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Mathematical Model for the Dynamics of Lassa Fever Incorporating Treatment and Isolation

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ABSTRACT

Lassa Fever (Hemorrhagic Fever) is a widespread disease cause by Mastomys rodent and cause serious health problem leading to loss of lives. This research aims to analyze some existing with the intention of modifying or developing new one Mathematical Model for the Dynamics of Lassa Fever Incorporating Treatment and Isolation. We establish the positivity, boundedness, diseases free and endemic equilibria, basic reproduction number, local and global stability and carried out numerical simulation of the modified model. We formulate and analyze deterministic mathematical model of nine compartments for the transmission dynamics of Lassa Fever infection using a non-linear ordinary differential equation. We investigated a dynamic behavior of the modified model and performed the qualitative analysis of the model. The system has two equilibrium points, namely the disease-free equilibrium and the endemic equilibrium points. The basic reproduction number was calculated using the next-generation matrix and the stability of the model equations were carried out using MATLAB R2021a. the finding of this study shows that Lassa Fever can be significantly curtailed having the basic reproduction number less than unity and that if the implementation of Lassa Fever treatment, isolation is very effective this can reduced or eliminate the number of infected individuals.

1. Introduction

Lassa Fever (LF) is one of many infectious diseases that are emerging or reappearing in some West African countries. It has caused widespread and serious health problems leading to loss of lives in West African countries, for instance Nigeria, Liberia, Ghana, Guinea, and Sierra Leone (Onah andCollins 2020). However, according to the Centers for Disease Control and Prevention (CDC), as well as the World Health Organization (WHO), the annual case count for LF ranges between 100,000 and 300,000, with an estimated 5,000 deaths in West Africa (Olugasa *et al.,* 2015).

LF was first described in the 1950s, and the viral particle was discovered in 1969 in the northern part of Nigeria, in a city called Lassa in Borno state. when two missionary nurses died from it in the town of Lassa in Borno, Nigeria (Bausch *et al.,* 2001). Lassa hemorrhagic fever is another name for Lassa fever, and it is contracted through the Lassa virus (LV). The multimammate rat *Mastomys Natalensis* which is of the genus family *Arena viridae* is the primary host of LV. The virus is primarily spread to humans through direct contact with contaminated food tainted by the urine or excrement of an infected rodent. Human-to-human transmission is uncommon, but it is possible if a person shares medical equipment with an infected person without proper sterilization. Furthermore, it could be transmitted by dust particles through mucous membranes or skin breaks in humans. Because of its ability to spread from infected animal to human, LF is classified as a zoonotic disease (Musa *et al.,* 2020). In humans, Lassa fever symptoms include headaches, chest pain, nausea, cough, vomiting, diarrhea, muscle pain, abdominal pain, sore throat, and fever. In severe cases, symptoms may include swelling of the face, low blood pressure, fluid in the lungs, and bleeding from the nose, mouth, or vagina. In a more severe case, this disease can result in death within two weeks of the onset of symptoms (Bakare *et al.,* 2020).

Signs and symptoms of Lassa fever typically occur 1–3 weeks after the patient comes in contact with the virus.

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For the majority of Lassa fever virus infections (approximately 80%), symptoms are mild and are undiagnosed. Mild symptoms include a slight fever, general weakness, and headache. In 20% of infected individuals, however, the disease may progress to more serious symptoms including hemorrhage (bleeding in gums, eyes, or nose), respiratory distress, repeated vomiting, facials welling, pain in the chest, back, abdomen, shock, and the neurological problem has also been described including hearing loss and tremors . Lassa fever is generally treated with the antiviral drug ribavirin, which has been very effective when given early in the course of the disease (Fichet-Calvet and Rogers, 2009).

In Nigeria, sporadic outbreaks of Lassa fever have been documented since 1969. The infection is endemic in several states including Edo, Ebonyi, Onitsha, Jos, Taraba, Nasarawa, Yobe, Rivers, and Ondo states. In 2012, for example, 623 suspected cases (108 laboratory confirmed), including 70 deaths, were recorded from 19 states in Nigeria (Nasir *et al.,* 2015; World Health Organisation, 2012). A total of 11 confirm cases of Lassa were recorded in Nigeria with high prevalence in Oyo State in 2014. Between January 1 and March 8, 2015, the Nigeria Centre for Disease Control (NCDC, 2016) Reported 21 cases of Lassa fever (44 Lab. confirm) and 1 death due to Lassa (CDC, 2015). Between August 2015 and January 2016, there were 239 suspected cases of LF (44 lab confirm), including 82 deaths, across 19 states including Anambra, Bauchi, Nasarawa, Niger, Delta, Ekiti, Ondo, Kogi, Ebonyi, Lagos, Osun, FCT, Taraba, Kano, Rivers, Edo, Plateau, Gombe, and Oyo states (NCDC, 2016; WHO, 2016). Similarly, the years 2016, 2017, 2018, and 2019 were not spared from Lassa fever in Nigeria with outbreaks across several states (statistics can be viewed on the Nigeria Centre for Disease Control (NCDC) website).

The outbreak of Lassa fever is highest in humans during the dry season, following multimammate rodent reservoir breeding during the rainy season. Studies have shown that seasonal timing of reproduction can affect the dynamics of host-pathogen systems (Bolzoni *et al.,* 2006). Seasonality has to do with the systematic peaks of diseases at a certain time of the year, and one of its drivers is the birth rate pulses which will be considered in this work. Understanding how seasonally varying parameters act as a forcing mechanism and investigating their dynamical consequences are part of our interest in this work. In this case, we are interested in understanding how such periodically forced modes permit us to better capture the observed pattern of recurrent epidemics deferent from the unforced models which predict damped oscillation toward the endemic equilibrium points (Keeling *et al.,* 2008).

Ogabi *et al* (2012) Proposed an SIR model for controlling Lassa fever in the northern part of the Edo State by considering two senatorial districts of the state with about two million people. Using the numerical approach, they analyzed the relation- ship between the susceptible, infected, and removed classes with three health policies. These health policies which consist of three sets of parameters representing the birth rate, the natural death rate, the transmission rate, and the rate of recovery were employed by the authors to simulate their results. They were able to show that the reproduction number is affected by these parameters, which indirectly tells that "the health policies" can control the disease, given the role of the reproduction number in disease dynamics. They were able to show also that the disease can be controlled if the transmission rate becomes less than the recovery rate. Bawa *et al* (2014) also did a study of Lassa fever dynamics by subdividing the rodent population into infant and adult classes. From their analyses of the disease-free and endemic equilibria, they established a global stability condition for the control of the disease, which is dependent on the reproduction number as obtained in their work.

