Asian Research Journal of Mathematics
2(3): 1-10, 2017; Article no.ARJOM.31201
ISSN: 2456-477X

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Sensitivity Analysis of Ebola Virus Model

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Authors' contributions

This work was carried out in collaboration between the authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ARJOM/2017/31201
Editor(s):
(1) Igor Ya. Subbotin, Department of Mathematics, National University, LA, CA, USA.
Reviewers:
(1) Anonymous, Gujarat University, India.
(2) Sanjay Mishra, IFTM University, India.
Complete Peer review History: http://www.sciencedomain.org/review-history/17637

Original Research Article

Received: 26th December 2016
Accepted: 9th January 2017
Published: 27th January 2017

Abstract

A Mathematical model of $(S, E, I_u, I_d, I_s, R, D)$ is presented to study the dynamical spread of Ebola in the population. Existence of the Local Stability of the disease–free equilibrium (DFE) was investigated via the threshold parameter (Reproduction number R_0) obtained using the next generation matrix technique. The result shows that the DFE is asymptotically stable at Reproduction number less than unity $(R_0 < 1)$. Reasonable sets of values for the parameter in the model were compiled from existing literatures and Sensitivity analysis indices R_0 around the baseline parameter value were computed, which shows that the most sensitive parameter to R_0 is the recruitment rate π followed by the rate at which exposed individuals are isolated due to contact tracing σ . Furthermore, the numerical computation of R_0 gave a value of 0.16, and numerical simulation was obtained which illustrates the effect of control parameters on the various compartments of the model.

Keywords: Ebola; sensitivity; body fluids; reproduction number; $(S, E, I_u, I_d, I_s, R, D)$*; stability.*

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1 Introduction

Ebola Haemorrhagic fever now known as Ebola virus disease (EVD) named after the river in Democratic Republic of Congo (formerly Zaire), is a severe often fatal illness in human [1,2]. The first two simultaneous outbreak of Ebola appeared in 1976 in Nzara Sudan, and in Yambuku, Democratic Republic of Congo [1,3]. The latter was in a village which was located near the Ebola River, from which the disease takes its name. It is a virulent filo virus that is known to affect humans and primates. It is 1 of 3 members of the filovirdae family (filo virus), along with genus Marburg virus and genus Cueva virus. Ebola virus comprises of 5 distinct species namely: Bundibugyo Ebola Virus (BDBV), Zaire Ebola virus (EBOV), Reston Ebola Virus (RESTV), Sudan Ebola Virus (SUDV) and Taiforest Ebola Virus (TAFV). BDBV, EBOV, and SUDV have been associated with large EVD outbreak in Africa, whereas RESTV and TAFV have not. The RESTV species found in Philippines and China Republic can infect humans, but no illness or death in humans from the species has been reported till date except BDBV. EBOV and SVDV have the same number of mortality rate [4,5].

Ebola can be introduced into human population through close contact with the secretions, blood, organs or other bodily fluids of infected animals. Infection has been documented through the handling of infected chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead in the rainforest in Africa. It then spread in the community through human to human transmission, with infection resulting from direct contact with the blood, secretions, organs or other bodily fluids of infected people, and indirect contact with environments contaminated with such fluids [1,4]. The incubation period of this deadly disease is 2 – 21days and infectious period is 4 -10 days [6]. Ebola symptoms includes "sudden onset of high fever greater than 38.6 degree Celsius or 101.5 degree Fahrenheit, fatigue, muscle pain, stomach pain, diarrhea sore throat, abdominal pain, unexplained hemorrhage and headache". If not managed well, this then rapidly progresses to vomiting of blood, rash, symptoms of impaired Kidney and Liver function, and in some cases it leads to both internal and external bleeding [4,7]. Most infected individuals die within 10days of their initial infection [8]. Burial ceremonies in which mourners have direct contact with the body of the deceased person can also play a role in the transmission of Ebola [2,3,9].

