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Modelling the Transmission Dynamics of the Lassa Fever Infection

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Abstract

Lassa fever is an acute hemorrhagic zoonotic illness that usually last for $2-21$ days duration occurring mostly in West African countries. Lassa virus being zoonotic means that, transmission of the disease from infected animal to human is possible with the animal reservoir or host being a rodent of the genus Mastomys. Currently, an ongoing outbreak in Nigeria has spread to 19 States of the country. Statistical figures indicated that, out of 615 suspected cases, 193 has been confirmed with 43 deaths of infected persons from Lassa fever in less than two months, giving a case fatality rate of 23.9%. In this paper, we developed a mathematical model for the transmission dynamics of the Lassa fever virus infection by splitting the infectious human population into symptomatic and asymptomatic infectious and assumed that the animal reservoirs do not recover once infected. We computed the model disease-free equilibrium E_0. We established the model basic reproduction numbers $R_{0,N}$ and $R_{0,H}$ for the animal reservoirs and the humans respectively and the associated reproduction numbers in the humans $R_{0,NH}$, $R_{0,H1}$, $R_{0,H2}$ and $R_{0,H3}$. The disease-free equilibrium was found to be locally and globally asymptotically stable if $R_{0,N}, R_{0,NH}, R_{0,H1}, R_{0,H2}, R_{0,H3} < 1$, and unstable if $R_{0,N}, R_{0,NH}, R_{0,H1}, R_{0,H2}, R_{0,H3} > 1$ using the next-generation matrix, linearization, comparison theorem and Lyapunov function methods. Qualitative analysis of the model revealed that, the disease becomes endemic in the rodents population and also do not die out of the human population over time without controlling the growth of the rodents population, preventing animal-human transmissions and improvement on the human recovery rates. The sensitivity analysis results using forward sensitivity index method indicated that, the reproduction numbers in the humans are most sensitive to the transmission rates, recovery rates and the natural mortality rates of the humans, while the reproduction number in the rodents is most sensitive to the transmission rate, hunting/predation rate and the natural mortality rate of the rodents. The numerical experiments of the model shows that if these parameters are controlled, the disease will be wiped out of the hosts populations over time.

Keywords: Asymptomatic, basic reproduction number, comparison theorem, invariance principle, stability analysis, Lassa fever, Lyapunov function, next-generation matrix, numerical simulation, sensitivity analysis

1.0 Introduction

Lass fever; an acute, hemorrhagic viral disease that occurs mainly in West African countries was first discovered in the town of Lassa in the North-East Nigeria in 1969 (World Health Organization, 2017; Danny, Donatus, Jacqueline, *et al*., 2012). Though first described in the 1950s, the virus causing the Lassa fever was not identified until 1969 (World Health Organization, 2017; Danny, Donatus, Jacqueline, *et al*., 2012). Lassa virus is a single-stranded RNA virus belonging to the virus family *Arenaviridae* (World Health Organization, 2017). The Lassa virus is a zoonotic disease that is primarily transmitted to humans from contact with infected animals; usually a rodent of the genus *Mastomys* commonly known as *multimammate* rat (World Health Organization, 2017; World Health Organization, 2018). The *Mastomys* rats infected with Lassa fever do not become ill, but can transmit the virus to humans and other primates through the shed of their urine and faeces (World Health Organization, 2017). Lassa fever is known to be endemic in Benin, Ghana, Liberia, Mali, Sierra Leone, and Nigeria, but probably exists in other African countries as well (World Health Organization, 2017; Danny, Donatus, Jacqueline, *et al*., 2012); World Health Organization, 2018).

The Lassa fever usually last for 2-21 days in humans, but because the clinical course of the disease is so variable and nonspecific, clinical diagnosis of the disease in affected patients at early stages has been difficult (World Health Organization, 2017; Danny, Donatus, Jacqueline, *et al*., 2012), and confirmatory laboratory diagnosis is not within the confines of many centers in West Africa (World Health Organization, 2017; Andrew, *et al.* (2013). About 80% of people infected with Lassa fever are asymptomatic (World Health Organization, 2017). The incubation period of the disease ranges from 6-21 days and the onset of the disease, when it is symptomatic, is usually gradual, starting with fever, general weakness, and malaise (World Health Organization, 2017). After few days of infection, followed headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhea, and

abdominal pain (World Health Organization, 2017). In severe cases of the disease, facial swelling, fluid in the lung cavity, bleeding from the mouth, nose, vagina or gastrointestinal tract and low blood pressure may also occur (World Health Organization, 2017). Protein may also be noted in the urine of an infected person (World Health Organization, 2017). However, shock, seizures, tremor, disorientation, and coma may also be seen in the later stages of infection (World Health Organization, 2017). Deafness occurs in 25% of patients who survived the disease (World Health Organization, 2017). In half of the infected cases, hearing returns partially after 1-3 months of recovery, and transient hair loss and gait disturbance may occur during recovery (World Health Organization, 2017).

Death usually occurs within the first 14 days of onset in fatal cases (World Health Organization, 2017). It is reported that, 1 out of each 5 infections results in severe disease case, where the virus affects several vital organs such as the liver, spleen and the kidneys (World Health Organization, 2017). The disease is especially severe late in pregnancies with maternal death and/or fetal loss occurring in more than 80% of the cases during third trimester (World Health Organization, 2017). The overall case-fatality rate is 1% and observed case-fatality rate among patients hospitalized with severe cases of the Lassa fever is 15% (World Health Organization, 2017). However, when presence of the disease is confirmed in a community, prompt isolation of affected patients, good infection prevention and control practices, and rigorous contact tracing can stop outbreaks (World Health Organization, 2017). Early supportive care with rehydration and symptomatic treatment of the infected persons improves survival and chances of recovery (World Health Organization, 2017). The antiviral drug ribavirin seems to be an effective treatment for the Lassa fever virus if given early in the course of clinical illness (World Health Organization, 2017). There is no evidence to support the role of ribavirin as post-exposure prophylactic treatment for the Lassa fever (World Health Organization, 2017). Generally, there is no licensed vaccine for Lassa fever virus (World Health Organization, 2017; Thomas, *et al*., 2005), and no experimental vaccine has completely protected nonhuman primates against Lassa fever (Thomas, *et al*., 2005).

The Lassa fever virus is usually transmitted to humans via contact with food or household items contaminated with rodents' urine or faeces (World Health Organization, 2017). Humans become infected with the Lassa fever virus from exposure to urine or faeces of an infected *Mastomys* rats (World Health Organization, 2017). The Lassa virus may also be transmitted between humans through direct contact with the blood, urine, faeces or other bodily secretions of an infected person with Lassa fever (World Health Organization, 2017). Currently, there is no epidemiological evidence supporting airborne spread of the Lassa fever virus among humans, but, person-to-person infections and laboratory transmission can also occur, especially in hospitals lacking adequate infection prevention and control measures (World Health Organization, 2017). Person-to-person transmission occurs in both community and healthcare settings where the virus may be spread by contaminated medical equipment, such as re-used needles (World Health Organization, 2017). Sexual transmission of the Lassa fever virus has also been reported (World Health Organization, 2017). Infections in humans typically occurs by direct or indirect exposure to animal excrement through the respiratory or gastrointestinal tracts (Public Health England, 2014). Inhalation of the tiny particles of infectious material (aerosol) is believed to be the most significant means of exposure (Public Health England, 2014). It is possible to acquire the infection through broken skin or mucous membranes that are directly exposed to infectious materials and so, transmission from person-to-person has been established (World Health Organization, 2017; Public Health England, 2014).

Outbreaks of the Lassa fever virus occurs regularly in West Africa with the most recent one in Nigeria (Amy, 2018). From 1 January 2018 through 18 March 2018, about 1495 suspected cases and 119 deaths have been reported in Nigeria from 19 States of the Federation including Anambra, Bauchi, Benue, Delta, Ebonyi, Edo, Ekiti, FCT Abuja, Gombe, Imo, Kaduna, Kogi, Lagos, Nassarawa, Ondo, Osun, Plateau, Rivers and Taraba (World Health Organization, 2018). During this period, 376 cases were confirmed, 9 were classified probable, 1084 were reported negative and 26 are pending; awaiting laboratory results (World Health Organization, 2018). Among the 376 confirmed and the 9 classified probable cases, 95 deaths were reported giving a case-fatality rate of the confirmed and probable cases to be 24.7% (World Health Organization, 2018). Similar reports about the current ongoing Lassa outbreaks and fatality cases in Nigeria can be found in (Ayodamola, 2018; Vanguard News, 2018). Since 1 January 2018, the number of Lassa fever cases increased from 10 to 70 weekly reported cases (World Health Organization, 2018). However, since mid-February 2018, there has been a downward trend in the weekly reported number of cases (World Health Organization, 2018). The Nigeria Center for Disease Control NCDC has built a laboratory in Ebonyi State that has the equipment needed to identify the Lassa fever virus, which is the fourth of its kind to be established by the institution in the country (Amy, 2018).

Mathematical modeling in epidemiology provides understanding of the mechanisms that influence the spread of diseases, and suggests control strategies. For some diseases, it is found that for a period of time, a part of the infectious class does not show the symptoms (Mohammed, AL-Smadi & Ghaleb, 2014). For modeling such

diseases SEIR models are used (Mohammed, AL-Smadi & Ghaleb, 2014). A general SEIR model with vertical transmission for the dynamics of an infectious disease was studied by El-Sheikh & El-Marouf (2003), where a fraction *p* and *q* of the offspring from the exposed and the infectious classes, respectively, were assumed to be infected at birth. The work of El-Sheikh & El-Marouf (2003) showed that once the disease appears, it eventually persists at the unique endemic equilibrium level. They finally used mathematical tools of differential analysis, persistence theory, Hopf-Andronov-Poincaré bifurcation, and linear system theory to deduce the existence of a family of periodic solutions that bifurcate from a positive interior equilibrium. A mathematical model for the transmission dynamics of the Lassa fever virus can be found in the work of Faniran (2017). In developing the model, Faniran (2017) neglected the latency/exposure period in the successive trends of infection progression in both humans and the animals. They also neglected human-to-human transmission of the virus in the human host and considered only animal-to-human transmission.

