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Investigating essential factors in the spread of lassa fever dynamics through sensitivity analysis

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Abstract

Lassa fever is a zoonotic acute viral illness caused by Lassa virus. Since there is no vaccine yet to protect against contracting the virus, it continues to spread in West Africa. In this paper, a mathematical model of lassa transmission that considers two classes of rats: house rat and bush rat, is proposed. Theoretically, global stability of the model disease-free and endemic equilibria are established by constructing a global Lyapunov function. Sensitivity indices of the basic reproduction number are derived using the normalised forward approach to evaluate the effectiveness of control measures. The disease-free equilibrium is globally asymptotically stable when the basic reproduction number $R_0 < 1$ and the unique endemic equilibrium is globally asymptotically stable when $R_0 > 1$. Results from sensitivity analysis reveals that rat biting rate for infectious house rats R_{FH} and infectious bush rats R_{FB}, transmission probability per contact with infectious house and bush rats (R_{FH} and R_{FB}), human recruitment rate and transmission probability per contact with infectious human hosts are highly significant in determining the severity of lassa infection. On the other hand, natural death rate of rats, natural death rate of human hosts, recovery and hospitalization rates of human hosts are critical for lassa transmission reduction. Plans that target the contact rate between house and bush rats (i.e use of indoor residual spray, fumigation of environment with pesticide) and those that target recovery rate of human hosts (i.e treatment of infectious human hosts) are recommended to control the disease.

Keywords: Lassa; basic reproduction number; stability; sensitivity analysis
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1. Introduction

Lassa fever is an acute hemorrhagic fever caused by Lassa virus (LAV), a bisegmented ambisense single-stranded RNA virus that belongs to the family old world Arenaviridisae spp [22]. It is prevalent in the West African sub-region where about 3-5 million individuals are infected yearly [6]. The transmission is through the droppings of the multimammate rat (mastomys natalensis spp) which serves as the reservoir to the virus. For more ecological background, the reader is referred to ([22], [6], [24]).

In recent times, several mathematical models have been formulated and analysed in the literature to study the transmission and spread of Lassa fever. Obabiyi et al., [16] analyzed the dynamics of Lassa infection with variable human and reservoir population. They employed maximum principle theorem to establish the positivity and boundedness of solutions. They also used Routh-Hurwitz criterion to establish the local stability of the disease-free equilibrium solution. They further made use of Maple software to show the graphical behaviour of the model compartmental classes. The results from their analysis show that the model is well posed and the disease-free equilibrium is locally stable for $R_0 < 1$. They therefore concluded that early diagnostic of infected humans, maintaining hygienic environment, use of new needle when taking injection and interim control of the rodent carrying the virus are the best strategy against the spread of the disease. In another development, Abdulhamid et al.[1] examined the effects of quarantine on transmission dynamics of Lassa fever. They employed next generation matrix operator method to calculate the basic reproduction number R_0. They also conducted numerical simulations using MATLAB. The results from their analysis showed that disease-free equilibrium is locally stable when $R_0 < 1$ and unstable when $R_0 > 1$. They concluded that the outlook of the effective control of Lassa virus is greatly enhanced if a control strategy based on using quarantine of the infectious human is implemented. Davies et al., [8] presented a deterministic mathematical model to investigate the effects of routine and pulse vaccination on Lassa dynamics between rodents and humans. They adopted a compartmental SEIR structure for humans and an SEI structure for rodents. They solved the model numerically using MATLAB. Their model showed that vaccination of 40-60 percent of infants reduces population incidence by 30-56 percent provided the vaccine has 70-90 percent effectiveness. They concluded that implementation of a vaccine in Lassa fever endemic areas could considerably reduce the disease incidence. For more comprehensive mathematical analysis of Lassa fever, see ([18], [17], [9], [20], [5], [19], [17], [10], [21]) and the references therein.

Motivated by Peter et al., [21], Okuongbe et al., [18] and Onuorah et al., [20], this paper presents a new mathematical model of Lassa fever that takes into account two classes of rats: house rat (i.e susceptible house rat, exposed house rat and infectious house rat) and bush rat (i.e susceptible bush rat, exposed bush rat and infectious bush rat), which is missing in the above literature. It is important to know that humans contact lassa fever disease from either house rat or bush rat. The disease is contacted from house and bush rats through contact or consumption. Our aim is to investigate essential factors that contribute to the spread of Lassa fever disease through sensitivity analysis. Hence qualitative and sensitivity analyses of Lassa fever model are presented incorporating the above compartments.

2. Model Formulation of Lassa Fever Disease

In this section, the transmission dynamics of Lassa fever is investigated. The total human hosts population N_H is sub-divided into five classes namely; the susceptible human hosts S_H, the exposed human hosts E_H, the infectious human hosts K_S, the hospitalized human host hosts K_P and the

recovered human hosts, R_H. Also, house rats population N_{RH}, is sub-divided into susceptible house rats R_{SH}, the exposed house rats R_{EH} and the infectious house rats R_{FH}. The bush rats population is sub-divided into susceptible bush rats R_{SB}, the exposed bush rats R_{EB} and the infectious bush rats R_{FB}. Thus, the total population N_H, N_S and N_B for human hosts, house rats and bush rats population are given by $N_H = S_H + E_H + K_S + K_P + R_H$, $N_S = R_{SH} + R_{EH} + R_{FH}$ and $N_B = R_{SB} + R_{EB} + R_{FB}$. We consider human-to-rat contact because research has shown that lassa fever transmission in most cases is as a result of contact between human and mastomys natalensis (rodent) [23] and therefore, we assume there is no human-to human transmission. The recruitment rates of human hosts, house rats and bush rats are respectively given by Λ_h, Λ_a and Λ_b. The parameter α is the biting rate of rat, the parameter ϕ is the transmission probability per contact with infectious house and bush rats while the parameter ϕ is the transmission probability per contact with infectious human hosts. The term $\alpha\psi S_H(R_{FH} + R_{FB})$ denotes the rate at which the human hosts S_H get infected by infectious house and bush rats while $\alpha\phi R_{SH}K_S$ refers to the rate at which susceptible house rats R_{SH} are infected by the infectious human hosts K_S and the term $\alpha\phi R_{SB}K_S$ denotes the rate at which the susceptible bush rats R_{SB} are infected by the infectious human hosts K_S. It is assumed that there is human-to-rat transmission. Also, it is assumed that progression rate for exposed house rats and exposed bush rats are not different and the transmission probability per contact with infectious human hosts for both house and bush rats are assumed to be the same. But the recruitment rate for human hosts, house rats and bush rats are assumed to be different. Moreover, we assume that population in K_S class can also recover without having to enter K_P class and all the human hosts in class K_P are 100% protected and so they do not contribute to the disease propagation.