The recent 2014 outbreak in West Africa reported that about 30% of infections were caused by a contact with the dead bodies that recently died of Ebola disease [2,10,11]. The number of dead bodies who recently died because of Ebola disease is related to the rate of the infection because of its burial process [2,10].

The threat posed by Ebola virus in human population initiated and prompted this research work to develop an epidemiological model that incorporated the dead individuals, infected undetected, infected detected and isolated individuals and to look into the Sensitivity analysis of the model.

2 Model Formulation

A dynamical system consisting ordinary differential equation is used to construct the Ebola disease model in this article. We assume that the human population is divided into seven (7) compartments namely: susceptible (S) exposed (E), Infected undetected (I_u), Infected detected (I_d), Infected isolated (I_s), Recovered (R), and death individuals (D). The govern model is given by the system of differential equations below:

$$\begin{aligned}
\frac{dS}{dt} &= \pi - \beta_1 S I_u - \beta_2 S I_d - \beta_3 S D - \mu S \\
\frac{dE}{dt} &= \beta_1 S I_u + \beta_2 S I_d + \beta_3 S D - \sigma E - \kappa E - \mu E \\
\frac{dI_u}{dt} &= (1-\omega)\kappa E - \gamma_1 I_u - \delta_u I_u - \mu I_u \\
\frac{dI_d}{dt} &= \omega\kappa E + \gamma_1 I_u - \gamma_2 I_d - \delta_d I_d - \mu I_d \\
\frac{dI_s}{dt} &= \sigma E + \gamma_2 I_d - \delta_s I_s - \alpha I_s - \mu I_s \\
\frac{dR}{dt} &= \alpha I_s - \mu R \\
\frac{dD}{dt} &= \delta_u I_u + \delta_d I_d + \delta_s I_s - \theta D
\end{aligned} \tag{1}$$

3 Analysis of the Model

3.1 Disease free equilibrium (DFE)

At equilibrium, (1) is set to be equal to zero.

That is: $$\frac{dS}{dt}=\frac{dE}{dt}=\frac{dI_u}{dt}=\frac{dI_d}{dt}=\frac{dI_s}{dt}=\frac{dR}{dt}=\frac{dD}{dt}=0 \quad (2)$$

The disease free equilibrium is obtained as:

$$(S,E,I_u,I_d,I_s,R,D)=\left(\frac{\pi}{\mu},0,0,0,0,0,0\right) \quad (3)$$

Table 1. Description of parameter of the model

Parameters	Description
π	Recruitment rate
β_2	Contact rate with undetected infected
β_2	Contact rate with detected infected
β_3	Contact rate with dead bodies
μ	Natural death rate
σ	The rate at which exposed individuals are isolated due to contact tracing
κ	Progression rate of individuals in exposed stage to active Ebola
ω	Endogenous reactivation rate
γ_1	Detection rate for infected undetected Individuals
γ_2	The rate at which Infected detected individuals are isolated
δ_u	Disease – induced death rate for undetected individuals
δ_d	Disease – induced death rate for detected individuals
δ_s	Disease – induced death rate for isolated infected individuals
α	Recovery rate of isolated individuals
θ	Burial rate

3.2 Basic reproduction number

Basic reproduction number plays a very important role in describing the qualitative analysis of the mathematical model of infectious disease. The basic reproduction number (R_0) measures the average number of secondary infected individual generated in his or her infectious period in the population of Susceptible [4]. It is known that if $R_0<1$, then the disease dies out and spread whenever it exceeds unity i. e $(R_0<1)$. Using the Next generation matrix techniques, the non–negative matrix F of the new infection terms (Transmission) and the non – singular matrix V of the other remaining transfer terms (Transition) are given by FV^{-1}:

