Available online www.jsaer.com

***Journal of Scientific and Engineering Research*, 2018, 5(6):1-9**

Research Article

ISSN: 2394-2630
CODEN(USA): JSERBR

Mathematical Model for Lassa Fever and Sensitivity Analysis

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Abstract In this paper, Lassa fever disease model was formulated. The model was divided into five compartments susceptible (S), latent (L), infected (I), isolated (I_s) and recovered (R) classes. The equilibrium states, basic reproduction number R_0 were obtained using generation matrix and their stabilities were analyzed using Descartes' rule of sign and comparison test. The results show that the disease free equilibrium is locally and globally asymptotically stable when $\beta\pi\gamma < \mu(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2)$. Finally, sensitivity analysis was carried out and it was shown that the parameter β is the most sensitive.

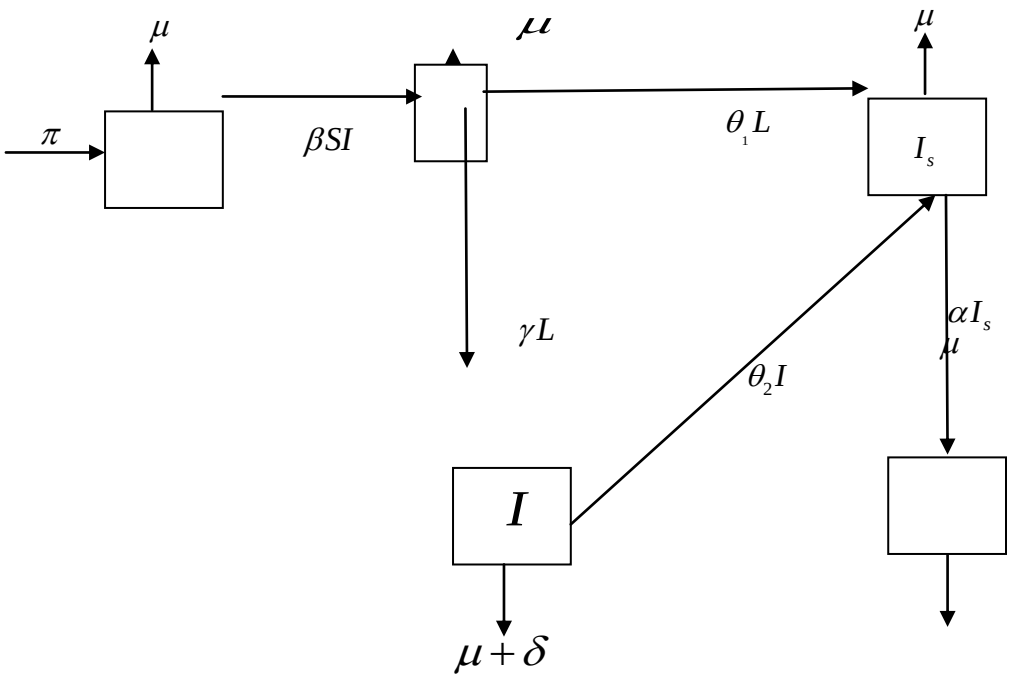
Keywords Lassa fever, Sensitivity, Basic reproduction number, isolated class and equilibrium