Based on the assumptions, the following system of ordinary differential equations are obtained:

$$\frac{dS_H}{dt} = \Lambda_h - \alpha\psi S_H(R_{FH} + R_{FB}) - \mu_h S_H, \tag{2.1}$$

$$\frac{dE_H}{dt} = \alpha\psi S_H(R_{FH} + R_{FB}) - (\beta + \mu_h)E_H, \tag{2.2}$$

$$\frac{dK_S}{dt} = \beta E_H - (\delta_1 + \tau_1 + \varepsilon + \mu_h)K_S, \tag{2.3}$$

$$\frac{dK_P}{dt} = \varepsilon K_S - (\delta_2 + \tau_2 + \mu_h)K_P, \tag{2.4}$$

$$\frac{dR_H}{dt} = \tau_1 K_S + \tau_2 K_P - \mu_h R_H, \tag{2.5}$$

$$\frac{dR_{SH}}{dt} = \Lambda_a - \alpha\phi R_{SH}K_S - \mu_r R_{SH}, \tag{2.6}$$

$$\frac{dR_{EH}}{dt} = \alpha\phi R_{SH}K_S - (\omega + \mu_r)R_{EH}, \tag{2.7}$$

$$\frac{dR_{FH}}{dt} = \omega R_{EH} - \mu_r R_{FH}, \tag{2.8}$$

$$\frac{dR_{SB}}{dt} = \Lambda_b - \alpha\phi R_{SB}K_S - \mu_r R_{SB}, \tag{2.9}$$

$$\frac{dR_{EB}}{dt} = \alpha\phi R_{SB}K_S - (\omega + \mu_r)R_{EB}, \tag{2.10}$$

$$\frac{dR_{FB}}{dt} = \omega R_{EB} - \mu_r R_{FB}. \tag{2.11}$$

With initial conditions

Table 1: Summary of the parameters

Parameter	Meaning	Value	Reference
μ_h	Natural death rate of human hosts	0.02	[7]
Λ_h	Recruitment rate of human hosts	0.0038	[7]
Λ_a	Recruitment rate of susceptible house rats	0.00001	[21]
Λ_b	Recruitment rate of susceptible bush rats	0.0001	Assumed
α	Biting rate of R_{FH} and R_{FB}	0.083	[20]
ψ	Transmission probability per contact with R_{FH} and R_{FB}	0.083	Assumed
β	Progression rate from E_H to K_S	0.08	[20]
ω	Progression rate of R_{SH} and R_{SB}	0.70	Estimate
τ_1, τ_2	Recovery rates of K_S and K_P	0.2	[21]
κ	Hospitalization rate	0.2	Assumed
δ_1	Disease-induced death rate of K_S	0.001	[3]
δ_2	Disease-induced death rate of K_P	0.001	Assumed
ϕ	Transmission probability per contact with K_S	0.75	[20]
μ_r	Natural mortality rate of rats	0.000167	[3]

$(S(0) = S_o > 0, E_H(0) = E_H^0(0) > 0, K_S(0) = I_S^o(0) > 0, K_P(0) = K_P^o(0) > 0, R_H(0) = R_H^o > 0, R_{SH}(0) = R_{SH}^o > 0, R_{EH}(0) = R_{EH}^o > 0, R_{FH}(0) = R_{FH}^o > 0, R_{SB}(0) = R_{EB}^o > 0, R_{EB}(0) = R_{EB}^o > 0, R_{FB}(0) = R_{FB}^o > 0)$

(2.1)-(2.3) are independent of the states K_P and R_H and after decoupling the equations for K_P and R_H from the model, we have the remaining equations of the model (2.1)-(2.11) which becomes

$$\frac{dS_H}{dt} = \Lambda_h - \alpha\psi S_H(R_{FH} + R_{FB}) - \mu_h S_H, \tag{2.12}$$

$$\frac{dE_H}{dt} = \alpha\psi S_H(R_{FH} + R_{FB}) - (\beta + \mu_h)E_H, \tag{2.13}$$

$$\frac{dK_S}{dt} = \beta E_H - (\delta_1 + \tau_1 + \varepsilon + \mu_h)K_S, \tag{2.14}$$

$$\frac{dR_{SH}}{dt} = \Lambda_a - \alpha\phi R_{SH}K_S - \mu_r R_{SH}, \tag{2.15}$$

$$\frac{dR_{EH}}{dt} = \alpha\phi R_{SH}K_S - (\omega + \mu_r)R_{EH}, \tag{2.16}$$

$$\frac{dR_{FH}}{dt} = \omega R_{EH} - \mu_r R_{FH}, \tag{2.17}$$

$$\frac{dR_{SB}}{dt} = \Lambda_b - \alpha\phi R_{SB}K_S - \mu_r R_{SB}, \tag{2.18}$$

$$\frac{dR_{EB}}{dt} = \alpha\phi R_{SB}K_S - (\omega + \mu_r)R_{EB}, \tag{2.19}$$

$$\frac{dR_{FB}}{dt} = \omega R_{EB} - \mu_r R_{FB}. \tag{2.20}$$

2.1. Condition for Disease Spread

The condition for disease spread which is the basic reproduction number R_0, is computed below. This is the difference between the rate of new infection in each infected compartment F and the rate

