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A Lyapunov functional for vaccination model on the dynamics of cholera epidemic with non-linear incidence of infection

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Abstract

A new deterministic susceptible-exposed-infectious-vaccinated-removed-pathogen (SEIVRB) cholera epidemic model with combined mass action incidence and saturated incidence rates is proposed and analyzed. A threshold level of vaccine coverage necessary for controlling or eradicating cholera has been determined and analyzed using the next generation matrix approach. It is shown that the higher values of vaccine coverage that are lower than the threshold value significantly reduces the number of infected individuals whenever basic reproduction number is less than unity, and the cholera would persist in the populations whenever the model basic reproduction number exceeds unity. The global stability for cholera free equilibrium state and cholera endemic equilibrium state of the model system is investigated using Lyapunov functional approach and Lasalle invariance principle, which are found to be globally asymptotically stable at both equilibrium states. Numerical simulations and graphical illustrations is presented to support the analytical results found in the study.

Keywords: Cholera; Saturated Incidence rate; Lyapunov function; Global stability; Reproduction number; Oral cholera vaccines

1. Introduction

Civil unrest and political crisis are responsible for approximately 1.3 billion people being at risk of cholera in endemic countries. It was reported that estimated 2.86 million cholera cases occur annually in endemic countries, in which most of the disease global burden is in sub Saharan Africa (60%) and South – East Asia (29%). Among these cases, there are an estimated 95 000 deaths [1]. About half of the cholera cases and deaths are estimated to occur in children under 5 years of age, but any age group may be affected. Cholera is an acute intestinal infection caused by ingestion of food or water contaminated with the bacterium Vibrio cholera 01 and 0139. It is a disease of poverty, closely linked to poor sanitation and lack of clean drinking water which mostly are the consequences of the unrest. It has a short incubation period of a few hours to five days, and is characterized in the majority of cases by acute, profuse watery diarrhea lasting from one day to a few days. In its extreme form, cholera can be rapidly fatal [2, 3, 4]. The disease occurs in both endemic and epidemics patterns. The method of transmission is by direct or indirect fecal contamination of water or food supplied by soiled hands, utensils or mechanical carrier such as flies [5].

In 2013, the WHO established an OCV stockpile. Vaccination is the most effective method of preventing infectious diseases; widespread immunity due to vaccination is largely responsible for the worldwide eradication of the diseases, for instance, in 1979 smallpox was the first infectious disease to be eliminated completely. The second eliminated disease was in 2010 a viral disease found only in cattle known as Rinderpest. Furthermore, viral diseases known as measles, polio and tetanus have nearly been eliminated from much of the world [6]. The number of cholera cases

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reported to World Health Organization was alarming. It was in 1885, the first development of a whole – cell injectable vaccine for cholera disease was made. Since that period, several vaccines were developed to control the outbreak and spread of diseases as well as total eradication of various infectious diseases [1]. Presently, there are three WHO pre-qualified oral cholera vaccines (OCV) as a game-changer in the fight against cholera. OCV takes effect immediately and works to prevent cholera for 2-3 years, effectively bridging emergency response and longer-term cholera control with a WASH focus. Dukoral (in 2001), Shanchol (in 2011), and Euvichol (in 2015). All three vaccines require two doses for full protection. Dukoral can be given to all individuals over the age of 2 years. There must be a minimum of 7 days, and no more than 6 weeks, delay between each dose. Children aged 2-5 years require a third dose. Two doses of Dukoral provide protection against cholera for 2 years. Shanchol and Euvichol are essentially the same vaccine produced by two different manufacturers, they are given to all individuals over the age of one year. However, there must be a minimum of two weeks' delay between each dose of these vaccines. Two doses of Shanchol and Euvichol provide protection against cholera for 3 years, while a single dose provides short term protection. To date, over 54 million doses of OCV have been delivered in 25 countries [7, 8, 9, 10].

In modeling, the transmission dynamics of infectious diseases, nonlinear incidence rates have played a significant role in certifying that the models establish reliable description of the disease dynamics. The commonest incidence rates such as Mass action law, with the form $\lambda S(t)I(t)$, the standard incidence with the form $\frac{\lambda S(t)I(t)}{N}$, the saturated incidence with the form $\frac{\lambda S(t)B(t)}{(k+B)}$ as well as separable incidence [11], have been applied to model cholera epidemics by many researchers to understand the dynamics of the disease [12].

Cholera dynamics is termed to have complexity in nature with both direct transmission (human to human) and indirect transmission (environments to human). In transmission dynamics of cholera diseases using both mass action and standard incidence functions would not be sufficient, because there are diverse biological mechanisms which may result in nonlinearities in the cholera transmission rates, a number of authors (see, for instance, [13, 12]) have employed a nonlinear incidence (saturated) function of the form, $\frac{\beta SB}{1+\tau B}$, to describe the transmission and spread of cholera disease. The need for the saturated incidence in cholera model is to describe the fact that the number of effective contact between susceptible and infectious individuals may saturate at high infective level due to the crowding of the infectious individuals (pathogens and humans) in the population or due to the precautionary measures (behavioral changes) exhibited by the susceptible individuals against the resurface of the disease. One of such precautionary measures by the susceptible, is the ability to provide measures to curtail the spread of the disease, such as hygiene and total sanitation reduce the amount of Vibrio Cholerae bacteria in the environment. In this work, we use a saturated incidence of the form $\beta_1 IS + \beta_1 \eta VS + \frac{\beta_2 B}{1+\tau B}$ to denote a saturating feature that inhibits the force of infection from unhygienic environments to susceptible humans.

