https://dx.doi.org/10.4314/dujopas.v9i4b.33
ISSN (Print): 2476-8316
ISSN (Online): 2635-3490
Dutse Journal of Pure and Applied Sciences (DUJOPAS), *Vol. 9 No. 4b December 2023*

Mathematical Modelling of The Transmission Dynamics and Control of Lassa Fever by Incorporating Isolation and Recovered with Complications Compartments

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Abstract

In this paper, a mathematical model on the transmission dynamics and control of Lassa fever was developed and analyzed. We considered two interacting populations of humans and rodents. The human population is divided into six compartments including the compartment of individuals that recovered with complications. And the rodent population is partitioned into three compartments. Existence of disease-free and endemic equilibriums was established. Using the next generation operator approach we find the effective reproduction number R_h *and* R_r *which signifies local asymptotic stability of the disease-free equilibrium whenever* R_h *and* R_r *is less than unity. Using Lyapunov theorem we further established the global asymptotical stability of the disease free equilibrium whenever* $R_h \leq 1$ *and* $R_r \leq 1$. *The paper has shown the possibility of a disease free equilibrium which can be globally stable.*

Keywords: Lassa fever, rodents, virus, isolation, complications, recovered.

INTRODUCTION

Lassa Fever is an acute Viral Hemorrhagic Fever (VHF) first isolated in Lassa town in the Yedseran river valley in the present Borno State of Northern Nigeria in 1969 (Tara, 2004). Since its initial discovery in Lassa – Nigeria, rural and Nosocomial outbreaks of Lassa fever have occurred repeatedly on other parts of Nigeria: Jos, Onisha, Zonkwa, Ekpoma (Tomori, *et al.* 1998). In 1969. An American missionary nurse named Laura Wine Came down with a troubling fever while working in the Nigeria town of Lassa. The local doctor thought it was probably malaria but Wine didn't respond to the usual treatments. She eventually died. Shortly after, two more nurses contacted the same mysterious disease. One also died. The other, Lily Pinneo, was evacuated to Columbia-Presbyterian hospital, and survived. From her blood, and that of her colleagues, scientists isolated a new virus, which they named after the town where the infection began. Since then, scientists have learned a lot about Lassa fever, and the virus that causes it. They discovered that it resides within the Multimammate mouse and jumps into people who eat food contaminated by the rodent's waste. They have shown that it is common in West Africa and causes many thousands of cases every year. (CDC, 2004). Promed, (2006) reported outbreaks in some cities of West African countries of Sierra leone, Liberia, Guinea, Cote d'ivoire, Ghana, Togo and Benin, no outbreak has ever been recorded

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in the United Kingdom, though isolated cases show evidence of viral circulation (Gunther *et al.* 2001). Many of those infected by Lassa fever virus do not develop symptoms. When symptoms occur they usually include fever, weakness, headaches, vomiting and muscle pains. Less commonly there may be bleeding from the mouth or gastrointestinal tract. The risk of death once infected is about one percent and frequently occurs within two weeks of the onset of symptoms. Among those who survive, about a quarter have hearing loss, which improves over time in about half (WHO 2016).

A total of 2787 confirmed cases and 516 deaths were reported in Nigeria from December, 2016 to September, 2020. Increase in number of cases and deaths were observed with 298, 528, 796 and 1165 confirmed cases and 79, 125, 158 and 158 deaths in 2017, 2018, 2019 and 2020 respectively. Over 60% of the cases were reported in two states, Edo and Ondo states. The lassa fever cases spread from 19 states in 2017 to 32 states and Federal Capital Territory (FCT) in 2020. Ondo state (25.39%) had the highest of death rate from lassa fever over the four years. (CDC, 2020). Lassa fever is endemic in Nigeria, Liberia, Sierra leone, Guinea and other West African Countries, affecting about 2-3 million persons with 5,000 – 10,000 fatalities annually (McCormick *et al.* 1987).

Despite various research works and the availability of various control strategies put in place by both the Government and other health organizations, the morbidity and mortality of the killer disease continue to increase globally. In the absence or limited access to pharmaceutical intervention such as vaccines and treatment, isolation remains one of the best choice of control strategy to reduce the transmission rate of infectious disease (WHO 2007). The effect of acquiring immunity, be it permanent or temporal have been of great interest to researches, aimed at gaining better insight into the complex transmission dynamics of infectious disease (li *et al.* 1999; Moghadas and Gumel, 2003; El-Doma, 2006; Kimbir, 2004).

MATERIALS

Bawa *et al.,* (2013), developed a mathematical model for lassa fever with five different compartments of susceptible humans S_h, infected humans I_h, infant reservoirs I_R, adult reservoirs A_R and lassa in the environment V. They obtained the basic reproduction number R_0 which can be used to control the transmission dynamics of the disease and established the conditions for local and global stability of the disease free equilibrium. Vital dynamics, standard incidence, disease induced death and infection due to humans, reservoirs and aerosol transmission were incorporated. The analysis reveals that the disease can be control if the R_0 is less than one regardless of the initial population profile. Thus, every effort must be put in place by all concerned to prevent the virus infection by reducing R_0 strictly less than

unity. The model equations are given below

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= b_H N_H - \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N}\right) S_H + \gamma I_H - \mu_H S_H \\
\frac{dI_H}{dt} &= \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N}\right) S_H - \left(\gamma + \mu_H + \delta_H\right) I_H \\
\frac{dI_R}{dt} &= b_R A_R - \left(\sigma + \mu_R + \delta_R\right) I_R \\
\frac{dA_R}{dt} &= \sigma I_R - \left(\mu_R + \delta_R\right) A_R \\
\frac{dV}{dt} &= e_H I_H + e_R A_R - \phi V
\end{aligned}\right\}$$

James *et al.,* (2015a) partitioned the human population into the susceptible class $S(t)$ and the infected class $I(t)$. Then the virus carrier (reservoir) population $R(t)$. The result of the model analysis showed that the zero equilibrium state of the model equation will be stable when the birth rate of the human population is less than the death rate i.e $\beta_1 < \mu_1$ and same when the birth rate of the vector is less than the total death rate i.e $\beta_1 < \mu_1 + \delta_2$. The model equations are given be

$$\left.\begin{aligned}
\frac{ds(t)}{dt} &= \beta_1 - \mu_1 S - \left(\alpha_1 I + \alpha_2 R\right) S + \left(\gamma + \left(1-\theta\right)\beta_1\right) I \\
\frac{dI(t)}{dt} &= \left(\alpha_1 I + \alpha_2 R\right) S - \left(\mu_1 + \delta_1 + \gamma\right) I + \theta\beta_1 I \\
\frac{dR(t)}{dt} &= \left(\beta_2 - \mu_2 - \delta_2\right) R
\end{aligned}\right\}$$

Faniran, (2017), A model with incidence of dynamics of lassa fever within human hosts and rodents vector is proposed in which the non-drug compliance rate is incorporated into the system, which is the rate at which infectious human hosts do not comply with drugs. Model analyses were carried out. Disease free and endemic equilibrium solution were obtained and their stability was analyzed. It was established that for the basic reproduction number, $R_0 < 1$, the disease free equilibrium solution is globally asymptotically stable so that the disease always dies out and if $R_0 > 1$, the disease free equilibrium is unstable. He observes that in order to reduce the basic reproduction number less than one, intervention strategies need to be focused on treatment and reduction on the contact between rodent vector and human host. Since the non-drug compliance rate of infectious human hosts causes reappearance of symptoms after a system free period, there is need to increase the parameter r_c which reduces the number of infectious human hosts who do not comply with drugs. There is also need for

