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Assessing the impact of isolation on the transmission dynamics of Lassa Fever

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Abstract

A non-linear deterministic mathematical model of Lassa fever with isolation of infected individuals is formulated and analysed. The model is shown to be well posed mathematically and epidemiologically. We obtained an important threshold parameter called the basic reproduction number $\mathcal{R}_0$. The presented model is shown to exhibits three equilibrium points each of which is proved to be globally asymptotically stable under certain condition on the associated threshold parameter. We further shown by numerical simulations that isolation of infected humans reduces the number of infected individuals in a society and contain the spread of lassa fever disease.

1. Introduction

Lassa fever, also known as the Lassa hemorrhagic fever (LHF), is an acute viral hemorrhagic illness with incubation period of six to twenty one days in humans and generated recurrent outbreaks in West Africa [3, 14, 34, 39]. The Lassa virus is an arenavirus, from the family of arenavirus that is mainly transmitted to humans through direct contact with food or household items contaminated with urine or stools from infected rodents [39, 20]. The human-to-human and laboratory transmissions could also be possible [39, 20]. Thus, LHF is largely a zoonotic disease, i.e., humans become infected when in contact with an infected animal [14, 33]. The disease is endemic in West Africa where the LHF risk areas approximately cover 80% of Sierra Leon and Liberia, 50% of Guinea, 40% of Nigeria, 30% of Benin, Coted'Ivoire and Togo and 10% of Ghana [2, 14]. Affecting about 2-3 million new infections annually and with 5,000-10,000 fatalities annually [26, 34]. About 80% of individuals infected with Lassa virus do not show symptoms [39] while about 1 in every 5 symptomatic infections result in severe cases in which numerous organs such as kidney, liver, spleen are affected [39].

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Much of the initial epidemiological information about Lassa fever was from investigations of hospitalized patients, many of whom had infection of nosocomial origin. Most instances were attributed to person-to-person transmission of the virus. Indeed, it was transmitted to hospital staff that led to the discovery of Lassa fever [6, 8, 16, 17, 18, 27]. It was discovered in 1969 in the village known as Lassa in Borno state of northern Nigeria [20, 33, 34]. The recognized human arenavirus infection history in Africa began in 1969 with the death of two medical missionaries mysteriously and the near-fatal illness of a third one [17]. An arenavirus was isolated from two of these patients [7] and given the name of Lassa virus after the town of Lassa, where the disease emerged [7]. Nosocomial outbreaks of LHF occurs repeatedly in Liberia, Nigeria and Sierra Leone [4, 14, 33].

The animal host (reservoir) of the LHF virus is a rodent of the genus Mastomysnatalensis called the multimammate rat which was found to be first infected with the virus in Nigeria and in Sierra Leon in 1972, and Guinea in 2006 [11, 14, 15, 20]. The infected rats do not become ill but they can shed the virus through their urine and stools [39, 14, 33]. Control of the rodent population has been largely unfeasible; therefore, measures frequently focus on keeping rats out of home and food items [39]. Further, there is evidence of vertical transmission in the rodent population [15], and the vertical transmission rate could be higher during the rainy season when the rodents are more involved in patrolling their houses for mating and breeding [15].

It takes six to twenty one days (Incubation period) 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, facial swelling, bleeding from mouth, nose, genital and gastrointestinal tract infection may develop [39]. The most common complication of Lassa fever after recovery is deafness [38] and marked by heart and kidney failure. No vaccine currently available against LHF [38]. However the antiviral drug ribavirin appears to be effective if administered early in the early course of clinical illness [14, 33, 39]. 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 a healthy individual coming in contact with an infected human, though this may not eradicate the disease [19]. 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 infectious disease [37].

WHO in 2018 included LF in the blueprint list of priority diseases, prioritized for research and development. The possibility that Lassa virus could be used as a biological weapon has raised the profile of the need for greater understanding of Lassa fever and for more effective control and treatment programs [34]. Many mathematical models have been designed and used to studied Lassa fever transmission dynamics mathematically, among them are [1, 5, 22, 28, 31]. In 2006, Okuonghae and Okuonghae [31] proposed a mathematical model to study the transmission dynamics of Lassa fever. They examined the steady states of their model for epidemic and endemic situations. The model analysis shows that in the interim control of the rodents carrying the virus and some isolation policy for infected individuals are the best strategies against the spread of the disease. A deterministic model for Lassa fever disease with vital dynamics was developed in [5]. Their model incorporated standard incidence rate, disease induced death and infection due to humans, reservoirs and aerosol (airborne) transmissions. They obtained the basic reproduction number, which can be used to control the transmission dynamics of the disease and established the conditions for local and global stabilities of the disease-free equilibrium. [25] use modelling approach to estimate the human-human transmission of Lassa fever at Kenema Government hospital

in Sierra Leone. The model analyses revels that almost 20% of the cases at that hospital are secondary cases arising from human-to-human transmission.
In the last decade, a deterministic mathematical model for the dynamics of lassa fever disease was proposed in [22]. Stability analysis of the model equilibrium points was carried out. In fact, they showed that the disease-free equilibrium point is stable when the birth rate of the human population is less than the death rate and the same when the birth rate of the reservoir is less than the total death rates. In our proposed model, we extend the model in [22] by incorporating isolation as a control measure and divide the reservoir population in to two. The aim of this study is to assess the impact of isolation on Lassa fever transmission dynamics. Indeed, the analysis shows that an increase in isolation rate reduces the human infected subpopulation.
The remaining part of the paper is organized as follows: the model is formulated in Section 2, and analyzed in Section 3. We present numerical results and give a concluding remark in Section 4.