1. Introduction

Lassa fever is an acute viral illness cause by Lassa virus and a zoonotic disease which is transmitted from an infected animal to human, person to person and occurs in the dry season as a result of dust particles from dead rats. The virus is known as Mastomy (Mastomy Natalensis), it can also be defined as a viral disease that attacks the liver, nervous system, spleen and kidney. It is an acute viral hemorrhagic fever (VHF) first isolated in a town called Lassa in the Yedseram River Valley in the present Borno State of Northern Nigeria in 1969 [1]. Many researchers have contributed and devoted a lot to of time to the investigation of Lassa fever. Some of the researchers are Okuonghae and Okuonghae [2] formulated a SIS model coupled to a population of rat species, for the transmission of Lassa fever disease. The equilibrium states of the model were obtained and examined the endemic and epidemic situations. They further calculated the basic reproductive number and gave conditions for disease outbreak. Onuorah et al [3] developed a Lassa fever model using the sex structure approach. Their model represented the transmission dynamics of the Lassa fever disease using a set of ordinary differential equations. They obtained the Disease free equilibrium. Their computation of basic reproduction number is 0.129 which is less than the one Castilo – Chavez et al [4] was used to obtain the Global Stability of Disease Free Equilibrium. James et al [5] developed the dynamics transmission of Lassa fever disease and showed that the zero equilibrium is stable when the birth rate of the human population is less than the death rate. Similarly, when the birth rate of the vector is less than the death rate. Omale and Edibo [6] studied the mathematical model for Lassa fever transmission with control strategies it was shown that the disease free equilibrium is locally asymptotically stable. In this paper the mathematical model of Lassa fever with isolated class is considered. The threat posed by Lassa virus in human population initiated and prompted this research work to develop an epidemiological model that incorporated the infected detected and isolated individuals and to obtain the Sensitivity analysis of the model.

2 Model Formulations

The model is divided into five compartments namely susceptible (S), latent (L), infected (I), isolated (I_s) and recovered (R) classes.



$$\frac{dS}{dt} = \pi - \beta IS - \mu S \tag{2.1}$$

$$\frac{dL}{dt} = \beta SI - \gamma L - \mu L - \theta_1 L \tag{2.2}$$

$$\frac{dI}{dt} = \gamma L - \mu I - \delta I - \theta_2 I \tag{2.3}$$

$$\frac{dI_s}{dt} = \theta_1 L + \theta_2 I - \mu I_s - \alpha I_s \tag{2.4}$$

$$\frac{dR}{dt} = \alpha I_s - \mu R \tag{2.5}$$

Where the parameters are as follows:

π = Recruitment rate β = Contact rate

μ = Natural death rate γ = Progression rate of individuals to infections class

θ_1 = Rate at which latently infected are isolated due to tracing

θ_2 = Rate at which infections individuals are isolated δ = Death due to the disease

α = Recovery rate of the isolated individuals S = Susceptible class

L = Latently class I = Infected class I_s = Isolated class

R = Recovered class

2.2 The Positive Invariant Region

The total population size is N= S+L+I+I_s +R (2.6)

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dL}{dt} + \frac{dI}{dt} + \frac{dI_s}{dt} + \frac{dR}{dt}$$

$$\pi - \mu(S + L + I + I_s + R) - \delta I \tag{2.7}$$

The positive invariant region can be obtained by using a Theorem

Theorem 2.1 the solutions of the system (2.1)-(2.5) are feasible for $t < 0$ if they enter the region D

Proof: Let $D = \{S, L, I, I_{s,}, R\} \in R^5$ be any solution of the system (2.1)-(2.5) with non-zero initial conditions. Assumed that there is no disease (2.7) becomes

$$\frac{dN}{dt} = \pi - \mu N \tag{2.8}$$

So that (2.8) gives

$$\frac{dN}{dt} + \mu N = \pi \tag{2.9}$$

On solving (2.9) and applying the initial condition $t = 0, N(0) = N_0$ yields

$$N \le \frac{\pi}{\mu} + \left(N_0 - \frac{\pi}{\mu} \right) e^{-\mu t} \tag{2.10}$$

As $t \to \infty$ in (2.10) the population N approaches $\frac{\pi}{\mu}$. Hence all feasible solution of(2.1)-(2.5) enter the region $D = \left\{ (S, L, I, I_{s,}, R) \in R^5 : S(0) \ge 0, L(0) \ge 0, I(0) \ge 0, I_s(0) \ge 0, R(0) \ge 0, N \le \frac{\pi}{\mu} \right\}$. Therefore, the region D is positively invariant and equations (2.1) to (2.5) are epidemiologically meaningful and mathematically well-posed in the domain D.

