BERKELEY PUBLICATION
AND RESEARCH INTERNATIONAL
09.30.2020
Journal of Med., Biological and Pharm. Sci. Vol. 13 No. 3

ON THE STABILITY ANALYSIS OF LASSA FEVER TRANSMISSION DYNAMICS

YUSUF BALAA*, KALABU SALISU AHMADA, ABDUL AUDU IBRAHIMA, IBRAHIM YUSUF INUWAA & AMINU HARUNAA
Department of Mathematics and Statistics, Federal Polytechnic Bauchi, Bauchi State.

ABSTRACT

In this research, a Lassa fever mathematical model has been developed. A non-linear ordinary differential equations were formulated to study the transmission dynamic of the model. We used the next generation operator method to obtain the basic reproduction number R_0, *which can be used to control the transmission dynamics of the disease. The local and global stability of the disease free- equilibrium were determined using Routh- Hurwitz criterion and Castillo-Chavez approach respectively. The disease-free equilibrium and the endemic equilibrium points were also obtained. The result of the analysis shows that, the disease-free equilibrium point is locally and globally asymptotically stable when the basic reproduction number* $R_0 < 1$ *and unstable when* $R_0 > 1$. *This simply means Lassa fever disease can*

Introduction:

Lassa fever is a viral disease that attacks the liver, nervous system, spleen and kidney. It is an acute viral hemorrhagic fever (VHF) first isolated in a town called Lassa in the *Yedseram* River Valley in the present Borno State of Northern Nigeria in 1969 (Tara, 2004; Akinpelu and Akinwande, 2018). It can also be defined as a zoonotic disease caused by Lassa virus (LASV), and is endemic in several West African countries, including Guinea, Liberia, Nigeria, and Sierra Leone; disease occurs both sporadically and as outbreaks (World Health Organization, 2018). However, some Lassa fever cases have been imported in the U.S and U.K through travelers who acquire the disease elsewhere

ISSN: 1211-4401

be controlled when the number of secondary infection is kept at barest minimum.

Keywords: *Lassa fever, model, Stability analysis, Transmission*

Tara, 2004). Population studies demonstrating serologic evidence of LASV infection and the presence of occasional sporadic Lassa fever cases in additional West African countries (i.e., Benin, Burkina Faso, Ghana, the Ivory Coast, Mali, and Togo) indicate that other areas of the region also may be at risk. *Mastomys natalensis* (i.e., the multimammate mouse which also is known as the multimammate rat) has long been considered the sole natural reservoir of LASV, but additional rodent reservoirs (*M. erythroleucus* and *H. pamfi*) recently have been discovered and may affect the distribution of Lassa fever. Primary transmission of the virus from animal hosts to humans typically occurs via exposure to excreta (urine or feces) or blood from LASV-infected rodents. Person-to-person and laboratory transmissions occur to a lesser extent and result from direct contact with the blood, tissue, urine, feces, or bodily secretions of an LASV-infected individual or reuse of contaminated medical equipment (World Health Organization, 2018).

Although public health officials often cite annual case estimates of 100,000 to 300,000 LASV infections and up to 5,000 deaths, these numbers are extrapolations from a single longitudinal study conducted over 30 years ago in Sierra Leone. The true public health burden of Lassa fever is unknown and represents a crucial gap in understanding the relative impact of Lassa fever in the affected West African countries. Existing Lassa fever surveillance data are limited and/or biased because they typically have been collected in conjunction with biomedical research projects located in areas where the disease already is recognized to be endemic. In contrast, seroprevalence studies in non-endemic areas have suggested high numbers of previously unrecognized infections, and more recent surveillance reports have observed substantial increases in the number and geographic spread of cases. Thus, the true incidence and spatial distribution of Lassa fever may be significantly underestimated. LASV

infection causes a wide spectrum of clinical manifestations; an estimated 80% of people with LASV infections have no or mild symptoms (and often are unrecognized and unreported), while the remaining 20% may progress to severe and life-threatening disease requiring hospitalization. Among survivors, the most common long-term *sequela* of Lassa fever is sensor neural hearing loss. The onset of Lassa fever is gradual and nonspecific with an incubation period ranging from 2 to 21 days; thus, it is clinically difficult to distinguish Lassa fever from other febrile illnesses that occur in West Africa such as malaria, typhoid, yellow fever, dengue, and Ebola virus disease (EVD) (WHO, 2018).

The onset of the disease, when it is symptomatic, is usually gradual, starting with fever, general weakness, and malaise. After a few days, headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhea, cough, and abdominal pain may follow. In severe cases facial swelling, fluid in the lung cavity, bleeding from the mouth, nose, vagina or gastrointestinal tract and low blood pressure may develop. Clinical diagnosis is often difficult, especially early in the course of the disease (WHO, 2018).

Lassa virus infections can only be diagnosed definitively in the laboratory using RT-PCR, ELISA, Antigen detection tests, or virus isolation. None of those tests are currently licensed. Early supportive care with rehydration and symptomatic treatment improves survival. Ribavirin has been widely used off-label to treat patients with LF based on the results of one clinical study performed in Sierra Leone in the 80's. Lastly, there is no licensed vaccine (WHO, 2018).

