Journal of the Nigerian Association of Mathematical Physics
Volume 47 (*July, 2018 Issue*), pp333– 340

A MATHEMATICAL MODEL FOR THE VACCINATION AGAINST EBOLA VIRUS

Haruna M., Abdul G. S and Ahu A. A.

Department of Mathematics and Statistics, College of Science and Technology, Kaduna Polytechnic, Kaduna, Nigeria.

Abstract

Hemorrhagic fever like Ebola remains a global health problem, and public health efforts today are geared towards focus on preventing/controlling it. In this paper, a susceptible-vaccinated-infectious-recovered-susceptible (SVIRS) model that addresses the vaccination against Ebola virus as well as the control of Ebola infection in human hosts is developed. It has been confirmed that the disease free equilibrium state is locally asymptotically stable when the basic reproductive number $R_0 < 1$ ***and the endemic equilibrium state is globally asymptotically stable when*** $R_0 > 1$***. A control measure parameter p incorporated into the model helps in preventing/controlling the transmission of Ebola viruses. Sensitivity indices of vaccination and Ebola control parameters show that the two parameters contributed negatively to the basic reproductive number*** R_0***.***

***Keywords*:** Ebola virus; Fruit bats; Vaccine; Immunity; Basic reproductive number

1.0 Introduction

Ebola is a virus disease with a high fatality rate that was first identified in Africa in 1976 [1]. Ebola hemorrhagic fever is a disease caused by one of five subspecies (i.e. strains) of the Ebola virus namely Zaire ebolavirus (EBOV), Bundibugyo ebolavirus (BDBV), Sudan ebolavirus (SUDV), Taï Forest ebolavirus (TAFV) and Reston ebolavirus (RESTV) [1]. Four of the strains can cause severe illness in humans and animals. The fifth, Reston virus, has caused illness in some animals, but not in humans [1]. The first human outbreaks occurred in 1976, one in northern Zaire (now Democratic Republic of the Congo or DRC) in Central Africa: and the other, in southern Sudan (now South Sudan) where it caused deadly epidemics [1,2]. The virus reemerged in Kikwit, Zaire, in 1995 and Gabon in 1996, causing additional, frightening epidemics [2].The virus is named after the Ebola River, where the virus was first recognized in 1976, according to the Centers for Disease Control and Prevention [1]. Ebola came in as a shocker to many people, more especially those living in West Africa countries, Nigeria included. The first case of Ebola in Nigeria was the one on 20th July 2014. This was when an infected man from Liberia arrived into Lagos by aeroplane. Before the death of the man five days later, he had already set off a chain of transmission [1,2]. A total of 20 people were infected by the Ebola virus in Nigeria. These people were those who had contact with the Liberian man who arrived in the airport in Lagos with the virus. The occurrence of Ebola virus in Nigeria claimed 8 lives in the country. Among the people who died, includes the nurse who treated the man and his doctor [2]. Deadly human Ebola outbreaks have been confirmed in the following countries Democratic Republic of the Congo (DRC), South Sudan, Gabon, Liberia, Nigeria and Sierra Leone [1].

Ebola is extremely infectious but not extremely contagious. It is infectious, because an infinitesimally small amount can cause illness [1]. Ebola could be considered moderately contagious, because the virus is not transmitted through the air [1]. Humans can be infected by other humans if they come in contact with body fluids such as blood, urine, feces, or saliva from an infected person or contaminated objects from infected persons[1]. Humans can also be exposed to the virus, for example, by butchering infected animals [1].

While the exact reservoir of Ebola viruses is still unknown, researchers believe the most likely natural hosts are fruit bats [3]. Bat is the only mammal that can fly. Bats have modified hands and arms that serve
as wings capable of sustained flight.

There are nearly 1000 living bat species, accounting for almost a quarter of all mammal species. These species are divided among two major groups. The Megachiroptera, or megabats, are large animals, commonly known as Old World fruit bats [3]. They are mainly fruit-eaters and are found only in tropical habitats of Africa, India, and Australasia. The Microchiroptera, or

Corresponding Author**:** Haruna M., Email: moshoodharuna@yahoo.com, Tel: +2348023445978

microbats, are smaller, eat a variety of foods from small mammals to fish, and are much more widely distributed [3]. However, studies published in 2005 suggested that fruit bats may carry the deadly Ebola virus in Africa and a horseshoe bat may be a host for the SARS virus in Asia.

Symptoms of Ebola typically include: weakness, fever, aches, diarrhea, and vomiting. Additional experiences include stomach pain, rash, red eyes, chest pain, muscle pain, throat soreness, difficulty in breathing or swallowing and internal bleeding [1,3,4]. Typically, symptoms appear 8-10 days after exposure to the virus, but the time it takes symptoms to develop, known as the incubation period can span 2 to 21 days [1,3]. The mortality rate of Ebola hemorrhagic fever ranges from 50 to 90 percent [1].

Unprotected health care workers are susceptible to infection because of their close contact with patients during treatment [1]. Gloves, gowns, and eye shields are necessary when caring for hemorrhagic fever patients [1,3].

Ebola is not transmissible if someone is asymptomatic and usually not after someone has recovered from it [1]. However, the virus has been found in semen for up to three months, and "possibly" is transmitted from contact with that semen, according to the CDC [1].

Mathematical models have been used to modelled haemorrhagic diseases like yellow fever, Dengue [5,6], and Lassa fever [3,7,8]. This paper considered '*SVIRS*' model which is a modified form of '*SIRS*' model by incorporating vaccinated class, V into the human component of the model. In this model, the susceptible individuals are in susceptible class, $S(t)$; the vaccinated individuals are in vaccinated class, $V(t)$; the infected individuals are in infected class, $I(t)$; while the recovered individuals are in recovered/immune class, $R(t)$, while $E(t)$ stands for Ebola virus, carrying and transmitting Ebola infection.