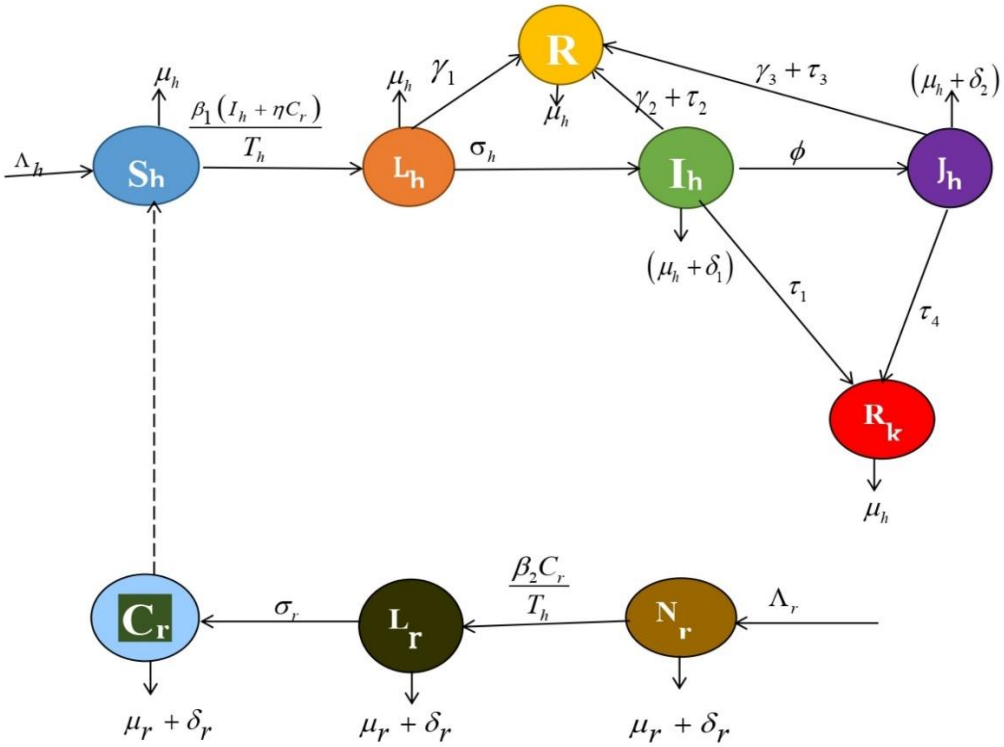
isolation of the infectious human hosts in order to reduce the spread of lassa fever. The model equations are;

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H - \frac{\alpha_1\alpha_2 S_H I_R}{N_H} + \gamma R_H + \tau_{nc} I_H - \mu_H S_H \\
\frac{dI_H}{dt} &= \frac{\alpha_1\alpha_2 S_H I_R}{N_H} - \tau_c I_H - r_c I_H - \tau_{nc} I_H - \delta I_H - \mu_H I_H \\
\frac{R_H}{dt} &= \tau_c I_H + r_c I_H - \gamma R_H - \mu_H R_H \\
\frac{dS_R}{dt} &= \Lambda_R - \frac{\alpha_1\alpha_3 S_R I_H}{N_H} - \mu_R I_R \\
\frac{dI_R}{dt} &= \frac{\alpha_1\alpha_3 S_R I_H}{N_H} - \mu_R I_R
\end{aligned}\right\}$$

This paper aimed at extending the work of Faniran (2017) by considering a model on the transmission dynamics of Lassa fever by incorporating isolation and recovered with complications compartment using all the model analysis tools described in the aforementioned authors.

METHODOLOGY

MODEL



The corresponding mathematical equations of the schematic diagram can be described by a system of ordinary differential equations given below.

MODEL EQUATIONS

$$\frac{dS_h}{dt} = \Lambda_h - \frac{\beta_1\left(I_h + \eta C_r\right)}{T_h} S_h - \mu_h S_h \tag{1}$$

$$\frac{dL_h}{dt} = \frac{\beta_1\left(I_h + \eta C_r\right)}{T_h} S_h - \left(\sigma_h + \gamma_1 + \mu_h\right) L_h \tag{2}$$

$$\frac{dI_h}{dt} = \sigma_h L_h - \left(\phi + \gamma_2 + \tau_1 + \tau_2 + \mu_h + \delta_1\right) I_h \tag{3}$$

$$\frac{dJ_h}{dt} = \phi I_h - \left(\tau_3 + \tau_4 + \gamma_3 + \mu_h + \delta_2\right) J_h \tag{4}$$

$$\frac{dR_k}{dt} = \tau_1 I_h + \tau_4 J_h - \mu_h R_k \tag{5}$$

$$\frac{dR}{dt} = \gamma_1 L_h + \left(\gamma_2 + \tau_2\right) I_h + \left(\gamma_3 + \tau_3\right) J_h - \mu_h R \tag{6}$$

$$\frac{dN_r}{dt} = \Lambda_r - \frac{\beta_2 C_r}{T_h} N_r - \left(\mu_r + \delta_r\right) N_r \tag{7}$$

$$\frac{dL_r}{dt} = \frac{\beta_2 C_r}{T_h} N_r - \left(\sigma_r + \mu_r + \delta_r\right) L_r \tag{8}$$

$$\frac{dC_r}{dt} = \sigma_r L_r - \left(\mu_r + \delta_r\right) C_r \tag{9}$$

Where

$$T_h = S_h + L_h + I_h + J_h + R_k + R \tag{10}$$

$$T_r = N_r + L_r + C_r \tag{11}$$

The following assumptions are taken into account in the construction of the model:

(i) There is homogeneous mixing of the population, where all people are equally likely to be infected by the infectious individuals in case of contact.

(ii) The natural recovery of the infectious individuals largely depends on the strongness of the immune system.

(iii) Government provides centre where individuals with lassa fever symptoms are isolated and treatment is administered to them.

$$\lambda_h = \frac{\beta_1\left(I_h + \eta C_r\right)}{T_h} \tag{12}$$

$$\lambda_r = \frac{\beta_2 C_r}{T_r} \tag{13}$$

$k_1 = \left(\sigma_h + \gamma_1 + \mu_h\right),\ k_2 = \left(\phi + \gamma_2 + \tau_1 + \tau_2 + \mu_h + \delta_1\right),\ k_3 = \left(\tau_3 + \tau_4 + \gamma_3 + \mu_h + \delta_2\right)$

$k_4 = \left(\gamma_2 + \tau_2\right),\ k_5 = \left(\gamma_3 + \tau_3\right),\ k_6 = \left(\mu_r + \delta_r\right),\ k_7 = \left(\sigma_r + \mu_r + \delta_r\right)$

Hence equations (1) - (9) becomes

$$\frac{dS_h}{dt} = \Lambda_h - \lambda_h S_h - \mu_h S_h \tag{14}$$

$$\frac{dL_h}{dt} = \lambda_h S_h - k_1 L_h \tag{15}$$

$$\frac{dI_h}{dt} = \sigma_h L_h - k_2 I_h \tag{16}$$

$$\frac{dJ_h}{dt} = \phi I_h - k_3 J_h \tag{17}$$

$$\frac{dR_k}{dt} = \tau_1 I_h + \tau_4 J_h - \mu_h R_k \tag{18}$$

$$\frac{dR}{dt} = \gamma_1 L_h + k_4 I_h + k_5 J_h - \mu_h R \tag{19}$$

$$\frac{dN_r}{dt} = \Lambda_r - \lambda_r N_r - k_6 N_r \tag{20}$$

$$\frac{dL_r}{dt} = \lambda_r N_r - k_7 L_r \tag{21}$$

$$\frac{dC_r}{dt} = \sigma_r L_r - k_6 C_r \tag{22}$$

Now, the human total population size $T_h(t)$ can be determine from the differential equation

$$\frac{dT_h}{dt} = \Lambda_h - \mu_h T_h - \delta_1 I_h - \delta_2 J_h \tag{23}$$

