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Mathematical Model and Stability Analysis for the Transmission Dynamics of Lassa Fever Epidemic in Nigeria with the Influence of Treatment

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Abstract: In this paper, we proposed, formulated and analyzed a SEIR deterministic mathematical model of Lassa fever in Nigeria, by consider the impact of treatment of infected individuals using standard incidence rate. The model is shown to be well posed mathematically and epidemiologically. The basic reproduction number R_0 that depends on ten parameters which is the important threshold has been obtained, together with the basic control parameters say transmission coefficient β_h and treatment coefficient γ that can help us to control the spread of the Lassa fever disease. The model is shown to exhibits two equilibrium points namely, the endemic equilibrium points and disease-free equilibrium points which is proved to be locally and globally asymptotically stable under certain condition on the associated threshold parameter. We further established that early treatment of infected populations reduces the number of infected individuals which as well leads to decreases in the spread dynamics of Lassa fever disease in a society.

Keyword: Lassa fever, mathematical model, basic reproduction number, stability analysis, control Parameters.

Introduction

Lassa fever is also called Lassa hemorrhagic fever, is an infectious disease and a zoonotic viral illness instigated by the Lassa virus, a single-stranded RNA virus from the Arenaviridae family [(Peterson *et al.*,2014, Ibrahim and Denes (2021)]. The mastomys natalensis which known as a multimammate rat is the main host of this virus that is dominant in Sub-Saharan African as one of the most common rodent species [(Zhao *et al.*, 2020), (Gibb *et al.*,2017)& Richmond and Baglole (2013)]. the viral particle responsible for cause of Lassa fever was first identified in 1969 at Borno state northern region of Nigeria.

However, the yearly estimated incidence in eastern and western regions of West Africa ranges from a hundred to three hundred thousand cases with nearly five thousand deaths[(Grenenky *et al.*,2017), (Mariem *et al.*, 2019) & (Olugasa *et al.*, 2015)] this momentum necessitated the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) to declared Lassa

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fever as endemic and a health challenge in Western African Accordingly. The countries at the highrisk for Lassa fever (belt) include Liberia, Guinea, Sierra Leone, and Nigeria[(Greenky *et al.*, 2017), (Musa *et al.*, 2020), (Davies *et al.*,2019) & (Peter *et al.*,2020)]. the largest epidemic was reported to be in Nigeria, with report of many outbreaks from the aforementioned countries over the years. The largest outbreak of Lassa fever that swept through eighteen out of the thirty-six states of the country is reported to be in Nigeria, with over 400 confirmed cases were reported (Maxmen 2018).

Although, the yearly increase of cases of Lassa virus has to do with various factor such as insufficient health facilities, polluted environment, and poor personal hygiene, to gather with the ecological climate factor rainfall and movement of harvested food into our communities. These activities are associated with an improve or increase in the host reservoir (mastomys rodents) to migrate from their natural habitation to the human environment, a reduce or diminished in the prevalence of Lassa fever is rely upon on human efforts in reducing the transmission proportion of this disease [(Zhao *et al.*,2020), (Onah and Collins (2020)].

Lassa fever has an incubation period between 6 and 21 days, hence, following this exposure period, infected humans are expected to start showing symptoms of the disease. Although about eighty percent of infected humans have only slight symptoms such as headaches, cough, muscle pain, sore throat, weakness, and fever. However, in severe cases, an infected human can develop more complications such as facial swelling, bleeding from the nose, respiratory distress, and low blood pressure [(Ibrahim and Denes (2021), (Peter et al., 2020) & (Bakare et al., 2020)]. In a more critical situation, this disease can lead to death within fourteen days after the first appearance of the symptoms, due to neurological problems[(Ibrahim and Denes (2021), (Bakare et al., 2020)]. The Lassa virus is primarily spread to humans through human contact with food or substances that are contaminated by the urine or feces of an infected rodent (Musa et al., 2020), while secondary infection from human-to-human and laboratory transmissions are likewise possible [(Davies et al., 2019), (Hamblion et al., 2018)]. Due to the absence of a vaccine against Lassa fever, prevention against infection has an important role in controlling the transmission of this disease in the population. Currently, since the eradication of mastomys rodent population is unrealistic, the present ways of avoiding the spread of this infection include the facilitation of good personal hygiene to avoid contact with infected rodents' secretions or excretions, and implementation of standard health facilities for effective testing, diagnosing and treatment of patients (Davies et al., 2019).

Literature reavel that there is no confirmed cure or vaccine exists for Lassa fever yet, however, ribavirin is an antiviral drug that has been declared as an effective treatment for Lassa fever patients, if administered at the premature period of the infection (Mariem *et al.*,2019), (Musa *et al.*,2020). Consequently, the transmission dynamics of the virus is still not yet fully comprehended limited and far from being complete. Therefore, it is then important to urgently conduct various researches and explore new methods and techniques, which can help to better understanding of the outbreak process and controlling the spread of the virus.

Over the decade, mathematical models have become vital tools in studying the dynamics of diseases in a given population. The recent development of the use of mathematical models such as [(Ibrahim and Denes (2021), (Diethelm, 2020)], has been developed for numerous diseases, to

answer specific questions in an attempt to contribute to the understanding of the epidemiology of such disease under study. More specifically, studies have been carried out to further provide information on the transmission dynamics of Lassa fever (see (Zhao *et al.*,2020),[(Mariem *et al.*,2019), (Olugasa *et al.*,2015) & (Musa *et al.*, 2020)], [Onah and Collins (2020)], (Bakare *et al.*,2020), [(Ma *et al.*,2016), (Alsaedi *et al.*, 2015)].

