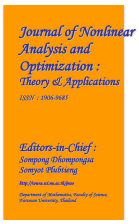
Journal of **N**onlinear **A**nalysis and **O**ptimization
Vol. 7, No. 2, (2016), 57-66
ISSN : 1906-9685
http://www.math.sci.nu.ac.th



A MATHEMATICAL ANALYSIS OF THE TRANSMISSION DYNAMICS OF EBOLA VIRUS DISEASES

MITUN KUMAR MOMDAL[1], MUHAMMAD HANIF[2] AND MD. HAIDER ALI BISWAS[1*]

[1]Mathematics Discipline, Science Engineering and Technology School, Khulna University, Khulna, Bangladesh; [2]Department of Applied Mathematics, Noakhali Science and Technology University, Noakhali, Bangladesh

ABSTRACT. A mathematical model to investigate the transmission dynamics of Ebola virus disease (EVD), which causes acute viral haemorrhagic fever, is established in this paper. Based on the mechanism and characteristic of EVD transmission, we propose a susceptible-exposed-infectious-recovered-susceptible (SEIRS) epidemic model with the understanding that the recovered individuals can become infected again. The equilibria of the model and their stability are discussed in detail. Basic reproduction number (R_0) is obtained by using the next generation approach and proved that the disease free equilibrium (DFE) of our system is locally asymptotically stable if $R_0 < 1$, which means that the disease can be eradicated under such condition in finite time and unstable if $R_0 > 1$. When the associated reproduction number, $R_0 > 1$ then the endemic equilibrium is stable, otherwise unstable. We contemplate our proposed model numerically and compare the results with existing literature.

KEYWORDS : Ebola Virus; SEIRS model; Equilibria; Basic reproduction number; Stability analysis.
AMS Subject Classification: 92D30, 93A30, 49K15, 35B35

1. INTRODUCTION

Ebola virus disease (EVD) also known as Ebola hemorrhagic fever (EHF) or simply Ebola, is a disease of humans and other primates caused by Ebolavirus. EVD is actually an important problem of public health, especially in West African regions. The disease was first identified in 1976 in two simultaneous outbreaks, one in Nzara, Sudan and the other in Yambuku, Democratic Republic of Congo (formerly Zaire). The latter occurred in a village near the Ebola River, from which the disease takes its name. The virus family Filoviridae includes three genera: Cuevavirus, Marburvirus and Ebolavirus. According to Pringle [15], there are five species that have been identified: Zaire, Bundibugyo, Sudan, Reston and Tai Forest.

* *Corresponding author.*
Email address : mhabiswas@yahoo.com.
Article history : Received 12 February 2016 Accepted 26 January 2018.

The transmission of Ebola virus can spread from human to human by direct contact with body fluids such as blood, saliva, mucus, vomit, sweat, tears, breast milk, urine and semen of an infected human or other animal, which were described by Kuhn et al. [9]. Pattyn et al. [14] stated that the spread of the disease through the air between primates, including humans, has not been documented in either laboratory or natural conditions. It is mentioned by Bowen et al. [6] semen or breast milk of a person after recovery from EVD may still carry the virus for several weeks to months. Fruit bats are believed to be the normal carrier in nature, able to spread the virus without being affected by it. Other diseases such as meningitis, malaria, typhoid fever and other viral hemorrhagic fevers may resemble EVD. By nature, Ebola is highly contagious and deadly and there are no drugs or proven Ebola virus-specific treatment at moment. Ebola can kill up to 90% of patients, although in this outbreak, the death rate has dropped below 50%, which gives credence to the fact that early detection and good medical care could be synonymous to possible recovery, which is not permanent since with no immunity, the recovered become susceptible again. Between 1976 and 2013, World Health Organization (WHO) reports a total of 24 outbreaks involving 1,716 cases. Ndanusa et al. [11] reported that the largest outbreak is the ongoing epidemic in West Africa, still affecting Liberia, Guinea and Sierra Leone. As of 11 August 2015, this outbreak has 27,984 reported cases resulting in 11,298 deaths.

