimes ignored, when the latent period is considered very short. Besides, the compartment of the recovered individuals cannot always be considered disease free, there are diseases where the host has never became resistant. Acronyms for epidemiology models are often based on the flow patterns between the compartments such as SI, SIR, SIS, SEIR MSEIR, MSEIRS, SEIRS SIRS, SEI, SEIS.

3.2 The SEIR Model

In this section we deal with the dynamics and control strategy of infectious disease to SEIR model. We proposed vaccination, escaping contact of infected people and environmental favour to recovery of infected people as a control strategy analyzing dynamics of virus by SEIR model. We base our analysis on an SEIR (Susceptible, Exposed, Infectious and Recovered) for the human infectious disease model. Since Vaccine can resist infectious disease and avoiding contact of infected people also helpful not to be infected. We can analyze the spread out and stability of infectious disease and we also can find out herd immunity threshold of infectious diseases by mathematical model of infectious diseases. In this regard, the SEIR type epidemic model is very crucial to study the dynamics of infectious diseases and to find out herd immunity threshold of infectious diseases. In this model, the targeted population is divided into four classes: Susceptible(S), Exposed (E), Infectious (E) and Recovered (Immune) (R) (Anderson and May, 1991). An SEIR model can represent several infectious of human for instance measles, pox, dengue and influenza. Here we focus on a generic SEIR model with particular influenza. Immunity is not heredity, therefore all people are considered susceptible by birth. The disease is also supposed to transmit to the individuals by horizontal incidence, that is, susceptible individuals become infected when they come in contact of infected individuals. This contact may be direct (touching, biting) or indirect (cough, air, sneeze). The infectious

population can either die or recovered completely and all those recovered (recovered from infection and vaccinated) are considered immune.

3.3 Model Formulation

Let $S(t), E(t), I(t)$ and $R(t)$ be the number of individuals in S, E, I and R compartments respectively at time t. The total population at time t is represented by $S(t) + E(t) + I(t) + R(t) = N(t)$. Several assumptions have been made to formulate the equation of the model. It is assumed that the population mix uniformly with no restriction of age, mobility or other social factors. For comprehensive analysis of the model, we assume birth rates and death rates occur at equal rates and the all new born are susceptible (no inherited immunity). We use symbol μ to represent average death rates as well as average birth rates (as equal). Therefore individuals are born into the susceptible class with rate μN (N denotes total number of population). An individual in the population must be considered as having an equal probability as every other individual of contacting the disease with rate β (which is considered transmission rate or contact or infection rate of the disease). Therefore, an infected makes contact and able to transmit the disease with βN others per unit time and the fraction of contacts of by an infected with a susceptible is $\frac{S}{N}$ .The number of new infectious in unit time per infective then is $\beta N(\frac{S}{N})$, giving the new infectious (or those leaving the susceptible category) as $\beta N\left(\frac{S}{N}\right) I = \beta SI$ (Brauer and Castillo-Chavez , 2011). Dynamics of virus, across the compartments of SEIR model is represented by the following diagram (Lenhart and Workman , 2007; Brauer and Castillo-Chavez, 2011 and Biswas, 2014a).

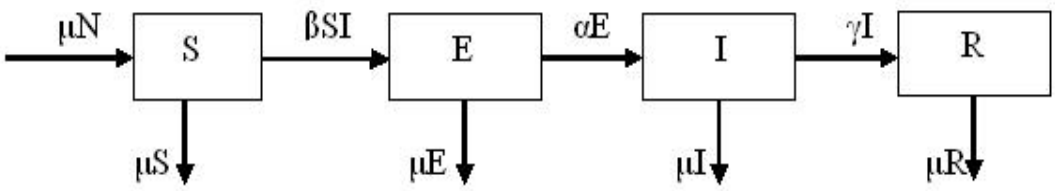

Figure 3.1: Schematic diagram of virus dynamics through SEIR model.

The parameter α is the rate at which exposed individuals become infectious (αE individuals leave exposed class and enter into infectious class per unit time) and γ is the rate at which infected individuals become recovered (αR individuals leave Infected class and enter into Recovered class per unit time). The following system of Ordinary Differential Equations (ODEs) is used to represent this SEIR model (Bubniakov´a , 2007).

$$\left.\begin{aligned} \frac{dS}{dt} &= \mu N - \mu S - \beta SI \\ \frac{dE}{dt} &= \beta SI - (\mu + \alpha)E \\ \frac{dI}{dt} &= \alpha E - (\mu + \gamma)I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned}\right\} \tag{3.1}$$

With initial conditions

$$S(t) = S_0 \geq 0, E(t) = E_0 \geq 0, I(t) = I_0 \geq 0, R(t) = R_0 \geq 0 \tag{3.2}$$

3.4 Equilibrium State

We know that the populations become a Disease Free Equilibrium (DFE) or Endemic Equilibrium (EE) according to the value of R_0. From the biological point of view it can be shown that if

$$\big(S(0), E(0), I(0), R(0)\big) \in \{(S, E, I, R) \in \{0, N\}^4, S \geq 0, E \geq 0, I \geq 0, R \geq 0, S + E + I + R = N\}$$

then $R_0 \leq 1$ implies

$$\lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = DFE$$

And $R_0 > 1, I(0) > 0$ implies

$$\lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = FE$$

Now set S, E, I, R as a proportion of the total population N, i.e.

$$s(t) = \frac{S(t)}{N}$$

$$e(t) = \frac{E(t)}{N}$$

$$i(t) = \frac{I(t)}{N}$$

$$r(t) = \frac{R(t)}{N}$$

and

$$r(t) = 1 - s(t) - e(t) - i(t)$$

then above four ODEs (Eqn. (3.1)) are reduced to three ODEs as follows:

$$\left.\begin{aligned} \frac{ds}{dt} &= \mu - (\mu + \beta i)s \\ \frac{de}{dt} &= \beta si - (\mu + \alpha)e \\ \frac{di}{dt} &= \alpha e - (\gamma + \mu)i \end{aligned}\right\} \quad (3.3)$$

The equilibrium points can be found by solving the equations which are obtained by setting the right side of equations in the model (3.3) to zero.

Then the above equations become as follows:

$$\mu - (\mu + \beta i)s = 0 \quad (3.4)$$

$$\beta si - (\mu + \alpha e = 0 \quad (3.5)$$

$$\alpha e - (\gamma + \mu)i = 0 \quad (3.6)$$

If i =0, then from equation (3.4) we get s = 1 and from equation (3.5), we get e = 0. Hence the Disease Free Equilibrium $(s, e, i) = (s_0, e_0, i_0)$is as follows:

$$(s_0, e_0, i_0) = (1,0,0)$$

Now we have to find the Endemic Equilibrium $(s, e, i) = (s^*, e^*, i^*)$. From equation (3.6) we have

$$e^* = \frac{\gamma+\mu}{\alpha} i \quad (3.6a)$$

Substituting the value of e in equation (3.5) we get,

$$s^* = \frac{(\mu+\alpha)(\gamma+\mu)}{\beta\alpha} \quad (3.5a)$$

Putting the value of s in equation (3.4) we get,

$$i^* = \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{\mu}{\beta} \quad (3.4a)$$

Therefore, Endemic Equilibrium(s^*, e^*, i^*) is given as follows:

$$(s^*, e^*, i^*) = \left(\frac{(\mu+\alpha)(\gamma+\mu)}{\beta\alpha}, \frac{\gamma+\mu}{\alpha}\left\{\frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{\mu}{\beta}\right\}, \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{\mu}{\beta}\right) \quad (3.7)$$

3.5 Estimation of Basic Reproduction Number (R_0)

It is stated earlier that the Basic Reproduction Number R_0, for our compartmental SEIR model, is estimated by next generation matrix method. In the Next generation operator (matrix) method, R_0 is defined as the spectral radius of next generation operator (matrix)

FV^{-1} where F be the matrix formed by new infection individuals in the compartments and V be the matrix formed by the net infected individuals in the compartments. For the formation of next generation operator, we have to determine two types of compartments – infected and non-infected. Let us assume that there are *n* compartments of which *m* are infected. We define the vector $\bar{x} = x_i$, where $i = 1,2,\cdots\cdots n$.We can form the next generation matrix (operator) FV^{-1} from the partial derivatives of F_i and V_i. Specifically if x_0 is the Disease Free Equilibrium then

$$F = \frac{\partial F_i(x_0)}{\partial(x_j)},$$

$$V = \frac{\partial V_i(x_0)}{\partial(x_j)}; i, j = 1,2,\cdots\cdots m.$$

where $F_i(\bar{x})$ be the new infections in compartment *i* and $V_i(\bar{x}) = V_i^-(\bar{x}) - V_i^+(\bar{x})$, here $V_i^+(\bar{x})$ is the transfer individuals into compartment *i* and $V_i^-(\bar{x})$ is the transfer of individuals out of *i* compartment.

In our SEIR model the numbers of infected compartments are two – exposed compartment and infected compartment. So from the SEIR model (as we have two types of compartments – infected and non-infected)

$$F_1(\bar{x}) = \beta IS$$

$$F_2(\bar{x}) = 0$$

$$V_1(\bar{x}) = (\mu + \alpha)E$$

$$V_2(\bar{x}) = (\mu + \alpha)I - \alpha E$$

Hence,

$$F = \frac{\partial F_i(x_i)}{\partial(x_j)} = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}$$

and

$$V = \frac{\partial V_i(x_i)}{\partial(x_j)} = \begin{pmatrix} \mu + \alpha & 0 \\ -\alpha & \mu + \gamma \end{pmatrix}$$

Now,

$$V^{-1} = \frac{1}{|V|}\begin{pmatrix} \mu + \gamma & \alpha \\ 0 & \mu + \alpha \end{pmatrix}$$

$$= \frac{1}{(\mu+\alpha)(\mu+\gamma)}\begin{pmatrix} \mu + \gamma & 0 \\ \alpha & \mu + \alpha \end{pmatrix}$$

$$= \begin{pmatrix} \frac{1}{(\mu+\alpha)} & 0 \\ \frac{\alpha}{(\mu+\alpha)(\mu+\gamma)} & \frac{1}{(\mu+\gamma)} \end{pmatrix}$$

Therefore,

$$FV^{-1} = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{(\mu+\alpha)} & 0 \\ \frac{\alpha}{(\mu+\alpha)(\mu+\gamma)} & \frac{1}{(\mu+\gamma)} \end{pmatrix}$$

$$=> FV^{-1} = \begin{pmatrix} \frac{\alpha\beta}{(\mu+\alpha)(\mu+\gamma)} & \frac{\beta}{(\mu+\gamma)} \\ 0 & 0 \end{pmatrix}$$

Therefore, the Spectral radius of FV^{-1} is known as basic reproduction number (R_0).
The characteristics equation $|FV^{-1} - \lambda I| = 0$ where I is the Identity matrix

$$=> \begin{vmatrix} \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma)} - \lambda & \frac{\beta\alpha}{(\mu+\gamma)} \\ 0 & 0 - \lambda \end{vmatrix} = 0$$

$$=> \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma)}\lambda - \lambda^2 = 0$$

$$\lambda = \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma)}, 0$$

Therefore the Spectral radius of FV^{-1} is the dominant eigenvalue of FV^{-1} is

$$\lambda = \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma)}$$

Hence the basic Reproduction number is as follows:

$$R_0 = \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma)} \quad (3.8)$$

3.6 Stability Analysis

The stability analysis of the disease-free and endemic equilibria are governed by the eigenvalues of the Jacobian matrix of system (3.3), evaluated at these points. For stability, we require that $Re(\lambda) < 0$, where λ is an eigenvalue of the linearized system evaluated at the respective steady states (Murray, 2002).

3.6.1 Stability of Disease free Equilibrium

Theorem 3.1: *The disease-free equilibrium* (s_0, e_0, i_0) *is locally asymptotically stable when* $R_0 < 1$.

Proof: The stability of the disease-free is determined by the following Jacobian matrix of system (3.3)

$$J = \begin{pmatrix} -(\mu + \beta i) & 0 & -\beta s \\ \beta i & -(\mu + \alpha) & \beta s \\ 0 & \alpha & -(\mu + \gamma) \end{pmatrix} \tag{3.9}$$

So the Jacobian at the Disease Free Equilibrium i.e at $(s_0, e_0, i_0) = (1,0,0)$ is

$$J_{DFE} = \begin{pmatrix} -\mu & 0 & -\beta \\ 0 & -(\mu + \alpha) & \beta \\ 0 & \alpha & -(\mu + \gamma) \end{pmatrix}$$

Now the characteristic equation of J_{DFE} is

$$|J_{DFE} - \lambda I| = 0$$

$$\Rightarrow \begin{vmatrix} -\mu - \lambda & 0 & -\beta \\ 0 & -(\mu + \alpha) - \lambda & \beta \\ 0 & \alpha & -(\mu + \gamma) - \lambda \end{vmatrix} = 0$$

$$\Rightarrow \lambda^3 + (3\mu + \alpha + \gamma)\lambda^2 + \{(\mu + \gamma)(\mu + \alpha) - \alpha\beta + \mu(2\mu + \gamma + \alpha)\}\lambda + \{\mu(\mu + \gamma)(\mu + \alpha) - \alpha\beta\} = 0$$

It can be written as a polynomial of λ

$$F(\lambda) = \lambda^3 + b_1\lambda + b_2\lambda + b_3 = 0 \tag{3.10}$$

where,

$$b_1 = (3\mu + \gamma + \alpha)$$

$$b_2 = \{(\mu + \gamma)(\mu + \alpha) - \alpha\beta + \mu(2\mu + \gamma + \alpha)\}$$

$$b_3 = \{\mu(\mu + \gamma)(\mu + \alpha) - \alpha\beta\}$$

By the Routh-Hurwitz condition (Murray, 2002) we require that $b_3 > 0$, $D_1 = b_1 > 0$ and $D_2 = b_1 b_2 - b_3 > 0$, for the eigenvalues (that is, roots of (3.10)) to have negative real parts.

