EFFECTS OF SENSITISATION AND EARLY TREATMENT ON FUTURE OUTBREAK OF LASSA FEVER IN NIGERIA

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Abstract

We exploit the dynamics of Lassa fever model with sex structure of the human population with the rat population. The objectives of the research were to: (i) solve for the equilibrium point of the disease free of the model; (ii) obtain basic reproduction number R_0, for the model; (iii) investigate local and global stability of the model; and (iv) analyze the sensitivity of parameters of the model. It was found that the disease free equilibrium point was locally asymptotically stable whenever the basic reproduction number (R_o) is less than one and unstable otherwise. The global stability of the model at disease free equilibrium was found. The analysis of the contribution of each parameter was performed using sensitivity analysis. All positive value parameters are in direct proportionality with the basic reproduction number R_o and all negative value parameters are inversely proportional to the basic reproduction number. Thus, increase in the values of all parameters with positive sensitivity value would increase R_o. Conversely, increase in the value of all parameters with negative sensitivity value would decrease R_o.

Keywords*: Epidemiology, stability analysis, differential equation, theorem.*

INTRODUCTION

The antiviral drug ribavirin seems to be an effective treatment for Lassa fever if given early on in the course of clinical illness. There is no evidence to support the role of ribavirin as post-exposure prophylactic treatment for Lassa fever WHO (2017)[9]. Early detection of disease will lessen the danger of disease endemic related to transmission among persons, particularly among relatives and

medical personnel. Lassa infection has been detached from semen a month and a half after intense ailment; in this manner the infection can be contracted with sexual accomplices by recuperating individuals Tara (2004)[8]. Asogun et al. (2016)[2] researched the direct cost of treatment of Lassa fever for an average Nigerian, which is expensive despite subsidy in medications and investigations by the government. Therefore efforts are geared towards reducing the economic burden of Lassa fever on patients and their families by advocating sensitisation and early treatment model.

Onuorah et al. (2016)[7] formulated a Lassa fever model with sex structure of both the human population and the rat population. In their model, human population were categorized according to their sexes as males and females, then they are subdivided into compartments as Susceptible and Infected males and female respectively. A new approach is proposed owning to the fact that Ribavirin is efficient in exposure prophylactic treatment. Incorporating the Exposed classes for both the male and female compartments in Onuorah et al. (2016)[7]. Below are some assumptions of the model considered.

1. The Exposed/Latent compartment can cause infections.
2. It is assumed that transmission by homosexualism (gay or lesbianism) is ignored.
3. Human population is divided into genders that are male and female.
4. It is assumed that treatments are more effective at the Asymptomatic/Exposed class.
5. It is assumed that Lassa fever occurs at all age groups

MATHEMATICAL FORMULATION OF THE PROBLEM

Based on the above assumptions, the system of nonlinear differential equations are formed, see detail information in tables 1 and 2

$$\left.\begin{aligned}
\frac{dR_1}{dt} &= \pi_r - \sigma R_1 - (\mu_r + \delta_1)R_1 \\
\frac{dR_2}{dt} &= \sigma R_1 - (\mu_r + \delta_1)R_2 \\
\frac{dS_1}{dt} &= \pi_h + \gamma_1 E_1 - G_1 - \mu_h S_1 \\
\frac{dE_1}{dt} &= G_1 - \mu_h E_1 - \gamma_1 E_1 - \varepsilon_1 E_1 \\
\frac{dI_1}{dt} &= \varepsilon_1 E_1 - (\mu_h + \delta_2)I_1 \\
\frac{dS_2}{dt} &= \gamma_2 E_2 + (1-\pi_h) - \mu_h S_2 - G_2 \\
\frac{dE_2}{dt} &= G_2 - \gamma_2 E_2 - \varepsilon_1 E_2 - \mu_h E_2 \\
\frac{dI_2}{dt} &= \varepsilon_2 E_2 - (\mu_h + \delta_2)I_2
\end{aligned}\right\} \quad (1)$$

where

$$G_1 = \beta_1 S_1 E_2 + \beta_2 S_1 I_2 + \beta_3 S_1 R_2 \quad (2)$$

$$G_2 = \beta_4 S_2 E_1 + \beta_5 S_2 I_1 + \beta_6 S_2 R_2 \quad (3)$$

and

$$\sigma = \beta_7 R_2 \quad (4)$$

$R_1(0) \geq 0, R_2(0) \geq 0, S_1(0) \geq 0, E_1(0) \geq 0, I_1(0) \geq 0, S_2(0) \geq 0, E_2(0) \geq 0, I_2(0) \geq 0$ are initial condition of the populations.

