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On the basic reproduction number of Lassa fever epidemics and its relationship with inter-epidemic period

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Abstract

Lassa fever is a deadly disease transmitted through ingestion of food that is contaminated with infected rodent's saliva, urine or excreta, infected person and inhalation of the aerosol. In this paper, we present a novel mathematical model that accounted for all the known Lassa fever transmission routes. We derived the basic reproduction number for the model and estimated the inter-epidemic period of infection disease. The goal of this paper is to find the relationship between the Lassa fever basic reproduction number and inter-epidemic period of infection disease. It was found that the basic reproduction number is inversely proportional to the square of inter-epidemic period of an infectious disease. Therefore, any policy or measures taken to reduce the basic reproduction number will definitely make the disease to take a very long time to re-emerge.

Keywords: Lassa fever; mathematical model; reproduction number; inter-epidemic period

1 Introduction

Lassa fever is an acute viral illness cause by Lassa virus. It belongs to the member of Arenavirus family. The disease was first described in the 1950s and the virus was identified in 1969, when two missionary nurses died from it in the town of Lassa in Borno state, Nigeria [2]. Lassa fever is endemic in West African countries such as Guinea, Liberia, Sierra Leone and Nigeria [6]. Studies show that about 500, 000 cases of Lassa fever occur per year in West Africa with approximately 5000 death [8]. The animal host of the Lassa virus is the rodents called Mastomys Natalensis [3].

Lassa fever can be transmitted through ingestion of food that is contaminated with infected rodent's saliva, urine or excreta, inhalation of the aerosol as occurs during the sweeping of an area where the droppings are present, contaminated needles or exposure to an infected aerosol in health care setting and person-to-person transmission occurs through body fluid exchange [11]. The symptoms of

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Lassa fever take up to three weeks to manifest [1]. They start with a lower fever, tiredness, body ache, sore throat and headache, nausea, vomiting and even diarrhea, high fever, swelling of the face, bleeding from the eyes or nose, breathing difficulties, severe pain in the back, chest and abdomen, shock, etc. [4]. There is no US approved vaccine for Lassa fever but it can be treated using Ribavirin which is effective during early stage of infectiousness [7]. Even though fatality is high, Lassa fever is still preventable and treatable.

Lassa fever outbreak Pattern/Prevalence in Nigeria: Current Reports

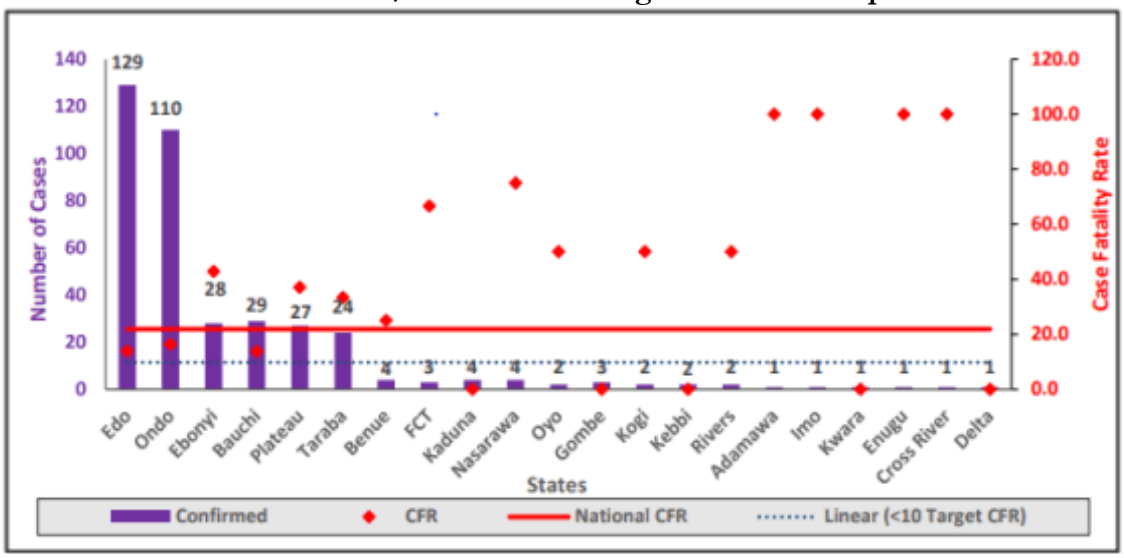

Figure 1: Confirmed Lassa fever cases in Nigeria with specific case fatality Rates (CFR) as at 24th February 2019