2. Model formulation

The total population of humans at time t, denoted by $N_h(t)$, is divided into susceptible individuals with risk of Lassa virus infection $S_h(t)$, infected individuals $I_h(t)$ and individuals in isolation $Q(t)$. Thus:

$$N_h(t) = S_h(t) + I_h(t) + Q(t).$$

While, the total population of rodents at time t denoted by $N_r(t)$, is divided into two compartments for susceptible rodents $S_r(t)$ and infected rodents $I_r(t)$, such that

$$N_r(t) = S_r(t) + I_r(t).$$

The susceptible population with risk of Lassa virus infection $S_h(t)$ is generated by recruitment of humans at a constant rate Π_h (all humans recruited into the population are assumed to be at risk of Lassa-infection), infected individuals who recover at a rate τ_1 and isolated individuals recovered at a rate τ_2. The population is decreased by natural death at a rate μ_h and by infection following effective contact with infected humans or rodents at the rates λ_1 given by $\lambda_1 = \frac{\beta_h I_h + \beta_r I_r}{N_h}$, the parameters β_h and β_r are the effective transmission probability per contact with infected humans and rodents respectively.

$$\frac{dS_h}{dt} = \Pi_h + \tau_1 I_h + \tau_2 Q - (\lambda_1 + \mu_h) S_h.$$

The population of infected individuals (I_h) is increased by infection at the rate λ_1 and diminished by recovery at the rate τ_1, isolation at the rate γ, natural death at the rate μ_h and death induced by the disease at a rate δ. Thus,

$$\frac{dI_h}{dt} = \lambda_1 S_h - (\tau_1 + \gamma + \delta + \mu_h) I_h.$$

The population of isolated individuals is generated as a result of isolating the infected individuals at the rate γ and decreased by recovery of individuals in the isolation at the rate τ_2, natural death μ_h and death induced by the disease δ. Such that,

$$\frac{dQ}{dt} = \gamma I_h - (\tau_1 + \delta + \mu_h) Q.$$

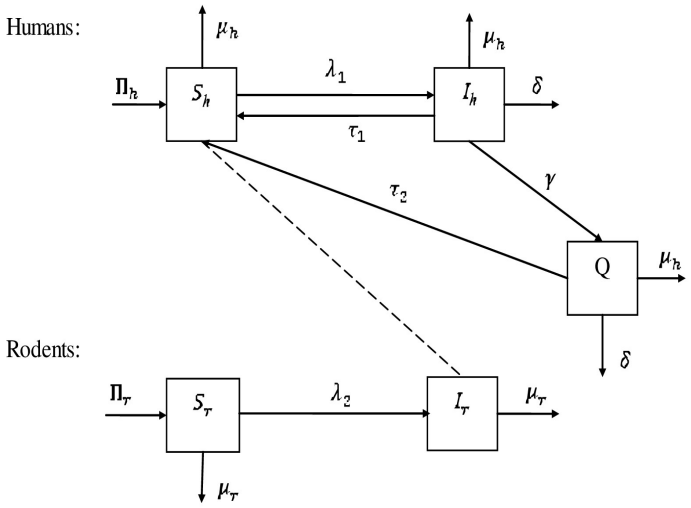
On the other hand, the population of susceptible rodents $S_r(t)$ is generated by recruitment of rodents into the population at constant rate Π_r and diminished by Lassa fever infection at a rate λ_2 given by $\lambda_2 = \frac{\beta_r I_r}{N_r}$ and natural death at the rate μ_r. Therefore,

$$\frac{dS_r}{dt} = \Pi_r - (\lambda_2 + \mu_r)S_r.$$

The population of infected rodents I_r is generated following the infection of susceptible rodents at the rate λ_2 and decreased only because of natural death mu_r. Hence,

$$\frac{dI_r}{dt} = \lambda_2 S_r - \mu_r I_r.$$

The following system of differential equations described the model for Lassa fever with isolation while the flow diagram of the model is shown in figure 1. The parameters and associated variables are presented in tables 1 and 2.



Figures 1: Flow diagram of model (2.1)

$$\begin{aligned}
\frac{dS_h}{dt} &= \Pi_h + \tau_1 I_h + \tau_2 Q - (\lambda_1 + \mu_h)S_h \\
\frac{dI_h}{dt} &= \lambda_1 S_h - (\tau_1 + \gamma + \delta + \mu_h)I_h \\
\frac{dQ}{dt} &= \gamma I_h - (\tau_1 + \delta + \mu_h)Q \\
\frac{dS_r}{dt} &= \Pi_r - (\lambda_2 + \mu_r)S_r \\
\frac{dI_r}{dt} &= \lambda_2 S_r - \mu_r I_r
\end{aligned} \tag{2.1}$$

where $\lambda_1 = \frac{\beta_h I_h + \beta_r I_r}{N_h}$ and $\lambda_2 = \frac{\beta_r I_r}{N_r}$. The system of equations ((2.1) extends the model proposed by [22] in some sense as follows:

i. Incorporating isolation as control measure;
ii. The population of the reservoir (rodents) is divided into susceptible and infected classes [6, 16, 25]; and
iii. Standard incidence rate used while bilinear incidence rate was used in [22].

We assume that

(a) Homogeneous mixing of the human and rodents populations such that there are equal chances of transmitting the virus.
(b) Successful treatment of Lassa fever does not guarantee permanent immunity. That is re-infection after recovery is possible [34],
(c) Natural recovery is possible,
(d) The virus does not kill the vector as in [22],
(e) Isolation of infected human is incorporated as a control measure,
(f) The population of the reservoir (rodents) is divided into susceptible and infected classes as in [6, 16, 25],
(g) the force of infection is via Standard incidence rate.

TABLE 1. Description of state variables of the model

Variable	Interpretation
N_h	Total population of humans
S_h	Population of susceptible humans with risk of Lassa virus infection
I_h	Population of Lassa-infected humans with symptoms of Lassa fever
Q	Population of isolated individuals
N_r	Total population of rodents
S_r	Population of susceptible rodents
I_r	Population of Lassa-infected rodents

TABLE 2. parameter description

Parameter	Description
Π_h	Recruitment rate for humans
β_h	Transmission probability from Humans to Humans
β_r	Transmission probability from Rodents to Rodents and Humans
μ_h, μ_r	Natural death rates of humans and rodents respectively
τ_1, τ_2	Recovery rate of infected and isolated humans respectively
γ	Progression rate of infected humans to isolation class
δ	Disease-induced death rate for humans

2.1. **Basic properties of the model.** Here, we present the basic qualitative features of the model (2.1) in the following propositions.