Mohammed *et al.,* (2015) in their work developed a transmission dynamic model for Lassa fever with human immigration. Model analysis was carried out to calculate the reproduction number, and sensitivity analysis of the model was also performed. Their results showed that the human immigration rate is the most sensitive parameter, followed by the human recovery rate as the second most sensitive parameter, and finally followed by the person-to-person contact rate. It was suggested that control strategies should target human immigration, effective drugs for treatment, and education to reduce person-to-person contact. Andrei *et al* (2018) in their paper, suggested that seasonal migratory dynamics of rodents played a key role in regulating the cyclic pattern of Lassa fever epidemics, but they had no explicit model

Bakare's research developed a non-autonomous system of nonlinear ordinary differential equations that capture the dynamics of LF transmission and seasonal variation in *Mastomys* rodent birth, the authors of the study evaluate Lassa fever disease intervention strategies by predicting optimal intervention best fit in controlling the disease in the population using the elasticity of the equilibria prevalence. Early ribavirin treatments, as well as an early combination of intervention strategies such as effective community hygiene, proper isolation of infected humans, and rodent elimination, will facilitate effective disease control in the population. A mathematical model of the transmission dynamics of Lassa fever infection with control in two different but complementary hosts is presented in (Bakare *et al.,* 2020). The model includes a death infectious human compartment that can infect a vulnerable individual. According

to the study's findings, the best way to control secondary transmission dynamics from human-to-human is to establish more Lassa fever diagnostic centers and use precautionary burial practices. (Dachollom *et al.,* 2020).

2. MATERIAL AND METHODS

2.1 Model Formulation

The model subdivides the human population $N_H(t)$ into six compartments as; susceptible $S_H(t)$, exposed $E_H(t)$, mild symptom $I_H^{ms}(t)$, severe symptom $I_H^{ss}(t)$, isolated $I_S(t)$ humans and recovered $R_H(t)$. So that;

$$N_H(t) = S_H(t) + E_H(t) + I_H^{ms}(t) + I_H^{ss} + I_S(t) + R_H$$

Also, the model subdivides the rodent population $N_R(t)$ into three compartments as; susceptible $S_R(t)$, exposed $E_R(t)$ and infectious $I_R(t)$ rodents, so that;

$$N_R(t) = S_R(t) + E_R(t) + I_R(t)$$

The population of susceptible humans S_H, are recruited by birth at a rate π_H. It reduces by infection, following contact with infected rodent at a rate β_R and exposed humans, at a rate β_H. The class is also increased due to contact with individuals with mild symptoms and severe symptoms at a rate θ and $(1\text{-}\theta)$ respectively, the susceptible population is further increased at a rate which recovered humans revert to susceptible class at a rate α_3 It further decreases due to natural death at a rate μ_H. So that;

$$\frac{dS_H}{dt} = \pi_H - \lambda_1 S_H + \alpha_3 R_H - \mu_H S_H$$

The population of exposed human E_H is generated following infection at a rate β_R and β_H due to infection with human and rodents. It decreases as a result of progression into the infection class with mild symptoms and severe symptoms at a rate $\theta\rho_H$ and $(1-\theta)\rho_H$ respectively. The class is further reduced due to natural death at rate μ_H. such that

$$\frac{dE_H}{dt} = \lambda_1 S_H - \left(\theta\rho_H + (1-\theta)\rho_H\right)E_H - \mu_H E_H$$

Mild symptom humans, I_H^{ms} are generated as a result of progression into the mild infected compartment due to the mild infection from the exposed class at the rate $\theta\rho_H$. It diminishes due to treatment, progression into isolation compartments at a rate α_1 and γ_1 respectively. It reduces due to natural death and diseases induced death at a rate μ_H and d_H respectively. So that:

$$\frac{dI_H^{ms}}{dt} = \theta\rho_H E_H - (\alpha_1 + \gamma_1 + \mu_H + d_H)I_H^{ms}$$

Severe symptom humans, I_H^{ss} class is generated as a result of progression into the infected class from the exposed class due to severe infection at a rate $\rho_H(1-\theta)$. The class diminishes due to progression into isolation class and recovery compartment at a rate γ_2 and α_2 respectively, it further reduces due to natural death and death due to severe symptoms at a rate μ_H and C_H respectively, so that:

$$\frac{dI_H^{ss}}{dt} = (1-\theta)\rho_H E_H - (\alpha_2 + \gamma_2 + \mu_H + \mathrm{C}_H)I_H^{ss}$$

The isolation class, I_S is generated due to progression from infected humans with mild symptoms and

infected humans with severe symptoms at a rate γ_1 and γ_2 respectively. It diminishes due to recovery and rate at which isolated humans result to susceptible again at a rate ε_H, μ_H and m_H respectively, so that

$$\frac{dI_S}{dt} = \gamma_1 I_H^{ms} + \gamma_2 I_H^{ss} - (\mu_H + \varepsilon_H + m_H) I_S$$

The recovered humans class, R_H are generated as a result of recovery from the mild symptom, severe symptoms and isolation at a rate α_1, α_2 and ε_H respectively, it diminishes due to natural death and rate at which recovered human lose their immunity such that at a rate μ_H and α_3 respectively, so that:

$$\frac{dR_H}{dt} = \alpha_1 I_H^{ms} + \alpha_2 I_H^{ss} + \varepsilon_H I_S - (\mu_H + \alpha_3) R_H$$

The population of susceptible rodents S_R are recruited at a rate π_R. It diminishes due to infection following contact with infected rodents at a rate β_R and by natural death μ_R, so that;

$$\frac{dS_R}{dt} = \pi_R - \lambda_2 S_R - \mu_R S_R$$

The populations of exposed rodents E_R is generated due to progression by infection at a rate β_R and β_H. It diminishes due to progression to infectious class at a rate σ_R, and are depleted as a result of natural death μ_R, so that;

$$\frac{dE_R}{dt} = \lambda_2 S_R - (\sigma_R + \mu_R) E_R$$

The population of infected rodents is increases due to exposed rodents moving into infected class at a rate σ_R and diminishes as a result of natural death and disease induced death at a rate μ_R and d_R, so that;

$$\frac{dI_R}{dt} = \sigma_R E_R - (\mu_R + d_R) I_R$$

The biological assumptions of the model are as follows:

i. Relapse in medicine in a recurrence of diseases after it has been apparently cured. So, relapse in Lassa fever connotes the recurrence of the virus after clinical treatment. So we assume that relapse can occur.

ii. Both mild and severe infected individuals are treated as follows: Mild symptom compartment are given conservative management (treatment) such as; adequate and oral fluid intent, save environment, vitamin A and C and calcium. While severe symptoms are given antibiotic, vitamin A and C, calcium and zinc tablet because of the pneumonia, IV fluids are given anti-coagulants and blood transfusion plus the mild treatment because of the bleeding tendencies (Dr. Aliyu T. 2021).

iii. We also assume that those that were treated could be re- infected and are factored back into the susceptible class for lack of permanent immunity.