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 and Sani, 2015; WHO, 2012). A total of 11 confirmed cases of Lassa were recorded in Nigeria with high prevalence in Oyo State in 2014. Between January 1st and 8th of March 2015, the Nigerian Center for Disease Control (NCDC) reported 21 cases of Lassa fever (4Lab. Confirmed) and 1death due to Lassa (WHO, 2015; CDC, 2015). Between August 2015 and January 2016,

there were 239 suspected cases of LF (44 Lab. Confirmed), including 82 deaths, across 19 states including; Bauchi, Nassarawa, Niger, Delta, Ekiti, Ondo, Kogi, Ebonyi, Lagos, Osun, FCT, Taraba, Kano, Rivers, Edo, Plateau, Gombe, Oyo States etc. (NCDC, 2016; WHO, 2016). Similarly the year 2016, 2017, 2018 and 2019 were not spared from Lassa fever in Nigeria with outbreaks across several states (Bakare, Are, Abolarin, Osanyinlusi, Ngwu Benitho and Ubaka Obiaderi, 2019).

For instance, in early 2018, Nigeria has witnessed an unprecedented LF outbreak, whereby the usual annual observed LF burden has been concentrated into one trimester. From 1st January to 29th April 2018, a total of 1878 suspected cases have been reported from 21 states. Of these, 420 were confirmed positive (WHO, 2018). Similarly, there were 1374 suspected with 420 confirmed cases and 93 confirmed death from week 1 to week 9 of 2019 from 21 states across 66 L .G .A, while around the same period in 2020, there were 3054 suspected cases, 775 confirmed positive cases and 132 confirmed death from 27 states across 118 L. G. A. (Nigeria center for disease control, 2020).This shows that there is a significant increase in suspected cases almost every year, hence the need for more research in order to curtail the spread of Lassa fever within the population. Mathematical modeling of Lassa fever has been employed by various researchers to study the dynamics of the disease transmission. Faniran (2017) presents a mathematical model that tracks the transmission dynamics of Lassa fever in a two-interacting human host and rodent vector populations. The model in-corporates a non-drug compliance rate in the parameters for the human population. The basic reproduction number is derived and the stability of the disease-free and endemic equilibrium points were analyzed. Bakare et'al (2019) presented a periodically-forced seasonal non-autonomous system of a non-linear ordinary differential equation developed to captures the dynamics of Lassa fever transmission and seasonal variation in the birth of mastomys rodents where time was measured in days to capture seasonality. It was shown that the model is epidemiologically meaningful and mathematically well-posed by using the results from the qualitative properties of the solution of the model. Akinpelu and Akiwande (2018) formulated a Lassa fever disease model

with sensibility analysis. The equilibrium states, basic reproduction number were obtained using generation matrix and their stabilities were analyzed using Descartes' rule of sign and comparison test. Their results show that the disease free equilibrium is locally and globally asymptotically stable when $\beta\pi y < \mu(y+\mu+\theta_1)(\mu+\delta+\theta_2)$. Finally, they carried out sensitivity analysis and it is shown that the parameter β is the most sensitive. James, Akinyemi and Bamidele (2016) presented a deterministic model for Lassa fever transmission in the presence of quarantine and permanent immunity. The model was validated for existence and uniqueness of solution. The threshold parameter for disease eradication R_0, was computed and used to investigate its global stability using Lyapunov function such that whenever $R_0 < 1$, the disease can be eradicated. Bawa, Abdulrahman, Jimoh and Adabara (2013) 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. They obtained the basic reproduction number, R_0, which can be used to control the transmission dynamics of the disease and thus, established the conditions for local and global stability of the disease-free equilibrium.

In this paper, we complement and extend on the work of Akinpelu and Akinwande (2018) by incorporating vector-to-human, vector-to-vector transmission and standard incidence rate in to the Lassa fever model with a view to study the dynamics of the disease transmission in the presence of Isolation of infected persons.

Model formulation

The model is partitioned in to eight (8) compartments which consists of human sub-population and vector (rodents) sub-population. The human population include susceptible human at time t, $S_h(t)$, the latently infected with Lassa fever virus at time t, $L_h(t)$, the infected human at time t, $I_h(t)$, the

isolated human after being infected with Lassa fever virus at time t, $I_s(t)$, the recovered human from Lassa fever infection at time t, $R_h(t)$. On the other hand, the vector (rodents) population composed of susceptible vector at time t, $S_v(t)$, the latently infected vector at time t, $L_v(t)$ and the infected vector at time t, $I_v(t)$. The total human and vector populations are given by

$$N_h(t) = S_h + L_h + I_h + I_s + R_h$$

$$N_v(t) = S_v + L_v + I_v$$

With initial conditions $S_h(0) = S_{h_0}, L_h(0) = L_{h_0}, I_h(0) = I_{h_0}, I_s(0) = I_{s_0}, R_h(0) = R_{h_0}$
$S_v(0) = S_{v_0}, L_v(0) = L_{v_0}, I_v(0) = I_{v_0}$

Hence, the description of how each of the eight (8) compartment evolved with time is presented below:

The susceptible human population $S_h(t)$, increases by the recruitment of new offspring through birth at the rate Λ_h, and due to loss of immunity from recovered class at a rate α_2. This population is reduced due to new infection which occurred as a result of interaction between susceptible human and infected human or vector at the quantity $\frac{\beta_1 I_h S_h}{N_h}$ and $\frac{\beta_2 I_v S_h}{N_h}$ respectively. The population is further reduced due to natural death at a rate μ_h.