Proposition 2.1. *The system of the equations* (2.1) *preserves positivity of solutions. In other words, the solutions* $(S_h(t), I_h(t), Q(t), S_r(t), I_r(t))$ *of model* (2.1) *are non-negative with positive initial data and remain positive* $\forall t > 0$.

Proof. Suppose that system (2.1) has positive initial conditions.

$$S_h(0) > 0, I_h(0) > 0, Q(0) > 0, S_r(0) > 0, I_r(0) > 0.$$

If by contradiction, we assume that for the first time t_1, $S_h(t)$ is not positive and $S_h(t) > 0$ for $0 < t < t_1$ with $S_h(t_1) = 0$. Then one can see by inspection from the second equation of model (2.1), that

$$\frac{dI_h}{dt} \geq -(\tau_1 + \gamma + \delta + \mu_h)I_h \quad \text{for } t \in [0, t_1),$$

and so, $I_h > 0$ for $t \in [0, t_1)$. Also, the first equation of (2.1), gives

$$\frac{dS_h}{dt} \geq -(\lambda_1 + \mu_h)S_h \quad \text{for } t \in [0, t_1).$$

Thus, $S_h(t_1) > 0$ contradicting the hypothesis that $S_h(t_1) = 0$. Therefore $S_h(t) > 0$. Now, applying similar approach as that of $S_h(t)$, one can easily verify that the remaining state variables $I_h(t), Q(t), S_r(t)$ and $I_r(t)$ are positive.

Proposition 2.2. *The following biologically feasible region of the model (2.1), the closed set*

$$D = \left\{ (S_h, I_h, Q, S_r, I_r) \in \mathbb{R}^5_+ : S_h + I_h + Q \leq \frac{\Pi_h}{\mu_h}, S_r + I_r \leq \frac{\Pi_r}{\mu_r} \right\}$$

is positively invariant and attract all positive solutions of the model.

Proof. It follows from model (2.1) that

$$\frac{dN_h}{dt} \leq \Pi_h - \mu_h N_h(t).$$

By a standard comparison theorem as in [23], we have

$$N_h(t) \leq N_h(0)e^{-\mu_h(t)} + \frac{\Pi_h}{\mu_h}(1 - e^{-\mu_h(t)}).$$

Similarly,

$$N_r(t) \leq N_r(0)e^{-\mu_r(t)} + \frac{\Pi_r}{\mu_r}(1 - e^{-\mu_r(t)}),$$

so that $\frac{dN_h}{dt} < 0, \frac{dN_r}{dt} < 0$ if $N_h > \frac{\Pi_h}{\mu_h}$ and $N_r > \frac{\Pi_r}{\mu_r}$, respectively. In particular, $N_h \leq \frac{\Pi_h}{\mu_h}$ and $N_r \leq \frac{\Pi_r}{\mu_r}$ if $N_h(0) \leq \frac{\Pi_h}{\mu_h}$ and $N_r(0) \leq \frac{\Pi_r}{\mu_r}$, respectively. Thus, the region D is positively-invariant. Furthermore, if $N_h(t) > \frac{\Pi_h}{\mu_h}$ and $N_r(t) > \frac{\Pi_r}{\mu_r}$ then either the solution enters D infinite time, or $N_h(t)$ approaches $\frac{\Pi_h}{\mu_h}, N_r(t)$ approaches $\frac{\Pi_r}{\mu_r}$ and the infected variable approaches zero. Hence, D is attracting (i.e. all solutions in $\mathbb{R}^5_+$ eventually approach, enter or stay in D). Hence the model is epidemiologically well-posed in D as in [21].

3. Analysis of the model

3.1. **Disease-free equilibrium.** In the absence of Lassa fever infection ($I_h = Q = I_r = 0$), system (2.1) reduces to

$$\begin{aligned} \frac{dS_h}{dt} &= \Pi_h - \mu_h S_h \\ \frac{dS_r}{dt} &= \Pi_r - \mu_r S_r \end{aligned} \tag{3.1}$$

so that the disease-free equilibrium denoted by ε_{0L} is given by

$$\varepsilon_{0L} = (S_h^*, I_h^*, Q^*, S_r^*, I_r^*) = \left(\frac{\Pi}{\mu_h}, 0, 0, \frac{\Pi}{\mu_h}, 0 \right).$$

For us to establish the linear stability of the equilibrium points of model (1) the threshold parameter called the basic reproduction number is required. This parameter can be computed using the next generation operator method [12, 13, 36] on the system (2.1). The matrices F (for the new infection terms) and V (for the transition terms) associated with the model (2.1) are given, respectively, by

$$\begin{pmatrix} \beta_h & 0 & \beta_r \\ 0 & 0 & 0 \\ 0 & 0 & 0\beta_r \end{pmatrix}, \begin{pmatrix} K_1 & 0 & 0 \\ -\gamma & K_2 & 0 \\ 0 & 0 & \mu_r \end{pmatrix},$$

with $K_1 = \tau_1 + \gamma + \delta + \mu_h, K_2 = \tau_2 + \delta + \mu_h$. It follows that the basic reproduction number of the model (2.1) is given by $\mathcal{R}_0 = \rho(FV^{-1})$ where ρ is the spectral radius of the matrix.

Hence,

$$\mathcal{R}_0 = \max\left\{\frac{\beta_h}{K_1}, \frac{\beta_r}{\mu_r}\right\} = \max\{\mathcal{R}_{0h}, \mathcal{R}_{0r}\}.$$

where $\mathcal{R}_{0h}$ is the basic reproduction number associated to humans while $\mathcal{R}_{0r}$ is the basic reproduction number associated to rodents. The threshold quantity $\mathcal{R}_0$ is the basic reproduction number of the model (2.1), which is the average number of new cases of infection caused by one typical infected Rodent/Human in a population consisting of only susceptible population.