Section 2 of this paper deals with formulation of the Ebola model, section 3 determines the basic reproduction number, the disease free equilibrium (i.e. zero or trivial) state, endemic equilibrium (i.e. non-zero or non-trivial) state (or point), section 4 analyses the stability of the disease free equilibrium and endemic equilibrium states, section 5 considers the impacts of Ebola vaccine and control measures on the model and section 6 deals with the conclusion and recommendations.

The aim of this study is to investigate the local and global stability of the disease free equilibrium and endemic equilibrium states of the Ebola virus model. And to also consider impacts of the Ebola vaccine on the model.

2.0 Model

2.1 Formulation of Model

This paper derives a dynamic system for Ebola disease so as to study the dynamics of the transmission and spread of the Ebola virus in human hosts. The model describes the dynamic of transmission of Ebola in human beings. Human population, in turn, is divided into susceptible individuals class, denoted by $\boldsymbol{S(t)}$, infected individuals class $\boldsymbol{I(t)}$, the vaccinated individuals class $\boldsymbol{V(t)}$, the recovered (and immune) individuals class $\boldsymbol{R(t)}$ and the total humans, $\boldsymbol{N = S + V + I + R}$ [9-25]. And $\boldsymbol{E(t)}$ for Ebola virus, that causes Ebola fever. The susceptible individual in susceptible class S becomes an infected individual in infected class I after interacting effectively with Ebola virus, infected and infectious individuals in infected human class I. Infectious individual in infected class I becomes recovered individual in recovered/immune class R, after taken Ribavirin, an antibiotic drugs that improved immunity of Ebola, Lassa fever victims. This individual's moved from recovered class to susceptible class after loss of immunity. Note that, α_1 and α_2 represent the transmission rates of Ebola virus from E to S and from I to S respectively; π and β are the natural birth rates of S and E respectively; μ_1 and μ_2 are the natural mortality rates for humans and Ebola virus respectively; ρ is the proportion of individuals in susceptible class vaccinated against Ebola virus; ω is the proportion of individuals in vaccinated class that returned to susceptible class as a result of waning Ebola virus vaccine; δ is the proportion of Ebola induced deaths in I; γ is the recovery rate of infected individuals in R; σ is the proportion of individuals in recovered/immune class that returned to susceptible class as a result of loss of temporary immunity from Ebola virus infection.

2.2 Assumptions

I. Viruses causing Ebola infection can be transmitted from infected individuals to susceptible individuals by direct contact and by the virus discharged to the environment by susceptible individuals.
II. Once an individual has suffered from Ebola infection, he gets temporary immunity to Ebola infection.
III. Recruitment of humans is through births, loss of temporary immunity, and loss of immunity due to waning of Ebola vaccine.
IV. There is additional deaths (Ebola induced deaths) δ to infected human I.
V. The birth and death rates of susceptibles are not the same.

2.3 Schematic Diagrams

In Figure 1, the four rectangles represent the four classes (i.e. subpopulations), while the circle represents Ebola viruses. The arrows represent the progressions, while the dotted line arrow represents the Ebola viruses discharged by the human hosts. And the straight line represents the interconnection between the individuals in susceptible class and the Ebola virus.

