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Sensitivity Analysis of the Dynamical Transmission and Control of Lassa Fever Virus

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Abstract

A non-linear deterministic model was considered to study the dynamics transmission and control of Lassa fever virus. The total population was divided into six mutually exclusive classes between human and rodents as susceptible human, infected human, treated human, removed human, susceptible rodents and infected rodents. Existence and uniqueness of the solution of the model were determined, the model threshold parameter was examined using next-generation operator method. The existence of disease-free equilibrium point and endemic equilibrium point was carried out. The model result shows that diseases free equilibrium is local asymptotically stable at $R_o < 1$ and unstable at $R_o > 1$, the model is globally asymptotically stable. Sensitivity analysis of the model parameters was carried out in order to identify the most sensitive parameters on the disease transmission. The results indicate that, the most sensitive parameter is the progression rate to active Lassa fever (γ), the next is the force of infection the susceptible human with the infected individuals' (λ). The least sensitive parameter is the treatment rate of infective class (θ). (γ) and (λ) are highly sensitive to the transmission of Lassa fever and every effort must be put in place by the agencies concern to check these parameters.

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1 Introduction

Lassa fever is caused by Lassa virus which belongs to the arena virus family and classified as group V(-)ss RNA. A rat that is common in endemic areas, known as masto-mysnatalensis is the natural host of the disease [1,2,3,4]. Humans are infected with this disease by eating foods that is contaminated with saliva, urine or excreta of the hosted Lassa virus rat. The incubation period of Lassa fever is 6 to 21 days. It can also be defined as a viral disease that attacks the liver, nervous system, spleen and kidney, causing them to bleed, hence the hemorrhagic fever [5]. Nosocomial transmission may occur through droplets by person to person contact or the contamination of needles [1] but the virus cannot be spread through casual contact (including skin-to-skin contact without exchange of body fluids) [5].

The symptoms and signs of the disease are similar to the symptoms and signs of malaria, typhoid and yellow fever [13]. The symptoms and signs include fever, nausea, vomiting, chest pain, puffy face, puffy cheeks, oedema, dehydration, conjunctiva injection, fainting attacks, bleeding from orifices, hypotension, shock and coma [1,6,2,7,8,9,3,10,4]. Approximately 15%- 20% of patients hospitalized for Lassa fever die from the illness. Studies show that about 500 000 cases of Lassa fever occur per year in West Africa with approximately 5000 death [11].

There is no US approved vaccine for Lassa fever but it can be treated using Ribavirin which is effective during an early stage of infectiousness [12]. Lassa fever can be prevented by using: Rodent –proof containers for food storage, Rodents control measures such as traps and rodenticides are to be used in and around human homes, Avoid eating rodent (rats), Avoid attracting rodents to house by cleanliness and healthy waste disposal practices, Isolation of patients till recovery is well advanced, Use of gown, gloves mask and cap, Careful segregation of biologically hazardous waste and Sterilizing all equipment used for the patients [13].

2 Mathematical Model

We considered Six (6) compartmental deterministic mathematical model using the S_H, I_H, T_H, R_H, S_R, *and* I_R to have a better understanding on the transmission and control of Lassa fever virus. The population size $N(t)$ is divided into two population: human population and rodent population, that are sub–divided into sub–classes which are Susceptible human S_H, Infected human I_H, Treated human T_H,Removed human R_H, Susceptible rodent S_R and Infected rodent I_R.

Where $$N_H = S_H + I_H + T_H + R_H \quad and \quad N_R = S_R + I_R \tag{1}$$

2.1 Susceptible human (S_H)

Susceptible human is a member of a human population who is at risk of becoming infected by a disease. The population of susceptible humans increases by the recruitment of sexually-active humans at a rate π_1 and the ones that are recovery from the disease. The population decreased by natural death at a rate μ_1 also, by force of infection of infected detected λ.

2.2 Infected human (I_H)

Infected human is a member of a human population who is infected and capable of transmitting the disease. The population of infected humans increases through the infection of susceptible human. The population is decreased by treatment rate of infectious, natural death and disease-induced death θ, μ_1 and d respectively.