2.3 Positivity Solution

Lemma 1: consider the initial $\{S(0) \ge 0, L(0) \ge 0, I(0) \ge 0, I_s(0) \ge 0, R(0) \ge 0\} \in D$ then the solution set $(S, L, I, I_{s,}, R)$ of the system of equations (2.1)-(2.5) is positive for all $t > 0$

Proof: from (2.1)

$$\frac{dS}{dt} = \pi - \beta IS - \mu S \ge -\mu S$$

$$\frac{ds}{dt} \ge -\mu S \tag{2.11}$$

So that the solution to (2.11) after using the initial becomes

$$S(t) = S(0) e^{-\mu t} \ge 0$$

From (2.2)

$$\frac{dL}{dt} = \beta SI - (\gamma + \mu + \theta_1) L \ge -(\gamma + \mu + \theta_1) L$$

$$\frac{dL}{dt} \ge -(\gamma + \mu + \theta_1) L \tag{2.12}$$

The solution to (2.12) with the application of the initial condition gives $L(t) = L(0) e^{-(\gamma + \mu + \theta_1)t} \ge 0$

Similarly, the remain equations can be verified that they are all positive for $t > 0$. Since $e^{\theta} > 0$ for all $\theta \in R$

2.4 Equilibrium States

2.4.1 The Disease Free Equilibrium (DFE) State: is absence of infection

Therefore the disease Free State equilibrium is $E_0 = \left(\frac{\pi}{\mu}, 0, 0, 0, 0 \right)$.

2.4.2 The Endemic Equilibrium State is when there is infection

Therefore the disease endemic state equilibrium is

$$E_e(S,L,I,I_s,R)=\begin{pmatrix} \dfrac{(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)}{\gamma\beta}, \dfrac{\gamma\beta\pi-\mu(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)}{\gamma\beta(\gamma+\mu+\theta_1)}, \\ \dfrac{\gamma\beta\pi-\mu(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)}{\beta(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)}, \\ \dfrac{(\theta_1(\gamma+\mu+\theta_1)+\theta_2\gamma)[\gamma\beta\pi-\mu(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)]}{\gamma\beta(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)}, \\ \dfrac{\alpha(\theta_1(\gamma+\mu+\theta_1)+\theta_2\gamma)[\gamma\beta\pi-\mu(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)]}{\mu\gamma\beta(\gamma+\mu+\theta_1)(\delta+\mu+\theta_2)} \end{pmatrix} \quad (2.13)$$

2.5 Basic Reproduction Number (R_0)

The basic reproduction R_0, is the most important threshold concerning any infectious disease, it helps in determining whether or not an infectious disease will spread through population. Since our focus is the population that spread the infection, equation (2.1) – (2.4) were considered, using Next Generation Matrix to obtain the basic reproduction number.

$$R_0=\rho\left(FV^{-1}\right)$$

$$FV^{-1}=\begin{pmatrix} \dfrac{\beta\pi\gamma}{\mu(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2)} & \dfrac{\beta\pi}{\mu(\mu+\delta+\theta_2)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$\Rightarrow R_0=\frac{\beta\pi\gamma}{\mu(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2)} \quad (2.14)$$

3. Stability Analysis of the Model

THEOREM 1: The disease free equilibrium of the system $(2.1-2.5)$ is locally asymptotically stable when $R_0<1.$

Proof: The Jacobian matrix of the system at disease free equilibrium is

$$J\left(\frac{\pi}{\mu},0,0,0,0\right)=\begin{bmatrix} -\mu & 0 & -\dfrac{\beta\pi}{\mu} & 0 & 0 \\ 0 & -(\gamma+\mu+\theta_1) & \dfrac{\beta\pi}{\mu} & 0 & 0 \\ 0 & \gamma & -(\mu+\delta+\theta_2) & 0 & 0 \\ 0 & \theta_1 & \theta_2 & -(\gamma+\alpha) & 0 \\ 0 & 0 & 0 & \alpha & -\mu \end{bmatrix}$$