And also, the total rodents population size $T_r(t)$ is written as

$$\frac{dT_r}{dt} = \Lambda_r - \mu_r T_r \tag{24}$$

Boundedness of Solution

Consider the region

$$D_1 = \left(S_h \geq 0 \quad L_h \geq 0 \quad I_h \geq 0 \quad J_h \geq 0 \quad R_k \geq 0 \quad R \geq 0 \quad N_r \geq 0 \quad L_r \geq 0 \quad C_r \geq 0\right) \tag{25}$$

It can be shown that the set D_1 is positively invariant and a global attractor of all positive solutions of the system (1)- (9)

Lemma 1: The region D_1 is positively invariant for the system (1) - (9)

Proof: The rate of change of the total human population is given as

$$\frac{dT_h}{dt} = \frac{dS_h}{dt} + \frac{dL_h}{dt} + \frac{dI_h}{dt} + \frac{dJ_h}{dt} + \frac{dR_k}{dt} + \frac{dR}{dt} \tag{26}$$

$$\frac{dT_h}{dt} = \Lambda_h - \mu_h T_h - \delta_1 I_h - \delta_2 J_h \tag{27}$$

By standard comparison theorem,

$$\frac{dT_h}{dt} + \mu_h T_h \leq \Lambda_h e^{\mu_h t} \tag{28}$$

Solving (28) using the integrating factor method

$$\frac{dT_h}{dt} e^{\mu_h t} + \mu_h T_h e^{\mu_h t} \leq \Lambda_h e^{\mu_h t} \tag{29}$$

$$\int \left(T_h e^{\mu_h t}\right) \leq \int \left(\Lambda_h e^{\mu_h t} dt\right) \tag{30}$$

$$T_h = T_h(0) e^{-\mu_h t} + \frac{\Lambda_h}{\mu_h}\left(1 - e^{-\mu_h t}\right) \tag{31}$$

And the rate of change for the rodents population

$$\frac{dT_r}{dt} = \frac{dN_r}{dt} + \frac{dL_r}{dt} + \frac{dC_r}{dt} = \Lambda_r - \mu_r T_r \tag{32}$$

By Standard comparison theorem,

$$\frac{dT_r}{dt} + \mu_r T_r \leq \Lambda_r e^{\mu_r t} \tag{33}$$

Solving (33) using the integrating factor method

$$\frac{dT_r}{dt} e^{\mu_r t} + \mu_r T_r e^{\mu_r t} \leq \Lambda_r e^{\mu_r t} \tag{34}$$

$$\int d\left(T_r e^{\mu_r t}\right) \leq \int \left(\Lambda_r e^{\mu_r t} dt\right) \tag{35}$$

$$T_r = T_r(0) e^{-\mu_r t} + \frac{\Lambda_r}{\mu_r}\left(1 - e^{-\mu_r t}\right) \tag{36}$$

$$\text{If } \textit{If } T_r(0) \leq \frac{\Lambda_r}{\mu_r} \textit{ then } T_r \leq \frac{\Lambda_r}{\mu_r}$$

So, D_1 is a positively invariant set under the flow described in (1) - (9)

Hence, no solution path leaves through and boundary of D_1. Also, since solution path cannot leave D_1, solutions remain non-negative for non-negative initial conditions. Solutions exist for all time t. In this region, the model (1) - (9) is said to be well posed mathematically and epidemiologically.

Existence of Equilibria, E^*

At equilibrium state the rate of change of each variable is equal to zero. i.e

$$\frac{dS_h}{dt} = \frac{dL_h}{dt} = \frac{dI_h}{dt} = \frac{dJ_h}{dt} = \frac{dR_k}{dt} = \frac{dR}{dt} = \frac{dN_r}{dt} = \frac{dL_r}{dt} = \frac{dC_r}{dt} = 0 \tag{37}$$

Thus, the model equations become

$$\Lambda_h - \lambda_h^* S_h^* - \mu_h S_h^* = 0 \tag{38}$$

$$\lambda_h^* S_h^* - k_1 L_h^* = 0 \tag{39}$$

$$\sigma_h L_h^* - k_2 I_h^* = 0 \tag{40}$$

$$\phi I_h^* - k_3 J_h^* = 0 \tag{41}$$

$$\tau_1 I_h + \tau_4 J_h - \mu_h R_k = 0 \tag{42}$$

$$\gamma_1 L_h^* + k_4 I_h^* + k_5 J_h^* - \mu_h R^* = 0 \tag{43}$$

$$\Lambda_r - \lambda_r^* N_r^* - k_6 N_r^* = 0 \tag{44}$$

$$\lambda_r^* N_r^* - k_7 L_r^* = 0 \tag{45}$$

$$\sigma_r L_r^* - k_6 C_r^* = 0 \tag{46}$$

From (38) to (46)

$$S_h^* = \frac{\Lambda_h}{\left(\lambda_h^* + \mu_h\right)},\ L_h^* = \frac{\Lambda_h \lambda_h^*}{k_1\left(\lambda_h^* + \mu_h\right)},\ I_h^* = \frac{\Lambda_h \sigma_h \lambda_h^*}{k_1 k_2\left(\lambda_h^* + \mu_h\right)},\ J_h^* = \frac{\Lambda_h \sigma_h \phi \lambda_h^*}{k_1 k_2 k_3\left(\lambda_h^* + \mu_h\right)}$$

$$R_k^* = \frac{\Lambda_h \sigma_h \tau_1 k_3 \lambda_h^* + \Lambda_h \sigma_h \tau_4 \phi \lambda_h^*}{k_1 k_2 k_3\left(\lambda_h^* + \mu_h\right)\mu_h},\ R^* = \frac{\Lambda_h \gamma_1 k_2 k_3 \lambda_h^* + \Lambda_h \sigma_h k_3 k_4 \lambda_h^* + \Lambda_h \sigma_h \phi k_5 \lambda_h^*}{k_1 k_2 k_3 \mu_h\left(\lambda_h^* + \mu_h\right)},$$

$$N_r^* = \frac{\Lambda_r}{\left(\lambda_r^* + k_6\right)},\ L_r^* = \frac{\Lambda_r \lambda_r^*}{k_7\left(\lambda_r^* + k_6\right)},\ C_r^* = \frac{\Lambda_r \sigma_r \lambda_r^*}{k_6 k_7\left(\lambda_r^* + k_6\right)} \tag{47}$$

For λ_r^*

From (13)

$$\lambda_r^* = \frac{\beta_2 C_r}{T_h}$$

$$\lambda_r^*\left(k_6k_7T_h^*\lambda_r^* + k_6k_6k_7T_h^*\left[1-\frac{\beta_2\Lambda_r\sigma_r}{k_6k_6k_7T_h^*}\right]\right)=0 \tag{48}$$

This implies that,

$$\lambda_r^*=0 \quad or \quad k_6k_7T_h^*\lambda_r^* + k_6k_6k_7T_h^*\left[1-\frac{\beta_2\Lambda_r\sigma_r}{k_6k_6k_7T_h^*}\right]=0 \tag{49}$$