However, Onah *et al.*, (2020) used optimal control theory to determine how to reduce disease transmission with minimal cost, by introducing different control intervention measures, such as external protection, treatment, isolation and rodent control, within the extended SIR–SI-type compartmental model. Musa *et al.*(2020) showed the presence of a forward bifurcation with a stability switch between the disease-free and the endemic equilibrium. Their model describing the interaction between humans and rodents including quarantine, isolation and hospitalization. Zhao *et al.*(2020) studied the epidemiological features of Lassa epidemics in various regions of Nigeria, and established the connection between the reproduction number and rainfall. They determined the infectivity of Lassa by the reproduction number estimated from four types of growth models, the models fitted to Lassa surveillance data and estimated the reproduction number in various regions. 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 (WHO, 2020)

In view of the above, Proper treatment of Lassa fever victims will play a significant role in controlling and spread of this virus. Consequently, treatment of Lassa fever virus needs to be acknowledged as an important factor that may attract urgent intervention for controlling Lassa virus epidemics, obviously, the Treatment interventions of Lassa fever victims has no clear status in our communities, hence the optimal policy need to be tractable. However, our study, extend the work done by James *et al.*(2015). And present a seven compartmental deterministic model, using a system of ordinary differential equations by incorporating exposed, treatment and recovery in to the human compartment and further subdivided the rodent compartment into two, in other to gain insight into the transmission dynamics of Lassa fever with treatment.

The model System description and formulation

This study will engross on the influence on transmission dynamics of Lassa fever virus diseases with treatment, concerning the progression of the infection in the human population. Consequently, our propose models extends the work done by James *et al.* (2015) in the following sense

- i. Incorporating exposed, treatment and recovered compartments with treatment as control measure, is not considered in James *et al.*(2015)
- ii. Sub dividing the reservoir population (rodents) In to susceptible and infected compartments. is not considered in James *et al.*(2015)
- iii. We extend our model to SEIR type while SIR model type was used in James *et al.*(2015)
- iv. The probability or proportion of susceptible to be becomes infectious in both humans and reservoir (rodents) population, is not considered in James *et al.*(2015)
- v. Standard incidence rate used while bilinear incidence rate was used in James *et al.* (2015)

Thus, the proposed extended model is formulated based on the following considerations.

- (a) Homogeneous mixing of members of the population under consideration with equal chances of transmitting the virus.
- (b) the Probability of susceptible individuals to be becomes infectious in the population under consideration by the proportion of (1θ) , with the transmission rate β and $0 \le \theta \le 1$.
- (c) Successful treatment of individuals to becomes recovered, does not guarantee permanent immunity. But they do confer some immunity from their primary infection, and since there is no absolute cure for Lassa fever, they may also have a relapse of the disease back into the infectious class.

Hence, the total human and population at time t, is divided into five (5) compartments such that $N_h(t) = S_h(t) + E_h(t) + I_h(t) + T_h(t) + R_h(t)$ and the total rodents population at time t is divided in to two (2) compartments such that $N_r(t) = S_r(t) + I_r(t)$.

In the model (1), $S_h(t)$; $E_h(t)$; $I_h(t)$; $T_h(t)$; $R_h(t)$; $S_r(t)$ and $I_r(t)$ are the state variables used to represent the Susceptible human, Exposed human, Infected human, Recovery human, Treated human, Susceptible mastomys rats' and Infected mastomys rats compartment respectively, with the assumptions that all parameters in the model (1) are constants.

Thus, the susceptible population with risk of Lassa virus infection $S_h(t)$ is generated by recruitment of humans at a constant rate Λ_h (all humans recruited into the population are assumed to be at risk of Lassa-infection), All infected individuals move into the susceptible population due to treatment failure at rate φ , the population is decreased by natural death at a rate μ , following the effective contact with β_h the human-to-human contact rate and β_r a mastomys rat-to-human contact rate.

The exposed population $E_h(t)$ is produced following the effective contact with β_h the human-tohuman contact rate and β_r a mastomys rat-to-human contact rate, and further reduce by the proportion of susceptible individuals that becomes infectious at $(1 - \theta)$ and natural death at a rate μ .

The infected population $I_h(t)$ is increased by ξ the proportion of exposed individuals that becomes infectious at $(1 - \theta)$, which decreased by ϕ a recovery rate of infectious human, and rates at which infected humans move to treatment class γ together with natural death of human population μ and the induced death of infectious individual at α_1 .

The population of treated individuals $T_h(t)$ is generated as a result of treatment of infected individuals at rate γ , and diminished by the ψ rate of recovery, all infected individuals move into the susceptible population due to treatment failure at rate φ , natural death at a rate μ , together with α_2 the induced death of individual under treatment.

The population of recovered individuals $R_h(t)$ is composed as a result of recovery of treated individuals at rate ψ together with recovery rate of infected individuals and decreased by natural death at a rate μ .

Similarly, the population of susceptible mastomys rat (rodents) $S_r(t)$ is generated by recruitment of rodents at a constant rate Λ_r , which decreased by the population of natural death at a rate ϑ , following the effective contact with β_r the transmission rate of mastomys rat-to-mastomys rat.

The population of infected mastomys rats (rodents) $I_r(t)$ is produced following the effective contact with β_r the transmission rate of mastomys rat-to-mastomys rat. and only diminished by natural death of mastomys rat's (rodents) at a rate ϑ .

Thus, the transfer diagram of the model system shown in Fig. 1. Together with above descriptions, yield the following model equations:

$$\frac{dS_h}{dt} = \Lambda_h + \varphi T_h - (\lambda_h + \mu) S_h$$

$$\frac{dE_h}{dt} = \lambda_h S - [\xi(1 - \theta) + \mu] E_h$$

$$\frac{dI_h}{dt} = \xi(1 - \theta) E_h - (\phi + \gamma + \mu + \alpha_1) I_h$$

$$\frac{dT_h}{dt} = \gamma I_h - (\psi + \varphi + \mu + \alpha_2) T_h$$

$$\frac{dR_h}{dt} = \varphi I_h + \psi T_h - \mu R_h$$

$$\frac{dS_r}{dt} = \Lambda_r - (\lambda_r + \vartheta) S_r$$

$$\frac{dI_r}{dt} = \lambda_h S_r - \vartheta I_r$$
(1)

With
$$\lambda_h = \frac{\beta_h I_h + \beta_r I_r}{N_h}$$
 and $\lambda_r = \frac{\beta_r I_r}{N_r}$ (2)

where β_h is the effective contact rate for human-to-human transmission, β_r is a mastomys rat-to-human effective contact rate.