Where:

$$F = \begin{pmatrix} 0 & \frac{\beta_1\pi}{\mu} & \frac{\beta_2\pi}{\mu} & 0 & \frac{\beta_3\pi}{\mu} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \qquad V = \begin{pmatrix} P_1 & 0 & 0 & 0 & 0 \\ -P_2 & P_3 & 0 & 0 & 0 \\ -\omega\kappa & -\gamma_1 & P_4 & 0 & 0 \\ -\sigma & 0 & -\gamma_2 & P_5 & 0 \\ 0 & -\delta_u & -\delta_d & -\delta_s & \theta \end{pmatrix} \tag{4}$$

Where: $P_1 = (\sigma + \kappa + \mu), P_2 = (1-\omega)\kappa, P_3 = (\gamma_1 + \delta_u + \mu), P_4 = (\gamma_2 + \delta_d + \mu), P_5 = (\delta_s + \alpha + \mu)$

The basic reproduction number, $R_0 = \rho(FV^{-1})$, is the spectral radius of the product FV^{-1}. Hence, for the model (1), we arrive at:

$$R_0 = \frac{\pi\left(\beta_1 P_2 P_4 P_5\theta + \kappa\omega\theta P_3 P_5\beta_2 + \theta P_2 P_5\beta_2\gamma_1 + \kappa\omega P_3 P_5\beta_3\delta_d + \kappa\omega P_3\beta_3\delta_s\gamma_2 + \sigma P_3 P_4\beta_3\delta_s + P_2 P_4 P_5\beta_3\delta_u + P_2 P_5\beta_3\delta_d\gamma_1 + P_2\beta_3\delta_s\gamma_1\gamma_2\right)}{\mu P_1 P_3 P_4 P_5\theta}$$

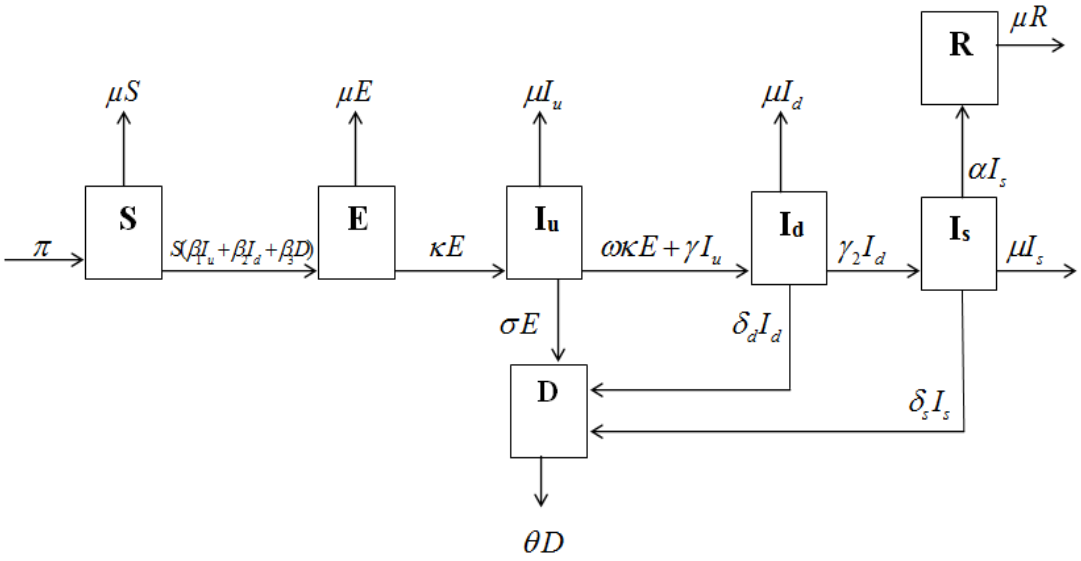

Fig. 1. The schematic illustration of the model

3.3 Local stability of the model

Using the basic reproduction number obtained for the model (1), we analyze the stability of the equilibrium point in the following result.