Using R_0 (from equation (3.8)) in b_2 and b_3 we get

$$b_2 = \beta\alpha\left(1 - \frac{1}{R_0}\right) + \mu(2\mu + \gamma + \alpha)$$

and

$$b_3 = \mu\alpha\beta\left(1 - \frac{1}{R_0}\right)$$

.

Therefore,

$$\begin{aligned} & b_1 b_2 - b_3 \\ &= (3\mu + \alpha + \gamma)\{\beta\alpha\left(\frac{1}{R_0} - 1\right) + \mu(2\mu + \alpha + \gamma)\} - \mu\beta\alpha\left(\frac{1}{R_0} - 1\right) \\ &= (3\mu + \alpha + \gamma)\beta\alpha\left(\frac{1}{R_0} - 1\right) + (3\mu + \alpha + \gamma)\mu(2\mu + \alpha + \gamma) - \mu\beta\alpha\left(\frac{1}{R_0} - 1\right) \\ &= \left(\frac{1}{R_0} - 1\right)\beta\alpha\{(3\mu + \alpha + \gamma) - \mu\} + (3\mu + \alpha + \gamma)\mu(2\mu + \alpha + \gamma) \\ &= \left(\frac{1}{R_0} - 1\right)\beta\alpha(2\mu + \alpha + \gamma) + (3\mu + \alpha + \gamma)\mu(2\mu + \alpha + \gamma) \end{aligned}$$

Here $D_1 = b_1 > 0$ is always true. Now $b_3 > 0$ and $b_1 b_2 - b_3 > 0$ will be true if and only if $R_0 < 1$. So Disease Free Equilibrium is stable if $R_0 < 1$ otherwise it is unstable.

3.6.2 Stability of Endemic Equilibrium

Theorem 3.2 *The Endemic equilibrium* (s^*, e^*, i^*) *is locally asymptotically stable when* $R_0 > 1$.

Proof:

By the help of equation (3.8) we have rewrite the Endemic Equilibrium equation (3.7) as follow

$$(s^*, e^*, i^*) = \left(\frac{1}{R_0}, \frac{\mu(R_0 - 1)}{R_0(\mu + \alpha)}, \frac{\mu(R_0 - 1)}{\beta}\right) \tag{3.11}$$

The local stability of the endemic equilibrium is determined by the following Jacobian matrix of system (3.3)

$$J = \begin{pmatrix} -(\mu + \beta i) & 0 & -\beta s \\ \beta i & -(\mu + \alpha) & \beta s \\ 0 & \alpha & -(\mu + \gamma) \end{pmatrix}$$

Using the value of (s^*, e^*, i^*) form equation (3.7) in above Jacobian matrix, we have the Jacobian at the endemic equilibrium point as follow:

$$=> J_{EE} = \begin{pmatrix} -\{\mu + \beta\frac{\mu(R_0-1)}{\beta}\} & 0 & -\beta\frac{1}{R_0} \\ \beta\frac{\mu(R_0-1)}{\beta} & -(\mu+\alpha) & \beta\frac{1}{R_0} \\ 0 & \alpha & -(\mu+\gamma) \end{pmatrix}$$

$$=> J_{EE} = \begin{pmatrix} -\mu - \mu R_0 + \mu & 0 & -\beta\frac{1}{R_0} \\ \mu(R_0-1) & -(\mu+\alpha) & \beta\frac{1}{R_0} \\ 0 & \alpha & -(\mu+\gamma) \end{pmatrix}$$

Using the value of R_0 form equation (3.8) in $(2,3)^{th}$ position, we get

$$=> J_{EE} = \begin{pmatrix} -\mu R_0 & 0 & -\beta\frac{1}{R_0} \\ \mu(R_0-1) & -(\mu+\alpha) & \frac{(\mu+\gamma)(\mu+\alpha)}{\alpha} \\ 0 & \alpha & -(\mu+\gamma) \end{pmatrix}$$

Now the characteristic equation of J_{EE} is

$$|J_{EE} - \lambda I| = 0$$

$$=> \begin{vmatrix} -(\mu R_0 + \lambda) & 0 & -\beta\frac{1}{R_0} \\ \mu(R_0-1) & -(\lambda+\mu+\alpha) & \frac{(\mu+\gamma)(\mu+\alpha)}{\alpha} \\ 0 & \alpha & -(\lambda+\mu+\gamma) \end{vmatrix} = 0$$

$$=> \lambda^3 + (2\mu + \gamma + \alpha + \mu R_0)\lambda^2 + \{(2\mu+\gamma+\alpha)\mu R_0\}\lambda + \mu(R_0-1)\{\mu^2 + \mu(\alpha + \gamma) + \alpha\gamma)\} = 0$$

It can be written as a polynomial of λ

$$F(\lambda) = \lambda^3 + p_1\lambda + p_2\lambda + p_3 = 0 \qquad (3.12)$$

where,

$$p_1 = 2\mu + \gamma + \alpha + \mu R_0$$
$$p_2 = \mu R_0(2\mu + \gamma + \alpha)$$
$$p_3 = \mu(R_0 - 1)\{\mu^2 + \mu(\alpha+\gamma) + \alpha\gamma)\}$$

By the Routh-Hurwitz condition (Murray, 2002), we require that $p_3 > 0$, $D_1 = p_1 > 0$ and $D_2 = p_1p_2 - p_3 > 0$, for the eigenvalues (that is, roots of (3.15)) to have negative real

parts, which means Stable equilibrium (Heffernan et al., 2005). It is obvious that $p_3 > 0$, $p_1 > 0$ for $R_0 > 1$.

Now, for third condition

$$D_2 = p_1 p_2 - p_3 > 0$$

We have,

$$p_1 p_2 - p_3 =$$
$$\{2\mu + \gamma + \alpha + \mu R_0\}\{\mu R_0(2\mu + \gamma + \alpha)\} - \mu(R_0 - 1)\{\mu^2 + \mu(\alpha + \gamma) + \alpha\gamma)$$
$$= \mu[R_0\{(3\mu + \gamma + \alpha)(\alpha + \gamma) + \mu^2(3 + 2R_0) + \gamma^2\} + \mu^2 + \mu(\alpha + \gamma) + \alpha\gamma]$$

which is greater than zero for all parameters value along with $R_0 > 1$. Therefore, by Routh-Hurwitz condition the endemic equilibrium is stable for $R_0 > 1$.

3.7 Herd Immunity Threshold

To control outbreak of the disease, the population have to be immunized. The percentage of the population that needs to be immunized for controlling the outbreak is the Herd Immunity Threshold (HIT) (Paul. et al., 2011 and Hethcote, 2000). We have proposed the HIT (H_T) as the sole immunization strategy. It protects directly the immunized individuals from infection and also provides protection of being susceptible individuals. To evaluate HIT, we use the equation, given in (Paul F. et al., 2011 and Hethcote, 2000), as follows:

$$H_T = 1 - \frac{1}{R_0} \tag{3.13}$$

3.8 Summary

In this chapter, a new deterministic model for the dynamics of influenza virus transmission is formulated and extensively analyzed to get control strategies. We can summarize the results obtained in this chapter as follows:

(i) The model (3.1) has a locally-asymptotically stable disease free equilibrium (*DFE*) (Theorem (3.1)) when the basic reproduction number R_0, which is derived by next generation method, is less than unity.

(ii) When the basic reproductive number R_0, is greater than one, there exists a unique endemic equilibrium (*EE*) of the model (3.1) (Theorem 3.2).

(iii) When outbreak occurs herd immunity threshold can be found by vaccinating the percentage of people obtain by the equation (3.13).

CHAPTER IV

Dynamics and Control Strategies of Influenza A (H1N1) Virus

4.1 Introduction

Influenza A (H1N1) is highly infectious and fatal disease which was first identified in Bangladesh at 2009. In this chapter, well-known SEIR model is considered to find the flow (transition) of people through different compartments regarding influenza A (H1N1) virus in perspective of Bangladesh. By using next generation matrix method, the Basic Reproduction Number (R_0) for pandemic influenza A (H1N1) virus is determined regarding the data of pandemic influenza A (H1N1) virus of Bangladesh (www.wikipedia/Demographics, 2015; ICDDR,B/news, 2015; and IEDCR/influenza, 2015). By the help of this R_0, the decision making parameter Herd Immunity Threshold (H_T), by which we can find the vaccinated number of population, is determined in perspective of Bangladesh. We have reformulated SEIR model by introducing vaccine. Moreover the disease free and endemic equilibrium of SEIR model is studied extensively according to the data considered. Also numerical solutions of the system of Ordinary Differential Equations (ODEs) of SEIR and vaccine induced SEIR models are done regarding data of Bangladesh and other simulated data. According to the numerical solutions, the trends of various aspects of the susceptible, exposed, infectious and recovered of the population regarding Bangladesh are discussed.

4.2 Mathematical Model

In analyzing the spread and control of infectious diseases, mathematical models have become important tools. For studying the dynamics of the pandemic novel influenza A (H1N1) virus, the model considered here is the Susceptible (S (t))-Exposed (E (t))-Infectious (I (t))-Recovered (R (t)) compartment model or in brief SEIR model (Lenhart and Workman, 2007; Brauer and Castillo-Chavez, 2011 and Biswas, 2014a).

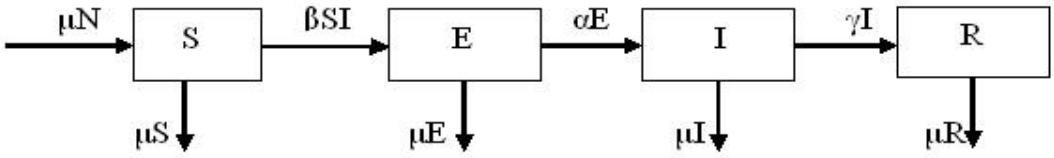

Figure 4.1: Transmission dynamics of Influenza A (H1N1) virus through SEIR epidemic model.

SEIR model is similar to SIR model (Kermack and McKendrick, 1927), except that before the individuals become infectious, of course he/she exposed to the environment. In this model, for the transmission dynamics of pandemic influenza (Figure 4.1), individuals are classified as Susceptible (S), Exposed (E), Infective (I) and Removed (R). Here symbol μ denotes average death rates as well as average birth rates (as equal), β be the transmission coefficient, α be the exposed coefficient and γ be the recovery coefficient.

The following system of Ordinary Differential Equations (ODEs) is used to represent this SEIR model (Bubniakov´a, 2007).

$$\left.\begin{aligned} \frac{dS}{dt} &= \mu N - \mu S - \beta SI \\ \frac{dE}{dt} &= \beta SI - (\mu + \alpha)E \\ \frac{dI}{dt} &= \alpha E - (\mu + \gamma)I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned}\right\} \tag{4.1}$$

with initial conditions,

$$S(t) = S_0 \geq 0, E(t) = E_0 \geq 0, I(t) = I_0 \geq 0, R(t) = R_0 \geq 0 \tag{4.2}$$

Here, $\alpha > 0, \beta > 0, \gamma > 0, \mu > 0$ and $S + E + I + R = N$

4.3 Equilibrium State

We know that the populations become Disease Free Equilibrium (DFE) or Endemic Equilibrium (EE) according to the value of R_0. From the biological point of view it can be shown that if

$$\big(S(0), E(0), I(0), R(0)\big) \in \{(S, E, I, R) \in \{0, N\}^4, S \geq 0, E \geq 0, I \geq 0, R \geq 0, S + E + I + R = N\}$$

then $R_0 \leq 1$ implies

$$\lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = DFE$$

and $R_0 > 1, I(0) > 0$ implies

$$\lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = FE$$

Now set S, E, I, R as a proportion of the total population N, as follow:

$$s(t) = \frac{S(t)}{N}$$
$$e(t) = \frac{E(t)}{N}$$
$$i(t) = \frac{I(t)}{N}$$
$$r(t) = \frac{R(t)}{N}$$

and

$$r(t) = 1 - s(t) - e(t) - i(t)$$

Then above four ODEs (4.1) are reduced to three ODEs as follows:

$$\left.\begin{aligned} \frac{ds}{dt} &= \mu - (\mu + \beta i)s \\ \frac{de}{dt} &= \beta si - (\mu + \alpha)e \\ \frac{di}{dt} &= \alpha e - (\gamma + \mu)i \end{aligned}\right\} \quad (4.3)$$

It is known that for the steady state Equilibrium

$$\frac{dK}{dt} = 0, \exists K \in \{s, e, i\}$$

Then the above equations become as follows:

$$\mu - (\mu + \beta i)s = 0 \quad (4.4)$$
$$\beta si - (\mu + \alpha)e = 0 \quad (4.5)$$
$$\alpha e - (\gamma + \mu)i = 0 \quad (4.6)$$

If $i = 0$, then from equation (4.4) we get $s = 1$ and from equation (4.5), we get $e = 0$. Hence the Disease Free Equilibrium $(s, e, i) = (s_0, e_0, i_0)$ is as follows:

$$(s_0, e_0, i_0) = (1,0,0)$$

Now we have to find the Endemic equilibrium$(s, e, i) = (s^*, e^*, i^*)$. From equation (4.6) we have

$$e^* = \frac{\gamma+\mu}{\alpha} i \tag{4.6a}$$

Substituting the value of e in equation (4.5) we get,

$$s^* = \frac{(\mu+\alpha)(\gamma+\mu)}{\beta\alpha} \tag{4.5a}$$

Putting the value of s in equation (4.4) we get,

$$i^* = \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{\mu}{\beta} \tag{4.4a}$$

Therefore, Endemic equilibrium is given as follows:

$$(s^*, e^*, i^*) = \left(\frac{(\mu+\alpha)(\gamma+\mu)}{\beta\alpha}, \frac{\gamma+\mu}{\alpha}\left\{\frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{\mu}{\beta}\right\}, \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{\mu}{\beta}\right) \tag{4.7}$$

4.4 Parameter Estimation for Influenza A (H1N1) Virus

In the previous chapter, by Next Generation Matrix Method, we have calculated Basic Reproduction Number (R_0) which is as follows:

$$R_0 = \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma)} \tag{4.8}$$

Now we will estimate other parameters with the help of following equations. It is known that the expected duration of infectious is the inverse of the removal rate (Hethcote, 2000 and www.ibmathsresources, 2014). So according to the definition (Hethcote, 2000 and www.wikipedia/Transmission, 2015) the removal rate (γ), Exposed rate (α) and transmission rate (β) are given as follows:

$$\gamma = \frac{1}{\text{mean infectious period}} \tag{4.9}$$

$$\alpha = \frac{1}{\text{mean latancy period}} \tag{4.10}$$

$$\beta = \frac{\text{effective contact}}{\text{total contact}} \tag{4.11}$$

4.5 Stability Analysis

Here we have just pointed out two important theorems related to stability analysis. It is noted that the proof of the theorems are represented in the Chapter III.