2.3 Treated human (T_H)

Treated human is a member of a human population who is infected but not infectious. The population of treated human increases through the treatment rate of infectious. The population of treated class diminished by the recovery rate of infected human and natural death at a rate μ_1. We assume that no one die of the disease in this class.

2.4 Susceptible rodent (S_R)

Susceptible rodent is a member of a rodent population who is at risk of becoming infected by a disease. The population of susceptible rodents increases by the recruitment π_2. The population decreased by the rate at which susceptible rodents become infected α and natural death at a rate μ_2.

2.5 Infected rodent (I_R)

Infected rodent individual is a member of a rodent population who is infected and capable of transmitting the disease. The population of infected rodents' increases through the rate at which susceptible rodent become infected α while the population is decreased by rate at which rodent infect human ρ and natural death μ_2.

2.6 Removed human (R_H)

Recovered human is a member of a human population who recovered from the disease .The population of removed human is increased by death rate due to the disease d, this population later decreased by natural death at the rate μ_1.

Hence, we have the following non-linear system of differential equations:

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= \pi_1 + rT_H + \rho I_R - \lambda\gamma S_H - \mu_1 S_H \\
\frac{dI_H}{dt} &= \lambda\gamma S_H - (d + \theta + \mu_1)\, I_H \\
\frac{dT_H}{dt} &= \theta I_H - (\mu_1 + r)T_H \\
\frac{dS_R}{dt} &= \pi_2 - (\alpha + \mu_2) S_R \\
\frac{dI_R}{dt} &= \alpha S_R - (\rho + \mu_2) I_R \\
\frac{dR_H}{dt} &= d\, I_H - \mu_1 R
\end{aligned}\right\} \tag{2}$$

With initial condition $S_H(0) > 0, I_H(0) \geq 0, T_H(0) \geq 0, R_H(0) \geq 0, S_R(0) > 0, I_R(0) \geq 0$

Table 1. Description of variables

Variables	Definitions
S_H	Susceptible human at time t
I_H	Infected human at time t
T_H	Treated human at time t
R_H	Removed human at time t
S_R	Susceptible rodent at time t
I_R	Infected rodent at time t

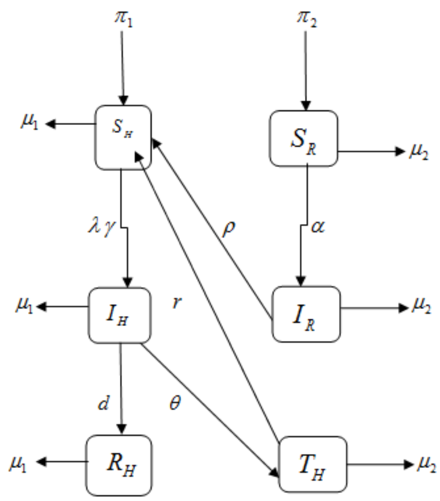

Table 2. Description of parameters

Parameters	Definitions
π_1	Recruitment rate into Susceptible human
π_2	Recruitment rate into Susceptible rodent
μ_1	Natural death rate in human
μ_2	Natural death rate in rodent
r	Recovery rate
θ	Treatment rate
d	Death rate due to the disease
ρ	Rate at which rodent infect human
α	Rate at which susceptible rodent become infected
c	Contact rate
γ	Progression rate to active Lassa fever
β	Probability of getting Lassa fever infection
N_H	Total population of human
N_R	Total population of rodent
λ	Force of infection

2.7 Existence and Uniqueness of the solution

Lemma 1: The closed set

$$D = \begin{Bmatrix} S_H + I_H + T_H + R_H + S_R + I_R : \left|S_H - S_H(0)\right| \le a,\ \left|I_H - I_H(0)\right| \le b, \left|T_H - T_H(0)\right| \le c, \\ \left|S_R - S_R(0)\right| \le d, \left|I_R - I_R(0)\right| \le e, \left|R_H - R_H(0)\right| \le f \end{Bmatrix}$$

then model in (2) has a unique solution in D

Proof: Consider the biologically-feasible region D, defined above. The model in (2) must be continuous and bounded in D.