As seen in Figure 1, statistics from NCDC shows that from January 1 to February 24, a total of 1249 suspected cases have been reported from 21 States including the FCT was at least one case was confirmed [10]. Of these, 381 were confirmed positive, 15 probable and 858 negatives (not a case). These states are Edo, Ondo, Bauchi, Nasarawa, Ebonyi, Plateau, Taraba, FCT, Adamawa, Gombe, Kaduna, Kwara, Benue, Rivers, Kogi, Enugu, Imo, Delta, Oyo, Kebbi and Cross River. The confirmed cases were spread out across 66 Local Government Areas in the 21 states [12].

Meanwhile, since the beginning of the year, 1279 suspected cases have been reported from 32 States including FCT. Also in the new reporting week eight, two new healthcare workers were affected in Edo State. This brings the total of health care workers who have been infected since the onset of the outbreak to 15. These health workers are located in seven states, Edo (7), Ondo (3), Ebonyi (1), Enugu (1), Rivers (1), Bauchi (1) and Benue (1) with one death in Enugu. So far, Edo, Ondo, Bauchi and Ebonyi has been topping the chart of the most infected states. Currently, 55 patients are being managed at various treatment centres across the country: Irrua Specialist Teaching Hospital (ISTH) treatment Centre (27), Federal Medical Centre Owo (9), Federal Teaching Hospital Abakiliki (1), Bauchi (1), Plateau (7) and Taraba (7), Gombe (1), Kaduna (1) and Kebbi (1).

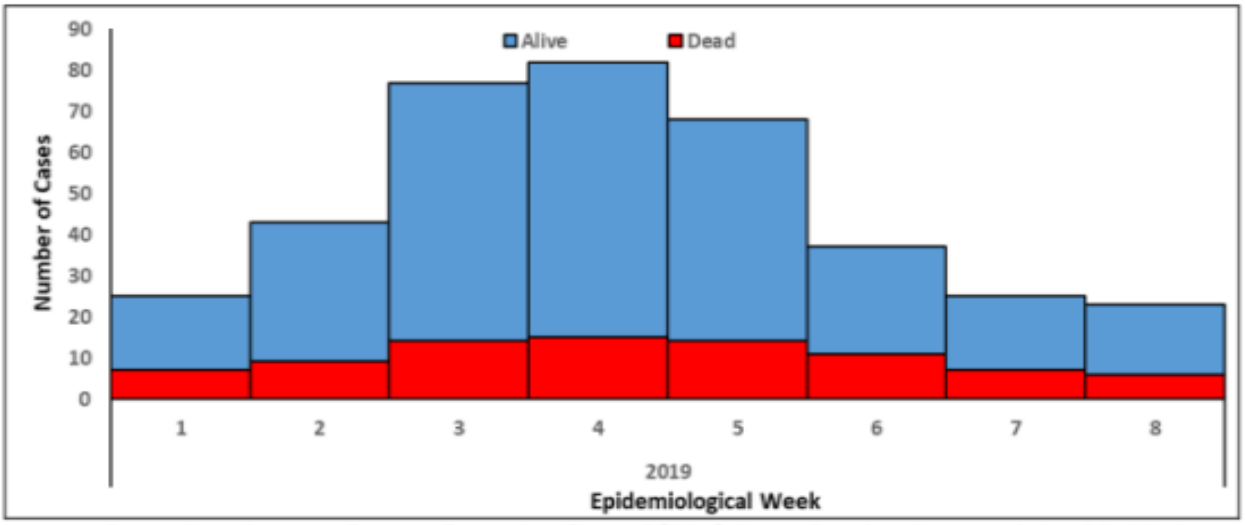

Figure 2. Epicurve of Lassa fever Confirmed (381) Cases in Nigeria - week 01-08, 2019