Theorem 4.1: The Disease Fee Equilibrium is locally stable if $R_0 < 1$, otherwise unstable.

Theorem 4.2: Endemic Equilibrium locally stable if $R_0 > 1$, otherwise unstable.

4.6 Herd Immunity Threshold for Influenza A(H1N1) Virus

We know that to control outbreak of the disease, the population has to be immunized. The percentage of the population that needs to be immunized for controlling the outbreak is the Herd Immunity Threshold (HIT) (Paul et al., 2011 and Hethcote, 2000). We have considered the HIT (H_T) as the sole immunization strategy. It protects directly the immunized individuals from infection and also provides protection of being susceptible individuals. The mathematical formula of HIT is as follows (Paul et al., 2011 and Hethcote, 2000):

$$H_T = 1 - \frac{1}{R_0} \tag{4.12}$$

4.7 Model Analysis

In order to evaluate the Herd Immunity Threshold as well as numerical analysis of the SEIR models, we have considered the information about influenza A (H1N1) virus as defined in (Gu, et al., 2011) and real numerical data in perspective of Bangladesh (www.wikipedia/Demographics, 2015; ICDDR,B/news-and, 2015 and IEDCR/ influenza, 2015). It is known that the latency period of A (H1N1) is 1 to 4 days and infectious period is one day prior to onset of symptoms to 7 days after symptom onset (Eccles, 2005 and Gu, et al., 2011). So the mean latency period of A (H1N1) is 2 days and mean infectious period is 3.5 days. Therefore by using equations (4.9) and (4.10), we have, $\gamma = 0.2857$, $\alpha = 0.5$ According to (ICDDR,B/news, 2015), from 18 June 2009 to 20 July 2009, 84 (assumed total contact) individuals had been tested and among them 24 (effective contact)

individuals were found influenza positive. Again for month July 2015, 258 (assumed total contact) individuals has been tested and among them 100 (effective contact) individuals were found influenza positive (IEDCR/ influenza, 2015). Therefore, we have

$$\beta_1 = \frac{24}{84},$$

$$\beta_2 = \frac{100}{258}$$

and $$\beta = \frac{\beta_1 + \beta_2}{2} = 0.3374$$

We have the death rate of population of Bangladesh is $\mu = 0.00001425$ per day and the total population of Bangladesh is N = 16,09,95,642 (www.wikipedia/Demographics, 2015 and www.populationpyramid/Bangladesh, 2015) . Using the value of β, α, γ and μ in Equation (4.8), we get $R_0 = 1.1809$. So Disease Free Equilibrium (s_0, e_0, i_0) = (1, 0, 0) is unstable as $R_0 = 1.1809 > 1$. From equations (4.7) and (4.8), we have Endemic Equilibrium

$$(s^*, e^*, i^*) = \left(\frac{1}{R_0}, \frac{\mu(R_0-1)}{R_0(\mu+\alpha)}, \frac{\mu(R_0-1)}{\beta}\right)$$

$$= (0.8486, 0.000004733, 0.000008283)$$

which is stable as $R_0 = 1.1809 > 1$. Moreover, from Equation (4.12), the Herd Immunity Threshold is found to be

$$H_T = 1 - \frac{1}{R_0} = 0.1531$$

Now the sensitivity will be analyzed for both Disease Free Equilibrium and Endemic Equilibrium points of the SIER model in perspective of Bangladesh. For these experiments, the death rate as well as the expose rate is considered to be fixed. On the other hand the transmission rate as well as the recovery rate is changed as shown in the Table 4.1. At first, the values of recovery rate (0.2857) are kept unchanged whereas the corresponding values of transmission rates are changed. Secondly keeping the value of transmission rate (0.3374) unchanged, we have varied the value of recovery rate. Finally we have calculated the R_0 values for each changed values of the removal rate (γ) as well as (β). The experimental results are displayed in the Table 4.1.

Table 4. 1 Sensitivity analysis of the Disease Free Equilibrium state and Endemic Equilibrium state for Influenza A(H1N1) virus

μ	β	α	γ	R_0	Nature of DFE state	Nature of EE state
0.00001425	*0.35*	0.5	0.2857	1.224965242	Unstable	Stable
0.00001425	**0.3374**	**0.5**	**0.2857**	**1.180866493**	**Unstable**	**Stable**
0.00001425	*0.30*	0.5	0.2857	1.049970207	Unstable	Stable
0.00001425	**0.2857223929**	0.5	0.2857	1	**Critical value**	**Critical value**
0.00001425	***0.27***	0.5	0.2857	0.944973186	Stable	Unstable
0.00001425	***0.25***	0.5	0.2857	0.874975173	Stable	Unstable
0.00001425	0.3374	0.5	*0.3*	1.124581197	Unstable	Stable
0.00001425	0.3374	0.5	**0.3373761344**	1	**Critical value**	**Critical value**
0.00001425	0.3374	0.5	***0.35***	0.963933281	Stable	Unstable
0.00001425	0.3374	0.5	***0.5***	0.674761538	Stable	Unstable
0.00001425	0.3374	0.5	*0.125*	2.69881541	Unstable	Stable

It is observed in the Table 4.1 that when the transmission rate (β) decreases (from 0.3374→ to 0.25) with unchanged of other parameters, then the Disease Free Equilibrium approaches unstable to stable and Endemic Equilibrium becomes unstable from stable as the value of R_0 decrease from 1.180866493 to less than one. Again keeping unchanged the value of all parameters except the value of recovery rate, we have observed that for the increasing of the value of recovery rate (from 0.2857 → to 0.5), the Disease Free Equilibrium again approaches unstable to stable as well as Endemic Equilibrium becomes unstable from stable as the value of R_0 decreases to less than one. That is, if transmission rate will decrease or recovery rate will increase then the Disease Free Equilibrium may become stable as well as Endemic Equilibrium approaches to unstable in perspective of Bangladesh. This implies that the disease will not spread out. What happen if we will consider the reverse strategy? From the experimental results, given in the Table 4.1, it is observed that when the transmission rate (β) increased or recovery rate (γ) decreased then R_0 becomes much greater than one and consequence the Disease Free Equilibrium

found to be unstable as well as Endemic Equilibrium becomes stable from unstable as well. Which implies disease will spread out. Now we will find the critical value of Transmission rate if other parameters are remained unchanged and critical value of recovery rate when other parameters are kept fix in perspective of Bangladesh. To find the critical value of Transmission rate (β*) we set R_0= 1(by keeping fix other parameters), in equation (4.8) we have **β*=0.2857223929**. Now to find the critical value of Recovery rate (γ*), we again set R_0= 1(by keeping fix other parameters), in equation (4.8) we have **γ*= 0.3373761344.** The experimental results regarding β* and γ* are also displayed in the table. Therefore, if all parameters are unchanged except the transmission rate, the disease will be spread out or controlled if the transmission rate be greater or less than the critical value of β*= **0.2857223929** respectively. Similarly, if all parameters are unchanged but only the recovery rate are varied, the disease will be spread out or controlled if the recovery rate be less or greater than the critical value of **γ*= 0.3373761344** respectively.

Again it is revealed that $R_0 > 1$ implies that the state of disease free equilibrium is unstable and the state of endemic equilibrium is stable. In the case of unstable state of disease free equilibrium and stable state of endemic equilibrium, diseases will spread out. To control of the spread out of disease, we need to calculate Herd Immunity Threshold. We have calculated the Herd Immunity Threshold, in perspective of Bangladesh (2015), which was 0.1531.

Moreover, we have performed numerical simulation of the model by using initial numerical solution in perspective of Bangladesh. For the initial numerical solution of the SIER model (equation (4.3) and equation $r(t) = 1 - s(t) - e(t) - i(t)$), in perspective of Bangladesh on March 2015, we have, $S(0) = 160995620$, $E(0) = 12$ (assumed), $I(0) = 10, R(0) = 0$ (IEDCR, 2015 and www.populationpyramid/Bangladesh, 2015). So dividing each of the terms by the total population of Bangladesh, N =160995642 (www.populationpyramid/Bangladesh, 2015), we have

$s(0) = 0.999998634$

$e(0) = 0.00000007453$

$i(0) = 0.00000006211$

and $r(0) = 0.$

We have also calculated the value of the parameters earlier that are given below:

$\mu = 0.00001425$

$\alpha = 0.5$

$\beta = 0.3374$

and $\gamma = 0.2857$

The numerical simulated of the model in perspective to Bangladesh are displayed in the Figure 4.2. It is observed in the Figure 4.2 that the initial outbreak occurs in Bangladesh and proportion of infectious has minimal effect on susceptible. One of the cause of this insignificance effect on susceptible is that the value of initial infectious $i(0) = 0.00000006211$ is too small.

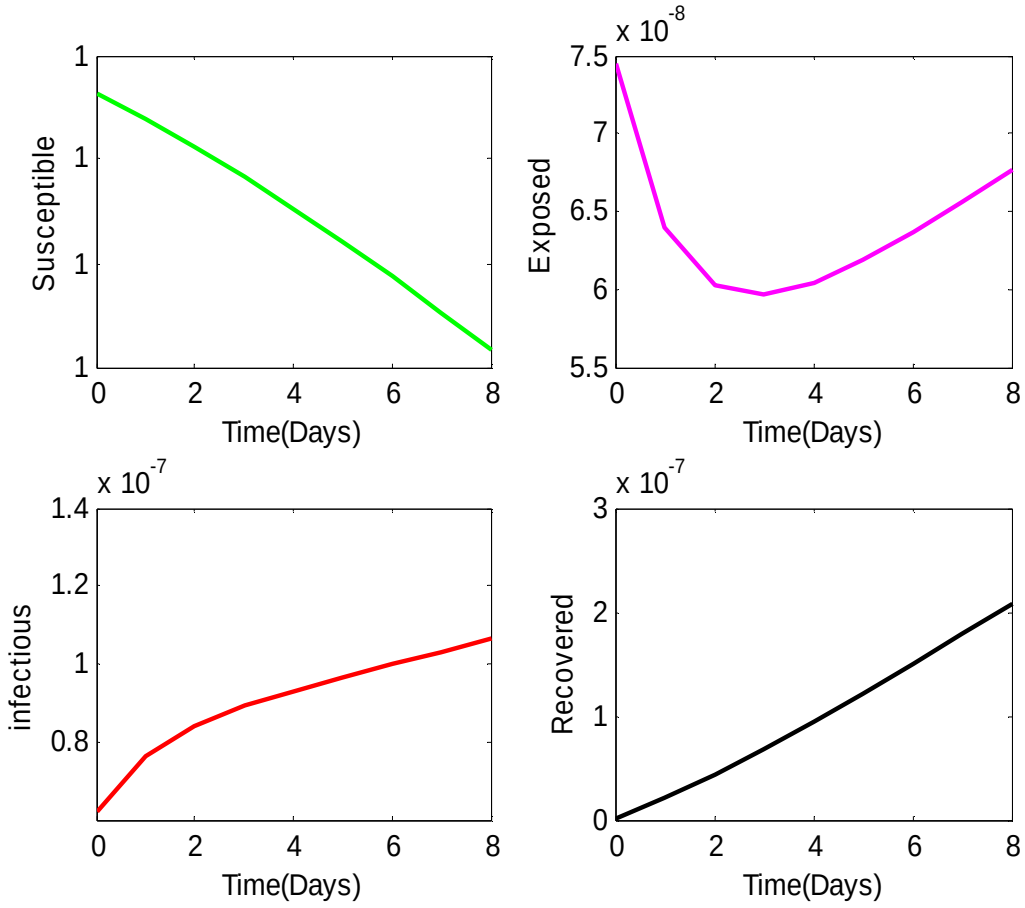

Figure 4.2: Dynamics of Influenza A (H1N1) through various compartments at the initial outbreak in Bangladesh