Therefore, $\left|\frac{dx_i}{dx_j}\right|, i, j = 1,2,3,4,5,6$ are continuous and bounded. All solution of the model (2) with initial conditions in D. Hence the model (2) has a unique solution in D, which means that the model (2) is epidemiologically and mathematically well posed.

2.8 Existence of Disease Free Equilibrium (DFE)

When there is no disease in the population, it is called DFE; it implies that

$$\frac{dS_H}{dt} = \frac{dI_H}{dt} = \frac{dT_H}{dt} = \frac{dS_R}{dt} = \frac{dI_R}{dt} = \frac{dR_H}{dt} = 0 \tag{3}$$

Let E_0 denotes the disease free equilibrium. We set $I_H^* = T_H^* = I_R^* = R_H^* = 0$

The model in (2) has disease free equilibrium given by

$$E_0 = (S_H^*,\ I_H^*, T_H^*, S_R^*, I_R^*, R_H^*) = \left(\frac{\pi_1}{\mu_1}, 0, 0, \frac{\pi_2}{\mu_2}, 0, 0\right) \tag{4}$$

2.9 Existence of Endemic Equilibrium Point (EEP)

When there is disease in the population, it is called EEP; it implies that

$$\frac{dS_H}{dt} = \frac{dI_H}{dt} = \frac{dT_H}{dt} = \frac{dS_R}{dt} = \frac{dI_R}{dt} = \frac{dR_H}{dt} = 0$$

And now solve model (2) simultaneously to get the endemic equilibrium point, it given below;

$$\left.\begin{array}{lll} S_R^{**} = \dfrac{\pi_2}{K_2} & I_R^{**} = \dfrac{\alpha \pi_2}{K_2 K_3} & S_H^{**} = \dfrac{NK_1}{\beta c} \\ I_H^{**} = \dfrac{K_4 (K_1 K_2 K_3 K_5 - \pi_2 \alpha \rho)}{\beta \gamma c K_3 (r\theta - K_1 K_4)} & & T_H^{**} = \dfrac{\theta (K_1 K_2 K_3 K_5 - \pi_2 \alpha \rho)}{\beta \gamma c K_3 (r\theta - K_1 K_4)} \\ R_H^{**} = \dfrac{d K_1 K_3 K_4 K_5}{\beta \gamma c \mu_1 (r\theta - K_1 K_4)} & & \end{array}\right\} \tag{5}$$

Where

$K_1 = d + \theta + \mu_1$ $K_2 = \alpha + \mu_2$ $K_3 = \rho + \mu_2$

$K_4 = \mu_1 + r$ $K_5 = \mu_1 N - \pi_1 \beta c \gamma$ $\lambda = \frac{\beta c I_H}{N}$

2.10 Basic reproduction number (R_0)

Using next generation matrix [14], the non-negative matrix F (new infection terms) and non-singular matrix V (other transferring terms) of the model are given respectively by;

$$F = \begin{pmatrix} \frac{\lambda \gamma \pi_1}{\mu_1} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ at DFE} \tag{6}$$

$$V = \begin{pmatrix} K_1 & 0 & 0 & 0 \\ -\theta & K_4 & 0 & 0 \\ 0 & 0 & K_3 & 0 \\ -d & 0 & 0 & \mu_1 \end{pmatrix} \tag{7}$$

And

$$F.V^{-1} = \begin{pmatrix} \frac{\lambda \gamma \pi_1}{K_1 \mu_1} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{8}$$

Thus;

$$R_0 = \frac{\lambda \gamma \pi_1}{K_1 \mu_1} \tag{9}$$

The threshold quantity R_0 is the basic reproduction number of the system (2) for Lassa fever virus. It is the average number of new secondary infections generated by a single infected individual in his or her infectious period [15].

