A Mathematical Modelling of Lassa Fever Dynamics with Non-drug Compliance Rate

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Abstract

This paper presents a mathematical model that tracks the transmission dynamics of Lassa fever in a two-interacting human host and rodent vector populations. The model incorporates a non-drug compliance rate in the parameters for the human population. The basic reproduction number is derived and the stability of the disease-free and endemic equilibrium points is analysed. A locally asymptotically stable disease-free equilibrium at the basic reproduction number less than unity is derived through the analysis of characteristic equation. It was established that the disease-free equilibrium point is globally asymptotically stable when the reproduction number, $R_o < 1$ and the disease always dies out. For $R_0 > 1$, the disease-free equilibrium point becomes unstable and the endemic equilibrium point is globally asymptotically stable.

Keywords: Lassa fever, non-drug compliance, basic reproduction number, compound matrices, stability.

1 Introduction

Lassa fever is an acute arena viral haemorrhagic fever caused by Lassa virus. It was first found in a town called Lassa in the Yedseram River Valley in the present Borno State of Northern Nigeria in 1969 [17]. The first victim is Laura Wine, 65 years old female nurse who works at Lassa Mission Hospital [9]. Lassa fever is endemic in Nigeria, Liberia, Sierra Leone, Guinea and other West African countries, affecting 2-3 million people with 5000-10000 fatalities annually [8]. Since its initial discovery in Lassa-Nigeria, rural and nosocomial outbreaks of Lassa fever have occurred repeatedly in other parts of Nigeria: Jos, Onitsha, Zorikwa, Ekpoma [18].

Proomed [14] reported outbreaks in some cities of West African countries of Sierra Leone, Liberia, Guinea. In Cote d'Ivoire, Ghana, Togo and Benin, no outbreak has ever been recorded, though isolation cases show evidence of viral circulation [2]. However, some Lassa fever cases have been imported in the U.S and U.K through travellers who acquire the disease elsewhere [17].

The carrier of Lassa virus is a small rodent (rat), the Multimammate rat of the genus Mastomys. Transmission occurs when an individual comes in contact directly with the blood, urine, faeces of rats and other body secretion of an infectious person [1]. Secondary human-to-human spread within a community may occur through inhalation or ingestion. Victims can also become infected through skin breaks and through mucous membranes from aerosol transmission from dust-borne particles. In some areas, the rodents are used as a food source,

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thus providing additional exposure to the infectious rat blood, as well as allowing ingestion of potentially contaminated meat.

The symptoms of Lassa fever develop 21 days after the infection with acute illness involving multi organs. Specific symptoms include fever, facial swelling, muscle fatigue, vomiting, cough, meningitis and hypertension. In some parts, neurological problems, including hearing loss, which may be transient or permanent, tremors and encephalitis have been described. [10].

Various theoretical studies have been carried out on mathematical modelling of Lassa fever transmission dynamics, focusing on a number of different issues. Okuonghae et al [11] formulated a SIS model coupled to a population of rat for the transmission of Lassa fever disease. They calculated the basic reproduction number for their model and gave conditions for disease outbreak. Ogabi et al. [12] developed a SIR model for controlling Lassa fever transmission in Northern part of Edo state, Nigeria. They advocated for health policies that will keep the basic reproduction number, R_o below 1, thereby keeping the transmission of the disease under control. Bawa et al. [1] developed a mathematical model for Lassa fever where they divided the human population into susceptible human S_H and the infectious human I_H and the reservoir population into infant I_R and the adult reservoir A_R and represented the virus in the environment by V. They explained that the virus compartment is generated from the urine and faeces of infected human and adult reservoirs. They recommended that effort should be made to keep the basic reproduction number below one. James et al. [5] developed a mathematical model of Lassa fever disease dynamics using a set of ordinary differential equations. They discovered that the zero equilibrium is stable when the birth rate of the human population is less than the death rate and same when the birth rate of the mastomysnatalensis (reservoir) is less than the total death rates. Onuorah et al. [13] 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. The total human population at time t denoted by $N_H(t)$ was sub-divided into four mutually exclusive sub-populations of Susceptible Male $S_1(t)$, Infected Male $I_1(t)$ Susceptible Female $S_2(t)$, Infected Female $I_2(t)$, such that $N_H(t) = S_1(t) + I_1(t) + S_2(t) + I_2(t)$. Similarly, the total Natural Reservoir/host population at time t, denoted by $N_R(t)$ was into dormant Reservoir host $R_1(t)$, active Reservoir host $R_2(t)$ such that $N_R(t) = R_1(t) + R_2(t)$. Their model had the following assumptions: Susceptible individuals, male/female can be infected through interaction with the active Reservoir (Mastomys Natelensis), and through sexual interaction with opposite sex. Two major controls were considered, the use of condom to reduce contact through sexual interaction and the use of pesticide/rat poison to kill the natural Reservoir (Mastomys Natelensis).