Now we have considered hospital based real data about influenza A(H1N1) from march 2015 to December 2015 of Bangladesh. The number of influenza infected people from

March 2015 to December 2015 obtained from (IEDCR/influenza, 2015) are displayed in the bar diagram (in Figure 4.3)

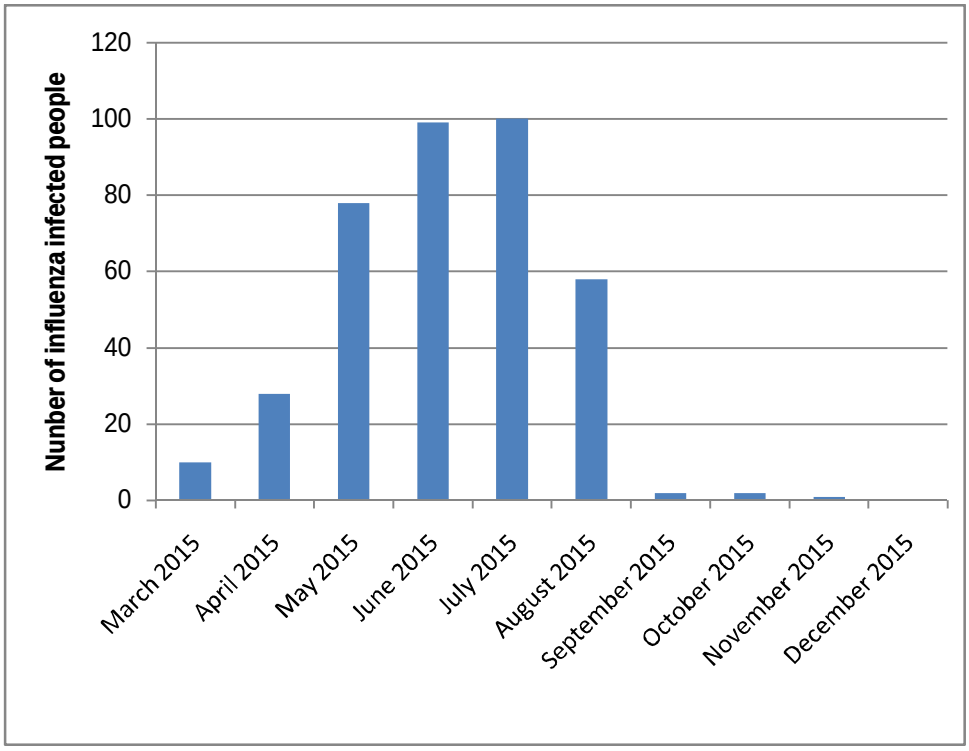

Figure 4.3: Real scenario of Influenza A(H1N1) outbreak in Bangladesh from March 2015 to December 2015

It is observed in the Figure 4.3 that initial outbreak, for influenza A (H1N1), is occurred in Bangladesh, which is also agreed with our numerical solution as well as with the decision based on Basic Reproduction Number.

4.8 Analysis of the Model after Proposed Vaccination

To control initial outbreak (to get Herd Immunity Threshold), we have to vaccinate 0.1531 portion of the population. Introducing $0.1513 = \omega$ portion vaccinated population, our proposed model's schematic diagram for dynamics of influenza A (H1N1) is shown in the Figure 4.4.

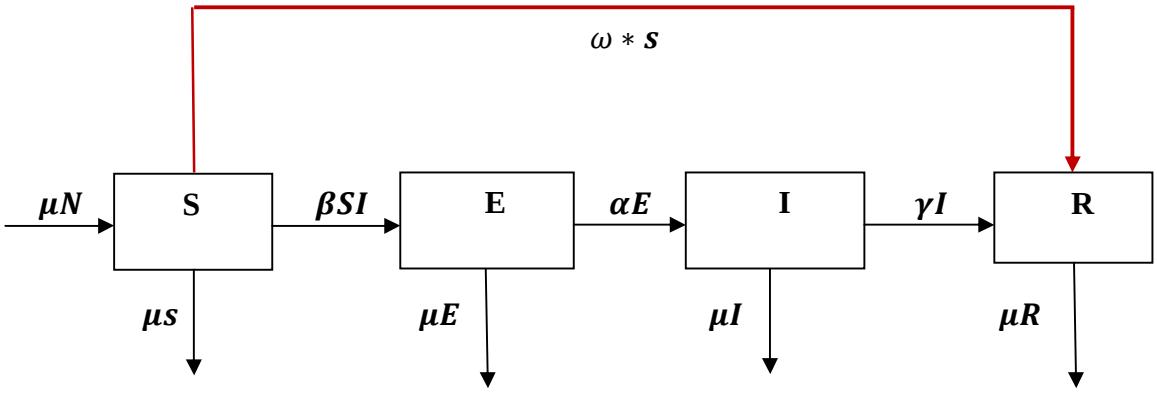

Figure 4.4: Transmission dynamics of Influenza A (H1N1) virus through SEIR epidemic model with vaccination.

After vaccination the modified system of Ordinary Differential Equations (ODEs) for vaccine induced SEIR model is given below:

$$\left.\begin{aligned} \frac{dS}{dt} &= \mu N - \mu S - \beta SI - \omega * S \\ \frac{dE}{dt} &= \beta SI - (\mu + \alpha)E \\ \frac{dI}{dt} &= \alpha E - (\mu + \gamma)I \\ \frac{dR}{dt} &= \gamma I - \mu R + \omega * S \end{aligned}\right\} \quad (4.13)$$

with initial conditions,

$$S(t) = S_0 \geq 0, E(t) = E_0 \geq 0, I(t) = I_0 \geq 0, R(t) = R_0 \geq 0 \quad (4.14)$$

Here, $\alpha > 0, \beta > 0, \gamma > 0, \mu > 0$ and $S + E + I + R = N$

Now setting S, E, I, R as a proportion of the total population N as well as follows:

$$s(t) = \frac{S(t)}{N}$$

$$e(t) = \frac{E(t)}{N}$$

$$i(t) = \frac{I(t)}{N}$$

$$r(t) = \frac{R(t)}{N}$$

and

$$r(t) = 1 - s(t) - e(t) - i(t) + \omega * s.$$

Then above four ODEs (4.13) are reduced to three ODEs as follows:

$$\left.\begin{aligned} \frac{ds}{dt} &= \mu - (\mu + \beta i)s - \omega * s \\ \frac{de}{dt} &= \beta si - (\mu + \alpha)e \\ \frac{di}{dt} &= \alpha e - (\gamma + \mu)i \end{aligned}\right\} \tag{4.14}$$

Now solving equation (4.14) with $r(t) = 1 - s(t) - e(t) - i(t) + \omega * s$ at initial outbreak we have obtained the values of $S(t)$, $E(t)$, $I(t)$ and $R(t)$ which are shown in the Figure 4.5.

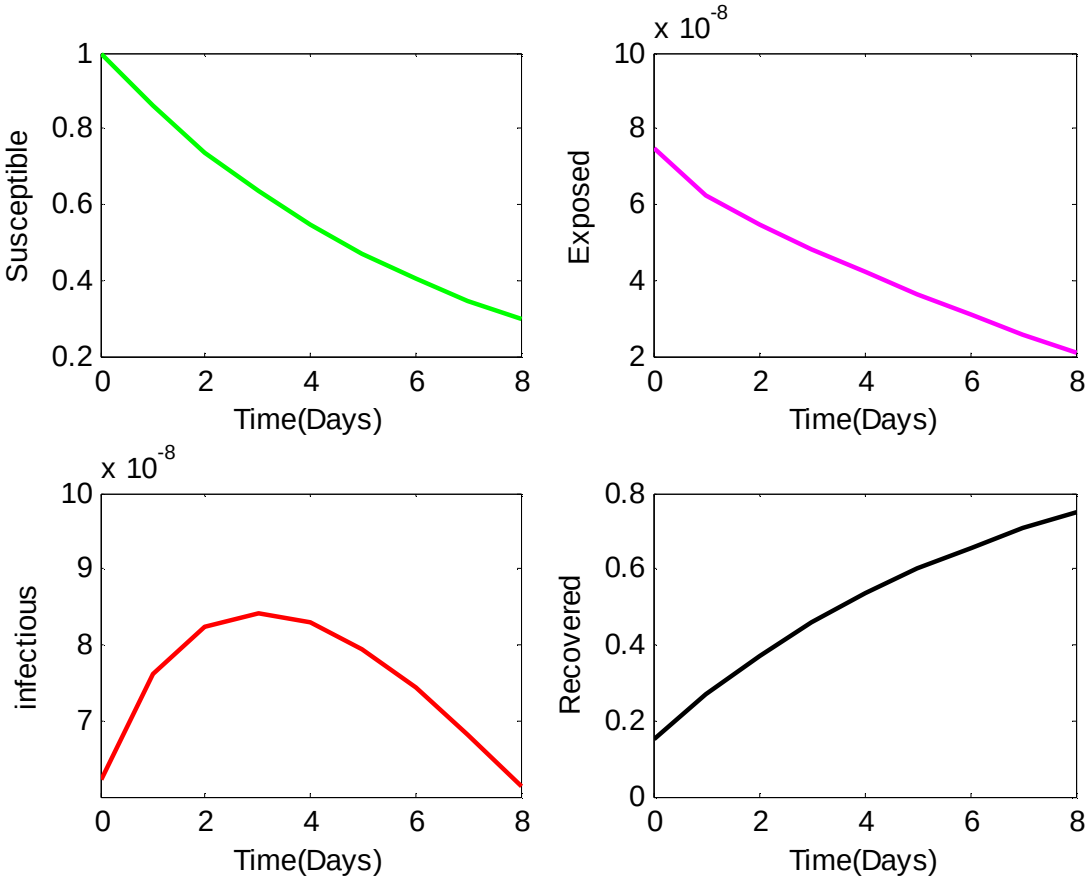

Figure 4.5: Dynamics of Influenza A (H1N1) through various compartments at the initial outbreak in Bangladesh after vaccine induced

It is observed in the Figure 4.5 that the portion of exposed population considerably decreased and recovered populations' portions dramatically increased, though the portion of infective population initial increase but after few days it is rapidly decreased. Which means that outbreak will come to control (disease will not spread out).

4.9 Comparison of SEIR and Proposed Vaccine Induced SEIR Model Regarding Numerical Simulation

Now we have carried out farther experiments to analyze the effect of proposed vaccine induced SEIR model. What happen if the proportion of infective is significantly large, keeping unchanged the value of the parameters? For this experiment, we varied the proportion of initial infective to $i(0) = 0.02$ as well as proportion of initial susceptible $s(0) = 0.89$ and initial susceptible to $e(0) = 0.01$ around the endemic equilibrium point for a period 10 days. The simulated results are shown in Figures 4.6- 4.9.

From Figure 4.6, we have observed that the proportion of susceptible decreases very slowly according to the SEIR (without vaccine) model but the proportion of susceptible decreases very rapidly according to the vaccine induced SEIR model within 10 days.

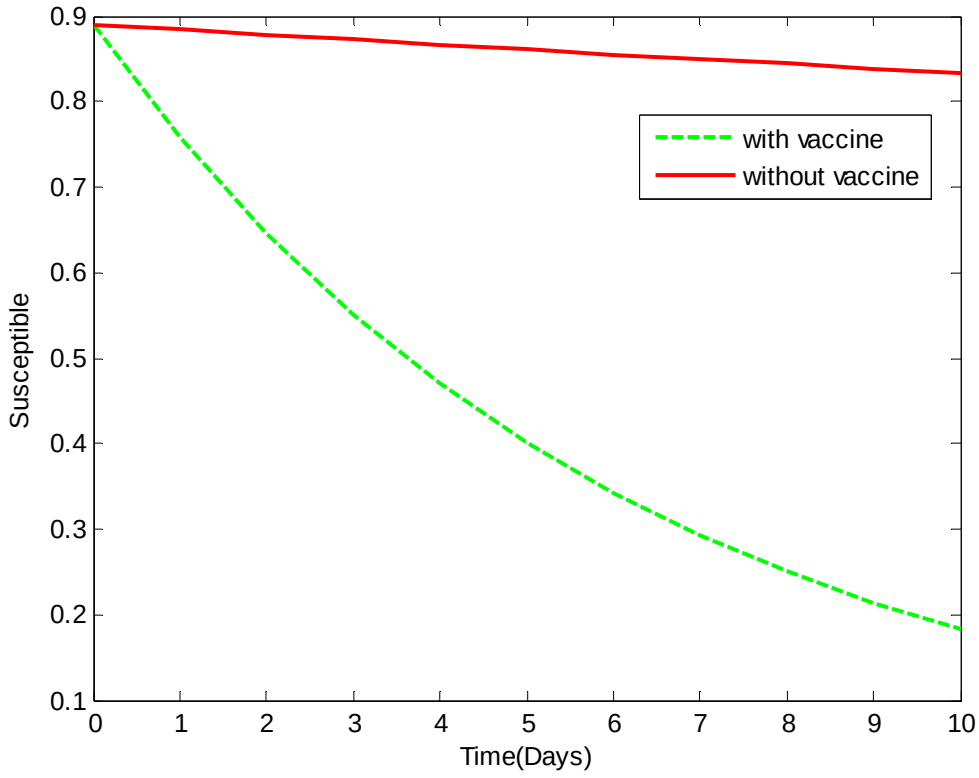

Figure 4.6: Numerical simulated values in susceptible compartments for vaccine induced and without vaccine SEIR models

