STABILITY ANALYSIS OF THE DISEASE-FREE EQUILIBRIUM STATE FOR LASSA FEVER DISEASE

Bawa, M.[*], Abdulrahman, S.[**], Jimoh, O. R.[**] & Adabara, N. U.[***]
[*]Department of Mathematics, Ibrahim Badamasi Babangida University, Lapai
[**]Department of Mathematics and Statistics, Federal University of Technology, Minna
[***]Department of Microbiology, Federal University of Technology, Minna
E-mail.: sirajo.abdul@futminna.edu.ng; Phone No: +234-805-8259616

Abstract
In this paper, we developed a deterministic model for Lassa fever disease in a population with vital dynamics, incorporating standard incidence rate, disease induced death and infection due to humans, reservoirs and aerosol (airborne) transmissions. We obtained the basic reproduction number, R_0 which can be use to control the transmission dynamics of the disease and thus, established the conditions for local and global stability of the disease-free equilibrium.

Keywords: Lassa fever, Disease-free equilibrium state, Basic reproduction number, Stability.

Introduction
Lassa fever is an acute viral illness caused by Lassa virus, named after Lassa town in Nigeria from where the first cases originated. Lassa virus is known to be responsible for a severe hemorrhagic fever characterized by fever, muscle aches, sore throat, nausea, vomiting, and chest and abdominal pain (Centers for Disease Control and Prevention, 2004). The disease is endemic in West Africa and has been reported in Sierra Leone, Guinea, Liberia, and Nigeria (Ogbu, Ajuluchukwu & Uneke, 2007). The number of Lassa fever virus infections per year in West Africa is estimated at about 300,000 to 500,000 with approximately 5000 deaths (World Health Organization, 2005). The most common complication of Lassa fever after recovery is deafness.

The reservoir of the Lassa virus is a small rodent, 'the multimammate rat' of the genus Mastomys. Since the rodent lives in a semi-domestic fashion near human dwellings, rodent-to-human transmission of the virus occurs via direct contact when they are caught and prepared for food. Human-to-human transmission may also occur when a person comes into contact with the virus in the blood, tissue, secretions, or excretions of an infected person. Furthermore, contact with the virus may occur when a person inhales tiny particles in the air contaminated with Lassa virus from infected humans or reservoirs urine or feces. This is called aerosol or airborne transmission, and is believe to be most significant means of exposure. The virus cannot be spread through casual contact (including skin-to-skin contact without exchange of body fluids) (Centers for Disease Control and Prevention, 2013).

In order to find an efficient way to control (prevent and treat) an infection, it is of great importance to establish its transmission dynamics. One main goal of mathematical epidemiology is to understand how to control and eradicate diseases (J. Ma & Z. Ma, 2006). Mathematical models are used extensively in the study of ecological and epidemiological phenomena (Kaplan & Brandeau, 1994). They are particularly helpful as experimental tools with which to evaluate and compare control procedures and preventive strategies, and to investigate the relative effects of various sociological, biological and environmental factors on the spread of diseases. This is so because they can help in figuring out decisions that are of significance importance on the outcomes and provide comprehensive examinations that enter into decisions in a way that human reasoning and debate cannot.

A mathematical model for Lassa fever was developed by (Okuonghae & Okuonghae, 2006) with three (3) compartments of Susceptible humans (*S*), Infected humans (*I*) and the rodent carrying the virus (*V*). Human-to-human (α) and rodent-to-human (β) infection contact rates were incorporated. They obtained the basic reproduction number, R_0 and established conditions for local stability of both the disease and endemic equilibria. In a similar development [8] developed an SIR model for controlling Lassa fever transmission in Northern part of Edo state, Nigeria with λ as the transmission rate of the disease. In this work, we therefore complement and extend the works of the aforementioned authors by having five (5) compartments of Susceptible humans (S_H), Infected humans (I_H), Infant reservoirs (I_R), Adult reservoirs (A_R), and Lassa virus in the environment (V). We also incorporated vital dynamics, standard incidence rate, disease induced death and human-to-human (β_1), rodent-to-human (β_2) and aerosol (β_3) infection contact rates.

Model Formulation

The S_H population are generated from daily recruitment of individuals through birth and recovery from infection given by $b_H N_H$ and γI_H respectively. They acquired infection and move to the I_H compartment via infection from I_H, A_R and V, given by $\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N_H}$. Natural death occurs in S_H and I_H classes at a rate μ_H. Individuals in the I_H compartment suffer additional death due to diseases at the rate δ_H.