Therefore, based on the above description and assumptions, the basic Lassa Fever Model leads to the following system of non-linear differential equations (1), the schematic diagram Figure 1 below, and the state variables and parameters indicated in the diagram are explained in Table 1.

$$
\left.
\begin{aligned}
\frac{dS_H}{dt} &= \pi_H - \lambda_1 S_H + \alpha_3 R_H - \mu_H S_H \\
\frac{dE_H}{dt} &= \lambda_1 S_H - \left(\theta\rho_H + (1-\theta)\rho_H\right) E_H - \mu_H E_H \\
\frac{dI_H^{ms}}{dt} &= \theta\rho_H E_H - (\alpha_1 + \gamma_1 + \mu_H + d_H) I_H^{ms} \\
\frac{dI_H^{ss}}{dt} &= (1-\theta)\rho_H E_H - (\alpha_2 + \gamma_2 + \mu_H + \mathrm{C}_H) I_H^{ss} \\
\frac{dI_S}{dt} &= \gamma_1 I_H^{ms} + \gamma_2 I_H^{ss} - (\mu_H + \varepsilon_H + m_H) I_S \\
\frac{dR_H}{dt} &= \alpha_1 I_H^{ms} + \alpha_2 I_H^{ss} + \varepsilon_H I_S - (\mu_H + \alpha_3) R_H \\
\frac{dS_R}{dt} &= \pi_R - \lambda_2 S_R - \mu_R S_R \\
\frac{dE_R}{dt} &= \lambda_2 S_R - \left(\sigma_R + \mu_R\right) E_R \\
\frac{dI_R}{dt} &= \sigma_R E_R - (\mu_R + d_R) I_R
\end{aligned}
\right\} \tag{1}
$$

where: $\lambda_1 = \beta_H (I_R + I_S + E_H + I_H^{ms} + I_H^{ss})$ and $\lambda_2 = \beta_R (E_R + E_H + I_R + I_H^{ss})$

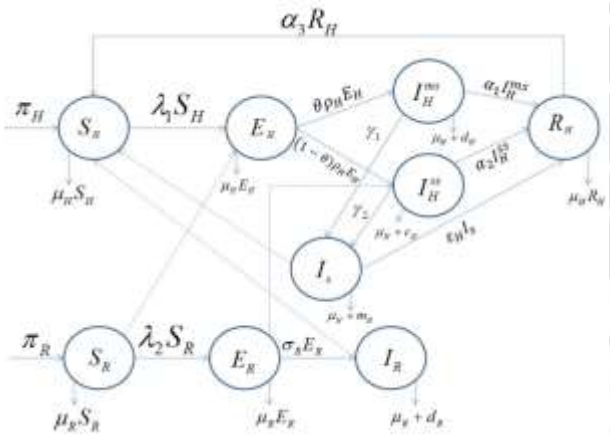

Figure 1: Schematic Diagram of the Model

Table 1: State variables description of the model

Variable	Description
$S_H(t)$	The number of susceptible human hosts at time t
$E_H(t)$	The number of exposed human hosts at time t

$I_H^{ms}(t)$	The number of mild symptoms human hosts at time t
$I_H^{ss}(t)$	The number of severe symptoms human hosts at time t
$R_H(t)$	The number of recovered human hosts at time t
$I_S(t)$	The number of isolated human hosts at time t
$S_R(t)$	The number of susceptible rodent vectors at time t
$E_R(t)$	The number of exposed rodent vector at time t
$I_R(t)$	The number of infectious rodent vectors at time t

Table 2: Parameters description of the model

Parameters	Description
π_H	Recruitment into susceptible humans class (birth rate)
π_R	Recruitment into susceptible rodents class (birth rate)
β_R	Contact rate of rodents
β_H	Contact rate of humans
γ_1	Rate of progression from infected mild symptom to isolation
γ_2	Rate of progression from infected severe symptoms to isolation
α_1	Rate of treatment of infected individuals with mild symptoms
α_2	Rate of treatment of infected individuals with severe symptoms
α_3	Rate at which recovered individuals revert back to susceptible
μ_H	Natural death rate of humans
μ_R	Natural death rate of rodents
c_H	Disease induced death at severe symptoms class
m_H	Disease induced death at isolated class
d_H	Disease induced death at mild symptoms class
d_R	Disease induced death at infectious rodent class
ρ_H	Progression rate of exposed individuals into infectious with mild symptoms
θ	Proportion of individuals that progresses into infectious with mild symptoms
$(1-\theta)$	Proportion of individuals that progresses into infectious with severe symptoms
σ	Progression rate from exposed to infectious rodent
λ_1, λ_2	Force of infections in humans and rodents
ε_H	Rate of treatment of infected individuals with isolated class

2.2 Boundedness and Invariant Region

In this section, some qualitative analyses of the model are performed. Firstly, we demonstrate two basic properties of the model, which are the invariant region and the non-negativity of the model solution.

2.2.1 Boundedness

The basic dynamical features of the model equations (1) will now be explored. For the model to be epidemiologically meaningful, it is important to prove that all variables are non-negative for all time, and a bounded solution exists. The model equations (1) are divided into two regions: $\Omega_H = \left[S_H, E_H, I_H^{ms}, I_H^{ss}, I_S, R_H\right] \in \mathbb{R}_+^6$ and $\Omega_R = \left[S_R, E_R, I_R\right] \in \mathbb{R}_+^3$, thus, $\Omega = \Omega_H \times \Omega_R \in \mathbb{R}_+^9$.