Theorem: The disease – free state, is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: The Jacobian matrix of the system (1) evaluated at the disease – free equilibrium point, obtained as

$$J=\begin{pmatrix} -\mu & 0 & -\frac{\beta_1\pi}{\mu} & -\frac{\beta_2\pi}{\mu} & 0 & 0 & -\frac{\beta_3\pi}{\mu} \\ 0 & -P_1 & \frac{\beta_1\pi}{\mu} & \frac{\beta_2\pi}{\mu} & 0 & 0 & \frac{\beta_3\pi}{\mu} \\ 0 & -P_2 & -P_3 & 0 & 0 & 0 & 0 \\ 0 & \omega\kappa & \gamma_1 & -P_4 & 0 & 0 & 0 \\ 0 & \sigma & 0 & \gamma_2 & -P_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha & -\mu & 0 \\ 0 & 0 & \delta_u & \delta_d & \delta_s & 0 & -\theta \end{pmatrix} \tag{5}$$

Where:

$$P_1=(\sigma+\kappa+\mu), P_2=(1-\omega)\kappa, P_3=(\gamma_1+\delta_u+\mu), P_4=(\gamma_2+\delta_d+\mu), P_5=(\delta_s+\alpha+\mu)$$

We need to show that all the eigenvalues of J are negative. The eigenvalues of the matrix J are the roots of the characteristic equation

$$\lambda^7+r_1\lambda^6+r_2\lambda^5+r_3\lambda^4+r_4\lambda^3+r_5\lambda^2+r_6\lambda+r_7=0 \tag{6}$$

Where

r_i (for $i=1,2...6$) are representative of some expressions

$$r_7=\pi\beta_1P_2P_4P_5\theta+\pi\kappa\omega\theta P_3P_5\beta_2+\pi\theta P_2P_5\beta_2\gamma_1+\pi\kappa\omega P_3P_5\beta_3\delta_d+\pi\kappa\omega P_3\beta_3\delta_s\gamma_2+\pi\sigma P_3P_4\beta_3\delta_s+$$
$$\pi P_2P_4P_5\beta_3\delta_u+\pi P_2P_5\beta_3\delta_d\gamma_1+\pi P_2\beta_3\delta_s\gamma_1\gamma_2-\mu\theta P_1P_3P_4P_5$$

Employing the Descartes' rule of signs [11], which states that all roots of polynomial (6) have negative real part and distinct, if and only if the coefficient r_i are negative for $i=1,2,3,4,5,6,7$.

Hence, it is *locally Asymptotically stable* if $r_7<0$:

Such that:

$$\begin{pmatrix}\pi\beta_1P_2P_4P_5\theta+\pi\kappa\omega\theta P_3P_5\beta_2+\pi\theta P_2P_5\beta_2\gamma_1+\pi\kappa\omega P_3P_5\beta_3\delta_d+\pi\kappa\omega P_3\beta_3\delta_s\gamma_2+\pi\sigma P_3P_4\beta_3\delta_s+\\ \pi P_2P_4P_5\beta_3\delta_u+\pi P_2P_5\beta_3\delta_d\gamma_1+\pi P_2\beta_3\delta_s\gamma_1\gamma_2-\mu\theta P_1P_3P_4P_5\end{pmatrix}<0 \tag{7}$$

Further simplification in terms of reproduction number yields

$$\frac{\pi\left(\beta_1P_2P_4P_5\theta+\kappa\omega\theta P_3P_5\beta_2+\theta P_2P_5\beta_2\gamma_1+\kappa\omega P_3P_5\beta_3\delta_d+\kappa\omega P_3\beta_3\delta_s\gamma_2+\sigma P_3P_4\beta_3\delta_s+P_2P_4P_5\beta_3\delta_u+P_2P_5\beta_3\delta_d\gamma_1+P_2\beta_3\delta_s\gamma_1\gamma_2\right)}{\mu P_1P_3P_4P_5\theta}<1 \tag{8}$$

Equation (8) implies $R_0<1$

Therefore, all the eigenvalues of the Jacobian matrix J have negative real parts when $R_0 < 1$, hence the disease-free equilibrium point is locally Asymptotically stable.