of transfer between each infected compartment G. Hence, we have

$$\begin{bmatrix} \frac{dE_H}{dt} \\ \frac{dK_S}{dt} \\ \frac{dR_{EH}}{dt} \\ \frac{dR_{FH}}{dt} \\ \frac{dR_{EB}}{dt} \\ \frac{dR_{FB}}{dt} \end{bmatrix} = F - G = \begin{bmatrix} \alpha\psi S_H(\nu R_{FH} + R_{FB}) \\ 0 \\ \alpha\phi R_{SH} K_S \\ 0 \\ \alpha\phi R_{SB} K_S \\ 0 \end{bmatrix} - \begin{bmatrix} r_1 E_H \\ -\beta E_H + r_2 K_S \\ (\omega + \mu_r) R_{EH} \\ -\omega R_{EH} + \mu_r R_{FH} \\ (\omega + \mu_r) R_{EB} \\ -\omega R_{EB} + \mu_r R_{FB} \end{bmatrix}$$

The Jacobian matrices J_F and J_G of F and G are found about E_0.

$$S = J_F J_G^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{\alpha\phi\Lambda_a}{\mu_r(\omega+\mu_r)} & \frac{\alpha\phi\Lambda_a\omega}{\mu_r^2(\beta_3+\mu_r)} & \frac{\alpha\phi\Lambda_b}{\mu_r(\omega+\mu_r)} & \frac{\alpha\phi\Lambda_b\omega}{\mu_r^2(\omega+\mu_r)} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\alpha\psi\Lambda_h}{\mu_h r_1} & \frac{\alpha\psi\Lambda_h\beta}{\mu_h r_2 r_1} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\alpha\psi\Lambda_h}{\mu_h r_1} & \frac{\alpha\psi\Lambda_h\beta}{\mu_h r_2 r_1} & 0 & 0 & 0 & 0 \end{bmatrix}$$

R_0 is the maximum eigenvalue of S given as

$$R_0 = \sqrt{\frac{\alpha^2\psi\Lambda_h\phi\omega\beta H_T}{r_1 r_2 \mu_h \mu_r^2(\omega+\mu_r)}}$$

where

$$\begin{aligned} r_1 &= \beta + \mu_h \\ r_2 &= \delta_1 + \tau_1 + \mu_h + \varepsilon \\ H_T &= \Lambda_a + \Lambda_b \end{aligned}$$

It is worthy to mention that initial lassa fever disease transmission is associated to the basic reproduction number R_0.

3. Stability Analysis

We shall establish the global stability of lassa-free and prevalence equilibrium solution below.

3.1. Global Stability of the Lassa-Free Equilibrium Solution

In order to guarantee the elimination of lassa fever disease regardless of the initial sizes of the subpopulations of the model (2.1)-(2.11), the establishment of a globally asymptotically stable disease-free equilibrium becomes necessary, which is demonstrated in the following result.

Theorem 3.1. *The Lassa-free equilibrium E_0 of the model is globally asymptotically stable in Γ if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof: Consider the Lyapunov function

$$\begin{aligned} L =& \frac{\beta H_T}{\mu_h r_1 r_2} E_H + \frac{H_T}{r_2 \mu_h} K_S + \frac{\mu_r R_0 H_T}{2\alpha\phi\Lambda_a \mu_h} R_{EH} + \frac{\mu_r(\omega+\mu_r) R_0 H_T}{2\alpha\phi\omega\Lambda_a \mu_h} R_{FH} \\ &+ \frac{\mu_r R_0 H_T}{2\alpha\phi\Lambda_b \mu_h} R_{EB} + \frac{\mu_r(\omega+\mu_r) R_0 H_T}{2\alpha\phi\omega\Lambda_b \mu_h} R_{FB}. \end{aligned}$$

Its time derivative is

$$\begin{aligned} \dot{L} =& \frac{\beta H_T}{\mu_h r_1 r_2}(\alpha\psi S_H(R_{FH}+R_{FB}) - r_1 E_H) + \frac{H_T}{r_2\mu_h}(\beta E_H - r_2 K_S) \\ &+ \frac{\mu_r R_0 H_T}{2\alpha\phi\Lambda_a\mu_h}(\alpha\phi R_{SH} K_S - (\omega+\mu_r) R_{EH}) + \frac{\mu_r(\omega+\mu_r) R_0 H_T}{2\alpha\phi\omega\Lambda_a\mu_h}(\omega R_{EH} - \mu_r R_{FH}) \\ &+ \frac{\mu_r R_0 H_T}{2\alpha\phi\Lambda_b\mu_h}(\alpha\phi R_{SB} K_S - (\omega+\mu_r) R_{EB}) + \frac{\mu_r(\omega+\mu_r) R_0 H_T}{2\alpha\phi\omega\Lambda_b\mu_h}(\omega R_{EB} - \mu_r R_{FB}) \end{aligned}$$

$$\begin{aligned} \dot{L} =& \frac{\beta H_T \alpha\psi S_H(R_{FH}+R_{FB})}{r_1 r_2 \mu_h} - \frac{H_T K_S}{\mu_h} + \frac{\mu_r R_0 H_T R_{SH} K_S}{2\Lambda_a\mu_h} + \frac{\mu_r R_0 H_T R_{SB} K_S}{2\Lambda_b\mu_h} \\ &- \frac{\mu_r(\omega+\mu_r) R_0 H_T \mu_r R_{FH}}{\alpha\phi\omega\Lambda_a} - \frac{\mu_r(\omega+\mu_r) R_0 H_T \mu_r R_{FB}}{\alpha\phi\omega\Lambda_b} \end{aligned}$$

$$\begin{aligned} \dot{L} &= \left[\frac{\beta H_T \alpha\psi S_H}{r_1 r_2 \mu_h} - \frac{\mu_r^2(\omega+\mu_r) R_0 H_T}{2\alpha\phi\omega H_T \mu_h}\right](R_{FH}+R_{FB}) + \left(\frac{\mu_r R_0 R_{SH}}{2\Lambda_a} + \frac{\mu_r R_0 R_{SB}}{2\Lambda_b} - 1\right)\frac{K_S H_T}{\mu_h} \\ &\leq \left[\sqrt{\frac{\beta\psi\Lambda_h\mu_r^2(\omega+\mu_r) H_T}{r_1 r_2 \phi\omega\mu_h}}(R_0 - 1)\right](R_{FH}+R_{FB}) + (R_0-1)\frac{K_S H_T}{\mu_h} \\ &\leq \left[\sqrt{\frac{\beta\psi\Lambda_h\mu_r^2(\omega+\mu_r) H_T}{r_1 r_2 \phi\omega\mu_h}}.(R_{FH}+R_{FB}) + \frac{K_S H_T}{\mu_h}\right](R_0 - 1) \end{aligned}$$