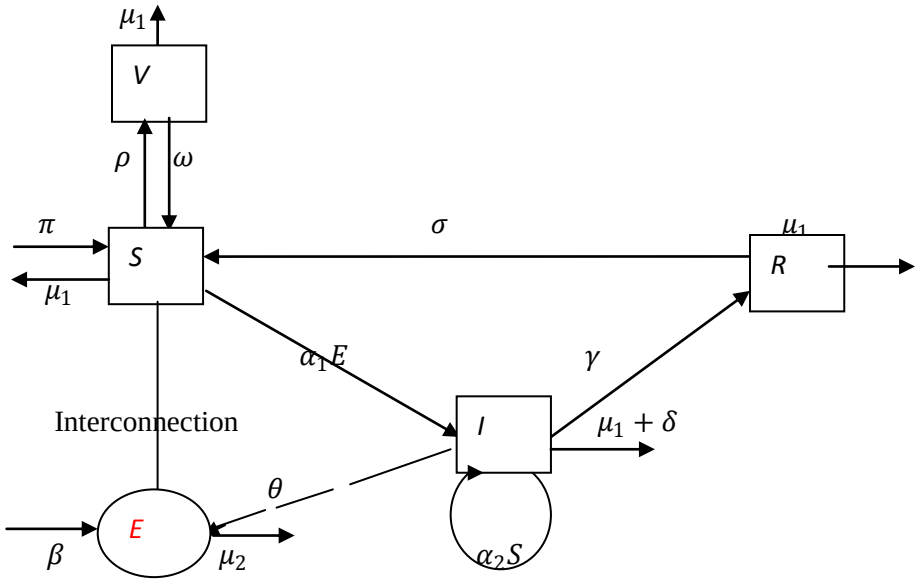

Figure 1 Schematic diagram showing progressions and probabilities for humans

2.4 Description of the Model

Beginning from the first four equations of malaria model (1) in which susceptible humans S grow at the rate of $\pi + \omega V - (\mu_1 + \rho)S$, where π is the natural birth rate, and μ_1 is the natural mortality rate. Those susceptible humans S who acquired the Ebola infection do so at the rates of $\alpha_1 ES$ and $\alpha_2 IS$ where α_1 is the transmission rate of Ebola from the Ebola virus E to the susceptible humans and α_2 is the transmission rate of Ebola from the infected individuals in infected class I to the susceptible humans. The rate at which the host infection in I occurs is given by $\alpha_1 SE$ and $\alpha_2 IS$. The I may either recover after treatment with an antibiotic for treating Ebola infection at the rate γ or die from the disease, with the rate $(\mu + \delta)$, where δ is the death as a result of the malaria infection. An individual in R class only die from natural causes. Then the last equation of model (1) represents Ebola viruses E. Ebola viruses grow at the rate of $\theta I + (\beta - \mu_2 - k)E$, where β is the natural birth rate, and μ_2 is the natural mortality rate of Ebola viruses. And θ is the rate of discharge of Ebola viruses from infected/infectious individuals into the environment, while k denotes the additional death as a result of washing of hands, protection against the virus by heath workers or care givers and fumigation of the environment.

2.5 Model Equation for Treatment of Malaria Infection

Here, the mathematical model for the Ebola vaccination using '*SVIRE'* approach is presented. By considering a human population in a settlement where the Ebola viruses/fruity Bats carrying Ebola viruses are present. The model equations are:

$$S' = \pi + \sigma R + \omega V - \alpha_1 SE - \alpha_2 IS - (\mu_1 + \rho)S \quad (1a)$$

$$V' = \rho S - (\mu_1 + \omega)V \quad (1b)$$

$$I' = \alpha_1 SE + \alpha_2 IS - ((\mu_1 + \delta + \gamma)I \quad (1c)$$

$$R' = \gamma T - (\mu_1 + \sigma)R \quad (1d)$$

$$E' = \theta I + \beta E - (\mu + k)E \quad (1e)$$

Let

$$S + V + I + R = N \quad (2)$$

3.0 Equilibrium States

There are two equilibrium states, the disease free equilibrium state $E^0 = (S^0, V^0 I^0, R^0, E^0)$, is a state where there is no epidemic and the endemic equilibrium $E^* = (S^*, V^*, I^*, R^*, E^*)$, is a state where there is epidemic.

3.1 Basic Reproductive Number

This is a number that gives the number of secondary infective cases of Ebola infection produced by an individual infected with Ebola infection during the effective period when introduced in a population of susceptibles [7-25].

The basic reproductive number R_0 is defined as the spectral radius of the 'next generation operator' [21]. The formulation of the operator involves determining two compartments, infected human and Ebola virus, from the model. The basic reproductive number R_0 of the Ebola model (1) is then determined by finding spectral radius of the next generation operator which is the eigenvalues of matrix FV^{-1}.

$$= \begin{pmatrix} \alpha_2 S^0 & \alpha_1 S^0 \\ 0 & 0 \end{pmatrix} \quad (3)$$

$$v = \begin{pmatrix} k_3 & 0 \\ \theta & k_5 - \beta \end{pmatrix} \quad (4)$$

$$R_0 = \rho(Fv^{-1}) = \begin{vmatrix} \frac{(\alpha_2(k_5-\beta)+\alpha_1\theta)S^0}{k_3(k_5-\beta)} - \lambda & \frac{\alpha_1 S^0}{k_5-\beta} \\ 0 & -\lambda \end{vmatrix} = 0 \quad (5)$$

$$\lambda^2 - \frac{(\alpha_2(k_5-\beta)+\alpha_1\theta)S^0}{k_3(k_5-\beta)}\lambda = 0 \quad (6)$$

From the characteristic equation (6), the eigenvalues λs' are

$\lambda_1 = 0$ or $\lambda_2 = \frac{(\alpha_2(k_5-\beta)+\alpha_1\theta)S^0}{k_3(k_5-\beta)}$ (7)

From (7),

$R_0 = \frac{(\alpha_2(k_5-\beta)+\alpha_1\theta)S^0}{k_3(k_5-\beta)}$ (8)

Equation (8) represents the basic reproductive number for Ebola fever [19-23]. The biological meaning of R_0 in (8) is that it defines the average number of new infections (patients) produced by one Ebola infected person when introduced into a population of susceptible persons. It follows then that if $R_0 > 1$, then the disease is able to invade host population. Otherwise, if $R_0 \leq 1$, the disease eventually disappears from the host population.

3.2 Determination of Equilibrium States

At equilibrium,

$S' = V' = I' = R' = R' = 0$ (9)

Applying equation (9) to system (1):

$\pi + \sigma R + \omega V - \alpha_1 ES - \alpha_2 IS - k_1 S = 0$ (10a)

$\rho S - k_2 V = 0$ (10b)

$\alpha_1 ES + \alpha_2 IS - k_3 I = 0$ (10c)

$\gamma I - k_4 R = 0$ (10d)

$\theta I + \beta E - k_5 E = 0$ (10e)

where

$k_1 = \rho + \mu_1$ (11)

$k_2 = \omega + \mu_1$ (12)

$k_3 = \delta + \gamma + \mu_1$ (13)

$k_4 = \sigma + \mu_1$ (14)

$k_5 = k + \mu_2$ (15)

From (10e),

$I = \frac{(k_5-\beta)}{\theta} E$ (16)

Substituting (16) into (10c) gives:

$E = 0$ (17)

Or

$S^* = \frac{k_3(k_5-\beta)}{\alpha_1\theta+\alpha_2(k_5-\beta)}$ (18)

Based on (17),

$V^0 = \frac{\rho\pi}{k_1k_2-\omega\rho}$ (19)

$S^0 = \frac{k_2\pi}{k_1k_2-\omega\rho}$ (20)

$I^0 = R^0 = E^0 = 0$ (21)

Therefore, the Disease free equilibrium DFE state

$E^0 = (S^0, V^0, 0,0,0)$ (22)

From (10b),

$V^* = \frac{\rho S^*}{k_2}$ (23)

From (10d),

$R^* = \frac{\gamma I^*}{k_4}$ (24)

From (10c)

$\alpha_1 E^* S^* + \alpha_2 I^* S^* = k_3 I^*$ (25)

Substituting (23), (24) and (25), gives

$I^* = \frac{k_3k_4(k_5-\beta)(k_1k_2-\omega\rho)}{k_2(k_3k_4-\sigma\gamma)(\alpha_1\theta+(k_5-\beta)\alpha_2)}(R_0 - 1)$ (26)

If $R_0 > 1$, then $I^* > 0$.