Table 2. Baseline parameters and values used in simulation

Parameters	Values	Reference
β_1	0.000118	Assumed
β_2	0.000118	Assumed
β_3	0.000118	Assumed
μ	0.02	[4]
σ	0.2	[4]
κ	0.6	[4]
ω	0.03	[4]
γ_1	0.12	[4]
γ_2	0.12	[4]
δ_u	0.937	[6]
δ_d	0.937	[6]
δ_s	0.937	[6]
α	0.225	Assumed
θ	0.8	[4]

4 Sensitivity Analysis

It is necessary to conduct an investigation to determine how sensitive the threshold quantity basic reproduction number is with respect to its parameters, this will facilitate us to know which of the parameters causes most reduction and most high impact on the reproduction number R_0. This analysis tells us how crucial and important each of the parameter is to the disease transmission, and this will helps the public health authorities in focusing on a well posed intervention strategy for preventing and controlling the spread of the disease in the population. The normalized forward sensitivity index of the reproduction number with respect to its parameter is computed.

Definition: If a variable 'c' depends differentiably on a parameter 'w', then the normalized forward sensitivity index of 'c' with respect to 'w' is denoted by X_c, which is defined as:

$$X_c = \frac{c}{w}\frac{\partial w}{\partial c}$$

As we have explicit formula for R_0, an analytical expression for the sensitive of R_0 is derived as

$$X_w^{R_0} = \frac{\partial R_0}{\partial w} \times \frac{w}{R_0} \tag{9}$$

The maple code was used to generate the Sensitivity index and the results obtained are given in Table 3 below:

Table 3. Sensitivity index of the basic reproduction number R_0

	Parameter	Sign	Value
1	π	+	1
2	β_1	+	0.24
3	β_2	+	0.034
4	β_3	+	0.415
5	μ	-	-0.54
6	σ	-	-0.61
7	κ	+	0.679
8	ω	-	-0.068
9	γ_1	-	-0.246
10	γ_2	-	-0.005
11	δ_u	-	-0.12
12	δ_d	-	-0.028
13	δ_s	+	0.019
14	α	-	-0.176
15	θ	-	-0.117

The positive sign of the sensitivity index of the basic reproduction number to the model parameters indicates that an increase (or decrease) in the value of each parameter in this category will leads to increase (or decrease) in the basic reproduction number of the disease, likewise the negative sign of the sensitivity index of the basic reproduction number to the model parameters indicates that an increase (or decrease) in the value of each parameter in this category will leads to decrease (or increase) in the basic reproduction number of the disease in the population. Thus, the index table above reveals that the most Sensitive parameter of our Reproduction number is the recruitment rate (π) and the rate at which exposed individuals are isolated due to contact tracing (σ).

5 Numerical Results and Discussion

In this phase, we study numerically the expression/behaviour of the system (1) employing some of the parameter values compatible with Ebola [4], [10] as given in Table 2 and by considering the initial conditions, $S(0)=1000,\ E(0)=500,\ I_u(0)=300,\ I_d(0)=250,\ I_s(0)=150,\ R(0)=100,\ D(0)=20.$

The numerical simulations are evaluated using the Rungi – Kutta order 4 embedded in mathematical software (Maple 18).