Therefore, $\dot{L} \leq 0$ for $R_0 \leq 1$ for $\dot{L} = 0$ if and only if $R_0 = 1$ or $K_S = 0$, $R_{FH} = 0$ and $R_{FB} = 0$. As a result, the largest compact invariant set in $\{(S_H, E_H, K_S, K_P, R_H, R_{SH}, R_{EH}, R_{FH}, R_{SB}, R_{EB}, R_{FB}) \in \Gamma : \dot{L} = 0\}$ is the E_0 and by Lyapunov-Lasalle's invariance principle, the lassa-free equilibrium point is globally asymptotically stable in Γ if $R_0 \leq 1$ and this completes the proof.□

The epidemiological implication of the above theorem is that lassa fever disease can be eradicated irrespective of the initial sizes of the sub-population of the model. This means that the sub-population that starts with lassa infection shrinks and never turns to epidemic for $R_0 < 1$.

3.2. Global Stability of Endemic Equilibrium Point

The endemic equilibrium solution at steady state is

$$E_1 = (S_H^*, E_H^*, K_S^*, R_{SH}^*, R_{EH}^*, R_{FH}^*, R_{SB}^*, R_{EB}^*, R_{FB}^*)$$

where

$$S_H^* = \frac{\Lambda_h}{D_h^* + \mu_h}$$
$$E_H^* = \frac{D_h^* \Lambda_h}{(D_h^* + \mu_h)(\beta + \mu_h)}$$
$$K_S^* = \frac{\beta \Lambda_h D_h^*}{r_2(D_h^* + \mu_h)(\beta + \mu_h)}$$
$$R_{SH}^* = \frac{\Lambda_a}{D_r^* + \mu_r}$$
$$R_{EH}^* = \frac{D_r^* \Lambda_a}{(\omega + \mu_r)(D_r^* + \mu_r)}$$
$$R_{FH}^* = \frac{\omega D_r^* \Lambda_a}{\mu_r(\omega + \mu_r)(D_r^* + \mu_r)}$$
$$R_{SB}^* = \frac{\Lambda_b}{D_r^* + \mu_r}$$
$$R_{EB}^* = \frac{D_r^* \Lambda_b}{(\omega + \mu_r)(D_r^* + \mu_r)}$$
$$R_{FB}^* = \frac{\omega D_r^* \Lambda_b}{\mu_r(\omega + \mu_r)(D_r^* + \mu_r)}$$

where the forces of infection for human hosts and rats at equilibrium state are

$$D_h^* = \alpha\psi(R_{FH}^* + R_{FB}^*)$$

and

$$D_r^* = \alpha\phi K_S^*$$

Substituting E_H^*, K_S^*, $R_{SH}^*, R_{EH}^*, R_{FH}^*, R_{SB}^*, R_{EB}^*$ and the expression for D_h^* and D_r^* in forces of infection for human hosts and rats gives the following linear equation:

$$AD_h^* + B = 0 \tag{3.1}$$

where

$$A = \mu_r(\omega + \mu_r)(\alpha\phi\beta\Lambda_h + \mu_r r_1 r_2 \mu_h)$$

and

$$B = \mu_r(\omega + \mu_r)(\mu_r r_1 r_2 \mu_h)(1 - R_0^2)$$

From (3.1) $D_h^* = \dfrac{-B}{A} \leq 0$ if $B \geq 0$ at $R_0 \leq 1$, and no endemic equilibrium exists. On the other hand, $D_h^* = \dfrac{-B}{A} > 0$ if $B < 0$ at $R_0 > 1$. Hence, an endemic equilibrium exists only at $R_0 > 1$. The theorem below summarizes the above result.

Theorem 3.2. *The model (2.12)-(2.20) has a unique endemic equilibrium whenever $R_0 > 1$, and no endemic equilibrium otherwise.*

We establish the global stability of the endemic equilibrium solutions of the model (2.1)-(2.11) below.

Theorem 3.3. *The unique endemic equilibrium E_1, is globally asymptotically stable whenever $R_0 > 1$.*

Proof: We employ Goh-Volterra type Lyapunov function [11]

Given the following equations which are satisfied by the endemic equilibrium point E_1:

$$\Lambda_h = \alpha\psi S_H^*(R_{FH}^* + R_{FB}^*) + \mu_h S_H^*, \tag{3.2}$$
$$\alpha\psi S_H^*(R_{FH}^* + R_{FB}^*) = r_1 E*_H, \tag{3.3}$$
$$\beta E_H^* = r_2 K_S^*, \tag{3.4}$$
$$\Lambda_a = \alpha\phi R_{SH}^* K_S^* + \mu_r R_{SH}^*, \tag{3.5}$$
$$\alpha\phi R_{SH}^* K_S^* = r_3 R_{EH}^*, \tag{3.6}$$
$$\omega R_{EH}^* = \mu_r R_{FH}^*, \tag{3.7}$$
$$\Lambda_b = \alpha\phi R_{SB}^* K_S^* + \mu_r R_{SB}^*, \tag{3.8}$$
$$\alpha\phi R_{SB}^* K_S^* = r_3 R_{EB}^*, \tag{3.9}$$
$$\omega R_{EB}^* = \mu_r R_{FB}^*. \tag{3.10}$$