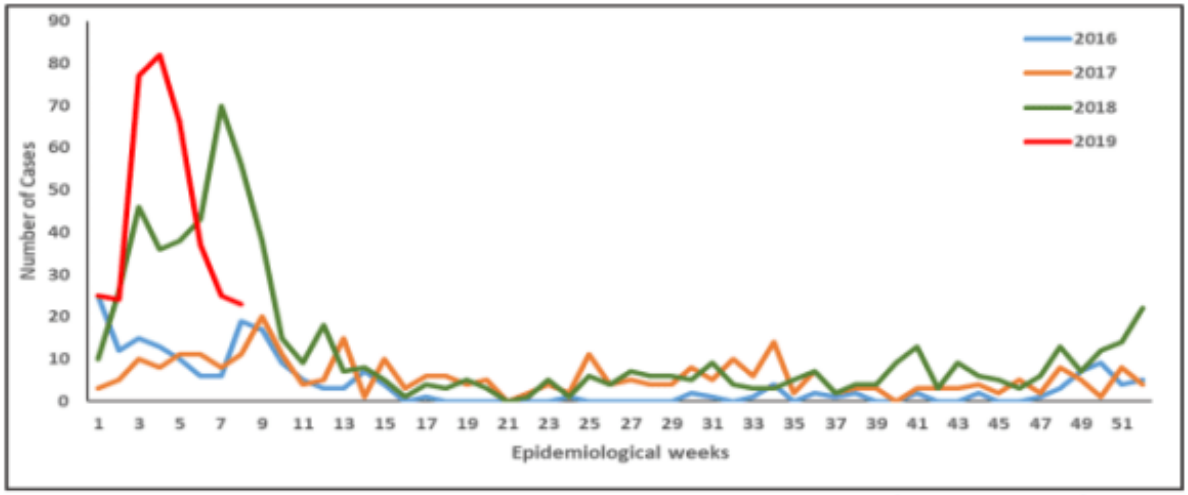

Figure 3 .Weekly trends of Lassa fever Confirmed Cases in Nigeria, 2016/week 01-2019/week 08

A total of 4499 contacts have been identified from 18 States. Of these 1987 are currently being followed up, 2461 have completed 21 days follow up, while 4 were lost to follow up. 77 symptomatic contacts have been identified, of which 47 have tested positive. NCDC said the multi-sectoral one health national rapid response teams (NCDC, NFELTP, Federal Ministry of Agricultural and Federal Ministry of Environment) is still working in Ondo, Edo and Ebonyi [1]. As part of the response coordination, NCDC said it has provided an ambulance to Federal Medical Centre, Owo Infection Control Centre. In fact, epidemiology is the backbone of public health.

Epidemiology has become an exciting area for the modern application of mathematics. Many of the innovations in epidemiology are fundamentally related to the mathematical sciences [5]. New insights into the mechanisms of population dynamics of infectious diseases are based on rigorous mathematical formulations, methods and models. A mathematical model is an explicit mathematical description of the simplified dynamics of a system [5]. Mathematical modelling is a set of techniques, tools, and equations that can be tailored to particular disciplines. It has proved its importance in understanding the dynamics of many biological processes. It is important to pay adequate attention to prevent the spread of such diseases by using effective measure through mathematical modelling. Thus, preventing and predicting Lassa fever is a matter of considerable concern in the epidemiological field. In particular, epidemic theory has been instrumental in our understanding of the threshold phenomena that govern the spread of most infectious diseases.

Among the various threshold parameters arising in epidemic theory perhaps the most useful is the basic reproduction number, usually denoted R_0. The basic reproduction number of an infectious agent in a given population is the average number of secondary infections which one typical infected individual would generate if the population were completely susceptible. It depends on the interaction between the infectious organism, its host and the environment. Some of the factors involved include the route of infection, the duration of the infectious period, the type and frequency of contacts between individuals in the population and the probability that a contact between an infectious and a susceptible individual will result in infection. This metric is useful because it helps determine whether or not an infectious disease can spread through a population. The roots of the basic reproduction concept can be traced through the work of Alfred Lotka, Ronald Ross, and others, but its first modern application in epidemiology was by George MacDonald in 1952, who constructed population models of the spread of malaria [14]. Knowledge of R_0 and related quantities is important in guiding policy decisions. This among others could be based on the outbreak pattern and inter-epidemic period of the disease, which corresponds to the interval between major epidemics of Lassa fever. Thus, there is considerable interest in investigating the inter-epidemic period of Lassa fever epidemics in Nigeria. In the present paper we concentrate on the relationship between reproduction number and inter-epidemic period based on a mathematical model of Lassa fever.