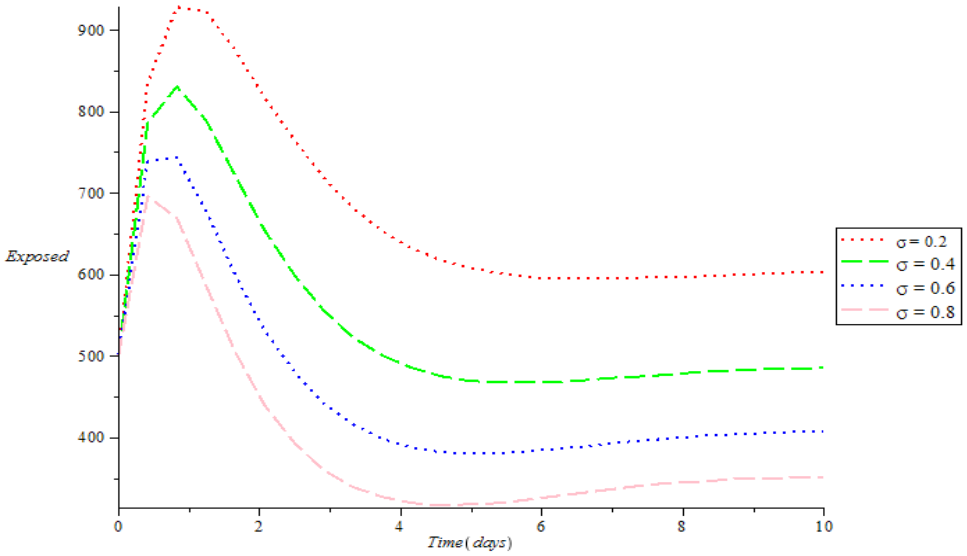

Fig. 2. The graph of exposed population against time where:
$\pi = 500, \beta_1 = 0.000118, \beta_2 = 0.000118, \beta_3 = 0.000118, \mu = 0.02, \sigma = 0.2...0.8, \kappa = 0.6, \omega = 0.03,$
$\gamma_1 = 0.12, \gamma_2 = 0.12, \delta_u = 0.937, \delta_d = 0.937, \delta_s = 0.937, \alpha = 0.225, \theta = 0.8$

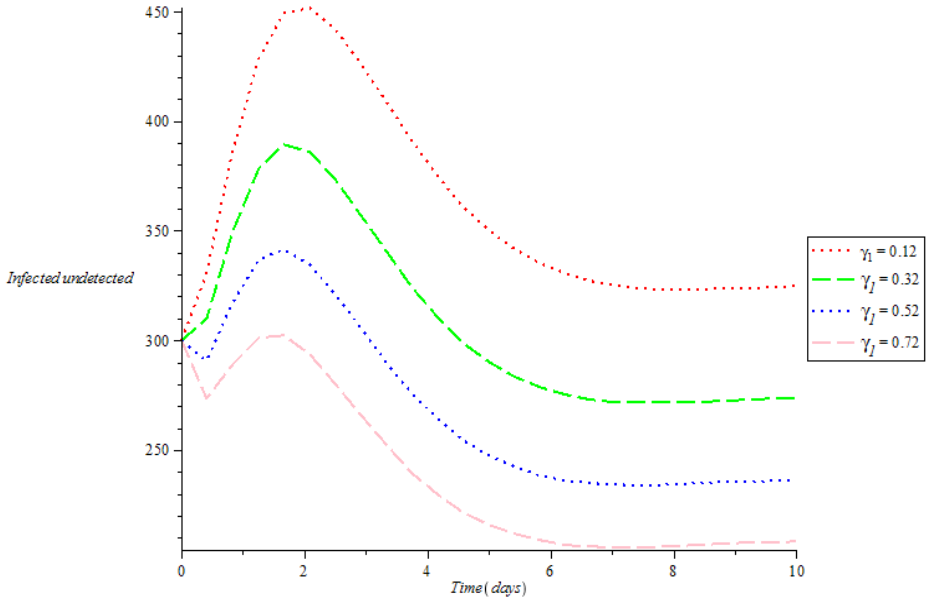

Fig. 3. The graph of Infected Undetected population against time where:
$\pi = 500, \beta_1 = 0.000118, \beta_2 = 0.000118, \beta_3 = 0.000118, \mu = 0.02, \sigma = 0.2, \kappa = 0.6, \omega = 0.03,$
$\gamma_1 = 0.12...0.72, \gamma_2 = 0.12, \delta_u = 0.937, \delta_d = 0.937, \delta_s = 0.937, \alpha = 0.225, \theta = 0.8$