Variables and Parameter Description

Below tables show the various state variables and parameters of the Model with meaning

Table 1: Variable description of the Model

State Variable	Description
$R_1(t)$	Dormant Rat compartment
$R_2(t)$	Active Rat compartment
$S_1(t)$	Susceptible male's compartment
$E_1(t)$	Exposed/Asymptomatic male's compartment
$I_1(t)$	Compartment of the infected male
$S_2(t)$	Compartment of the Susceptible female
$E_2(t)$	Exposed/Asymptomatic female's compartment
$I_2(t)$	Infected female's compartment

Table 2: Parameter description of the model

Parameter	Description
π_h	The rate of recruitment of human males either by birth or immigrant.
ε_1	The proportion of uninformed human males to infected class.
γ_1, γ_2	The recovery rates of patients from the Exposed classes.
π_r	The rate of recruitment of Rat to the dormant compartment.
β_1	Force of infections between S_1E_2.
μ_r , μ_h	Natural deaths of the Rats and Human populations respectively.

ε_2	The proportion of uninformed human females to the infected class.
$(1-\pi_h)$	The rate of recruitment of female either by birth or immigrant.
β_7	Force of infection between Dormant Rat and Active Rat population.
δ_1	Death rate of Rats as result of the use of rat poisoning.
δ_2	Death rate of Humans due to infection.
β_2	Force of infection between $S_1 I_2$.
β_3	Force of infection between $S_1 R_2$.
β_4	Force of infection between $S_2 E_1$.
β_5	Force of infection between $S_2 I_1$.
β_6	Force of infection between $S_2 R_2$.

METHOD OF SOLUTION

The Reproduction Number R_0 of the Model

The nature of behaviour of the model is known in the computation of a reproduction number. One of the thresholds that shows disease persistence or dying-off in the given community is the reproduction number, defined as the total number of secondary infectives which one infective would produce in its entire life in population that are completely susceptible. The possibility of a future out-break is known by the value of the basic reproductive number R_o. Driessche and Wathmough (2002), developed the next generation approach to fine the basic reproduction number R_o of Epidemiological models.

Lemma

If x_o is a Disease Free Equilibrium (DFE) of the model above satisfying:

- $x \geq 0$, then $\mathsf{F}_i, \mathsf{V}^-, \mathsf{V}^+ \geq 0$ for $i = 1,2,\cdots,n$
  - If $x_i = 0$ then $\mathsf{V}_i = 0$ (Nobody leaves the compartment)

- $\mathsf{F}_i = 0, i > m$ (m is the number of infective classes)
- If $x \in X_s$, then $\mathsf{F}_i = 0$ and $\mathsf{V}_i = 0$ for all $i = 1,2,\cdots,m$
- If $\mathsf{F}(x)$ is the set to zero then all the eigenvalues of $D\mathsf{F}(x)$ have negative real parts.

then,the negative derivative $D\mathsf{F}(x_o)$ and $D\mathsf{V}(x_o)$ are partitioned as

$$D\mathsf{F}(x_o) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, D\mathsf{V}(x_o) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix} \tag{5}$$

where F and V and $n \times n$ matrices defined by

$$F = \left[\frac{\partial \mathsf{F}(x_o)}{\partial x_j} \right] \quad and \quad V = \left[\frac{\partial \mathsf{V}(x_o)}{\partial x_j} \right] \tag{6}$$

with $1 \le n \le m$. F is non-negative and V is non-singular matrix.

Following Diekmann et al. (1990)[5], the basic reproduction number R_0

$$R_o = \rho(FV^{-1}) \tag{7}$$

Where $\rho(r)$ denotes the spectral radius or largest eigenvalues.

From the governing equation, the following are obtained

The Disease Free Equilibrium (DFE)

$$E_o(S_1, E_1, I_1, S_2, E_2, I_2, R_1, R_2) = (\frac{\pi_h}{\mu_h}, 0, 0, \frac{(1-\pi)}{\mu_h}, 0, 0, \frac{\pi_r}{\mu_r}, 0) \tag{8}$$

$$F = \begin{bmatrix} \frac{\beta_7 \pi_r}{Q_1} & 0 & 0 & 0 & 0 \\ \frac{\beta_3 \pi_h}{\mu_h} & 0 & 0 & \frac{\beta_1 \pi_h}{\mu_h} & \frac{\beta_2 \pi_h}{\mu_h} \\ \frac{\beta_6 (1-\pi_h)}{\mu_h} & \frac{\beta_4 (1-\pi_h)}{\mu_h} & \frac{\beta_5 (1-\pi_h)}{\mu_h} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \tag{9}$$