The population of latently infected human $L_h(t)$, increases due to the migration of newly infected persons from the susceptible population at the proportion $\frac{\beta_1 I_h S_h}{N_h}$ and $\frac{\beta_2 I_v S_h}{N_h}$ respectively. This population is decreased by the transfer of individuals to either Isolation $I_s(t)$ or infected $I_h(t)$ classes at the rate γ_1 and φ respectively. The population is further reduced due to natural death at the rate μ_h.

The infected human $I_h(t)$, is increased by the transfer of individuals from the latent infection $L_h(t)$, at the rate φ. This population is reduced due to the migration of individuals to isolation compartment for treatment at the rate w and is further decreased as a result of natural death and disease induced death at the rate μ_h and δ_h respectively.

The isolated human $I_s(t)$, is increased due to migration of human with latent infection $L_h(t)$ and infected human $I_h(t)$ at the rate γ_1 and w respectively. This population is reduced due to the transfer of individual to recovered population at the rate α_1. The population is further reduced due to natural death at the rate μ_h.

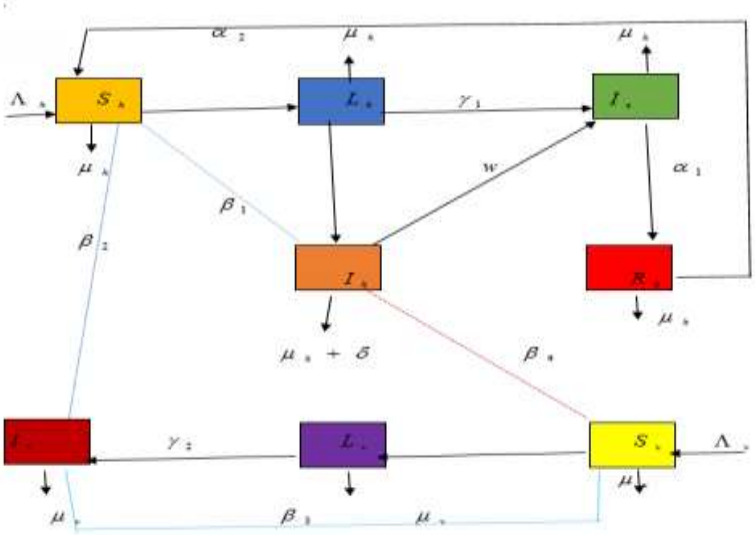
The recovered human $R_h(t)$, is increased due to migration of individuals from isolated human $I_s(t)$ at the rate α_1. This population is reduced due to loss of immunity and the transfer of such individuals to susceptible human $S_h(t)$, at the rate α_2. The population also decreased due to natural death at the rate μ_h.

The susceptible vector (rodents) population $S_v(t)$, is increased due to birth of new rodent offspring at the rate Λ_v. This population of rodent is decreased as a result of interaction between susceptible vector and infected vector or human by the proportion $\frac{\beta_3 I_v S_v}{N_v}$ and $\frac{\beta_4 I_h S_v}{N_v}$ respectively. This population is also reduced by natural death at the rate μ_v.

The Latently infected vector $L_v(t)$, is increased due to migration of newly infected individuals from the pool of susceptible vector population $S_v(t)$, by the quantity $\frac{\beta_3 I_v S_v}{N_v}$ and $\frac{\beta_4 I_h S_v}{N_v}$ respectively. This population Is reduced due to transfer of latently infected vector (rodents) $L_v(t)$, to the infected vector (rodents) compartment $I_v(t)$, at the rate γ_2 and due to natural death at the

rate μ_v. The infected vector (rodents) $I_v(t)$, is increased due to migration of latent infected vector (rodent) $L_v(t)$, at the rate γ_2 and is reduced due to natural death at the rate μ_v.

Model diagram



The model equations

$$\frac{dS_h}{dt} = \Lambda_h - \frac{\beta_1 I_h S_h}{N_h} - \frac{\beta_2 I_v S_h}{N_h} + \alpha_2 R_h - \mu_h S_h$$

$$\frac{dL_h}{dt} = \frac{\beta_1 I_h S_h}{N_h} + \frac{\beta_2 I_v S_h}{N_h} - (\gamma_1 + \varphi + \mu_h) L_h$$

$$\frac{dI_h}{dt} = \varphi L_h - wI_h - (\mu_h + \delta) I_h$$

$$\frac{dI_s}{dt} = \gamma_1 L_h + wI_h - (\alpha_1 + \mu_h) I_s \qquad (1)$$

$$\frac{dR_h}{dt} = \alpha_2 I_s - (\alpha_2 + \mu_h) R_h$$

$$\frac{dS_v}{dt} = \Lambda_v - \frac{\beta_3 I_v S_v}{N_v} - \frac{\beta_4 I_h S_v}{N_v} - \gamma_2 L_v - \mu_v S_v$$