In the light of the foregoing, there is an urgent and serious need to have coordinated responses from all angles in order to combat against the EVD effectively. As part of this coordinated approach, we use the mathematical modeling for describing the EVD transmission, because mathematical modeling is an equation or set of equations that successfully describes the physical problem or phenomenon. Already many authors have developed mathematical models to improve our understanding of the dynamics and spread of this gigantic infectious disease. An EVD transmission model to the reported daily numbers of incident cases and deaths during the outbreak in Nigeria is fitted by Althaus et al. [1]. Osemwinyen et al. [13] introduced a modified SIR model in which they included a quarantined group to refine their proposed model and equally used it to simulate the transmission dynamics of the EVD. Chowell et al. [7] modeled the course of the outbreaks of ebola disease via an SEIR epidemic model by including a smooth transition in the transmission rate after control interventions were put in place. A simple ebola virus transmission model is developed by Deepa [8]. For more details on EVD transmission we refer readers to the references within as well as for some recent developments of other infectious diseases in [2, 3, 4, 5, 10, 12].

In this paper, we attempt to propose a SEIRS model that can be used to study how to reduce the spread of ebola epidemics. We propose this model with the understanding that the recovered individuals can become infected again. The first section of this paper formulates a SEIRS model for transmission of EVD, the second section analyzes the model and the last section simulates the model. The simulation is compared to the theoretical calculation by using ODE45 solvers written in MATLAB programming language.

2. MODEL FORMULATION

In this section, we formulate a SEIRS compartmental model to hit off the transmission dynamics of EVD. In order to describe the model equations, we assume that the total population (N) is divided into four different classes, which are the susceptible, (S) are people that have never come into contact with ebola virus, the

TABLE 1. Parameters used in the model with their description and values

Parameter	Description	Value (day^{-1})
A	Recruitment rate	9863
β	Effective contact rate with infectious individuals	0.90
μ	Natural death removal rate	0.0000548
γ	Rate at which exposed individuals become infectious	0.083
δ	Recovery rate	0.15
σ	Death removal rate due to EVD	0.025
ρ	Rejoin rate from recovered to susceptible class	0.023

exposed, (E) are people who have come into contact with the disease but are not yet infective, the infectious, (T) are people who have become infected with ebola virus and are able to transmit the virus, and recovered, (R) are people that have recovered from EVD. The model parameters are defined in TABLE 1 and the transmission of EVD are shown in FIGURE 1.

The susceptible class S is increased by birth or immigration at the rate A. It is decreased by infection following contact with infected individuals at the rate $\frac{\beta I}{N}$, and diminished by natural death of people at the rate μ. To determine the rate at which people become exposed in the population, the first term is considered in the susceptible class which is the rate at which susceptible, by meeting infective, become exposed is $\frac{\beta I}{N}$. This class is decreased by the rate γ at which the exposed individuals become infectious and diminished by natural death at the rate μ.The infectious class I is generated by breakthrough of exposed individuals at the rate γ. This class is decreased by recovery from infection at the rate δ and diminished by natural death and disease induced death at a rate μ and σ. The recovered class R is increased by those that recover from the infection at the rate δ and reduced by the number of people that rejoin to the susceptible class at the rate ρ and by natural death rate μ.

The model is illustrated by the following schematic diagram

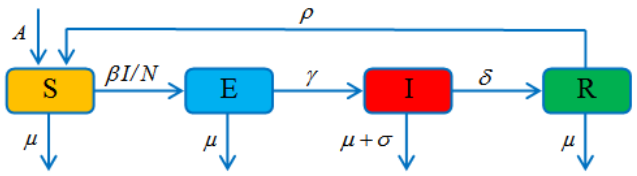


FIGURE 1. Diagram showing the compartmental model for SEIRS

The corresponding mathematical equations can be described by the following system of ordinary differential equations:

$$\frac{dS}{dt} = A - \frac{\beta IS}{N} + \rho R - \mu S \tag{2.1}$$

$$\frac{dE}{dt} = \frac{\beta IS}{N} - \gamma E - \mu E \tag{2.2}$$

$$\frac{dI}{dt} = \gamma E - \delta I - \sigma I - \mu I \tag{2.3}$$

$$\frac{dR}{dt} = \delta I - \rho R - \mu R \tag{2.4}$$

with, $N = S + E + I + R$.

3. MODEL ANALYSIS

In this section we find out the disease free equilibrium (DFE), endemic equilibrium (EE), basic reproduction number and the stability of equilibrium points.