Lyapunov is a Russian mathematician which in 1892, developed a method for the analysis of the stability of ordinary differential equations. The method employs an appropriate auxiliary function, called a Lyapunov function. In recent years, Lyapunov's method becomes an important tool which has been used to establish the local and global stability of equilibrium in various forms of models arising in Mathematical biology and Mathematical epidemiology [14]. There are no standard methods for constructing Lyapunov functions in epidemiological models with saturated incidence rate and therefore it is often difficult to construct Lyapunov function [15].

In recent literatures on Lyapunov function with mass action incidence to study global stability for epidemiological model includes [16, 17]. The standard incidence was used in the construction of Lyapunov function by [18, 19] to study global stability for different models. The saturated incidence rate was used by [20, 21] to investigate global stability and dynamics of a models.

The study extended the work of Lawal and Sule [21] and applied the mathematical analysis on the work of [22], by using the approach of Korobeinikov [23] as first used by Goh Volterra in his work to study the stability of a predator-prey ecosystem [24]. We define a Lyapunov function as:

$$V(x,y) = S - S^* - S^* \ln\frac{S}{S^*} + E - E^* - E^* \ln\frac{E}{E^*} + \sum_{i=1}^{n} u_i \left(I - I^* - I^* \ln\frac{I}{I^*} \right) + b\left(R - R^* - R^* \ln\frac{R}{R^*} \right)$$

.

This paper was organized into sections as follows: Section 1 briefly discussed the role of incidence rates in the mathematical modeling of cholera disease. Section 2 presents the model formulation and description of the cholera carrier. Qualitative analysis and the model basic properties, as well as global stability behavior, are discussed in section 3. The model is simulated and plotted to support the analytical results obtained in section 4. The conclusion and references are given in section 5.

2. Model Formulation

The study consider a human population $N_H(t)$ divided into compartments of susceptible, exposed, infectious, vaccinated, and removed individuals, with numbers at time t denoted by $S(t)$, $E(t)$, $I(t)$, $V(t)$ and $R(t)$ respectively, that is $N_H(t) = S(t) + E(t) + I(t) + V(t) + R(t)$. The pathogen population $N_B(t)$ at time t denoted by $B(t)$.

The following assumptions were considered to design the vaccination model of cholera carrier:

- Population have equal access to vaccination.
- Using combine incidence rates of the form $\beta_1 IS + \beta_1 \eta VS + \dfrac{\beta_2 B}{1+\tau B}$
- re-infection of vaccinated individual may occur.
- modification parameter to reduce the shedding rate of vaccinated individuals.

Using mentioned assumptions, the below model equations are established showing the interaction between different populations: Thus, the model formulation is governed by the following system of nonlinear differential equations as presented by [22]:

$$\frac{dS}{dt} = \pi - \left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1+\tau B} \right] S(t) - \mu S(t) \quad \text{..... (1)}$$

$$\frac{dE}{dt} = (1-\rho)\left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1+\tau B} \right] S(t) - (\mu + \theta) E(t) \quad \text{..... (2)}$$

$$\frac{dI}{dt} = \rho\left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1+\tau B} \right] S(t) + \theta E(t) - (\mu + \delta + \alpha + \gamma_1) I(t) \qquad (3)$$

$$\frac{dV}{dt} = \alpha I(t) - (\mu + \psi\delta + \gamma_2) V(t) \quad \text{.....(4)}$$

$$\frac{dR}{dt} = \gamma_1 I(t) + \gamma_2 V(t) - \mu R(t) \quad \text{..... (5)}$$

$$\frac{dB}{dt} = \varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi B(t) \text{..... (6)}$$

Subject to the initial conditions

$$\left.\begin{aligned} S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0 \\ V(0) = V_0,\ R(0) = R_0,\ B(0) = B_0 \end{aligned}\right\} \text{..... (7)}$$

Table 1 Description of Variables used in the Vaccination Model Simulations

Variable	Description
$S(t)$	Susceptible Individuals
$E(t)$	Exposed Individuals
$I(t)$	Infective Individuals
$V(t)$	Vaccinated Individuals
$R(t)$	Removed Individuals
$B(t)$	Pathogen Individuals

Table 2 Description of Parameters and their values used in the Vaccination Model Simulations