Figure 1. The Lassa fever flow diagram for human and rodent population

Description of the State Variables and the Parameters of the Flow Chart Model

Symbol of the Variable	Description
$S_h(t)$	Susceptible human compartment
$E_h(t)$	Exposed human compartment
$I_h(t)$	Infected human compartment
$T_h(t)$	Treatment compartment
$R_h(t)$	Recovery human compartment
$S_r(t)$	Susceptible mastomys rats' compartment
$I_r(t)$	Infected mastomys rats' compartment

Table 1. The state variables of the flow chart model system

Symbol of the	Descriptions
Parameters	
Λ_h and Λ_r	Rate of recruitment of susceptible human and mastomys rat's population
μ	Rate of natural death in human
θ	Rate of natural death in mastomys rat's
Ψ	Recovery rate of treated individuals
ϕ	Recovery rate of infected individuals
arphi	Rate of treatment failure
γ	Rate of treatment (Rates at which infected humans move to treatment class)
$(1-\theta)$	Proportion of new exposed individual that become symptomatically infected
ξ	Rate at which an exposed individual becomes infectious
$lpha_1$ and $lpha_2$	Rate of induced death of infectious individual and individual under treatment.
	Respectively
eta_h	The Transmission rate of human population
β_r	The Transmission rate of mastomys rat's population

Table 2. The Parameters of the Flow Chart Model System

Positivity and Boundedness

Now let us prove the positivity and boundedness of the solutions of our model to ensure that the system of differential equations in (1), is mathematically well defined and biologically meaningful.

Theorem1.Let the initial coditions $S_h(0) > 0$, $E_h(0) > 0$, $I_h(0) > 0$, $T_h(0) > 0$, $R_h(0) > 0$, $S_r(0) > 0$, and $I_r(0) > 0$, then the solution of $S_h(t)$, $E_h(t)$, $I_h(t)$, $T_h(t)$, $R_h(t)$, $S_r(t)$ and $I_r(t)$ of the model system (1) are positive for all $t \ge 0$.

Proof. Suppose S(t) is not positive, then there exists a first time, say $t^* > 0$, such that $S_h(t) > 0$ For all $t \in [0, t^*)$ and $S_h(t^*) = 0$. By inspection of the equation of $E_h(t)$, we have that

$$\frac{dE_h}{dt} \ge -[\xi(1-\theta)+\mu]E_h(t), for \ t \in [0,t^*),$$

Hence, it follows that,

$$E_h > 0 \text{ for } t \in [0, t^*).$$

Thus, it is clear from the first equation of model system (1) that

$$\frac{dS_h}{dt} \ge -(\lambda_h + \mu)S_h(t), for \ t \in [0, t^*).$$

It follows that $S_h(t^*) > 0$ which contradicts $S_h(t^*) = 0$. therefore, $S_h(t)$ is positive. Using similar approach as that for $S_h(t)$, it is easy to show that $E_h(0) > 0$, $I_h(0) > 0$, $T_h(0) > 0$, $R_h(0) > 0$, $S_r(0) > 0$, and $I_r(0) > 0$. Hence the proof.

Invariant Region

In order to retain the biological feasible region of the model system (1) we consider the biologically feasible region consisting of

 $\Delta = \Delta_h \times \Delta_r \in \mathbb{R}^5_+ \times \mathbb{R}^2_+$

with

$$\Delta_h = \{S_h, E_h, I_h, T_h, R_h \in \mathbb{R}^5_+ : N_h \leq \frac{\Lambda_h}{n} \}$$

And

$$\Delta_r = \{ S_r, I_r, \in \mathbb{R}^2_+ : N_r \leq \frac{\Lambda_r}{\vartheta} \}$$

It can be shown that the set Δ is a positively invariant set and global attractor of this system. This implies any phase trajectory initiated anywhere in the nonnegative region \mathbb{R}^7_+ enters the feasible region Δ and remains in thereafter.

Lemma 1. The biological feasible region $\Delta = \Delta_h \cup \Delta_r \subset \mathbb{R}^5_+ \times \mathbb{R}^2_+$ of the Lassa fever model (1) is positively invariant with nonnegative initial conditions in \mathbb{R}^7_+ .

Proof

The following steps are followed to establish the positive invariance of Δ (i.e., solutions in Δ remain in Δ for all t > 0). The rate of change of the total human and rodent populations N_h and N_r respectively, are obtained by adding the respective components of model (1) which result to

$$\frac{dN_h(t)}{dt} = \Lambda_h - \mu N_h(t) - \{(\alpha_1)I_h(t) + (\alpha_2)T_h(t)\} and$$
$$\frac{dN_r(t)}{dt} = \Lambda_r - \vartheta N_r(t)$$

so that,

$$\frac{dN_h(t)}{dt} \le \Lambda_h - \mu N_h(t) \text{ and } \frac{dN_r(t)}{dt} \le \Lambda_r - \vartheta N_r(t)$$
(2)

Hence, $N_h(t) \le \mu N_h(0) e^{\mu t} + \frac{\Lambda_h}{\mu} (1 - e^{-\mu t})$ and $N_r(t) \le \vartheta N_r(0) e^{\vartheta t} + \frac{\Lambda_r}{\vartheta} (1 - e^{-\vartheta t})$.

In particular, $N_h(t) \leq \frac{\Lambda_h}{\mu}$ and $N_r(t) \leq + \frac{\Lambda_r}{\vartheta}$ if the total human population and rodent population at the initial instant of time, $N_h(0) \leq \frac{\Lambda_h}{\mu}$ and $N_r(0) \leq + \frac{\Lambda_r}{\vartheta}$, respectively. So, the region Δ is positively invariant. Thus, it is consequently adequate to consider the dynamics of Lassa fever governed by model (1) in the biological feasible region Δ , where the model is considered to be

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epidemiologically and mathematically well posed see (Lakshmikanthan, et al 1989; Ojo, et al, 2017).