Another mathematical model for the transmission dynamics of the Lassa fever infection was developed by Omale & Edibo (2015). In the development of the model, they also neglected the latency/exposure period in the successive trends of infection progression in both humans and the animals and considered re-infection after recovery from the treatment intervention in the humans. They considered liner incidence transmission in the animals and the force of infection in the model did not account for animal-to-human transmission. A deterministic mathematical model for transmission dynamics of Lassa fever with quarantine policy was constructed in the work of Tolulope, Akinyemi & Bamidele (2015). In their work, they divided the infectious human population into two; the quarantine and un-quarantine human and considered both contribute to human-to-human transmission of the virus in the human host. They subdivided the animal population into adults and infant reservoirs and assumed only the adults contributes in animal-to-human transmission of the Lassa virus. In the model, they assumed humans recover with permanent immunity.

The work of Onuorah, Akinwande, Nasir & Ojo (2016) subdivided the human host into males and females and the animal reservoirs into active and inactive reservoirs when developing their model. They incorporated sexual transmission of the virus among sexually active humans as one of the means of transmitting the disease in humans. Sensitivity analysis of parameters in the basic reproduction number of their model revealed that, the reproduction number is most sensitive to parameters representing human birth, condom efficacy and compliance rates. In the work of Adewale, Olopade, Adeniran, & Oyedemi (2016), they developed a mathematical model for the transmission dynamics of the Lassa fever virus with proposed isolation of infectious humans as control strategy on the spread of the disease among humans. The model in James, Abdulrahman, Akinyemi & Akinwande (2015) studied the transmission dynamics of the Lassa fever virus in humans only. The SIR model in the work did not consider the animal reservoirs in the transmission dynamics of the virus.

Therefore, in this paper, we developed a mathematical model for the transmission dynamics of the Lassa fever virus infection by incorporating latency/exposure period in the trends of infection progression in both humans and animal reservoirs. And since almost 80% of Lassa fever cases in humans are asymptomatic, we divided the infectious human population into symptomatic and asymptomatic infectious humans. We considered animal-to-human and human-to-human transmission in the dynamics of the virus in the human host. The description of the dynamics of the model is presented in details in the following section.

2.0 Model Formulations

In this section, we present the development of the Lassa fever model in this paper. The definitions and representation of the model parameters, and the model assumptions are highlighted in the model description in the following subsection.

2.1 Description of the model

The model in this paper divided the host population into two; the non-human primates and/or some wild rodents (animal reservoirs), and the humans host population. The non-human primate population $N_N(t)$ at time t, was further divided into Susceptible (S_N), Exposed (E_N) and Infected (I_N) subpopulations. Susceptible non-human primates and/or some wild animals are recruited into (S_N) at a constant rate Λ. A susceptible primate/wild rodent in (S_N) become exposed to the Lassa fever and move to (E_N) after getting into contact with an infected non-human primate from (I_N) at a rate λ_N, with

$$\lambda_N = \beta_{NN} \frac{I_N}{N_N} \tag{1}$$

where β_{NN} is the product of effective contact rate and probability of the non-human primate getting infected per contact. After the disease-incubation period in primates, an exposed primate in (E_N) proceeds to the infected class (I_N) at a rate ν. The infected primates/wild rodents in (I_N) which are capable of infecting other animals when they come into effective contact does not recover naturally from the Lassa fever infection. All non-human primates in the model experience natural mortality rate μ and are being hunted by humans and other predators at a uniform rate κ.

The total human host population $N_H(t)$ at time t, was also divided into Susceptible (S_H), Exposed (E_H), Asymptomatic $(I_{H,A})$, Symptomatic $(I_{H,S})$, and Removed (R_H) human subpopulations. It is assumed that symptomatic and asymptomatic humans are equally infectious. Susceptible humans are recruited into (S_H) at a constant birth rate b. A susceptible individual in (S_H) become exposed to the Lassa fever virus and move to (E_H) after getting into contact with an infectious human or non-human primates/wild rodent at a rate λ_H, with

$$\lambda_H = \beta_{NH}\frac{I_N}{N_N} + \beta_{HH}\frac{(I_{H,A}+I_{H,S})}{N_H} \tag{2}$$

where β_{NH} is the product of the effective contact rate and probability of the human being infected per contact with an infectious non-human primate animal, and β_{HH} is the product of the effective contact rate and the probability of the human being infected with the Lassa Fever virus after getting into contact with an infectious human per contact. After the incubation period, a proportion $\rho \in [0,1]$ of the Exposed human in (E_H) develop symptoms of the Lassa Fever and proceeds to the symptomatic class $(I_{H,S})$ at a rate $\rho\varepsilon$ while the remaining proportion $(1-\rho)$ does not develop symptoms of the Lassa Fever and becomes asymptomatic, thus moving to the class $(I_{H,A})$ at a rate $(1-\rho)\varepsilon$; where ε is the disease-incubation rate in the humans. It is assumed that, humans die from the Lassa fever only when they have developed one or more symptoms of the virus. Therefore, individuals in $(I_{H,A})$ either develop symptoms naturally at a rate ω and move to $(I_{H,S})$ or recover naturally due to their immunity at a rate γ and move to (R_H) with permanent immunity. Individuals in $(I_{H,S})$ either recover with permanent immunity into (R_H) at a rate δ or die due to the virus at a constant rate ϕ. All individuals in the human subpopulations suffer natural mortality at a constant uniform rate d. All parameters of the model are strictly nonnegative and will assume values presented in Table 1 during simulations and sensitivity analysis.

2.2 Model Equations

From the description of the model in *2.1* above, we derived the following model equations

$$\dot{S_N} = \Lambda - \left(\mu + \kappa + \beta_{NN}\frac{I_N}{N_N}\right)S_N \tag{3}$$

$$\dot{E_N} = \beta_{NN}\frac{I_N}{N_N}S_N - (\mu+\kappa+\nu)E_N \tag{4}$$

$$\dot{I_N} = \nu E_N - (\mu+\kappa)I_N \tag{5}$$

$$\dot{S_H} = b - \left(d + \beta_{NH} \frac{I_N}{N_N} + \beta_{HH} \frac{I_{H,A} + I_{H,S}}{N_H} \right) S_H \tag{6}$$

$$\dot{E_H} = \left(\beta_{NH} \frac{I_N}{N_N} + \beta_{HH} \frac{I_{H,A} + I_{H,S}}{N_H} \right) S_H - (d + \varepsilon) E_H \tag{7}$$

$$\dot{I_{H,A}} = (1-\rho)\varepsilon E_H - (d + \omega + \gamma) I_{H,A} \tag{8}$$

$$\dot{I_{H,S}} = \rho\varepsilon E_H + \omega I_{H,A} - (d + \phi + \delta) I_{H,S} \tag{9}$$

$$\dot{R_H} = \gamma I_{H,A} + \delta I_{H,S} - dR_H \tag{10}$$

$$N_N(t) = S_N + E_N + I_N \tag{11}$$

$$N_H(t) = S_H + E_H + I_{H,A} + I_{H,S} + R_H \tag{12}$$

Subject to the following nonnegative initial conditions:

$$S_N(0) > 0, E_N(0) \geq 0, I_N(0) \geq 0 \tag{13}$$

$$S_H(0) > 0, E_H(0) \geq 0, I_{H,A}(0) \geq 0, I_{H,S}(0) \geq 0, R_H(0) \geq 0 \tag{14}$$

with

$$\begin{cases} S_N(0) + E_N(0) + I_N(0) \leq N_N(0) \\ S_H(0) + E_H(0) + I_{H,A}(0) + I_{H,S}(0) + R_H(0) \leq N_H(0) \end{cases} \tag{15}$$

3.0 Model Analyses

In this section, we begin the model analysis by showing that all feasible solutions of the model system are uniformly bounded in a proper subset of Ω. Thus, the feasible region

$$\Omega = \left\{ \left(S_N, E_N, I_N, S_H, E_H, I_{H,A}, I_{H,S}, R_H \right) \in \mathbb{R}_+^8 : N_N \leq \frac{\Lambda}{(\mu + \kappa)}, N_H \leq \frac{b}{d} \right\} \tag{16}$$

is considered. Therefore, differentiating equation (11) and (12) representing the total populations of the animal reservoirs and the humans, with proper substitutions and simplifications, we have:

$$\dot{N_N}(t) = \Lambda - (\mu + \kappa) N_N \tag{17}$$

and;

$$\begin{aligned} \dot{N_H}(t) &= b - dN_H - \phi I_{H,S} \\ \dot{N_H}(t) &\leq b - dN_H \end{aligned} \tag{18}$$

Applying the result in Birkhof & Rota (1989) on the differential equation in (17) and the differential inequality in (18), we obtained:

$$\begin{cases} N_N(t) = N_N(0)e^{-(\mu+\kappa)t} + \dfrac{\Lambda}{(\mu+\kappa)}\left(1-e^{-(\mu+\kappa)t}\right) \\ N_H(t) \le N_H(0)e^{-dt} + \dfrac{b}{d}\left(1-e^{-dt}\right) \end{cases} \tag{19}$$

where $N_N(0)$ and $N_H(0)$ are the initial populations of the animal reservoirs and the humans respectively. Therefore, $0 \le N_N \le \dfrac{\Lambda}{(\mu+\kappa)}$ and $0 \le N_H \le \dfrac{b}{d}$ as $t \Rightarrow \infty$. This implies that, $\dfrac{\Lambda}{(\mu+\kappa)}$ and $\dfrac{b}{d}$ are the upper bounds for the animal reservoir population $N_N(t)$ and the human population $N_H(t)$ respectively, as long as $N_N(0) \le \dfrac{\Lambda}{(\mu+\kappa)}$ and $N_H(0) \le \dfrac{b}{d}$. Hence, the feasible solution of the model equations in (3)-(12) enters the region Ω which is a positively invariant set. Thus, the system described by the model system in (3)-(12) is both mathematically and epidemiologically well-posed. Therefore, for an initial starting point $x \in \Omega$, the trajectory of x lies in Ω, and so it is sufficient to restrict our analysis on Ω. Obviously, under the dynamics described by the model equations in (3)-(12), the closed set Ω is hence a positively invariant set.