$$V = \begin{bmatrix} Q_1 & 0 & 0 & 0 & 0 \\ 0 & Q_2 & 0 & 0 & 0 \\ 0 & -\varepsilon & Q_3 & 0 & 0 \\ 0 & 0 & 0 & Q_4 & 0 \\ 0 & 0 & 0 & -\varepsilon_2 & Q_5 \end{bmatrix} \tag{10}$$

where $Q_1 = \mu_r + \delta_1,\ Q_2 = \mu_h + \gamma_1 + \varepsilon_1, Q_3 = \mu_h + \delta_2$ and $Q_4 = \mu_h + \gamma_2 + \varepsilon_2$ Then

$$V^{-1} = \begin{bmatrix} \frac{1}{Q_1} & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{Q_2} & 0 & 0 & 0 \\ 0 & \frac{\varepsilon_1}{Q_2 Q_3} & \frac{1}{Q_3} & 0 & 0 \\ 0 & 0 & 0 & \frac{\varepsilon_2}{Q_3 Q_4} & \frac{1}{Q_3} \end{bmatrix} \tag{11}$$

Therefore,

$$R_o = \rho(FV^{-1}) = \text{Maximum } \mathrm{R_i} \text{ for i} = (1,2) \tag{12}$$

$$R_1 = \frac{\beta_7 \pi_r}{Q_1^2} \tag{13}$$

and

$$R_2 = \frac{\sqrt{Q_2 Q_4 (1-\pi_h)(Q_3^2 \beta_1 \beta_4 + Q_3 \beta_1 \beta_5 + Q_3 \beta_2 \beta_4 \varepsilon_2 + \beta_2 \beta_5 \varepsilon_1 \varepsilon_2)}}{\mu_h Q_2 Q_4 Q_1} \tag{14}$$

By Driessche and Wathmough (2002)[6], the Basic reproduction number for Vector-host model can be written in the form

$$R_o = \sqrt{R_1 R_2} \tag{15}$$

$$R_o = \sqrt{\frac{\beta_7 \pi_r}{Q_1^2} \frac{(Q_2 Q_4 (1-\pi_h)(Q_3^2 \beta_1 \beta_4 + Q_3 \beta_1 \beta_5 + Q_3 \beta_2 \beta_4 \varepsilon_2 + \beta_2 \beta_5 \varepsilon_1 \varepsilon_2))^{1/2}}{\mu_h Q_2 Q_4 Q_1}} \tag{16}$$

Local Stability Analysis of the Model at Disease Free Equilibrium DFE

Theorem 1

The disease free equilibrium of the model is stable if $R_o < 1$ and unstable otherwise.

Proof

The Jacobian matrix of the governing model equations evaluated at disease free equilibrium given as

$$J_o = \begin{bmatrix} -Q_1 & \frac{-\beta_7 \pi_r}{\mu_r} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_7 \pi_r}{\mu_r} - Q_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{-\beta_3 \pi_h}{\mu_h} & -\mu_h & \gamma_1 & 0 & 0 & \frac{-\beta_1 \pi_H}{\mu_h} & \frac{-\beta_2 \pi_h}{\mu_h} \\ 0 & \frac{\beta_3 \pi_h}{\mu_h} & 0 & -Q_2 & 0 & 0 & \frac{\beta_1 \pi_H}{\mu_h} & \frac{\beta_2 \pi_h}{\mu_h} \\ 0 & 0 & 0 & \varepsilon_1 & -Q_3 & 0 & 0 & 0 \\ 0 & \frac{-\beta_6 (1-\pi_h)}{\mu_h} & 0 & \frac{-\beta_4 (1-\pi_h)}{\mu_h} & \frac{-\beta_5 (1-\pi_h)}{\mu_h} & -\mu_h & \gamma_2 & 0 \\ 0 & \frac{\beta_6 (1-\pi_h)}{\mu_h} & 0 & \frac{\beta_4 (1-\pi_h)}{\mu_h} & \frac{\beta_5 (1-\pi_h)}{\mu_h} & 0 & -Q_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \varepsilon_2 & -Q_3 \end{bmatrix} \tag{17}$$

Using the trace-determinant approach, the disease free equilibrium is locally stable if the trace of J_o is less than zero and the determinant of J_o is greater than zero.