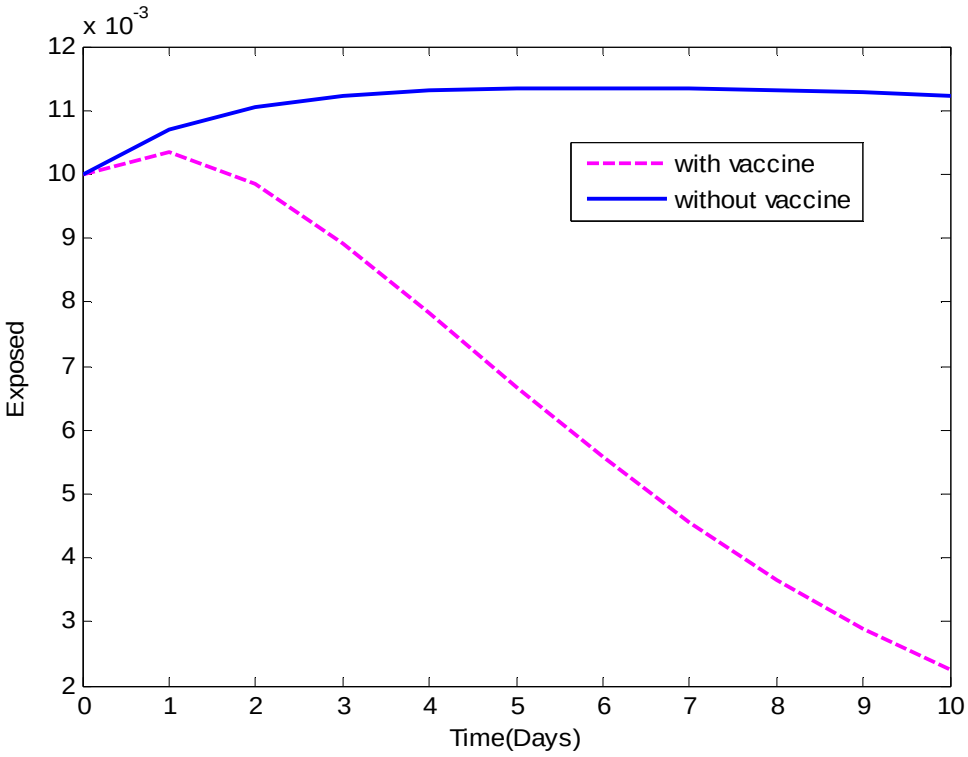

Figure 4.7: Numerical simulated values in exposed compartments for vaccine induced and without vaccine SEIR models.

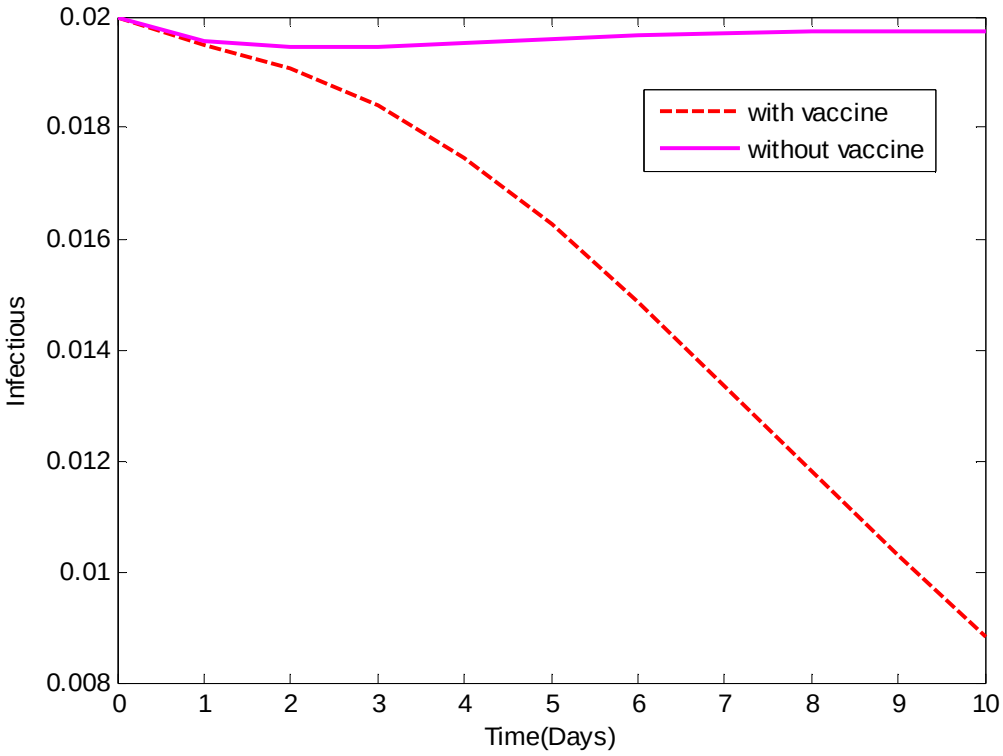

Figure 4.8: Numerical simulated values in infectious compartments for vaccine induced and without vaccine SEIR models.

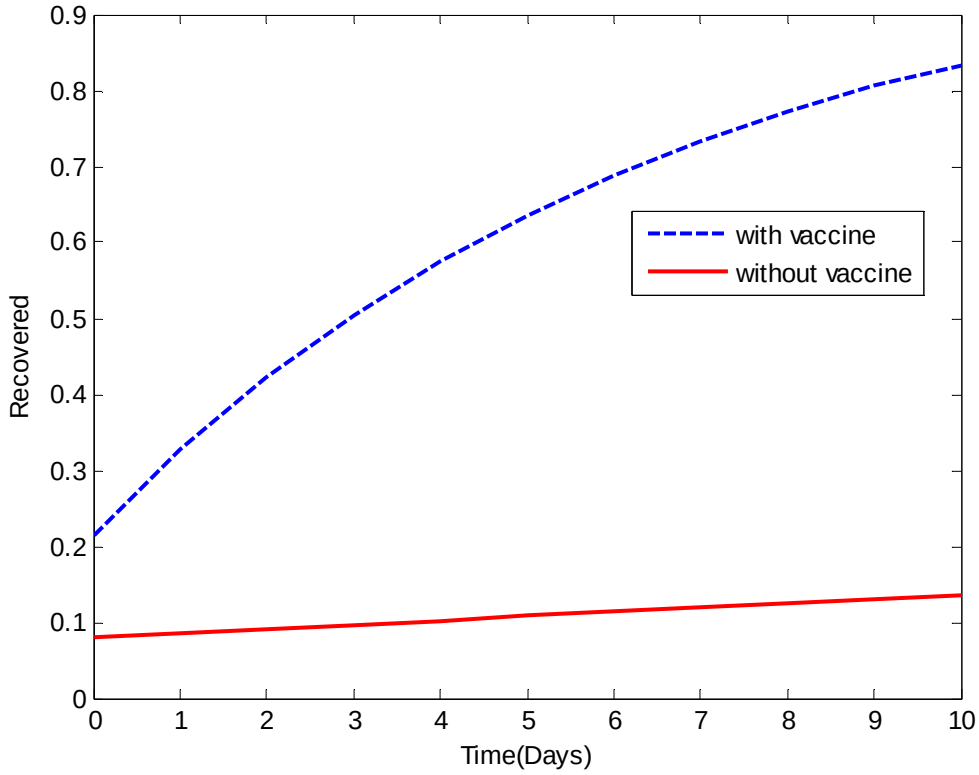

Figure 4.9: Numerical simulated values in recovered compartments for vaccine induced and without vaccine SEIR models.

It is also observed in the Figure 4.7 that according to the SEIR (without vaccine) model the proportion of exposed does not decrease rather increases whereas according to the vaccine induced SEIR model the proportion of exposed dramatically decreases after initial increase for about one day within 10 days.

It is noticed in the Figure 4.8 that the proportion of infectious though initial decreases (for about one day) but after day it is slowly increasing regarding SEIR (without vaccine) model. On the other hand the proportion of infectious initial decreases slowly but about one day later it is significantly decreasing for the vaccine induced SEIR model within 10 days.

Finally we have observed in the Figure 4.9 that the proportion of recovered increases very slowly in SEIR (without vaccine) model and significantly increases in vaccine induced SEIR model within 10 days.

4.10 Summary

In this chapter we have first analyzed the SEIR model in perspective of Bangladesh. It is observed that according to the data about AV1N1 virus in Bangladesh (2015), the numerically estimated Basic Reproduction number (R_0), by using the SEIR epidemiological model, is greater than one in perspective of Bangladesh. According to the model as $R_0 > 1$, so the disease should spread out. Now it is observed that during 2015 the disease was spread out. That is the inference of the model is agreed with real scenario (2015). Moreover the sensitivity analysis revealed that whenever the transmission rate is increased or recovery rate is decreased, the disease spread, but whenever the transmission rate is decreased or recovery rate is increased then the value of estimated R_0 becomes less than one, this implies the disease dies out. In the experiments we have also estimated the critical value of transmission rate (when other parameters except β assumed unchanged) and recovery rate (when other parameters except γ assumed unchanged). If it is possible to apply some mechanism (like closing school, preventing mass gathering etc) by which the value of β can be made less than β^*(**0.2857223929**) then spread out of disease can be controlled. Similarly if it is possible to apply some mechanism (like applying drug, environment support etc) by which the value of γ can be made greater than γ^*(**0.3373761344**) then spread out of disease can be controlled.

From the analysis of the numerical data regarding Bangladesh (2015) we have HIT which is 0.1531. According to the definition of HIT 15.31% population should be vaccinated to stop the disease spread out. Therefore we have modified the SEIR model and say vaccine induced SEIR model in which 15.31% population is vaccinated and so removed it to Recovery compartment.

Now in the numerical simulation, it is observed in the Figures 4.6 to 4.9., that vaccine induced SEIR model give better result than normal SEIR (without vaccine induced) model in all compartments. Vaccine induced SEIR model exhibited a sharp decline in the proportion of susceptible than normal SEIR model. Furthermore the recovered population increases dramatically with time in vaccine induced SEIR model compare to normal SEIR model. This result implies that as the susceptible population transferred to recovered compartment quickly, provide herd immunity.

When a disease spreads out then an inevitability concern is finding the controlling strategy of spread out disease. In this study our controlling strategy is vaccinating for which we have found the Herd Immunity Threshold. In perspective of Bangladesh (2015), for influenza A (H1N1) we have found that the Herd Immunity Threshold is 0.1531, by using SEIR model. Which means that vaccinating 15.31% population of Bangladesh can robustly control spreading of the pandemic novel influenza A (H1N1) virus when outbreak occurs. Moreover the numerical solution of our proposed vaccine induced SEIR model affirm that after vaccinating 15.31% susceptible population outbreak can be controlled.

CHAPTER V

Dynamics and Control Strategies of Nipah Virus (NiV)

5.1 Introduction

In the previous Chapter we have discussed one of the most Infectious disease namely influenza A (H1N1) virus in perceptive of Bangladesh. But recently another very transmittable disease namely Nipah Virus (NiV) comes out with outbreak in Bangladesh. It is one of the most frightening menaces for population of the most part of the world (especially developing countries). But the characteristics of this virus are some bits difference with influenza A (H1N1) virus. It is known that the vaccine of influenza A (H1N1) virus is available in Bangladesh. But vaccine regarding Nipah Virus (NiV) is not available in Bangladesh yet.

Most infectious disease can be annihilated by sufficient and suitable steps for instance educational campaign, social distance, social awareness, treatment and vaccination. The infectious diseases become epidemic when no necessary steps taken. To control the outbreak of infectious diseases we should take some required steps, particularly those for which vaccine is not available. Furthermore, it is well known that prevent is better than cure. There are some diseases in our environment for which vaccine is not available and treatment is also limited, but preventive measures can play a vital rule for such diseases. Nipah Virus (NiV) is a kind of disease for which vaccine is not applicable and treatment facility is also limited.

In this chapter we will understand transmission dynamics of Nipah virus by an epidemiological compartmental model (SEIR model) regarding data from Bangladesh. Sensitivity of Disease Free Equilibrium state and Endemic Equilibrium state will be analyzed extensively to find control strategy. We will propose to quarantine people to control outbreak of Nipah virus. The number of quarantine people will be determined by basic reproduction number. We will reformulate SEIR model introducing quarantine

population. We will determine numerical solutions of the system of Ordinary Differential Equations (ODEs) of SEIR and quarantine population induced SEIR models regarding data of Bangladesh and other simulated data. According to the numerical solutions, the trends of various aspects of the susceptible, exposed, infectious and recovered of the population regarding Bangladesh will be discussed.