Consider the following Goh-Volterra Lyapunov function

$$\begin{aligned} V = &\left(S_H - S_H^* - S_H^* \ln\frac{S_H}{S_H^*}\right) + \left(E_H - E_H^* - E_H^* \ln\frac{E_H}{E_H^*}\right) + a\left(K_S - K_S^* - K_S^* \ln\frac{K_S}{K_S^*}\right) \\ &+ \left(R_{SH} - R_{SH}^* - R_{SH}^* \ln\frac{R_{SH}}{R_{SH}^*}\right) + \left(R_{EH} - R_{EH}^* - R_{EH}^* \ln\frac{R_{EH}}{R_{EH}^*}\right) \\ &+ b\left(R_{FH} - R_{FH}^* - R_{FH}^* \ln\frac{R_{FH}}{R_{FH}^*}\right) + \left(R_{SB} - R_{SB}^* - R_{SB}^* \ln\frac{R_{SB}}{R_{SB}^*}\right) \\ &+ \left(R_{EB} - R_{EB}^* - R_{EB}^* \ln\frac{R_{EB}}{R_{EB}^*}\right) + c\left(R_{FB} - R_{FB}^* - R_{FB}^* \ln\frac{R_{FB}}{R_{FB}^*}\right) \end{aligned}$$

where

$$a = \frac{\alpha\phi(R_{SH}^* + R_{SB}^*)}{r_2}, \quad b = \frac{\alpha\psi S_H^*}{\mu_r} = c$$

with the Lyapunov time derivative obtained as

$$\begin{aligned} \dot{V} = &\left(1 - \frac{S_H^*}{S_H}\right) S_H' + \left(1 - \frac{E_H^*}{E_H}\right) E_H' + a\left(1 - \frac{K_S^*}{K_S}\right) K_S' + \left(1 - \frac{R_{SH}^*}{R_{SH}}\right) R_{SH}' + \left(1 - \frac{R_{EH}^*}{R_{EH}}\right) R_{EH}' \\ &+ b\left(1 - \frac{R_{FH}^*}{R_{FH}}\right) R_{FH}' + \left(1 - \frac{R_{SB}^*}{R_{SB}}\right) R_{SB}' + \left(1 - \frac{R_{EB}^*}{R_{EB}}\right) R_{EB}' + c\left(1 - \frac{R_{FB}^*}{R_{FB}}\right) R_{FB}' \end{aligned}$$

$$\begin{aligned}\dot{V} = &\left(1-\frac{S_H^*}{S_H}\right)(\Lambda_h - \alpha\psi S_H(R_{FH}+R_{FB}) - \mu_h S_H) + \left(1-\frac{E_H^*}{E_H}\right)(\alpha\psi S_H(R_{FH}+R_{FB}) - r_1 E_H)\\ &+ a\left(1-\frac{K_S^*}{K_S}\right)(\beta E_H - r_2 K_S) + \left(1-\frac{R_{SH}^*}{R_{SH}}\right)(\Lambda_a - \alpha\phi R_{SH}K_S - \mu_r R_{SH})\\ &+ \left(1-\frac{R_{EH}^*}{R_{EH}}\right)(\alpha\phi R_{SH}K_S - r_3 R_{EH}) + b\left(1-\frac{R_{FH}^*}{R_{FH}}\right)(\omega R_{EH} - \mu_r R_{FH})\\ &+ \left(1-\frac{R_{SB}^*}{R_{SB}}\right)(\Lambda_b - \alpha\phi R_{SB}K_S - \mu_r R_{SB}) + \left(1-\frac{R_{EB}^*}{R_{EB}}\right)(\alpha\phi R_{SB}K_S - r_3 R_{EB})\\ &+ c\left(1-\frac{R_{FB}^*}{R_{FB}}\right)(\omega R_{EB} - \mu_r R_{FB})\end{aligned}$$

Using (3.2), (3.5) and (3.8), we have

$$\begin{aligned}\dot{V} = &\left(1-\frac{S_H^*}{S_H}\right)(\alpha\psi S *_H (R_{FH}^*+R_{FB}^*) + \mu_h S_H^* - \alpha\psi S_H(R_{FH}+R_{FB}) - \mu_h S_H)\\ &+ \left(1-\frac{E_H^*}{E_H}\right)(\alpha\psi S_H(R_{FH}+R_{FB}) - r_1 E_H) + a\left(1-\frac{K_S^*}{K_S}\right)(\beta E_H - r_2 K_S)\\ &+ \left(1-\frac{R_{SH}^*}{R_{SH}}\right)(\alpha\phi R_{SH}^* K_S^* + \mu_r R_{SH}^* - \alpha\phi R_{SH}K_S - \mu_r R_{SH}) + \left(1-\frac{R_{EH}^*}{R_{EH}}\right)(\alpha\phi R_{SH}K_S - r_3 R_{EH})\\ &+ b\left(1-\frac{R_{FH}^*}{R_{FH}}\right)(\omega R_{EH} - \mu_r R_{FH}) + \left(1-\frac{R_{SB}^*}{R_{SB}}\right)(\alpha\phi R_{SB}^* K_S^* + \mu_r R_{SB}^* - \alpha\phi R_{SB}K_S - \mu_r R_{SB})\\ &+ \left(1-\frac{R_{EB}^*}{R_{EB}}\right)(\alpha\phi R_{SB}K_S - r_3 R_{EB}) + c\left(1-\frac{R_{FB}^*}{R_{FB}}\right)(\omega R_{EB} - \mu_r R_{FB})\end{aligned}$$