$$\frac{dL_v}{dt} = \frac{\beta_3 I_v S_v}{N_v} + \frac{\beta_4 I_h S_v}{N_v} - (\gamma_2 + \mu_v) L_v$$

$$\frac{dI_v}{dt} = \gamma_2 L_v - \mu_v I_v$$

TABLE 1: VARIABLES /PARAMETERS

SYMBOLS	*DESCRIPTION*
$S_h(t)$	Susceptible human at time t
$S_v(t)$	Susceptible vector (rodents) at time t
$L_h(t)$	Latently infected human at time t
$I_h(t)$	Infected human at time t
$I_s(t)$	Isolated human at time t
$R_h(t)$	Recovered human at time t
$L_v(t)$	Latently infected vector (rodent) at time t
$I_v(t)$	Infected vector (rodent) at time t
$\beta_i (i = 1,2,3,4)$	Transmission rate
Λ_h	Recruitment rate in to susceptible human population
Λ_v	Recruitment rate in to susceptible vector population
μ_h	Natural death rate in human population
μ_v	Natural death rate in vector population
γ_1	Migration rate from human with Latent infection in to Isolation compartment
γ_2	Migration rate from latent to infected vector
α_1	Migration rate from human in Isolation to recovered compartment
α_2	Migration rate of recovered human to susceptible compartment
φ	Migration rate from human in latent stage to infected population

ω	Migration from infected human to isolation compartment
δ	Disease induced death in human population

Result of the analysis of the model

In this section we present the basic results of the model as follow:

Positivity of the solution

It is important that, epidemiological models which deals with populations remains positive at all the time. We wish to show that the solution of the model (1) always is non-negative provided that the initial solution values are non-negative.

Theorem 3.1 Let the initial solution set $\{S_h(0)>0, L_h(0)>0, I_h(0)>0, I_s(0)>0, R_h(0)>0, S_v(0), L_v(0)>0, I_v(0)>0\} \in R_+^8$, then the solution set $\{S_h(t), L_h(t), I_h(t), I_s(t), R_h(t), S_v(t), L_v(t), I_v(t)\}$ is positive for all time $t>0$.

Proof:

Since, $$\frac{dS_h}{dt} = \Lambda_h - \frac{\beta_1 I_h S_h}{N_h} - \frac{\beta_2 I_v S_h}{N_h} + \alpha_1 R_h - \mu_h S_h$$

By standard comparison theorem,

$$\frac{dS_h}{dt} \geq \frac{\beta_1 I_h S_h}{N_h} - \frac{\beta_2 I_v S_h}{N_h} - \mu_h S_h$$

$$\frac{dS_h}{dt} \geq \frac{(\beta_1 I_h + \beta_2 I_v) S_h}{N_h} - \mu_h S_h$$

$$\frac{dS_h}{dt} \geq -(\lambda + \mu_h) S_h \quad \text{where} \quad \lambda = \frac{\beta_1 I_h + \beta_2 I_v}{N_h}$$

By separating the variable and integrating we get

$\ln S_h(t) \geq -\int (\lambda + \mu_h) dt + c$ and taking the exponential of both sides we obtain

$S_h(t) \geq A e^{-\int (\lambda+\mu_h) dt + c}$ where $A = e^c$

Applying the initial condition $t=0$ we get

$S_h(t) \geq S_h(0)e^{-(\lambda+\mu_h)t} > 0.$

(2)

In the same fashion, we see that for the remaining equations in (1) the solution set is positive for all time $t>0$.

Invariant region

It is expected that, an epidemiological model describes a population whose size is bounded within a given region. Hence, the model equation (1) will be analyzed in a biologically feasible region as follows;

Theorem 3.2: The closed set $\Omega = \Omega_1 \cup \Omega_2 \subset R_+^5 \times R_+^3$

Where $\Omega_1 = \left\{(S_h, L_h, I_h, I_s, R_h) \in R_+^5 : N_h \leq \frac{\Lambda_h}{N_h}\right\} \quad \Omega_2 = \left\{(S_v, L_v, I_v) \in R_+^3 : N_v \leq \frac{\Lambda_v}{N_v}\right\}$

is positively invariant and attracting with respect to system (1).