Substituting (26) into (16) and (24), give

$E^* = \frac{\theta k_3k_4(k_1k_2-\omega\rho)}{k_2(k_3k_4-\sigma\gamma)(\alpha_1\theta+(k_5-\beta)\alpha_2)}(R_0 - 1)$ (27)

$R^* = \frac{\gamma k_3(k_5-\beta)(k_1k_2-\omega\rho)}{k_2(k_3k_4-\sigma\gamma)(\alpha_1\theta+(k_5-\beta)\alpha_2)}(R_0 - 1)$ (28)

Substituting (18) into (23), gives

$V^* = \frac{\rho k_3(k_5-\beta)}{k_2(\alpha_1\theta+(k_5-\beta)\alpha_2)}$ (29)

Therefore, EE state,

$E^* = (S^*, V^*, I^*, R^*, E^*)$ (30)

3.2.1 Existence of Disease Free Equilibrium State

Here, the existence of disease free equilibrium state using the following proposition will be established:

Proposition 1: A disease free equilibrium state of the system (1) exists at the point

$$S = \frac{k_2\pi}{k_1k_2-\omega\rho}, V = \frac{\rho\pi}{k_1k_2-\omega\rho}, I = 0, R = 0, E = 0 \quad (31)$$

Proof: Let the disease free equilibrium point be defined by

$$S = S^0, I = I^0, T = T^0, R = R^0, U = U^0, V = V^0 \quad (32)$$

Consider (32) to be an arbitrary equilibrium point at which (31) holds. Substituting (32) into system (10) at E^0,

$$-k_1S^0 + \omega V^0 = -\pi \quad (33a)$$

$$\rho S^0 - k_2V^0 = 0 \quad (33b)$$

$$I^0 = R^0 = E^0 = 0 \quad (33c)$$

From the first and second equations of the system (33),

$$V^0 = \frac{\rho\pi}{k_1k_2-\omega\rho} \quad (34)$$

And

$$S^0 = \frac{k_2\pi}{k_1k_2-\omega\rho} \quad (35)$$

Hence, from (33*c*), (34), and (35) the proposition is proved.

3.2.2 Endemic Equilibrium State

To find the endemic equilibrium (ee) state of the treatment model (1), which is the equilibrium state where the Ebola fever persists. Solve the system of equations (10) at E^*, where the solution to (10) satisfies the following conditions:

$$\begin{pmatrix} E^* = \{(S^*, V^*, I^*, R^*, E^*): S^* > 0, V^* > 0, I^* > 0, \\ R^* > 0, E^* > 0;\ N = S^* + V^* + I^* + R^*; E^*\} \end{pmatrix} \quad (36)$$

System (10) at E^*, becomes

$$\pi + \sigma R^* + \omega V^* - \alpha_1E^*S^* - \alpha_2I^*S^* - k_1S^* = 0 \quad (37a)$$

$$\rho S^* - k_2V^* = 0 \quad (37b)$$

$$\alpha_1E^*S^* + \alpha_2I^*S^* - k_3I^* = 0 \quad (37c)$$

$$\gamma I^* - k_4R^* = 0 \quad (37d)$$

$$\theta I^* + \beta E^* - k_5E^* = 0 \quad (37e)$$

Equation (30) is the solution to system (37).

3.2.2.1 Existence of Endemic Equilibrium State

The existence of endemic equilibrium state will be established using the following proposition:

Proposition 2: The endemic equilibrium state of the system (1) exists if the basic reproductive number $R_0 > 1$.

Proof

From (18), (26) – (29):

$$S^* > 0, V^* > 0, I^* > 0, R^* > 0, E^* > 0 \quad (38)$$

Whenever $R_0 - 1 > 0$. Therefore endemic equilibrium E^*exists.

4.0 Stability Analysis

Stability analyses of disease free equilibrium (dfe) and endemic equilibrium (ee) states are carried out to test whether the two equilibrium states are stable at long run or not. The local stability of disease free equilibrium state and global stability of endemic equilibrium state using Jacobian method were established in sections 4.1 and 4.3 respectively. Also the global stability of dfe using the method in [24] and the local stability of endemic equilibrium state using Lynapunov method were established in sections 4.2 and 4.4 respectively.

4.1 Local Stability of Disease Free Equilibrium State E^0

Proposition3: The disease free equilibrium state E^0 is locally asymptotically stable whenever $R_0 < 1$.