Solving the above

$$\lambda_r^* = k_6\left[\frac{\beta_2\Lambda_r\sigma_r}{k_6k_6k_7T_h^*}-1\right] \tag{50}$$

For λ_h

From (12)

$$\lambda_h = \frac{\beta_1\left(I_h+\eta C_r\right)}{T_h}$$

After Substituting, we have

$$\lambda_h^* = \frac{\beta_1\left(\frac{\Lambda_h\sigma_h\lambda_h^*}{k_1k_2\left(\lambda_h^*+\mu_h\right)}+\frac{\Lambda_r\sigma_r\eta\lambda_r^*}{k_6k_7\left(\lambda_r^*+k_6\right)}\right)}{T_h} \tag{51}$$

Substituting $\lambda_r^*=0$ in (51) we've

$$\lambda_h^* = \frac{\beta_1\left(\frac{\Lambda_h\sigma_h\lambda_h^*}{k_1k_2\left(\lambda_h^*+\mu_h\right)}\right)}{T_h} \tag{52}$$

$$\lambda_h^*\left(k_1k_2T_h\lambda_h^* + k_1k_2\mu_hT_h - \beta_1\Lambda_h\sigma_h\right)=0 \tag{53}$$

$$\text{Either } \lambda_h^*=0, \quad or \quad k_1k_2T_h\lambda_h^* + k_1k_2\mu_hT_h - \beta_1\Lambda_h\sigma_h=0 \tag{54}$$

$$\lambda_h^* = \mu_h\left[R_h-1\right] \tag{55}$$

Therefore, the four different equilibriums are given as

1) $\lambda_h^*=0$ *and* $\lambda_r^*=0$ (56)

2) $\lambda_h^* = \mu_h\left[\frac{\beta_1\Lambda_h\sigma_h}{k_1k_2\mu_hT_h}-1\right]$ *and* $\lambda_r^*=0$ (57)

3) $\lambda_h^*=0$ *and* $\lambda_r^* = k_6\left[\frac{\beta_2\Lambda_r\sigma_r}{k_6k_6k_7T_h^*}-1\right]$ (58)

$$\textbf{4)}\quad \lambda_h^{\,*} = \mu_h\left[\frac{\beta_1\Lambda_h\sigma_h}{k_1k_2\mu_hT_h}-1\right] \text{ and } \lambda_r^{\,*} = k_6\left[\frac{\beta_2\Lambda_r\sigma_r}{k_6k_6k_7T_h^{\,*}}-1\right] \tag{59}$$

3.4 Disease Free Equilibrium State (E^0)

At the disease free equilibrium state there is absence of infection. Thus, all the infected classes will be zero and the entire population will comprise of susceptible human and rodents.

Lemma 2: A diseases free equilibrium state of the model exists at the point.

$$\left(S_h \quad L_h \quad I_h \quad J_h \quad R_k \quad R \quad N_r \quad L_r \quad C_r\right) = \left(\frac{\Lambda_h}{\mu_h} \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad \frac{\Lambda_r}{k_6} \quad 0 \quad 0\right) \tag{60}$$

Proof: At the disease-free equilibrium state, let
Consider an arbitrary equilibrium, this gives

$$\Lambda_h - \mu_h S_h^{\,0} = 0 \tag{61}$$

$$\Lambda_r - k_6 N_r^{\,0} = 0 \tag{62}$$

$$L_h^{\,0} = I_h^{\,0} = J_h^{\,0} = L_r^{\,0} = C_r^{\,0} = 0 \tag{63}$$

From (61), gives

$$S_h^{\,0} = \frac{\Lambda_h}{\mu_h} \tag{64}$$

From (62), gives

$$N_r^{\,0} = \frac{\Lambda_r}{k_6} \tag{65}$$

Hence the Lemma is proved.

Basic reproduction number and Local stability of the disease free equilibrium

The basic reproduction number (denoted by R_0) is a measure of how transferable a disease is. It is the average number of people that a single infectious person will infect over the course of their infection. A better widely accepted and used method in finding R_0 that reflect its biological meaning is the next generation operator approach described by Diekmann and Heesterbeek (2000) and subsequently analysed by Van de Driessche and Watmough (2002).
Helen and Maria (2009) defined the effective reproduction number as the parameter that estimates the average number of secondary cases per infectious case in a population made up of both susceptible and non- susceptible hosts. It is obtained by taking the largest (dominant) eigen-value (spectral radius) of the next generation matrix (Driessche and Watmough, 2012).

$$R_0 = \left[\frac{\partial f_i\left(x_0\right)}{\partial\left(x_j\right)}\right]\left[\frac{\partial V_i\left(x_0\right)}{\partial x_i}\right]^{-1} \tag{66}$$

$$F=\begin{pmatrix}0 & \beta_1 & 0 & 0 & \beta_1\eta\\ 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & \beta_2\\ 0 & 0 & 0 & 0 & 0\end{pmatrix} \qquad V=\begin{pmatrix}k_1 & 0 & 0 & 0 & 0\\ -\sigma_h & k_2 & 0 & 0 & 0\\ 0 & -\phi & k_3 & 0 & 0\\ 0 & 0 & 0 & k_7 & 0\\ 0 & 0 & 0 & -\sigma_r & k_6\end{pmatrix} \tag{67}$$

In order to determine the matrix V^{-1}, we use the Gauss-Jordan elimination method as explained in Kreyszig (2005) and Stroud and Booth (2003).
The final computation gives

$$FV^{-1}=\begin{pmatrix}\frac{\beta_1\sigma_h}{k_1k_2} & \frac{\beta_1}{k_2} & 0 & \frac{\beta_1\eta\sigma_r}{k_6k_7} & 0 & \frac{\beta_1\eta}{k_6}\\ 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & \frac{\beta_2\sigma_r}{k_6k_7} & \frac{\beta_2}{k_6}\\ 0 & 0 & 0 & 0 & 0 & 0\end{pmatrix} \tag{68}$$

The spectral radius is given by

$$\rho\left(FV^{-1}\right)=\max\left\{\frac{\beta_1\sigma_h}{k_1k_2},\frac{\beta_2\sigma_r}{k_6k_7}\right\} \tag{69}$$

The following result is established using Van den Driessche & Watmough, 2002.

Theorem 1: The DFE of the system (1) - (9) is locally asymptotically stable if $R_h<1$ and $R_r<1$ and unstable if $R_h>1$ and $R_r>1$.

The value R_h is the humans effective reproduction number since there is the presence of control strategies and R_r is the rodents basic reproduction number.
The threshold quantity R_h is the humans effective or control reproduction number for the model (1) - (9). By Theorem 1, Lassa fever is eliminated from the human population when $R_h<1$ and rodents population when $R_r<1$ if the initial sizes of the populations of the model are in the region of attraction of D. However, the disease free equilibrium may not be globally asymptotically stable even if $R_h<1$ and $R_r<1$ in the case when a backward bifurcation occurs. That is, there is the presence of a stable EEP co-existing with the DFE.

Global stability of disease free equilibrium $\left(E^0\right)$

Global stability of equilibrium removes the restrictions on the initial conditions of the model variables. In global asymptotic stability, solutions approach the equilibrium for all initial conditions. There are many ways of proving the global stability of disease free equilibrium which include among others the Lyapunov theorem and the Castillo-Chavez, *et. al* (2002).