5.2 Formulation of Model

Nipah virus is a zoonotic virus and transmitted first from animal to human. Once it has been transmitted to human, then it continuously transmit through human to human (H2H) by the close contact of infected individuals due to its high infectivity (Biswas, 2012 and Biawas, 2014b). Biawas (2012 and 2014b) discussed dynamics of Nipah virus by SIR model. Here we will discuss dynamics of Nipah Virus by SEIR type infectious disease model in the form of a set of ordinary differential equations rather than SIR model. Because it is known that the patient of Nipah infected pass through 5-14 days of latency period after infection. So let us suppose that $S\ (t)$, $E\ (t)$, $I\ (t)$ and $R\ (t)$ are the number of individuals in the Susceptible, Exposed, Infectious and Recovered classes at time t respectively. The transition among the various compartments can be explained by the following parameters:

β be the transmission rate

μ be the average death rates as well as average birth rates (as equal)

α be the exposed rate

γ be the recovery rate

d be the disease induced death rate

We have transmission dynamics flow chart for Nipah virus as follows:

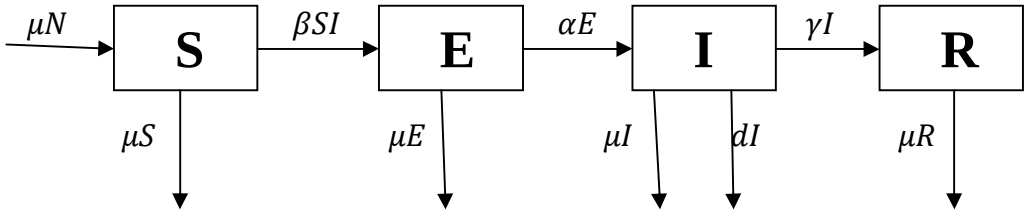

Figure 5.1: Transmission dynamics of Nipah virus (NiV) through SEIR epidemic model.

The following system of Ordinary Differential Equations (ODEs) is used to represent this SEIR model (Bubniakov´a, 2007).

$$\left.\begin{aligned} \frac{dS}{dt} &= \mu N - \mu S - \beta SI \\ \frac{dE}{dt} &= \beta SI - (\mu + \alpha)E \\ \frac{dI}{dt} &= \alpha E - (\mu + \gamma + d)I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned}\right\} \tag{5.1}$$

With initial conditions,

$$S(t) = S_0 \geq 0, E(t) = E_0 \geq 0, I(t) = I_0 \geq 0, R(t) = R_0 \geq 0 \tag{5.2}$$

Here, $\alpha > 0, \beta > 0, \gamma > 0, \mu > 0, d > 0$ and $S + E + I + R = N$

5.3 Equilibrium State

We know that the populations become a Disease Free Equilibrium (DFE) or Endemic Equilibrium (EE) according to the value of R_0. From the biological point of view it can be shown that if

$$\big(S(0), E(0), I(0), R(0)\big) \in \{(S, E, I, R) \in \{0, N\}^4, S \geq 0, E \geq 0, I \geq 0, R \geq 0, S + E + I + R = N\}$$

then $R_0 \leq 1$ implies

$$\lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = DFE$$

and $R_0 > 1, I(0) > 0$ implies

$$\lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = FE$$

Now set S, E, I, R as a proportion of the total population N, i.e.

$$s(t) = \frac{S(t)}{N}$$

$$e(t) = \frac{E(t)}{N}$$

$$i(t) = \frac{I(t)}{N}$$

$$r(t) = \frac{R(t)}{N}$$

and

$$r(t) = 1 - s(t) - e(t) - i(t)$$

then above four ODEs (Eqn. (5.1)) are reduced to three ODEs as follows:

$$\left.\begin{aligned}\frac{ds}{dt} &= \mu - (\mu + \beta i)s \\ \frac{de}{dt} &= \beta si - (\mu + \alpha)e \\ \frac{di}{dt} &= \alpha e - (\gamma + \mu + d)i\end{aligned}\right\} \tag{5.3}$$

It is known that for the steady state Equilibrium

$$\frac{dK}{dt} = 0, \exists K \in \{s, e, i\}$$

Then the above equations become as follows:

$$\mu - (\mu + \beta i)s = 0 \tag{5.4}$$

$$\beta si - (\mu + \alpha)e = 0 \tag{5.5}$$

$$\alpha e - (\gamma + \mu + d)i = 0 \tag{5.6}$$

If $i = 0$, then from equation (5.4) we get $s = 1$ and from equation (5.5), we get $e = 0$. Hence the Disease Free Equilibrium $(s, e, i) = (s_0, e_0, i_0)$ is as follows:

$$(s, e, i) = (1,0,0)$$

Now we have to find the Endemic Equilibrium $(s, e, i) = (s^*, e^*, i^*)$. From equation (5.6) we have

$$e^* = \frac{\gamma+\mu+d}{\alpha} i \tag{5.6a}$$

Substituting the value of e in equation (5.5) we get,

$$s^* = \frac{(\mu+\alpha)(\gamma+\mu+d)}{\beta\alpha} \tag{5.5a}$$

Putting the value of s in equation (5.4) we get,

$$i^* = \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu+d)} - \frac{\mu}{\beta} \tag{5.4a}$$

Therefore, Endemic equilibrium is given as follows:

$$(s^*, e^*, i^*) = \left(\frac{(\mu+\alpha)(\gamma+\mu+d)}{\beta\alpha}, \frac{\gamma+\mu+d}{\alpha}\left\{\frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu+d)} - \frac{\mu}{\beta}\right\}, \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu+d)} - \frac{\mu}{\beta}\right) \tag{5.7}$$

5.4 Parameter Estimation for Nipah Virus

Applying Next Generation Matrix Method we have calculated Basic Reproduction Number (R_0) as follows:

$$R_0 = \frac{\beta\alpha}{(\mu+\alpha)(\mu+\gamma+d)} \tag{5.8}$$

Now we will estimate other parameters with the help of following equations (5.9) – (5.11). As it is known that the expected duration of infectious is the inverse of the removal rate (Hethcote, 2000 and www.ibmathsresources, 2014). So according to the definition (Hethcote, 2000 and www.wikipedia/Transmission, 2015) the removal rate (γ), Exposed rate (α) and transmission rate (β) are given as follows:

$$\gamma = \frac{1}{\text{mean infectious period}} \tag{5.9}$$

$$\alpha = \frac{1}{\text{mean latancy period}} \tag{5.10}$$

$$\beta = \frac{\text{effective contact}}{\text{total contact}} \tag{5.11}$$

5.5 Stability Analysis

As we have considered SEIR model so we need again the following theorems as stated earlier:

Theorem 4.1: The Disease Fee Equilibrium is locally stable if $R_0 < 1$, otherwise unstable.

Theorem 4.2: Endemic Equilibrium locally stable if $R_0 > 1$, otherwise unstable.

5.6 Herd Immunity Threshold for Nipah Virus

To control outbreak of the disease, the population have to stay away from close contact of infected population. The percentage of the population that needs to be stay away from close contact of infected population for controlling the outbreak is the Herd Immunity Threshold (HIT) (Paul. et al., 2011 and Hethcote, 2000). We have proposed the HIT (H_T) as the sole **quarantine** strategy by campaign (closing mass gathering duration of outbreak). It protects directly the **quarantine** individuals from infection and also provides protection of being susceptible individuals. To evaluate HIT, we use the equation, given in (Paul. et al., 2011 and Hethcote, 2000), as follows:

$$H_T = 1 - \frac{1}{R_0} \tag{5.12}$$

5.7 Model Analysis

In order to evaluate the Herd Immunity Threshold as well as numerical analysis of the SEIR models, we have considered the information Nipah virus as defined in (CDC/nipah,

2018; WHO/nipah, 2018 and IEDCR/nipah, 2018) and real numerical data in perspective of Bangladesh (www.wikipedia/Demographics, 2015; IEDCR/nipah, 2018 and IEDCR/nipah-outbreak, 2013) .The latency period of Nipah Virus is 2 to 12 days (IEDCR, 2018) and infectious period is 3 to14 days (CDC/nipah, 2018). So the mean latency period of Nipah virus is 7 days and mean infectious period is 8.5 days.

Therefore, by using equations (5.9) and (5.10), we have, $\gamma = 0.11764706$, $\alpha = 0.14285714$ and disease induced death rate $d = 0.053$ (IEDCR/nipah-outbreak, 2013). From (Biswas, 2014b) we have $\beta = 0.75$.

We have the death rate of population of Bangladesh is $\mu = 0.00001425$ per day and the total population of Bangladesh is N= 157,157,394 (www.wikipedia/Demographics, 2015 and www.populationpyramid/Bangladesh, 2013).

Using the value of β, α, γ, d and μ in (5.8) we get $\boldsymbol{R_0 = 4.3942}$. So Disease Free Equilibrium $(s_0, e_0, i_0) = (1,0,0)$ is unstable as $R_0 = 4.3942 > 1$. From equation (5.7) and (5.8), we have Endemic Equilibrium

$$(s^*, e^*, i^*) = \left(\frac{1}{R_0}, \frac{\mu(R_0-1)}{R_0(\mu+\alpha)}, \frac{\mu(R_0-1)}{\beta}\right)$$

$$= (0.22757271, 0.00007704, 0.00006449)$$

which is stable as $R_0 = 4.3942 > 1$. Moreover, from Equation (5.12), the Herd Immunity Threshold is found to be

$$H_T = 1 - \frac{1}{R_0} = 0.7725.$$

Now the sensitivity will be analyzed for both Disease Free Equilibrium and Endemic Equilibrium points of the SIER model in perspective of Bangladesh. For these experiments the natural death rate, disease induced date rate and the expose rate is considered to be fixed. On the other hand the transmission rate as well as the recovery rate is changed as shown in the Tables 5.1. At first, the values of recovery rate ($\gamma = 0.117647059$) are kept unchanged whereas the corresponding values of transmission rates are changed. Secondly keeping the value of transmission rate ($\beta = 0.75$) constant, we have varied the value of recovery rate. Finally we have calculated the R_0values for each changed values of (γ) as well as(β). The experimental results are displayed in the Table 5.1.

Table 5.1 Sensitivity analysis of the Disease Free Equilibrium state and Endemic Equilibrium state of Nipah virus

μ	β	α	γ	d	R_0	Nature of DFE	Nature of EE
0.00001425	**0.75**	**0.14285714**	**0.11764706**	**0.053**	**4.3942308**	**Unstable**	**Stable**
0.00001425	0.5	0.14285714	0.11764706	0.053	2.9294872	Unstable	Stable
0.00001425	0.3	0.14285714	0.11764706	0.053	1.7576923	Unstable	Stable
0.00001425	0.2	0.14285714	0.11764706	0.053	1.1717948	Unstable	Stable
0.00001425	**0.170678334**	0.14285714	0.11764706	0.053	1	**Critical value**	**Critical value**
0.00001425	0.16	0.14285714	0.11764706	0.053	0.93743592	Stable	Unstable
0.00001425	0.75	0.14285714	0.2	0.053	2.96396426	Unstable	Stable
0.00001425	0.75	0.14285714	0.6	0.053	1.14840556	Unstable	Stable
0.00001425	0.75	0.14285714	0.65	0.053	1.06672830	Unstable	Stable
0.00001425	0.75	0.14285714	**0.696910945**	0.053	1	**Critical value**	**Critical value**
0.00001425	0.75	0.14285714	0.75	0.053	**0.93388778**	Stable	Unstable

From Table 5.1 we observed that when the transmission rate (β) decreases (**0.75**→0.16) with unchanged of other parameters, then the Disease Free Equilibrium approaches unstable to stable and Endemic Equilibrium becomes unstable from stable as the value of R_0decrease from **4.3942308** to less than one. Again keeping unchanged the value of all parameters except the value of recovery rate, we have observed that for the increasing of

the value of recovery rate (**0.11764706→**0.75), the Disease Free Equilibrium again approaches unstable to stable as well as Endemic Equilibrium becomes unstable from stable as the value of R_0 decreases to less than one. Which implies that if transmission rate decrease or recovery rate increase then the Disease Free Equilibrium may become stable as well as Endemic Equilibrium approaches to unstable in perspective of Bangladesh. This concludes that the disease will not spread out. What happen if we will consider the reverse strategy? From the experimental results, given in the Table 5. 1, we observe that when the transmission rate (β) increased or recovery rate (γ) decreased then R_0 becomes much greater than one and consequence the Disease Free Equilibrium found to be unstable as well as Endemic Equilibrium becomes stable from unstable as well. Which implies disease will spread out. Now we will find the critical value of Transmission rate if other parameters are remained unchanged and critical value of recovery rate when other parameters are kept fix in perspective of Bangladesh. To find the critical value of Transmission rate (β*) we set $R_0 = 1$ (by keeping fix other parameters), in equation (5.8) we have **β*=0.170678334**. Now to find the critical value of Recovery rate (γ*), we again set $R_0 = 1$ (by keeping fix other parameters), in equation (5.8) we have **γ*= 0.696910945.** The experimental results regarding β* and γ* are also displayed in the table. Therefore, if all parameters are unchanged except the transmission rate, the disease will be spread out or controlled if the transmission rate be greater or less than the critical value of β*= **0.170678334** respectively. Similarly, if all parameters are unchanged but only the recovery rate are varied, the disease will be spread out or controlled if the recovery rate be less or greater than the critical value of **γ*= 0.696910945** respectively.

Again it is revealed that $R_0 > 1$ implies the state of disease free equilibrium is unstable and the state of endemic equilibrium is stable. In the case of unstable state of disease free equilibrium and stable state of endemic equilibrium, diseases will spread out. To control of the spread out of disease, we need to calculate Herd Immunity Threshold. In perspective of Bangladesh, we have calculated the Herd Immunity Threshold to 0.7725.