By applying Jacobian method to system (10),

$$J(E^0) = \begin{vmatrix} -(k_1+\lambda) & \omega & -\alpha_2S^0 & \sigma & -\alpha_1S^0 \\ \rho & -(k_2+\lambda) & 0 & 0 & 0 \\ 0 & 0 & -(k_3-\alpha_2S^0+\lambda) & 0 & \alpha_1S^0 \\ 0 & 0 & \gamma & -(k_4+\lambda) & 0 \\ 0 & 0 & \theta & 0 & -(k_5-\beta+\lambda) \end{vmatrix} = 0 \quad (39)$$

$$\lambda^5 + A_1\lambda^4 + A_2\lambda^3 + A_3\lambda^2 + A_4\lambda + A_5 = 0 \quad (40)$$

Where

$$A_1 = k_3 + k_5 - \beta - \alpha_2S^* + k_4 + k_1 + k_2 \quad (41)$$

$$A_2 = \begin{pmatrix} k_3(k_5-\beta)(1-R_0) + (k_4+k_1+k_2)(k_3+k_5-\beta-\alpha_2S^*) \\ +k_4(k_1+k_2) + (k_1k_2-\omega\rho) \end{pmatrix} \quad (42)$$

$$A_3 = \begin{pmatrix} (k_4+k_1+k_2)k_3(k_5-\beta)(1-R_0) + \\ \big(k_4(k_1+k_2) + (k_1k_2-\omega\rho)\big)(k_3+k_5-\beta-\alpha_2S^0) + k_4(k_1k_2-\omega\rho) \end{pmatrix} \quad (43)$$

$$A_4 = \begin{pmatrix} \big(k_4(k_1+k_2) + (k_1k_2-\omega\rho)\big)k_3(k_5-\beta)(1-R_0) \\ +k_4(k_1k_2-\omega\rho)(k_3+k_5-\beta-\alpha_2S^0) \end{pmatrix} \quad (44)$$

$$A_5 = k_4(k_1k_2-\omega\rho)k_3(k_5-\beta)(1-R_0) \quad (45)$$

The eigenvalues of (40) are have negative real parts, since A_1, A_2, A_3, A_4, and A_5 are all positive whenever $R_0 < 1$. By applying Routh-Hurwith criteria, the dfe, E^0 state of model (1) is locally asymptotically stable (l.a.s). The biological implication of the above proposition is that Ebola infection can be controlled from the host population when $R_0 - 1 < 0$.

4.2 Global Stability of Disease Free Equilibrium State E^0

The restrictions on the initial conditions of the state variables are removed through global stability of equilibrium. For all initial conditions, solutions approach the equilibrium in global asymptotic stability [24]. The global stability of dfe, E^0, is analyzed using the method in [24].

Proposition 4: The disease free equilibrium, E^0 of model (1) is globally asymptotically stable in region D if $R_0 < 1$.

Proof: the two conditions (H1) and (H2) as in [24] must be satisfied for $R_0 < 1$, so as to establish the global stability of the dfe [23].

The model (1) is rewritten as:

$$X_1^{'} = F(X_1, X_2) \quad (46a)$$

$$X_2^{'} = G(X_1, X_2) \quad (46b)$$

$$G(X_1, 0) = 0 \quad (46c)$$

Where $X_1 = (S^0, V^0, R^0)$ and $X_2 = (I^0, E^0)$.

The uninfected populations are the components of X_1, while the infected populations are the components of X_2; $X_1 \in R^3$ and $X_2 \in R^2$:

$$E^0 = (X_1^*, 0) \quad (47)$$

Where

$$X_1^* = (N, 0) \quad (48)$$

Where

$$N = (N, E) \quad (49)$$

The first condition for the global asymptotical stability (g.a.s) of X_1^* is

$$X_1^{'} = F(X_1, 0) = \begin{bmatrix} \pi + \omega V^0 + \sigma R^0 - k_1 S^0 \\ \rho S^0 - k_2 V^0 \\ k_3 R^0 \end{bmatrix} \quad (50)$$

Equation (50) is a system of linear differential equations. Solutions to system (50) are:

$$S^0(t) = e^{-\left(\frac{k_1 k_2 - \omega\rho}{k_2}\right)t}\left(S^0(0) - \frac{k_2\pi}{k_1 k_2 - \omega\rho}\right) + \frac{k_2\pi}{k_1 k_2 - \omega\rho} \quad (51)$$

$$V^0(t) = e^{-\left(\frac{k_1 k_2 - \omega\rho}{k_2}\right)t}\left(V^0(0) - \frac{\rho\pi}{k_1 k_2 - \omega\rho}\right) + \frac{\rho\pi}{k_1 k_2 - \omega\rho} \quad (52)$$

$$R^0(t) = e^{-k_4 t} R^0(0) \quad (53)$$

Clearly, from (51) – (53), $S^0(t) + V^0(t) + R^0(t) \to \frac{(k_2+\rho)\pi}{k_1 k_2 - \omega\rho}$ as $t \to \infty$ regardless of the values of the initial conditions: $S^0(t)$, $V^0(t)$, and $R^0(t)$. Hence, X_1^* is globally asymptotically stable.

For the second condition, let

$$A = \begin{pmatrix} -k_3 + \alpha_2 \frac{k_2\pi}{k_1 k_2 - \omega\rho} & \alpha_1 \frac{\rho\pi}{k_1 k_2 - \omega\rho} \\ \theta & -k_5 + \beta \end{pmatrix} \quad (54)$$

Matrix (54) is an M-matrix where the off-diagonal elements are non-negative.

$$G(X_1, X_2) = \begin{pmatrix} \alpha_1 S^0 E^0 + \alpha_2 S^0 I^0 - k_3 I^0 \\ \theta I^0 - (k_5 - \beta) E^0 \end{pmatrix} \quad (55)$$

$$\hat{G}(X_1, X_2) = AX_2 - G(X_1, X_2) \quad (56)$$

Substituting (54) and (55) into (56), gives

$$\hat{G}(X_1, X_2) = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \quad (57)$$

From (57), the dfe state, E^0 is globally asymptotically stable (g.a.s.) whenever the basic reproductive number $R_0 < 1$. Hence, the disease free equilibrium state, E^0 is locally and globally stable as analyzed above, the Ebola infection disappears from the host population. Otherwise, the dfe, E^0 is unstable. Hence, the test for local and global asymptotic stability of endemic equilibrium state, E^* are carried out using the following propositions:

4.3 Local Stability of Endemic Equilibrium State E^*

Proposition 5: The endemic equilibrium state E^* of model (1) is locally asymptotically stable $R_0 < 1$.