Ignoring some terms and further simplification give

$$\begin{aligned}\dot{V} =&\alpha\psi S_H^*(R_{FH}^*+R_{FB}^*) + (r_1+r_3)R_{EH}^* + r_3 R_{EB}^* + a r_2 K_S^* + b\mu_r R_{FH}^* - c\mu_r R_{FB}^*\\ &- \frac{\alpha\psi(S_H^*)^2(R_{FH}^*+R_{FB}^*)}{S_H} - \frac{\alpha\psi S_H E_H^*(R_{FH}+R_{FB})}{E_H} - a\frac{\beta E_H K_S^*}{K_S} - \frac{\alpha\phi(R_{SH}^*)^2 K_S^*}{R_{SH}}\\ &- \frac{\alpha\phi R_{SH}K_S R_{EH}^*}{R_{EH}} - \frac{b\omega R_{EH}R_{FH}^*}{R_{FH}} - \frac{\alpha\phi(R_{SB}^*)^2 K_S^*}{R_{SB}} - \frac{\alpha\phi R_{SB}K_S R_{EB}^*}{R_{EH}} - \frac{c\omega R_{EB}R_{FB}^*}{R_{FB}}\\ &+ 2\mu_h S_H^* - \frac{\mu_h(S_H^*)^2}{S_H} - \mu_h S_H - \frac{\mu_r(R_{SH}^*)^2}{R_{SH}} - \frac{\mu_r(R_{SB}^*)^2}{R_{SB}} - \mu_r R_{SH}\\ &- \mu_r R_{SB} + 2\mu_r R_{SH}^* + 2\mu_r R_{SB}^* + \alpha\phi R_{SH}^* K_S^* + \alpha\phi R_{SB}^* K_S^*\end{aligned}$$

Replacing a and b by their values and exploiting (3.2)-(3.7) give

$$a\beta = \frac{\alpha\phi K_S^*(R_{SH}^*+R_{SB}^*)}{E_H^*} \tag{3.11}$$

$$b\omega = \frac{\alpha\psi S_H^* R_{FH}^*}{R_{EH}^*} \tag{3.12}$$

$$c\omega = \frac{\alpha\psi S_H^* R_{FB}^*}{R_{EB}^*} \tag{3.13}$$

Using (3.2)-(3.10) and (3.11)-(3.13), we have

$$\begin{aligned}\dot{V} =&\mu_h S_H^* \left(2 - \frac{S_H^*}{S_H} - \frac{S_H}{S_H^*}\right) + 3(\alpha\psi(R_{FH}^* + R_{FB}^*))S_H^* - \frac{\alpha\psi(S_H^*)^2 R_{FH}^* + R_{FB}^*}{S_H} \\ &- \frac{\alpha\psi S_H E_H^*(R_{SH} + R_{FB})}{E_H} - \frac{\alpha\phi(K_S^*)^2 E_H(R_{SH}^* + R_{SB}^*)}{E_H^* K_S} + \mu_r R_{SH}^* \left(2 - \frac{R_{SH}^*}{R_{SH}} - \frac{R_{SH}}{R_{SH}^*}\right) \\ &+ 3(\alpha\phi K_S^*)R_{SH}^* - \frac{\alpha\phi(R_{SH}^*)^2 K_S^*}{R_{SH}} - \frac{\alpha\phi R_{SH} K_S R_{EH}^*}{R_{EH}} - \frac{\alpha\psi S_H^* R_{EH}(R_{FH}^*)^2}{R_{EH}^* R_{FH}} \\ &+ \mu_r R_{SB}^* \left(2 - \frac{R_{SB}^*}{R_{SB}} - \frac{R_{SB}}{R_{SB}^*}\right) + 3(\alpha\phi K_S^*)R_{SB}^* - \frac{\alpha\phi(R_{SB}^*)^2 K_S^*}{R_{SB}} - \frac{\alpha\phi R_{SB} K_S R_{EB}^*}{R_{EB}} \\ &- \frac{\alpha\psi S_H^* R_{EB}(R_{FB}^*)^2}{R_{EB}^* R_{FB}}\end{aligned}$$

$$\begin{aligned}\dot{V} =&\mu_h S_H^* \left(2 - \frac{S_H^*}{S_H} - \frac{S_H}{S_H^*}\right) + \mu_r R_{SH}^* \left(2 - \frac{R_{SH}^*}{R_{SH}} - \frac{R_{SH}}{R_{SH}^*}\right) + \mu_r R_{SB}^* \left(2 - \frac{R_{SB}^*}{R_{SB}} - \frac{R_{SB}}{R_{SB}^*}\right) \\ &+ \alpha\psi(R_{FH}^* + R_{FB}^*)S_H^* \left(3 - \frac{S_H^*}{S_H} - \frac{S_H E_H^*(R_{FH} + R_{FB})}{S_H^*(R_{FH}^* + R_{FB}^*)E_H} - \frac{\phi(K_S^*)^2 E_H}{\psi S_H^* E_H^* K_S}\right) \\ &+ \alpha\phi R_{SH}^* K_S^* \left(3 - \frac{R_{SH}^*}{R_{SH}} - \frac{R_{SH} K_S R_{EH}^*}{R_{SH}^* K_S^* R_{EH}} - \frac{\psi(R_{FH}^*)^2 R_{EH} S_H^*}{\phi R_{SH}^* K_S^* R_{EH}^* R_{FH}}\right) \\ &+ \alpha\phi R_{SB}^* K_S^* \left(3 - \frac{R_{SB}^*}{R_{SB}} - \frac{R_{SB} K_S R_{EB}^*}{R_{SB}^* K_S^* R_{EB}} - \frac{\psi(R_{FB}^*)^2 R_{EB} S_H^*}{\phi R_{SB}^* K_S^* R_{EB}^* R_{FB}}\right)\end{aligned}$$

Using arithmetic-geometric means inequality, i.e., $n - (a_1 + a_2 + ... + a_n) \leq 0$, where $a_1.a_2...a_n = 1$ and $a_1, a_2, ..., a_n > 0$, it follows that $\dot{V} \leq 0$ with $V = 0$ if and only if $S_H = S_H^*$, $E_H = E_H^*$, $K_S = K_S^*$, $R_{SH} = R_{SH}^*, R_{EH} = R_{EH}^*, R_{FH} = R_{FH}^*$, $R_{SB} = R_{SB}^*, R_{EB} = R_{EB}^*, R_{FB} = R_{FB}^*$

Hence, the largest compact invariant subset of the set where $\dot{V} = 0$ is

$$(S_H, E_H, K_S, R_{SH}, R_{EH}, R_{FH}, R_{SB}, R_{EB}, R_{FB}) = (S_H^*, E_H^*, K_S^*, R_{SH}^*, R_{EH}^*, R_{FH}^*, R_{SB}^*, R_{EB}^*, R_{FB}^*)$$

and by classical stability theorem of Lyapunov and LaSalle's Invariance Principle, it follows that every solution in Γ approaches E_1 for $R_0 > 1$ as $t \to \infty$.