Theorem 1. The closed set

$$\Omega = \Omega_H \times \Omega_R \tag{2}$$

with $\Omega_H = \left\{S_H, E_H, I_H^{ms}, I_H^{ss}, I_S, R_H \in \mathbb{R}_+^6 : N_H \le \frac{\pi_H}{\mu_H}\right\}$ and $\Omega_R = \left\{S_R, E_R, I_R \in \mathbb{R}_+^3 : N_R \le \frac{\pi_R}{\mu_R}\right\}$ is positively invariant with respect to the model (1).

Proof: The total human population is denoted by N_H and given by

$$N_H(t) = S_H + E_H + I_H^{ms} + I_H^{ss} + I_S + R_H$$

And is differentiated and summed together to obtain

$$N_H(t) = \pi_H - \mu_H N - d_H I_H^{ms} - c_H I_H^{ss} - m_H I_S \tag{3}$$

But by standard comparison and rearranging equation (3), we obtain a first-order differential inequality:

$$\frac{dN}{dt} \le \pi_H - \mu_H N$$

Which is solved by integrating factor method to obtain

$$N(t) \ge N_0 e^{-\mu_H t} + \frac{\pi_H}{\mu_H}(1 - e^{-\mu_H t})$$

So as $t \to \infty$, $N_H(t) \le \frac{\pi_H}{\mu_H}$. A similar approach yields a similar result for the rat population: $N_R(t) \le \frac{\pi_R}{\mu_R}$. Thus, we have shown that Ω is positively invariant and attracts all solutions of equation (1) in finite time. This guarantees that our investigations and analyses will be carried out in a feasible region and that every solution of our model having initial conditions in Ω will always remain in Ω for all $t > 0$.

2.2.2 Positivity of solutions

Theorem 2. Let $\left(S_H(0), E_H(0), I_H^{ms}(0), I_H^{ss}(0), I_S(0), R_H(0), S_R(0), E_R(0), I_R(0)\right) \ge 0$ be the initial states of the model (1). Then every solution $\left(S_H(t), E_H(t), I_H^{ms}(t), I_H^{ss}(t), I_S(t), R_H(t), S_R(t), E_R(t), I_R(t)\right) \ge 0$ for all time $t > 0$.

Proof. From the first equation of our model (1),

$$\dot{S}_H = \pi_H - \lambda_1 S_H + \alpha_3 R_H - \mu_H S_H$$

This equation can be expressed without loose of generality, after eliminating the positive term as an inequality

$$\frac{dS_H}{dt} \geq -(\lambda_1 + \mu_H)S_H$$

Integrating both side using separation of variables, we have

$$S_H \geq ce^{-(\lambda_1+\mu_H)t} \tag{4}$$

At time $t = 0$, $S_H(0) = c_1$ substituting for c_1 into equation (4), we obtain

$$S_H(t) \geq S_0 e^{-(\lambda_1+\mu_H)t}$$

Hence, $S_H(t) > 0$ (is positive).

Therefore, any solution of S_H with positive initial data will remain positive $\forall t > 0$. In the same manner, it can be shown that $E_H(t) \geq 0,\ E_H(t) \geq 0,\ I_H^{ms}(t) \geq 0, I_H^{ss}(t) \geq 0, I_S(t) \geq 0, R_H(0) \geq 0,\ S_R(0) \geq 0, E_R(0) \geq 0, I_R(0) \geq 0$.

3. Model Analysis

In this section, we shall examine the equilibrium solutions, obtain the basic reproduction number, conduct the stability analysis of the Lassa Fever free equilibrium (LFFE), Lassa Fever endemic equilibrium (LFEE), the local and global stability of the RABV free equilibrium. At equilibrium, we set

$$\left.\begin{aligned}
&\pi_H - \lambda_1 S_H + \alpha_3 R_H - \mu_H S_H = 0\\
&\lambda_1 S_H - (\theta\rho_H + (1-\theta)\rho_H)E_H - \mu_H E_H = 0\\
&\theta\rho_H E_H - (\alpha_1 + \gamma_1 + \mu_H + d_H)I_H^{ms} = 0\\
&(1-\theta)\rho_H E_H - (\alpha_2 + \gamma_2 + \mu_H + \mathrm{C}_H)I_H^{ss} = 0\\
&\gamma_1 I_H^{ms} + \gamma_2 I_H^{ss} - (\mu_H + \varepsilon_H + m_H)I_S = 0\\
&\alpha_1 I_H^{ms} + \alpha_2 I_H^{ss} + \varepsilon_H I_S - (\mu_H + \alpha_3)R_H = 0\\
&\pi_R - \lambda_2 S_R - \mu_R S_R = 0\\
&\lambda_2 S_R - (\sigma_R + \mu_R)E_R = 0\\
&\sigma_R E_R - (\mu_R + d_R)I_R = 0
\end{aligned}\right\} \tag{5}$$

3.1 Lassa Fever Free Equilibrium

This is achieved if there is no Lassa Fever infection in the community, which means that the number of infected rats, infected humans, treated humans and recovered humans are zero, that is $E_H = I_H^{ms} = I_H^{ss} = I_S = E_R = I_R = 0$. The Lassa Fever free equilibrium of model equations (1) is obtained and is given by (6)

$$\begin{aligned}
E_0 &\equiv (S_H^0, E_H^0, I_H^{ms}, I_H^{ss}, I_S^0, R_H^0, S_R^0, E_R^0, I_R^0)\\
&= \left(\frac{\pi_H}{\mu_H}, 0, 0, 0, 0, 0, \frac{\pi_R}{\mu_R}, 0, 0\right)
\end{aligned} \tag{6}$$