Existence and Stability of Lassa fever free equilibrium (LFFE)

The Lassa fever free equilibrium of model (1) is obtained at the steady-state solution in the absence of Lassa fever infection, there in by setting the right-hand side of equation (1) equal to zero, such that $S_h^* = E_h^* = I_h^* = T_h^* = R_h^* = S_r^* = I_r^* = 0$ and solve it simultaneously we get the disease-free equilibrium state denoted by \mathcal{E}_0 and is given by

$$\mathcal{E}_{0} = (S_{h}^{*}, E_{h}^{*}, I_{h}^{*}, T_{h}^{*}, R_{h}^{*}, S_{r}^{*}, I_{r}^{*}) = \left(\frac{\Lambda_{h}}{\mu}, 0, 0, 0, 0, \frac{\Lambda_{r}}{\vartheta}, 0\right)$$
(3)

Basic reproduction number

The next-generation matrix method is used on system (1) for determining the reproduction number \mathcal{R}_0 . The epidemiological quantity \mathcal{R}_0 , called the reproduction number, measures the typical number of Lassa fever cases that a Lassa fever-infected individual can generate in a human population that is completely susceptible (Lakshmikantham, *et al*, 1989; Oke, *et al*, 2020).

The matrices F and V for the new infection terms and the remaining transfer or transition terms are shown below, it follows that the basic reproduction number of model system (1) is calculated as follows

$$\begin{vmatrix} Gain \ to \ E \\ Gain \ to \ I \\ Gain \ to \ I \\ Gain \ to \ I \\ Gain \ to \ I_{r} \\ losses \ from \ E \\ losses \ from \ I \\ losses \ from \ I_{r} \end{vmatrix} = \begin{pmatrix} (\frac{\beta_{h}I_{h}+\beta_{r}I_{r}}{N_{h}})S_{h} \\ 0 \\ 0 \\ (\frac{\beta_{h}I_{h}+\beta_{r}I_{r}}{N_{h}})S_{r} \\ (\frac{\beta_{r}I_{r}}{N_{r}})S_{r} \\ [\xi(1-\theta)+\mu]E_{h} \\ -\xi(1-\theta)E_{h} + (\phi+\gamma+\mu+\alpha_{1})I_{h} \\ -\gamma I_{h} + (\psi+\phi+\mu+\alpha_{2})T_{h} \\ \vartheta I_{r} \end{vmatrix}$$

That is by considering the most relevant equations in the model system (1) say, $E_h(t)$, $I_h(t)$, $T_h(t)$ and $I_r(t)$, thus, the gain (the new infection terms) and losses (the transfer or transition terms) expressions associated with the model (1) using next generation method gives

$$Gain \Rightarrow F = \begin{pmatrix} 0 & \beta_h & 0 & \beta_r \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_r \end{pmatrix}$$
$$Losses \Rightarrow V = \begin{pmatrix} K_1 & 0 & 0 & 0 \\ -K_2 & K_3 & 0 & 0 \\ 0 & -\gamma & K_4 & 0 \\ 0 & 0 & 0 & \vartheta \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{K_1} & 0 & 0 & 0\\ \frac{K_2}{K_1 K_3} & \frac{1}{K_3} & 0 & 0\\ \frac{\gamma K_2}{K_1 K_3 K_4} & \frac{\gamma}{K_3 K_4} & \frac{1}{K_4} & 0\\ 0 & 0 & 0 & \frac{1}{\vartheta} \end{pmatrix}$$

Where $K_1 = [\xi(1-\theta) + \mu], K_2 = \xi(1-\theta), K_3 = (\phi + \gamma + \mu + \alpha_1) \text{ and } K_4 = (\psi + \phi + \mu + \alpha_2)$ (4)

Thus, the spectral radius of the next-generation FV^{-1} , is the basic reproduction \mathcal{R}_0 of the model (1) it follows then that the associated reproduction number denoted by \mathcal{R}_0 , is obtained as follows:

$$\mathcal{R}_0 = \frac{\vartheta \beta_h K_2 + \beta_r K_1 K_3}{K_1 K_3 \vartheta} \tag{5}$$

With
$$\mathcal{R}_{0h} = \frac{\beta_h K_2}{K_1 K_3}$$
 and $\mathcal{R}_{0r} = \frac{\beta_r}{\vartheta}$ (6)

Where \mathcal{R}_{0h} defined the basic reproduction number of human population and \mathcal{R}_{0r} defined the basic reproduction number of rodents respectively.

Stability Analysis

Lemma 2: The disease – free equilibrium (DFE) of the (LASV) model system (1), given \mathcal{E}_0 , is locally asymptotically stable if $\mathcal{R}_0 < 1$ and \mathcal{E}_0 is unstable if $\mathcal{R}_0 > 1$.

Proof.

We prove the Lemma 2 using linearization method. The Jacobian matrix associated with the LASV model at the DFE, $\mathcal{E}_0 = (S_h^*, E_h^*, I_h^*, T_h^*, R_h^*, S_r^*, I_r^*) = (\frac{\Lambda_h}{u}, 0, 0, 0, 0, 0, \frac{\Lambda_r}{\vartheta}, 0)$ is given by

 $J(\varepsilon_0) = \begin{pmatrix} -\mu & 0 & -\beta_h & \phi & 0 & 0 & \beta_r \\ 0 & -K_1 & 0 & 0 & 0 & 0 \\ 0 & K_2 & -K_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma & -K_4 & 0 & 0 & 0 \\ 0 & 0 & \phi & \psi & -\mu & 0 & 0 \\ 0 & 0 & \phi & \psi & -\mu & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\vartheta - \beta_r \\ 0 & 0 & 0 & 0 & 0 & 0 & -\vartheta \end{pmatrix}$ (7)

With K_1, K_2, K_3 , and K_4 same as in (4)

The eigenvalues can be determined by solving the characteristic equation $|J - \lambda I| = 0$. Now Evaluating the eigenvalues of the Jacobian matrix J we found that the following eigenvalues $-K_4$, $-K_3$, $-K_1$, $-\vartheta$, $-\mu$, $-\vartheta$ and $-\mu$ are all real and negative. Hence, ε_0 is locally asymptotically stable whenever $\mathcal{R}_0 < 1$, and the above lemma has been proved accordingly.