Parameters	Description	Value	Source
η	Modification Parameter	$0-1$	Varied
μ	Natural death	0.2	Estimate
β_1	Force of infection in human susceptible	0.05	Estimate
β_2	Force of infection in pathogen	0.05	[25]
ψ_1	Modification parameter associated with vaccinated reduced failure	0.001	Varied
ρ	Fast progression rate	$0-1$	Varied
ε	Shedding rate	0.01	[25]
α	vaccine rate	$0-1$	Varied
γ_1	Natural recovery rate	0.2	[26]
γ_2	Vaccine recovery rate	$0-1$	Varied
ψ	Modification parameter associated with reduced mortality	0.05	Estimate
ϕ	Decay of vibrio	0.02	Estimate
τ	Saturation constant	$0-0.02$	Varied
θ	Progression rate E to I	0.3	Estimate
δ	Induced death	0.015	[27]
π	Recruitment	0.6	Estimate

3. Mathematical Analysis

3.1 Basic Properties of the Model

The model system describes the dynamic of the Vaccination Model of the Cholera Epidemic with Non-linear Incidence of Infection. Before analyzing the dynamics of the model presented by, [22] we briefly discuss the basic properties of the model system (1-6). Though, the model monitors changes in the human population, therefore it is assumed that all the model variables and parameters to be nonnegative for all, $t \geq 0$.

3.1.1 Positivity of Solutions

It is assumed that all the variables and parameters of the model are non-negative. By adding up the equations of the model system (1-6) we obtain

$$\frac{dN(t)}{dt} = \pi - \mu N(t) \qquad (8)$$

We claim the following results

3.2 Theorem 1 (Positivity)

Let, $\Omega = \left[S, E, I, V, R, B \in R_+^6 : S(0) > 0, E(0) > 0, I(0) > 0, V(0) > 0, R(0) > 0, B(0) > 0 \right]$, then the solutions set of $\{S(t), E(t), I(t), V(t), R(t), B(t)\}$, of the vaccination model system $(1-6)$ with non-negative initial conditions (7), remains non-negative for all $(t \geq 0)$.

Proof. Given that the initial conditions $S(0), E(0), I(0), V(0), R(0), B(0)$ are non-negative. It is observed that from the first model equation we deduce that for all, $(t > 0)$.

$$\frac{dS}{dt} = \pi - \left[\beta_1 (I + \eta V) + \frac{\beta_2 B}{1 + \tau B} \right] S(t) - \mu S(t) \qquad (9)$$

Then,

$$\frac{dS}{dt} \geq \pi - \mu S(t) \qquad (10)$$

On solving we get

$$S(t) = \frac{\pi}{\mu} + k\ell^{-\mu t} \qquad (11)$$

Applying initial condition, we get

$$S(t) = \frac{\pi}{\mu} + \left(S_0 - \frac{\pi}{\mu} \right) \ell^{-\mu t} \geq 0 \qquad (12)$$

Where, S_0 is the population of susceptible individuals at, $t = 0$. Similarly, the remaining five equations are obtained that $E(0), I(0), V(0), R(0), B(0) \geq 0$. Therefore, we establish that any solution of the vaccination model system $(1-6)$ is such that, $\{(S, E, I, V, R, B)\} \in R_+^6$.

Theorem 2 (Boundedness)

All solution of model system $(1-6)$ is bounded and remain in the region, Ω_N.

Where,

$$\Omega_N = \left\{ \{(S, E, I, V, R, B)\} \in R_+^6 : 0 \leq \left(S(t) + E(t) + I(t) + V(t) + R(t) + B(t) \right) \leq \frac{\pi}{\mu} \right\} \qquad (13)$$

Proof: From equation (5) the total human population

$$N_H(t) = S(t) + E(t) + I(t) + V(t) + R(t) \qquad (14)$$

This implies that,

$$\frac{dN_H}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dV}{dt} + \frac{dR}{dt} = \pi - \mu N_H - \delta(I + \psi V) \qquad (15)$$

In the absence of cholera infection, there is no death from cholera, that is, $\delta = 0$, then we obtain

$$\frac{dN_H(t)}{dt} \leq \pi - \mu N_H(t) \qquad (16)$$

By integration and simplifying and applying comparison theorem as presented by [28], we get

$$N_H(t) \le N(0)\ell^{-\mu t} + \frac{\pi}{\mu}\left(1-\ell^{-\mu t}\right) \qquad (17)$$

As $t \to \infty$, the total human population size N_H approaches $0 \le N_H \le \frac{\pi}{\mu} \Rightarrow N_H \to \frac{\pi}{\mu}$. Therefore, the feasible solution set of the human population for the system (1-5) enters the region

$$\Omega_H = \left\{ (S, E, I, V, R) \in R_+^5 : 0 \le \left(S(t) + E(t) + I(t) + V(t) + R(t)\right) \le \frac{\pi}{\mu} \right\} \qquad (18)$$

Similarly, the pathogen population for any solution set in B_+^1. Let

$$N_B = B = \varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi B(t) \qquad (19)$$

But, $I, V \in N_H$ and $N_H = \frac{\pi}{\mu}$ then

$$N_B = \frac{\pi}{\mu}\varepsilon(1+\psi_1) - \phi B \qquad (20)$$

Then,

$$\frac{dN_B(t)}{dt} + \phi B(t) = \frac{\pi}{\mu}\varepsilon(1+\psi_1) \qquad (21)$$