Proof: By applying Jacobian method to the system of equations (37),

$$J(E^0) = \begin{vmatrix} -(B_1 + k_1 + \lambda) & \omega & -\alpha_2 S^* & \sigma & -\alpha_1 S^* \\ \rho & -(k_2 + \lambda) & 0 & 0 & 0 \\ B_1 & 0 & -(B_2 + \lambda) & 0 & \alpha_1 S^* \\ 0 & 0 & \gamma & -(k_4 + \lambda) & 0 \\ 0 & 0 & \theta & 0 & -(B_3 + \lambda) \end{vmatrix} = 0 \quad (58)$$

Where

$$B_1 = \alpha_1 S^* E^* + \alpha_2 S^* I^* \quad (59)$$

$$B_2 = k_3 - \alpha_2 S^* \quad (60)$$

$$B_3 = k_5 - \beta \quad (61)$$

Therefore, the characteristic equation of (58) is

$$\lambda^5 + C_1\lambda^4 + C_2\lambda^3 + C_3\lambda^2 + C_4\lambda + C_5 = 0 \quad (62)$$

Where

$$C_1 = k_4 + k_3 + k_5 - \beta - \alpha_2 S^* + k_1 + k_2 + \alpha_1 S^* E^* + \alpha_2 S^* I^* \quad (63)$$

$$C_2 = (k_1 + k_2)(k_4 + k_3 + k_5 - \beta - \alpha_2 S^*) + (k_1 k_2 - \omega\rho) + k_4(k_4 + k_3 + k_5 - \beta - \alpha_2 S^*) + (\alpha_1 S^* E^* + \alpha_2 S^* I^*)(k_3 + k_4 + k_2 + B_3) \quad (64)$$

$$C_3 = \begin{pmatrix} (k_1 + k_2)k_4(k_4 + k_3 + k_5 - \beta - \alpha_2 S^*) \\ +(k_1 k_2 - \omega\rho)k_4(k_4 + k_3 + k_5 - \beta - \alpha_2 S^*) \\ +(\alpha_1 S^* E^* + \alpha_2 S^* I^*)\big((k_2 + B_3)(k_3 + k_4) + k_3 k_4 - \sigma\gamma + k_2 B_3\big) \end{pmatrix} \quad (65)$$

$$C_4 = (k_1 k_2 - \omega\rho)(k_3 + k_5 - \beta - \alpha_2 S^*)k_4 + (\alpha_1 S^* E^* + \alpha_2 S^* I^*)\big((k_3 k_4 - \sigma\gamma)(k_2 + B_3) + (k_3 + k_4)k_2 B_3\big) \quad (66)$$

$$C_5 = (\alpha_1 S^* E^* + \alpha_2 S^* I^*)(k_3 k_4 - \sigma\gamma)k_2 B_3 \quad (67)$$

The eigenvalues of (62) have negative real parts, since C_1, C_2, C_3, C_4,, and C_5 are all positive whenever $R_0 > 1$. By applying Routh-Hurwith criteria, the endemic equilibrium, E^* state of model (1) is globally asymptotically stable (g.a.s).

4.4 Global Stability of Endemic Equilibrium State E^*

To analyse the global stability of endemic equilibrium state, apply Lynapunov function to system (10).

Proposition 6: The endemic equilibrium state E^* of model (1) is globally asymptotically stable if $R_0 > 1$.

Proof

$$U'(S,I,T,R,U,V) = \left(1 - \frac{S^*}{S}\right)S' + \left(1 - \frac{V^*}{V}\right)V' + \left(1 - \frac{I^*}{I}\right)I' + \left(1 - \frac{R^*}{R}\right)R' + \left(1 - \frac{E^*}{E}\right)E' \quad (68)$$

Substituting (10) into (68),

$$U'(S,I,T,R,U,V) = \left(1 - \frac{S^*}{S}\right)(\pi + \omega V + \sigma R - (\alpha_1 E + \alpha_2 I + k_1)S) + \left(1 - \frac{V^*}{V}\right)(\rho S - k_2 V) + \left(1 - \frac{I^*}{I}\right)((\alpha_1 E + \alpha_2 I)S - k_3 I) + \left(1 - \frac{R^*}{R}\right)(\gamma I - k_4 R) + \left(1 - \frac{E^*}{E}\right)(\theta I - k_5 E) \quad (69)$$

$$U'(S,I,T,R,U,V) = \left(1 - \frac{S^*}{S}\right)\begin{bmatrix}(\alpha_1 E^* + \alpha_2 I^*)S^* - (\alpha_1 E + \alpha_2 I)S + \\ k_1 S^* - k_1 S + \sigma R + \rho V - \sigma R^* - \rho V^*\end{bmatrix} + \left(1 - \frac{V^*}{V}\right)(k_2 V^* - k_2 V) + \left(1 - \frac{I^*}{I}\right)\begin{pmatrix}(\alpha_1 E + \alpha_2 I)S - \\ (\alpha_1 E^* + \alpha_2 I^*)S^*\end{pmatrix} + \left(1 - \frac{R^*}{R}\right)(k_4 R^* - k_4 R) + \left(1 - \frac{E^*}{E}\right)[(k_5 - \beta)E^* - (k_5 - \beta)E] \quad (70)$$