2 Mathematical model description

The model sub-divides the total human population at time t, namely; $S_h(t)$ denoting the number of susceptible individuals, $E_h(t)$ the exposed non-infectious individuals, $I_h(t)$ denoting the number of infectious individuals (infected and diagnosed or symptomatic) and $R_h(t)$, denoting the number of recovered individuals. The total rodent (rats) population at time t, is divided into susceptible rodents, $S_r(t)$, exposed rodents, $E_r(t)$ and infectious rodents, $I_r(t)$. The susceptible human population increases due to recruitment at Λ_h, a loss of immunity from the recovered class at a rate ψ and recovered humans without immunity at a rate $(1-\upsilon)$. The susceptible human population reduces as a result of a contact with an infectious rodent and a sexual contact with infected humans, aerosols and a natural death at a rate μ_h. The exposed human population increases the transmission routes and reduces due to a transition of individuals from the class of exposed to the infected class at a rate of κ and a natural death at a rate of μ_h. The infected humans may recover with temporary immunity at a rate υ and progress to recovered class while the remaining proportion recovers

without immunity and become susceptible at a rate $(1-\upsilon)$, while ϕ is the proportion of humans who recovered spontaneously. The infected human population reduces by natural death and induced death at rates μ_h and δ respectively. The recovered human population reduces by natural death at a rate μ_h and loss of immunity at a rate ψ. The susceptible rodent population increases due to recruitment at a rate Λ_r which represents the growth rate of rodents. The population of the rodents reduces upon contact with infected humans, where β_3 is the transmission probability per contact by an infected humans, natural death at a rate μ_r. The exposed rodent population increases and reduces by breakthrough into infectious class at the rate α_r, natural death at a rate μ_r. The infectious rodent population increases due to breakthrough from exposed class at a rate α_r and reduces due to natural death at a rate μ_r. Another aspect of the transmission route is the opportunistic airborne transmission-infectious that naturally cause disease by small airborne particles (aerosol) that contain microorganisms. Riley and Nardell [5] present a standard model of airborne infection usually referred to as the Wells-Riley equation. The modified version of Wells-Riley equation is used to describe airborne transmission route in this Lassa fever model. The exponent represents the degree of exposure to infection and $1-e^{-rt}$ is the probability of a single susceptible being infected. Thus, putting the above formulations and assumptions together gives the following human-rodent model, given by system of ordinary differential equations below as:

$$
\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \phi(1-\nu)I_h + \psi R_h - \beta_1\sigma I_r S_h - \beta_2\varepsilon I_h S_h - \eta\left(1-e^{-rt}\right)S_h - \mu_h S_h \\
\frac{dE_h}{dt} &= \beta_1\sigma I_r S_h + \beta_2\varepsilon I_h S_h + \eta\left(1-e^{-rt}\right)S_h - (\kappa+\mu_h)E_h \\
\frac{dI_h}{dt} &= \kappa E_h - \phi(1-\nu)I_h - \phi\nu I_h - (\delta+\mu_h)I_h \\
\frac{dR_h}{dt} &= \phi\nu I_h - (\psi+\mu_h)R_h \\
\frac{dS_r}{dt} &= \Lambda_r - \beta_3\vartheta I_h S_r - \mu_r S_r \\
\frac{dE_r}{dt} &= \beta_3\vartheta I_h S_r - (\alpha+\mu_r)E_r \\
\frac{dI_r}{dt} &= \alpha E_r - \mu_r I_r
\end{aligned}
\qquad (1)
$$

The associated model variables and parameters are described in Table 1.