By standard comparison theorem, we obtain

$$N_B(t) \le \frac{\pi\varepsilon(1+\psi_1)}{\mu\phi}\left(1-\ell^{-\mu t}\right) \qquad (22)$$

As $t \to \infty$, the total pathogen population size N_B approaches

$$0 \le N_B(t) \le \frac{\pi\varepsilon(1+\psi_1)}{\mu\phi} \qquad (23)$$

This indicates that the feasible solution set of the pathogen population enter into the region, Ω_B.

$$\Omega_B = \left\{ B \in B_+^1 : N_B \le \frac{\pi\varepsilon(1+\psi_1)}{\mu\phi} \right\}, \quad \text{where } \mu\phi > 0 \qquad (24)$$

Therefore. The solution of the model $(1-6)$ with the initial condition (7) is bounded in the invariant region, Ω_N for all $t > 0$. Hence, the model is well posed.

3.3 Equilibria Points and Basic Reproduction Number

At each of the equilibrium points of the model, $(1-6)$,

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dV}{dt} = \frac{dR}{dt} - \frac{dB}{dt} = 0 \qquad (25)$$

Thus, the following results are establishing.

3.3.1 Cholera Free Equilibrium

At the Cholera free state, there is no Cholera disease in the human population which implies, $E = I = B = 0$.

Thus, the Cholera free equilibrium of the model $(1-6)$ is given by

$$p^0 = \left(S^0, E^0, I^0, V^0, R^0, B^0\right) = (S, 0, 0, 0, 0, 0) \qquad (26)$$

With, $S = \frac{\pi}{\mu}$

3.3.2 Endemic Equilibrium

There are arbitrary small Cholera infections that will not disappear in the population. Thus, there is an equilibrium point $\left(S^*, E^*, I^*, V^*, R^*, B^*\right)$ with $E^*, I^*, B^* > 0$ such that, $N^*(t) = S^*(t) + E^*(t) + I^*(t) + V^*(t) + R^*(t) + B^*(t)$.

However, on algebraic manipulation we obtained the following results for endemic equilibrium point of the model, $(1-6)$.

$$S^* = \frac{\pi}{\mu R_0} \qquad (28)$$

$$E^* = \frac{\mu(R_0 - 1)(1-\rho)\pi}{\mu R_0 Q_1} \qquad (29)$$

$$I^* = \frac{\mu(R_0 - 1)\pi L_2}{\mu R_0 Q_1 Q_2} \qquad (30)$$

$$V^* = \frac{\mu\alpha(R_0 - 1)\pi L_2}{\mu R_0 Q_1 Q_2 Q_3} \qquad (31)$$

$$R^* = \frac{\pi L_2 (R_0 - 1)\left[\gamma_1 Q_3 + \alpha\gamma_2\right]}{\mu R_0 Q_1 Q_2 Q_3} \qquad (32)$$

$$B^* = \frac{\pi L_1 \mu(R_0 - 1)}{\mu R_0 \phi Q_1 Q_2 Q_3} \qquad (33)$$

$$\text{Where, } \left.\begin{array}{l} Q_1 = \mu + \theta \ , \ Q_2 = \mu + \delta + \alpha + \gamma_1 \ , Q_3 = \mu + \psi\delta + \gamma_2 \ , \\ L_1 = Q_3\varepsilon L_2 + \varepsilon\psi_1\mu L_2 \ , \ L_2 = Q_1\rho + \theta L_3 \ , L_3 = 1-\rho \end{array}\right\} \qquad (34)$$

3.4 Reproduction Number

The basic reproduction number R_0 as defined by Diekmann [29] is the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness. Using the method of next generation matrix explained in details by [30] and applied by [31]. Thus, the basic reproduction number of the model system $(1-6)$ with mass action incidence function denoted by R_0 is the spectral radius of FV^{-1}.

Let,

- $F_i(x)$ be the rate of appearance of new infection in compartment i.
- $V_i^+(x)$ be the transfer of individuals into compartments i by all other means.
- $V_i^-(x)$ be the rate of transfer of individuals out of compartments i.
- P_0 be the disease free equilibrium point.

Thus, the basic reproduction number of the model system $(1-6)$ with mass action incidence function denoted by R_0 is the spectral radius of FV^{-1}.

Let, $F = \begin{bmatrix} 0 & (1-\rho)\beta_1 \frac{\pi}{\mu} & (1-\rho)\beta_1\eta \frac{\pi}{\mu} & (1-\rho)\beta_2 \frac{\pi}{\mu} \\ 0 & \rho\beta_1 \frac{\pi}{\mu} & \rho\beta_1\eta \frac{\pi}{\mu} & \rho\beta_2 \frac{\pi}{\mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$ (35), $V = \begin{bmatrix} Q_1 & 0 & 0 & 0 \\ -\theta & Q_2 & 0 & 0 \\ 0 & -\alpha & Q_3 & 0 \\ 0 & -\varepsilon & -\varepsilon\psi_1 & \phi \end{bmatrix}$ (36)

