Stability Analysis of Lassa fever with Quarantine and Permanent Immunity

Tolulope O. James
Department of Mathematics,
Kebbi StateUniversity of Science and Technology,
Aleiro, Kebbi State,
Nigeria
Email tolujam@yahoo.com

Akinyemi,S.T.
Department of Mathematics
University of Ilorin,
Kwara State,
Nigeria
Email: Sammysalt047@gmail.com

BamideleOluwade
Department of Computer Science,
University of Ilorin,
Ilorin,Kwara State,
Nigeria
Email: deleoluwade@yahoo.com

ABSTRACT

A deterministic model for Lassa fever transmission in the presence of quarantine and permanent immunity ispresented and analyzed.The model was validated for existence and uniqueness of solution. The threshold parameter for disease eradication, R_0 was computed and used to investigate its global stability using Lyapunov functionsuchthat whenever $R_0 < 1$, the disease can be eradicated.

Keywords: Lassa fever, quarantine,permanent immunity,existence and uniqueness of solution, stability.

1. INTRODUCTION

Lassa fever is an acute viral hemorrhagic fever named after a town in Borno State, Nigeriain 1969. It is a zoonotic disease (i.e. a disease which can be transmitted from an animal to man)that attacks the nervous system, spleen, liver and kidney etc. In 2014, Lassa fever was endemic in Benin, Guinea, Liberia, SierraLeone and parts of Nigeria. The Mastomy rat is the animal reservoir of Lassa virus that usually infects human, when exposed to the host's urine and faeces. Lassa fever is also transmitted through direct contact with the blood, urine, faeces or other bodily secretions of an infected person.It takes six to twenty one days for the symptoms of Lassa fever

to be apparent, which usually begin with fever, sore throat,headache,chest pain etc,while at chronic stage,low blood pressure, facialswelling, bleeding from mouth,nose,vagina andgastrointestinal tract infectionmay develop (WHO, 2015).

Since ancient time, isolation/quarantine has been a major strategy in controlling the spread of infectious diseases such as leprosy. The essence of isolation is to reduce the chances of an healthy individual coming in contact with an infected human, though this may not eradicate the disease (Gummel, 2009).In the absence or limited access to pharmaceutical interventions such as vaccines and treatment, isolation remains one of the best choices of control strategy to reduce the transmission rate of infectiousdisease (WHO, 2007).The effect of acquiring immunity, be it permanent or temporal have been of great interest to researchers, aimed at gaining better insight into the complex transmission dynamics of infectious diseases (Li et al., 1999;Moghadas and Gummel, 2003; El-Doma,2006; Kimbir,2004).However for SIR (Susceptible-Infected-Recovered) and SEIR (Susceptible-Exposed-Infected-Recovered) models, recovered individuals are assumed to acquire permanent immunity due to treatment or vaccine and can no longer become susceptible to the disease. Several authors (Okuonghae and Okuonghae,2006;Inyama,2009; Bawa et al.,2013;James et al.,2015;) have also studied Lassa fever transmission mathematically, in the presence of vital factors that may trigger or curtail its prevalence.

In this paper, the stability of a model of lassa fever with quarantine and permanent immunity is analyzed. That is, quarantine/isolation and permanent immunity is introducedinto the work done in(Bawa et al.,2013).It should be noted thatthe effect of quarantine in infectious models with little or no consideration to Lassa feverwas studied in (Gummel, 2009; Hethcote et al.,2002).An earlier general work presents a necessary condition for the qualitative stability of a system of differential equations (Oluwade et al.,2001).The rest of this paper is organized as follows:Section 2 presents the model formulation. In Section 3, existence and uniqueness results are presented while in Section 4, results on local and global stability of disease-free equilibrium are stated. Section 5 concludes the paper.

2.MODEL FORMULATION

The model is constructed by first dividing the total human population N_H into four mutually exclusive compartments, which are the susceptible human (S_H) ,unquarantine (I_H) individuals, quarantine (I_Q) individuals andpermanent immune individuals(recovered) (R) .Infant reservoir (I_R) and adult reservoir (A_R) are the subclasses of the total reservoir population (N_R) and V denote the population ofLassa virus in the environment.