The model considered in this paper differs from that of previous work because it incorporates the rate at which infectious humans do not comply with drug into parameters of human population. Motivated by the 2017 Lassa fever reoccurrence in Nigeria, a deterministic mathematical model is developed and analysed to investigate the impact of non-drug compliance rate on the spread of Lassa fever in order to model the dynamics of the disease and to make decisions on controlling it.

The paper is organized as follows: In section 2, compartmental model formulation for the transmission dynamics of Lassa fever is obtained. Section 3 deals with the qualitative analysis

of Lassa fever model. Section 4 deals with discussion of results and concludes the modelling work.

2 Compartmental Model Formulation for the Transmission Dynamics of Lassa Fever

The model sub-divides the total human population denoted by N_H, into sub-populations of susceptible human hosts (S_H), infectious human hosts (I_H), and recovered human hosts so that $N_H = S_H + I_H + R_H$.

The total rodent vector population, denoted by N_R, is sub-divided into susceptible rodent vector (S_R) and infected rodent vector (I_R) so that $N_R = S_R + I_R$.

The susceptible human population is generated by the recruitment of individuals into the population at a rate Λ_h. The population reduces when the infectious rodent vectors interact with susceptible human hosts at rates α_1 and α_2. The population increases when the recovered human hosts lose immunity at a rate γ. It increases again when the infectious human hosts are given medication by their doctors but do not comply with drug at a rate τ_{nc}. It also reduces when susceptible human hosts die naturally.

The population of the infectious human hosts is generated by the interaction of the infectious rodent vectors with the population of susceptible human hosts at rates α_1 and α_2. It reduces when the infectious human hosts comply with drug at a rate τ_c. It also reduces when the infectious human hosts do not comply with drug at a rate τ_{nc}. It reduces again when the infectious human hosts are educated to comply with drug after being given medication by their doctors at a rate r_c. It moreover reduces when the infectious human hosts die as a result of Lassa fever at a rate δ. It again reduces due to natural death at a rate μ_H.

The recovered human hosts are generated by the infectious human hosts who are given medication by their doctors and comply with drug at a rate τ_c. It increases when the non-drug compliant human hosts are educated to comply with drug at a rate $r_c\tau$. The population reduces when the recovered human hosts lose immunity at a rate γ. It also reduces when the recovered human hosts die naturally at a rate μ_H.

The susceptible rodent vector population is generated by the recruitment of rodent vectors into the population at a rate Λ_R. The population reduces when the susceptible rodent vectors interact with infectious rodent vectors at rates α_1 and α_3. It decreases again due to natural death at a rate μ_R.

The population of infectious rodent vector is generated by the interaction of susceptible rodent vectors with infectious rodent vectors at rates α_1 and α_3. It decreases due to natural death at a rate μ_R.

The model has the following variables and parameters and the unit of time is days:
$S_H(t)$ = the number of susceptible human hosts at time t
$I_H(t)$ = the number of infectious human hosts at time t