Theorem 3.1. *The disease-free equilibrium ε_{0L} of the system (2.1) is locally asymptotically stable on the biologically feasible region D if $\mathcal{R}_0 < 1$ and is unstable when $\mathcal{R}_0 > 1$.*

Proof. Linearizing system (2.1) around the equilibrium ε_{0L}, we obtain the Jacobian matrix

$$J(\varepsilon_{0L}) = \begin{pmatrix} -\mu_h & \tau_1 - \beta_h & \tau_2 & 0 & \beta_r \\ 0 & \beta_h - K_1 & 0 & 0 & \beta_r \\ 0 & \gamma & -K_2 & 0 & 0 \\ 0 & 0 & 0 & -\mu_r & -\beta_r \\ 0 & 0 & 0 & 0 & \beta_r - \mu_r \end{pmatrix}.$$

One can observe that the first three eigenvalues of the matrix $J(\varepsilon_{0L})$ are

$$\rho_1 = -\mu_h, \rho_3 = \beta_r - \mu_r = \mu_r(\mathcal{R}_{0L} - 1) \text{ and } \rho_3 = -\mu_r.$$

Then the remaining two eigenvalues are for the 2×2 sub matrix of $J(\varepsilon_{0L})$, denoted by $J^*(\varepsilon_{0L})$ which is obtained by deleting the first row with first column, the fifth row with the fifth column and the fourth row and the fourth column of $J(\varepsilon_{0L})$.

$$J^*(\varepsilon_{0L}) = \begin{pmatrix} \beta_h - K_1 & 0 \\ \gamma & -K_2 \end{pmatrix}.$$

It follows that the eigenvalues of $J^*(\varepsilon_{0L})$ which is a lower triangular matrix are the entries along the main diagonal. That is, $\rho_4 = \beta_h - K_1 = K_1(\mathcal{R}_{0h} - 1)$ and $\rho_5 = -K_2$. Thus, the five eigenvalues of $J(\varepsilon_{0L})$ are real and negative if $\mathcal{R}_{0h} < 1$ and $\mathcal{R}_{0r} < 1$ so that $\mathcal{R}_0 < 1$. Hence the DFE, ε_{0L} is locally asymptotically stable whenever $\mathcal{R}_0 < 1$.
The local asymptotic stability of the DFE allow us to investigate its global stability result in the following theorem.

Theorem 3.2. *The disease-free equilibrium ε_{0L} of model (2.1) is globally asymptotically stable in the interior of D if $\mathcal{R}_0 < 1$.*

Proof. We are to prove this theorem using Comparison theorem. The rate of change of the infected compartments of model (2.1) can be written in the form

$$\frac{dX}{dt} = (\mathcal{F} - \mathcal{V})X - JX, \tag{3.2}$$

where

$$X = \begin{pmatrix} I_h \\ Q \\ I_r \end{pmatrix}, \quad \mathcal{F} = \begin{pmatrix} \beta_h & 0 & \beta_r \\ 0 & 0 & 0 \\ 0 & 0 & \beta_r \end{pmatrix}, \quad \mathcal{V} = \begin{pmatrix} K_1 & 0 & 0 \\ -\gamma & K_2 & 0 \\ 0 & 0 & \mu_r \end{pmatrix}.$$

Thus

$$JX = \begin{pmatrix} \beta_h - K_1 & 0 & \beta_r \\ \gamma & -K_2 & 0 \\ 0 & 0 & \beta_r - \mu_r \end{pmatrix} \begin{pmatrix} I_h \\ Q \\ I_r \end{pmatrix} - \begin{pmatrix} \frac{\beta_h I_h + \beta_r I_r}{N_h} S_h - K_1 I_h \\ \gamma I_h - K_2 Q \\ \frac{\beta_r I_r}{N_r} S_r - \mu_r I_r \end{pmatrix}$$

$$= \begin{pmatrix} \beta_h \left(1 - \frac{S_h}{N_h}\right) & 0 & \beta_r \left(1 - \frac{S_r}{N_r}\right) \\ \gamma & -K_2 & 0 \\ 0 & 0 & \beta_r \left(1 - \frac{S_r}{N_r}\right) \end{pmatrix} \begin{pmatrix} I_h \\ Q \\ I_r \end{pmatrix}.$$

It follows that J is a non-negative matrix since $S_h \leq N_h \leq \frac{\Pi_h}{\mu_h}, S_r \leq N_r \leq \frac{\Pi_r}{\mu_r}$. Then

$$\frac{dX}{dt} \leq (\mathcal{F} - \mathcal{V})X. \tag{3.3}$$

Using the fact that the eigenvalues of the matrix $\mathcal{F} - \mathcal{V}$ all have negative real parts (as per our local stability result, where $\rho(\mathcal{F}\mathcal{V}^{(} - 1)) < 1$ if $\mathcal{R}_0 < 1$, which is equivalent to $\mathcal{F} - \mathcal{V}$ having eigenvalues with negative real parts when $\mathcal{R}_0 < 1$ [36]. It follows that the linearized differential inequality system (3.3) is stable whenever $\mathcal{R}_0 < 1$. Consequently, $(I_h, Q, I_r) \to (0, 0, 0)$ as $t \to \infty$. Thus, by comparison theorem, $(I_h, Q, I_r) \to (0, 0, 0)$ as $t \to \infty$. Substituting $I_h = Q = I_r = 0$ in (3.2) gives $S_h(t) \to S_h^*$ as $t \to \infty$ and $S_r(t) \to S_r^*$ as $t \to \infty$. Thus, $(S_h(t), I_h(t), Q(t), I_r(t)) \to (S_h^*, 0, 0, 0, S_r^*)$ as $t \to \infty$ for $\mathcal{R}_0 < 1$. Thus, ε_{0L} is globally asymptotically stable if $\mathcal{R}_0 < 1$.