3.1. **Disease free equilibrium.** For equilibrium point, we set the equations (2.1)-(2.4) equal to zero, that is

$$A - \frac{\beta IS}{N} + \rho R - \mu S = 0 \tag{3.1}$$

$$\frac{\beta IS}{N} - \gamma E - \mu E = 0 \tag{3.2}$$

$$\gamma E - \delta I - \sigma I - \mu I = 0 \tag{3.3}$$

$$\delta I - \rho R - \mu R = 0 \tag{3.4}$$

To determine the disease free equilibrium, substitute $E = I = R = 0$ then the equation (3.1) stands,

$$A - \mu S = 0$$
$$\therefore S = \frac{A}{\mu}$$

Hence the disease free equilibrium is $(\frac{A}{\mu}, 0, 0, 0)$.

3.2. **Endemic equilibrium.** From the equations (3.1)-(3.4) we obtain,

$$S = \frac{AN + \rho RN}{\beta I + \mu N} \tag{3.5}$$

$$E = \frac{\beta IS}{N(\gamma + \mu)} \tag{3.6}$$

$$I = \frac{\gamma E}{\delta + \sigma + \mu} \tag{3.7}$$

$$R = \frac{\delta I}{\rho + \mu} \tag{3.8}$$

Using equations (3.6) and (3.7) we have,

$$E = \frac{\beta S}{N(\gamma + \mu)} \frac{\gamma E}{\delta + \sigma + \mu}$$

$$\therefore S = \frac{N(\gamma+\mu)(\delta+\sigma+\mu)}{\beta\gamma} \tag{3.9}$$

Substituting the value of S and R in (3.5) we obtain

$$I = \frac{\beta\gamma AN - \mu N^2(\gamma+\mu)(\delta+\sigma+\mu)}{\beta N(\gamma+\mu)(\delta+\sigma+\mu) - \frac{\beta\gamma\rho\delta}{\rho+\mu}} \tag{3.10}$$

Hence from (3.6) and (3.8) we obtain,

$$E = \frac{(\delta+\sigma+\mu)\beta\gamma AN - \mu N^2(\gamma+\mu)(\delta+\sigma+\mu)^2}{\beta N(\gamma+\mu)(\delta+\sigma+\mu) - \frac{\beta\gamma\rho\delta}{\rho+\mu}} \tag{3.11}$$

and

$$R = \frac{\beta\gamma\delta AN - \mu\delta N^2(\gamma+\mu)(\delta+\sigma+\mu)}{\beta N(\rho+\mu)(\gamma+\mu)(\delta+\sigma+\mu) - \beta\gamma\rho\delta} \tag{3.12}$$

If the endemic equilibrium point is (S^*, E^*, I^*, R^*) then,

$$S^* = \frac{N(\gamma+\mu)(\delta+\sigma+\mu)}{\beta\gamma},$$

$$E^* = \frac{(\delta+\sigma+\mu)\beta\gamma AN - \mu N^2(\gamma+\mu)(\delta+\sigma+\mu)^2}{\beta N(\gamma+\mu)(\delta+\sigma+\mu) - \frac{\beta\gamma\rho\delta}{\rho+\mu}},$$

$$I^* = \frac{\beta\gamma AN - \mu N^2(\gamma+\mu)(\delta+\sigma+\mu)}{\beta N(\gamma+\mu)(\delta+\sigma+\mu) - \frac{\beta\gamma\rho\delta}{\rho+\mu}} \text{ and}$$

$$R^* = \frac{\beta\gamma\delta AN - \mu\delta N^2(\gamma+\mu)(\delta+\sigma+\mu)}{\beta N(\rho+\mu)(\gamma+\mu)(\delta+\sigma+\mu) - \beta\gamma\rho\delta}.$$