3.1 Model Disease-Free Equilibrium

Using standard mathematical approaches, we established the model Disease-Free Equilibrium (DFE) point E_0. The DFE was obtained by solving the model equations simultaneously with $I_N = I_{H,A} = I_{H,S} = 0$, which is given as:

$$E_0 = \left(S_N, E_N, I_N, S_H, E_H, I_{H,A}, I_{H,S}, R_H\right) = \left(\frac{\Lambda}{\mu+\kappa}, 0, 0, \frac{b}{d}, 0, 0, 0, 0\right) \tag{20}$$

Here, it is important to note that, in the absence of the Lassa fever infection, the animal reservoir population is bounded by birth, natural mortality and the hunting rates only and the human population is bounded by birth and natural mortality rates only, i.e.;

$$S_N \approx N_N \to \frac{\Lambda}{\mu+\kappa} \text{ and } S_H \approx N_H \to \frac{b}{d} \tag{21}$$

3.2 The Basic Reproduction Number

The basic reproduction number of the model was computed using the next-generation matrix as defined in Van den Driessche & Watmough (2002), and Diekmann, Heesterbeek & Metz (1990). It is defined to be largest eigenvalue or spectral radius of the characteristic equation $\left|FV^{-1} - \psi I\right| = 0$, where ψ is an eigenvalue associated with the matrix FV^{-1}. Using the notations in Diekmann, Heesterbeek & Metz (1990) for the model system, the associated matrices F and V for the new infectious terms and the remaining transition terms, evaluated at the DFE are respectively obtained as follows:

$$F_i = \begin{bmatrix} \beta_{NN}\dfrac{I_N}{N_N}S_N \\ 0 \\ \left(\beta_{NH}\dfrac{I_N}{N_N}+\beta_{HH}\dfrac{I_{H,A}+I_{H,S}}{N_H}\right)S_H \\ 0 \\ 0 \end{bmatrix}, \quad V_i = \begin{bmatrix} +(\mu+\kappa+\nu)E_N \\ -\nu E_N+(\mu+\kappa)I_N \\ +(d+\varepsilon)E_H \\ -(1-\rho)\varepsilon E_H+(d+\omega+\gamma)I_{H,A} \\ -\rho\varepsilon E_H-\omega I_{H,A}+(d+\phi+\delta)I_{H,S} \end{bmatrix} \tag{22}$$

such that $i=1,2,3,4,5$. Therefore, the associated matrices F and V for the new infectious terms and the remaining transition terms are computed from the following Jacobian matrices:

$$F = \begin{bmatrix} \frac{\partial F_1}{\partial E_N} & \frac{\partial F_1}{\partial I_N} & \frac{\partial F_1}{\partial E_H} & \frac{\partial F_1}{\partial I_{H,A}} & \frac{\partial F_1}{\partial I_{H,S}} \\ \frac{\partial F_2}{\partial E_N} & \frac{\partial F_2}{\partial I_N} & \frac{\partial F_2}{\partial E_H} & \frac{\partial F_2}{\partial I_{H,A}} & \frac{\partial F_2}{\partial I_{H,S}} \\ \frac{\partial F_3}{\partial E_N} & \frac{\partial F_3}{\partial I_N} & \frac{\partial F_3}{\partial E_H} & \frac{\partial F_3}{\partial I_{H,A}} & \frac{\partial F_3}{\partial I_{H,S}} \\ \frac{\partial F_4}{\partial E_N} & \frac{\partial F_4}{\partial I_N} & \frac{\partial F_4}{\partial E_H} & \frac{\partial F_4}{\partial I_{H,A}} & \frac{\partial F_4}{\partial I_{H,S}} \\ \frac{\partial F_5}{\partial E_N} & \frac{\partial F_5}{\partial I_N} & \frac{\partial F_5}{\partial E_H} & \frac{\partial F_5}{\partial I_{H,A}} & \frac{\partial F_5}{\partial I_{H,S}} \end{bmatrix}, \quad V = \begin{bmatrix} \frac{\partial V_1}{\partial E_N} & \frac{\partial V_1}{\partial I_N} & \frac{\partial V_1}{\partial E_H} & \frac{\partial V_1}{\partial I_{H,A}} & \frac{\partial V_1}{\partial I_{H,S}} \\ \frac{\partial V_2}{\partial E_N} & \frac{\partial V_2}{\partial I_N} & \frac{\partial V_2}{\partial E_H} & \frac{\partial V_2}{\partial I_{H,A}} & \frac{\partial V_2}{\partial I_{H,S}} \\ \frac{\partial V_3}{\partial E_N} & \frac{\partial V_3}{\partial I_N} & \frac{\partial V_3}{\partial E_H} & \frac{\partial V_3}{\partial I_{H,A}} & \frac{\partial V_3}{\partial I_{H,S}} \\ \frac{\partial V_4}{\partial E_N} & \frac{\partial V_4}{\partial I_N} & \frac{\partial V_4}{\partial E_H} & \frac{\partial V_4}{\partial I_{H,A}} & \frac{\partial V_4}{\partial I_{H,S}} \\ \frac{\partial V_5}{\partial E_N} & \frac{\partial V_5}{\partial I_N} & \frac{\partial V_5}{\partial E_H} & \frac{\partial V_5}{\partial I_{H,A}} & \frac{\partial V_5}{\partial I_{H,S}} \end{bmatrix} \tag{23}$$

After proper substitutions and evaluations of the matrices in (23) at the DFE, we have;

$$F = \begin{bmatrix} 0 & \beta_{NN} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \dfrac{b\beta_{NH}(\mu+\kappa)}{d\Lambda} & 0 & \beta_{HH} & \beta_{HH} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \tag{24}$$

$$V = \begin{bmatrix} (\mu+\kappa+\nu) & 0 & 0 & 0 & 0 \\ -\nu & (\mu+\kappa) & 0 & 0 & 0 \\ 0 & 0 & (d+\varepsilon) & 0 & 0 \\ 0 & 0 & -(1-\rho)\varepsilon & (d+\omega+\gamma) & 0 \\ 0 & 0 & -\rho\varepsilon & -\omega & (d+\phi+\delta) \end{bmatrix} \tag{25}$$

Thus, the inverse of the matrix in (25) was obtained as;

$$V^{-1}=\begin{bmatrix} \frac{1}{(\mu+\kappa+\nu)} & 0 & 0 & 0 & 0 \\ \frac{\nu}{(\mu+\kappa)(\mu+\kappa+\nu)} & \frac{1}{(\mu+\kappa)} & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{(d+\varepsilon)} & 0 & 0 \\ 0 & 0 & \frac{(1-\rho)\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)} & \frac{1}{(d+\omega+\gamma)} & 0 \\ 0 & 0 & \frac{[\omega+(d+\gamma)\rho]\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)(d+\phi+\delta)} & \frac{\omega}{(d+\omega+\gamma)(d+\phi+\delta)} & \frac{1}{(d+\phi+\delta)} \end{bmatrix} \quad (26)$$

Therefore, evaluating the characteristic polynomial equation $|FV^{-1}-\psi I|=0$, we obtained the following basic reproduction numbers for the model:

$$R_{0,N}=\frac{\nu\beta_{NN}}{(\mu+\kappa)(\mu+\kappa+\nu)} \quad (27)$$

and

$$R_{0,H}=\frac{\beta_{HH}(1-\rho)\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)}+\frac{\beta_{HH}[\omega+(d+\gamma)\rho]\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)(d+\phi+\delta)} \quad (28)$$

$$R_{0,H}=R_{0,H1}+R_{0,H2} \quad (29)$$

where $R_{0,N}$ and $R_{0,H}$ are the basic reproduction numbers of the animal reservoirs and the humans in the model respectively, and, $R_{0,H1}$ and $R_{0,H2}$ are the individual basic reproduction numbers of the asymptomatic and the symptomatic humans respectively.

3.3 Stability Analysis
3.3.1 Local Stability Analysis

Theorem 1: Given that $R_{0,H3}=\frac{\beta_{HH}\rho\varepsilon}{(d+\varepsilon)(d+\phi+\delta)}$, the Disease-Free Equilibrium (DFE) of the model is locally asymptotically stable if $R_{0,N}, R_{0,H1}, R_{0,H3}<1$ and unstable if $R_{0,N}, R_{0,H1}, R_{0,H3}>1$.