3.2. **Rodent disease-free equilibrium (RDFE).** The Rodent disease-free equilibrium (RDFE) point of the model (2.1), is an equilibrium point where the compartment of infected rodent is empty. That is, when only $I_r = 0$. We denote such an equilibrium point by $\varepsilon_{1L} = (S_h^{**}, I_h^{**}, Q_,^{**} S_r^{**}, I_r^{**})$. Then setting the right hand-side of model (2.1) to zero, we obtain after algebraic manipulations that

$$\begin{aligned} S_h^{**} &= \frac{\Pi_h K_1 K_2}{K_1 K_2 (\lambda_1^{**} + \mu_h) - \lambda_1^{**}(\tau_1 K_2 + \tau_2 \gamma)} \\ I_h^{**} &= \frac{\Pi_h K_2 \lambda_1^{**}}{K_1 K_2 (\lambda_1^{**} + \mu_h) - \lambda_1^{**}(\tau_1 K_2 + \tau_2 \gamma)} \\ Q^{**} &= \frac{\Pi_h \gamma \lambda_1^{**}}{K_1 K_2 (\lambda_1^{**} + \mu_h) - \lambda_1^{**}(\tau_1 K_2 + \tau_2 \gamma)} \\ S_r^{**} &= \frac{\Pi_r}{\mu_r}, \quad I_r^{**} = 0, \end{aligned} \tag{3.4}$$

with $\lambda_1^{**} = \frac{\beta_h^{**} I_h^{**}}{N_h^{**}}$ and $\lambda_2^{**} = 0$. Then

$$\lambda_1^{**}(S_h^{**} + I_h^{**} + Q^{**}) - \beta_h^{**} I_h^{**} = 0$$

so that using equation (3.4), we obtain after algebraic manipulations that $\lambda_1^{**} = \frac{K_1 K_2 (\mathcal{R}_{0h} - 1)}{K_2 + \gamma}$. It follows that the unique solution is positive if and only if $\mathcal{R}_{0h} > 1$.

Theorem 3.3. *The RDFE point (ε_{1L}) of model (2.1), if it exists, is globally asymptotically stable in D when $\mathcal{R}_{0h} > 1$.*

Proof. Suppose ε_{1L} exists and $\mathcal{R}_0 > 1$. Then consider the following nonlinear Lyapunov function of Goh-Volterra type.

$$W = \left(S_h - S_h^{**} - S_h^{**} \ln \frac{S_h}{S_h^{**}}\right) + \left(I_h - I_h^{**} - I_h^{**} \ln \frac{I_h}{I_h^{**}}\right) + \left(Q - Q^{**} - Q^{**} \ln \frac{Q}{Q^{**}}\right) + \left(S_r - S_r^{**} - S_r^{**} \ln \frac{S_r}{S_r^{**}}\right)$$

The time derivative of $F(t)$ along solutions of model (2.1) is given by

$$\begin{aligned} \dot{W} &= \left(1 - \frac{S_h^{**}}{S_h}\right)\dot{S}_h + \left(1 - \frac{I_h^{**}}{I_h}\right)\dot{I}_h + \left(1 - \frac{Q^{**}}{Q}\right)\dot{Q} \\ &\quad + \left(1 - \frac{S_r^{**}}{S_r}\right)\dot{S}_r \end{aligned} \tag{3.5}$$

At the steady state ε_{1L}, we have the following relations

$$\Pi_h = \lambda_1^{**} S_h^{**} + \mu_h S_h^{**},\ K_1 = \frac{\lambda_1^{**} S_h^{**}}{I_h^{**}},\ K_2 = \frac{\gamma I_h^{**}}{Q^{**}}\ \Pi_r \quad = \mu_r S_r^{**}, \tag{3.6}$$

Then, considering term by term in equation (3.5) starting with the first term, we have

$$\begin{aligned} \left(1 - \frac{S_h^{**}}{S_h}\right)\dot{S}_h &= \left(1 - \frac{S_h^{**}}{S_h}\right)(\Pi_h - \lambda_1 S_h - \mu_h S_h) \\ &= \left(1 - \frac{S_h^{**}}{S_h}\right)(\lambda_1^{**} S_h^{**} + \mu_h S_h^{**} - \lambda_1 S_h - \mu_h S_h) \\ &= (\lambda_1^{**} + \mu_h) S_h^{**} \left(2 - \frac{S_h^{**}}{S_h} - \frac{S_h}{S_h^{**}}\right) \end{aligned} \tag{3.7}$$

Following equation (3.7), we have

$$\left(1 - \frac{I_h^{**}}{I_h}\right)\dot{I}_h = \lambda_1^{**} S_h^{**} \left(1 - \frac{I_h}{I_h^{**}}\right) + \lambda_1 S_h \left(1 - \frac{I_h^{**}}{I_h}\right),$$

$$\left(1 - \frac{Q^{**}}{Q}\right)\dot{Q} = \gamma I_h^{**} \left(2 - \frac{Q}{Q^{**}} - \frac{Q^{**}}{Q}\right),$$

$$\left(1 - \frac{S_r^{**}}{S_r}\right)\dot{S}_r = \mu_r S_r^{**} \left(2 - \frac{S_r}{S_r^{**}} - \frac{S_r^{**}}{S_r}\right)$$

Now, using the fact that $S_h \leq S_h^{**}$, we obtain

$$\begin{aligned} \dot{F} &\leq (\lambda_1^{**} + \mu_h) S_h^{**} \left(2 - \frac{S_h^{**}}{S_h} - \frac{S_h}{S_h^{**}}\right) + \lambda_h^{**} S_h^{**} \left(2 - \frac{I_h}{I_h^{**}} - \frac{I_h^{**}}{I_h}\right) \\ &\quad + \gamma I_h^{**} \left(2 - \frac{Q}{Q^{**}} - \frac{Q^{**}}{Q}\right) + \mu_r S_r^{**} \left(2 - \frac{S_r}{S_r^{**}} - \frac{S_r^{**}}{S_r}\right) \end{aligned}$$

It follows from arithmetic-geometric inequality, that

$$\left(2 - \frac{S_h^{**}}{S_h} - \frac{S_h}{S_h^{**}}\right) \leq 0, \quad \left(2 - \frac{I_h}{I_h^{**}} - \frac{I_h^{**}}{I_h}\right) \leq 0,$$

and

$$\left(2-\frac{Q}{Q^{**}}-\frac{Q^{**}}{Q}\right)\leq 0,\quad \left(2-\frac{S_r}{S_r^{**}}-\frac{S_r^{**}}{S_r}\right)\leq 0,$$

Thus, $\dot{W}\leq 0$ if $\mathcal{R}_{0h}>1$ and $\dot{W}=0$ only when $S_h=S_h^{**}, I_h=I_h^{**}, Q=Q^{**}, S_r=S_r^{**}$. Then $\dot{W}$ is a Lyapunov function and by LaSalle Invariance principle [24] the equilibrium point ε_{1L} is the only positive invariant set contained in $\{(S_h,I_h,Q,S_r,0):\dot{W}=0\}$. Hence ε_{1L} is globally asymptotically stable in D.