Rearranging (70) further, gives:

$$U' = k_1 S^*\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + \mu_1 V^*\left(2 - \frac{V^*}{V} - \frac{V}{V^*}\right) + \mu_1 R^*\left(2 - \frac{R^*}{R} - \frac{R}{R^*}\right) + (k_5 - \beta)E^*\left(2 - \frac{E^*}{E} - \frac{E}{E^*}\right) + \alpha_2 I^* S^*\left(4 - \frac{S^*}{S} - \frac{S}{S^*} - \frac{I^*}{I} - \frac{I}{I^*}\right) + \alpha_1 E^* S^*\left(4 - \frac{S^*}{S} - \frac{E}{E^*} - \frac{I^*}{I} - \frac{E}{E^*}\frac{I^*}{I}\frac{S}{S^*}\right) + \rho V^*\left(3 - \frac{V^*}{V} - \frac{S^*}{S} - \frac{S^*}{S}\frac{V}{V^*}\right) + \sigma R^*\left(3 - \frac{S^*}{S} - \frac{R^*}{R} - \frac{S^*}{S}\frac{R}{R^*}\right) \quad (71)$$

$$U' = -\rho V^*\left(\frac{V^*}{V} + \frac{S^*}{S} + \frac{S^*}{S}\frac{V}{V^*} - 3\right) - \sigma R^*\left(\frac{S^*}{S} + \frac{R^*}{R} + \frac{S^*}{S}\frac{R}{R^*} - 3\right) - \alpha_2 I^* S^*\left(\frac{S^*}{S} + \frac{S}{S^*} + \frac{I^*}{I} + \frac{I}{I^*} - 4\right) - \alpha_1 E^* S^*\left(\frac{S^*}{S} + \frac{E}{E^*} + \frac{I^*}{I} + \frac{E}{E^*}\frac{I^*}{I}\frac{S}{S^*} - 4\right) - k_1 S^*\frac{(S - S^*)^2}{S} - \mu_1 V^*\frac{(V - V^*)^2}{V} - \mu_1 R^*\frac{(R - R^*)^2}{R} - (k_5 - \beta)E^*\frac{(E - E^*)^2}{E} \quad (72)$$

If $E^* > 0$ then $\frac{dU}{dt} \leq 0$. Thus, E^* is globally asymptotically stable [18,20]. This is the state where Ebola fever persists in the host population. That is, Ebola will remain in the population, since infectious humans still remain in the population, because they have not died or recovered.

5.0 Impacts of Ebola Vaccine/Control Measures on the Model

To investigate the impacts of Ebola vaccine/control measures on the Ebola model, sensitivity analyses of vaccination rate and control measure(s) ρ, k are carried out on the reproductive number with respect to ρ and k. Applying the normalized forward sensitivity index with respect to ρ and k [11, 25], which is the relative change of basic reproductive number, R_0 with relative change of treatment and recovery ρ and k. Mathematically,

$$\frac{\rho}{R_0}\frac{\partial R_0}{\partial \rho} = -\frac{\rho}{(k_2 + \rho)} \quad (73)$$

Equation (73) shows that the vaccination rate ρ has negative impacts on the production of new infective. That is, the higher the vaccination rate ρ, the lower the number of new infected persons (Ebola infected patients) in infected class $I(t)$, this means that both infected individuals and Ebola virus will reduce drastically due to Ebola vaccine been given to the susceptible individuals in susceptible class $S(t)$.

$$\frac{k}{R_0}\frac{\partial R_0}{\partial k} = -\frac{k\alpha_1\theta}{(\mu_2 + k - \beta)(\mu_2 + k - \beta + \alpha_1\theta)} \quad (74)$$

Equation (74) shows that the control/preventive measures k in form of i. washing of hands with antiseptic soap/sanitizer ii. Abstinence from eating/butchering infected animals like fruit bats that are reservoir for Ebola viruses iii. Wearing of protective kits i.e. gloves, gowns, and eye shields by health care workers/providers when caring for Ebola fever patients.

The rate k has negative impacts on the production of new infective in infected class $I(t)$. That is, the higher the parameter k, the lower the number of new infected persons (Ebola infected patients), this means that both infected individuals and Ebola virus will reduce drastically due to control/preventive measures taken against Ebola viruses.

6.0 Conclusion and Recommendations

Incorporating vaccinated class $V(t)$ and Ebola control measure k into the model helps in preventing/controlling the transmission of Ebola virus E(t). A system of five ordinary differential equations is used in formulating Ebola vaccination model. The basic reproductive number R_0 is determined using Next Generation Method. Existence of disease-free equilibrium (dfe) and endemic equilibrium (ee) states were established. The local and global stabilities of disease free equilibrium state and endemic equilibrium state were analyzed and it was discovered that disease free equilibrium and endemic equilibrium states are locally and globally asymptotically stable. In conclusion, the local and global stabilities of dfe show that Ebola infection will not persist in the host community if $R_0 < 1$, otherwise the infection will persist (i.e. spread). The paper recommends mass production of the Ebola vaccine by the State and Federal government of Nigeria (S-FGN), World Health Organization (WHO), as well as other corporate organizations. Furthermore, the enlightenment campaigns by both the S-FGN be intensified so as prevent future occurrence of Ebola in Nigeria and other Ebola endemic countries.