Variable	Description
S_h	Number of Susceptible humans
E_h	Number of Exposed humans
I_h	Number of Infectious humans
R_h	Number of Recovered humans
S_r	Number of Susceptible rodents
E_r	Number of Exposed rodents
I_r	Number of Infectious rodents

Table 1: Description of the state variables of the model

Parameters	Description
Λ_h	Recruitment level of humans
Λ_r	Recruitment level of rodents
δ	Per capita Lassa-induced death rate
ψ	Recovered human loss of immunity
ϕ	Spontaneous individual recovery
β_1	Transmission rate per contact by an infectious rodent
β_2	Transmission rate per contact by an infective through sexual activity
β_3	Transmission rate per contact by an infected human
η	Relative infectiousness of individuals with aerosol
μ_h	Natural mortality rate for humans
μ_r	Natural mortality rate for rodents
κ	Progression rate of human from exposed to infected
α	Progression rate of rodents from exposed to infected
σ	Contact rate of rodent per human per unit time
ϑ	Relative human-to-rodent transmissibility of infected humans
ε	Relative human-to-human transmissibility of infected humans
r	Rate of exposure to aerosol
v	Recovery with temporary immunity

Table 2: Description of the parameters of the Lassa fever model

2.1 Positivity and boundedness of solutions

For the Lassa fever transmission model (1) to be epidemiologically meaningful, it is important to prove that all its state variables are non-negative for all time. In other words, solutions of the model system (1) with non-negative initial data will remain non-negative for all time $t > 0$.

Theorem 1: Let the initial data be $\{(S_h(0), E_h(0), I_h(0), R_h(0), S_r(0), E_r(0), I_r(0)) \geq 0\} \in \Omega$. Then the solution set $\{S_h(t), E_h(t), I_h(t), R_h(t), S_r(t), E_r(t), I_r(t)\}$ of the system (1) is positive for all $t > 0$.

Proof: From the first equation of the model system (1) we have

$$\frac{dS_h}{dt} = \Lambda_h + \phi(1-\nu) I_h + \psi R_h - \beta_1 \sigma I_r S_h - \beta_2 \varepsilon I_h S_h - \eta\left(1-e^{-rt}\right) S_h - \mu_h S_h$$

$$= \Lambda_h + \phi(1-\nu) I_h + \psi R_h - \left(\beta_1 \sigma I_r + \beta_2 \varepsilon I_h + \eta\left(1-e^{-rt}\right) + \mu_h\right) S_h$$

$$\geq -\left(\beta_1 \sigma I_r + \beta_2 \varepsilon I_h + \eta\left(1-e^{-rt}\right) + \mu_h\right) S_h$$

$$\int \frac{dS_h}{S_h} \geq -\int \left(\beta_1 \sigma I_r + \beta_2 \varepsilon I_h + \eta\left(1-e^{-rt}\right) + \mu_h\right) dt$$

$$\Rightarrow S_h(t) \geq S_h(0) e^{-\int \left(\beta_1 \sigma I_r + \beta_2 \varepsilon I_h + \eta\left(1-e^{-rt}\right) + \mu_h\right) dt} \geq 0$$

It can similarly be shown that $E_h(t) > 0, I_h(t) > 0, R_h(t) > 0, S_r(t) > 0, E_r(t) > 0, I_r(t) > 0$ for all $t > 0$.

2.2 Invariant Region

Theorem 2: Let $(S_h, E_h, I_h, R_h, S_r, E_r, I_r)$ be the solution of the system (1) with initial conditions and the biological feasible region $\Omega := \Omega_h \times \Omega_r$ with $\Omega_h := \left\{(S_h, E_h, I_h, R_h) \in \mathbb{R}_+^4 : N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$ and $\Omega_r := \left\{(S_r, E_r, I_r) \in \mathbb{R}_+^3 : N_r \leq \frac{\Lambda_h}{\mu_r}\right\}$. Then, Ω is positively invariant and attracting with respect to the flow described by system (1). The rate of change of the humans and rodent populations is given in equation below, it follows that