Theorem 2: The disease free equilibrium, E^0 of (1) - (9) is globally asymptotically stable (GAS) if $R_h\le1$ and $R_r\le1$ and Unstable if $R_h>1$ and $R_r>1$.

Proof: Constructing a linear lyapunov function to prove the GAS of the DFE when $R_h \leq 1$

We now select the infected classes to construct the lyapunov function:

$$V = P_1 L_h + P_2 I_h + P_3 J_h + P_4 L_r + P_5 C_r \tag{70}$$

For V to be a lyapunov function, the coefficients must be chosen such that $P_1 > 0, P_2 > 0, P_3 > 0, P_4 > 0$ and $P_5 > 0$

Take the time derivative of V and substitute the corresponding right hand side of (70) into the derivative of V. We then have

$$\dot{V} = P_1 \dot{L_h} + P_2 \dot{I_h} + P_3 \dot{J_h} + P_4 \dot{L_r} + P_5 \dot{C_r} \tag{71}$$

$$\dot{V} = P_1 \left(\frac{\beta_1 \left(I_h + \eta C_r \right)}{T_h} S_h - k_1 L_h \right) + P_2 \left(\sigma_h L_h - k_2 I_h \right) + P_3 \left(\phi I_h - k_3 J_h \right) + P_4 \left(\frac{\beta_2 C_r}{T_r} N_r - k_7 L_r \right) + P_5 \left(\sigma_r L_r - k_6 C_r \right) \tag{72}$$

$$\dot{V} \leq k_1 k_2 \left(\frac{\beta_1 \sigma_h}{T_h} S_h - 1 \right) I_h - k_3 J_h + k_6 k_7 C_r \left[\frac{\beta_2 \sigma_r C_r N_r}{k_6 k_7 T_r} - 1 \right] \tag{73}$$

Therefore,

$$\dot{V} \leq k_1 k_2 \left[R_h - 1 \right] I_h - k_3 J_h + k_6 k_7 C_r \left[R_r - 1 \right] \tag{74}$$

$\dot{V} \leq 0$ if $R_h \leq 1$ and $R_r \leq 1$, additionally $\dot{V} = 0$ if $I_h = 0$ and $C_r = 0$. Therefore, for $L_h = I_h = J_h = L_r = C_r = 0$, it shows that $S_h(t) \to \Lambda_h / \mu_h, and\ \Lambda_r / \mu_r$, as $t \to \infty$.

Hence the largest compact invariant set in $\left\{ \left(S_h, L_h, I_h, J_h, R_k, R, S_r, L_r, I_r \right) \in D_1 : \dot{V} \leq 0 \right\}$ is the singleton set E^0.Therefore from LaSalle's invariant principle, we conclude that E^0 is globally asymptotically stable in D_1 if $R_h \leq 1$ and $R_r \leq 1$.

3.7 Endemic Equilibrium Point (E^{**})

The endemic equilibrium state is the state in which the disease persists in both humans and rodents populations. That is the coordinates should satisfy the conditions:

$$E^{**}=\left\{\begin{pmatrix}S_h\\L_h\\I_h\\J_h\\R_k\\R\\N_r\\L_r\\C_r\end{pmatrix}\middle|\begin{array}{c}S_h\geq 0\\L_h\geq 0\\I_h\geq 0\\J_h\geq 0\\R_k\geq 0\\R\geq 0\\N_r\geq 0\\L_r\geq 0\\C_r\geq 0\\S_h+L_h+I_h+J_h+R_k+R\leq T_h, N_r+L_r+C_r\leq T_r\end{array}\right\} \quad (75)$$

Lemma 3: The endemic equilibrium state of the model (1) - (9) exist if the human control reproduction number, $R_h>1$ and rodents reproduction number, $R_r>1$.

Proof: At the endemic equilibrium point, let
Consider the system (38) - (46), gives

$$S_h^{**}=\frac{\Lambda_h}{\left(\lambda_h^{**}+\mu_h\right)},\ L_h^{**}=\frac{\Lambda_h\lambda_h^{**}}{k_1\left(\lambda_h^{**}+\mu_h\right)},\ I_h^{**}=\frac{\Lambda_h\sigma_h\lambda_h^{**}}{k_1k_2\left(\lambda_h^{**}+\mu_h\right)},$$

$$J_h^{**}=\frac{\Lambda_h\sigma_h\phi\lambda_h^{**}}{k_1k_2k_3\left(\lambda_h^{**}+\mu_h\right)},\ R_k^{**}=\frac{\Lambda_h\sigma_h\tau_1k_3\lambda_h^{**}+\Lambda_h\sigma_h\tau_4\phi\lambda_h^{**}}{k_1k_2k_3\left(\lambda_h^{**}+\mu_h\right)\mu_h},$$

$$R^{**}=\frac{\Lambda_h\gamma_1k_2k_3\lambda_h^{**}+\Lambda_h\sigma_hk_3k_4\lambda_h^{**}+\Lambda_h\sigma_h\phi k_5\lambda_h^{**}}{k_1k_2k_3\mu_h\left(\lambda_h^{**}+\mu_h\right)},\ N_r^{**}=\frac{\Lambda_r}{\left(\lambda_r^{**}+k_6\right)}$$

$$L_r^{**}=\frac{\Lambda_r\lambda_r^{**}}{k_7\left(\lambda_r^{**}+k_6\right)},\ C_r^{**}=\frac{\Lambda_r\sigma_r\lambda_r^{**}}{k_6k_7\left(\lambda_r^{**}+k_6\right)} \quad (76)$$

Now, as earlier proved for positivity of solutions, it is observed that λ_h^{**} cannot be negative but can be greater than or equal to zero. Thus, $\lambda_h^{**}=0$

Hence, a unique Lassa fever endemic equilibrium exist (i.e $\lambda_h^{**}>0$) when $R_0>1$.

Now at E^{**}, implies that

$$\lambda_h^{*}=\beta_1\left\{\frac{\Lambda_h\sigma_h\lambda_h^{*}}{k_1k_2\left(\lambda_h^{*}+\mu_h\right)}+\frac{\Lambda_r\sigma_r\lambda_r^{*}}{k_6k_7\left(\lambda_r^{*}+k_6\right)}\right\}\times\frac{1}{T_h} \quad (77)$$

By simplification

$$\left\{k_1k_2k_6k_6k_7T_h\left[R_r-1\right]+k_1k_2k_6k_6k_7T_h\right\}\lambda_h^{*2}-k_1k_2k_6k_6k_7\mu_hT_h\lambda_h^{*}\left[R_h-1\right]\left[R_r-1\right]$$
$$-k_1k_2k_6k_6k_7\mu_hT_h\lambda_h^{*}\left[R_h-1\right]-\Lambda_r\sigma_r\eta k_1k_2k_6\lambda_h^{*}\left[R_r-1\right]-\Lambda_r\sigma_r\eta k_1k_2k_6\mu_h\left[R_r-1\right]=0 \quad (78)$$

$$A\,\lambda_h^{*2} - B\,\lambda_h^{*} - C = 0 \quad (79)$$

Where

$$A = k_1k_2k_6k_6k_7T_h\left[R_r-1\right]+k_1k_2k_6k_6k_7T_h \quad (80)$$

$$B = k_1k_2k_6k_6k_7\mu_hT_h\left[R_h-1\right]\left[R_r-1\right]-k_1k_2k_6k_6k_7\mu_hT_h\left[R_h-1\right] \quad (81)$$

$$C = \Lambda_r\sigma_r\eta k_1k_2k_6\mu_h\left[R_r-1\right] \quad (82)$$

$$A\lambda_h^{**2}-B\lambda_h^{**}=0 \quad (83)$$

By factorization

$$\lambda_h^{**}\left(A\lambda_h^{**}-B\right)=0 \quad (84)$$

Either

$$\lambda_h^{**}=0 \quad or \quad \lambda_h^{**}=\frac{B}{A} \quad (85)$$

By substituting (80) and (81), we have

$$\lambda_h^{**}=\frac{k_1k_2k_6k_6k_7\mu_hT_h\left[R_h-1\right]\left[R_r-1\right]-k_1k_2k_6k_6k_7\mu_hT_h\left[R_h-1\right]}{k_1k_2k_6k_6k_7T_h\left[R_r-1\right]+k_1k_2k_6k_6k_7T_h} \quad (86)$$

$$\lambda_h^{**}=\mu_h\left[R_h-1\right] \quad (87)$$

Thus, (87) greater than unity if $R_h>1$ and $R_r>1$. Substituting into (38) - (46), gives an equilibrium state,