The epidemiological implication of the above result is that lassa fever disease will establish itself whenever $R_0 > 1$, in the population.

4. Sensitivity Analysis and Conclusion

In order to discover the essential factors responsible for lassa fever transmission and prevalence, a sensitivity analysis of the model (2.12)-(2.20) is carried out. Following the approach by [4], we define sensitivity index of a variable to a parameter as the ratio of relative change in the variable to the relative change in the parameter. Sensitivity analysis is a useful tool to identify how closely input parameters are related to parameters and it also helps to determine level of change, necessary for an input parameter to find the desired value of a predictor parameter.

When the variable is a differentiable function of the parameter, the sensitivity index may be alternatively defined using partial derivatives.

Definition 4.1. *The normalized forward sensitivity index of a variable, $u(p)$, that depends differentiably on a parameter, p, is defined as:*

$$N_p^u = \frac{\partial u}{\partial p} \times \frac{p}{u}$$

for $u \neq 0$

Consequently, we derive analytical expression for the sensitivity index of R_0 as

$$N_{p_i}^{R_0} = \frac{\partial R_0}{\partial p_i} \times \frac{p_i}{R_0}$$

where $p_i, i \in \mathbb{N}$ denotes each parameter involved in R_0, R_0 is defined as

$$R_0 = \sqrt{\frac{\alpha^2 \psi \Lambda_h \phi \omega \beta H_T}{r_1 r_2 \mu_h \mu_r^2 (\omega + \mu_r)}}$$

where

$$\begin{aligned} r_1 &= \beta + \mu_h \\ r_2 &= \delta_1 + \tau_1 + \mu_h + \varepsilon \\ H_T &= \Lambda_a + \Lambda_b \end{aligned}$$

We have Table 2 which summarizes the sensitivity indices on R_0 with respect to parameters i.e

$$N_\alpha^{R_0}, N_\psi^{R_0}, N_{\Lambda_h}^{R_0}, N_\phi^{R_0}, N_{\Lambda_b}^{R_0}, N_\beta^{R_0}, N_{\Lambda_a}^{R_0}, N_\omega^{R_0}, N_{\mu_r}^{R_0}, N_{\mu_h}^{R_0}, N_\tau^{R_0}, N_\varepsilon^{R_0}, N_{\delta_1}^{R_0}$$

4.1. Interpretation of sensitivity Indices obtained in Table 2

It can be observed from the results for sensitivity analysis that R_0 is most sensitive to biting rate of infectious rats R_{FH} and R_{FB} α, in a positive sense and natural mortality rate of rats μ_r, in a negative sense. Furthermore, we observe that transmission probability per contact with infectious rats (R_{FH} and R_{FB}) ψ, human recruitment rate Λ_h, transmission probability per contact rate with infectious human hosts ϕ, bush rat recruitment rate Λ_b, rate of progression for exposed human β, house rat recruitment rate Λ_a and progression rate for both house and bush rats ω have a direct effect on the severity of clinical lassa fever. Clinical lassa fever control should aim at eradicating or reducing these parameters. On the other hand, natural death rate of human host μ_h, recovery rate of infectious human host τ, rate of hospitalization ε and lassa-induced death rate for infectious human host δ_1 are shown to reduce R_0 when their efficacy are improved. By rank, the parameters $\alpha\psi, \Lambda_h, \phi$ are the most influential parameters in the model (2.12-2.20), followed by $\mu_r, \mu_h, \tau, \varepsilon$. Consequently, the sensitivity indices for the model are graphically shown above. As a result of the sensitivity analysis, the following suggestions are made:

(1) Reducing the number of contacts between human hosts and rats through a reduction in the number of rats and a reduction in the number of bites that human hosts will tolerate, could be an effective control measure against the growing of lassa fever disease because it reduces the value of α

Table 2: Numerical values of sensitivity indices of R_c with respect to parameter involved .

Parameter symbol	Sensitivity Index
α	1.00000
ψ	+0.50000
Λ_h	+0.50000
ϕ	+0.50000
Λ_b	+0.45454
β	+0.10000
Λ_a	+0.04545
ω	+0.00011
μ_r	-0.6952639
μ_h	-0.3430359
τ	-0.0517594
ε	-0.0069012
δ_1	-0.0457381

and ψ
(2) Adherence to prophylactic drugs after an exposure to infection could reduce the rate of progression of exposed human hosts β to infectious human hosts
(3) Hospitalizing after screening the infectious human hosts, could be an efficient control measure because it reduces transmission probability per contact with infectious human hosts ϕ.
(4) Increasing the recovery rate τ of infectious human hosts, could control the number of infectious human hosts. This needs not only patients cooperate with treatment actively but also relevant departments should study new and effective medicine for the treatment of lassa fever. This can improve recovery rate of infectious human hosts.