Similarly, the I_R population are generated from daily recruitment through birth, given by $b_R A_R$. They progresses to A_R at the rate σ. Natural death and death due to hunting occurs in both I_R and A_R classes at a rate μ_R and δ_R respectively.

The V compartment is generated from urine and faeces of infected individuals and adult reservoirs at the rates e_H and e_A respectively. The virus is reduced from the environment due to natural death and other environmental factors.

The corresponding mathematical equations of the above description are given by a system of ordinary differential equations below:

$$\frac{dS_H}{dt} = b_H N_H - \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N_H} \right) S_H + \gamma I_H - \mu_H S_H \quad (1)$$

$$\frac{dI_H}{dt} = \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N_H} \right) - \left(\gamma + \mu_H + \delta_H \right) I_H \quad (2)$$

$$\frac{dI_R}{dt} = b_R A_R - \left(\sigma + \mu_R + \delta_R \right) I_R \quad (3)$$

$$\frac{dA_R}{dt} = \sigma I_R - \left(\mu_R + \delta_R \right) A_R \quad (4)$$

$$\frac{dV}{dt} = e_H I_H + e_R A_R - \phi V \quad (5)$$

where,

$$N_H(t) = S_H(t) + I_H(t) \quad (6)$$

and

$$N_R(t) = I_R(t) + A_R(t) \quad (7)$$

so that

$$\frac{dN_H}{dt} = (b_H - \mu_H)N_H - \delta_H I_H \quad (8)$$

and

$$\frac{dN_R}{dt} = (b_R - \mu_R - \delta_R)N_R \quad (9)$$

in the biological - feasible region:

$$\Omega = \left\{ \begin{array}{l} (S_H, I_H, I_R, A_R, V) \in \Re_+^5 : 0 \le S_H, 0 \le I_H, 0 \le I_R, 0 \le A_R, 0 \le V; \\ \qquad\qquad S_H + I_H = N_H; \; I_R + A_R = N_R \end{array} \right\} \quad (10)$$

which can be shown to be positively invariant with respect to the system (1) – (5).

The symbols used in the model are listed below:

S_H	Susceptible humans
I_H	Infected humans
I_R	Infant reservoirs
A_R	Adult reservoirs
V	Lassa virus in the environment
N_H	Total number of human population
N_R	Total number of reservoirs population
b_H	Per capital birth rate of humans
b_R	Per capital birth rate of the reservoirs
μ_H	Per capital natural death rate of humans
μ_R	Per capital natural death rate of reservoirs
δ_H	Lassa fever-induced death rate
δ_R	Mortality rate of reservoirs due to hunting
β_1	Effective contact rate for humans
β_2	Effective contact rate between reservoirs and human
β_3	Effective contact rate between Lassa virus and human (airborne transmission)
γ	Rate of recovery from I_H to S_H
σ	Progression rate from I_R to A_R

e_I Contribution of infected individual's to Lassa virus in the environment

e_A Contribution of adult reservoir to Lassa virus in the environment

ϕ Loss rate of Lassa virus in the environment

3. Model Analysis

3.1 Existence of disease-free equilibrium state, E_f

At the disease-free equilibrium state we have absence of infection. Thus, all the infected classes will be zero and the entire population will comprise of only susceptible individuals.

Theorem 1: A disease-free equilibrium state of the model exists at the point

$$E_f = \left(S_H^*, I_H^*, I_R^*, A_R^*, V^*\right) = \left(\frac{b_H N_H^*}{\mu_H}, 0, 0, 0, 0\right)$$

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

$$\frac{dS_H}{dt} = \frac{dI_H}{dt} = \frac{dI_R}{dt} = \frac{dA_R}{dt} = \frac{dV}{dt} = 0 \quad (11)$$

Let

$$\left(S_H, I_H, I_R, A_R, V\right) = \left(S_H^*, I_H^*, I_R^*, A_R^*, V^*\right) \quad (12)$$

at equilibrium state. Then from equations (1) - (5), (11) and (12) we have

$$b_H N_H^* - \left(\frac{\beta_1 I_H^* + \beta_2 A_R^* + \beta_3 V^*}{N_H^*}\right) S_H^* + \gamma I_H^* - \mu_H S_H^* = 0 \quad (13)$$

$$\left(\frac{\beta_1 I_H^* + \beta_2 A_R^* + \beta_3 V^*}{N_H^*}\right) S_H^* - \left(\gamma + \mu_H + \delta_H\right) I_H^* = 0 \quad (14)$$

$$b_R A_R^* - \left(\sigma + \mu_R + \delta_R\right) I_R^* = 0 \quad (15)$$

$$\sigma I_R^* - \left(\mu_R + \delta_R\right) A_R^* = 0 \quad (16)$$

$$e_I I_H^* + e_A A_R^* - \phi V^* = 0 \quad (17)$$

Now, from (15), we have

$$I_R^* = \frac{b_R A_R^*}{\left(\sigma + \mu_R + \delta_R\right)} \quad (18)$$

Substituting (18) into (16), we have

$$A_R^* \left(\frac{\sigma b_R - \left(\mu_R + \delta_R\right)\left(\sigma + \mu_R + \delta_R\right)}{\left(\sigma + \mu_R + \delta_R\right)}\right) = 0 \quad (19)$$