Hence, the endemic equilibrium state of model exist if $R_h>1$ and $R_r>1$

RESULTS AND DISCUSSION

Variables and Population Dependent Parameters Values

The model variables and population dependent parameters values usually have to be estimated base on Lassa Fever epidemiology and the demographic profile of the population concerned. Hypothetical values and Nigeria demographic values for variables and population dependent parameters of the model are set out in Table 4.1 Reasons for these values are explained in details except for hypothetical variables values which were assumed.

Table 4.1: Hypothetical, Nigeria (2019) Model Variables and population dependent parameters Values

S/N	Variable/ parameters	Nigeria Values
1	$S_h(t)$	202,713,887
2	$L_h(t)$	32,000
3	$I_h(t)$	16,000
4	$J_h(t)$	12,000
5	$R_k(t)$	20,000
6	$R(t)$	5,000
7	$S_r(t)$	10,946,000
8	$L_r(t)$	6,998,000
9	$I_r(t)$	4,000
10	$T_h(t)$	202,802,887
11	$T_r(t)$	11,000,000
12	μ_h	0.00005
13	μ_r	0.0009
14	Λ_h	10,140
15	Λ_r	3,666,300

Population Independent Parameters Value

Population independent parameters values usually have to be estimated based on the Lassa Fever epidemiology and published data. In table 4.2 parameter values are set out.

Table 4.2 The Values for Population independent parameters of the model

S/N	Parameter	Value	Unit	Source(s)
1.	β_1	0.5	-	Adewale et al. (2016)
2.	β_2	0.6	-	Adewale et al. (2016)
3.	δ_1, δ_2	0.01,0.15	Individuals/day	WHO (2017)
4.	δ_r	0.5	Rodents/day	Assumed
5.	γ_1	0.04	Individuals/day	Obasi and Mbah (2019)
6.	γ_2	0.006	Individuals/day	Obasi and Mbah (2019)
7.	γ_3	0.37	Individuals/day	Obasi and Mbah (2019)
8.	σ_h	0.048	Individuals/day	Adewale et al. (2016)
9.	σ_r	0.7	Rodents/day	Assumed
10.	τ_1	0.05	Individuals/day	Obasi and Mbah (2019)

11.	τ_2	0.01	Individuals/day	Obasi and Mbah (2019)
12.	τ_3	(0,1)	-	Control parameter
13.	η	0.16	-	Adewale et al. (2016)
14.	ϕ	(0,1)	-	Control parameter

Validation and Extension of Analytical Results by Numerical Method

Numerical methods of solutions for differential equations are of great importance to the engineers, epidemiologist and physicist because practical problems often lead to differential equations that cannot be solved exactly by straight forward analytical methods. Also, there are differential equations as for which the solutions in terms of formulas are so complicated that one prefers to apply a numerical method to such equations since numerical method have no such limitations. Numerical experiment is also performed to demonstrate the concordance of the numerical results with the theoretical results. That is, it confirms (validate), extend and illustrate the various theoretical (analytical) results obtained.

We used Maple software to obtain the numerical simulation of the model (1) to (9). Initial variables and parameters value are from Table 4.1 and 4.2. We then presented some numerical simulations to monitor the dynamics of the full model for various values and associate it with the effective basic reproduction number in order to confirm our analytical results on the global stability of the disease free equilibrium as well as show the global stability of the endemic equilibrium.

Global asymptotic stability of equilibrium

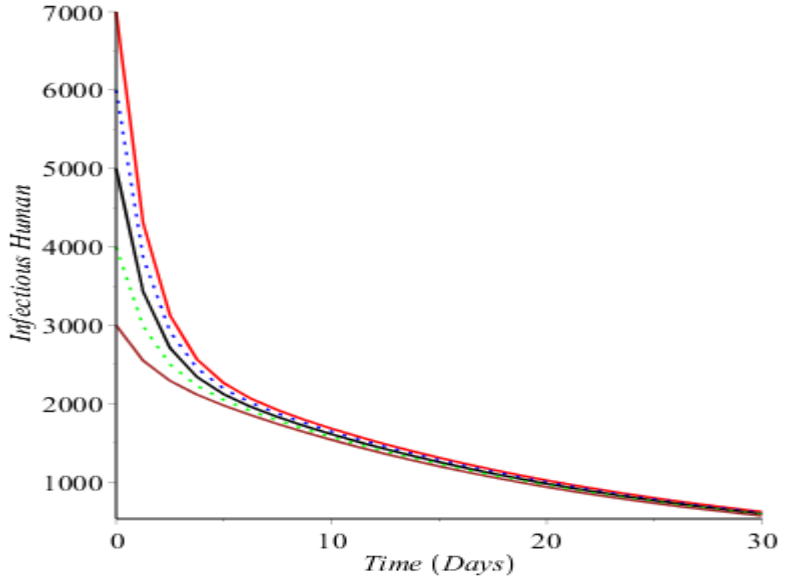


Fig. 4.1: Global asymptotic stability of the disease free equilibrium whenever $R_C < 1$, i.e $R_C = 0.4032 < 1$. The curves are plotted with $\beta_1 = 0.5, \delta_1 = 0.01$ and $\phi = 0.001$ and the remaining parameters are as in Table 4.2. With different initial condition of infectious humans, this clearly shows that the disease dies out in the human population irrespective of how large the initial infectious humans are introduced into the society as long as the control reproduction numbers are less than unity.

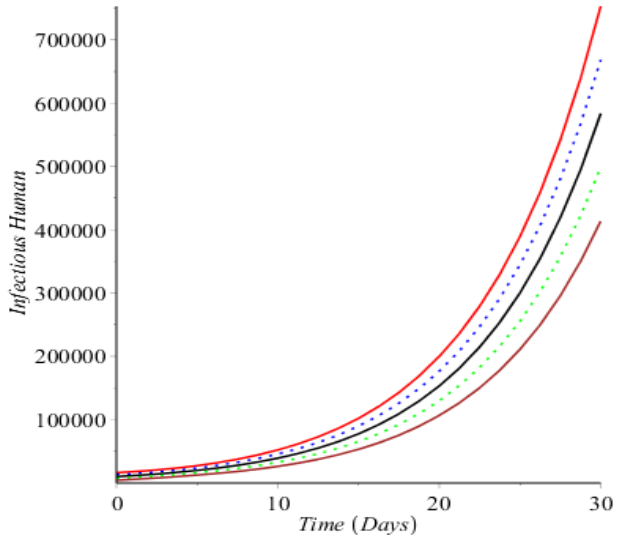


Fig. 4.2: The Global asymptotic stability of the endemic equilibrium point whenever $R_C > 1$ i.e $R_C = 1.6260 > 1$. The curves are plotted with $\beta_1 = 0.2$, $\delta_1 = 0.000003$ and $\phi = 0.001$ the remaining parameters are as in Table 4.2. With different initial condition of infectious humans, this indicates that the disease persists in the society irrespective of how small the initial infectious humans are introduced into the society as long as the effective reproduction numbers are greater than unity.