Thus, the characteristics equation is given by

$$\left|JE_0 - \lambda I\right| = \begin{bmatrix} -\mu-\lambda & 0 & -\frac{\beta\pi}{\mu} & 0 & 0 \\ 0 & -(\gamma+\mu+\theta_1)-\lambda & \frac{\beta\pi}{\mu} & 0 & 0 \\ 0 & \gamma & -(\mu+\delta+\theta_2)-\lambda & 0 & 0 \\ 0 & \theta_1 & \theta_2 & -(\gamma+\alpha)-\lambda & 0 \\ 0 & 0 & 0 & \alpha & -\mu-\lambda \end{bmatrix} = 0 \quad (2.15)$$

$\lambda_1 = -\mu, \lambda_2 = -\mu,\ \lambda_3 = -(\mu+\alpha)$ and

$$\lambda^2 + \left[(\gamma+\mu+\theta_1)+(\mu+\delta+\theta_2)\right]\lambda + \left[(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2) - \frac{\beta\pi\gamma}{\mu}\right] = 0 \quad (2.16)$$

By Descartes' rule of signs: Number of positive roots of any polynomials is equal to the number of times the signs of coefficients of each term changes.

For the roots of equation (2.16) to be negative it implies that

$$(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2) - \frac{\beta\pi\gamma}{\mu} > 0$$

$$\frac{\beta\pi\gamma}{\mu(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2)} < 1 \quad (2.17)$$

This implies that the disease free equilibrium is locally asymptotically Stable since $\beta\pi\gamma < \mu(\gamma+\mu+\theta_1)(\mu+\delta+\theta_2)$

THEOREM 2:- The disease free equilibrium of the system [2.1-2.5] is globally asymptotically stable whenever $R_0 < 1$ but unstable if $R_0 > 1$.

Proof: using the Comparison theorem [7] for the global stability. By defining comparison method $\left|F - V\right|$

$$F = \begin{pmatrix} 0 & \frac{\beta\pi}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} (\gamma+\mu+\theta_1) & 0 & 0 \\ -\gamma & (\mu+\delta+\theta_2) & 0 \\ -\theta_1 & -\theta_2 & (\mu+\alpha) \end{pmatrix} \quad (2.18)$$

$$\left|(F-V) - \lambda I\right| = \begin{vmatrix} -(\gamma+\mu+\theta_1)-\lambda & \frac{\beta\pi}{\mu} & 0 \\ \gamma & -(\mu+\delta+\theta_2)-\lambda & 0 \\ \theta_1 & \theta_2 & -(\mu+\alpha)-\lambda \end{vmatrix} = 0 \quad (2.19)$$

The Characteristics polynomial of equation (2,20) gives

$$\lambda_1 = -(\mu+\alpha) \quad (2.20a)$$

and $$\left[\lambda^2+\left(\left(\gamma+\mu+\theta_1\right)+\left(\mu+\delta+\theta_2\right)\right)\lambda+\left(\left(\gamma+\mu+\theta_1\right)\left(\mu+\delta+\theta_2\right)-\frac{\beta\pi\gamma}{\mu}\right)\right]=0 \quad (2.20b)$$

By applying Descartes rule of signs to equation (2.20b) gives

$$\frac{\beta\pi\gamma}{\mu\left(\gamma+\mu+\theta_1\right)\left(\mu+\delta+\theta_2\right)}<1$$

$$\Rightarrow R_0<1 \quad (2.22)$$

Thus, by the comparison method, the disease free equilibrium is Globally Asymptotically Stable.