3.3. **Basic reproduction number.** The basic reproduction number (R_0) is an important part of epidemiological model. It is defined as the expected numbers of secondary cases produced by an infected individual during its entire period of infectiousness. If $R_0 < 1$, then throughout the infectious period, each infective will produce less than one new infective on the average. This in turn implies that the disease will die out and if$R_0 > 1$, then throughout the infectious period, each infective will produce more than one new infective on the average. This in turn implies that the disease will persist. It is obtained from the largest eigenvalue of the next generation matrix, FV^{-1}.
Here,

$$F = \begin{bmatrix} \frac{\partial F_1}{\partial E} & \frac{\partial F_1}{\partial I} \\ \frac{\partial F_2}{\partial E} & \frac{\partial F_2}{\partial I} \end{bmatrix} = \begin{bmatrix} 0 & \frac{\beta S}{N} \\ 0 & 0 \end{bmatrix}; \text{ where, } \begin{bmatrix} F_1 \\ F_2 \end{bmatrix} = \begin{bmatrix} \frac{\beta IS}{N} \\ 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} \frac{\partial V_1}{\partial E} & \frac{\partial V_1}{\partial I} \\ \frac{\partial V_2}{\partial E} & \frac{\partial V_2}{\partial I} \end{bmatrix} = \begin{bmatrix} \gamma+\mu & 0 \\ -\gamma & \gamma+\delta+\mu \end{bmatrix}; \text{ where, } \begin{bmatrix} V_1 \\ V_2 \end{bmatrix} = \begin{bmatrix} (\gamma+\mu)E \\ -\gamma E + (\delta+\sigma+\mu)I \end{bmatrix}$$

Now,

$$V^{-1} = \frac{1}{(\gamma+\mu)(\delta+\sigma+\mu)} \begin{bmatrix} \delta+\sigma+\mu & 0 \\ \gamma & \gamma+\mu \end{bmatrix}. \tag{3.13}$$

At disease free equilibrium,

$$F = \begin{bmatrix} 0 & \beta \\ 0 & 0 \end{bmatrix}. \tag{3.14}$$

Therefore at disease free equilibrium,

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

$$= \frac{1}{(\gamma+\mu)(\delta+\sigma+\mu)} \begin{bmatrix} \beta\gamma & \beta(\gamma+\mu) \\ 0 & 0 \end{bmatrix}. \tag{3.15}$$

The largest eigenvalue of FV^{-1} is $\frac{\beta\gamma}{(\gamma+\mu)(\delta+\sigma+\mu)}$. Therefore, the basic reproduction number, $R_0 = \frac{\beta\gamma}{(\gamma+\mu)(\delta+\sigma+\mu)}$.

3.4. **Stability of the equilibrium points.** To investigate the stability at the equilibrium points, we present the following theorems.

Theorem 3.1. *The disease free equilibrium* $(\frac{A}{\mu}, 0, 0, 0)$ *of the system (2.1)-(2.4) is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

Proof. The Jacobian matrix of (2.1)-(2.4) is

$$J(S,E,I,R) = \begin{bmatrix} -\frac{\beta I}{N} - \mu & 0 & -\frac{\beta S}{N} & \rho \\ \frac{\beta I}{N} & -(\gamma+\mu) & \frac{\beta S}{N} & 0 \\ 0 & \gamma & -(\delta+\sigma+\mu) & 0 \\ 0 & 0 & \delta & -(\rho+\mu) \end{bmatrix}, \tag{3.16}$$

at disease free equilibrium point the matrix becomes

$$J_{DFE} = \begin{bmatrix} -\mu & 0 & -\beta & \rho \\ 0 & -(\gamma+\mu) & \beta & 0 \\ 0 & \gamma & -(\delta+\sigma+\mu) & 0 \\ 0 & 0 & \delta & -(\rho+\mu) \end{bmatrix} \tag{3.17}$$

Now equating the characteristic equation to zero for the eigenvalue ω we get,

$$(\mu+\omega)(\rho+\mu+\omega)(a_0\omega^2 + a_1\omega + a_2) = 0 \tag{3.18}$$

with, $a_0 = 1 > 0, a_1 = \gamma + \delta + \sigma + 2\mu$ and $a_2 = \dfrac{1 - R_0}{R_0}$.