Global Asymptotic Stability of Equilibrium of Rodents Population

The Global asymptotic stability of the disease free equilibrium and endemic equilibrium of the model were analytically shown in Theorem 2 and 5 respectively. Also, they are numerically supported by Fig. 4.3 and 4.4

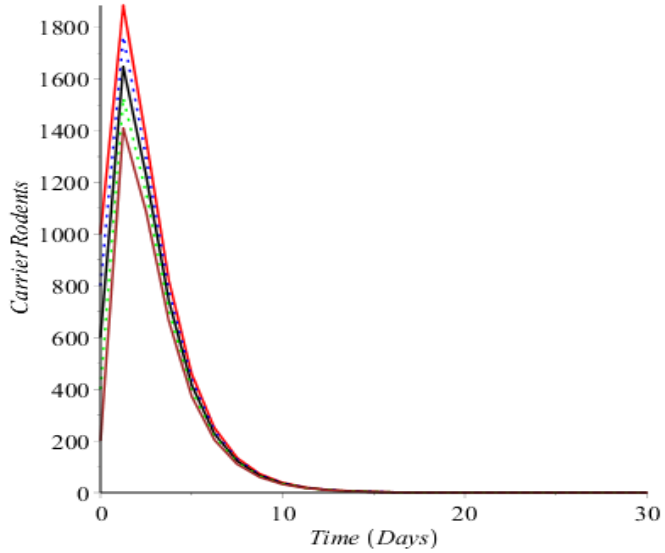


Fig. 4.3: Global asymptotic stability of the disease free equilibrium whenever $R_C < 1$, i.e $R_C = 0.62376 < 1$. The curves are plotted with $\beta_1 = 0.5$, $\delta_1 = 0.01$ and $\phi = 0.6$ and the remaining parameters are as in Table 4.2. With different initial condition of carrier rodents, this clearly shows that the disease dies out in the human population irrespective of how large the initial carrier rodents are introduced into the society as long as the control reproduction numbers are less than unity.

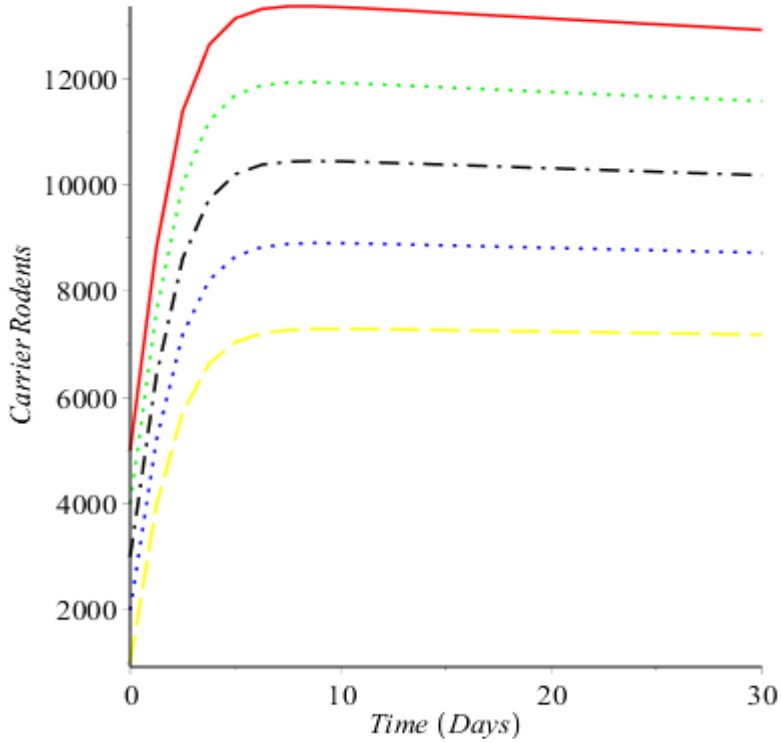


Fig. 4.4: The Global asymptotic stability of the endemic equilibrium point whenever $R_C > 1$ i.e $R_C = 1.8947 > 1$. The curves are plotted with $\beta_2 = 0.2$, $\sigma_r = 0.8$, $\delta_r = 0.09$ and the remaining parameters are as in Table 4.2. With different initial condition of carrier rodents, this clearly shows that the disease is endemic in the rodents' population irrespective of how small the initial carrier rodents are introduced into the rodents population as long as the effective reproduction numbers are greater than unity.

Assessing the Impact of killing Rodents to Human Population

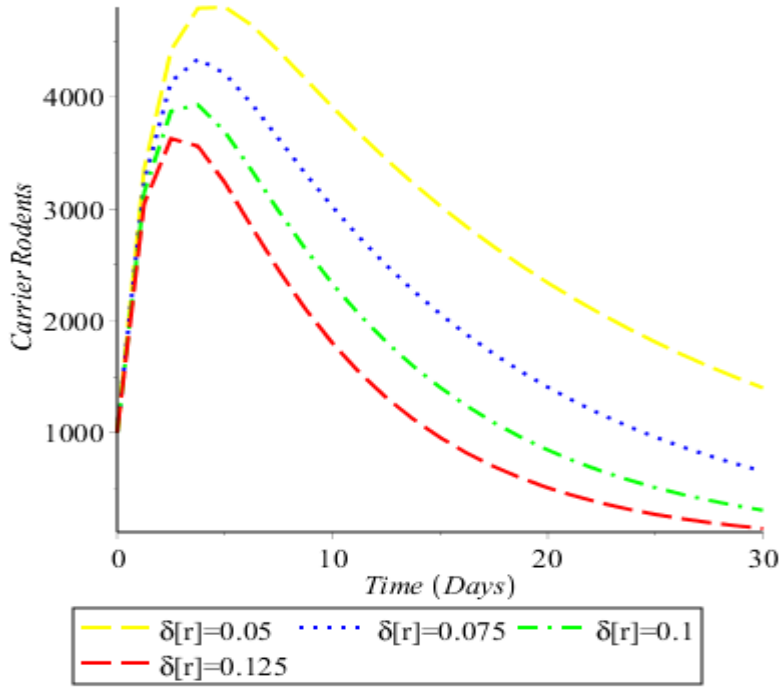
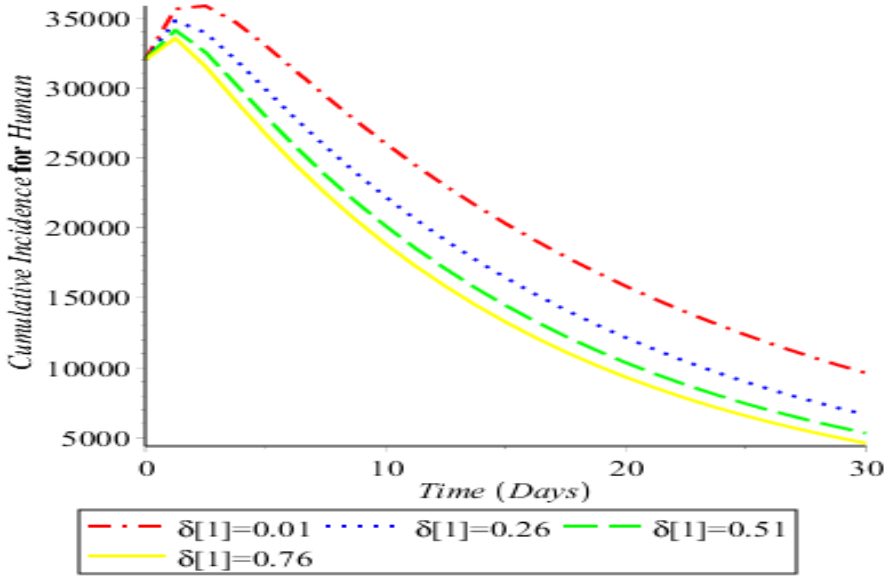