Thus, the set of eigenvalues corresponding to the product to matrix, FV^{-1}, and in which the dominant eigenvalue is the basic reproduction number,

$$R_0 = \frac{\pi A_1 \left[\beta_1\phi(Q_3+\alpha\eta)+\beta_2\varepsilon(Q_2+\alpha\psi_1)\right]}{\mu\phi Q_1 Q_2 Q_3} \quad (37)$$

Where,

$$A_1 = \rho Q_1 + (1-\rho)\theta, \quad Q_1 = \mu+\theta, \quad Q_2 = \mu+\delta+\alpha+\gamma_1, \quad Q_3 = \mu+\psi\delta+\gamma_2 \quad (38)$$

Theorem 3

The cholera free equilibrium, p_0 of the model system $(1-6)$ is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.

3.4.1 Biological remarks

The epidemiological implication of the above result is that cholera epidemic governed by model equations (1-6) can be eliminated from the population whenever an influx by infectious individual into the population is small such that $R_0 < 1$ In a disease with recovery with any initial population size, if the susceptible (and infected) reproduction ratio is less than unity, then the total population eventually disappear and it persists if otherwise.

4. Stability analysis

4.1 Global Stability of the Cholera free equilibrium for the vaccination epidemic model

We claim the following result:

Theorem 4

The Cholera free equilibrium is globally asymptotically stable whenever, $R_0 < 1$.

Proof. Consider the following Lyapunov function

$$L = \frac{A_1\theta}{Q_1Q_2Q_3}E + \frac{A_1}{Q_2Q_3}I + \frac{\beta_1\phi\eta+\beta_3\varepsilon\psi_1}{Q_3}V + \beta_3 D \quad (39)$$

Where $A_1 = \beta_1\phi(Q_3+\alpha\eta)+\beta_2\varepsilon(Q_3+\alpha\psi_1)$

With Lyapunov derivative (where a dot represents differentiation with respect to t)

$$\dot{L} = \frac{A_1\theta}{Q_1Q_2Q_3}E + \frac{A_1}{Q_2Q_3}I + \frac{\beta_1\phi\eta+\beta_3\varepsilon\psi_1}{Q_3}V + \beta_3 D \quad (40)$$

$$\left.\begin{aligned}\dot{L} = \frac{A_1\theta}{Q_1Q_2Q_3}\left((1-\rho)\Gamma S(t) - Q_1E(t)\right) + \frac{A_1}{Q_2Q_3}\left(\rho\Gamma S(t) + \theta E(t) - Q_2I(t)\right) + \\ \frac{\beta_1\phi\eta + \beta_3\varepsilon\psi_1}{Q_3}\left(\alpha I(t) - Q_3V(t)\right) + \beta_3\left(\varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi B(t)\right)\end{aligned}\right\} \quad (41)$$

Where, $\Gamma = \beta_1\left(I + \eta V\right) + \frac{\beta_2 B}{1+\tau B}$, $Q_1 = \mu + \theta$, $Q_2 = \mu + \delta + \alpha + \gamma_1$, $Q_3 = \mu + \psi\delta + \gamma_2$

$$\left.\begin{aligned}\dot{L} = \frac{A_1\theta}{Q_1Q_2Q_3}\left((1-\rho)\left[\beta_1\left(I + \eta V\right) + \frac{\beta_2 B}{1+\tau B}\right]S(t) - Q_1E(t)\right) + \frac{A_1}{Q_2Q_3}\left(\rho\left[\beta_1\left(I + \eta V\right) + \frac{\beta_2 B}{1+\tau B}\right]S(t) + \theta E(t) - Q_2I(t)\right) + \\ \frac{\beta_1\phi\eta + \beta_3\varepsilon\psi_1}{Q_3}\left(\alpha I(t) - Q_3V(t)\right) + \beta_3\left(\varepsilon I(t) + \varepsilon\psi_1 V(t) - \phi B(t)\right)\end{aligned}\right\} \quad (42)$$

Simplifying with $\frac{S}{1+\tau B} \le S \le \frac{\pi}{\mu}$, We get,

$$\ddot{L} \le \phi\left[\beta_1\left(I + \eta V\right) + \beta_2 B\right]\left(R_0 - 1\right) \qquad (43)$$

Thus, $\dot{L} \le 0$ if $R_0 \le 1$ with $\dot{L} = 0$ if and only if $I = V = 0$. Substituting in $I = V = 0$ in $(1-6)$ shows that $B(t) \to 0$ as $t \to \infty$ as $S \to \frac{\pi}{\mu}$ as $t \to \infty$. Further, the largest compact invariant set in

$$\left\{\left(S(t), E(t), I(t), V(t), R(t), B(t)\right) \in \Omega : \dot{L}\left(S(t), E(t), I(t), V(t), R(t), B(t)\right) = 0\right\}$$

is the singleton P_0. It follows from LaSalle's Invariance Principle [32] that every solution to the system $(1-6)$ with initial condition in Ω converges to the Disease-Free Equilibrium as $t \to \infty$ whenever $R_0 \le 1$. Hence, it is Globally Asymptotically Stable as $\left(S(t), E(t), I(t), V(t), R(t), B(t)\right) \to \left(\frac{\pi}{\mu}, 0, 0, 0, 0, 0\right)$ as $t \to \infty$.