Basic Assumption

i) Humans are only recruited into the susceptible class.

ii)Theforce of infection is given by a standard incidence as

$$\left(\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N}\right) \quad (1)$$

where N is the population and the constants $\beta_1, \beta_2, \beta_3, \beta_4 =$ Effective contact rate of susceptible human with unquarantine, quarantine individuals, adult reservoirs and lassa virus in the environment respectively.

iii) Individuals moved to the R only from (I_H) and (I_Q) due to permanent immunity confer on them as a result of effective treatment.

The described model are governed by the following differential equations.

$$\begin{aligned}
\frac{dS_H}{dt} &= b_H N_H - \left(\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N}\right) S_H - \mu_H S_H \\
\frac{dI_H}{dt} &= \left(\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N}\right) S_H - \left(\theta + \gamma_1 + \mu_H + \delta_H\right) I_H \\
\frac{dI_Q}{dt} &= \theta I_H - \left(\gamma_2 + \mu_H + \delta_H\right) I_Q \\
\frac{dR}{dt} &= \gamma_1 I_H + \gamma_2 I_Q - \mu_H R \\
\frac{dI_R}{dt} &= b_R A_R - \left(\mu_R + \delta_R + \sigma\right) I_R \\
\frac{dA_R}{dt} &= \sigma I_R - \left(\mu_R + \delta_R\right) A_R \\
\frac{dV}{dt} &= e_R A_R + e_Q I_Q + e_H I_H - \phi V
\end{aligned} \quad (2)$$

The R compartment appeared only once,hence it won't be considered in the analysis in this paper, where:

$S_H =$ Susceptible human

$I_H =$ Unquarantine human

$I_Q =$ Quarantine human

$I_R =$ Infant reservoirs

$A_R =$ Adult reservoirs

$N_H =$ Total human population

N_R = Total reservoir population

b_H = Recruitment rate of human

b_R = Recruitment rate of reservoirs

μ_H , μ_R = Natural death rate of human and reservoirs respectively.

δ_H = Lassa induced death rate of human.

δ_R = Mortality rate of reservoirs due to hunting

$\beta_1, \beta_2, \beta_3, \beta_4$ = Effective contact rate of susceptible human with unquarantine,quarantine individuals,adult reservoirs and lassa virus in the environment respectively.

θ = Progression rate from I_H to I_Q .

γ_1, γ_2 = Progression rate from I_H and I_Q to R respectively due to permanent immunity obtained from effective treatment.

σ = Progression rate from I_R to A_R .

$e_{H,} e_{Q,} e_R$ = Shedding rate of Lassa virus into the environment from I_H, I_Q and A_R respectively

3.EXISTENCE AND UNIQUENESS RESULTS.

First, we formulate atheorem on theexistence of aunique solution of system (3):

$$\left.\begin{aligned} x_1' &= f_1(t, x_1, \cdots, x_n) \\ x_2' &= f_2(t, x_1, \cdots, x_n) \\ &\vdots \\ x_n' &= f_n(t, x_1, \cdots, x_n) \end{aligned}\right\} \tag{3}$$

and establish the proof.

The above may be expressed in a compact form as

$$x_i' = f_i(t, x), x(t_0) = x_0, i = 1, \cdots, n \tag{4}$$

Definition3.1

Let D denote the region

$$|t - t_0| \le a, \ \| x - x_0 \| \le b, \ x = (x_1, x_2, \cdots, x_n), \ x_0 = (x_{10}, x_{20}, \cdots, x_n) \tag{5}$$

and suppose that $f(t, u)$ satisfies Lipschitz condition.

$$\| f(t,x_1) - f(t,x_2) \| \leq k \| x_1 - x_2 \| \tag{6}$$

whenever the pairs (t,x_1) and (t,x_2) belong to D, where k is a positive constant. Then, there is a constant $\delta > 0$ such that there exists a unique continuous vector solution $\underline{x}(t)$ of the system (3) in the interval $|t - t_0| \leq \delta$. It is essential to note that condition (7) is satisfied by the requirement that $\frac{\partial f_i}{\partial x_j}$ $i, j = 1,2,\cdots,n$ are continuous and bounded in D.

The region of interest is

$$0 \leq \xi \leq R$$

and a bounded solution of the form

$$0 \leq R < \infty$$

is found in the region D, whose partial derivatives satisfy $\delta \leq \xi \leq 0$, where ξ and δ are positive constants.

Theorem 3.2

Let D denote the region $0 \leq \xi \leq R$. Then, the system (3) has a unique solution which is bounded and continuous in D.