Global Stability of Lassa Fever-Free Equilibrium

The global stability of the Lassa fever-free equilibrium \mathcal{E}_0 of the model system (1), can be examine since \mathcal{E}_0 is locally asymptotically stable from above lemma.

Theorem 2 The Lassa fever disease-free equilibrium \mathcal{E}_0 is globally asymptotically stable (GAS) of model system (1) if $\mathcal{R}_0 < 1$, in the interior of Δ .

Proof. Comparisons theorem allow us to prove the above theorem in the following sense. Now let consider the next generation matrix together with the infected compartments as

Then the rate of change of the infected compartments of model (1) can be written in the form

$$\frac{dZ}{dt} = (F - V)Z - JZ$$
(8)

So that

It can be observed that *J* is a non-negative matrix since $S_h(t) \le N_h(t) \le \frac{\Lambda_h}{\mu}$ and $S_r(t) \le N_r(t) \le \frac{\Lambda_r}{\vartheta}$ In the invariant set. Hence it follows that $\frac{dZ}{dt} \le (F - V)Z$ (9)

Considering the fact that eigenvalues of the matrix F - V all have negative real parts, which coincide with our local stability result, where $\rho(FV^{-1}) < 1$ if $R_0 < 1$, (Van den Driessche and

Watmough 2002)). It follows that the linearized differential inequality of (9) is stable whenever $R_0 < 1$. Consequently, $(E_h, I_h, T_h, I_r) \rightarrow (0,0,0,0)$ as $t \rightarrow \infty$. Thus, by comparison theorem, $(E_h, I_h, T_h, I_r) \rightarrow (0,0,0,0)$ as $t \rightarrow \infty$. Substituting $E_h = I_h = T_h = I_r = 0$ in (8) gives $S_h(t) \rightarrow S_h^*$ as $t \rightarrow \infty$ and $S_r(t) \rightarrow S_r^*$ as $t \rightarrow \infty$. Thus, $(S_h(t), E_h, I_h(t), T_h, R_h, S_r(t), I_r(t)) \rightarrow (S_h^*, 0,00,0, , S_r^*, 0)$ as $t \rightarrow \infty$ for $R_0 < 1$. Thus, ε_0 is GAS if $R_0 < 1$. **Existence and Stability of Endemic Equilibria**

Lassa fever endemic equilibrium points of model (1) is obtained at the steady-state solution in the presence of Lassa fever infection in the population. there in by setting the right-hand side of equation (1) equal to zero and solve it simultaneously in terms of the associated form of infection we get the Lassa fever endemic equilibrium points state denoted by \mathcal{E}_1 and is given by $\mathcal{E}_1 = (S_h^{**}, E_h^{**}, I_h^{**}, T_h^{**}, R_h^{**}, S_r^{**}, I_r^{**})$, Therefore, the endemic equilibrium point of the model system (1) is obtained as

$$S_{h}^{**} = \frac{K_{1}K_{3}K_{4}\Lambda_{h}}{(K_{1}K_{3}K_{4} - \gamma\varphi K_{2})\lambda_{h}^{**} + \mu K_{1}K_{3}K_{4}}$$

$$E_{h}^{**} = \frac{K_{3}K_{4}\Lambda_{h}\lambda_{h}^{**}}{(K_{1}K_{3}K_{4} - \gamma\varphi K_{2})\lambda_{h}^{**} + \mu K_{1}K_{3}K_{4}}$$

$$I_{h}^{**} = \frac{K_{2}K_{4}\Lambda_{h}\lambda_{h}^{**}}{(K_{1}K_{3}K_{4} - \gamma\varphi K_{2})\lambda_{h}^{**} + \mu K_{1}K_{3}K_{4}}$$

$$T_{h}^{**} = \frac{K_{2}\gamma\Lambda_{h}\lambda_{h}^{**}}{(K_{1}K_{3}K_{4} - \gamma\varphi K_{2})\lambda_{h}^{**} + \mu K_{1}K_{3}K_{4}} \quad (10)$$

$$R_{h}^{**} = \frac{(\gamma\psi + \phi K_{4})K_{2}\gamma\Lambda_{h}\lambda_{h}^{**}}{((K_{1}K_{3}K_{4} - \gamma\varphi K_{2})\lambda_{h}^{**} + \mu K_{1}K_{3}K_{4})\mu}$$

$$S_{r}^{**} = \frac{\Lambda_{r}}{\lambda_{r}^{**} + \vartheta}, \qquad I_{r}^{**} = \frac{\lambda_{r}^{**}\Lambda_{r}}{\vartheta(\lambda_{r}^{**} + \vartheta)}.$$

With the force of infections

$$\lambda_h^{**} = \frac{\beta_h I_h^{**} + \beta_r I_r^{**}}{N_h^{**}} \quad and \quad \lambda_r^{**} = \frac{\beta_r I_r^{**}}{N_r^{**}} \tag{11}$$

Where $N_h^{**} = (S_h^{**} + E_h^{**} + I_h^{**} + T_h^{**} + R_h^{**})$ and $N_r^{**} = (S_r^{**} + I_r^{**})$ From equation (9) $\lambda_r^{**} = \frac{\beta_r I_r^{**}}{N_r^{**}}$

implies that

$$\begin{split} \lambda_r^{**}N_r^{***} &- \beta_r I_r^{**} = 0\\ \Rightarrow (\lambda_r^{**} - \beta_r)I_r^{**} + \lambda_r^{**}S_r^{**} = 0. \end{split}$$

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$$\Rightarrow (\lambda_r^{**} - \beta_3) \frac{\lambda_r^{**} \Lambda}{\vartheta(\lambda_r^{**} + \vartheta)} + \lambda_r^{**} \frac{\Lambda}{(\lambda_r^{**} + \vartheta)} = 0$$
$$\Rightarrow \frac{\lambda_r^{**} \Lambda(\lambda_r^{**} - \beta_r + \vartheta)}{\vartheta(\lambda_r^{**} + \vartheta)} = 0$$