Proof: Let $N_h = S_h + L_h + I_h + I_s + R_h, \quad N_v = S_v + L_v + I_v$

By taking the time derivative of the above and solving we obtain

$\frac{dN_h}{dt} \leq \Lambda_h - \mu_h N_h$

By separation of variable and integrating we get

$\frac{-1}{\mu_h}\ln(\Lambda_h - \mu_h N_h) \leq t + c$

On simplifying and taking the exponentials of both sides we have

$\Lambda_h - \mu_h N_h(t) \leq Ae^{-\mu t}$ where $A = e^{-\mu c}$ is a constant

By applying the initial condition $t=0$ we obtain

$$N_h(t) \leq \frac{\Lambda_h}{\mu_h} - \frac{(\Lambda_h - \mu_h N_h(0))}{\mu_h}e^{-\mu t} \qquad (3)$$

As $t \to \infty$, the population size $N_h \to \frac{\Lambda_h}{\mu_h}$ which implies that $0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}.$

Using the same approach, we also show that $\frac{dN_v}{dt} = \frac{d}{dt}(S_v + L_v + I_v) = \frac{dS_v}{dt} + \frac{dL_v}{dt} + \frac{dI_v}{dt}$ yielded the following result

$$N_v(t) \leq \frac{\Lambda_v}{\mu_v} - \frac{(\Lambda_v - \mu_v N_v(0))}{\mu_v}e^{-\mu t} \qquad (4)$$

ISSN: 1211-4401

as $t \to \infty$ the population size of the vector $N_v \to \frac{\Lambda_v}{\mu_v}$ which implies that $0 \le N_v \le \frac{\Lambda_v}{\mu_v}$. Thus, the feasible solution set of the system of the model is positively-invariant in the region Ω. Hence, it is sufficient to study the dynamic of the model in Ω, since it is epidemiologically and mathematically well-posed.

Disease-free equilibrium

Now, to obtain the disease–free equilibrium we set the model equation (1) to zero and solved to get

$$\left(S_h, L_h, I_h, I_s, R_h, S_v, L_v, I_v\right) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0\right) \quad (5)$$

This indicates that, in the absence of Lassa fever disease, the susceptible population of human and the vector changes in proportion of their birth rate to their death rate.

Endemic equilibrium point

To calculate the endemic equilibrium point where $L_h \neq 0,\ I_h \neq 0,\ I_s \neq 0,\ L_v \neq 0,\ I_v \neq 0,$ we equate the system of equation (1) to zero and then solved to get the following result:

$$\left.\begin{aligned}
S_h^* &= \frac{\Lambda_h + \alpha_2\alpha_1 I_s^*}{K + \mu_h} \\
L_h^* &= \frac{\Lambda_h + \alpha_2\alpha_1 I_s^*}{(\mu_h + 1)(\gamma_1 + \varphi + \mu_h)} \\
I_h^* &= \frac{(\Lambda_h + \alpha_2\alpha_1 I_s^*)\varphi}{(\mu_h + 1)(\gamma_1 + \varphi + \mu_h)(w + \mu_h + \delta)} \\
I_s^* &= \frac{\Lambda_h(\gamma_1 + \omega\varphi)}{(\mu_h + 1)(\gamma_1 + \varphi + \mu_h)((1-\alpha_2)\alpha_1 + \mu_h)} \\
R_h^* &= \frac{\Lambda_h(\gamma_1 + \omega\varphi)}{(\mu_h + 1)(\gamma_1 + \varphi + \mu_h)(1 - \alpha_2 + \mu_h)(\alpha_2 + \mu_h)} \\
S_v^* &= \frac{\Lambda_v}{K^* + \mu_v} \\
L_v^* &= \frac{\Lambda_v}{(\mu_v + 1)(\gamma_2 + \mu_v)} \\
I_v^* &= \frac{\Lambda_v\gamma_2}{(\mu_v + 1)(\gamma_2 + \mu_v)\mu_v}
\end{aligned}\right\} \quad (6)$$

ISSN: 1211-4401

where $K = \frac{\beta_1 I_h + \beta_2 I_v}{N_h}$ and $K^* = \frac{\beta_3 I_v + \beta_4 I_h}{N_v}$

Basic Reproduction number

The basic reproduction number, R_0, is the average number of secondary infections caused by an infectious individual during his/her entire life as an infectious individual. The threshold epidemiological of Lassa fever denoted by $R_0 = \rho(FV^{-1})$, where ρ denotes the spectral radius. Applying the next generation method, we obtained

$$R_0 = \rho(FV^{-1}) = \sqrt{\frac{\varphi a + \gamma_2 d + ad + bc}{q_2 q_1 q_4 q_5}} \quad (7)$$

Where, $a = \frac{\beta_1 \Lambda_h}{\mu_h N_h}, \quad b = \frac{\beta_2 \Lambda_h}{\mu_h N_h}, \quad c = \frac{\beta_4 \Lambda_v}{\mu_v N_v}, \quad d = \frac{\beta_3 \Lambda_v}{\mu_v N_v}$

$$q_1 = (\gamma_1 + \varphi + \mu_h)(w + \mu_h + \delta)\mu_v, q_2 = (w + \mu_h + \delta)(\alpha_1 + \mu_h)(\gamma_2 + \mu_v)$$

$$q_3 = (\gamma_1 + \varphi + \mu_h)(\alpha_1 + \mu_h)(\gamma_2 + \mu_v), q_4 = (w + \mu_h + \delta)(\gamma_2 + \mu_v)\mu_v, q_5 = (\gamma_1 + \varphi + \mu_h)(\alpha_1 + \mu_h)\mu_v$$

Local stability of the disease free equilibrium point for Lassa fever disease.

Theorem 3.3: The disease free equilibrium point E^0 of the model is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable otherwise.