As seen from (17), the trace of $J_o < 0$ if

$$\frac{\beta_7 \pi_r}{\mu_r} - Q_1 = Q_1(\frac{\beta_7 \pi_r}{Q_1^2} - 1) = Q_1(R_1 - 1) < 0. \tag{18}$$

Thus, when $R_1 < 1$

Determinant of J_o is given by

$$| J_o | = (\pi_r \beta_7 - Q_1^2)(L\pi_h(Q_3^2 \beta_1 \beta_4 + Q_3 \beta_1 \beta_5 \varepsilon + Q_3 \beta_2 \beta_5 \varepsilon_1 \varepsilon_2) - \mu_h^2 \phi Q_2 Q_3^2 Q_4) \tag{19}$$

$$| J_o | = Q_1^2 (R_1 - 1)(R_2^2 - 1)\mu_h^2 \phi Q_2 Q_3^2 Q_4 \tag{20}$$

$$| J_o | = \mu_h^2 Q_1^2 Q_2 Q_3^2 Q_4 (R_1 - 1)(R_2 + 1)(R_2 - 1) > 0 \tag{21}$$

Thus, the disease free equilibrium is locally asymptotically stable if $R_o < 1$ (that is $R_1 < 1$ and $R_2 < 1$).

Global Stability of the Model at Disease Free Equilibrium

The method outlined in Berhe H.W. and D.M. (2019)[3] shall be used to investigate the global asymptotic stability of the disease free equilibrium of the model. This method entails that, the Model equations be written as

$$X'(t) = F(X, Y) \tag{22}$$

$$Y'(t) = G(X, Y), G(X, 0) = 0 \tag{23}$$

where $X \in R^n$ denotes the number of non infectious individuals and $Y \in R^n$ denotes the number of infected individual. Let $Z_o = (X^*, 0)$ denote the disease free equilibrium of the Model, then Z_o is globally asymptotically stable if the following conditions are satisfied.

(H1) For

$$X'(t) = F(X, Y) \tag{24}$$

X^* is globally asymptotically stable.

(H2) $G(X,Y) = AI - \hat{G}(X,Y) \geq 0$ (25)

for (X,Y) $\in A$

where $A = D_y \hat{G}(X^*,0)$ is an M-matrix.

Theorem 2

The disease free equilibrium $Z_o = (X^*,0)$ is globally asymptotically stable provided $R_o < 1$ and the conditions stated in (H1) and (H2) above are satisfied.

Proof

The governing Model equations are written in the form of noninfectious and infectious classes, so that $X = (R_1, S_1, S_2)^T$, $Y = (R_2, E_1, E_2, I_1, I_2)^T$ and $X^* = (\frac{\pi_r}{Q_1}, \frac{\pi_h}{\mu_h}, \frac{(1-\pi_h)}{\mu_h})^T$ then,

$$F(X,0) = \begin{pmatrix} \pi_r - Q_1 R_1 \\ \pi_h - \mu_h S_1 \\ (1-\pi_h) - \mu_h S_2 \end{pmatrix} \quad (26)$$

and the solution is given by

$$R_1(t) = \frac{\pi_r}{Q_1} e^{Q_1 t} + R_1(0) e^{-Q_1 t} \quad (27)$$

$$S_1(t) = \frac{\pi_h}{\mu_h} e^{\mu_h t} + S_1(0) e^{-\mu_h t} \quad (28)$$

$$S_2(t) = \frac{(1-\pi_h)}{\mu_h} e^{\mu_h t} + S_2(0) e^{-\mu_h t} \quad (29)$$

thus, as $t \to \infty$ $R_1(t) \to \frac{\pi_r}{Q_1}$, $S_1(t) \to \frac{\pi_h}{\mu_h}$ and $S_2(t) \to \frac{(1-\pi_h)}{\mu_h}$ independently of $R_1(0)$, $S_1(0)$ and $S_2(0)$ respectively.