Proof

Let

$$f_1 = b_H N_H - \left(\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N} \right) S_H - \mu_H S_H \tag{7}$$

$$f_2 = \left(\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N_H} \right) S_H - K_1 I_H \tag{8}$$

$$f_3 = \theta I_H - K_2 I_Q \tag{9}$$

$$f_4 = b_R A_R - K_3 I_R \tag{10}$$

$$f_5 = \sigma I_R - K_4 A_R \tag{11}$$

$$f_6 = e_R A_R + e_Q I_Q + e_H I_H - \phi V \tag{12}$$

Where $K_1 = \theta + \gamma_1 + \mu_H + \delta_H, K_2 = \gamma_2 + \mu_H + \delta_H, K_3 = \mu_R + \delta_R + \sigma, K_4 = \mu_R + \delta_R$

Thus, the partial derivatives of equations (7)-(12) are given below

$$\left|\frac{\partial f_1}{\partial S_H}\right| = \left|-\left[\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N} + \mu_H\right]\right| < \infty, \left|\frac{\partial f_1}{\partial I_H}\right| = \left|\frac{-\beta_1 S_H}{N}\right| < \infty, \left|\frac{\partial f_1}{\partial I_Q}\right| = \left|\frac{-\beta_2 S_H}{N}\right| < \infty, \left|\frac{\partial f_1}{\partial I_R}\right| = 0 < \infty,$$

$$\left|\frac{\partial f_1}{\partial A_R}\right| = \left|\frac{-\beta_3 S_H}{N}\right| < \infty, \left|\frac{\partial f_1}{\partial V}\right| = \left|\frac{-\beta_4 S_H}{N}\right| < \infty$$

$$\left|\frac{\partial f_2}{\partial S_H}\right| = \left|\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N}\right| < \infty, \left|\frac{\partial f_2}{\partial I_H}\right| = \left|\frac{\beta_1 S_H}{N} - K_1\right| < \infty, \left|\frac{\partial f_2}{\partial I_Q}\right| = \left|\frac{\beta_2 S_H}{N}\right| < \infty, \left|\frac{\partial f_2}{\partial I_R}\right| = 0 < \infty,$$

$$\left|\frac{\partial f_2}{\partial A_R}\right| = \left|\frac{\beta_3 S_H}{N}\right| < \infty, \left|\frac{\partial f_2}{\partial V}\right| = \left|\frac{\beta_4 S_H}{N}\right| < \infty$$

$$\left|\frac{\partial f_3}{\partial S_H}\right| = \left|\frac{\partial f_3}{\partial I_R}\right| = \left|\frac{\partial f_3}{\partial A_R}\right| = \left|\frac{\partial f_3}{\partial V}\right| = 0 < \infty, \left|\frac{\partial f_3}{\partial I_H}\right| = |\theta| < \infty, \left|\frac{\partial f_3}{\partial I_Q}\right| = |-K_2| < \infty$$

$$\left|\frac{\partial f_4}{\partial S_H}\right| = \left|\frac{\partial f_4}{\partial I_H}\right| = \left|\frac{\partial f_4}{\partial I_Q}\right| = \left|\frac{\partial f_4}{\partial V}\right| = 0 < \infty, \left|\frac{\partial f_4}{\partial I_R}\right| = |-K_3| < \infty, \left|\frac{\partial f_4}{\partial A_R}\right| = |b_R| < \infty$$

$$\left|\frac{\partial f_6}{\partial S_H}\right| = \left|\frac{\partial f_6}{\partial I_R}\right| = 0 < \infty, \left|\frac{\partial f_6}{\partial I_Q}\right| = |e_Q| < \infty \left|\frac{\partial f_6}{\partial I_H}\right| = |e_H| < \infty, \left|\frac{\partial f_6}{\partial A_R}\right| = |e_R| < \infty, \left|\frac{\partial f_6}{\partial V}\right| = |-\phi| < \infty$$

Obviously, all the partial derivatives are continuous and bounded. Hence, Theorem 3.2 shows that in the region D there exists a unique solution of system (3).

We now establish the existence of disease-free equilibrium and basic reproductive number.