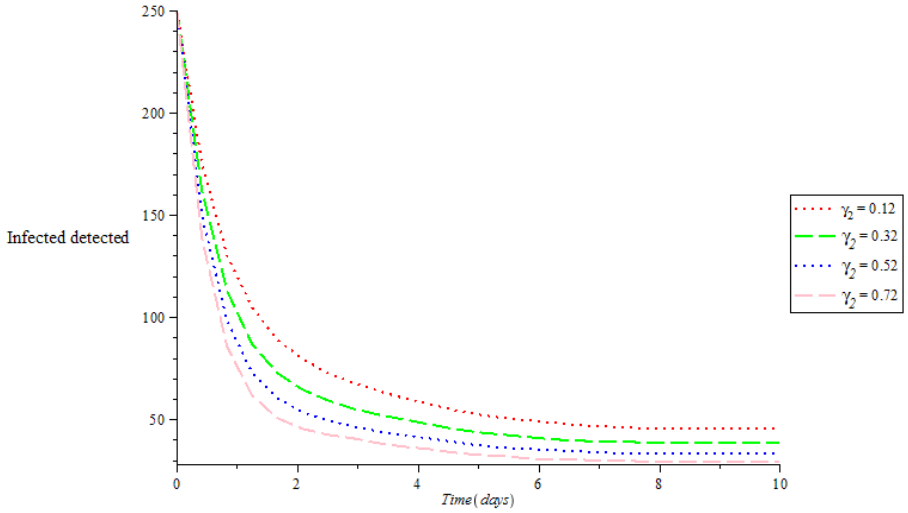

Fig. 4. The graph of infected detected population against time where:
$\pi = 500, \beta_1 = 0.000118, \beta_2 = 0.000118, \beta_3 = 0.000118, \mu = 0.02, \sigma = 0.2, \kappa = 0.6, \omega = 0.03,$
$\gamma_1 = 0.12, \gamma_2 = 0.12...0.72, \delta_u = 0.937, \delta_d = 0.937, \delta_s = 0.937, \alpha = 0.225, \theta = 0.8$

6 Conclusion

This paper presented and analyzed an epidemic model of $(S, E, I_u, I_d, I_s, R, D)$ for Ebola virus disease to gain more insight into the dynamical spread of the disease in the population. The results of the analysis are highlighted as follows:

(i) The research shows the existence of the disease free.
(ii) The disease free equilibrium of the model is locally asymptotically stable when the reproduction number is less than unity i.e. $(R_0 < 1)$.
(iii) Sensitivity analysis reveals that the most sensitive parameter to the basic reproduction number R_0 is the recruitment rate π, followed by the rate at which exposed individuals are isolated due to contact tracing σ.

Numerical simulation shows the effects of the control parameters on some of the various compartment of the model. Fig. 2 shows the effect of σ in the exposed population. It shows that when the isolation of Exposed individual is sufficiently large, it reduces the exposed individuals and increases the isolated individuals tremendously, while Fig. 3 shows the effect of γ_1 on the infected undetected population. It shows that when the detection rate of undetected individuals due to contact tracing is very low, the infected undetected individuals increases tremendously which will cause the total amount of infected individuals to increase in that population. Fig. 4 shows the effect of γ_2 on the infected detected population. It shows that the higher the rate at which infected detected individuals move to isolated individuals due to isolation techniques, the lower would be the infected detected individuals in the population.

7 Further Research

The basic reproduction number computed (0.16) is low; still the virus is fast spreading in the countries in the world. This calls for a further in-depth study on the Bifurcation analysis which will place a sensory that reducing the reproduction number R_0 is not enough to show that the virus will be contained.

Competing Interests

Authors have declared that no competing interests exist.

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DOI: 10.15224/ 978-1-63248-075-0-41

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