Thus,

$$A_R^* = 0 \quad (20)$$

or

$$\left(\sigma b_R - \left(\mu_R + \delta_R\right)\left(\sigma + \mu_R + \delta_R\right)\right) = 0 \quad (21)$$

Now, substituting (20) into (16), we obtained

$$I_R^* = 0 \quad (22)$$

and then substituting (20) and (22) into (17), we obtained

$$V^* = 0 \quad (23)$$

Thus, we have

$$I_R^* = A_R^* = V^* = 0 \quad (24)$$

Next, we consider equation (13) and (14) - the human sub-populations. Substituting (24) into (13), we have

$$S_H^* = \frac{\left(b_H N_H^* + \gamma I_H^*\right) N_H^*}{\left(\beta_1 I_H^* + \mu_H N_H^*\right)} \quad (25)$$

Substituting (24) and (25) into (14), we have

$$I_H^* \left(\frac{\beta_1 \left(b_H N_H^* + \gamma I_H^*\right) - \left(\gamma + \mu_H + \delta_H\right)\left(\beta_1 I_H^* + \mu_H N_H^*\right)}{\left(\beta_1 I_H^* + \mu_H N_H^*\right)} \right) = 0 \quad (26)$$

Thus,

$$I_H^* = 0 \quad (27)$$

or

$$\left(\beta_1 S_H^* - \left(\gamma + \mu_H + \delta_H\right) N_H^*\right) = 0 \quad (28)$$

Thus, substituting (27) into (25), we obtained

$$S_H^* = \frac{b_H N_H^*}{\mu_H} \quad (29)$$

Hence, a disease-free equilibrium of the model exists at:

$$E_f = \left(S_H^*, I_H^*, I_R^*, A_R^*, V^*\right) = \left(\frac{b_H N_H^*}{\mu_H}, 0, 0, 0, 0 \right) \quad (30)$$

3.2 Effective basic reproduction number, R_c

One of the most important concerns about any infectious disease is its ability to invade a population. The basic reproduction number, R_0 is a measure of the potential for disease spread in a population, and is inarguably "one of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory" (Heesterbeek & Dietz, 1996). It represents the average number of secondary cases generated by an infected individual if introduced into a susceptible population with no immunity to the disease in the absence of interventions to control the infection. If $R_0 < 1$, then on average, an infected individual produces less than one newly infected individual over the course of his infection period. In this case, the infection may die out in the long run. Conversely, if $R_0 > 1$, each infected individual produces, on average more than one new infection, the infection will be able to spread in a population. A large value of R_0 may indicate the possibility of a major epidemic.

Using the next generation operator technique described by (Diekmann & Heesterbeek, 2000) and subsequently analyzed by (Vanden & Watmough, 2005), we obtained the basic reproduction number, R_0 of the model equations (1) - (5) which is the spectral radius (ρ) of the next generation matrix, K.

i.e.

$R_C = \rho K$, where $K = FV^{-1}$

Now,

$$F = \begin{pmatrix} \frac{\beta_1 b_H}{\mu_H} & 0 & \frac{\beta_2 b_H}{\mu_H} & \frac{\beta_3 b_H}{\mu_H} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} K_1 & 0 & 0 & 0 \\ 0 & K_2 & -b_R & 0 \\ 0 & -\sigma & K_3 & 0 \\ -e_I & 0 & -e_A & \phi \end{pmatrix}$$

where

$$K_1 = \gamma + \mu_H + \delta_H \quad (31a)$$

$$K_2 = \sigma + \mu_R + \delta_R \quad (31b)$$

$$K_3 = \mu_R + \delta_R \quad (31c)$$

Thus,

$$R_0 = \frac{b_H}{(\gamma + \mu_H + \delta_H)\mu_H}\left(\beta_1 + \frac{e_I \beta_3}{\phi}\right) \quad (32)$$