2.11 Local Stability of the DFE

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

Proof: To determine the local stability of E_0, the following Jacobian matrix is computed corresponding to equilibrium point E_0. Considering the local stability of the disease free equilibrium at $\left(\frac{\pi_1}{\mu_1}, 0, 0, \frac{\pi_2}{\mu_2}, 0, 0 \right)$.

We have

$$J_G = \begin{pmatrix} -(\mu_1+\lambda) & 0 & r & 0 & \rho & 0 \\ 0 & -(K_1+\lambda) & 0 & 0 & 0 & 0 \\ 0 & \theta & -(K_5+\lambda) & 0 & 0 & 0 \\ 0 & 0 & 0 & -(K_2+\lambda) & 0 & 0 \\ 0 & 0 & 0 & \alpha & -(K_3+\lambda) & 0 \\ 0 & d & 0 & 0 & 0 & -(K_3+\lambda) \end{pmatrix} \quad (10)$$

The characteristics polynomial of the above matrix is given by

$$B_6\lambda^6 + B_5\lambda^5 + B_4\lambda^4 + B_3\lambda^3 + B_2\lambda^2 + B_1\lambda + B_0 = 0 \quad (11)$$

And

$$B_0 = \lambda\gamma\pi_1 - K_1\mu_1$$

Thus by Routh – Hurwitz criteria, E_o is locally asymptoticly stable as it can be seen for

$$B_1 > 0, B_2 > 0, B_3 > 0, B_4 > 0, B_1 B_3 - B_3 > 0 \ \textit{and} \ B_1 B_2 B_3 - B_3^2 - B_1^2 B_4 > 0 \quad (12)$$

Thus, using $B_0 > 0$

$$B_0 = \frac{\lambda\gamma\pi_1}{K_1\mu_1} < 1 \quad (13)$$

Hence $R_0 < 1$

The result from Routh Hurwitz criterion shows that, all eigen-values of the polynomial are negative which shows that the disease free equilibrium is locally asymptotically stable.

2.12 Global Stability of the DFE

Theorem 2: The disease free-equilibrium of the system in (2) is globally asymptotically stable(GAS) whenever $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: The proof is based on using the comparison theorem [16]. The rate of change of the variables representing the infected component of the system can be written as follows.

$$\begin{pmatrix} \frac{dI_H}{dt} \\ \frac{dT_H}{dt} \\ \frac{dI_R}{dt} \\ \frac{dR_H}{dt} \end{pmatrix} = (F - V)\begin{pmatrix} I_H \\ T_H \\ I_R \\ R_H \end{pmatrix} - F_i \begin{pmatrix} I_H \\ T_H \\ I_R \\ R_H \end{pmatrix} \quad (14)$$

At the DFE, $(S_H^*, I_H^*, T_H^*, S_H^*, I_R^*, R_H^*) = \left(\frac{\pi_1}{\mu_1}, 0, 0, \frac{\pi_2}{\mu_2}, 0, 0\right)$

Consequently, equation (14) becomes

$$\begin{pmatrix} \frac{dI_H}{dt} \\ \frac{dT_H}{dt} \\ \frac{dI_R}{dt} \\ \frac{dR_H}{dt} \end{pmatrix} \le (F-V) \begin{pmatrix} I_H \\ T_H \\ I_R \\ R_H \end{pmatrix} \tag{15}$$

According to [14], all eigenvalues of the matrix F – V have negative real parts. i.e $\left|(F-V)-\lambda I\right| = 0$

$$(F-V)-\lambda I = \begin{pmatrix} \left(\frac{\lambda\gamma\pi_1}{\mu_1} - K_1\right) - \lambda & 0 & 0 & 0 \\ \theta & -(K_4+\lambda) & 0 & 0 \\ 0 & 0 & -(K_3+\lambda) & 0 \\ d & 0 & 0 & -(\mu_1+\lambda) \end{pmatrix} \tag{16}$$

The characteristics polynomial of the above matrix was found and can be written as

$$g(\lambda) = \lambda^4 + F_1\lambda^3 + F_2\lambda^2 + F_3\lambda + F_4 = 0 \tag{17}$$

Since, $F_1 > 0, F_2 > 0, F_3 > 0, and\ F_4 > 0,$

Hence, all eigen-values are negative which implies that disease-free equilibrium is globally asymptotically stable.