3.2 Basic Reproduction Number

Using the next generation matrix method on our system of Equation (1) and following the notations used in Van Driessche and Watmough, (2002), the matrix F_i (of new infections) and the matrix V_i (of the transfer of species

between compartments) are given, respectively, by

$$F=\begin{pmatrix} \beta_H S_H & \beta_H S_H & \beta_H S_H & 0 & 0 & \beta_H S_H \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \beta_R S_R & 0 & \beta_R S_R & 0 & \beta_R S_R & \beta_R S_R \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{7}$$

and

$$V=\begin{pmatrix} A_1 & 0 & 0 & 0 & 0 & 0 \\ -\theta\rho_H & A_2 & 0 & 0 & 0 & 0 \\ A_3 & 0 & A_4 & 0 & 0 & 0 \\ 0 & -\gamma_1 & -\gamma_2 & A_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & A_6 & 0 \\ 0 & 0 & 0 & 0 & -\sigma_R & A_7 \end{pmatrix} \tag{8}$$

with: $A_1=\theta\rho_H+(1-\theta)\rho_H+\mu_H$, $A_2=\alpha_1+\gamma_1+\mu_H+d_H$, $A_3=-(1-\theta)\rho_H$, $A_4=\alpha_2+\gamma_2+\mu_H+c_H$, $A_5=\mu_H+\varepsilon_H+m_H$, $A_6=\sigma_R+\mu_R$, and $A_7=\mu_R+d_R$

such that

$$V^{-1}=\begin{pmatrix} \frac{1}{A_1} & 0 & 0 & 0 & 0 & 0 \\ \frac{\theta\rho_H}{A_1A_2} & \frac{1}{A_2} & 0 & 0 & 0 & 0 \\ -\frac{A_3}{A_1A_4} & 0 & \frac{1}{A_4} & 0 & 0 & 0 \\ \frac{\theta A_4\gamma_1\rho_H-A_2A_3\gamma_2}{A_2A_1A_4A_5} & \frac{\gamma_1}{A_2A_5} & \frac{\gamma_2}{A_4A_5} & \frac{1}{A_5} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{A_6} & 0 \\ 0 & 0 & 0 & 0 & \frac{\sigma_R}{A_6A_7} & \frac{1}{A_7} \end{pmatrix} \tag{9}$$

Hence, the basic reproduction number, (R_0), of the model (1) computed as the spectral radius $\left(\rho\left(FV^{-1}\right)\right)$ of the matrix $\left(FV^{-1}\right)$ is obtained as

$$R_0=\frac{1}{2}M_8+\frac{1}{2}M_1+\frac{1}{2}\sqrt{M_1^2-2M_1M_8+4M_4M_6+M_8^2} \tag{10}$$

with:

$$M_1 = \frac{\beta_H \pi_H}{\mu_H A_1} + \frac{\beta_H \pi_H \theta \rho_H}{\mu_H A_1 A_2} - \frac{\beta_H \pi_H A_3}{\mu_H A_1 A_4},\ M_4 = \frac{\beta_H \pi_H \sigma_R}{\mu_H A_6 A_7},\ M_6 = \frac{\beta_R \pi_R}{\mu_R A_1} - \frac{\beta_R \pi_R A_3}{\mu_R A_1 A_4}$$
$$M_8 = \frac{\beta_R \pi_R}{\mu_R A_6} + \frac{\beta_R \pi_R \sigma_R}{\mu_R A_6 A_7},$$

Lemma 1: The disease-free equilibrium (DFE) of the model (1) is locally asymptotically stable (LAS) whenever the basic reproduction number $R_0 < 1$ and unstable when $R_0 > 1$.

3.3 Global Stability of the Lassa-Fever Free Equilibrium

We used Castillo-Chavez theorem (Castillo-Chavez *et al.,* 2002) to investigate the global asymptotic stability of the disease-free state. For the theorem to work, we rewrite (3.7) to (3.15) in the form

$$\left.\begin{aligned} \frac{dX}{dt} &= H(X,Z) \\ \frac{dZ}{dt} &= G(X,Z), G(X,0) = 0 \end{aligned}\right\} \tag{11}$$

where $X = \left(S_H, R_H, S_R\right)$ and $Z = \left(E_H, I_H^{ms}, I_H^{ss}, I_S, E_R, I_R\right)$. Here the components of $X \in \mathbb{R}^3$ denote the uninfected human and rodent compartments and $Z \in \mathbb{R}^6$ denote the infected human and rodents population. The disease-free equilibrium of the system now becomes $E^0 = \left(X^*, 0\right)$. To guarantee global asymptotic stability, the following two condition must be met.

i. $\frac{dX}{dt} = H\left(X, 0\right), X^*$ is globally asymptotically stable (GAS)

ii. $G\left(X,Z\right) = PZ - \hat{G}\left(X,Z\right) \geq 0$ for $\left(X,Z\right) \in \Omega$

where $P = D_Z G\left(X^*, 0\right)$ is an M matrix (the off diagonal element of P are non-negative) and Ω is the region where the model is biologically meaningful. If the system satisfies condition (i) and (ii) then the following theorem holds

Theorem 3: The fixed point $E^0 = \left(X^*, 0\right)$ is globally asymptomatic stability (GAS) equilibrium provided that $R_0 < 1$ and the assumption (i) and (ii) satisfied (Patrick *et al.,* 2020)

Proof: Since $X = \left(S_H, R_H, S_R\right)$ and $Z = \left(E_H, I_H^{ms}, I_H^{ss}, I_S, E_R, I_R\right)$ then

$$H(X,Z) = \begin{pmatrix} \pi_H - \lambda_1 S_H + \alpha_3 R_H - \mu_H S_H \\ \alpha_1 I_H^{ms} + \alpha_2 I_H^{ss} + \varepsilon_H I_S - \left(\mu_H + \alpha_3\right) R_H \\ \pi_R - \lambda_2 S_R - \mu_R S_R \end{pmatrix} \tag{12}$$

then

$$H\left(X,0\right) = \begin{pmatrix} \pi_H - \mu_H S_H \\ 0 \\ \pi_R - \mu_R S_R \end{pmatrix} \tag{13}$$

and

$$G(X,Z) = PZ - \hat{G}(X,Z)$$

where

$$G(X,Z) = \begin{pmatrix} \lambda_1 S_H - (\theta\rho_H + (1-\theta)\rho_H)E_H - \mu_H E_H \\ \theta\rho_H E_H - (\alpha_1 + \gamma_1 + \mu_H + d_H) I_H^{ms} \\ (1-\theta)\rho_H E_H - (\alpha_2 + \gamma_2 + \mu_H + c_H) I_H^{ss} \\ \gamma_1 I_H^{ms} + \gamma_2 I_H^{ss} - (\mu_H + \varepsilon_H + m_H) I_S \\ \lambda_2 S_R - (\sigma_R + \mu_R) E_R \\ \sigma_R E_R - (\mu_R + d_R) I_R \end{pmatrix} \tag{14}$$