3.3. **Endemic equilibrium.** The endemic equilibrium (EE) point of the system (2.1) is the steady state where the disease persists in the population. That is when at least one of the infected compartments of the model is non-empty. Let $\varepsilon_{2L}=(S_h^{***},I_h^{***},Q^{***},S_r^{***},I_r^{***})$ be an endemic equilibrium solution of the model (2.1). Then equating the right hand side of model (2.1) to zero, we obtain

$$\begin{aligned}
S_h^{***}&=\frac{\Pi_h K_1K_2}{K_1K_2(\lambda_1^{***}+\mu_h)-\lambda_1^{***}(\tau_1K_2+\tau_2\gamma)}\\
I_h^{***}&=\frac{\Pi_h\lambda_1^{***}K_2}{K_1K_2(\lambda_1^{***}+\mu_h)-\lambda_1^{***}(\tau_1K_2+\tau_2\gamma)}\\
Q^{***}&=\frac{\Pi_h\lambda_1^{***}\gamma}{K_1K_2(\lambda_1^{***}+\mu_h)-\lambda_1^{***}(\tau_1K_2+\tau_2\gamma)}\\
S_r^{***}&=\frac{\Pi_r}{\lambda_2^{***}+\mu_r}\\
I_r^{***}&=\frac{\lambda_2^{***}\Pi_r}{\mu_r(\lambda_2^{***}+\mu_r)}
\end{aligned}\tag{3.8}$$

with

$$\lambda_1^{***}=\frac{\beta_h^{***}I_h^{***}+\beta_r^{***}I_r^{***}}{N_h^{***}},\quad \lambda_2^{***}=\frac{\beta_r^{***}I_r^{***}}{N_r^{***}}.\tag{3.9}$$

Then from (3.9), we have

$$\begin{aligned}
&\lambda_1^{***}(S_h^{***}+I_h^{***}+Q^{***}-\beta_h^{***}I_h^{***}+\beta_r^{***}I_r^{***}=0,\\
&\lambda_2^{***}(S_r^{***}+I_r^{***})-\beta_r^{***}I_r^{***}=0.
\end{aligned}\tag{3.10}$$

Using (3.8) and simplifying, equation (3.10) becomes

$$\begin{aligned}
&\Pi_h\mu_r(\lambda_2^{***}+\mu_r)[\lambda_1^{***}K_2(\lambda_1^{***}-\beta_h^{***})+\lambda_1^{***}K_1K_2+\gamma*\lambda_1^{***2}]\\
&-\beta_r^{***}\lambda_2^{***}\Pi_r[K_1K_2(\lambda_1^{***}+\mu_h)-\lambda_1^{***}(\tau_1K_2+\tau_2\gamma)]=0,\\
&(\lambda_2^{***}-\beta_r^{***}+\mu_r^{***})\lambda_2^{***}=0.
\end{aligned}\tag{3.11}$$

Thus, the second equation of (3.11) gives $\lambda_2^{***}=\beta_r^{***}-\mu_r^{***}$ and the second equation of (3.8) becomes a quadratic equations in λ_1^{***}

$$A\lambda_1^{***2}+B\lambda_1^{***}+C=0,\tag{3.12}$$

where

$$\begin{aligned}
A&=\Pi_h(K_2+\gamma)\\
B&=\Pi_hK_1K_2(1-\mathcal{R}_{0h})+\Pi_r(\delta+\mu_h)(\gamma+K_2)(1-\mathcal{R}_{0r})\\
C&=\Pi_rK_1K_2\mu_h(1-\mathcal{R}_{0r}).
\end{aligned}\tag{3.13}$$

It can be seen that the coefficient A is always positive while the sign of B and C depends on the values of the reproduction numbers. It follows that,

(i) If $R_{0h} > 1$ and $R_{0r} > 1$ (i.e., $\mathcal{R}_0 > 1$), then $B < 0$ and $C < 0$ so that there is only one sign change in the sequence of coefficients A, B, C. Thus, there is one positive real root of (3.12) by Descartes rule of signs.

(ii) Both B and C are positive when $R_{0h} < 1$ and $R_{0r} < 1$. Then there is no change in the sequence of coefficients of (3.12). Therefore, equation (3.12) has no positive real roots.

(iii) If $R_{0h} > 1$ and $R_{0r} < 1$ then there is either two sign changes or no sign change in the sequence of coefficients of (3.12). Thus there are two or no positive real roots of equation (3.12).

(iv) If $R_{0h} > 1$ and $R_{0r} > 1$, there is one sign change in the sequence of coefficients A, B, C of (3.9). Thus, there exists at most one positive real root.

Consequently, equation (3.12) together with (3.13) has at least one endemic equilibrium point.