Remarks: thus, the epidemiological implication was that the infected fraction (the sum of the exposed and the infectious fractions) of the population vanishes in time so the Cholera dies out.

4.2 Global Stability of the Endemic Equilibrium Point E^* of the Vaccination Model of a Cholera Carrier: Special case

The analyses in this section will be carried out for the special case of the model with no fast progression rate of susceptible to infective class, no saturation constant and no Modification parameter associated with reduced mortality of vaccinated individuals. The model equation for the special case, setting $\rho = \tau = \psi = 0$ in $(1-6)$ to obtain

$$\left.\begin{aligned}\frac{dS}{dt} &= \pi - \left[\beta_1\left(I + \eta V\right) + \beta_2 B\right]S(t) - \mu S(t) \\ \frac{dE}{dt} &= (1-\rho)\left[\beta_1\left(I + \eta V\right) + \beta_2 B\right]S(t) - Q_1E(t) \\ \frac{dI}{dt} &= \rho\left[\beta_1\left(I + \eta V\right) + \beta_2 B\right]S(t) + \theta E(t) - Q_2I(t) \\ \frac{dV}{dt} &= \alpha I(t) - Q_3V(t) \\ \frac{dB}{dt} &= \varepsilon I(t) - \phi B(t)\end{aligned}\right\} \quad (44)$$

Thus, R_0 at special case is given as:

$$R_0 = \frac{\pi\theta\left[\beta_1\phi\left(Q_3+\alpha\eta\right)+\beta_2\varepsilon Q_3\right]}{\mu Q_1 Q_2 Q_3}$$

At endemic steady state, it yields

$$\left.\begin{aligned}
\pi &= \left[\beta_1\left(I^*+\eta V^*\right)+\frac{\beta_2 B^*}{1+\tau B^*}\right]S^*(t)-\mu S^*(t)\\
Q_1E^*(t) &= (1-\rho)\left[\beta_1\left(I^*+\eta V^*\right)+\frac{\beta_2 B^*}{1+\tau B^*}\right]S^*(t)\\
\theta E^*(t) &= Q_2 I^*(t)\\
\alpha I^*(t) &= Q_3 V^*(t)\\
\varepsilon I^*(t) &= \phi B^*(t)
\end{aligned}\right\} \quad (45)$$

Using the approach of Korobeinikov [22] of the following non-linear function, we define a Lyapunov function as

$$\left.\begin{aligned}
L_1 = \left[S-S^*-S^*\ln\frac{S}{S^*}\right]+\left[E-E^*-E^*\ln\frac{E}{E^*}\right]+\frac{Q_1}{\theta}\left[I-I^*-I^*\ln\frac{I}{I^*}\right]\\
+\frac{\beta_1\eta S^*}{Q_3}\left[V-V^*-V^*\ln\frac{V}{V^*}\right]+\frac{\beta_2 S^*}{\phi}\left[B-B^*-B^*\ln\frac{B}{B^*}\right]
\end{aligned}\right\} \quad (46)$$

with Lyapunov derivative given by

$$\dot{L}_1 = \left[1-\frac{S^*}{S}\right]\dot{S}+\left[1-\frac{E^*}{E}\right]\dot{E}+\frac{Q_1}{\theta}\left[1-\frac{I^*}{I}\right]\dot{I}+\frac{\beta_1\eta S^*}{Q_3}\left[1-\frac{V^*}{V}\right]\dot{V}+\frac{\beta_2 S^*}{\phi}\left[1-\frac{B^*}{B}\right]\dot{B} \quad (47)$$

With simplification, to obtain

$$\left.\begin{aligned}
\dot{L}_1 = \left[1-\frac{S^*}{S}\right]\left(\pi-\left[\beta_1\left(I+\eta V\right)+\beta_2 B\right]S(t)-\mu S(t)\right)+\left[1-\frac{E^*}{E}\right]\left(\left[\beta_1\left(I+\eta V\right)+\beta_2 B\right]S(t)-Q_1E(t)\right)\\
+\frac{Q_1}{\theta}\left[1-\frac{I^*}{I}\right]\left(\theta E(t)-Q_2 I(t)\right)+\frac{\beta_1\eta S^*}{Q_3}\left[1-\frac{V^*}{V}\right]\left(\alpha I(t)-Q_3 V(t)\right)+\frac{\beta_2 S^*}{\phi}\left[1-\frac{B^*}{B}\right]\left(\varepsilon I(t)-\phi B(t)\right)
\end{aligned}\right\} \quad (48)$$