2.13 Sensitivity analysis

Sensitivity analysis is a crucial analysis that shows the importance of each parameter to disease transmission [14]. The sensitivity index of parameters with respect to the basic reproduction number was calculated, to know how crucial each parameter is to the disease transmission; intervention control strategies that target such parameter should be employed in the control/prevention of Lassa fever virus.

Definition 1.The normalized forward sensitivity index of a variable ω that depends differentiable on a parameter p is defined as:

$$X_P^{\omega} = \frac{\partial\omega}{\partial P} \times \frac{P}{\omega}. \tag{18}$$

As we have explicit formula for R_o, we derive an analytical expression for the sensitivity of R_o as

$$X_P^{R_o} = \frac{dR_o}{dP} \times \frac{P}{R_o} \tag{19}$$

The signs of the sensitivity index of R_0 are as shown in Table 3.

Table 3. Signs of sensitivity index of R_0

Parameter	Parameter value	Sensitivity value	Sensitivity index
λ	0.0712 (Assumed)	0.99999999999	Positive
γ	0.72 (Assumed)	1	Positive
π_1	0.000215 [17]	0	Positive
μ_1	0.0000548 [17]	-1.000101	Negative
d	0.01 [13]	-0.0185166	Negative
θ	0.53 (Assumed)	-0.981	Negative

2.14 Numerical Simulation

Numerical simulation was carried out by MAPLE 18 software using Runge-Kutta method of order four with the set of parameter values given in Table 3. Control and dynamic spread of Lassa fever virus are checked simultaneously on susceptible human, infected human, treated human, susceptible rodent, infected rodent and removed human, since the spread of Lassa fever virus is a function of time. $S_H(0)=10000, I_H(0)=2000, T_H(0)=600$ $, S_R(0)=200, I_R(0)=125$, $R_H(0)=500$. Figs. 1-4 below are the results obtained from numerical simulation of the Lassa fever virus model with the dynamic spread and control.