Moreover, we have performed initial numerical solution and numerical simulation of the model. For the initial numerical solution of the SIER model (equation (5.3) and equation ($r(t) = 1 - s(t) - e(t) - i(t)$), in perspective of Bangladesh on February 2013, we have,

$S(0) = 157157358$, $E(0) = 20$ (assumed), $I(0) = 16$ and $R(0) = 0$ (IEDCR/nipah-outbreak, 2013 and www.population pyramid/Bangladesh, 2013). So dividing each of the terms by the total population of Bangladesh, $N = 157157394$ (www.population pyramid/Bangladesh, 2013),

we have

$s(0) = 0.9999997709$,

$e(0) = 0.0000001272$,

$i(0) = 0.0000001018$

and

$r(0) = 0$ respectively.

As calculated earlier that the value of

$\mu = 0.00001425$,

$\alpha = 0.14285714$

$\beta = 0.75$

$d = 0.053$

and

γ=0.11764706

The numerical results are given in the Figures 5.2 and 5.2, reveal that the initial outbreak occurred in Bangladesh and proportion of infectious has minimal effect on susceptible. One of the cause of this insignificance effect on susceptible is that the value of initial infectious $i(0) = 0.0000001018$ is very small.

Now we have hospital based real data about Nipah virus from February 2013 to May 2013 of Bangladesh (IEDCR/nipah-outbreak, 2013), which is shown in bar diagram (in Figure 5.3).

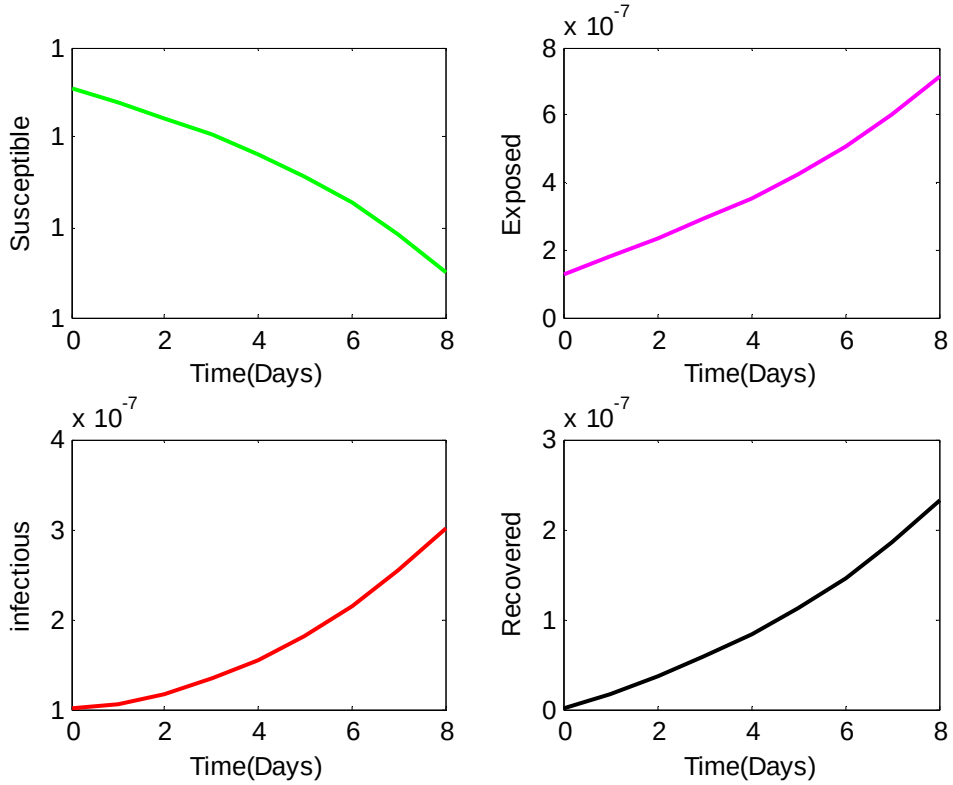

Figure 5.2: Dynamics of Nipah virus through various compartments at the initial outbreak in Bangladesh.

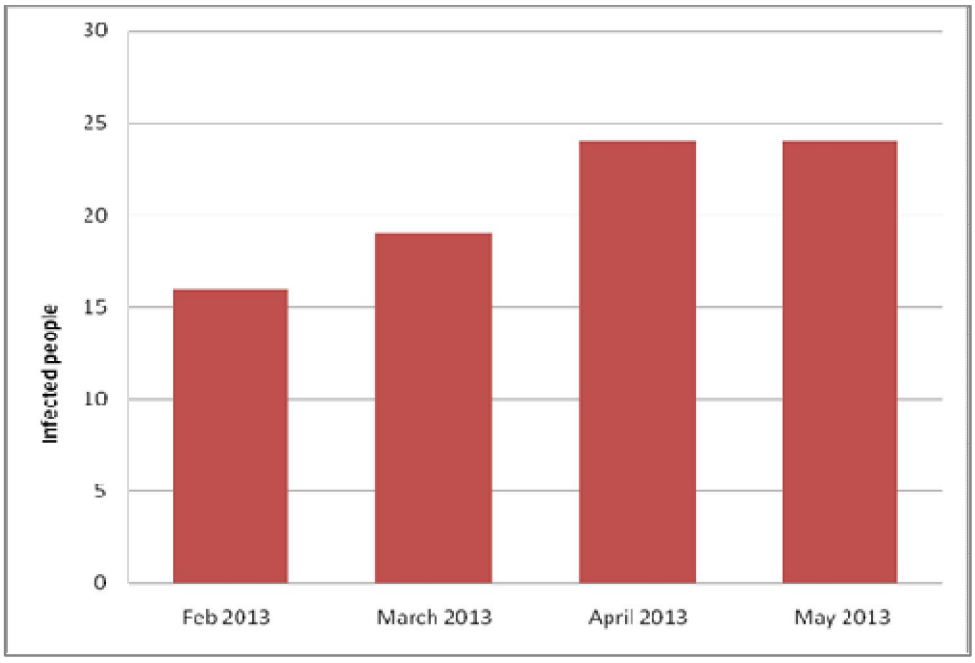

Figure 5.3: Real scenario of Nipah virus outbreak in Bangladesh from February 2013 to May 2013.

From the Figure 5.3 of real data, we have seen that initial outbreak occur for Nipah virus in Bangladesh, which also confer with our numerical solution's Figure 5.3 as well as with decision based on Basic Reproduction Number R_0

5.8 Analysis of the Model after Proposed Control

To control initial outbreak (to get Herd Immunity Threshold), we have to control 0.7725 portion of the population from being susceptible. Introducing $0.7725 = \psi$ portion Quarantine population, the schematic diagram of our proposed model for dynamics of Nipah virus would be as follows:

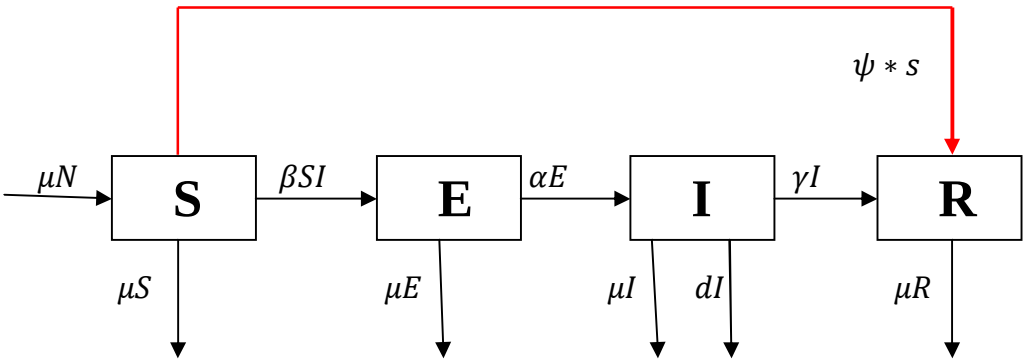

Figure 5.4: Transmission dynamics of Nipah virus through control induced SEIR epidemic model.

We get the following system of Ordinary Differential Equations (ODEs) for control induced SEIR model:

$$\left.\begin{aligned} \frac{dS}{dt} &= \mu N - \mu S - \beta SI - \psi * S \\ \frac{dE}{dt} &= \beta SI - (\mu + \alpha)E \\ \frac{dI}{dt} &= \alpha E - (\mu + \gamma + d)I \\ \frac{dR}{dt} &= \gamma I - \mu R + \psi * S \end{aligned}\right\} \qquad (5.13)$$

with initial conditions,

$$S(t) = S_0 \geq 0, E(t) = E_0 \geq 0, I(t) = I_0 \geq 0, R(t) = R_0 \geq 0$$

Here, $\alpha > 0, \beta > 0, \gamma > 0, \mu > 0, d > 0$ and $S + E + I + R = N$

Now setting S, E, I, R as a proportion of the total population N, i.e.

$$s(t) = \frac{S(t)}{N}$$

$$e(t) = \frac{E(t)}{N}$$

$$i(t) = \frac{I(t)}{N}$$

$$r(t) = \frac{R(t)}{N}$$

and

$$r(t) = 1 - s(t) - e(t) - i(t) + \psi * s$$

then above four ODEs (Eqn. (5.13)) are reduced to three ODEs as follows:

$$\left.\begin{aligned} \frac{ds}{dt} &= \mu - (\mu + \beta i)s - \psi * s \\ \frac{de}{dt} &= \beta si - (\mu + \alpha)e \\ \frac{di}{dt} &= \alpha e - (\gamma + \mu + d)i \end{aligned}\right\} \quad (5.14)$$

Now solving equation (5.14) with $r(t) = 1 - s(t) - e(t) - i(t) + \psi * s$ at initial outbreak we get following Figure 5.5.

From the Figure 5.5 we have observed that portion of exposed population considerably decreased and recovered populations' portions dramatically increased, side by side portion of infective population noticeably decreased after initial increase. Which means that outbreak will come to control (disease will not spread out). We will get herd immunity threshold after Quarantine $\psi = 0.7725$ portion of susceptible population, as we campaign to keep stay away 0.7725 portion of susceptible population.

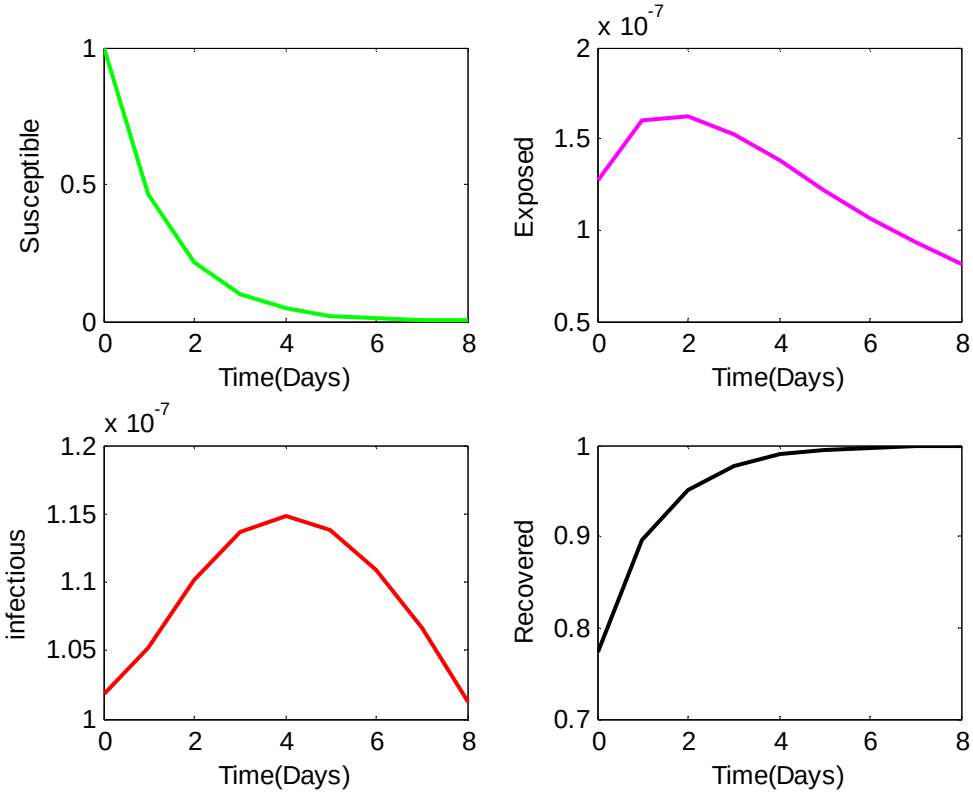

Figure 5.5: Dynamics of Nipah through various compartments at the initial outbreak in Bangladesh after control induced.

5.9 Comparison of SEIR and Control Induced SEIR Model Regarding Numerical Simulation

What happen if the proportion of infective is significantly large, keeping unchanged the value of the parameters? For this experiment, we varied the proportion of initial infective to $i(0) = .09$ as well as proportion of initial susceptible $s(0) = 0.88$ and $e(0) = 0.03$ around the endemic equilibrium point for a period 12 days. The simulated results are shown in Figures 5.6- 5.9.

From Figure 5.6 we observed that the proportion of susceptible gradually decreases in SEIR model and very rapidly decreases in control induced SEIR model within 12 days.