Using

$$\left.\begin{aligned}
\pi &= \left[\beta_1\left(I^*+\eta V^*\right)+\beta_2 B^*\right]S^*(t)+\mu S^*(t)\\
Q_1 &= \frac{\left[\beta_1\left(I^*+\eta V^*\right)+\beta_2 B^*\right]S^*(t)}{E^*(t)}\\
Q_2 &= \frac{\theta E^*(t)}{I^*(t)}\\
V^*(t) &= \frac{\alpha I^*(t)}{Q_3}\\
\phi &= \frac{\varepsilon I^*(t)}{B^*(t)}
\end{aligned}\right\} \quad (49)$$

And with further simplification, we get

$$\left.\begin{aligned} L_1 = \mu S^*\left[2-\frac{S^*}{S}-\frac{S}{S^*}\right]+\beta_1 I^* S^*\left[3-\frac{S^*}{S}-\frac{SIE^*}{S^*I^*E}-\frac{I^*E}{IE^*}\right] \\ +\beta_1\eta V^* S^*\left[4-\frac{S^*}{S}-\frac{SVE^*}{S^*V^*E}-\frac{I^*E^*}{IE^*}-\frac{V^*I}{VI^*}\right]+\beta_2 B^* S^*\left[4-\frac{S^*}{S}-\frac{BSE^*}{B^*S^*E}-\frac{I^*E}{IE^*}-\frac{B^*I}{BI^*}\right] \end{aligned}\right\} \quad (50)$$

Hence, for $R_0>1$, $\dot{L}\le 0$, where $\dot{L}=0$ holds only when $S=S^*, I=I^*, E=E^*, V=V^*, B=B^*$. Further, the only largest invariant set in $\left\{(S,E,I,V,B)\in\Omega:\dot{L}=0\right\}$ is reduced to the endemic equilibrium. Hence, (S,E,I,V,B) is attractive. Because of LaSalle's invariance Principle [32], the endemic equilibrium E^* of system $(1-6)$ is Globally Asymptotically Stable in the interior Ω.

The epidemiological implication of Theorem 5 is that cholera can persist in the population whenever the intervention strategies are not adhered to and the associated basic reproduction is greater than one.

Theorem 5

The unique endemic equilibrium of the reduced model $(1-6)$, with $\rho=\tau=\psi=0$, is Globally Asymptotically Stable in the interior Ω whenever $R_0>1$.

5. Numerical Simulations

The numerical analysis of the theoretical result obtained in the proposed model is presented. This is achieved by using the set of parameter values given in Table 1, and whose sources are mainly from literature as well as assumptions satisfying the stability conditions. The proposed vaccination model system $(1-6)$ was simulated using Maple software with different initial population size as follows:

$$\left.\begin{aligned} &1.\ \mathrm{S}(0)=1.5;\ \mathrm{E}(0)=0.6;\mathrm{I}(0)=0.48;\ \mathrm{V}(0)=0.27;\ \mathrm{R}(0)=0.15;\ \mathrm{P}=15 \\ &2.\ \mathrm{S}(0)=2.0;\mathrm{E}(0)=0.5;\ \mathrm{I}(0)=0.15;\ \mathrm{V}(0)=0.3;\ \mathrm{R}(0)=0.05;\ \mathrm{P}=20 \\ &3.\ \mathrm{S}(0)=1.4;\ \mathrm{E}(0)=0.55;\mathrm{I}(0)=0.46;\ \mathrm{V}(0)=0.3;\ \mathrm{R}(0)=0.29;\ \mathrm{P}=10 \\ &4.\ \mathrm{S}(0)=2.15;\mathrm{E}(0)=0.35;\ \mathrm{I}(0)=0.25;\ \mathrm{V}(0)=0.2;\ \mathrm{R}(0)=0.15;\ \mathrm{P}=8 \end{aligned}\right\} \quad (51)$$

5.1 Numerical Results on the Global Stability of the Vaccination Model of Cholera Carrier, when, $R_0<1$.

In Figure 1 (a-f), the time plot of model in section 5 was presented to verify the theoretical results of the vaccination model, this was achieved by using set of parameter value given in Table 2, for ρ = 0.2; η = 0.001; α = 0.8; γ2 = 0.5 for $R_0<1$ = 0.9129 < 1. Figure 1 (a) shows that the population of susceptible individual $S(t)$ increase to approach S^* (i.eπ μ = 0.6 0.2 = 3). In Figure 1 (b), shows that the population of the Exposed $E(t)$ decrease to approach E^* (i.e. zero). In Figure 1 (c), the population of symptomatic infectious, $I(t)$ decrease to approach I^* (i.e. zero). In Figure 1 (d), the vaccinated individuals population $V(t)$ decreases to approach V^* (i.e. zero) to enter recovered population. In Figure 1 (e), the recovered population $R(t)$ decreases due to temporary immunity to becomes susceptible again and approach R^* (i.e. zero). In Figure 1 (f), the population concentration of vibrio cholera $B(t)$ also decrease at first then slightly approach B^*.