Proof: The proof of the theorem can be established by constructing a Jacobian matrix for the model system evaluated at the DFE. The Jacobian matrix evaluated at the DFE was constructed as:

$$J_{E_0}=\begin{bmatrix} -(\mu+\kappa) & 0 & -\beta_{NN} & 0 & 0 & 0 & 0 & 0 \\ 0 & -(\mu+\kappa+\nu) & \beta_{NN} & 0 & 0 & 0 & 0 & 0 \\ 0 & \nu & -(\mu+\kappa) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\frac{b\beta_{NH}(\mu+\kappa)}{d\Lambda} & -d & 0 & -\beta_{HH} & -\beta_{HH} & 0 \\ 0 & 0 & \frac{b\beta_{NH}(\mu+\kappa)}{d\Lambda} & 0 & -(d+\varepsilon) & \beta_{HH} & \beta_{HH} & 0 \\ 0 & 0 & 0 & 0 & (1-\rho)\varepsilon & -(d+\omega+\gamma) & 0 & 0 \\ 0 & 0 & 0 & 0 & \rho\varepsilon & \omega & -(d+\phi+\delta) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & \delta & -d \end{bmatrix} \quad (30)$$

We used elementary row operations as used by Usman & Adamu (2017) and Usman, Adamu & Tahir (2016) to row-reduce the Jacobian matrix in (30) to an upper triangular matrix and obtained the following eigenvalues from the leading diagonal of the reduced Jacobian matrix:

$$\psi_1 = -(\mu+\kappa), \qquad \psi_2 = -(\mu+\kappa+\nu), \qquad \psi_3 = -(1-R_{0,N}), \qquad \psi_4 = -d(1-R_{0,N}),$$
$$\psi_5 = -(d+\varepsilon)(1-R_{0,N}), \qquad \psi_6 = -(1-R_{0,N})(1-R_{0,H1}),$$
$$\psi_7 = -\left[(1-R_{0,H1})(1-R_{0,H3}) - (d+\varepsilon)^2(d+\omega+\gamma)(d+\phi+\delta)(R_0+R_{0,H3})\right],$$
$$\psi_8 = -d(1-R_{0,N})(1-R_{0,H1})\left[(1-R_{0,H1})(1-R_{0,H3}) - (d+\varepsilon)^2(d+\omega+\gamma)(d+\phi+\delta)(R_0+R_{0,H3})\right]$$

where $R_{0,H3} = \dfrac{\beta_{HH}\rho\varepsilon}{(d+\varepsilon)(d+\phi+\delta)}$, is the average basic reproduction number of the symptomatic human population. Therefore, $\psi_{3,4,and\,5} < 0$ if $R_{0,N} < 1$, and $\psi_{6,7,and\,8} < 0$ if $R_{0,H1}, R_{0,H3} < 1$. Hence, the DFE is locally asymptotically stable if $R_{0,N}, R_{0,H1}, R_{0,H3} < 1$, which complete the proof of the Theorem 1.

3.3.2 Global Stability Analysis

Theorem2: The Disease-Free Equilibrium (DFE) of the model is globally asymptotically stable if $R_{0,N}, R_{0,H1}, R_{0,H2}, R_{0,H3} < 1$ and unstable if $R_{0,N}, R_{0,H1}, R_{0,H2}, R_{0,H3} > 1$.

Proof: The proof of Theorem 2 will be established using the comparison theorem as used by Usman, Adamu & Umar (2017) and Shaban & Hawa (2014). Thus, by the comparison theorem, the rate of change of the variables representing the infectious compartments of the animal reservoirs and the humans in the model can be compared in equation (31) and the inequality in (32).

$$\begin{bmatrix} E_N' \\ I_N' \\ E_H' \\ I_{H,A}' \\ I_{H,s}' \end{bmatrix} = (F-V)\begin{bmatrix} E_N \\ I_N \\ E_H \\ I_{H,A} \\ I_{H,S} \end{bmatrix} - S_N^0\theta_1\begin{bmatrix} E_N \\ I_N \\ E_H \\ I_{H,A} \\ I_{H,S} \end{bmatrix} - S_H^0\theta_2\begin{bmatrix} E_N \\ I_N \\ E_H \\ I_{H,A} \\ I_{H,S} \end{bmatrix} \qquad (31)$$

Where F and V are defined earlier in (24) and (25) respectively, S_N^0 and S_H^0 are the populations of the animal reservoirs and the humans respectively at the DFE, and, θ_1 and θ_2 are nonzero matrices (to be specified). Since $S_N^0 \le N_N^0$ and $S_H^0 \le N_H^0$, then (31) can be written as

$$\begin{bmatrix} E_N' \\ I_N' \\ E_H' \\ I_{H,A}' \\ I_{H,s}' \end{bmatrix} \le (F-V)\begin{bmatrix} E_N \\ I_N \\ E_H \\ I_{H,A} \\ I_{H,S} \end{bmatrix} \qquad (32)$$

Therefore, the matrix $(F-V)$ was obtained as

$$(F-V)=\begin{bmatrix} -(\mu+\kappa+\nu) & \beta_{NN} & 0 & 0 & 0 \\ \nu & -(\mu+\kappa) & 0 & 0 & 0 \\ 0 & \frac{b\beta_{NH}(\mu+\kappa)}{d\Lambda} & -(d+\varepsilon) & \beta_{HH} & \beta_{HH} \\ 0 & 0 & (1-\rho)\varepsilon & -(d+\omega+\gamma) & 0 \\ 0 & 0 & \rho\varepsilon & \omega & -(d+\phi+\delta) \end{bmatrix} \quad (33)$$

Evaluating the characteristic polynomial equation $|(F-V)-\psi I|=0$, we obtained the following eigenvalues:

$\psi_9=-(\mu+\kappa+\nu)$, $\psi_{10}=-(1-R_{0,N})$, $\psi_{11}=-(d+\varepsilon)(1-R_{0,N})$, $\psi_{12}=-(1-R_{0,N})(1-R_{0,H1})$,

$\psi_{13}=-\left[(1-R_{0,H1})(1-R_{0,H3})-(d+\varepsilon)^2(d+\omega+\gamma)(d+\phi+\delta)\left((R_{0,H1}R_{0,H3})+R_{0,H2}\right)\right]$.

Therefore, clearly, $\psi_{10,11,12,13}<0$ if $R_{0,N},R_{0,H1},R_{0,H2},R_{0,H3}<1$. This implies, all the eigenvalues of the matrix in (33) have negative real parts showing that the matrix in (33) is stable for $R_{0,N},R_{0,H1},R_{0,H2},R_{0,H3}<1$. Consequently, using the model equations in $(3)-(12)$, $(E_N,I_N,E_H,I_{H,A},I_{H,S})\Rightarrow(0,0,0,0,0)$ as $t\Rightarrow\infty$. Evaluating the model system $(3)-(10)$ at $E_N=I_N=E_H=I_{H,A}=I_{H,S}=0$ gives $S_N^0=\frac{\Lambda}{(\mu+\kappa)}$, $S_H^0=\frac{b}{d}$ and $R\Rightarrow 0$ as $t\Rightarrow\infty$ for $R_{0,N},R_{0,H1},R_{0,H2},R_{0,H3}<1$. The proof of Theorem 2 can be finalized by construction and study of a Lyapunov function as follows:

Given $R_{0,N},R_{0,NH},R_{0,H1}<1$, with $R_{0,NH}=\frac{\beta_{NH}(1-\rho)\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)}$, then there exist only the DFE $E_0=(S_N,E_N,I_N,S_H,E_H,I_{H,A},I_{H,S},R_H)=\left(\frac{\Lambda}{\mu+\kappa},0,0,\frac{b}{d},0,0,0,0\right)$. Thus, by considering a Lyapunov function candidate $V=V(S_N,E_N,I_N,S_H,E_H,I_{H,A},I_{H,S},R_H):\mathbb{R}^8\to\mathbb{R}^+$ defined by

$V=V(S_N,E_N,I_N,S_H,E_H,I_{H,A},I_{H,S},R_H)=\chi_1E_N+\chi_2E_H$, such that $\chi_1,\chi_2>0$ (34)

Clearly, $V>0$. Differentiating both sides of (34) with respect to time, we obtained

$$\dot{V}=\chi_1\dot{E}_N+\chi_2\dot{E}_H \quad (35)$$

Substituting the values of $\dot{E}_N$ and $\dot{E}_H$ from equation (4) and (7) into equation (35), we get

$$\dot{V}=\chi_1\left[\beta_{NN}\frac{I_N}{N_N}S_N-(\mu+\kappa+\nu)E_N\right]+\chi_2\left[\beta_{NH}\frac{I_N}{N_N}+\frac{\beta_{HH}(I_{H,A}+I_{H,S})}{N_H}S_H-(d+\varepsilon)E_H\right] \quad (36)$$

Since $S_N=N_N$ and $S_H=N_H$ at the DFE, then (36) can be simplified to

$$\dot{V}=\chi_1\left[\beta_{NN}I_N-(\mu+\kappa+\nu)E_N\right]+\chi_2\left[\beta_{NH}\frac{I_N}{N_N}+\beta_{HH}(I_{H,A}+I_{H,S})-(d+\varepsilon)E_H\right] \quad (37)$$

Solving for E_N and E_H in (5) and (8), and substituting the values in (37) we obtained

$$\dot{V} = \chi_1\left[\beta_{NN} I_N - (\mu+\kappa+\nu)E_N\right] + \chi_2\left[\beta_{NH}\frac{I_N}{N_N} + \beta_{HH}\left(I_{H,A}+I_{H,S}\right) - (d+\varepsilon)E_H\right]$$

$$\dot{V} = \chi_1\left[\beta_{NN} I_N - (\mu+\kappa+\nu)\frac{(\mu+\kappa)}{\nu}I_N\right] + \chi_2\left[\beta_{NH}\frac{I_N}{N_N} + \beta_{HH}\left(I_{H,A}+I_{H,S}\right) - (d+\varepsilon)\frac{(d+\omega+\gamma)}{(1-\rho)\varepsilon}I_{H,A}\right]$$

$$= \frac{\chi_1(\mu+\kappa)(\mu+\kappa+\nu)(R_{0,N}-1)I_N}{\nu} + \frac{\chi_2(d+\varepsilon)(d+\omega+\gamma)}{(1-\rho)\varepsilon}\left[R_{0,NH}\frac{I_N}{N_N} + R_{0,H1}I_{H,S} + (R_{0,H1}-1)I_{H,A}\right]$$

$$\leq \frac{\chi_1(\mu+\kappa)(\mu+\kappa+\nu)(R_{0,N}-1)I_N}{\nu} + \frac{\chi_2(d+\varepsilon)(d+\omega+\gamma)\left[(R_{0,NH}-1)\frac{I_N}{N_N} + (R_{0,H1}-1)I_{H,A} + (R_{0,H1}-1)I_{H,S}\right]}{(1-\rho)\varepsilon} \qquad (38)$$

where $R_{0,NH} = \dfrac{\beta_{NH}(1-\rho)\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)}$.