Proof: Let model (1) be

$$\left.\begin{aligned}
F_1 &= \Lambda_h - \frac{\beta_1 I_h S_h}{N_h} - \frac{\beta_2 I_v S_h}{N_h} + \alpha_2 R_h - \mu_h S_h \\
F_2 &= \frac{\beta_1 I_h S_h}{N_h} + \frac{\beta_2 I_v S_h}{N_h} - \gamma_1 L_h - \varphi L_h - \mu_h L_h \\
F_3 &= \varphi L_h - w I_h - (\mu_h + \delta) I_h \\
F_4 &= \gamma_1 L_h + w I_h - \alpha_1 I_s - \mu_h I_s \\
F_5 &= \alpha_1 I_s - \alpha_2 R_h - \mu_h R_h \\
F_6 &= \Lambda_v - \frac{\beta_3 I_v S_v}{N_v} - \frac{\beta_4 I_h S_v}{N_v} - \gamma_2 L_v - \mu_v S_v \\
F_7 &= \frac{\beta_3 I_v S_v}{N_v} + \frac{\beta_4 I_h S_v}{N_v} - \gamma_2 L_v - \mu_v L_v \\
F_8 &= \gamma_2 L_v - \mu_v L_v
\end{aligned}\right\} \quad (8)$$

Thus, the Jacobian matrix of system (1) is obtained as follow

$$\left|J\left(E^{0}\right)-\lambda I\right|=0 \tag{9}$$

$$\begin{vmatrix} -n_1-\lambda & 0 & \frac{-\beta_1\Lambda_h}{\mu_h N_h} & 0 & \alpha_2 & 0 & 0 & \frac{-\beta_2\Lambda_h}{\mu_h N_h} \\ 0 & -n_2-\lambda & \frac{\beta_1\Lambda_h}{\mu_h N_h} & 0 & 0 & 0 & 0 & \frac{\beta_2\Lambda_h}{\mu_h N_h} \\ 0 & \varphi & -n_3-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_1 & w & -n_4-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \alpha_1 & -n_5-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -n_6-\lambda & -\gamma_2 & \frac{-\beta_3\Lambda_v}{\mu_v N_v} \\ 0 & 0 & \frac{\beta_4\Lambda_v}{\mu_v N_v} & 0 & 0 & 0 & -n_7-\lambda & \frac{\beta_3\Lambda_v}{\mu_v N_v} \\ 0 & 0 & 0 & 0 & 0 & 0 & \gamma_2 & -n_8-\lambda \end{vmatrix}=0 \tag{10}$$

$$n_1=-\mu_h, n_2=-(\gamma_1+\varphi+\mu_h), n_3=-(w+\mu_h+\delta), n_4=-(\alpha_1+\mu_h), n_5=-(\alpha_2+\mu_h),$$
$$n_6=-\mu_v, n_7=-(\gamma_2+\mu_v), n_8=-\mu_v$$

We observed that the first four eigenvalues have negative real part as follow

$\lambda_1=-\mu_h, \lambda_4=-(\alpha_1+\mu_h), \lambda_5=-(\alpha_1+\mu_h), \lambda_6=-\mu_v$ so that equation (10) reduces to

$$\begin{vmatrix} -n_2-\lambda & c_{31} & 0 & c_{51} \\ c_{22} & -n_3-\lambda & 0 & 0 \\ 0 & c_{33} & -n_4-\lambda & c_{53} \\ 0 & 0 & c_{44} & -n_8-\lambda \end{vmatrix}=0 \tag{11}$$

where $c_{22}=\varphi, c_{31}=\frac{\beta_1\Lambda_h}{\mu_h N_h}, c_{33}=\frac{\beta_4\Lambda_v}{\mu_v N_v}, c_{44}=\gamma_2, c_{51}=\frac{\beta_2\Lambda_h}{\mu_h N_h}, c_{53}=\frac{\beta_3\Lambda_v}{\mu_v N_v}$

The remaining four eigenvalues were obtained from the determinant of the 4×4 matrix:

which yield the polynomial equation

$$A_1\lambda^4+A_2\lambda^3+A_3\lambda^2+A_4\lambda+A_0=0 \tag{12}$$

where

$$\left.\begin{aligned} A_1&=1 \\ A_2&=\left(n_3+n_7\right)+\left(n_2+n_8\right)\left(n_3n_7\right) \\ A_3&=\left(n_2+n_8\right)\left(n_3+n_7\right)+\left(n_2n_8\right)+\left(n_3n_7\right)+c_{53} \\ A_4&=\left(n_2n_8\right)\left(n_3n_7\right)+\left(n_2n_8\right)\left(n_3+n_7\right)+\left(n_2+n_3\right)c_{53}+c_{22}c_{31} \\ A_0&=\left(n_2n_3c_{53}+n_7c_{22}c_{31}\right)+\left(c_{33}c_{51}c_{22}-c_{51}c_{53}c_{22}\right) \end{aligned}\right\} \tag{13}$$