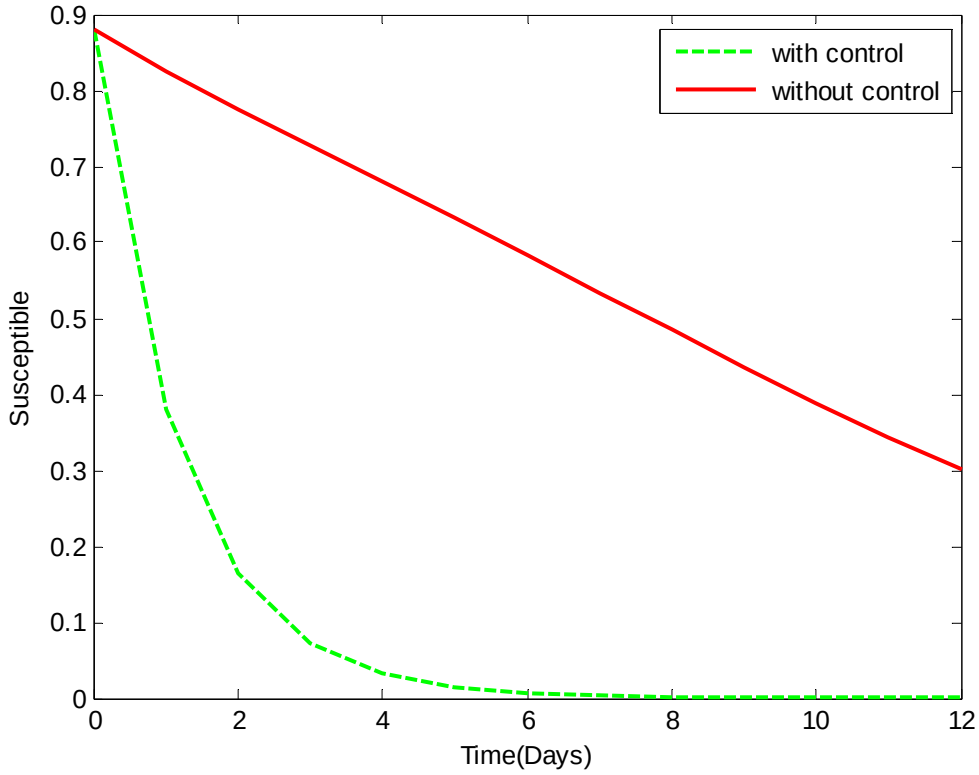

Figure 5.6: Numerical simulated values in susceptible compartments for control induced and without control induced SEIR models.

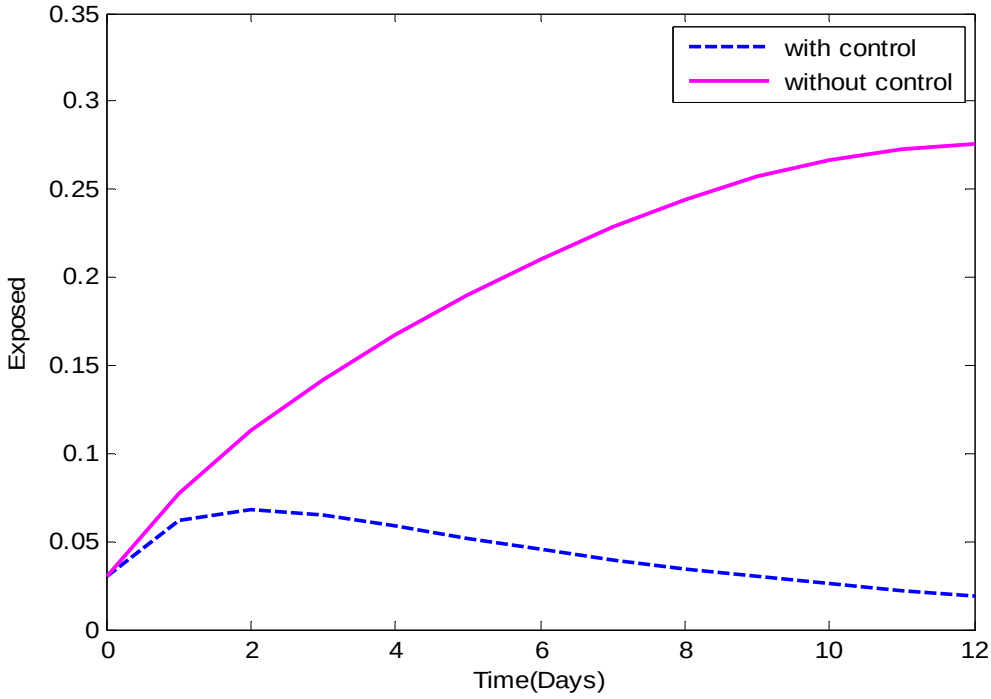

Figure 5.7: Numerical simulated values in exposed compartments for control induced and without control induced SEIR models.

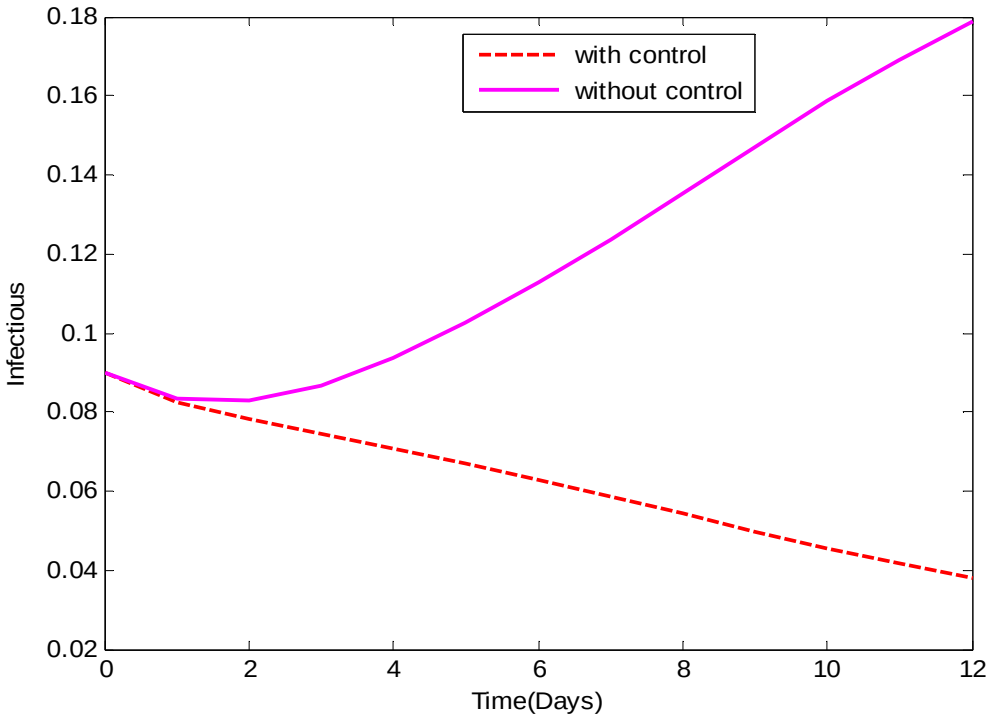

Figure 5.8: Numerical simulated values in infectious compartments for control induced and without control induced SEIR models.

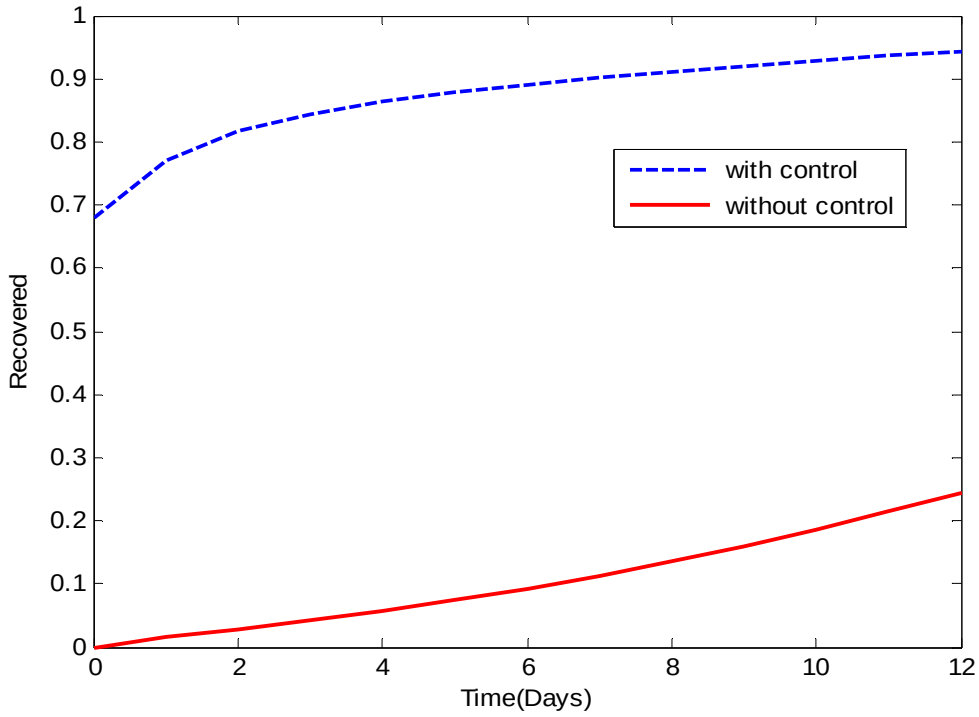

Figure 5.9: Numerical simulated values in recovered compartments for control induced and without control induced SEIR models.

From Figure 5.7 we observed that the proportion of exposed progressively increases in SEIR model and decreases after initial increase for about two days in control induced SEIR model within 12 days.

From Figure 5.8 we observed that the proportion of infectious increases after initial decrease for about two days in without control induced SEIR model and dramatically decreases in control induced SEIR model within 12 days.

From Figure 5.9 we observed that the proportion of recovered increases very slowly in without control induced SEIR model and sharply increases in control induced SEIR model within 12 days.

5.10 Summary

In perspective of Bangladesh, the estimated Basic Reproduction number (R_0) for the SEIR epidemiological model is greater one which indicates that disease will spread out. The sensitivity analysis revealed that whenever the transmission rate is increased or recovery rate is decreased, the disease spreads, but whenever the transmission rate is decreased or recovery rate is increased then the value of estimated R_0 becomes less than one, this implies the disease dies out. In the experiments we have also estimated the critical value of transmission rate (when other parameters except β assumed unchanged) and recovery rate (when other parameters except γ assumed unchanged). If it is possible to apply some mechanism (like closing school, preventing mass gathering and using mask and gloves etc) by which the value of β can be made less than **β*(0.170678334)** then spread out of disease can be controlled. Similarly if it is possible to apply some mechanism (like applying drug, environment support, hygienic foods etc) by which the value of γ can also be made greater than **γ*(0.696910945)** then spread out of disease can be controlled.

From the simulation Figures 5.6 to 5.9, it may conclude that the proposed control induced SEIR model give better result than without control induced SEIR model in all compartments Control induced SEIR model exhibited a sharp decline in the proportion of susceptible than normal SEIR model. Furthermore the recovered population increases dramatically with time in control induced SEIR model compare to normal SEIR model.

This result implies that as the susceptible population transferred to recovered compartment quickly, provide herd immunity.

If a disease spreads out then an inevitability concern is finding the controlling strategy to prevent spread out of that disease. In this study our controlling strategy is keeping away population from close contact of infected population (by creating awareness by campaign through media, wearing mask and gloves while caring patient of Nipah virus) which give the Herd Immunity Threshold. In perspective of Bangladesh, for Nipah virus, we have found that the Herd Immunity Threshold is 0.7725, by using SEIR model. Which means that controlling 77.25% population from close contact of infected population of Bangladesh can robustly control spreading of Nipah virus when outbreak occurs (assuming the parameters will be unchanged). The numerical solution of our proposed control induced SEIR model affirm that after keeping away from close contact of infected people of 77.25% susceptible population outbreak can be controlled.

CHAPTER VI

Conclusions

There is no doubt that mathematical modeling is essential in planning and formulation of policy on contagious diseases. As is the case with modeling, in general, there will always be the quest for more appropriate and accurate models. The kind of models we have been studying in this dissertation can be refined in many different ways. We focused on the SEIR model. In particular we studied its stability properties, paying particular attention to basic reproductive number to get Herd Immunity Threshold. By SEIR model we have analyzed dynamics of Influenza A (H1N1) virus and Nipah virus in perspective of Bangladesh and got their control strategies. The findings are as follows:

Findings for Influenza A (H1N1) virus:

- By the help of the value of Basic Reproduction Number, it is possible to draw conclusion whether the infectious disease spread out or not.
- Reduction of transmission rate can control the disease.
- Increase of the recovery rate can control the outbreak of the disease.
- If *15.13%* population of Bangladesh vaccinated then outbreak would be controlled. Our proposed vaccine induced SEIR model confirmed that issue. So in future if outbreak occur estimating basic reproduction (at initial stage) we would be able to find the vaccinating percentage of people to control the outbreak.

Findings for Nipah virus:

- It is possible to draw conclusion whether the infectious disease spread out or not on basis the number of Basic reproduction number.
- Reduction of transmission rate can control the disease.
- Increase of the recovery rate can control the outbreak of the disease.
- If *77.25%* population of Bangladesh kept away from close contact of Nipah infected population (by creating awareness through media, closing mass gathering

and wearing gloves and musk whiling caring infected people) then outbreak would be controlled. Our proposed control induced SEIR model confirmed that concern. So, in future, if outbreak occurs estimating basic reproduction (at initial stage) we would be able to find the controlling percentage of people to control the outbreak.

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