The first two eigenvalues have negative real parts and the other two eigenvalues have negative real parts if and only if $a_2 > 0$, i.e., $R_0 < 1$. Hence completes the proof. □

Theorem 3.2. *The endemic equilibrium of the system (2.1)-(2.4) is locally asymptotically stable if $R_0 > 1$, otherwise unstable.*

Proof. We present the following Jacobian matrix of (2.1)-(2.4) for proving the theorem,

$$J(S,E,I,R) = \begin{bmatrix} -\dfrac{\beta I}{N} - \mu & 0 & -\dfrac{\beta S}{N} & \rho \\ \dfrac{\beta I}{N} & -(\gamma+\mu) & \dfrac{\beta S}{N} & 0 \\ 0 & \gamma & -(\delta+\sigma+\mu) & 0 \\ 0 & 0 & \delta & -(\rho+\mu) \end{bmatrix}, \tag{3.19}$$

at endemic equilibrium point the matrix becomes,

$$J_{EE} = \begin{bmatrix} -\dfrac{\beta X}{N} - \mu & 0 & -\dfrac{\beta}{R_0} & \rho \\ \dfrac{\beta X}{N} & -(\gamma+\mu) & \dfrac{\beta}{R_0} & 0 \\ 0 & \gamma & -(\delta+\sigma+\mu) & 0 \\ 0 & 0 & \delta & -(\rho+\mu) \end{bmatrix} \tag{3.20}$$

where, $X = \dfrac{R_0 A - \mu N}{\beta - \dfrac{R_0 \rho \delta}{\rho + \mu}}$.

The characteristic polynomial of J_{EE} is,

$$P(\omega) = a_0\omega^4 + a_1\omega^3 + a_2\omega^2 + a_3\omega + a_4 \tag{3.21}$$

where, $a_0 = 1 > 0$, $a_1 = X + \rho + \gamma + \delta + \sigma + 4\mu$, $a_2 = (X+\mu)(\rho+\mu) + (X + \rho + 2\mu)(\gamma + \delta + \sigma + 2\mu)$, $a_3 = (X+\mu)(\rho+\mu)(\gamma+\delta+\sigma+2\mu) + \dfrac{\beta\gamma X}{R_0}$ and $a_4 = X(\gamma+\mu)(\delta+\sigma+\mu)(\rho+\mu+R_0\delta)$.

Note that all coefficients of $P(\omega)$ are positive for $R_0 > 1$. Thus by the Routh-Hurwitz criteria, all roots of $P(\omega)$ have negative real parts if $a_1a_2 > a_3$ and $a_1a_2 > a_3 + a_1^2a_4$. It is possible only when $R_0 > 1$, thus the endemic equilibrium point is stable if $R_0 > 1$, otherwise unstable. □

4. NUMERICAL RESULTS

For the purpose of model validation as well as in order to ensure that the proposed model is agreement with reality, numerical simulations are carried out using the data provided in TABLE 1. Varying the values of parameters, the graphs are plotted to investigate the effect of some parameters on the transmission dynamics of EVD. The results are displayed in FIGURE 2-4. The result for the value of parameters (see TABLE 1) is displayed in FIGURE 2.

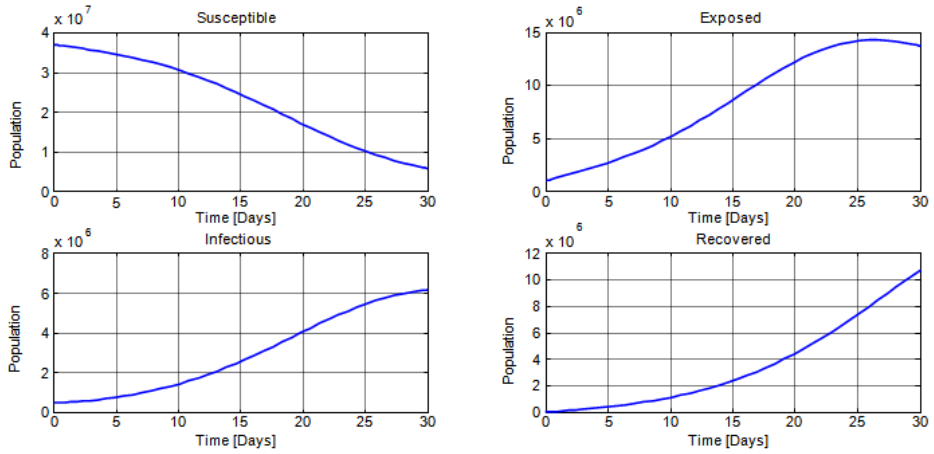


FIGURE 2. Variation of the population with time (30 days) for $R_0 = 5.65 > 1$.