Therefore, for $\chi_1 = \dfrac{\nu}{(\mu+\kappa)(\mu+\kappa+\nu)} > 0$ and $\chi_2 = \dfrac{(1-\rho)\varepsilon}{(d+\varepsilon)(d+\omega+\gamma)} > 0$, (38) can be written as

$$\dot{V} = (R_{0,N}-1)I_N + \left[(R_{0,NH}-1)\frac{I_N}{N_N} + (R_{0,H1}-1)(I_{H,A}+I_{H,S})\right], \qquad \Leftrightarrow \dot{V} \leq 0 \qquad (39)$$

It is important to note that $\dot{V} = 0$ only if $I_N = I_{H,A} = I_{H,S} = 0$. This implies, substituting $I_N = I_{H,A} = I_{H,S} = 0$ into the equations for $\dot{S_N}$ and $\dot{S_H}$ in (4) and (6) shows that $S_N \to \dfrac{\Lambda}{(\mu+\kappa)}$ and $S_H \to \dfrac{b}{d}$ as $t \to \infty$. Therefore, the maximum invariant set in $\left\{(S_N, E_N, I_N, S_H, E_H, I_{H,A}, I_{H,S}, R_H) \in \Omega : \dot{V} \leq 0\right\}$ is the singleton set $\{E_0\}$. Hence the global stability of the DFE E_0 if $R_{0,N}, R_{0,NH}, R_{0,H1} < 1$ follows from the LaSalle's invariance principle which completes the proof of Theorem 2 (LaSalle, 1976; Tewa & Bowong, 2009).

4.0 Results

4.1 Analytic Results

In this paper, we have developed a mathematical model for the transmission dynamics of the Lassa fever virus infection. The model development and the model equations were presented in section 2. We have established the disease-free equilibrium (DFE) E_0 of the model. The DFE of the model was presented in section 3, with $E_0 = (S_N, E_N, I_N, S_H, E_H, I_{H,A}, I_{H,S}, R_H) = \left(\dfrac{\Lambda}{\mu+\kappa}, 0, 0, \dfrac{b}{d}, 0, 0, 0, 0\right)$. We have also computed the basic reproduction numbers of the model for the animal reservoirs $R_{0,N}$, and for the humans $R_{0,H}$ using the next generation matrix method. Establishment of the model basic reproduction number yielded four more different associated basic reproduction numbers in the human population viz: $R_{0,NH}$, $R_{0,H1}$, $R_{0,H2}$ and $R_{0,H3}$. These basic reproduction numbers of the model serves as threshold for measuring new infections in the host's populations. The disease-free equilibrium was proved to be locally asymptotically stable if $R_{0,N}, R_{0,H1}, R_{0,H3} < 1$ and unstable if $R_{0,N}, R_{0,H1}, R_{0,H3} > 1$ using linearization plus row-reduction method, and globally asymptotically

stable if $R_{0,N}, R_{0,H1}, R_{0,H2}, R_{0,H3}, R_{0,NH} < 1$ and unstable if $R_{0,N}, R_{0,H1}, R_{0,H2}, R_{0,H3}, R_{0,NH} > 1$ using the comparison theorem and Lyapunov functions methods.

4.2 Qualitative Results

We have conducted some numerical experiments to study the qualitative behavior of the model in this paper. We have carried out numerical simulations of the model and sensitivity analysis of parameters in the basic reproduction numbers of the model. These results are presented in section 4 of this paper. Values of parameters of the model in Table 1 were sourced from the existing literatures and assumed were otherwise for the purpose of illustrations. In the numerical simulations, we first studied the natural dynamics of the disease without interventions of any kind using the parameter values in Table 1 and the result of the experiment was presented in Figure 1. We later carried out another experiment in order to know at which parameter values, the infectious populations in the animal reservoirs and the humans will die out and become asymptotic to zero. These parameter values are presented in Table 2 and the results of the experiment are presented in Figure 2. In each case, we computed the numerical values of the basic reproduction numbers of the model and presented them along with the graphs in Figure 1 and 2. The numerical simulations were carried out using MATLAB R2016B using an assumed initial populations. We have also conducted sensitivity analysis of parameters in the reproduction numbers of the model using the forward sensitivity index method. Parameter values in the Table 1 were used for this analysis and the result is presented in Table 3. These sensitivity indices indicates the dominance of the parameters in the reproduction numbers and how an increase in a parameter value might have affected the corresponding reproduction number; whether positively or negatively.

4.2.1 Numerical Simulations

Numerical simulations for the model were carried out using the parameter values in Table 1 and 2. Thus, parameters in Table 1 were sourced from the existing literatures on Lassa fever where available, and assumed for the purpose of illustrations to fit the model analyses where otherwise. While the parameters in Table 2 were chosen carefully so that the infectious compartments of the model dies out asymptotically. The program codes were written and implemented on MATLAB R2016b encoded with ODE45 solver to simulate the model system using the parameter values in Table 1 and 2, using an initial population of $S_N = 250$, $E_N = 125$, $I_N = 75$, $S_H = 80000$, $E_H = 3000$, $I_{H,A} = 1600$, $I_{H,S} = 400$ and $R_H = 200$. The results of the simulations are presented in Figure 1 and 2. In each of the simulations, the basic reproduction numbers of the model were computed numerically using the parameter values in the Table 1 and 2, and presented along with the curves.

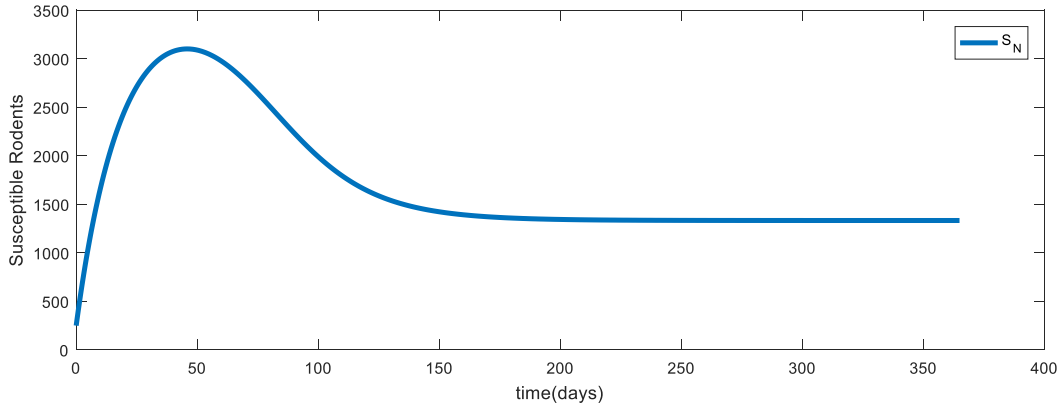
Table 1: Model Parameter Values

Parameter	Dimension	Value	Source
Λ	$Days^{-1}$	20	*
b	$Days^{-1}$	500	*
μ	$Days^{-1}$	0.04	Assumed
κ	$Days^{-1}$	0.01	*
d	$Days^{-1}$	0.02	[15]
ϕ	$Days^{-1}$	0.01	[16]
ν	$Days^{-1}$	0.03	*
ρ	$Days^{-1}$	0.2	[1]
$\frac{1}{\varepsilon}$	$Humans \times Days^{-1}$	$6-21$	[1]
ω	$Days^{-1}$	0.01	*

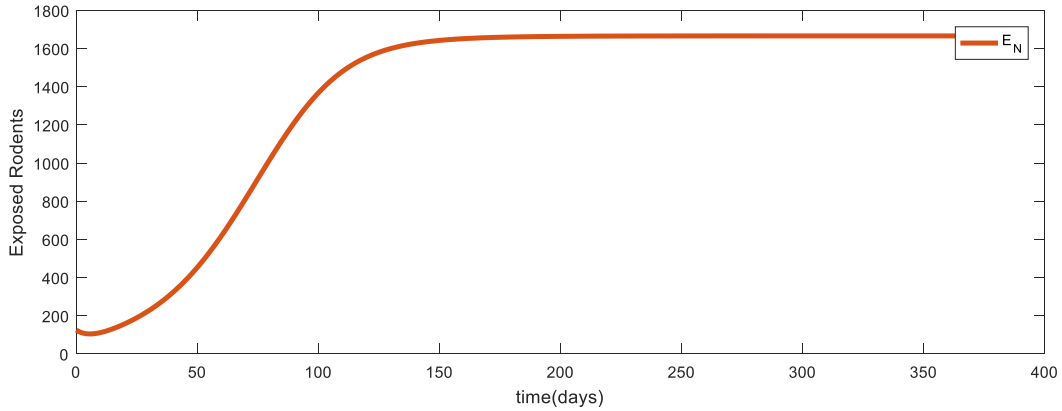
$\frac{1}{\gamma}$	$Humans \times Days^{-1}$	$2-21$	$[1,2]$
$\frac{1}{\delta}$	$Humans \times Days^{-1}$	$6-30$	$[1,2]$
β_{NN}	1	0.2	[16]
β_{NH}	1	0.00002	*
β_{HH}	1	0.002	*

Hypothetically Estimated

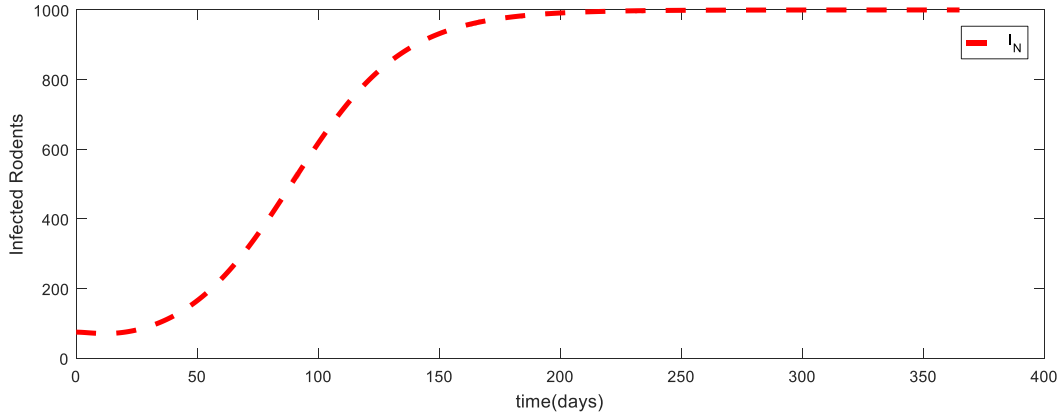
(a)