Hence, X^* is globally asymptotically stable and (H1) is satisfied. Next,

$$\hat{G}(X,Y) = \begin{bmatrix} \frac{\beta_7\pi_r}{\mu_r} - Q_1 & 0 & 0 & 0 & 0 \\ \frac{\beta_3\pi_h}{\mu_h} & -Q_2 & 0 & \frac{\beta_1\pi_h}{\mu_H} & \frac{\beta_2\pi_h}{\mu_h} \\ 0 & \varepsilon_1 & -Q_3 & 0 & 0 \\ \frac{\beta_6(1-\pi_h)}{\mu_h} & \frac{\beta_4(1-\pi_h)}{\mu_h} & \frac{\beta_5(1-\pi_h)}{\mu_h} & Q_4 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} R_2 \\ E_1 \\ I_1 \\ E_2 \\ I_2 \end{bmatrix} - \begin{bmatrix} \beta_7 R_2 R_2 - Q_1 R_2 \\ (\beta_1 E_2 + \beta_2 I_2 + \beta_3 R_2) S_1 - Q_2 E_1 \\ \varepsilon_1 E_2 - Q_3 I_1 \\ (\beta_4 E_1 + \beta_5 I_1 + \beta_6 R_2) S_2 - Q_4 E_2 \\ \varepsilon_2 E_2 - Q_3 I_2 \end{bmatrix} \tag{30}$$

$$\hat{G}(X,Y) = \begin{bmatrix} \beta_7 R_2 (\frac{\pi_r}{\mu_r} - R_1) \\ (\beta_3 R_2 + \beta_2 I_2 + \beta_1 E_2)(\frac{\pi_h}{\mu_h} - S_1) \\ 0 \\ (\beta_4 E_1 + \beta_5 I_1 + \beta_6 R_2)(\frac{1-\pi_h}{\mu_h} - S_2) \\ 0 \end{bmatrix} \tag{31}$$

Since $\frac{\pi_r}{\mu_r} \geq R_1$, $\frac{\pi_h}{\pi_h} \geq S_1$ and $\frac{1-\pi_h}{\mu_h} \geq S_h$ thus, $\hat{G}(X,Y) \geq 0$. This satisfies condition (H2), hence the disease free equilibrium is globally asymptotically stable.

Sensitivity Analysis of the Model

Relative importance of key parameters in Mathematical modeling are examined via the sensitivity analysis. Here, various parameters responsible for the disease transmission in two Models are analyzed. A recent example is the work of Onuorah et al. (2016)[7] and Abdullahi et al. (2015)[1]. The sensitivity quantity R_o with respect to the various parameter is given as

$$\Upsilon_{kj}^{R_o} = \frac{\partial R_o}{\partial k_j} \times \frac{k_j}{R_o} \tag{32}$$

Where k_j stands for the various parameters of the Models. The tables below show sensitivity analysis of parameters of the model.

Table 3: **Sensitivity Analysis of the Model**

Parameter	**Value**	**References**	**Sensitivity**
π_r	0.0020	Assumed	+0.5000
π_h	0.0380	CIA (2015)[4]	+0.0001
β_1	0.4200	Onuorah et al. (2016)[7]	+0.2460
β_2	0.5000	Onuorah et al. (2016)[7]	+0.0003
β_3	0.3200	Onuorah et al. (2016)[7]	+0.0001
β_4	0.5000	Onuorah et al. (2016)[7]	+0.0049
β_5	0.5000	Onuorah et al. (2016)[7]	+0.2451
β_6	0.5000	Onuorah et al. (2016)[7]	+0.0000
β_7	0.0320	Onuorah et al. (2016)[7]	+0.5000
δ_1	0.0010	Onuorah et al. (2016)[7]	-0.0033
δ_2	0.0010	Onuorah et al. (2016)[7]	+0.2144
γ_1	0.3000	Onuorah et al. (2016)[7]	+0.2459
γ_2	0.2000	Onuorah et al. (2016)[7]	-0.4902
μ_h	0.0030	Onuorah et al. (2016)[7]	+0.0353
μ_r	0.4500	Onuorah et al. (2016)[7]	-1.4966

Interpretation of Sensitivity Index for R_o

In the above table, all positive value parameters are in directly proportional to the basic reproduction number R_o and all negative value parameter are inversely proportional to the basic reproduction number. Increase in the values of all parameters with positive sensitivity index would increase R_o while increase in the values of all parameters with negative sensitivity index would decrease R_o

CONCLUSION

This research work focused on the dynamics of lassa fever in Nigeria. A deterministic model of a system of nonlinear differential equations formulated was analysed. Existence of Disease Free Equilibrium (DFE) of model was found. The basic reproduction number R_o was calculated for the model to establish the important threshold parameter that either culminates in disease spread or its removal. Local and global stabilities at Disease Free Equilibrium were established. Sensitivity analysis of parameters of the Model revealed that reduction of parameter values like "forces of infection" lead to reduction of basic reproduction number while increase in parameter values like recovery rates result to reduction of the basic reproduction number.

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