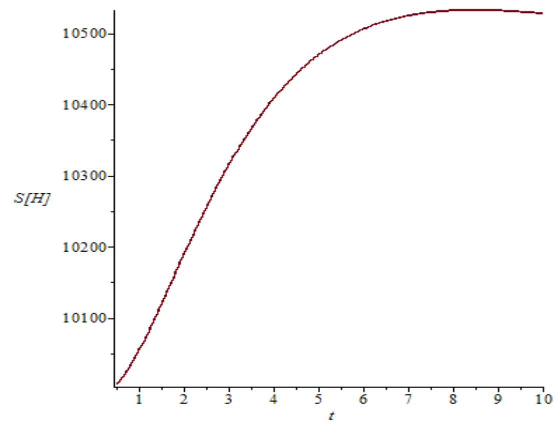

Fig. 1. Suscetipible human

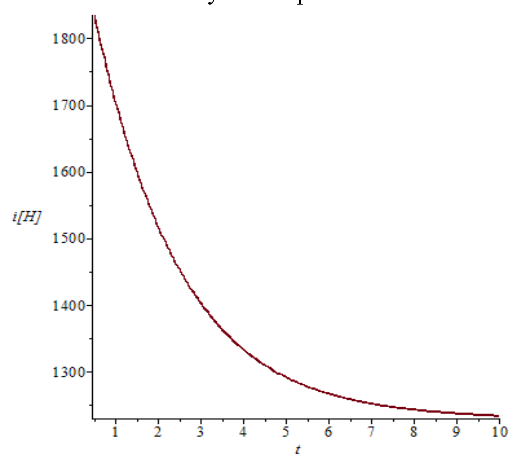

Fig. 2. Infected human

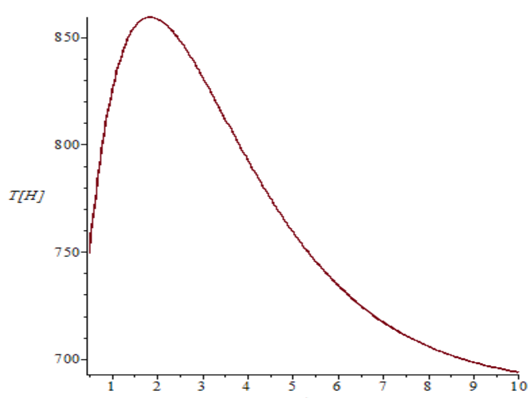

Fig. 3. Treatment human

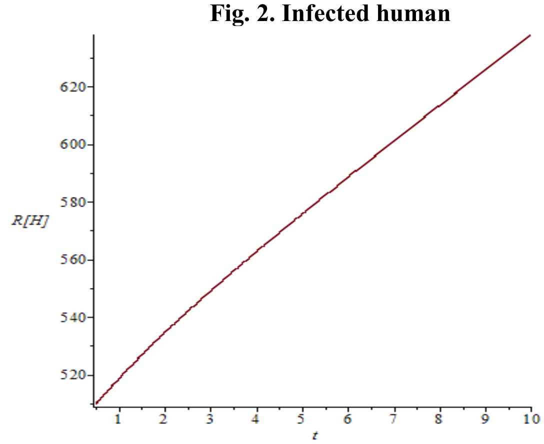

Fig. 4. Removed human

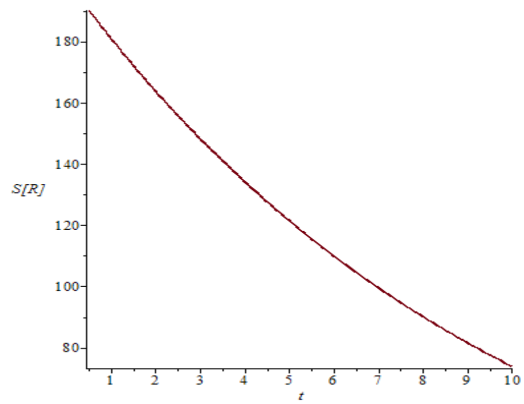

Fig. 5. Suscetipible rodents

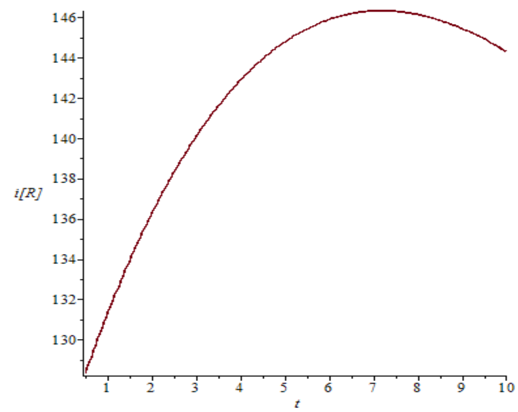

Fig. 6. Infected rodents

3 Results and Discussion

In this study, Six (6) deterministic epidemiological model of (S_H, I_H, T_H, S_R, I_R, R_H) are presented to gain insight into the control and dynamical spread of Lassa fever virus disease. Fig. 1; the population of susceptible human continue to increase with time in the presence of good medical control, Fig. 2; the population of infected human decrease continually with time in the presence of good medical control, meaning that the disease can be controlled and over time the disease will fade out. Fig. 3; the population of the treated human firstly increase between the 1st two month of the infection and later decrease after the 2nd month when good control has been put in place and good medical care while in Fig. 4, the population of removed human increase steady with time also in Fig. 5, the population of susceptible rodent decrease steady with time, controlling the population of the rodent that can be affected with the disease. Fig. 6; the population of the infected rodent firstly increases and after the 7th month the population start to decrease which indicate the population of the rodent that affected with the disease is under control

4 Conclusion

In conclusion, Sensitivity analysis of the model parameters was carried out in order to identify the most sensitive parameters on the disease transmission. The results indicate that the most sensitive parameter is the progression rate to active Lassa fever (γ), the next is the force of infection the susceptible human with the infected individuals' (λ). The least sensitive parameter is the treatment rate of infective class (θ). (γ) and (λ) parameters that are highly sensitive to the transmission of Lassa fever and every effort must be put in place by the agencies concern to check these parameters.