Let ε_0 denote the disease free equilibrium, i.e. in the absence of infection,all infectiveclasses will be equated to zero. Thus

$$\varepsilon_0 = \left(S^*, I_H^*, I_Q^*, I_R^*, A_R^*, V^*\right) = \left(\frac{b_H N_H}{\mu_H}, 0, 0, 0, 0, 0\right)$$

The linear stability of ε_0 is investigated using the basic reproductive number denoted by R_0, which is defined as a threshold parameter that represents the mean number of secondary cases a typical single infection will generate in a totally naïve/susceptible population during his/her entire period of infectiousness(Maliyoniet al., 2012). Thus it is computed using the next generation approach as shown in (Diekmann and Heesterbeek, 2000; Driessche and Watmough, 2002),where F (non-negative) and V (non-singular) denote the new infection and transition term at ε_0 respectively.

Therefore

$$F=\begin{bmatrix} \frac{\beta_1 b_H}{\mu_H} & \frac{\beta_2 b_H}{\mu_H} & 0 & \frac{\beta_3 b_H}{\mu_H} & \frac{\beta_4 b_H}{\mu_H} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \quad V=\begin{bmatrix} K_1 & 0 & 0 & 0 & 0 \\ -\theta & K_2 & 0 & 0 & 0 \\ 0 & 0 & K_3 & -b_R & 0 \\ 0 & 0 & -\sigma & K_4 & 0 \\ -e_H & -e_Q & 0 & -e_H & \phi \end{bmatrix}$$

Hence $R_0=\rho\left(FV^{-1}\right)=\dfrac{b_H\left(\beta_1 K_2\phi+\beta_2\theta\phi+\beta_4\left[e_H K_2+e_Q\theta\right]\right)}{\mu_H\phi K_1 K_2}$ (13)

where ρ is the spectral radius (dominant eigenvalue in magnitude) of the next generation matrix, FV^{-1}.

4.STABILITY OF DISEASE FREE EQUILIBRIUM

First, we prove the local stability of disease-free equilibrium, ε_0

THEOREM4.1
The disease-free equilibrium ε_0 of the model is locally asymptotically stable (LAS) if $R_0<1$.

PROOF

$$\frac{dI_H}{dt}=\left(\frac{\beta_1 I_H+\beta_2 I_Q+\beta_3 A_R+\beta_4 V}{N_H}\right)\left(N_H-I_H-I_Q\right)-K_1 I_H$$
$$\frac{dI_Q}{dt}=\theta I_H-K_2 I_Q$$
$$\frac{dI_R}{dt}=b_R A_R-K_3 I_R$$
$$\frac{dA_R}{dt}=\sigma I_R-K_4 A_R$$
$$\frac{dV}{dt}=e_R A_R+e_Q I_Q+e_H I_H-\phi V$$
(14)

The Jacobian matrix of the above system evaluated at ε_0 is obtained as

$$J(\varepsilon_0)=\begin{bmatrix} \beta_1-K_1 & \beta_2 & 0 & \beta_3 & \beta_4 \\ \theta & -K_2 & 0 & 0 & 0 \\ 0 & 0 & -K_3 & 0 & 0 \\ 0 & 0 & \sigma & -K_4 & 0 \\ e_H & e_Q & 0 & e_R & -\phi \end{bmatrix}$$

Using elementary row transform, to have

$$\begin{bmatrix} \beta_1-K_1 & \beta_2 & 0 & \beta_3 & \beta_4 \\ 0 & \dfrac{K_2\beta_1-K_1K_2+\theta\beta_2}{-\beta_1+K_1} & 0 & \dfrac{\theta\beta_3}{-\beta_1+K_1} & \dfrac{\theta\beta_4}{-\beta_1+K_1} \\ 0 & 0 & -K_3 & b_R & 0 \\ 0 & 0 & 0 & \dfrac{-K_3K_4+\sigma b_R}{K_3} & 0 \\ 0 & 0 & 0 & 0 & \dfrac{-\left(\beta_1K_2\phi-\phi K_1K_2+\beta_2\theta\phi+\beta_4\left[e_HK_2+e_Q\theta\right]\right)}{K_2\beta_1-K_1K_2+\theta\beta_2} \end{bmatrix}$$

Hence the eigenvalues are

$$\lambda_1=\beta_1-K_1,\lambda_2=\frac{K_2\left[\beta_1-K_1\right]+\beta_2\theta}{-\left(\beta_1-K_1\right)},\lambda_3=-K_3,\lambda_4=\frac{-K_3K_4+\sigma b_R}{K_3},\lambda_5=\frac{\beta_1K_2\phi-\phi K_1K_2+\beta_2\theta\phi+\beta_4\left[e_HK_2+e_Q\theta\right]}{K_2\left[\beta_1-K_1\right]+\beta_2\theta}$$