Thus,
$$\lambda_r^{**} - \beta_r + \vartheta = 0$$
 since $\lambda_r^{**} \neq 0$,
and so $\lambda_r^{**} = \beta_r - \vartheta$ (13)
Also, From (9) $\lambda_h^{**} = \lambda_h^{**} = \frac{\beta_h l_h^{**} + \beta_r l_r^{**}}{N_h^{**}}$
implies that

 $\lambda_{h}^{**}N_{h}^{**} - (\beta_{r}I_{r}^{**} + I_{h}^{**}\beta_{h}) = 0$ $\Rightarrow \lambda_{h}^{**}(S_{h}^{**} + E_{h}^{**} + I_{h}^{**} + T_{h}^{**} + R_{h}^{**}) - (\beta_{r}I_{r}^{**} + I_{h}^{**}\beta_{h}) = 0$ (14) Substituting (8) and (10) into (11) we have the following quadratic equation in team of λ_{h}^{**}

$$a\lambda_h^{**2} + b\lambda_h^{**} + c = 0 \tag{15}$$

With

$$\begin{split} a &= \Lambda_h \vartheta \left(\gamma \mu K_2 + \gamma \psi K_2 + \mu K_2 K_4 + \mu K_3 K_4 + \varphi K_2 K_4 \right) \\ b &= K_1 K_3 K_4 \Lambda_h \vartheta \mu (1 - \mathcal{R}_{0h}) + K_1 K_3 K_4 \Lambda_r \vartheta \mu (1 - \mathcal{R}_{0r}) + K_2 \gamma \varphi \mu \Lambda_r (\beta_r - \vartheta) \\ c &= \mu^2 K_1 K_2 K_4 \Lambda_r \vartheta (1 - \mathcal{R}_{0r}) \end{split}$$

It can be observed that the coefficient a is always positive while the sign of b and c depends on the values of the reproduction numbers \mathcal{R}_{0h} and \mathcal{R}_{0r} with $\beta_r - \vartheta \neq 0$. since $\mathcal{R}_0 < 1$, it follows by Descartes rule of signs that,

- i. If $R_{0h} > 1$ and $R_{0r} > 1$, then b < 0 and c < 0 then there is only one sign change in the sequence of coefficients a, b, c. Thus, there is one positive real root of (15).
- ii. If both *b* and *c* are positive when $R_{0h} < 1$ and $R_{0r} < 1$. Then there is no change in the sequence of coefficients, therefore, equation (15) has no positive real root.
- iii. If $R_{0h} > 1$ and $R_{0r} < 1$ then there either two sign changes or no sign change in the sequence of coefficients of (15). Then there two or no positive real root of (15).
- iv. If $R_{0h} < 1$ and $R_{0r} > 1$, there is one sign change in the sequence of coefficients a, b, c. Then there exists at most one positive real root of (15)

Consequently, apart from the root $\lambda_h^{**} = 0$, by Descartes rule of signs, there exists at least one positive real root for (15) whenever $\mathcal{R}_0 > 1$. Hence, the model (1) has at least one endemic equilibrium point whenever $\mathcal{R}_0 > 1$.

Data fitting and Estimation of the Parameter

The Nigeria Centre for Disease Control (NCDC) reported cases of Lassa fever for suspected cases and confirmed cases for a period from 2019 to 2020 where used to validate model (1).



Figure 2. The cumulative suspected and confirmed cases of Lassa fever in Nigeria from 2019 to 2020

The pictorial representation of number of cumulative suspected and confirmed cases for the aforementioned period is shown in Fig.2. Moreover, the number of suspected and Confirmed Cases of Lassa Fever from 2019 – 2020 are depicted in Fig. 3, and Fig. 4 respectively.



Figure 3. The suspected cases of Lassa fever in Nigeria from 2019 to 2020



Figure 4. The confirmed cases of Lassa fever in Nigeria from 2019 to 2020

This study considers the Lassa fever confirmed cases for the aforementioned period in fitting model (1) to the data, the following parameter values where adopted from the literature, $\Lambda_h = 68088$; $\Lambda_r = 557$; $\alpha_1 = 0.485$; $\alpha_2 = 0.485$; see (Ojo *et al.*, Collins *et al.*).

Thus, according to (Central Intelligence Agency) the average lifespan of a person in Nigeria is 60.45 years. Additionally, the total human population (N_h) of Nigerians is reported to be 214, 028, 302. As a result, we computed the recruitment rate using N_h as we assumed by the invariant region that $N_h = \frac{\Lambda_h}{\mu}$. Similar to this, the natural death of rodent is ϑ calculated using the formula $\vartheta = \frac{1}{\vartheta_0}$, where $\vartheta_0 = 1$ year represents the typical lifespan of multimammate rat (Ibrahim *et al.2021*). Also, we consider the entire population of rodents to be $N_r = 90,000$, allowing us to calculate the rodent recruitment rate as $N_r \times \vartheta$. Since Nigeria Centre for Disease Control states that Lassa fever takes 6 to 21 days to incubate. We used the Lassa fever model (1) to the compute cumulative number of cases reported from 219 to 2020 in order to derive the values for the remaining parameter values.

We developed a program code written and implemented on MATLAB ODE45 solvers, using model data fitting techniques, via conventional nonlinear least squares methods, as shown in Table 3. The pictorial diagrammatical representation for the data fitting of the model (1) using the cumulative confirmed cases is shown in figure 5. Moreover, the data fitting parameter values where used to carryout sensitivity analyses and simulations.