References

[1] CNN Library, Ebola Fast Facts, Updated May 24, 2017, Retrieved 8/6/2017. http://edition-m.cnn.com /2014/04/11/health/ebola-fast-facts/index.html?r=https%3A%2F%2Fwww.google.com%2F

[2] 10 Facts About Ebola Occurrence in Nigeria, Retrieved 8/6/2017. http://www.visitnigeria.com.ng/10-facts-ebola-occurence-nigeria/

[3] Gordon, D. G. (2009). Bat. Microsoft Encarta Premium, Microsoft® Encarta® 2009 [DVD]. Redmond, WA: Microsoft Corporation.

[4] Microsoft Encarta Premium (2009). Hemorrhagic Fever. Microsoft® Encarta® 2009 [DVD]. Redmond, WA: Microsoft Corporation.

[5] Kongnuy, R., Naowanich, E., & Pongsumpun, P. (2011). Analysis of a dengue disease transmission model with clinical diagnosis in Thailand. *International Journal of Mathematical Models and Methods in Applied Sciences*. *3*(5), 594-601.

[6] Feng, Z. & Jorge X. V. (1997). Competitive exclusion in a vector-host model for the dengue fever. *Journal of Mathematical Biology*. *35*, 523-544.

[7] Haruna, M., Okeowo. G. F. & Idoko, J. E. (2010). A Mathematical model for endemic lassa with constant human and populations. *Journal of the Nigerian Association of Mathematical Physics*. *29*, 55-112.

[8] Sirajo, Abdulrahman. (2013). Stability analysis of the disease free equilibrium state for disease. *Journal of Science, Tech., Maths and Educ. 9*(2), 115-123. Retrieved 8/11/2016.

[9] Garba, S.M. & Gumel, A.B. (2010). Mathematical recipe for HIV elimination in Nigeria. *Journal of Nigerian Mathematical Society*. *29*, 55-112.

[10] Iyare B.S.E & Osagiede, F.E.U. (2011). A variable human population model for malaria disease with direct transmission. *International Journal of Academic Research*. *3*(5), 344-348.

[11] Mushayabasa, S. (2011). Impact of vaccine on controlling typhoid fever in Kassena-Nankana District of Upper East of Ghana: Insight from a Mathematical Model, *Journal of Modern Mathematics and Statistics*. *5*(2), 54-59.

[12] Adeboye, K. R. & Haruna, M. (2015[b]). A mathematical model for the control of transmission of typhoid fever. *Journal of the Nigerian Association of Mathematical Physics*. *29*(1) 167 - 172.

[13] Lawi, G. O., Mugisha, J. Y. T. & Omolo-Ongati, N. (2011). Mathematical model for malaria and meningitis co-infection among children. *Applied Mathematical Sciences. 5*(47), 2337-2359.

[14] Lawi, G. O., Mugisha, J. Y. T. & Omolo-Ongati, N. (2013). Modeling co-infection of paediatric malaria and pneumonia. *International Journal of Mathematical Analysis. 7*(9), 413-424.

[15] Pongsumpun, P. (2010). Mathematical model for the transmission of two plasmodium malaria. *International Journal of Biological and Life Science*. *6* (3), 138-142

[16] Blyuss, K. B. & Kyrychko, Y. N. (2005). On a basic model of a two-disease epidemic. *Journal of Applied Mathematics and Computation*. *160*, 177-187. doi:10.1016/j.amc.2003.10.033

[17] Ashrafur Rahman, S. M. & Zou, X. (2011). Flu epidemics: a two-strain flu model with a single vaccination. *Journal of Biological Dynamics*. *5*(5), 376-390. http://dx.doi.org/10.1080/7513758.2010.510213

[18] Haruna, M. (2015). Development of mathematical model for the control of malaria and typhoid co-infection using susceptible-infectious-recovered-susceptible (sirs) approach. Ph.D. Thesis, Minna, Nigeria: Federal University of Technology.

[19] Adeboye, K. R. & Haruna, M. (2014). Mathematical modelling of co-existence of *plasmodium* and *salmonella typhi* in human. *Journal of Mathematical Sciences*. *3*(1) 641 - 656.

[20] Adeboye, K. R. & Haruna, M. (2015[a]). A mathematical model for the transmission and control of malaria and typhoid co-infection using *SIRS* approach. *Researchjournali's Journal of Mathematics*. 2(2), 1 – 24.

[21] Heffernan, J. M. Smith, R. J. & Wahl, L. M. (2005). Perspectives on the basic reproductive ratio. *Journal of Royal Society Interface*. *42*, 1-12. doi:10.1098/rsif.2005.0042

[22] Castillo-Chavez C, Feng, Z. & Huang, W. (2002). On the computation of R_0 and its role on global stability. In C. Castillo-Chavez, S. Blower, P. van der Driessche, D. Kirschner, A. Yakubu (Eds). *Mathematical Approaches for Emerging and Reemerging Infectious Diseases*: *Vol 125 An Introduction. The IMA Volumes in Mathematics and its Applications* (*pp* 229 – 250), New York: Springer Verlag.

[23] Diekmann O., Heesterbeek, J. A. P., & Metz, J. A. J. (1990). On the definition and computation of basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology*. *28*, 365-382.

[24] Abdulrahman, S. (2014). A mathematical model for the transmission dynamics of hepatitis B virus. Minna, Nigeria: PhD Thesis, Federal University of Technology.

[25] Chitnis, N., Hyman, J. M., & Cushing, J. M. (2008). Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. *Bulletin of Mathematical Biology*. *70*, 1272-1296. doi: 10.1007/s11538-008-9299-0.