According to FIGURE 2 we notice a gradual drop of susceptible group with the increasing of time. The number of exposed begins to rise from its initial state and after rising at highest point the group falls down gradually. The infected also begins to increase from its initial position and the recovered people gradually increasing over time. Again if we reduce the effective contact rate between infected and susceptible as well as the rate at which exposed individuals become infectious, as: $\beta = 0.75,\ \gamma = 0.063,\ \delta = 0.45,\ \sigma = 0.15,\ \rho = 0.023$ and $\mu = 0.0000548$. Then we get the new result which is shown in FIGURE 3.

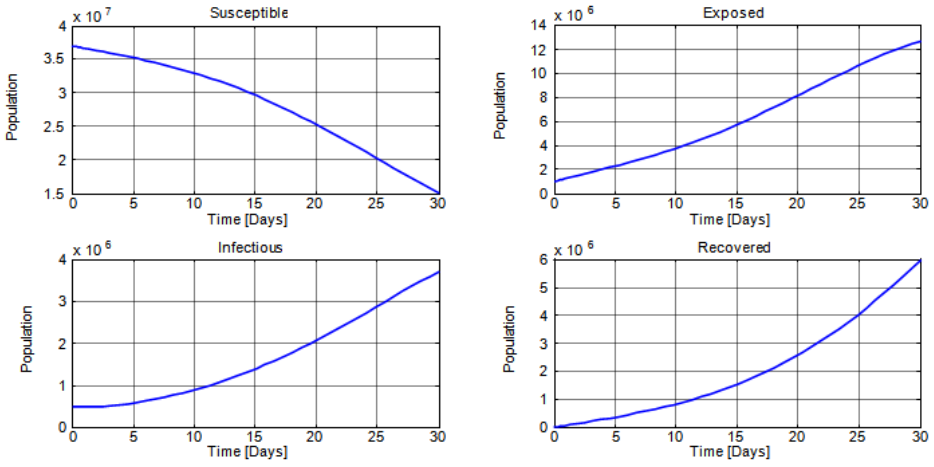


FIGURE 3. Variation of the population with time (30 days) for $R_0 = 1.25 > 1$.

FIGURE 3 shows relatively similar curves but with little change over FIGURE 2. Here we see a gradual dropping of susceptible group and gradual rising of recovered group. The change of exposed group is not like as FIGURE 2. In FIGURE 2 the exposed group reaches at a highest point then falls down but in FIGURE 3 the exposed group is always increasing with the increase of time. Also for the values of $\beta = 0.55,\ \gamma = 0.043,\ \delta = 0.45,\ \sigma = 0.15,\ \rho = 0.023$ and $\mu = 0.0000548$, the new result is shown in FIGURE 4.

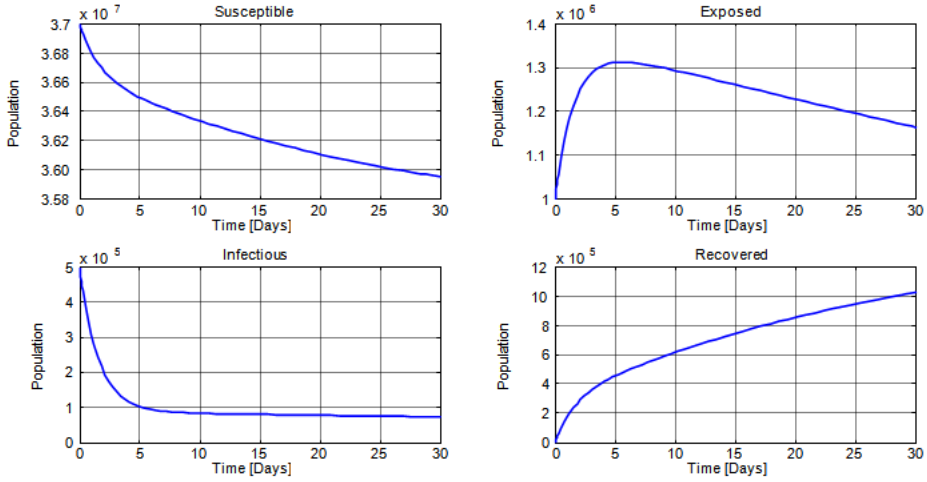


FIGURE 4. Variation of the population with time (30 days) for $R_0 = 0.91 < 1$.