When $\lambda_i<0$ for all $i=1,2...,5,$ the system is said to be locally asymptotically stable(LAS) at DFE. Itis obvious that $\lambda_3<0$,but since the system is LAS,it implies that

$$\lambda_1<0,K_2\left[\beta_1-K_1\right]+\beta_2\theta<0,-K_3K_4+\sigma b_R<0,\beta_1K_2\phi-\phi K_1K_2+\beta_2\theta\phi+\beta_4\left[e_HK_2+e_Q\theta\right]<0,$$

hence is readily seen from $\beta_1K_2\phi-\phi K_1K_2+\beta_2\theta\phi+\beta_4\left[e_HK_2+e_Q\theta\right]<0$,that $R_0<1$ .This complete the proof.

The global stability of disease-free equilibrium will now be established.

Theorem4.2

The DFE of model(2) is globally asymptotically stable(GAS) in D if $R_0<1$ and unstable if otherwise.

Proof

Consider the Lyapunov function

$$L=Q_1I_H+Q_2I_Q+Q_3I_R+Q_4A_R+Q_5V \qquad (15)$$

where $Q_1 = \frac{\mu_H R_0}{b_H}, Q_2 = \frac{\beta_2\phi + \beta_4 e_Q}{K_2\phi}, Q_3 = \frac{\sigma[\beta_3\phi + \beta_4 e_R]}{\phi(K_3K_4 - b_R\sigma)}, Q_4 = \frac{K_3[\beta_3\phi + \beta_4 e_R]}{\phi(K_3K_4 - b_R\sigma)}, Q_5 = \frac{\beta_4}{\phi}$ (16)

Differentiating (15) with respect to time, we obtain:

$$\dot{L} = Q_1\dot{I}_H + Q_2\dot{I}_Q + Q_3\dot{I}_R + Q_4\dot{A}_R + Q_5\dot{V}$$

$$\dot{L} = Q_1\left\{\left(\frac{\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V}{N_H}\right)S_H - K_1 I_H\right\} + Q_2\left(\theta I_H - K_2 I_Q\right) + Q_3\left(b_R A_R - K_3 I_R\right) +$$

$$Q_4\left(\sigma I_R - K_4 A_R\right) + Q_5\left(e_R A_R + e_Q I_Q + e_H I_H - \phi V\right)$$

Since $S_H \le S_H^* = \frac{b_H N_H}{\mu_H}$, *implying that* $\frac{S_H}{N_H} \le \frac{b_H}{\mu_H}$

$$\dot{L} \le Q_1\left\{\left(\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V\right)\frac{b_H}{\mu_H} - K_1 I_H\right\} + Q_2\left(\theta I_H - K_2 I_Q\right) + Q_3\left(b_R A_R - K_3 I_R\right) +$$

$$Q_4\left(\sigma I_R - K_4 A_R\right) + Q_5\left(e_R A_R + e_Q I_Q + e_H I_H - \phi V\right) \quad (17)$$

With the aid of (16),(17) is simplified as

$$\dot{L} \le \left(\beta_1 I_H + \beta_2 I_Q + \beta_3 A_R + \beta_4 V\right)\left(R_0 - 1\right) \le 0$$

since $\dot{L} < 0$ if and only if $R_0 < 1$ and $\dot{L} = 0$ if and only if $I_H = I_Q = A_R = V = 0$ .The largest compact invariant set in $\left\{\left(S_H, I_H, I_Q, I_R, A_R, V\right) \in D : \dot{L} = 0\right\}$ is the singleton $\{\varepsilon_0\}$. Therefore, by LaSalle invariance principle,every solution to system (2) with initial conditions in D approaches ε_0 as $t \to \infty$. Thus, since the region D is positively-invariant, the DFE is GAS in D if $R_0 < 1$.

5. CONCLUSION

In this paper, we presented a deterministic model of Lassa fever transmission with quarantine and permanent immunity.The existence and uniqueness of the solutions to the model were also proved. Furthermore, the stability of the model at the disease-free equilibrium(DFE) was established.In particular, usingLyapunov function, it was shown thatwhenever $R_0 < 1$, the model is globally asymptotically stable at DFE.This implies that the diseases can be eradicated irrespective of the initial population size, provided $R_0 < 1$.

Public health workers can educate participants on the importance of the incorporated vital dynamics on the transmission of Lassa fever by using the presented model as a study material or guide for seminars, workshop or training programs.

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