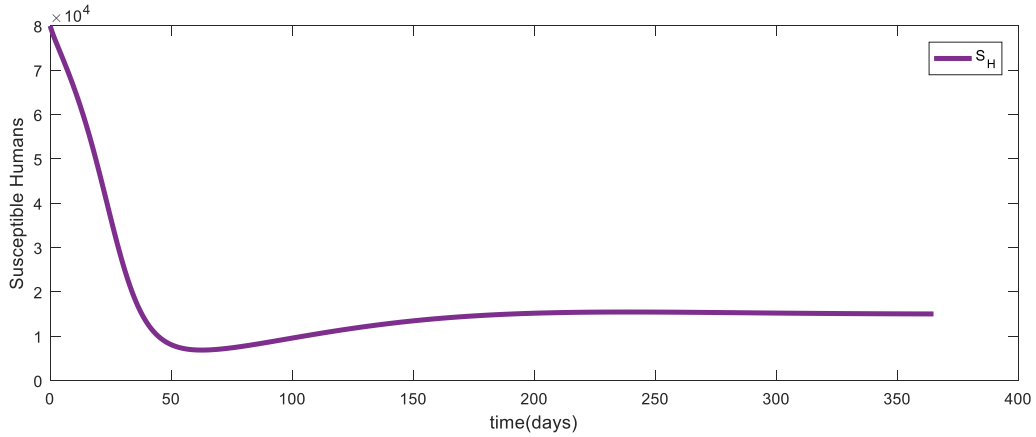
(b)



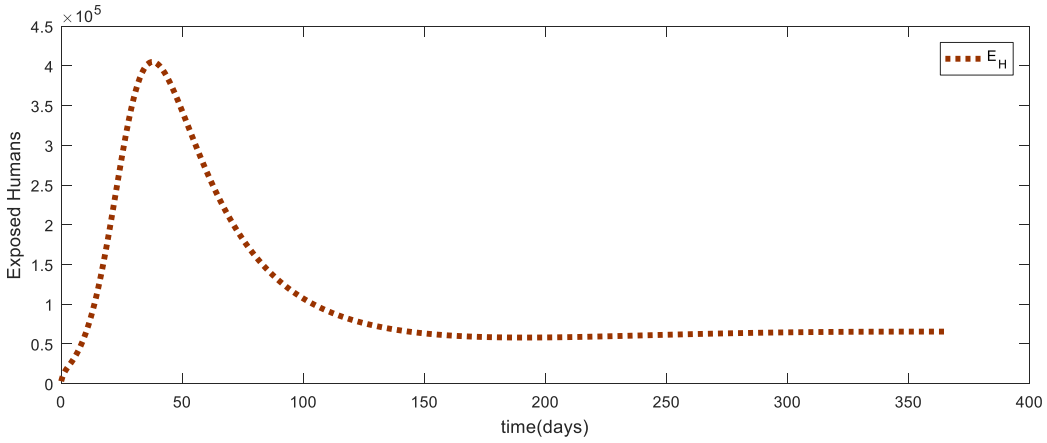
(c)


Infected Rodents
time(days)
I_N
0
200
400
600
800
1000
0
50
100
150
200
250
300
350
400

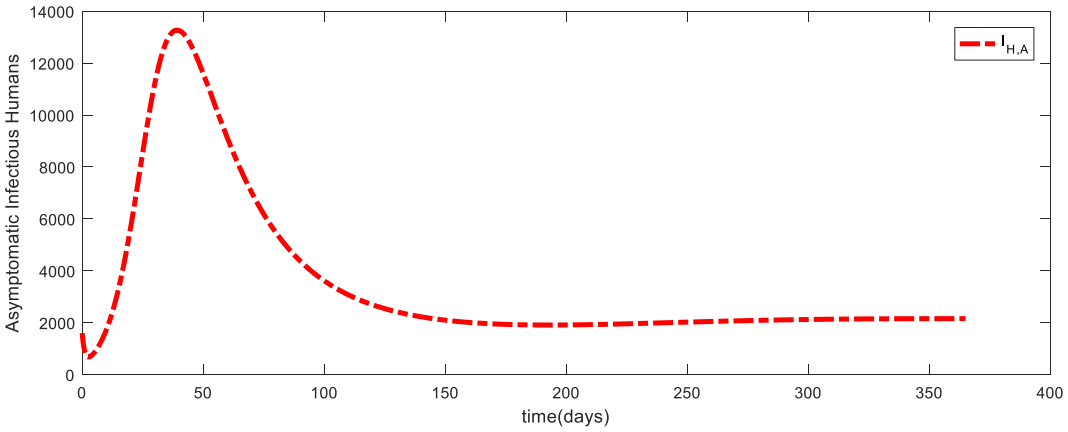
(d)


×10^4
Susceptible Humans
time(days)
S_H
0
1
2
3
4
5
6
7
8
0
50
100
150
200
250
300
350
400

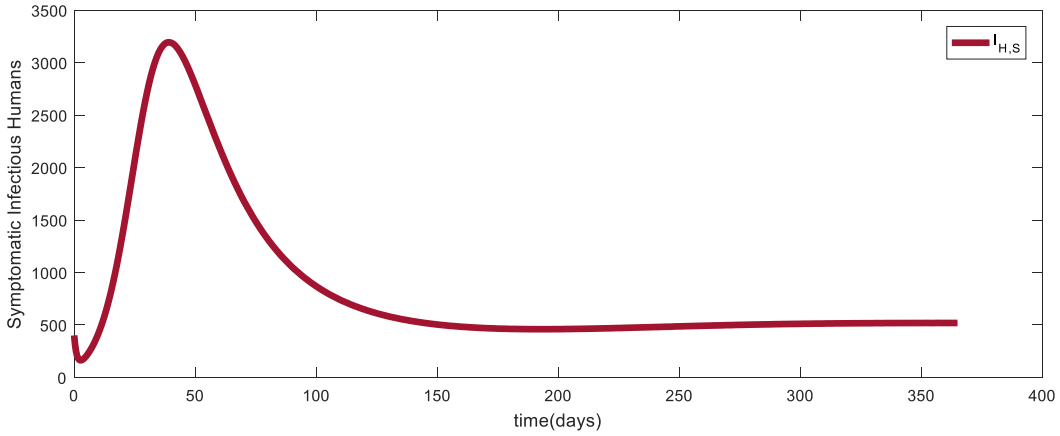
(e)


×10^5
Exposed Humans
time(days)
E_H
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
0
50
100
150
200
250
300
350
400

(f)



(g)



(h)

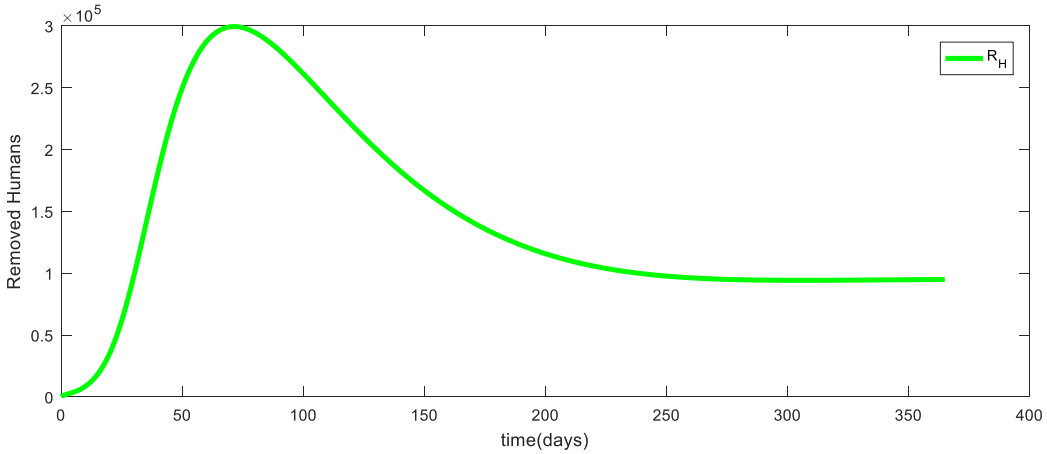
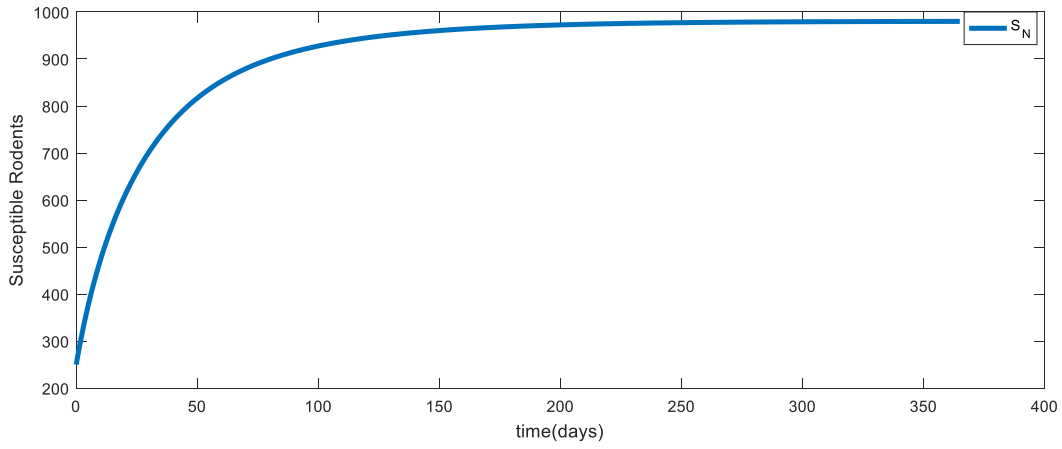


Figure 1: Results of Simulations with Parameter Values on Table 1, where $R_{0,N}=1.5$, $R_{0,NH}=1.315\times10^{-5}$, $R_{0,H1}=1.315\times10^{-3}$, $R_{0,H2}=3.165\times10^{-4}$, $R_{0,H3}=3.29\times10^{-4}$ and $R_{0,H}=1.6315\times10^{-3}$.