and $P = D_Z G(X,0)$ in the Jacobian of $G(X,Z)$ with respect to Z, such that

$$P = \begin{pmatrix} \beta_H S_H - \theta\rho_H - (1-\theta)\rho_H & \beta_H S_H & \beta_H S_H & \beta_H S_H & 0 & \beta_H S_H \\ \theta\rho_H & -\alpha_1 - \gamma_1 - \mu_H - d_H & 0 & 0 & 0 & 0 \\ (1-\theta)\rho_H & 0 & -\alpha_2 - \gamma_2 - \mu_H - c_H & 0 & 0 & 0 \\ 0 & \gamma_1 & \gamma_2 & -\mu_H - \varepsilon_H - m_H & 0 & 0 \\ \beta_R S_R & 0 & \beta_R S_R & 0 & S_R\beta_R - \mu_R - \sigma_R & \beta_R S_R \\ 0 & 0 & 0 & 0 & \sigma_R & -\mu_R - d_R \end{pmatrix} \tag{15}$$

and

$$Z = \left(E_H, I_H^{ms}, I_H^{ss}, I_S, E_R, I_R\right)^T \tag{16}$$

so that,

$$PZ = \begin{pmatrix} \left(\beta_H \frac{\pi_H}{\mu_H} - \theta\rho_H - (1-\theta)\rho_H\right)E_H + \beta_H \frac{\pi_H}{\mu_H} I_H^{ms} + \beta_H \frac{\pi_H}{\mu_H} I_H^{ss} + \beta_H \frac{\pi_H}{\mu_H} I_S + \beta_H \frac{\pi_H}{\mu_H} I_R \\ \theta\rho_H E_H - (\alpha_1 + \gamma_1 + \mu_H + d_H) I_H^{ms} \\ (1-\theta)\rho_H E_H - (\alpha_2 + \gamma_2 + \mu_H + c_H) I_H^{ss} \\ \gamma_1 I_H^{ms} + \gamma_2 I_H^{ss} - (\mu_H + \varepsilon_H + m_H) I_S \\ \beta_R \frac{\pi_R}{\mu_R} E_H + \beta_R \frac{\pi_R}{\mu_R} I_H^{ss} + \left(\beta_R \frac{\pi_R}{\mu_R} - \mu_R - \sigma_R\right)E_R + \beta_R \frac{\pi_R}{\mu_R} I_R \\ \sigma_R E_R - (\mu_R + d_R) I_R \end{pmatrix} \tag{17}$$

then

$$PZ - G(X,Z) = \hat{G}(X,Z)$$

and

$$\hat{G}(X,Z)=\begin{pmatrix}\hat{G}_1(X,Z)\\ \hat{G}_2(X,Z)\\ \hat{G}_3(X,Z)\\ \hat{G}_4(X,Z)\\ \hat{G}_5(X,Z)\\ \hat{G}_6(X,Z)\end{pmatrix}=\begin{pmatrix}\beta_H\frac{\pi_H}{\mu_H}\left(E_H+I_H^{ms}+I_H^{ss}+I_S+I_R\right)\left(1-\frac{S_H}{N_H}\right)\\ 0\\ 0\\ 0\\ \beta_R\frac{\pi_R}{\mu_R}\left(E_H+E_R+I_H^{ss}+I_R\right)\left(1-\frac{S_R}{N_R}\right)\\ 0\end{pmatrix} \tag{18}$$

Therefore, $\hat{G}(X,Z)\geq 0$ if and only if, $\hat{G}_1(X,Z)\geq 0$ if $S_H\leq N_H$ and $\hat{G}_5(X,Z)\geq 0$ if $S_R\leq N_R$. Condition (i) and (ii) holds and therefore E_0^* is Globally Asymptomatically Stable (GAS).

4 Numerical Simulation

To illustrate the theoretical results, numerical simulations were carried out. Model variables and parameters value for the numerical simulations source are listed in Table 4.1 and Table 4.2 below. Whenever parameter values were not available in the literature, we assumed realistic values for the purpose of illustration.

Table 4.1: Variable values used for numerical simulations

Variables	Values	Reference
$S_H(0)$	1200	Assumed
$E_H(0)$	35	Assumed
$I_H^{ms}(0)$	90	Assumed
$I_H^{ss}(0)$	50	Assumed
$R_H(0)$	25	Assumed
$I_S(0)$	45	Assumed
$S_R(0)$	400	Assumed
$E_R(0)$	13	Assumed
$I_R(0)$	22	Assumed

Table 4.2: Parameters values used for numerical simulations

Parameters	Values	Reference
π_H	0.038	Abdulhamid and Hussaini 2018
π_R	0.05	Ogabi 2012
β_R	0.43	Abdulhamid and Hussaini 2018
β_H	0.4	Abdulhamid and Hussaini 2018
γ_1	0.5	Patrick *et al.,* 2020
γ_2	0.024	Musa *et al.,* 2020
α_1	0.108	Musa *et al.,* 2020
α_2	0.446	Musa *et al.,* 2020
α_3	0.00578	Musa *et al.,* 2020
μ_H	0.018182	Abdulhamid and Hussaini 2018
μ_R	0.1858	Ogabi 2012
c_H	0.485	Musa *et al.,* 2020
m_H	0.269	Musa *et al.,* 2020
d_H	0.1133	NCDC 2018
d_R	0.123	Assumed
ρ_H	0.7869	Richmond and Bagole 2003
θ	0.815	Musa *et al.,* 2020
σ	0.32	Musa *et al.,* 2020
ε_H	0.18	Richmond and Bagole 2003

4.1 Numerical experiments

The following Figures 4.1 to 4.11 are graphical representation showing the behavior of the infectious human in various stages of Lassa Fever over a period of time.

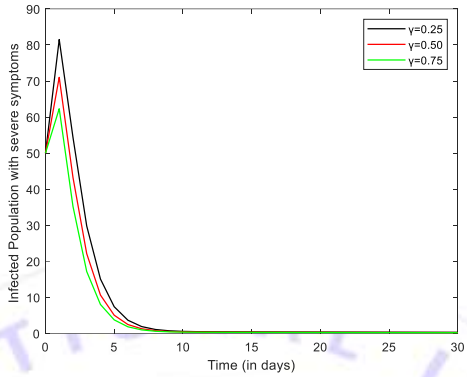

Figure. 4.1: Impact of Isolation and Treatment with human-to-human transmission on Severe Symptoms Infected Population at different rate of isolation.