Theorem 3.4. *A unique endemic equilibrium point ε_{02} of model (2.1), if it exist, is globally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. Suppose $\mathcal{R}_0 > 1$ so that ε_{02}, exists. We consider a nonlinear Lyapunov function of Goh-Volterra kind as follows:

$$\begin{aligned} F = &\left(S_h - S_h^{***} - S_h^{***}\ln\frac{S_h}{S_h^{***}}\right) + \left(I_h - I_h^{***} - I_h^{***}\ln\frac{I_h}{I_h^{***}}\right) \\ &+ \left(Q - Q^{***} - Q^{***}\ln\frac{Q}{Q^{***}}\right) + \left(S_r - S_r^{***} - S_r^{***}\ln\frac{S_r}{S_r^{***}}\right) \\ &+ \left(I_r - I_r^{***} - I_r^{***}\ln\frac{I_r}{I_r^{***}}\right) \end{aligned} \tag{3.14}$$

The time derivative of $F(t)$ along solutions of model (2.1) is given by

$$\begin{aligned} \dot{F} = &\left(1 - \frac{S_h^{***}}{S_h}\right)\dot{S}_h + \left(1 - \frac{I_h^{***}}{I_h}\right)\dot{I}_h + \left(1 - \frac{Q^{***}}{Q}\right)\dot{Q} \\ &+ \left(1 - \frac{S_r^{***}}{S_r}\right)\dot{S}_r + \left(1 - \frac{I_r^{***}}{I_r}\right)\dot{I}_r \end{aligned} \tag{3.15}$$

At the steady state ε_{2L}, we have the following relations

$$\begin{aligned} &\Pi_h = \lambda_1^{***}S_h^{***} + \mu_h S_h^{***},\ K_1 = \frac{\lambda_1^{***}S_h^{***}}{I_h^{***}},\ K_2 = \frac{\gamma I_h^{***}}{Q^{***}} \\ &\Pi_r = \lambda_2^{***}S_r^{***} + \mu_r S_r^{***},\ \mu_r = \frac{\lambda_2^{***}S_r^{***}}{I_r^{***}} \end{aligned} \tag{3.16}$$

Then, from equation (3.15) above considering term by term starting with the first term, we have

$$\begin{aligned}\left(1-\frac{S_h^{***}}{S_h}\right)\dot{S}_h &= \left(1-\frac{S_h^{***}}{S_h}\right)(\Pi_h-\lambda_1 S_h-\mu_h S_h)\\ &= \left(1-\frac{S_h^{***}}{S_h}\right)(\lambda_1^{***}S_h^{***}+\mu_h S_h^{***}-\lambda_1 S_h-\mu_h S_h)\\ &= (\lambda_1^{***}+\mu_h)S_h^{***}\left(2-\frac{S_h^{***}}{S_h}-\frac{S_h}{S_h^{***}}\right)\end{aligned} \tag{3.17}$$

Using similar argument as in equation (3.15), we have

$$\begin{aligned}\left(1-\frac{I_h^{***}}{I_h}\right)\dot{I}_h &= \lambda_1^{***}S_h^{***}\left(1-\frac{I_h}{I_h^{***}}\right)+\lambda_1 S_h\left(1-\frac{I_h^{***}}{I_h}\right),\\ \left(1-\frac{Q^{***}}{Q}\right)\dot{Q} &= \gamma I_h^{***}\left(2-\frac{Q}{Q^{***}}-\frac{Q^{***}}{Q}\right),\\ \left(1-\frac{S_r^{***}}{S_r}\right)\dot{S}_r &= (\lambda_2+\mu_r)S_r^{***}\left(2-\frac{S_r}{S_r^{***}}-\frac{S_r^{***}}{S_r}\right)\\ \left(1-\frac{I_r^{***}}{I_r}\right)\dot{I}_r &= \lambda_2^{***}S_r^{***}\left(2-\frac{I_r}{I_r^{***}}-\frac{I_r^{***}}{I_r}\right)\end{aligned}$$

Now, using the fact that $S_h \le S_h^{***}, I_h \le I_h^{***}, S_r \le S_r^{***}$ and $I_r \le I_r^{***}$, we have

$$\begin{aligned}\dot{F} \le{}& (\lambda_1^{***}+\mu_h)S_h^{***}\left(2-\frac{S_h^{***}}{S_h}-\frac{S_h}{S_h^{***}}\right)+\lambda_1^{***}S_h^{***}\left(2-\frac{I_h}{I_h^{***}}-\frac{I_h^{***}}{I_h}\right)\\ &+\gamma I_h^{***}\left(2-\frac{Q}{Q^{***}}-\frac{Q^{***}}{Q}\right)+(\lambda_2+\mu_r)S_r^{***}\left(2-\frac{S_r}{S_r^{***}}-\frac{S_r^{***}}{S_r}\right)\\ &+\lambda_2^{***}S_r^{***}\left(2-\frac{I_r}{I_r^{***}}-\frac{I_r^{***}}{I_r}\right)\end{aligned}$$

Applying arithmetic-geometric inequality, we have

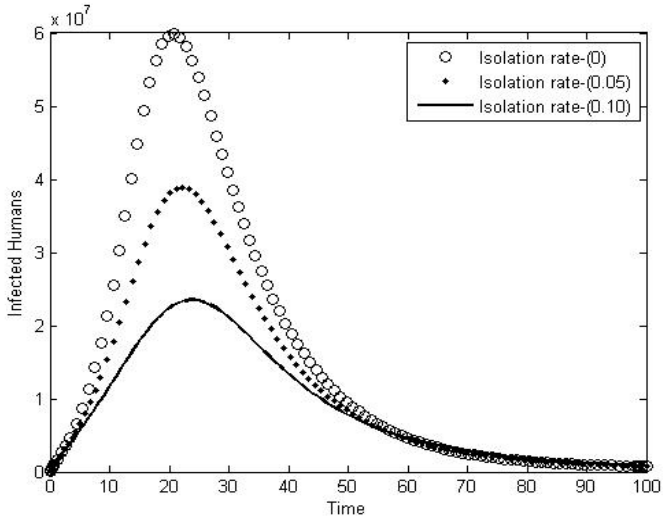
$$\begin{aligned}&\left(2-\frac{S_h^{***}}{S_h}-\frac{S_h}{S_h^{***}}\right)\le 0, \quad \left(2-\frac{I_h}{I_h^{***}}-\frac{I_h^{***}}{I_h}\right)\le 0,\\ &\left(2-\frac{Q}{Q^{***}}-\frac{Q^{***}}{Q}\right)\le 0, \quad \left(2-\frac{S_r}{S_r^{***}}-\frac{S_r^{***}}{S_r}\right)\le 0,\\ &\left(2-\frac{I_r}{I_r^{***}}-\frac{I_r^{***}}{I_r}\right)\le 0\end{aligned}$$

It follows that $\dot{F}\le 0$ if $\mathcal{R}_0>1$ and $\dot{F}=0$ when $S_h=S_h^{***}, I_h=I_h^{***}, Q=Q^{***}, S_r=S_r^{***}$ and $I_r=I_r^{***}$. Therefore, $\dot{F}$ is a Lyapunov function of system (2.1). We conclude this theorem with similar argument as in the proof of Theorem 3.3.