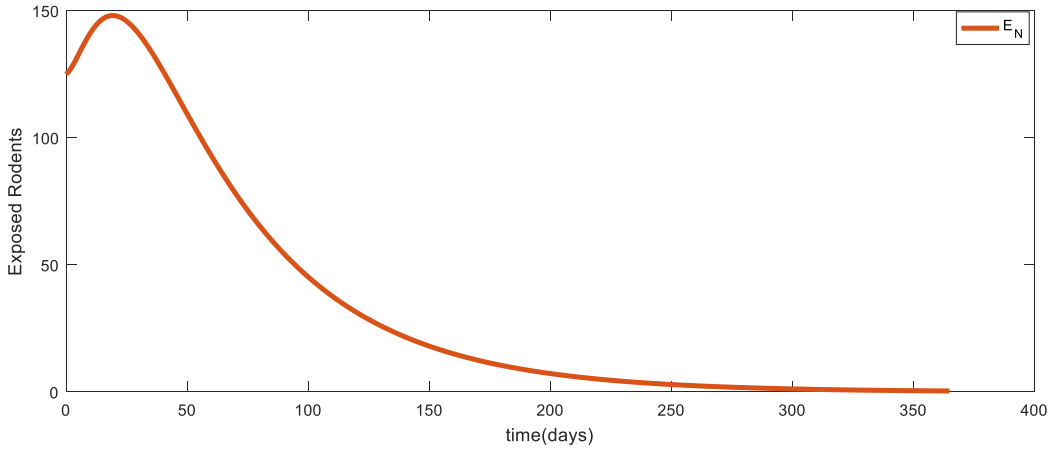
Table 2: Model Parameter Values

Parameter	Dimension	Value
Λ	$Days^{-1}$	50
b	$Days^{-1}$	500
μ	$Days^{-1}$	0.05
κ	$Days^{-1}$	0.01
d	$Days^{-1}$	0.02
ϕ	$Days^{-1}$	0.02
ν	$Days^{-1}$	0.03
ρ	$Days^{-1}$	0.2
ε	$Days^{-1}$	0.05
ω	$Days^{-1}$	0.2
γ	$Days^{-1}$	0.8
δ	$Days^{-1}$	0.9
β_{NN}	1	0.2
β_{NH}	1	0.00001
β_{HH}	1	0.00002

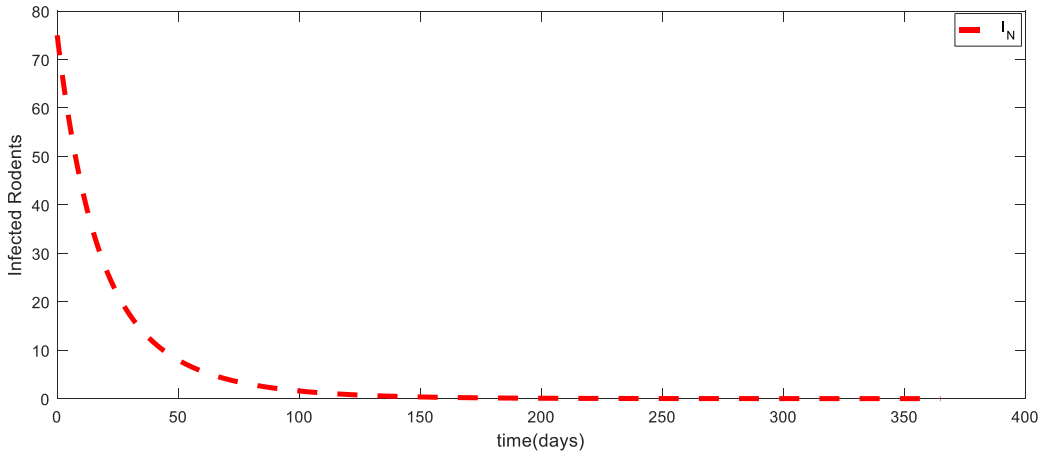
(a)



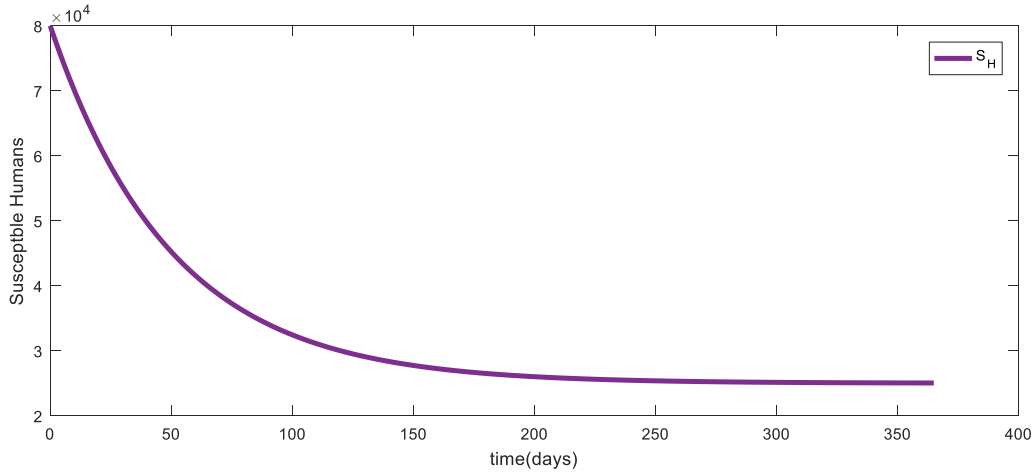
(b)


Exposed Rodents
time(days)
E_N
0
50
100
150
200
250
300
350
400

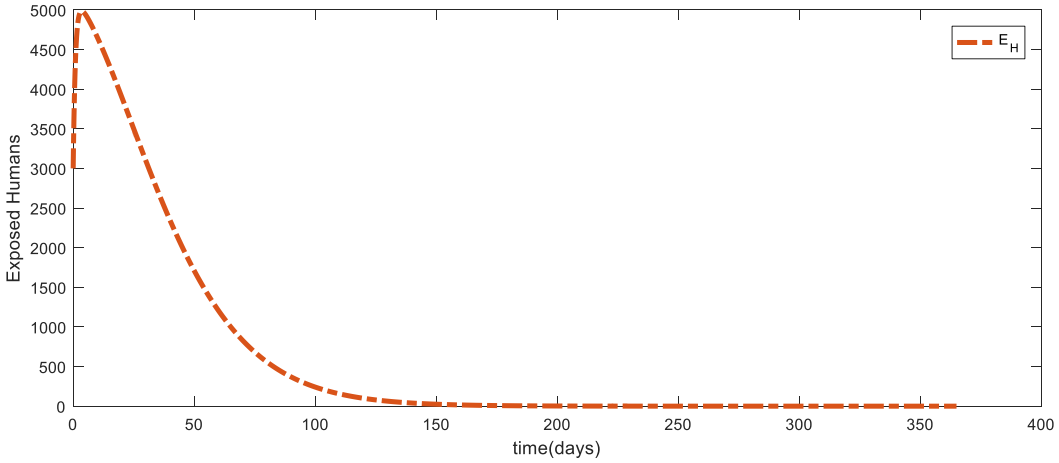
(c)


Infected Rodents
time(days)
I_N
0
10
20
30
40
50
60
70
80
0
50
100
150
200
250
300
350
400

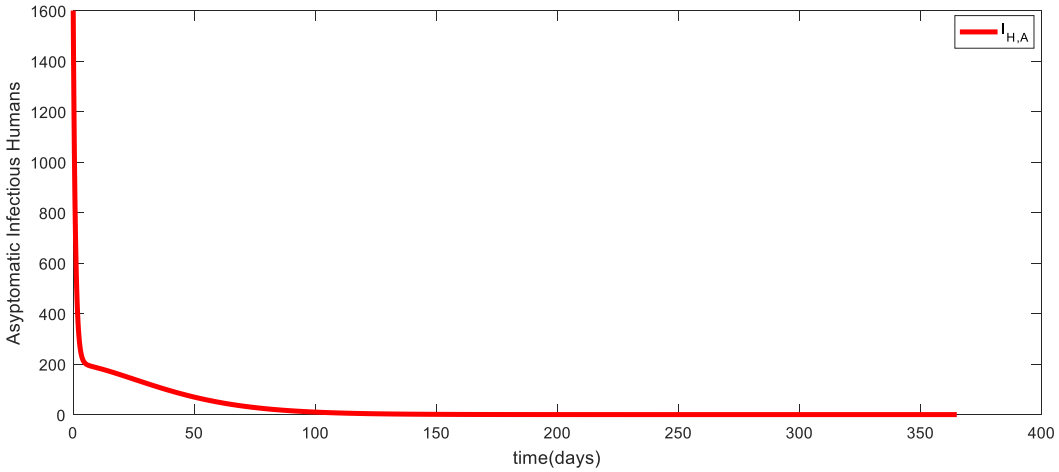
(d)


×10^4
Susceptble Humans
time(days)
S_H
2
3
4
5
6
7
8
0
50
100
150
200
250
300
350
400