ISSN: 1211-4401

By applying Routh-Hurwitz criterion which states that all roots of the polynomial equation (12) have negative real part if and only if the coefficients A_i, are positive and the determinant of the matrices $H_i > 0$ for $i = 0, 1, 2, 3, 4$,(see Olaniyi and Obabiyi 2013). From (13), we noticed that $A_1 > 0, A_2 > 0, A_3 > 0, A_4 > 0,$ and if $R_0 < 1$, then $A_0 > 0.$ The Hurwitz matrices for the polynomial (13) are found to be positive as presented below

$$H_1 = A_3 > 0,\ H_2 = \begin{vmatrix} A_3 & A_1 \\ 1 & A_2 \end{vmatrix} > 0,\ H_3 = \begin{vmatrix} A_3 & A_1 & 0 \\ 1 & A_2 & A_0 \\ 0 & A_3 & A_1 \end{vmatrix} > 0,\ H_4 = \begin{vmatrix} A_3 & 1 & 0 & 0 \\ A_1 & A_2 & A_3 & 1 \\ 0 & A_0 & A_1 & A_2 \\ 0 & 0 & 0 & A_0 \end{vmatrix} > 0$$

Therefore, all the eigenvalues of the polynomial (12) have negative real parts, implying that $\lambda_2 < 0, \lambda_3 < 0, \lambda_7 < 0, \lambda_8 < 0$. Since all the values of $\lambda_i < 0,$ for $i = 1, 2, 3, \ldots\ldots 8$ when $R_0 < 1$ we conclude that the disease-free equilibrium point is locally asymptotically stable.

Global stability of the disease-free equilibrium

We used the method of Castillo-Chavez, Feng and Huang (2002) to obtain the global stability of the disease-free equilibrium point. Two conditions which guarantee the global stability of the disease-free state were considered. Therefore, our system of equations (1) is re-write in the following form;

$$\left.\begin{aligned} \frac{dX}{dt} &= F(X, Z) \\ \frac{dZ}{dt} &= G(X, Z), G(X, 0) = 0 \end{aligned}\right\} \qquad (14)$$

Where $X = (S_h, R_h, S_v)$ denotes the number of uninfected individuals in human and vector populations and $X \in R^3$, while $Z = (L_h, I_h, I_s, L_v, I_v)$ denotes the number of infected individuals and $Z \in R^5$. We represent the disease-free state by $E^0 = (X^0, 0)$ .The following two conditions H_1 and H_2 must be met to guarantee a global asymptotic stability:

$H_1: for \frac{dX}{dt} = F(X,0), X^0$ is globally asymptotically stable

$H_2: G(X,Z) = CZ - G(X,Z), where G(X,Z) \geq 0, for (X,Z) \in \Omega$

Where $C = D_Z G(X^0, 0)$ is an M-matrix (the off diagonal of C are non-negative) and Ω is the biological feasible region.

Lemma 1: The point $K^0 = (X^0, 0)$ is called stable global asymptotic equilibrium point, if in addition $R_0 < 1$ and the conditions H_1 and H_2 holds. The following theorem is developed.

Theorem 3.4: Let $R_0 < 1$. Then the disease-free equilibrium is globally asymptotically stable.

Proof: Let $X = (S_h, R_h, S_v)$, $Z = (L_h, I_h, I_s, L_v, I_v)$ and $K^0 = (X^0, 0)$ where

$$X^0 = \left(\frac{\Lambda_h}{\mu_h}, 0, \frac{\Lambda_v}{\mu_v}\right)$$

$$\left.\begin{aligned} &\Rightarrow X \in R^3 \\ &\frac{dS_h}{dt} = \Lambda_h - \frac{\beta_1 I_h S_h}{N_h} - \frac{\beta_2 I_v S_h}{N_h} + \alpha_1 R_h - \mu_h S_h \\ &\frac{dR_h}{dt} = \alpha_2 I_s - \alpha_1 R_h - \mu_h R_h \\ &\frac{dS_v}{dt} = \Lambda_v - \frac{\beta_3 I_v S_v}{N_v} - \frac{\beta_4 I_h S_v}{N_v} - \gamma_2 L_v - \mu_v S_v \end{aligned}\right\} \quad (15),$$

$$F(X,0) = \begin{pmatrix} \Lambda_h - \mu_h S_h \\ 0 \\ \Lambda_v - \mu_v S_v \end{pmatrix} \quad (16)$$

$$\left.\begin{aligned} &X \in R^5 \Rightarrow \\ &\frac{dL_h}{dt} = \frac{\beta_1 I_h S_h}{N_h} + \frac{\beta_2 I_v S_h}{N_h} - (\gamma_1 + \varphi + \mu_h) L_h \\ &\frac{dI_h}{dt} = \varphi L_h - w I_h - (\mu_h + \delta) I_h \\ &\frac{dI_s}{dt} = \gamma_1 L_h + w I_h - (\alpha_2 + \mu_h) I_s \\ &\frac{dL_v}{dt} = \frac{\beta_3 I_v S_v}{N_v} + \frac{\beta_4 I_h S_v}{N_v} - (\gamma_2 + \mu_v) L_v \\ &\frac{dI_v}{dt} = \gamma_2 L_v - \mu_v I_v \end{aligned}\right\} \quad (17)$$