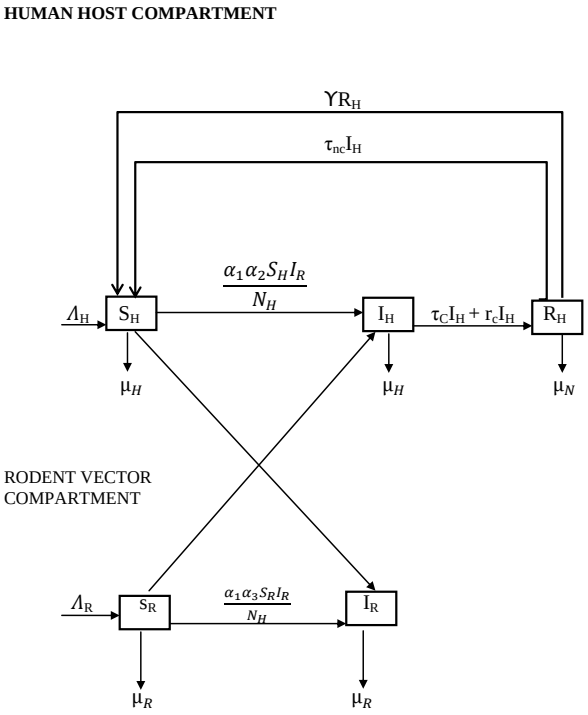

Figure 1: Compartmental Diagram for Lassa fever Model Incorporating Non-Drug Compliance Rate

$R_H(t)$ = the number of recovered human hosts at time t
$S_R(t)$ = the number of susceptible rodent vectors at time t
$I_R(t)$ = the number of infectious rodent vectors at time t
$N_H(t)$ = total human population
$m = \frac{N_R}{N_H}$ = the number of infectious rodent vectors per human host
α_1 = the rate of transmission resulting from interaction between infectious rodent vectors and susceptible human hosts
α_2 = concentration of Lassa virus that produces infection
α_3 = progression rate from susceptible rodent vector to infectious rodent vector
τ_c = rate at which infectious human hosts comply with drug
τ_{nc} = rate at which infectious human hosts do not comply with drug
r_c = rate at which infectious human hosts are educated to comply with drug
δ = death rate of infectious human hosts due to the disease
γ = rate of loss of immunity in human hosts

2.1 Assumptions of the Model

The following assumptions were made in order to formulate the equations of the model:
(a). Susceptible human host is infected through interaction with the infectious rodent vector.
(b). Susceptible rodent vector becomes infectious when it comes in contact with infectious human host.
(c). Some infectious human hosts who are given medication by their doctors and comply with drug get, treated fully and move to the recovered human host compartment.
(d). Some infectious human hosts who are given medication by their doctors but do not comply with drug, get treated partially and move to the susceptible human compartment.
(e). Small proportion of active virus are still in the system of partially treated human hosts.
(f). The partially treated infectious human hosts due to non-drug compliance rate do not show symptoms for some time, but sooner or later, recrudescence occurs, that is, reappearance of symptoms after a symptom free period.
(g). Susceptible rodent vector is infected through the interaction with the infectious human host.
(h). Interaction between susceptible rodent vector and infectious rodent vector is ignored.
(i). Human to human spread of the disease is ignored.
(j). Recovered human hosts have temporary immunity that can be lost and are again susceptible to reinfection.

Applying the assumptions, variables and parameters above, the Lassa fever model is formulated:

$$\frac{dS_H}{dt} = \Lambda_H - \frac{\alpha_1\alpha_2 S_H I_R}{N_H} + \gamma R_H + \tau_{nc} I_H - \mu_H S_H \tag{2.1}$$

$$\frac{dI_H}{dt} = \frac{\alpha_1\alpha_2 S_H I_R}{N_H} - \tau_c I_H - r_c I_H - \tau_{nc} I_H - \delta I_H - \mu_H I_H \tag{2.2}$$

$$\frac{R_H}{dt} = \tau_c I_H + r_c I_H - \gamma R_H - \mu_H R_H \tag{2.3}$$

$$\frac{dS_R}{dt} = \Lambda_R - \frac{\alpha_1\alpha_3 S_R I_H}{N_H} - \mu_R S_R \tag{2.4}$$

$$\frac{I_R}{dt} = \frac{\alpha_1\alpha_3 S_R I_H}{N_H} - \mu_R I_R \tag{2.5}$$

3 Qualitative Analysis of Lassa Fever Model

In this section, conditions that guarantee local and global stability of the disease-free equilibrium E_0 are stated and proved. But before then, the model shall be analysed proportionally. To do this, the total population sizes N_H and N_R can be determined by $S_H + I_H + R_H = N_H$ and $S_R + I_R = N_R$ or from the differential equations