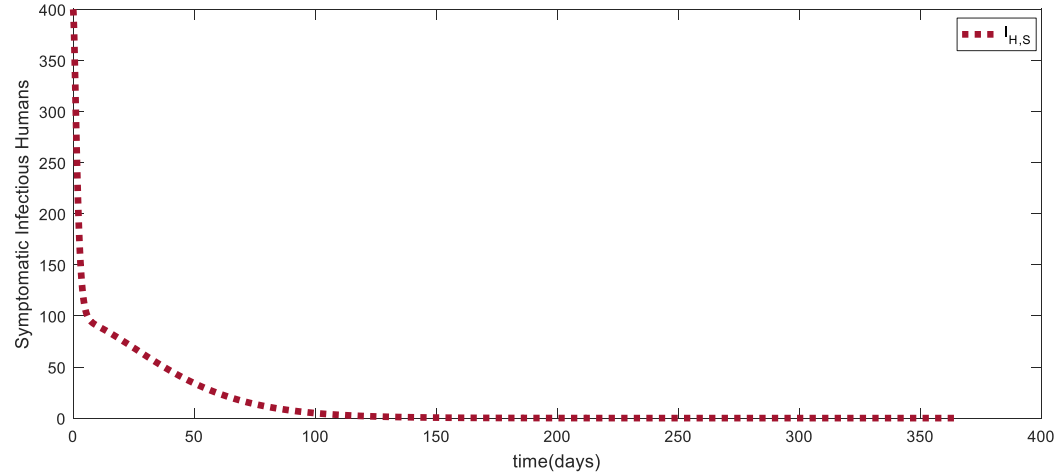
(e)


Exposed Humans
time(days)
E_H
0
500
1000
1500
2000
2500
3000
3500
4000
4500
5000
0
50
100
150
200
250
300
350
400

(f)


Asyptomatic Infectious Humans
time(days)
I_H,A
0
200
400
600
800
1000
1200
1400
1600
0
50
100
150
200
250
300
350
400

(g)


Symptomatic Infectious Humans
time(days)
I_H,S
0
50
100
150
200
250
300
350
400
0
50
100
150
200
250
300
350
400

(h)

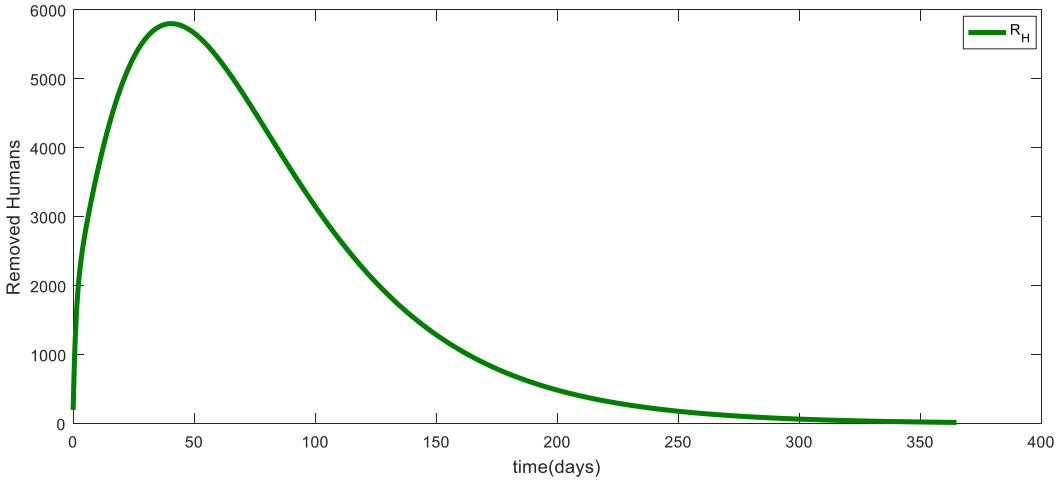


Figure 2: Results of Simulations with Parameter Values on Table 2, where $R_{0,N} = 0.1111$, $R_{0,NH} = 5.6022\times10^{-6}$, $R_{0,H1} = 1.1204\times10^{-5}$, $R_{0,H2} = 5.4234\times10^{-6}$, $R_{0,H3} = 3.0395\times10^{-6}$ and $R_{0,H} = 1.6627\times10^{-5}$.

4.2.2 Sensitivity Analysis of Parameters in the Basic Reproduction Numbers

Sensitivity indices allow us to measure the relative change in a variable when a parameter changes (Adamu & Usman, 2018). The normalized forward sensitivity index of a variable to a parameter as defined in Adamu & Usman (2018)] and Chitnis Hyman & Cushing (2008) is the ratio of the relative change in the variable to the relative change in the parameter. When the variable is a differentiable function of the parameter, the sensitivity index may be alternatively defined using partial derivatives from the following:

Definition: *The normalized forward sensitivity index of a variable* τ *that depends, differentiably, on a parameter* p *, is defined as*

$$\Upsilon_p^{\tau} = \frac{\partial \tau}{\partial p} \times \frac{p}{\tau} \qquad (40)$$

We used the parameter values in Table 1 for the sensitivity analysis of parameters in the reproduction numbers. The results of the analysis indicates that, indices with positive signs increases the value of R_0 when the corresponding parameters are increased and indices with negative signs decreases the value of R_0 with increase in the corresponding parameters, while zero indices indicates that R_0 is not dependent on the corresponding parameter. The sensitivity indices of the parameters are presented in Table 3.

Table 3: Table of Sensitivity Indices of Parameters in the Basic Reproduction Numbers

	$R_{0,N}$	$R_{0,NH}$	$R_{0,H1}$	$R_{0,H2}$	$R_{0,H3}$	$R_{0,H}$
μ	–1.300	0.000	0.000	0.000	0.000	0.000
κ	–0.325	0.000	0.000	0.000	0.000	0.000
d	0.000	–0.427	–0.427	–0.898	–0.425	–1.325
ϕ	0.000	0.000	0.000	–0.425	–0.013	–0.425
ν	+0.625	0.000	0.000	0.000	0.000	0.000
ρ	0.000	–0.250	–0.250	+0.935	+1.000	+0.685
ε	0.000	+0.400	+0.400	+0.400	+0.400	+0.800
ω	0.000	–0.014	–0.014	+0.051	0.000	+0.037
γ	0.000	–0.959	–0.959	–0.050	0.000	–1.009
δ	0.000	0.000	0.000	–0.963	–0.963	–0.963
β_{NN}	+1.000	0.000	0.000	0.000	0.000	0.000
β_{NH}	0.000	+1.000	0.000	0.000	0.000	0.000
β_{HH}	0.000	0.000	+1.000	+1.000	+1.000	+2.000

5.0 Discussions

In this paper, we have developed a mathematical model for the transmission dynamics of the Lassa fever infection. In developing the model, we divided the hosts population into animal reservoirs and humans coexisting together. We assumed that the animals do not recover once infected. We further divided the infectious human population into two; symptomatic and asymptomatic infectious due to an identified increase in the asymptomatic human infectious cases in the dynamics of the disease, and assumed that both symptomatic and asymptomatic humans are equally infectious. We have carried out analytic and qualitative analysis of the developed model. The analytic model analysis established a unique disease-free equilibrium that is locally and globally asymptotically stable for all values of R_0 less than 1 and unstable for all values R_0 greater than 1. The numerical simulations results in Figure 1 presented the natural dynamics of the Lassa fever infection which suggested that, once the disease is introduced into the animal host, it persisted and becomes endemic in the population. This can be seen from the graphs in Figure 1 (b) and (c) which shows the exposed and infected rodents subpopulations growing exponentially. The graphs in Figure 1 (e), (f) and (g) indicates that there is exponential increase in human infections which subsided naturally with time, but the disease do not die out of the human population. This can be linked to the fact that, the disease is endemic in the rodent's population and if human contacts with the animals is not prevented, the infection will keep spreading in the human population over time. The results of the numerical simulations in Figure 2 indicated that, with improved recovery rates in the human population, prevented rodent-human transmission and control on population of the rodents, the Lassa fever virus will be wiped out of the host populations over time. This assertions can be deducted from the sensitivity analysis results in Table 3. The sensitivity indices of the recovery rates γ and δ for the asymptomatic and symptomatic humans are both negative in all the basic reproduction numbers of the human population. While the sensitivity indices of the natural mortality rate μ and the hunting rate κ in the rodent's population are negative for the animal reservoir's reproduction number $R_{0,N}$. The results of the sensitivity analysis in Table 3 indicates that, indices with positive signs increases the value of R_0 when the corresponding parameters are increased and indices with negative signs decreases the value of R_0 with increase in the corresponding parameters, while zero index

indicates that R_0 is not dependent on the corresponding parameter. Signs of the sensitivity indices of some parameters in R_0 keeps alternating across the reproduction numbers of the humans. As seen in the sensitivity analysis table, the sensitivity index of the parameter ω is negative in $R_{0,NH}$ and $R_{0,H1}$, but positive in $R_{0,H2}$ and $R_{0,H}$. This can be explained as; thus, the presence of the parameter ω in the asymptomatic infectious human compartment $I_{H,A}$ causes transfer of individuals out of the compartment and as such, any reproduction number associated with that compartment will decrease with corresponding increase in the parameter ω. While the presence of the parameter ω in the symptomatic infectious human compartment $I_{H,S}$ brings in new infectious terms into the compartment and as such, any reproduction number associated with that compartment will increase with corresponding decrease in the parameter ω. The same can be said about the sensitivity index of the parameter ρ.

6.0 Conclusion

We studied analytic and qualitative behavior of a mathematical model for the transmission dynamics of the Lassa fever virus infection in this paper. Results of the analytic analysis indicated that, the disease-free equilibrium of the model is both locally and globally asymptotically stable if the reproduction number of the model is less than 1 and unstable if it is greater than 1. Qualitative analysis of the model revealed that, the disease becomes endemic in the rodents population and also do not die out of the human population over time without controlling the growth of the rodents population, preventing animal-human transmissions and improvement on the recovery rates of the humans. The results of our analysis indicated that, the reproduction numbers in the humans are most sensitive to the transmission rates, recovery rates and the natural mortality rates of the humans, while the reproduction number in the rodents is most sensitive to the transmission rate, hunting/predation rate and the natural mortality rate of the rodents. Numerical experiments of the model shows that if this parameters are controlled, the disease will be wiped out of the hosts populations over time.

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