Table 1: Baseline parameter values for the model (2.1) – (2.5)

Parameter	Values	References
β	0.05	[3]
π	0.15	[3]
γ	0.9	[3]
μ	0.02	[8]
θ_1	0.5	[3]
θ_2	0.6	[3]
δ	0.3	[3]
α	0.6	[3]

Sensitivity Analysis

It is necessary to determine how sensitive the threshold quantity basic reproductive number with respect to its parameters. This analysis reveals how crucial each of the parameter is to the disease transmission. Therefore, the sensitive index is defined using partial derivatives by

$$\Gamma_w^{R_0}=\frac{\partial R_0}{\partial w}\times\frac{w}{R_0} \quad (2.23)$$

Where the normalized forward sensitivity index of R_0 that depends differentially on a parameter w

Table 2: Sensitivity indices of the basic Reproduction number R_0

S/N	Parameter	Sign	Result
1	β	$+ve$	1
2	π	$+ve$	0.9999999999806459
3	γ	$+ve$	0.3661971829
4	μ	$-ve$	-1.035823637
5	θ_1	$-ve$	-0.3521126761
6	θ_2	$-ve$	-0.6521739128
7	δ	$-ve$	-0.3260869564

Numerical Simulation

In this study, the numerical solution for the five compartments model (2.1) – (2.5) were obtained using some of the parameter values as given in Table 1. The simulations were conducted using the Runge-Kuta method (rkf45) embedded in Maple 13.

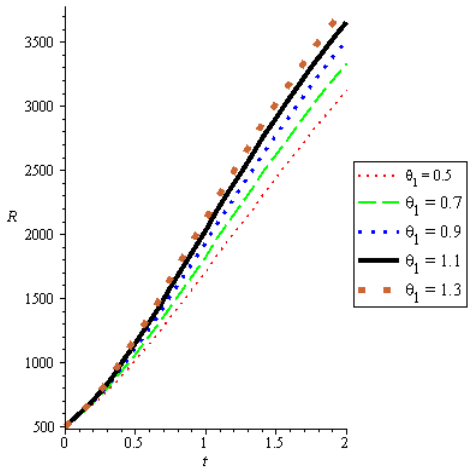


Figure 1: The graph of Recovery rate $R(t)$ *against time* t *for different values of rate at which latently infected are isolated due to tracing.*

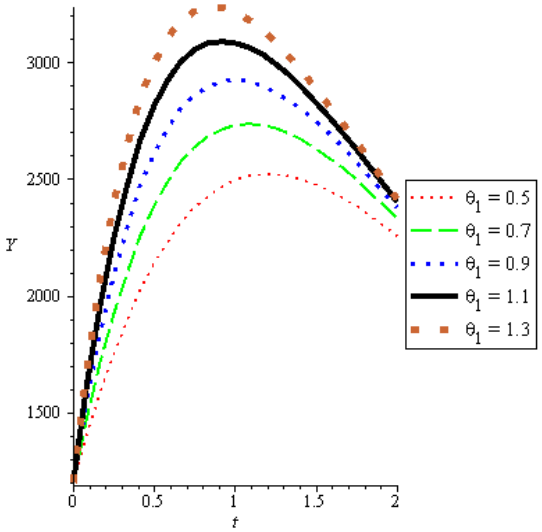


Figure 2: The graph of isolated class $Y(t)$ *against time* t *for different values of rate at which latently infected are isolated due to tracing*

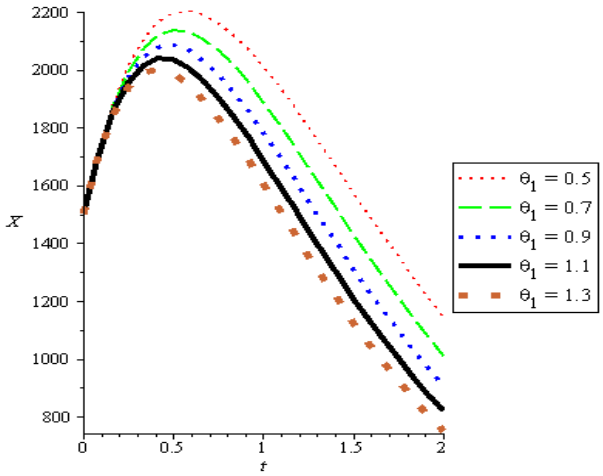


Figure 3: The graph of infected class $X(t)$ *against time* t *for different values of rate at which latently infected are isolated due to tracing.*