Figure 5. Data fitting of cumulative confirmed cases of Lassa fever model (1) From 2019 to 2020

Paramete r	Descriptions	Value	Source
Λ_h	Rate of recruitment of susceptible human	68088	Ojo et al., (2022)
Λ_r	Rate of recruitment of susceptible mastomys rat's	557	Ojo et al., (2022)
μ	Rate of natural death in human	0.0000005 4	Fitted

θ	Rate of natural death in mastomys rat's	0.7681	Fitted
Ψ	Recovery rate of treated individuals	1.2257	Fitted
ϕ	Recovery rate of infected human	1.0849	Fitted
arphi	Rate of treatment failure	0.7258	Fitted
γ	Rate of treatment	3.1602	Fitted
α_1	Rate of induced death of infectious	0.484	Collins <i>et al.,</i>
	individual		(2023)
α_2	Rate of induced death of individual under	0.484	Collins <i>et al.,</i>
	treatment		(2023)
θ	Proportion of new exposed individual	0.0416	Fitted
	that become symptomatically infected		
ξ	Rate at which an exposed individual	1.7665	Fitted
	becomes infectious		
β_h	The Transmission rate of human	0.1316	Fitted
β_r	The Transmission rate of mastomys rat's	0.0248	Fitted

 Table 3. Value of Parameters for the Lassa Fever Model (1)

Sensitivity Analysis

To evaluate the relationship between the model value parameters, we developed a Sensitivity analysis codes using Partial Rank Correlation Coefficients (PRCC) imbedded in MATLABR2022b in model (1) to assess the most sensitive epidemiological parameters (musa *et al.*, 2020). The sensitivity indices values together with the parameter values is shown in Figure 6 for further illustration of the numerical outcome. However, the results of the analysis revealed that the positive values of the parameters θ , ξ , β_h , β_r and Λ_r is linked to an increase in the spread of Lassa fever. Moreover, a drop in the negative values of the parameters Λ_h , γ , ψ ϕ and ϕ is related to an increase in the transmission of Lassa fever. Figure 6 depicted, the maximum negative values of the sensitivity index are natural mortality rate of rats ϑ and rate of treatment γ , while the maximum positive values are transmission rate of mastomys rat's β_r and Transmission rate of human β_h . Consequently, the findings indicate that a rise (or decrease) in the value of β_r and β_h will result in a corresponding increase (or reduction) in the reproduction number. Additionally, an increase (or decrease) in the value of ϑ will result in a corresponding decrease (or increase) in the number of rats.



Figure 6. Sensitivity indices of the Lassa fever reproduction number using partial rank correlation coefficient (PRCC)

Finally, the Lassa fever sensitivity analysis indicates that any control measures that lessen the likelihood of transmission and the rate at which rats are recruited into the population alongside with early treatment of Lassa fever victims will successfully reduce the spread of the disease. **Numerical simulations and discussion**

We developed a program code written and implemented on MATHEMATICA to simulate the model (1) utilizing demographic data of Nigeria. All the parameter values that were used is shown in Table 3. These values were derived by fitting the actual NCDC data to the model system. Consequently, we support our theoretical conclusions, by exploring the impact of the most sensitive parameters on the reproduction number after the sensitivity analysis's findings. Most importantly, in order to forecast the eradication of Lassa disease in Nigeria, we also investigate the dynamical behavior of model (1) under various scenarios (that is, in increasing or decreasing order). Notably, we defined the total infected human population as the sum of exposed human and Infected deceased population that is ($E_h + I_h$) since Lassa fever exposed humans can transmit the infection, and chose our initial conditions as follows, the first cumulative suspected case of Lassa fever is assumed to be in the first exposed human population, which is given as $E_h(0) = 1340$. The first cumulative confirmed case of Lassa fever is assumed to be in the initial infectious human population, which is given as $I_h(0) = 476$, with the initial treatment of human population to be $T_h(0) = 0$, while the initial recovered human population is assumed to be given as, $R_h(0) = 0$. We calculate the initial susceptible population as $S(0) = N_h(0) - N_h(0) = N_h(0) + N_h(0) = N_h(0) + N_h(0) = N_h(0) + N_h(0) = N_h(0) + N_h(0) + N_h(0) = N_h(0) + N_h(0)$

[$E_h(0) + I_h(0) + T_h(0) + R_h(0)$] because the reported total human population of Nigeria is $N_h(0) = 214,028,302$. Moreover, the susceptible rodents' population and infected rodents' population initial conditions are assumed to be $S_r(0) = 30000$ and $I_r(0) = 20000$ respectively.



Figure 7. plot showing the Simulations of Lassa fever model (1) of susceptible human population with the effects of control parameters μ in (*a*), Λ_h in (*b*), β_h in (*c*) and β_r in (*d*), using different initial conditions represented by different colours with parameter values given in Table 3.

We explored the effect of some parameters on the reproduction number \mathcal{R}_0 based on the results from the sensitivity analysis, Since the reproduction number is the threshold quantity that determines the control or spread of disease in the population.

Hence, the susceptible human population was presented in fig.7(a, b, c, d), with figure 7(a) indicating that, the natural death rate μ has negative impact on the susceptible human population, and it is obvious that as time progress the susceptible human population will continue to decrease as the natural death rate increase.

Figure 7(b) shows that the recruitment rate of susceptible human Λ_h has a positive impact for increasing the susceptible human population.

Figure 7 (c) presents the effect of transmission probability from human-to-human (β_h) on susceptible human population respectively. However, the changes in the susceptible human population shows a very insignificant progression or neutral effect.

Figure 7(d) presents the effect of transmission probability from rodent-to-human (β_r) on susceptible human population respectively. However, the changes in the susceptible human population shows a very insignificant progression or neutral effect.





Figure 7. plot showing the Simulations of Lassa fever model (1) of exposed human population with the effects of control parameters μ in (a), φ in (b), β_h in (c) and β_r in (d), in (e) and ξ in (f) using different initial conditions represented by different colors with parameter values given The Explosed human population was presented in fig.8 (a, b, c, d, e, f), with figure 8 (a) indicating that, the natural death rate μ has negative impact on the exposed human population, and it's obvious that as time progress the susceptible human population will continue to decrease as the natural death rate increase. Figure 8 (b) shows that the rate of treatment failure φ in exposed human population has a very insignificant progression or neutral effect.

Similarly, figure 8 (c) and (d) shows the positivity impact for increasing the exposed human population in presence of transmission probability from human-to-human (β_h) and rodent-to-human (β_r) on exposed human population respectively.