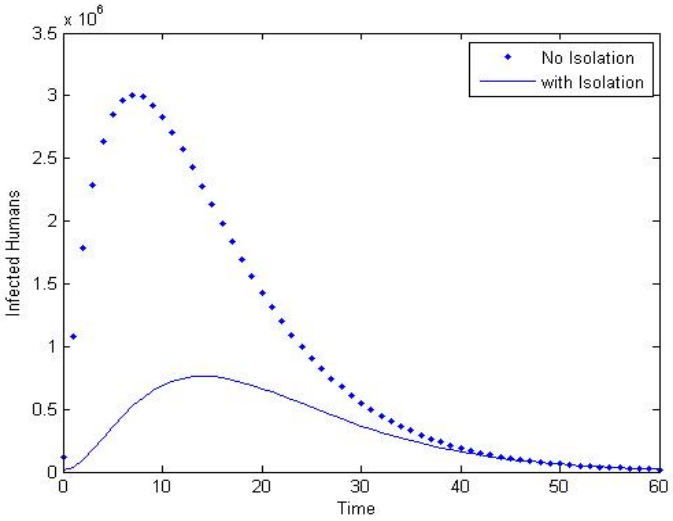
4. Numerical results and Conclusion

4.1. **Numerical simulations.** To investigate the positive impact of isolation of infected individuals on the dynamics of lassa fever disease, we simulate model (2.1) using the data presented in Table 4.1. We first consider the effect of isolation rate γ and then the effects of isolation when the basic reproduction number $\mathcal{R}_0$ is less than and greater than unity. Figure 2, shows that an increase in the isolation rate of infected humans leads to the decrease of infected humans subpopulation. Moreover, one can observe from Figure 2 that when $\gamma = 0$ the infected humans population is 60 million, increasing γ to 0.05 results in reducing the infected human to around 40 million while when $\gamma = 0.1$ the population declined to about 22 million.

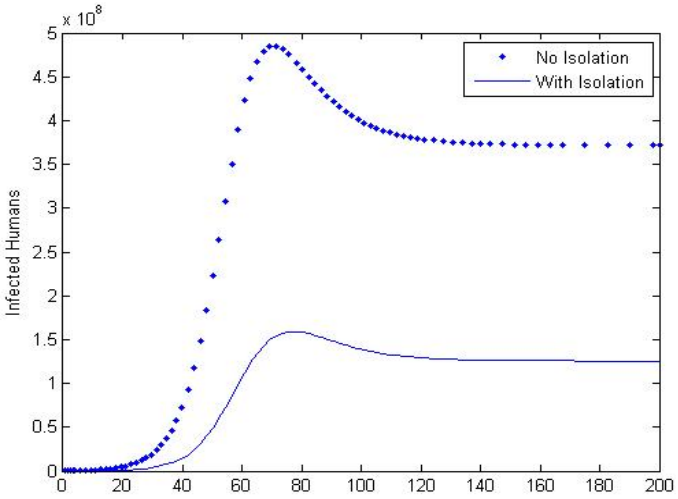
For the impact of isolation on model (2.1) when the basic reproduction number $\mathcal{R}_0 = 0.4042 < 1$, Figure 3 indicates that without isolation the infected humans could reach 3 million and the presence of isolation strategy the infected humans are about 0.8 million. On the other hand, the infected humans could be 490 million without isolation and decline to about 150 million with isolation strategy if $\mathcal{R}_0 = 3.7707 > 1$. In general, isolating infected human from the population decreases the number of infected individuals thereby containing the spread of the virus in a population.



Figures 2: Simulation results showing the impact of isolation rate on infected humans



Figures 3: Graph of infected humans with and without isolation when $\mathcal{R}_0 < 1$.



Figures 4: Graph of infected humans with and without isolation when $\mathcal{R}_0 > 1$ at $\beta_h = 0.844$.

TABLE 3. parameter description

Parameter	Range/Baseline value	Reference
Π_h	68.088	[30]
β_h, β_r	0.0844, 0.0372	[30], estimated
μ_h, μ_r	0.018182, 0.1858	[9, 32, 35]
τ_1	0.0614	[30]
τ_2	[0.01,0.18]	[34]
γ	[0.05,0.08]	[26]
δ	[0.0452,0.1133]	[29]
Π_r	946	[26]

Conclusions: In this paper, a mathematical model is developed and analysed to study the transmission dynamics of Lassa fever with isolation of infected individuals as a control measure. The model incorporates isolation as a control measure and divide the reservoir population into two as an extension of the model proposed in [22]. We first show that there exists a domain where our model is well posed mathematically and epidemiologically. The model is shown to exhibits three equilibrium points namely; disease-free equilibrium (DFE), denoted by ε_{0L}, Rodent disease-free equilibrium (RDFE), (ε_{1L}), and endemic state represented by ε_{2L}. Furthermore, each equilibrium point is proved to be globally asymptotically stable under certain condition on the associated threshold parameter either $\mathcal{R}_{0r}$ or $\mathcal{R}_{0h}$.
In order to complete our analysis, we simulate model (2.1) using the parameter values in table 3 to investigate the positive impact of isolation strategy in the transmission dynamics of lassa fever. Indeed, Figure 2 reveals that an increase of isolation rate decreases the number of infected individuals which results in containing the spread of the virus. Figure 3 and Figure 4 also show that the presence of isolation strategy decreases drastically the number of infected individuals in a society.

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