3.3 Local stability of disease free equilibrium, E_f

We used the Jacobian stability approach to prove the stability of the disease-free equilibrium state. Using the relation

$$I_R = N_R - A_R \quad (33)$$

allows us as explained in (Hethcote, 2000) and (Benyah, 2013) to attack (1) - (5) by studying the subsystem:

$$\frac{dS_H}{dt} = b_H N_H - \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N_H}\right) S_H + \gamma I_H - \mu_H S_H \quad (34)$$

$$\frac{dI_H}{dt} = \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N_H}\right) S_H - (\gamma + \mu_H + \delta_H) I_H \quad (35)$$

$$\frac{dA_R}{dt} = \sigma(N_R - A_R) - (\mu_R + \delta_R) A_R \quad (36)$$

$$\frac{dV}{dt} = eI_H + eA_R - \phi V \quad (37)$$

Linearization of the equations (34) - (37) at E_f, gives the Jacobian matrix

$$J(E_f) = \begin{pmatrix} -\mu_H & -\left(\frac{\beta_1 b_H}{\mu_H} - \gamma\right) & -\frac{\beta_2 b_H}{\mu_H} & -\frac{\beta_3 b_H}{\mu_H} \\ 0 & -\left(K_1 - \frac{\beta_1 b_H}{\mu_H}\right) & \frac{\beta_2 b_H}{\mu_H} & \frac{\beta_3 b_H}{\mu_H} \\ 0 & 0 & -(\sigma + K_3) & 0 \\ 0 & e_I & e_A & \phi \end{pmatrix} \quad (38)$$

Using elementary row-transformation, we have

$$J\left(E_f\right)=\begin{pmatrix} -\mu_H & -\left(\frac{\beta_1 b_H-\gamma\mu_H}{\mu_H}\right) & -\frac{\beta_2 b_H}{\mu_H} & -\frac{\beta_3 b_H}{\mu_H} \\ 0 & -\left(\frac{K_1\mu_H-\beta_1 b_H}{\mu_H}\right) & \frac{\beta_2 b_H}{\mu_H} & \frac{\beta_3 b_H}{\mu_H} \\ 0 & 0 & -\left(\sigma+K_3\right) & 0 \\ 0 & 0 & 0 & M \end{pmatrix} \quad (39)$$

where

$$M=\frac{-\phi\left(K_1\mu_H-\beta_1 b_H\right)+e_I\beta_3 b_H}{\left(K_1\mu_H-\beta_1 b_H\right)} \quad (40)$$

Thus, the eigenvalues are

$$\lambda_1=-\mu_H<0,\ \lambda_2=-\left(K_1-\frac{\beta_1 b_H}{\mu_H}\right)<0,\ \lambda_3=-\left(\sigma+K_3\right)<0$$

and

$$\lambda_4=M=\frac{-\phi\left(K_1\mu_H-\beta_1 b_H\right)+e_I\beta_3 b_H}{\left(K_1\mu_H-\beta_1 b_H\right)}$$

now, for λ_4 to be negative, we must have

$$\frac{-\phi\left(K_1\mu_H-\beta_1 b_H\right)+e_I\beta_3 b_H}{\left(K_1\mu_H-\beta_1 b_H\right)}<0.$$

simplifying, we have

$$\frac{b_H}{\left(\gamma+\mu_H+\delta_H\right)\mu_H}\left(\beta_1+\frac{e_I\beta_3}{\phi}\right)<1.$$

Thus, $\lambda_4<0$ if $R_0<1$ implying all the eigenvalues have negative real parts, we therefore, established the following result.

Theorem 2: The disease-free equilibrium E_f of the model is locally asymptotically stable (LAS) if $R_0<1$.

3.4 Global stability of disease free equilibrium, E_f

The epidemiological implication of the theorem is that Lassa fever can be eliminated (control) from the population when $R_0<1$, if the initial size of the sub-populations of the model are in the basin of attraction of the DFE.

In order to ensure that the disease is independent of the initial size of the sub-populations of the model, it is necessary to show that the DFE is globally- asymptotically stable (GAS). One common approach in studying the global asymptotic stability of the DFE is to construct an appropriate Lyapunov function.

Theorem 3: The disease- free equilibrium E_f of (1) - (5) is globally asymptotically stable (GAS) in Ω if $R_0\le 1$.