$$\frac{dN_H}{dt} = \Lambda_H - \mu_H N_H - \delta I_H \tag{3.1}$$

$$\frac{dN_R}{dt} = \Lambda_R - \mu_R N_R \tag{3.2}$$

which are derived by adding Eqs. (2.1)-(2.3) for the human population and (2.4) and (2.5) for rodent vector population. Now we do the scaling by making the transformation $s_h = \frac{S_H}{N_H}$; $i_h = \frac{I_H}{N_H}$ $r_h = \frac{R_H}{N_H}$; $s_r = \frac{S_R}{N_R}$; $i_r = \frac{I_R}{N_R}$; $m = \frac{N_R}{N_H}$. This is done by differentiating the fractions with respect to time t and simplifying as follows:

$$\begin{aligned}
\frac{ds_h}{dt} &= \frac{1}{N_H}\left[\frac{dS_H}{dt} - s_h\frac{dN_H}{dt}\right] \\
&= \lambda_h(1-s_h) - \alpha_1\alpha_2 m s_h i_r + \gamma r_h + \tau_{nc} i_h + \delta s_h i_h \\
\frac{di_h}{dt} &= \frac{1}{N_H}\left[\frac{dI_H}{dt} - i_h\frac{dN_H}{dt}\right] \\
&= \alpha_1\alpha_2 m s_h i_r - (\tau_c + r_c + \delta + \lambda_h + \tau_{nc}) i_h + \delta i_h^2 \\
\frac{dr_h}{dt} &= \frac{1}{N_H}\left[\frac{dR_H}{dt} - r_h\frac{dN_H}{dt}\right] \\
&= (\tau_c + r_c) i_h - (\gamma + \lambda_h) r_h + \delta i_h r_h \\
\frac{ds_r}{dt} &= \frac{1}{N_H}\left[\frac{dS_R}{dt} - s_r\frac{dN_H}{dt}\right] \\
&= \lambda_r - (1 - s_r) - \alpha_1\alpha_3 m s_r i_h \\
\frac{di_r}{dt} &= \frac{1}{N_H}\left[\frac{dI_R}{dt} - i_r\frac{dN_H}{dt}\right] \\
&= \alpha_1\alpha_3 m s_r i_h - \lambda_r i_r
\end{aligned}$$

subject to the restrictions $s_h + i_h + r_h = 1$ and $s_r + i_r = 1$. Using the relations $r_h = 1 - s_h - i_h$ and $s_r = 1 - i_r$ lead to study the system of differential equations

$$\frac{ds_h}{dt} = \lambda_h(1 - s_h) - \alpha_1\alpha_2 m s_h i_r + \gamma(1 - s_h - i_h) + \tau_{nc} + \delta s_h i_h \tag{3.3}$$

$$\frac{di_h}{dt} = \alpha_1\alpha_2 m s_h i_r - (\tau_c + r_c + \lambda_h + \delta + \tau_{nc})i_h + \delta i_h^2 \tag{3.4}$$

$$\frac{di_r}{dt} = \alpha_1\alpha_3(1 - i_r)i_h - \lambda_r i_r \tag{3.5}$$

in the feasible region (i.e. where the model makes biological sense)
$T = \{(s_h, i_h, i_r) \in R_+^3 : 0 \leq s_h, 0 \leq i_h, s_h + i_h \leq 1, 0 \leq i_r \leq 1\}$
Equilibrium points are obtained by setting the right hand-sides of (3.3)-(3.5) to zero and the system takes the form

$$\lambda_h(1 - s_h) - \alpha_1\alpha_2 m s_h i_r + \gamma(1 - s_h - i_h) + \tau_{nc} + \delta s_h i_h = 0 \tag{3.6}$$

$$\alpha_1\alpha_2 m s_h i_r - (\tau_c + r_c + \lambda_h + \delta + \tau_{nc})i_h + \delta i_h^2 = 0 \tag{3.7}$$