Fig. 4.5: It is well known how rodents are disseminated in every nook and cranny of our homes where a large number of this rodents harbor and transmit the lassa virus to humans. As such, rodents are further reduced in the population due to human activities i.e physical killing, hunting, the use of trap, spray of poisonous powder etc. Fig. 4.5 shows the impact of killing this rodents, to the human population. It shows clearly how drastic the rodents population reduces due to human activities. Conclusively, this implies the more the rodents are reduced in the society, the closer we are to mitigating lassa fever virus in our society. Intensifying human activities which lead to reduction in rodent population will go a long way in curbing the spread of lassa fever in the human population.

Impact of Induce Death of Human



Cumulative Incidence Varying Different Control Parameters

Variation of control parameter will be considered in this section. All the parameter values used here are in Table 1 above with $R_C = 1.2456$.

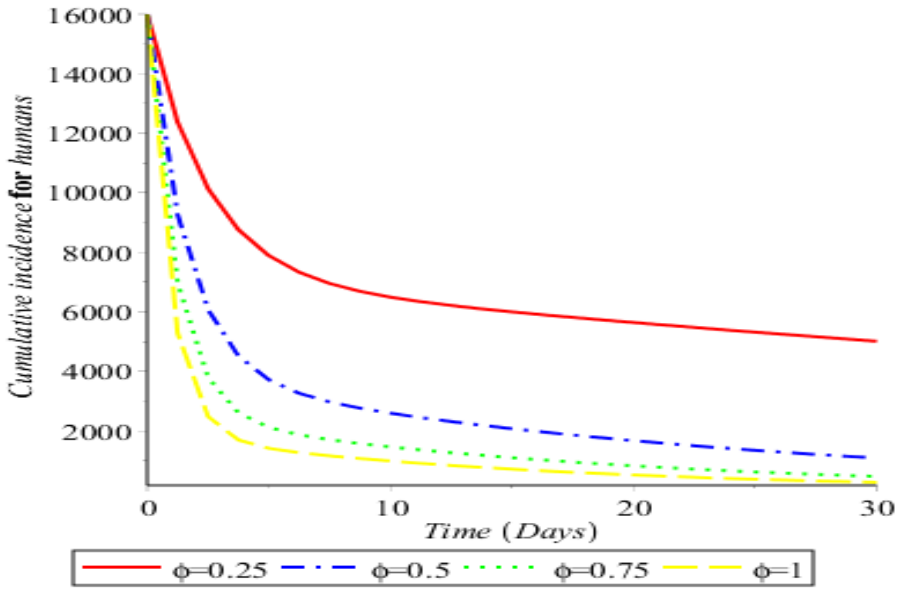


Fig. 4.7: Cumulative Incidence for Humans Varying Isolation Rate

Fig. 4.7 shows clearly the role played by isolating infectious humans in curbing the menace of lassa-fever in the society. The infectious humans is a function of isolation rate. The graph shows how massively the number of infection falls due to isolation. The solid line represents the rate at which the disease persists in the society, but adopting isolation as a control strategy in the population of infectious human the disease dies out, the broken line represents how the disease is being curtailed in a very short period of time. Increase in the isolation rate of infectious humans is seen to have a positive impact on the dynamics of lassa fever as this leads to a reduction in the cumulative number of cases.

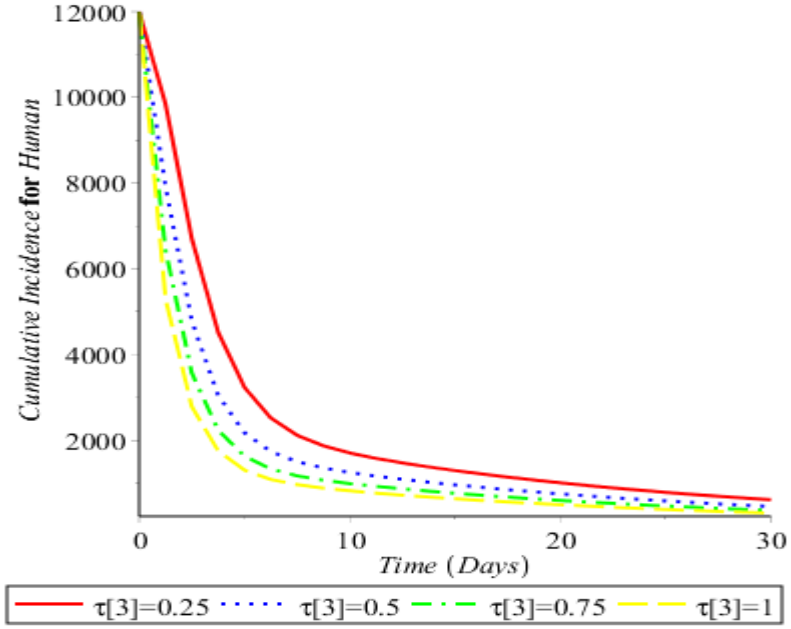


Fig. 4.8: Cumulative Incidence for Humans Varying Treatment Rate

Fig. 4.8 is showing the cumulative incidence for humans varying treatment rate. Ribavirin, an antiviral drug is considered to be the most effective to lassa-fever patient. The graph shows if given in the early days in the course of the illness. With this control strategy, the broken line in fig. 4.8 keep approaching zero which is an indication that the disease dies out completely from the population.

CONCLUSION

This work has been examined, using deterministic model for the Lassa Fever Virus transmission dynamics in a population, the model has various control strategies that could be implemented to bring down the burden of Lassa fever in a society. The following findings are made:

1) The model consists of four equilibriums: Disease free equilibrium in both humans and rodents' population endemic in humans' population only, endemic in rodents' population only and endemic in both population,
2) Existence and local stability of disease free equilibrium (DFE) if $R_h \leq 1$ and $R_r \leq 1$.
3) Global stability of disease free equilibrium if $R_h \leq 1$ and $R_r \leq 1$.
4) Existence and local stability of endemic equilibrium point (EEP) if $R_h > 1$ and $R_r > 1$
5) Global stability of endemic equilibrium point (EEP) if $R_h > 1$ and $R_r > 1$.

6) Applying all the control parameters in this model simultaneously leads to a smooth and unique way of curbing Lassa Fever in a society.
7) Reducing rodents population helps in Lassa fever mitigation in a society.

The following contribution to knowledge where achieved:

1) The work has improved on the existing models on the transmission dynamics and control of Lassa Fever disease.
2) The work has shown positive ways to control Lassa Fever in any society,
3) The work has shown the possibility of a disease free equilibrium which can be globally stable.

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