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

$$\frac{dN_r(t)}{dt} \leq \Lambda_r - \mu_r N_r(t)$$

A standard comparison theorem [5] can then be used to show that

$N_h(t) \leq N_h(0) e^{-\mu_h t} + \frac{\Lambda_h}{\mu_h}\left(1-e^{-\mu_h t}\right)$ and $N_r(t) \leq N_r(0) e^{-\mu_r t} + \frac{\Lambda_r}{\mu_r}\left(1-e^{-\mu_r t}\right)$. In particular,

$N_h(t) \leq \frac{\Lambda_h}{\mu_h}$ and $N_r(t) \leq \frac{\Lambda_r}{\mu_r}$ if $N_h(0) \leq \frac{\Lambda_h}{\mu_h}$ and $N_r(0) \leq \frac{\Lambda_r}{\mu_r}$ respectively.

Thus, the region Ω is positively-invariant. Hence, the system is biologically meaningful and mathematically well-posed in the domain Ω. In this domain it is therefore sufficient to consider the dynamics of the flow generated by the model system (1).

3 Reproduction Number and Stability of Equilibrium Points

The infectiousness of that disease can be encapsulated in basic reproduction number, a number describing how widely a pathogen is likely to spread in a given population. This is defined as the expected number of secondary cases that would arise from a single primary case introduced into a fully susceptible population [5, 6, and 9]. If $R_0 < 1$ the disease cannot persist in the population and will, over time, be eliminated. If $R_0 > 1$, the disease persists. Hence the objective of a disease elimination programme is to reduce the basic reproduction ratio below one. If epidemiologists know enough about a pathogen's R_0, the hope is that they can predict aspects of its next outbreak – and hopefully prevent small-scale outbreaks from becoming large-scale epidemics.

The Lassa fever model (1) has a DFE, obtained by setting the right-hand sides of the equations in the model to zero, given by

$$\xi_0 = \left(S_h^*, E_h^*, I_h^*, R_h^*, S_r^*, E_r^*, I_r^*\right) = \left(\frac{\Lambda_h}{\eta\left(1-e^{-rt}\right)+\mu_h}, 0, 0, 0, \frac{\Lambda_r}{\mu_r}, 0, 0\right).$$

The linear stability of ξ_0 can be established using the next generation operator method [5] on the system (1), the matrices F and V, for the new infection terms and the remaining transfer terms, are, respectively, given by

$$F = \begin{pmatrix} 0 & \beta_2\varepsilon S_h^* & 0 & \beta_1\sigma S_h^* \\ 0 & 0 & 0 & 0 \\ 0 & \beta_3\vartheta S_r^* & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} (\kappa+\mu_h) & 0 & 0 & 0 \\ -\kappa & (\phi+\mu_h+\delta) & 0 & 0 \\ 0 & 0 & (\alpha+\mu_r) & 0 \\ 0 & 0 & -\alpha & \mu_r \end{pmatrix}$$

It follows that the reproduction number of the Lassa fever system (1), denoted by R_0, is

$$R_0 = \frac{1}{2}\left(\frac{\beta_2\varepsilon\kappa\Lambda_h}{(\kappa+\mu_h)(\phi+\mu_h+\delta)\left(\eta(1-e^{-rt})+\mu_h\right)} + \sqrt{\left(\frac{\beta_2\varepsilon\kappa\Lambda_h}{(\kappa+\mu_h)(\phi+\mu_h+\delta)\left(\eta(1-e^{-rt})+\mu_h\right)}\right)^2 + \frac{4\alpha\sigma\vartheta\kappa\beta_1\beta_3\Lambda_h\Lambda_r}{\mu_r^2(\alpha+\mu_r)(\kappa+\mu_h)(\phi+\mu_h+\delta)\left(\eta(1-e^{-rt})+\mu_h\right)}}\right).$$

The model was qualitatively analyzed for the existence and stability of the disease-free equilibrium and endemic equilibrium points. The disease-free equilibrium has been shown to be both locally asymptotically stable and globally asymptotically stable when $R_0 < 1$. It was also shown that the endemic equilibrium point, exists for $R_0 > 1$ and has been noted that this endemic equilibrium is unique and globally asymptotically stable. The implication of the above result to public health is that if the control strategy for Lassa fever can force the reproduction number to below the value of one, then Lassa fever can be eliminated from the population [see 5 for details].