Competing Interests

Authors have declared that no competing interests exist.

References

[1] Eze KC, Salami TAT, Eze IC, Pogoson AE, Omordia N, Ugochukwu MO. High Lassa fever activity in Northern Part of Edo State, Nigeria: Re-analysis of Confirmatory Test Results. African Journal of Health Sciences. 2010;16(3-4):52-56.

[2] Fisher-Hoch SP, Tomori O, Nasidi A, Perez- Oronoz G.I, Fakile Y, Hutwagner L, McCormick JB. Review of cases of Nosocomial Lassa fever in Nigeria: The high price from poor medical practice. British Medical Journal. 1995;311:857-859.

[3] McCormick J.B, King I.J, Webb P.A, Scribner C.L, Craven R.B, Johnson K.M, Elliot L.H, Belmont-Williams R, 1986, Lassa fever. Effective Therapy with Ribavirin. New England Journal of Medicine, 314: 20-26.

[4] Richmond JK, Baglole DJ. Lassa fever: Epidemiology, clinical features and social consequences. British Medical Journal. 2003;327:1271-1275.

[5] Frame JD, Baldwin JM, Gocke DJ, Troup JM. Lassa fever, a new virus disease of man from West Africa. Am. J. Trop. Med. Hyg. 1970;19:670–676.

[6] Fisher-Hoch SP, Hutwagner L, Brown B, McCormick JB. Effective vaccine for Lassa fever. Journal of Virology. 2000;74:6777-6783.

[7] Lassa fever-Nigeria (Edo), 2004 Feb 14, (Cited 2004 Dec 8). Available:http://www.promedmail.org, archive number 20040214.0487

[8] Lassa fever, Suspected-Nigeria (Edo), 2001 March 19 (Cited 2004 Dec 8). Available:http://www.promedmail.org, archive number 20010319.0552.

[9] Okoror LE, Esumeh FI, Agbonlahor DE, Umolu DI. Lassa virus: Seroepidemiological Survey of Rodents Caught in Ekpoma and Environs, Tropical Doctor. 2005;35:16-17.

[10] Omilabu SA, Badaru SO, Okokhere P, Asogun D, Drosten C, Emmerich P, Becker-Zaija B, Schmitz H, Gunther S. Lassa fever, Nigeria 2003 and 2004, Emerging Infectious Diseases. 2005;11:1642-1644.

[11] World Health Organization. Lassa fever. WHO Newsletter, Geneva, Switzerland; 2005.

[12] McCormick JB, Webb PA, Krebs JW, Johnson KM, Smith ES. A prospective study of the epidemiology and ecology of Lassa fever. J Infect Dis. 1987;155:437-444.

[13] Omale D, Edibo Thomas E. Mathematical models for lassa fever transmission with control strategies, computing, information systems. Development Informatics & Allied Research Journal 2014;6(4):25-32. Available: www.cisdijournal.net

[14] Akanni JO, Akinpelu FO, Oladejo JK, Opaleye SE. Sensitivity analysis of the dynamical spread of Ebola virus disease. International Journal of Chemistry, Mathematics and Physics (IJCMP). 2017;01(01):1-10.

[15] Anderson RM, May RM. Infectious disease of humans. Oxford University Press, Oxford; 1991.

[16] Akanni JO, Akinpelu FO. An HIV/AIDs model with vertical transmission, treatment and progression rate. Asian Research Journal of Mathematics. 2016;1(4):1-17. Article no.ARJOM.28549.

[17] Olaniyi S, Obabiyi OS. Mathematical model for malaria transmission dynamics in human and mosquito populations with nonlinear forces of infection. International journal of pure and applied Mathematics. 2013;88(1):125-156. ISSN: 1311-8080 (printed version); ISSN: 1314-3395 (on- line version), Available: http://www.ijpam.eu; doi:http://dx.doi.org/10.12732/ijpam.v88i1.10.

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