$$\frac{di_r}{dt} = \alpha_1\alpha_3(1 - i_r)i_h - \lambda_r i_r = 0 \tag{3.8}$$

3.1 Local stability of disease-free equilibrium point E_0

Lemma 1: The disease-free equilibrium E_0 is locally stable if $R_0 < 1$ and unstable if $R_0 > 1$.
Proof: In the absence of infection, the model has a steady state, E_0, called the disease-free equilibrium, where $E_0 = (1, 0, 0)$. To establish the local stability of this equilibrium, the Jacobian of (3.6)-(3.8) is computed and evaluated at E_0. The local stability of E_0 is determined based on the signs of the eigenvalues of this Jacobian. The equilibrium E_0 is locally stable if the real part of these eigenvalues are all negative. At the steady state of the model, the Jacobian matrix is given by

$$J_E = \begin{bmatrix} -(\lambda_h + \alpha_1\alpha_2 m i_r + \gamma - \delta i_h & \tau_{nc}) - \gamma + \delta s_h & -\alpha_1\alpha_2 m s_h \\ \alpha_1\alpha_2 m i_r & -A_T + 2\delta i_h & \alpha_1\alpha_2 m s_h \\ 0 & \alpha_1\alpha_3(1 - i_r) & -\lambda_r - \alpha_1\alpha_3 i_h \end{bmatrix} \tag{3.9}$$

The Jacobian matrix in (3.9) at E_0 gives

$$J_{E_0} = \begin{bmatrix} (\lambda_h + \gamma) & -\tau_{nc} - \gamma + \delta & -\alpha_1\alpha_2 m \\ 0 & -A_T & \alpha_1\alpha_2 m \\ 0 & \alpha_1\alpha_3 & -\lambda_r \end{bmatrix} \tag{3.10}$$

where

$$A_T = \tau_c + r_c + \lambda_h + \delta + \tau_{nc}$$

Evaluating the eigenvalues at the Jacobian matrix gives

$$-(\lambda_h + \gamma),\ \frac{-(A_T + \lambda_r) \pm \sqrt{(A_T + \lambda_r)^2 - 4A_T\lambda_r(1 - R_0)}}{2}$$

where

$$R_0 = \frac{\alpha_1^2\alpha_2\alpha_3 m}{A_T\lambda_r}$$

We obtain the reproductive number R_0 by expressing (3.3)-(3.5) as the difference between the rate of new infection in each infected compartment A and the rate of transfer between each infected compartment B

$$\begin{bmatrix} \frac{di_h}{dt} \\ \frac{i_r}{dt} \end{bmatrix} = S - T = \begin{bmatrix} \alpha_1\alpha_2 m s_h i_r \\ \alpha_1\alpha_3 m s_r i_h \end{bmatrix} - \begin{bmatrix} (\tau_c + r_c + \lambda_h + \delta + \tau_{nc})i_h + \delta i_h^2 \\ \lambda_r i_r \end{bmatrix}$$

The Jacobian matrices J_S and J_T of S and T are found about E_0.

$$D = J_S J_T^{-1} = \begin{bmatrix} 0 & \frac{\alpha_1\alpha_3 m}{\lambda_r} \\ \frac{\alpha_1\alpha_2 m}{\tau_c + r_c + \lambda_h + \delta + \tau_{nc}} & 0 \end{bmatrix}$$

R_0 is the maximum eigenvalue of D given as $R_0 = \frac{\alpha_1^2\alpha_2 m\alpha_3}{A_T\lambda_r}$ where $A_T = \tau_c + r_c + \lambda_h + \delta + \tau_{nc}$ It is easy to see that the two eigenvalues have negative real parts if $R_0 < 1$, therefore, the disease-free equilibrium E_0 is locally asymptotically stable.

3.2 Global Stability of Disease-Free Equilibrium E_0

Theorem 1: The disease-free equilibrium $E_0 = (1, 0, 0)$ of (3.3)-(3.5) is globally asymptotically stable in T if $R_0 \leq 1$ and unstable if $R_0 > 1$.