4 Inter-epidemic Period of Lassa Fever

This means occurring between epidemics of disease. That is, the period of recurrent outbreak of disease. In unforced susceptible, exposed, infectious, recovered (SEIR) models of directly

transmitted diseases, incidence is predicted to exhibit damped oscillations with an approximate inter-epidemic period (T):

$$T = 2\pi\sqrt{AD} \qquad (2)$$

where A is the average age of first infection, while D is the sum of latent interval and the infectious interval of the disease. The result based on the model showed increase in inter-epidemic period as the average age of infection increases. The estimation of inter-epidemic period is shown in Table 3.

A (years)	T (years)	A (years)	T (years)
1	14	11	46
2	20	12	48
3	24	13	50
4	28	14	52
5	31	15	54
6	34	16	55
7	37	17	57
8	39	18	59
9	42	19	60
10	44	20	62

Table 3: Estimation of inter-epidemic periods of Lassa fever

Table 3 revealed the estimation of inter-epidemic periods of Lassa fever from the mathematical model. It shows the increase in inter-epidemic period as the average age of infection increases. The plot of the inter-epidemic period against the average age of infection is shown below.

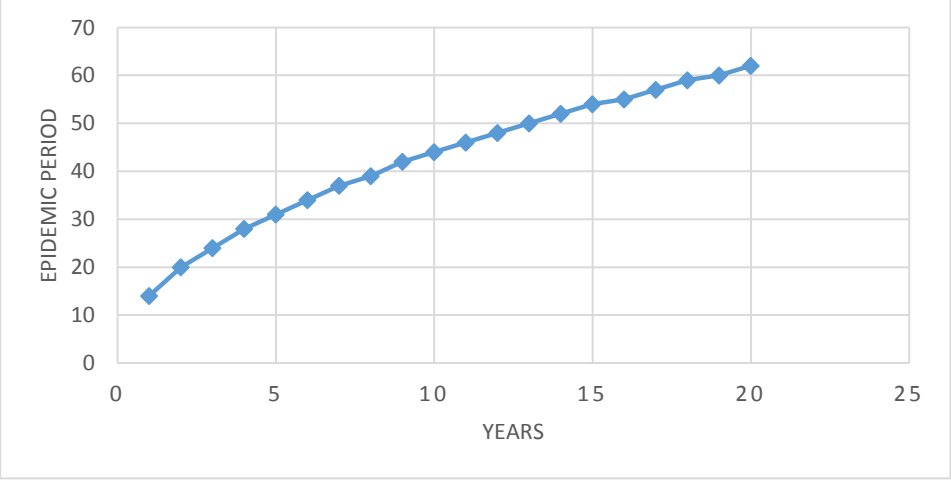

Figure 4**:** Plot of the inter-epidemic period against the average age of infection

4.1 Relationship between Reproduction Number and Inter-epidemic Period of Infectious Disease

Recall that the average age of first infection, A is inversely related with the basic reproduction number, R_0 [14].

$$A = \frac{\kappa_1}{R_0}$$

$$\Rightarrow \frac{T^2}{4\pi^2} = AD = \frac{\kappa_1 D}{R_0} \Rightarrow T^2 R_0 = 4\pi^2 \kappa_1 D = \kappa_2$$

$$\Rightarrow R_0 = \frac{\kappa_2}{T^2} \Rightarrow R_0 \propto \frac{1}{T^2}$$

This indicates that the basic reproduction number is inversely proportional to the square of inter-epidemic period of an infectious disease. This implies that increase in R_0 would decreased T^2. Epidemiologically, any policy or measures taken to reduce the basic reproduction number will definitely make the disease to take a very long time to re-emerge. This by implication goes to show that introduction of effective control measures will lead to a very long time for the re-emergence of infectious disease.