The results displayed in FIGURE 4, indicates a more interesting result than in FIGURE 2 and 3. Here the susceptible group is reducing as like as FIGURE 2 and 3 but infected group is reducing from its initial state which is more changed than FIGURE 2 and 3. The exposed group is increasing first and reach at a peak then falls down gradually. The recovered always increasing over time. Therefore a greater percentage of the population is alive, though still susceptible.

5. CONCLUSIONS

The world is currently having a difficult time fighting against Ebola virus. In spite of that, this deadly virus must be dealt with. This is not merely fighting against a disease; it is an event where different nations and companies cooperate for the common cause. In this paper, we came up with a mathematical model that can be applied to the fight against EVD. First, we fitted a compartmental SEIRS model to describe the transmission dynamics of EVD, then analyzed the model briefly and at last simulated shortly the model numerically with the help of known nonlinear solver coded.

REFERENCES

1. .L. Althaus, N. Low, E.O. Musa, F. Shuaib and S. Gsteiger, Ebola virus disease outbreak in Nigeria: Transmission dynamics andrapid control, Epidemics, **11**(2015), 80-84.
2. .H.A. Biswas, Model and control strategy of the deadly Nipah virus (NiV) infections in Bangladesh, Research and Reviews in Biosciences, **6**(12) (2012), 370-377.

3. .H.A. Biswas, Optimal Control of Nipah Virus (NiV) Infections: A Bangladesh Scenario, Journal of Pure and Applied Mathematics: Advances and Applications, **12**(1) (2014), 77-104.
4. .H.A. Biswas, AIDS epidemic worldwide and the millennium development strategies: A light for lives, HIV and AIDS Review, **11**(4) (2012), 87-94.
5. .H.A. Biswas, L.T. Paiva and M.D.R. de Pinho, A SEIR model for control of infectious diseases with constraints, Mathematical Biosciences and Engineering, **11**(4) (2014), 761-784.
6. .T.W. Bowen, G. Lloyd, W.J. Harris, G.S. Platt, A. Baskerville and E.E. Vella, Viral haemorrhagic fever in southern Sudan and northern Zaire, Preliminary studies on the aetiological agent, Lancet, **1**(8011) (1977), 571-573.
7. . Chowel, N.W. Hengartner, C, Castillo-Chavez, P.W. Fenimore and J.M. Hyman, The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda, Journal of Theoretical Biology, **229** (2004), 119-126.
8. .S. Deepa, S. Nallamalli, L.N.S. Naik and G.V.S. Teja, Mathematical Model for Transmission of Ebola, Procedia Computer Science, **48** (2015), 741-745.
9. .H. Kuhn, S. Becker, H. Ebihara, T.W. Geisbert, K.M. Johnson, Y. Kawaoka, W.I. Lipkin, A.I. Negredo, S.V. Netesov, S.T. Nichol, G. Palacios, C.J. Peters, A. Tenorio, V.E. Volchkov and P.B. Jahrling, Proposal for a revised taxonomy of the family Filoviridae: classification, names of taxa and viruses, and virus abbreviations, Archives of Virology, **155**(12) (2010), 2083-2103.
10. .K. Mondal and M.H.A. Biswas, Modeling the Transmission Dynamics of the Nipah Virus Infection, Proceedings of 1st International Conference on Mathematics and Its Applications, Mathematics Discipline, Khulna University, Khulna, Bangladesh, 23rd December 2015, 22-26.
11. . Ndanusa, S. Abdulrahman and A. Abdulmalik, A Mathematical Model for Controlling the Spread of Ebola Virus Disease in Nigeria, International Journal of Humanities and Management Sciences, **3**(3) (2015), 144-148.
12. .M. Neilan and S. Lenhart, An Introduction to Optimal Control with an Application in Disease Modeling, DIMACS Series in Discrete Mathematics, **75** (2010), 67-81.
13. .C. Osemwinyen and A. Diakhaby, Mathematical Modelling of the Transmission Dynamics of Ebola Virus, Applied and Computational Mathematics, bf 4(4) (2015), 313-320.
14. . Pattyn, G. van der Groen, W. Jacob, P. Piot and G. Courteille, Isolation of Marburg-like virus from a case of haemorrhagic fever in Zaire, Lancet, **309**(8011), (1977) 573-574.
15. .R. Pringle, Virus taxonomy-San Diego 1998, Archives of Virology, **143**(7) (1998), 1449-1459.