Proof: Consider the Lyapunov function $L = \alpha_1\alpha_3 i_h + A_T i_r$ where $A_T = \tau_c + r_c + \lambda_h + \delta + \tau_{nc}$. Its derivative along the solutions of (3.3)-(3.5) is

$$\begin{aligned} L' &= \alpha_1\alpha_3\frac{di_h}{dt} + A_T\frac{i_r}{dt} \\ &= \alpha_1^2\alpha_2 m\alpha_3 s_h i_r - \alpha_1\alpha_3 i_h[A_T - \delta i_h] + A_T[\alpha_1\alpha_3 i_h(1 - i_r) - \lambda_r i_r] \\ &= \alpha_1^2\alpha_2 m\alpha_3 s_h i - r - A_T\lambda_r i_r + \alpha_1\alpha_3 i_h(\delta i_h - A_T i_r) \\ &= A_T\lambda_r i_r(\frac{\alpha_1^2\alpha_2 m\alpha_3 s_h}{A_T\lambda_r} - 1) + \alpha_1\alpha_3 i_h(\delta i_h - A_T i_r) \\ &= A_T\lambda_r i_r(R_0 s_h - 1) - \alpha_1\alpha_3 i_h(A_T i_r - \delta i_h) \\ &\leq A_T\lambda_r i_r(R_0 s_h - 1) \leq 0 \quad \text{if} \quad R_0 \leq 1 \end{aligned}$$

It is shown that $L' \leq 0$ if $R_0 \leq 1$ and the equality, $L' = 0$ holds when $R_0 = 1$ and $i_h = i_r = 0$. If $R_0 > 1$, then $L' > 0$ when s_h is sufficiently close to 1 except when $i_h = i_r = 0$. From Lyapunov-Lasalle's Theorem(see[J.K. Hale, 1969]), this implies that all paths in T approach the largest positive invariant subset of the set where $L' = 0$ is $(s_h, i_h, i_r) \in T$. On the boundary of T where $i_h = i_r = 0$ $(s_h - axis)$, $s_h' = (\lambda_h + \gamma)(1 - s_h)$ so that $s_h = (1 + e^{-(\lambda_h+\gamma)t}) \to 1$ as $t \to \infty$. Thus all solutions paths in T will approach the disease-free equilibrium point E_0. Hence the disease-free equilibrium point is globally asymptotically stable and this completes the proof of Theorem 1.

3.3 Global Stability of Endemic Equilibrium E_1

We need to establish the global stability of the unique endemic equilibrium point of the disease when it persists. In order to do that, we shall use the property of competitive systems[15,16,3] and additive compound matrices and differential equations[7] for the analysis of our system. The following definitions (see[4]) are used to establish the stability of the orbit:
Definition 1: The orbit Γ is orbitally stable if and only if for each $\epsilon > 0$, there exists a δ such that any solution $\tilde{x}$, for which the distance of $\tilde{x}(0)$ from Γ is less than δ, remains a distance less than ϵ from Γ, for all $t \geq 0$.

Definition 2: The orbit Γ is asymptotically orbitally stable, if it is orbitally stable and the distance of $\tilde{x}(t)$ from Γ also tends to zero as $t \to \infty$.

Since (3.3)-(3.5) is a 3-dimensional competitive system that is convex in D, the following theorem stated and proved in [6] for a system of an SEIR model is used to generalize results of systems that are competitive, persistent and have the property of stability of periodic orbits.

Theorem 1: For $n = 3$ and D convex and bounded and suppose that (3.3)-(3.5) is competitive, permanent and have the property of stability of periodic orbits. If $\tilde{x}_0$ is the only equilibrium point in intD, and if it is locally asymptotically stable, then it is globally asymptotically stable in intD.

Proof: In order to analyze the global stability of the endemic equilibrium, the additive compound matrices approach as in [6,7] is used. From the Jacobian matrix J_E, the second additive compound matrix is given by

$$J_E^{[2]} = \begin{bmatrix} -(B - 3\delta i_h) & \alpha_1\alpha_2 m s_h & \alpha_1\alpha_2 m s_h \\ \alpha_1\alpha_3(1 - i_r) & -(C - \delta i_h) & \tau_{nc} - \gamma + \delta s_h \\ 0 & \alpha_1\alpha_2 m i_r & -(D - 2\delta i_h) \end{bmatrix} \tag{3.11}$$

where

$$\begin{aligned} B &= (A_T + \lambda_h + \alpha_1\alpha_2 m i_r + \gamma) \\ C &= \lambda_h + \lambda_r + \alpha_1\alpha_3 i_h + \gamma + \alpha_1\alpha_2 m i_r \\ D &= A_T + \lambda_r + \alpha_1\alpha_3 i_h \end{aligned}$$