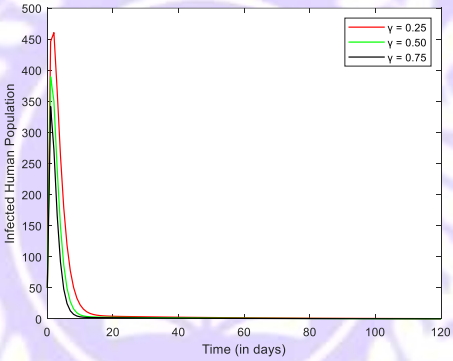

Figure. 4.2: Impact of Isolation and Treatment with human-to-human transmission on Mild Symptoms Infected Human Population at different rate of isolation.

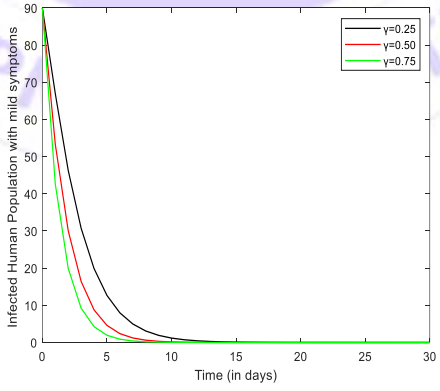

Figure. 4.3: Impact of Isolation and Treatment without human-to-human transmission on Mild Symptoms Infected

Human Population at different rate of isolation.

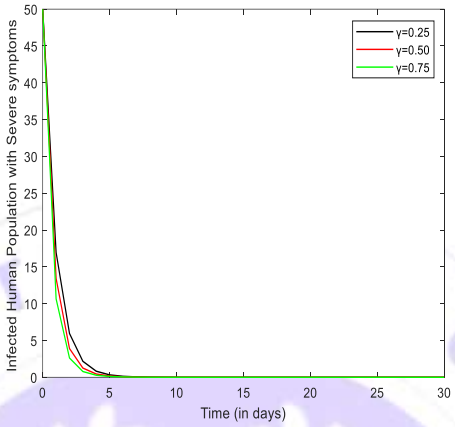

Figure. 4.4: Impact of Isolation and Treatment without human-to-human transmission on Severe Symptoms Infected Population at different rate of isolation.

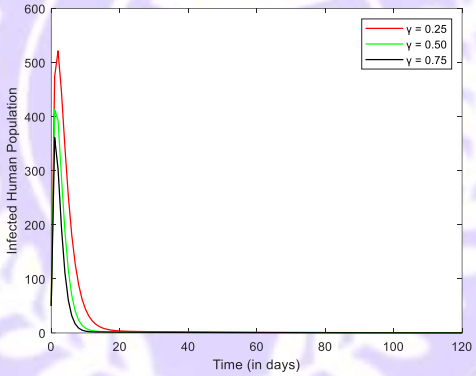

Figure. 4.5: Impact of Isolation only with human-to-human transmission on Infected Human Population at different rate of isolation.

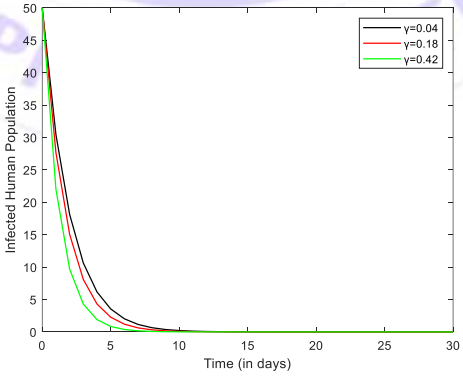

Figure. 4.6: Impact of Isolation only without human-to-human transmission on Infected Human Population at different

rate of isolation.

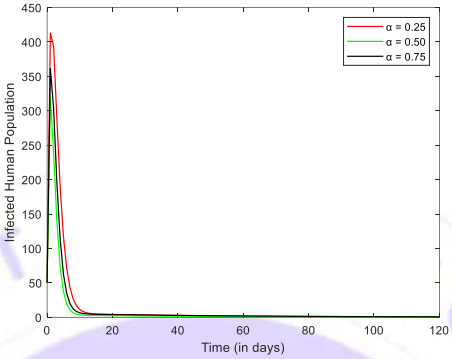

Figure. 4.7: Impact of Treatment only with human-to-human transmission on Infected Human Population at different rate of isolation.

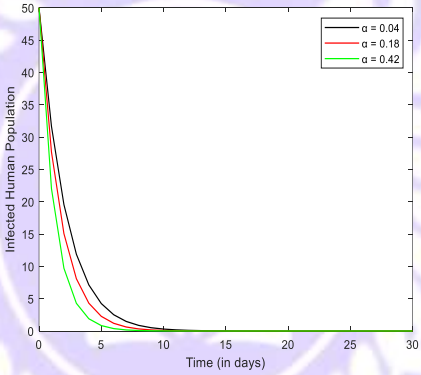

Figure. 4.8: Impact of Treatment only without human-to-human transmission on Infected Human Population at different rate of isolation.

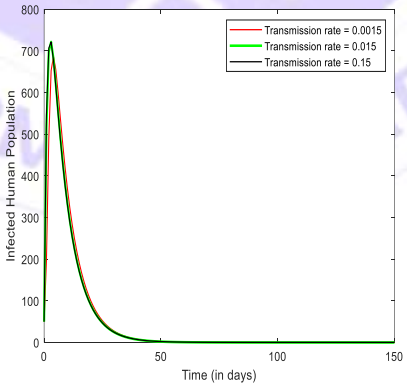

Figure. 4.9: Infected Human Population without treatment and isolation at different rate of human-human transmission.

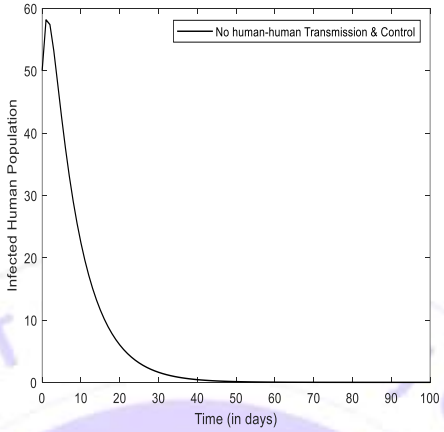

Figure. 4.10: Infected Human Population without human-human transmission, isolation and treatment