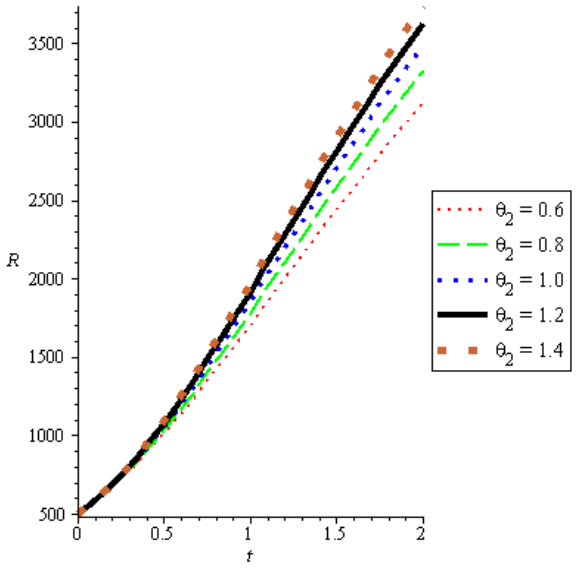


Figure 4: The graph of Recovered class $R(t)$ *against time* t *, with initial condition 500, varying rate at which infectious individuals are isolated.*

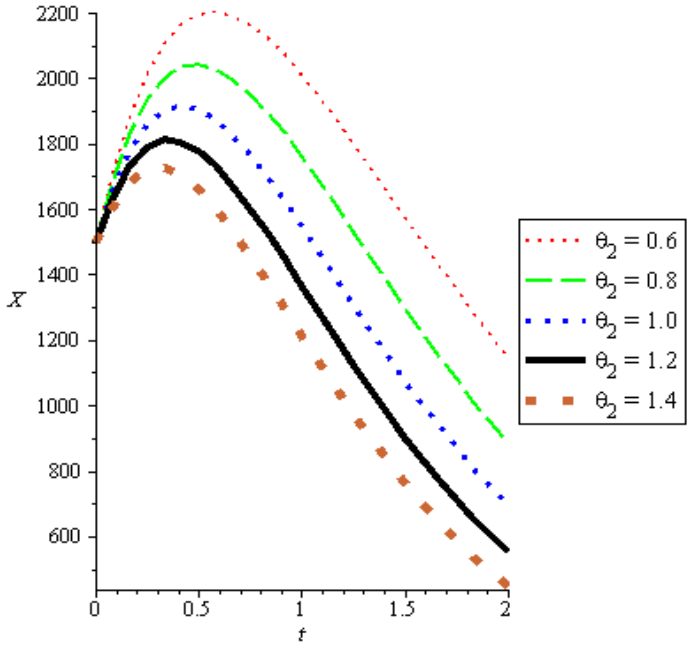


Figure 5: The graph of isolated class $X(t)$ *against time* t *for different values of rate at which the infections individuals are isolated*

4. Discussion of Results

Figure 1 shows the rate at which latently infected isolated increase the recovered class, which implied that there will be reduction in number of infected individuals. Figure 2 shows the isolated class against time, with different values of rate at which latently infected are isolated, the isolated class also increases. Figure 3 reveals that the latently infected are isolated increases and the infected class decreases. Figure 4 shows the Recovered class against time, with different values of rate at which infectious individuals increases the isolated, therefore, increases the Recovered class. Figure 5 shows the isolated class against time, with different values of rate at which infections individuals are isolated, the isolated class decreases and they were moving to the recovery class faster.

Conclusion

A mathematical model of five compartments was formulated. The disease free equilibrium point of the model was performed. The Local and Global stability was obtained and analyzed based on the basic reproduction number which shows that $R_0 < 1$. The sensitivity analysis shows that the most sensitive parameters to the basic reproduction number R_0 are the contact rate β

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