4.2. Conclusion

An eight-compartment model describing the transmission of lassa fever disease between three interacting populations, namely, human hosts, house rats and bush rats, are presented. The formulated model governed by systems of ordinary differential equations were qualitatively and quantitatively analysed to gain more insight into the transmission and spread of lassa fever disease. The lassa-free equilibrium and persistence were determined and their stability properties were investigated through an explicit formula for a threshold parameter known as the basic reproduction number, R_0. This threshold was derived using next generation matrix method. For a threshold less than one, a globally asymptotically stable lassa-free equilibrium was shown while the disease persistence was revealed to be globally asymptotically stable for R_0 greater than one. The formulated lassa fever model led to a sensitivity analysis with a view to examining the factors most responsible for the transmission and spread of the disease. We found that rat biting rate α, transmission probability per contact with R_{FH} and R_{FB} ψ, human recruitment rate Λ_h and transmission probability per contact with K_s, among other parameters with positive sensitivity index, contributes most significantly to the persistence of lassa fever disease in the population.

References

[1] A. Abdulhamid, N. Hussaini, *Effects of quarantine on transmission dynamics of Lassa fever*, Infectious Disease of poverty, 11(1)(2006) 397-407.

[2] I.S. Abdulraheem, *Public health importance of lassa fever epidemiology, clinical features and current management review of literature*, Afr. J. Clin. Exp Microbiol., 3(2002) 33-37.

[3] F.O. Akinpelu, R. Akinwande, *Mathematical model for lassa fever and sensitivity analysis*, Journal of Scientific and Engineering Research, 5(5)(2008) 1-9.

[4] L.M. Arriola, J.M. Hyman, *Being sensitive to uncertainty*, Journal of Computing and Engineering,9(2)(2007) 10-20.

[5] M.Bawa, S. Abdulrahaman, O.R. Jimoh, Adabara Nu, *Stability analysis of the disease-free equilibrium state of Lassa fever disease. Journal of Science and Technology, Mathematics and Education*, 9(2)(2013) 115-123.

[6] M.J.Buchmeier, J.C. de la Torre, C.J.Peters Arenaviridae, *The viruses and their replication*, Fields Virology,(2007) 1791-1827.

[7] Central Intelligence Agency, World fact book for the year 2014, *Retrieved on 20 February 2016 from* `http://www.cia/library/publication/the-worldfactbook/geos/ni.htm`, (2015)

[8] J. Davies, K. Lokuge, K.Glass, *Routine and pulse vaccination for Lassa virus could reduce high levels of endemic disease: A mathematical modeling study*, Vaccine, 37(26)(2019) 3451-3456.`Journalhomepage:www.elsevier.com/locate/vaccine`

[9] K.C. Eze, T.A.T. Salami, I.C. Eze, A.E.Pogoson, N.Omodia, M.Ugochukwu, *High Lassa fever activities in Northern part of Edo State, Nigeria: Re-analysis of confirmatory test result*, African Journal of Health Sciences, 16(34)(2010), 52-56.

[10] T.S. Faniran, *A mathematical modelling of lassa fever dynamics with non-drug compliance rate*, International Journal of Mathematics Trends and Technonlogy, 5(47)(2017) 305–317.

[11] H. Guo, M.Y. Li, *Global stability in a mathematical model of tuberculosis*, Canadian Applied Mathematics Quaterly, 4(2) (2006).

[12] T.O.James, S.Abdulrahaman, S.Akinyemi, N.I.Akinwande, *Dynamics transmission of Lassa fever disease*, International Journal of Innovation and Research in Educational Sciences, 2(1)(2015) 2349-5219.

[13] A.Korobeinikov, *A global properties of infectious disease model with nonlinear incidence*, Bulletin of Mathematical Sciences, 8(78)(2014) 3889-3904.

[14] M.Y.Li, J.S. Mouldowney, *Global stability for the SEIR model in epidemiolgy*, Journal of Mathematical Biosciences, 125(1995) 155-164.

[15] S.C. Nwasuka, I.E. Nwachukwu, P.C. Nwachukwu, *Mathematical model of the transmission dynamics of Lassa fever with separation of infected individuals and treatment as control measures*, Journal of Advances in Mathematics and Computer Science, 32(6)(2019) 1-15.

[16] O.S. Obabiyi, A.A.Onifade, *Mathematical model for Lassa fever transmission dynamics with variable human and reservoir population*, International Journal of Differential Equations and Applications, 16(1)(2017) 67-91.

[17] C.O.Ogabi, T.V.Olusa,M.A. Madufor, *Controlling Lassa fever transmission in Northern part of Edo State, Nigeria using SIR model*, New York Science Journal, 5(12)(2012) 190-197.

[18] D. Okuongbe, R. Okuongbe, *A mathematical model for Lassa fever*, Journal of National Association of Mathematical Physics, 10(2017) 457-464.

[19] S.A.Omilabu, S.O.Badaru,P. Okokhere, D. Asogun, C.Drosten, P. Emmerich, *Lassa fever, Nigeria, 2003, and 2004*, Emerging Infectious Diseases, 11(10)(2005) 1642-1644.

[20] O. Onuorah Martins,S. Ojo Moses, J. Usman Dahiru , A. abdulkadir, *Basic reproduction number for the spread and control of Lassa fever*, Int. Journal of Mathematics Trends and Technology (IJMTT),30(1) (2016) 1-7.

[21] O.J. Peter, A.I. Abioye, F.A. Oguntolu, T.A. Owolabi, M.O. Ajisope, A.G. Zakari, T.G. Shaba, *Modelling and optimal control analysis of Lassa fever disease*, Informatics in Medicine Unlocked (Elsevier), 20(2020) 100419.

[22] J.M.Rojek,S. Kunz, *Cell entry by human pathogenic arenaviruses*, Cell Microbol, 10(4)(2008) 828-835.

[23] I.B. Sule, I.B. Wada, A.A. Abubakar et al., *Outbreak of a highly virulent Lassa fever virus in Kano State, Nigeria: An investigation report 2015-2016*, International Journal of Scientific and Engineering Research,8(1)(2017) 613-619.

[24] J. W. Ufberg, D.J.Karres, *Update on emerging infections: news for the centers for disease control and prevention. Imported Lassa fever-New Jersey, 2004*, Ann Emerg Med, 45(3)(2005) 323-326.

[25] World Health Organization, Lassa, (2017)