From the second additive compound matrix above, we have a linear system with respect to the solutions $s_h(t), i_h(t), i_r(t)$ written as
$w_1'(t) = -(B - 3\delta i_h(t))w_1(t)$
$w_2'(t) = \alpha_1\alpha_3(1 - i_r(t))w_1(t) - (C - \delta i_h(t))w_2(t) + (\tau_{nc} - \gamma + \delta s_h(t))w_3(t)$
$w_3'(t) = \alpha_1\alpha_2 m i_r(t)w_2(t) - (D - 2\delta i_h(t))w_3(t)$
In order to prove that the system $J_E^{[2]}$ is asymptotically stable, we shall use the following Lyapunov function that is positive but not differentiable everywhere:
$V(w_1(t), w_2(t), w_3(t)) = \sup\{|w_1|, \frac{i_h(t)}{i_r(t)}(|w_2| + |w_3|)\}$
Denoting the left- hand side derivative of V(t) by $D_+V(t)$, we get the following inequalities:

$$\begin{aligned} D_+(|w_1(t)|) &\leq -(B - \delta i_h(t))|w_1(t)| + \alpha_1\alpha_2 m s_h(|w_2(t) + w_3(t)|) \\ &\leq -(B - 3\delta i_h(t))|w_1(t)| + \frac{\alpha_1\alpha_2 m s_h(t) i_r(t)}{i_h(t)}\left(\frac{i_h(t)}{i_r(t)}|w_2(t)| + |w_3(t)|\right) \quad (3.12) \\ D_+(|w_2(t)|) &\leq \alpha_1\alpha_3(1 - i_r)|w_1(t)| - (C - \delta i_h(t))|w_2(t)| + (\tau_{nc} - \gamma + \delta s_h(t))|w_3(t)| \quad (3.13) \\ D_+(|w_3(t)|) &\leq (\alpha_1\alpha_2 m i_r)|w_2(t)| - (D - 2\delta i_h(t))|w_3(t)| \quad (3.14) \end{aligned}$$

We also have

$$\begin{aligned} D_+\frac{i_h(t)}{i_r(t)}(|w_2(t)| + |w_3(t)|) &= \left[\frac{i_h'(t)}{i_h(t)} - \frac{i_r'(t)}{i_r(t)}\right]\frac{i_h(t)}{i_r(t)}(|w_2(t)| + |w_3(t)|) \\ &\quad + \frac{i_h(t)}{i_r(t)}D_+(|w_2(t)| + |w_3(t)|) \quad (3.15) \end{aligned}$$

Adding (3.13) and(3.14), we have

$$D_+(|w_2(t)| + |w_3(t)|) = \alpha_1\alpha_3(1 - i_r(t))|w_1(t)| - (C - \alpha_1\alpha_2 m i_r - \delta i_h)|w_2(t)|$$

$$+(\tau_{nc} - \gamma + \delta s_h(t) + 2\delta i_h(t) - D)|w_3(t)|$$

$$= \alpha_1\alpha_3(1 - i_r(t))w_1(t) - (\lambda_h + \lambda_r + \alpha_1\alpha_3 i_h + \gamma - \delta i_h(t))w_2(t)$$

$$-(\lambda_h + \lambda_r + \alpha_1\alpha_3 i_h + \gamma - \delta i_h(t) + \tau_{nc} + \tau_c + r_c - \delta(1 - s_h(t) - i_h(t)))\, w_3(t)$$

$$\leq \alpha_1\alpha_3(1 - i_r(t))|w_1(t)| - (\lambda_h + \lambda_r + \alpha_1\alpha_3 i_h + \gamma - \delta i_h(t))(|w_2(t) + |w_3(t)|) \quad (3.16)$$