Conclusion

In this work, we have presented a novel and realistic mathematical model that incorporate all the known transmission routes into Lassa fever epidemiology. The basic reproduction number for this model, R_0, has been derived and the inter-epidemic period of infection disease was examined. A significant result of the present study for Lassa fever epidemics in Nigeria is that the inter-epidemic period, which corresponds to the interval between major epidemics of Lassa fever, increases as the average age of infection increases. This result was supported by a theory based on the mathematical model for epidemics of Lassa fever disease. From this result, it can be said that the inter-epidemic period is useful to estimate the effect of intervention on Lassa fever incidences quantitatively. Thus, there is a possibility to investigate the inter-epidemic period for the Lassa fever data for the states in Nigeria. Hence, for long-term and effective control strategy for Lassa fever in Nigeria, it is important to continue the investigation of the inter-epidemic period of Lassa fever disease epidemics, as well as the investigation of control measures, antibody prevalence antiviral strains of the disease.

The paper highlighted the relationship between the Lassa fever basic reproduction number and inter-epidemic period of infection disease. It was found that the basic reproduction number is inversely proportional to the square of inter-epidemic period of an infectious disease. It is hoped that this work would motivate epidemiological researchers to collect relevant data to better understand the relationship between basic reproduction number and inter-epidemic period of infectious diseases. Therefore, any policy or measures taken to reduce the basic reproduction number will definitely make the disease to take a very long time to re-emerge.

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References

[1] Centre for Disease Control (CDC) (2005). Guidelines for preventing the transmission of mycobacterium tuberculosis in health-care settings. *Morbidity and Mortality Weekly Report* (MMWR), 54 (No. RR-17):1–140. Atlanta: Centers for Disease Control and Prevention.

[2] Central Intelligence Agency (2015). *World fact book for the year 2014*. Retrieved on 20 February 2016 from http:/www.cia/library/publication/the-world fact book/geos/ni.htm

[3] Fisher-Hoch S.P., Tomori O., Nasidi A., Perez-Oronoz G.I., Fakile Y., and Hutwagner L. (1995). Review of cases of nosocomial Lassa fever in Nigeria: The high price of poor medical practice. *Biomedical Journal*, 311, 857–869.

[4] Numfor, E. S (2010). Mathematical modelling, simulation and time series analysis of seasonal epidemics. *M.Sc Thesis, East Tenessee State University*.

[5] Obasi, C (2018). Developing and analyzing mathematical models of transmission and Controls of Lassa fever dynamics. *A PhD seminar presented to the Department of Mathematics, University of Nigeria, Nsukka.*

[6] Ogbu,O. E., Ajuluchukwu, C. J. and Uneke, C.J. (2007). Lassa fever in West Africa sub-region: An overview. *Journal of Vector Borne Diseases,* 44, 1-11.

[7] Okosun, K and Smith, R (2017). Optimal control analysis of malaria-schistosomiasis co-infection dynamics. *Math. Biosci. Engineer*, 14 (2), 337-405.

[8] Okuonghae D. and Okuonghae R. (2006). A Mathematical model for Lassa fever. *Journal of the Nigerian Association of Mathematical Physics*, 10,457-464.

[9] Onuorah M.O., Ojo M .S., Usman D.J and Ademu, A (2016). Basic reproductive number for the spread and control of Lassa fever. *International Journal of Mathematics Trends and Technology* (IJMTT), 30 (1), 1-7.

[10] Peter O.J. et al (2018). Sensitivity analysis of the parameters of a cholera model. *J. Appl. Sci. Environ. Manage*. 22 (4), 477-481.

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

[12] World Health Organization (2004). Centre for disease control. Imported Lassa fever. *Morbidity Mortal Weekly Reports*, 53(38), 894-897.

[13] Hay S., Myers M., Burke D., Vaughn D., Endyi T., Anandai N., Shanksi D., Snow R. and Rogers D. (2000). Etiology of inter-epidemic periods of mosquito-borne disease. *Proceedings of the National Academy of Sciences*, Vol. 97 (16), 9335–9339.

[14] Farrington C.P., Kanaan M.N. and Gay N.J. (2001). Estimation of the basic reproduction number for infectious diseases from age-stratified serological survey data. *Appl. Statist.*, 50, Part 3, pp. 251-292.