Proof: Consider the Lyapunov function:

$$L = e_H I_H + (\gamma + \mu_H + \delta_H)V \quad (41)$$

its derivatives along the solutions of the model equations is

$$L' = e_I I_H{}' + (\gamma + \mu_H + \delta_H)V' \quad (42)$$

$$= e_I \left\{ \left(\frac{\beta_1 I_H + \beta_2 A_R + \beta_3 V}{N_H} \right) S_H - (\gamma + \mu_H + \delta_H) I_H \right\}$$

$$+ (\gamma + \mu_H + \delta_H)\{e_I I_H + e_A A_R - \phi V\}$$

$$= \frac{e_I \beta_1 I_H S_H}{N_H} + \frac{e_I \beta_2 A_R S_H}{N_H} + \frac{e_I \beta_3 V S_H}{N_H} + (\gamma + \mu_H + \delta_H) e_A A_R - (\gamma + \mu_H + \delta_H)\phi V$$

$$= \frac{e_I \beta_2 A_R S_H}{N_H} + (\gamma + \mu_H + \delta_H) e_A A_R$$

$$+ \frac{(\gamma + \mu_H + \delta_H)\phi V S_H}{N_H} \left\{ \frac{e_I I_H \beta_1}{\phi(\gamma + \mu_H + \delta_H)V} + \frac{e_I \beta_3}{(\gamma + \mu_H + \delta_H)\phi} - 1 \right\}$$

Now, since $S_H \le \frac{b}{\mu}$ and $\frac{e_I I_H}{\phi V} \le \frac{e_I I_H + e_A A_R}{\phi V}$, we have

$$L' \le (\gamma + \mu_H + \delta_H)\phi V \left\{ \frac{b_H}{\mu_H (\gamma + \mu_H + \delta_H)} \left(\beta_1 + \frac{e_I \beta_3}{\phi} \right) - 1 \right\}$$

i.e.

$$L' \le (\gamma + \mu_H + \delta_H)\phi V \{R_0 - 1\}$$

when $R_0 \le 1$, $L' \le 0$; the equality $L' = 0$ holds when $R_0 = 1$ and $V = 0$. Thus $V = 0$ is the largest invariant subset in the set $L' = 0$. Thus, according to the asymptotical stability theorem of Lyapunov-LaSalle theorem (see (Miller & Michel, 1982), E_f is overall globally asymptotically stable in $\Re_+^5$ and hence, the result is proved.

Conclusion

In this paper, we developed a new mathematical model which incorporated some important factors that plays significant role in the transmission dynamics and control of Lassa fever. These factors are: vital dynamics, standard incidence, disease induced death and infection due to humans, reservoirs and aerosol (airborne) transmissions. We obtained the basic reproduction numbers, R_0. Our analysis reveals that the disease can be control if the basic reproduction number, 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.

Finally, there is need for further research work on the effects of various control strategy such as vaccination, personal hygiene and hunting on the transmission dynamics of Lassa fever disease.

References

Benyah, F. (2008). *Introduction to epidemiological modelling.* 10th Regional College on Modeling Simulation and Optimization, University of Cape Coast, Ghana.

Centers for Disease Control and Prevention (2013). Lassa fever fact sheet.

Centers for Disease Control and Prevention. Imported Lassa fever. MMWR Morb Mortal Wkly Rep. 53(38), 894-897 (2004).

Diekmann, O. & Heesterbeek, J. A. P. (2000). *Mathematical epidemiology of infectious diseases: Model building, analysis and integration.* New York: John Wiley.

Heesterbeek, J. A. P. & Dietz, K. (1996). The concept of R_0 in epidemic theory. Stat. Neerl. 50, 89-110.

Hethcote, W. (2000). The mathematics of infectious diseases. *SIAM Review. 42(4), 599-653.*

Kaplan, E. & Brandeau, M. (1994). *Modelling AIDS and the AIDS Epidemic.* New York: Raven.

Ma, J. & Ma, Z. (2006). Epidemic threshold conditions for seasonally forced SEIR models. *Journal of Mathematical Biosciences and Engineering, 3(1),161 – 172.*

Miller, R. K. & Michel, A. N. (1982). *Ordinary differential equations.* New York: Academic Press.

Ogabi, C. O., Olusa, T. V. & Madufor, M. A. (2012). Controlling Lassa fever in Northern part of Edo State, Nigeria, Using SIR Model. *New York Sci. J., 5(12),190 - 197.*

Ogbu, O., Ajuluchukwu, E. &. Uneke, C. J. (2007). Lassa fever in West Africa sub-region: An overview. *J. Vect. Borne Dis. 44, 1-11.*

Okuonghae, D. & Okuonghae, R. (2006). A mathematical model for Lassa fever. *J. of the Nigerian Ass. of Math. Physics, 10, 457 - 464.*

Vanden, P. D. & Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences, 180, 29 – 48.*

World Health Organization (2005). Lassa fever Newsletter. Geneva.