Substituting (3.16) into (3.15) yields

$$\begin{aligned}
&D_+\frac{i_h(t)}{i_r(t)}(|w_2(t)|+|w_3(t)|)\\
&\leq \frac{i_h(t)}{i_r(t)}\left[\frac{i_h'(t)}{i_h(t)}-\frac{i_r'(t)}{i_r(t)}\right](|w_2(t)|+|w_3(t)|)\\
&+\frac{i_h(t)}{i_r(t)}(\alpha_1\alpha_3(1-i_r(t)))|w_1(t)|\left[-(\lambda_h+\lambda_r+\alpha_1\alpha_3 i_h+\gamma-\delta i_h(t))(|w_2(t)|+|w_3(t)|)\right]\\
&\leq \alpha_1\alpha_3(1-i_r(t))\frac{i_h(t)}{i_r(t)}(|w_1(t)|)\\
&+\left[\frac{i_h'(t)}{i_h(t)}-\frac{i_r'(t)}{i_r(t)}-\lambda_h-\lambda_r-\alpha_1\alpha_3 i_h-\gamma+\delta i_h(t)\right]\frac{i_h(t)}{i_r(t)}(|w_2(t)+w_3(t)|) \qquad (3.17)
\end{aligned}$$

From (3.12) and (3.17), we have

$D_+V(t)\leq \sup(g_1(t),g_2(t))V(t)$,
where

$$g_1(t)=-(B-3\delta i_h(t))+\frac{\alpha_1\alpha_2 m s_h(t)i_r(t)}{i_h(t)} \qquad (3.18)$$

$$\begin{aligned}
g_2(t)&=\alpha_1\alpha_3(1-i_r(t))\frac{i_h(t)}{i_r(t)}\\
&+\left(\frac{i_h'(t)}{i_h(t)}-\frac{i_r'(t)}{i_r(t)}-\lambda_h-\lambda_r-\alpha_1\alpha_3 i_h(t)-\gamma+\delta i_h(t)\right) \qquad (3.19)
\end{aligned}$$

Using the expressions from (3.7) and (3.8) given by

$$\begin{aligned}
\frac{\alpha_1\alpha_2 m s_h(t)i_v(t)}{i_h(t)} &= \frac{i_h'(t)}{i_h(t)}+\tau_{nc}+\tau_c+r_c+\lambda_h+\delta-\delta i_h\\
\alpha_1\alpha_3(1-i_r)\frac{i_h(t)}{i_r(t)} &= \frac{i_r'(t)}{i_r(t)}+\lambda_r
\end{aligned}$$

(3.18) and (3.19) simplify to

$$g_1(t) = \frac{i_h'(t)}{i_h(t)}+[2\delta i_h(t)-(\lambda_h+\alpha_1\alpha_2 m i_r)] \qquad (3.20)$$

$$g_2(t) = \frac{i_h'(t)}{i_h(t)}+[\delta i_h-(\lambda_h+\alpha_1\alpha_3 i_r(t)+\gamma)] \qquad (3.21)$$

so that

$$\sup\{g_1(t),g_2(t)\}\leq \frac{i_h'(t)}{i_h(t)}-\delta \qquad (3.22)$$

From (3.22), we have

$$\lim_{w\to+\infty}\int_0^w \sup\{g_1(t), g_2(t)\}dt \leq \lim_{w\to+\infty}[\ln i_h(t)]_0^w$$
$$-\delta w = -\delta w < 0 \tag{3.23}$$

This shows that the periodic solution $(s_h(t), i_h(t), i_r(t))$ is asymptotically stable. This establishes the fact that the endemic equilibrium point of the disease is globally stable.

4 Discussion

A model with incidence of dynamics of Lassa fever within human hosts and rodent vector is proposed in which the non-drug compliance rate is incorporated into the system, which is the rate at which infectious human hosts do not comply with drug. The class of the recovered human is refilled by the infectious human hosts who comply with drug and infectious humans who are educated to take their drug. The model was then reformulated in terms of the proportions of the classes of the respective populations. Model analyses were carried out. Disease-free and endemic equilibrium solution were obtained and their stability was analysed respectively.

It was established that for the basic reproduction number, $R_0 < 1$, the disease-free equilibrium solution is globally asymptotically stable so that the disease always dies out, and if $R_0 > 1$, the disease-free equilibrium is unstable. We observe that in order to reduce the basic reproduction number below 1, intervention strategies need to be focused on treatment and reduction on the contact between mosquito vector and human host.

Since the non-drug compliance rate of infectious human hosts causes reappearance of symptoms after a symptom free period, there is need to increase the parameter r_c which reduces the number of infectious human hosts who do not comply with drug. There is also need for isolation of the infectious human hosts in order to reduce the spread of Lassa fever.

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