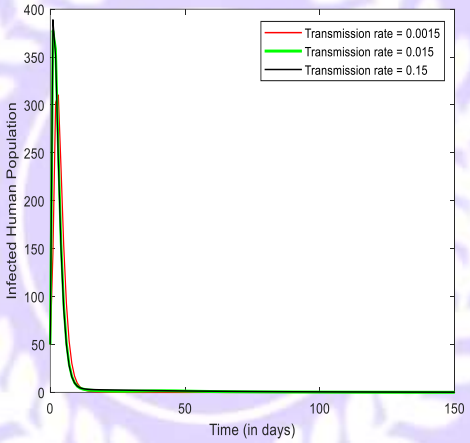

Figure. 4.11: Infected Human Population with varying human-human transmission and treatment and isolation rate (α=0.18; γ=0.5)

Discussion of Findings

We established the positivity of the solution and the invariant region which implies that the model solution was positive and bounded. In addition, the disease-free and endemic equilibrium of the model and its stability analysis were established showing the region where the model is well posed mathematically and epidemiologically. We also obtained the model's reproduction number using the next generation matrix techniques which shows that $R_0 < 0$ which implies epidemiologically that the disease Lassa Fever can be eradicated. Lastly, the local and global stability of the disease free-equilibrium is rigorously studied based on this R_0 . It was observed that the disease-free equilibrium is locally as well as globally asymptomatically stable whenever the basic reproduction number is less than unity (i.e. Lasa fever dies out in the population)

Numerical of the proposed epidemic model describing the transmission dynamic of Lassa Fever using the estimated parameters shown in the Table 4.1. The result is demonstrated in order to explore the dynamical influence of possible control strategies on the incidence of the infection. The numerical simulation was categories into eleven experiments namely; impact of isolation and treatment with human-to-human transmission on severe symptoms

infected population at different rate of isolation, impact of isolation and treatment with human-to-human transmission on mild symptoms infected population at different rate of isolation, impact of isolation and treatment without human-to-human transmission on mild symptoms infected human population at different rate of isolation, impact of isolation and treatment without human-to-human transmission on severe symptoms infected population at different rate of isolation, impact of human-to-human transmission on infected human population t different rate of isolation, impact of isolation only without human-to-human transmission on infected human population at different rate of isolation, impact of treatment only with human-to-human transmission on infected human population at different rate of isolation, impact of treatment only without human-to-human transmission on infected human population at different rate of isolation, infected human population without treatment and isolation at different rate of human-human transmission, infected human population without human-human transmission, isolation and treatment, infected human population with varying human-human transmission and treatment and isolation rate $(\alpha = 0.18, \gamma = 0.5)$.

Figure 4.1 shows that the impact of isolation and treatment with human-to-human transmission on severe symptoms infected population at different rate of isolation. The population of infectious human reduced slowly as the treatment is increasing, when the treatment rate was 0.25, the infectious human population rise up to 80 before starting to decrease to zero, the infectious human population reduced to zero while at 0.50 treatment rate, while at 0.75 the infectious human population reduced to zero. Therefore, the simulation indicates that the treatment rate at various interval of isolation play a vital role in decreasing the Lassa Fever disease.

Figure 4.2 shows that the impact of isolation and treatment with human-to-human population on mild symptoms infected human population at different rate of isolation. The population of infectious human is reducing slowly as the treatment is increasing, when the treatment rate is 0.25, the infectious human population rise up to 460 before starting to reduce to zero, while at 0.50 and 0.75. The infectious human population rise up to 390 and 340 respectively before decreasing to zero. Therefore, the simulation shows that as the treatment increase the disease decrease.

Figure 4.3 and 4.4 show a great reduction in the number of infectious human population. It reduced to zero at different rate of isolation. The disease decreases as the treatment increase. Figure 4.5 shows that the impact of isolation only with human-to-human transmission on infected human population at different rate of isolation. The population of infected individuals reduces, when the treatment rate is 0.25, the infectious individuals rise up to 520 before starting to decrease to zero, while at 0.50 and 0.75, the infectious individual rise up to 410 and 360 respectively before starting to decrease to zero. Figure 4.6 exhibits a decreasing prevalence of Lassa fever infection with increasing infection transmission rates $(\gamma = 0.04; 0.18; 0.42)$. The figures reveal that with isolation of the infected human, the disease can be eradicate in the shortest possible time.

Figure 4.7 shows decreasing prevalence of Lassa fever infection with increasing treatment rates $(\alpha = 0.25; 0.50; 0.75)$ with isolation. The stronger the treatment rate the shorter it takes for eradication of the disease. Figure 4.8 considers treatment only without human-to-human transmission on infected human population at different rate of isolation. By increasing treatment rate $(\alpha = 0.04; 0.18; 0.42)$. The disease can be eradicated in shortest possible time. The implication of this result is that effective treatment of infected humans can be useful intervention and eradication of Lassa Fever.

Figure 4.9 consider human population without treatment and isolation at different rate of human-human transmission. The population of infected individuals rise up to 670 at the rate of 0.0015 and 710 at the rate of 0.015 and 0.15 before started to decrease to 30. Thus, for effective preventive strategy, effort should be geared at reducing the infection transmission rate. Figure 4.10 shows the infected human population without human-human transmission, isolation and treatment. Without human-human transmission and in the absence of treatment and isolation. With the basic reproduction number $R_0 < 0$ in each case shows the convergence of the solution profile to the disease-free equilibrium (DFE). Thus, for effective preventive strategy, effort should be geared at reducing the infection transmission rate.

Finally, Figure 4.11 shows the infected human population with varying human-human transmission, treatment and isolation rate $(\alpha = 0.18; \gamma = 0.5)$. This figure shows that with combination of treatment and isolation of infected individuals as a control strategy, is effective for control and eradication of Lassa Fever.

5. Conclusion

This research work, developed a mathematical model to study the transmission dynamics of Lassa Fever. This study modified and extended the model by (Patrick *et al.,* 2020) by incorporating treatment and isolation. The disease-free and endemic equilibrium state were obtained and the basic reproduction number R_0 was computed using the next generation method. We conducted numerical simulation using MATLAB R2021a. Based on the results obtained, it was concluded that infection transmission rate (rodent-to-human and human-to-human) constitute and essential key to preventive strategies against Lassa Fever pandemic. It also shows that effective treatment and isolation of infected human is crucial as a control measure against any pandemics. A mathematical model of Lassa Fever with Isolation and Treatment was developed. The invariant region, positivity of the solution and the basic reproduction number of the model were obtained together with the disease-free and endemic equilibrium point. We also analyzed the local and global stability we also carried out the numerical simulation of the model. The implementation of isolation and treatment is very effective and can significantly curtailed the spread of Lassa Fever.

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