Figure 8 (e) shows that the Proportion of new exposed individual that become symptomatically infected θ in exposed human population has a stability between 0 and 1.

Similarly, figure 8 (f) indicate that the rate at which an exposed individual becomes infectious ξ shows a very significant or positivity impact for increasing the exposed human population in the order of smaller value of ξ respectively.



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Figure 9. plot showing the Simulations of Lassa fever model (1) of infected human population with the effects of control parameters μ in (*a*), β_h in (*b*), φ in (*c*), γ in (*d*), α_1 in (*e*) and ϕ in (*f*) using different initial conditions represented by different colours with parameter values given in Table 3.

The infected human population was presented in fig.9 (a, b, c, d, e and f), with figure 9 (a) indicating that, the natural death rate μ has negative impact on the infected human population, and it's obvious that as time progress the infected human population will continue to decrease as the natural death rate increase.

Figure 9 (b) shows that the transmission probability from human-to-human (β_h) has a very significant progression in infected human population

Moreover, figure 9 (c) shows that the rate of treatment failure φ in infected human population has a very insignificant progression or neutral effect.

Figure 9 (d), (e) and (f) indicate that the rate at which an infected human population shows a very significant or positivity impact for increasing the infected human population in the order of smaller value.





Figure 10. plot showing the Simulations of Lassa fever model (1) of treated human population with the effects of control parameters μ in (*a*), β_1 in (*b*), φ in (*c*), ξ in (*d*), ϑ in (*e*), ς in (*f*), α_2 in (*g*) and γ_2 in (*h*) using different initial conditions represented by different colors with parameter values given in Table 3.

infected deceased human population was presented in fig.10 (a, b, c, d, and e,), with figure 10 (a) shows the effect or progression of natural death rate μ on treated human population. and it's obvious that as time progress the treated human population will continue to decrease as the natural death rate increase and vice versa.

Figure 10 (b) indicated that the if rate of treatment on infected human population increases as time progress the causality decreases and vice versa. Moreover, figure 10 (c) shows the positivity impact of recovery of treated individuals and we can easily observe from the graph that a very significant or positivity impact for increasing the recovery of treated of human population in the order of smaller value.

Figure 10 (d) shows that *the* rate of treatment failure has a very significant or positivity impact for increasing the recovery of treated of human population.

Similarly, figure 10 (e) shows the influence of negative or decrease progression of induced death of individual under treatment

Consequently, plot showing the Simulations of Lassa fever model (1) of the rodent's population are as follows:





Figure 14: (a) shows the effects of control parameters of in (a), π_r in (b) and p_r in (c) using againstation where it depicts that as the rodent's death rate increases the susceptible rodent's population decreases at time progress, and it's obvious that the susceptible rodent's population has negative impact as time progresses.

figure 11 (b) shows that the influence of recruitment rate Λ_r of susceptible rodent's has a positive impact for increasing the susceptible rodent's population.

Also, figure 11 (c) presents the effect of transmission probability of the on susceptible rodent population against time where it depicts that as the transmission rate increases the susceptible rodent population decreases at different value.



Figure 12. plot showing the Simulations of Lassa fever model (1) of infected rodents' population with the effects of control parameters ψ in (*a*), Λ in (*b*) and β_3 in (*c*) using different initial conditions represented by different colours with parameter values given in

The **figure**³¹² (a) shows the effect of rodent's natural death rate ϑ on infected rodents' population against time where it depicts that as the rodent's death rate increases the infected rodent's population decreases at time progress.

figure 12 (b) shows the effect of recruitment rate on infected rodent's population, it is noted that the effect is significantly increasing and more steadily as time progress and that has a positive impact for increasing the susceptible rodent's population.

Similarly, figure 10 (e) shows the influence of progression rate transmission of rodent on infected rodents' population, and it can be notedly seen that the effect is positive at slowly state.

Conclusions

In this paper, a deterministic mathematical model of Lassa fever epidemic with influence of treatment was formulated and analyzed. We obtain the basic reproduction number \mathcal{R}_0 via next generation matrix method, we have shown that if \mathcal{R}_0 is greater than one, means the disease is spreading and also the number of infected individual increases as well. the disease-free equilibrium points and the endemic equilibrium point has been established. We have proven that the disease – free equilibrium (DFE) of the (LASV) model system is locally asymptotically stable if $\mathcal{R}_0 < 1$ and ε_0 is unstable if $\mathcal{R}_0 > 1$. This show that the early treatment of Lassa fever is necessary and meaningful.

However, the results of the analysis revealed that the positive values of the parameters θ , ξ , β_h , β_r and Λ_r is linked to an increase in the spread of Lassa fever and a drop in the negative values of the parameters Λ_h , γ , ψ , ϕ and φ is related to an increase in the transmission of Lassa fever. Figure 6 depicted, the maximum negative values of the sensitivity index are natural mortality rate of rats ϑ and rate of treatment γ , while the maximum positive values are transmission rate of mastomys rat's β_r and Transmission rate of human β_h . Consequently, the findings indicate that a rise (or decrease) in the value of β_r and β_h will result in a corresponding increase (or reduction) in the reproduction number. Additionally, an increase (or decrease) in the value of ϑ will result in a corresponding decrease (or increase) in the number of rats.

Lastly, the Lassa fever sensitivity analysis indicates that any control measures that lessen the likelihood of transmission and the rate at which rats are recruited into the population alongside with early treatment of Lassa fever victims will successfully reduce the spread of the disease.

Recommendations

To decrease the transmission of disease;

- i. Keeping the remaining parameters constant, the transmission rate (β_h) and the coefficient (ξ) should be less than 0 respectively.
- ii. Keeping the remaining parameters constant, the treatment failure rate (ϕ) should be less than 0.
- iii. Keeping the remaining parameters constant, the Lassa fever induced death rate for infectious individual rate (α_1) should be greater than 0.
- iv. Keeping the remaining parameters constant, the treatment rate (γ) should be greater than 1.

v. Government needs to increase or adopt the principle of screening or testing, and managing population of infected family with effective and sufficient medication to protect non-infected population.

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