$$C=\begin{bmatrix} -(\gamma_1+\varphi+\mu_h) & \frac{\beta_1 S_h}{N_h} & 0 & 0 & \frac{\beta_1 S_h}{N_h} \\ \varphi & -(w+\mu_h+\delta) & 0 & 0 & 0 \\ \gamma_1 & w & -(\alpha_1+\mu_h) & 0 & 0 \\ 0 & \frac{\beta_4 S_v}{N_v} & 0 & -(\gamma_2+\mu_v) & \frac{\beta_3 S_v}{N_v} \\ 0 & 0 & 0 & \gamma_2 & -\mu_v \end{bmatrix} \quad (18)$$

$$G(X,Z)=\begin{pmatrix} G_1(X,Z) \\ G_2(X,Z) \\ G_3(X,Z) \\ G_4(X,Z) \\ G_5(X,Z) \end{pmatrix}=\begin{pmatrix} \beta_1 I_h+\beta_2 I_v\left(1-\frac{S_h}{N_h}\right) \\ 0 \\ 0 \\ \beta_3 I_h+\beta_4 I_v\left(1-\frac{S_v}{N_h}\right) \\ 0 \end{pmatrix}\begin{pmatrix} L_h \\ I_h \\ I_s \\ L_v \\ I_v \end{pmatrix} \quad (19)$$

Therefore, the population is bounded and $G(X,Z)\geq 0$.Obviously, C is an M-matrix. Hence all the two conditions H_1 and H_2 hold, then by lemma 1, the disease-free equilibrium E^0 is globally asymptotically stable when $R_0<1$

Conclusion:

We have studied a Lassa fever model where vector to human and vector to vector contacts were incorporated. The analytical result indicates that, the disease-free equilibrium is locally and globally asymptotically stable when the basic reproduction number $R_0<1$ and unstable when $R_0>1$.This simply means Lassa fever disease can be controlled when the number of secondary infection is kept at barest minimum.

REFERENCES

Akinpelu, F.O. & Akinwande, R. (2018). Mathematical Model for Lassa fever and Sensitivity Analysis. *Journal of scientific and engineering research*, 5(6), 1-9.

Bakare, E. A. Z., Are, E. B. Z., Abolarin, O. E. Z., Osanyinlusi S. A. Y., Ngwu Benitho, Z. & Ubaka Obiaderi, N. (2019). Mathematical Modelling and Analysis of Transmission Dynamics of Lassa fever. TETFUND Institution Based Research funded by Federal Government of Nigeria.

Bawa, M., Abdulrahman, S., Jimoh, O. R. & Adabara, N. U. (2013) .Stability Analysis of the Disease-Free Equilibrium State for Lassa Fever Disease. *Journal of Science,*

Technology, Retrieved from *Mathematics and Education (JOSTMED),* 9(2), 115-123. https://www.researchgate.net/publication/245024578 on 12th April, 2020.

Castillo-Chavez, C., Feng, Z. & Huang, W. (2002). On the Computation of R_0 and its Role on Global Stability. *Institute for mathematics and its applications*, 125,229.

Center for Disease Control and Prevention. Lassa fever Fact Sheet; 2015.

Faniran, T. S. (2017). A Mathematical Modelling of Lassa fever Dynamics with Non-drug Compliance Rate. *International journal of mathematics trends and technology (IJMTT),* 47 (5), 305-318.

James, T. O., Akinyemi, S. T. & Bamidele, O. (2016). Stability Analysis of Lassa fever with Quarantine and Permanent Immunity. *International Journal of Applied Science and Mathematical Theory,* 1(8), 1-11. Retrieved from www.iiardonline.org on 12th April, 2020.

Nasir I. A. and Sani F. M. (2015). Outbreaks, Pathogen Containment and Laboratory Investigations of Lassa fever in Nigeria: How Prepared Are We? International Journal of tropical disease & Health; 10(1): 1-10.

Nigeria Centre for Disease Control (NCDC) (2016). Lassa Fever Outbreak In Nigeria Daily Situation Report No. 12: (20 January, 2016).

Nigeria Centre for Disease Control (2020). Lassa Fever Situation Report; week 9: 24th February to 1st March 2020. Retrieved from www.ncdc.gov.ng on 28 march 2020.

Olaniyi, S. & Obabiyi,O.S (2013). Mathematical Model For Malaria Transmission Dynamics In Human And Mosquito Populations With Nonlinear Forces Of Infection. *International journal of pure and applied mathematics*, 88 (1), 125-156.

Tara, K. H. (2004). Virology notes in Lassa fever. Retrieved on March 10, 2012 from www.taraharper.com/v lass.html.

World Health Organization (2018). R&D Roadmap Documents and Guidance Draft for Public comment.

World Health Organization, (2018). Efficacy trials of Lassa Therapeutics: endpoints, trial design, site selection.

World Health Organization. Lassa fever in Nigeria: Global alert and response; 2012. One Health, STEPS Working Paper 83, Brighton: STEPS Centre.

World Health Organization. Fact sheet on Lassa fever. Last accessed 2015. 2015; 10(11).

World Health Organization (2016). Lassa fever - Nigeria.