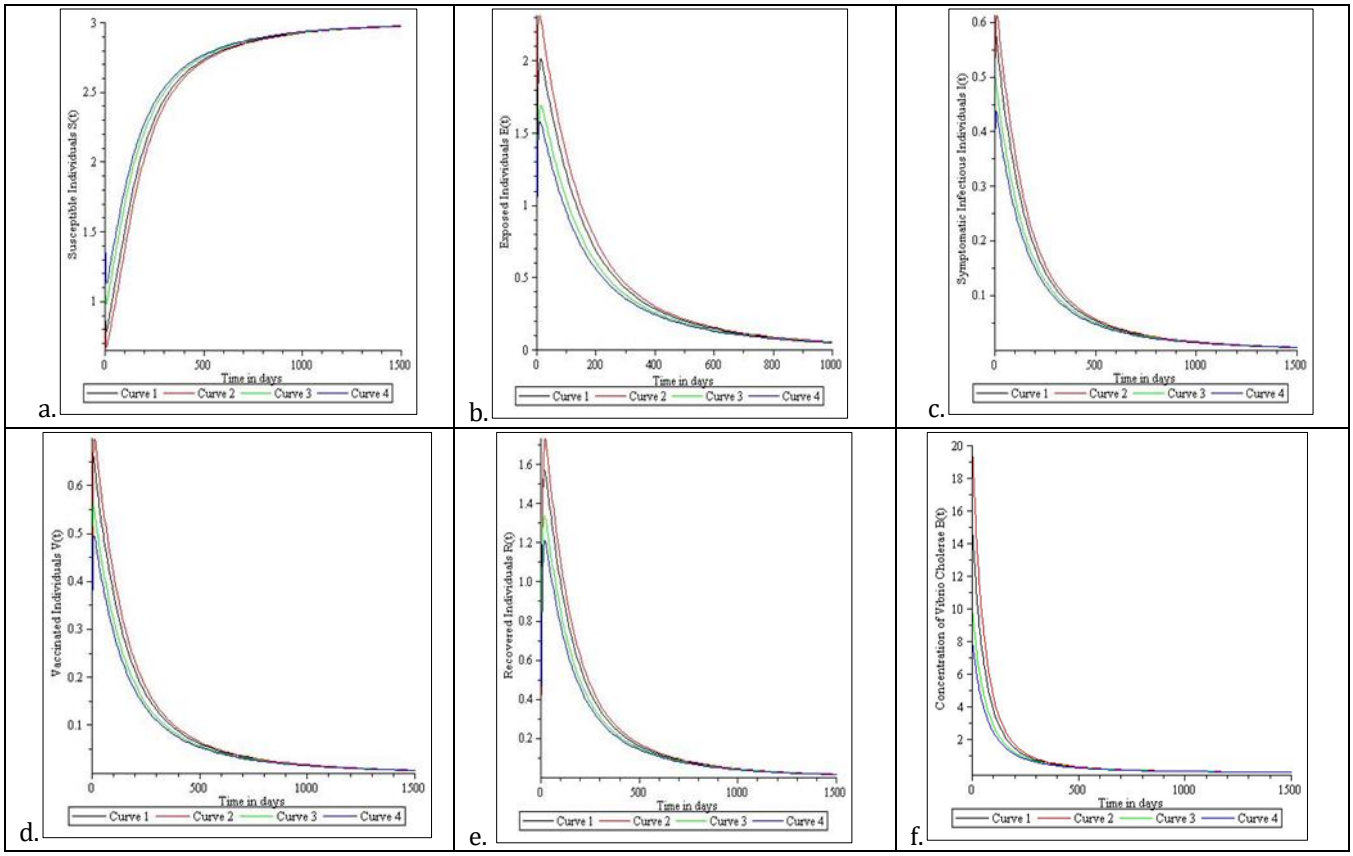

Figure 1 Time series simulations of the model $(1-6)$, showing the total number of populations as a function of time, with different initial conditions. Parameter values used are as given in Table 2, with $R_0 < 1$. (a) $S(t)$ for $R_0 < 1$ (b) $E(t)$ for $R_0 < 1$ (c) $I(t)$ for $R_0 < 1$ (d) $V(t)$ for $R_0 < 1$ (e) $R(t)$ for $R_0 < 1$ (f) $B(t)$ for $R_0 < 1$.

5.2 Results on the Global Stability of the Endemic State of the Vaccination on Model of the Cholera Carrier, whenever, $R_0 > 1$.

This section presents a numerical simulation of model in section 5, using a set of parameter values given in Table 2 with: $\rho = 0; \tau = 0; \psi_1 = 0; \beta_1 = 1; \alpha = 0.8; \gamma_2 = 0.5; \eta = 1$ for $R_0 > 1$ = 3.1046 > 1. In Fig 2 (a), it was observed that, the population of susceptible individuals $S(t)$ increase to approach, S^{**}. In Figure 2 (b) the population of exposed $E(t)$ decrease at first then it steadily tends to approach, E^{**}. In Fig 2 (c) the symptomatic infectious population $I(t)$ at first decrease, then steadily approach, I^{**}. In Figure 2 (d) vaccinated population, $V(t)$ at first decrease then tend to, V^{**}. In Figure 2 (e), the recovered population $R(t)$ decrease at first then approach, R^{**}. In Figure 2 (f), the Pathogen population, $B(t)$ decrease at first then steadily tend to approach, B^{**}.

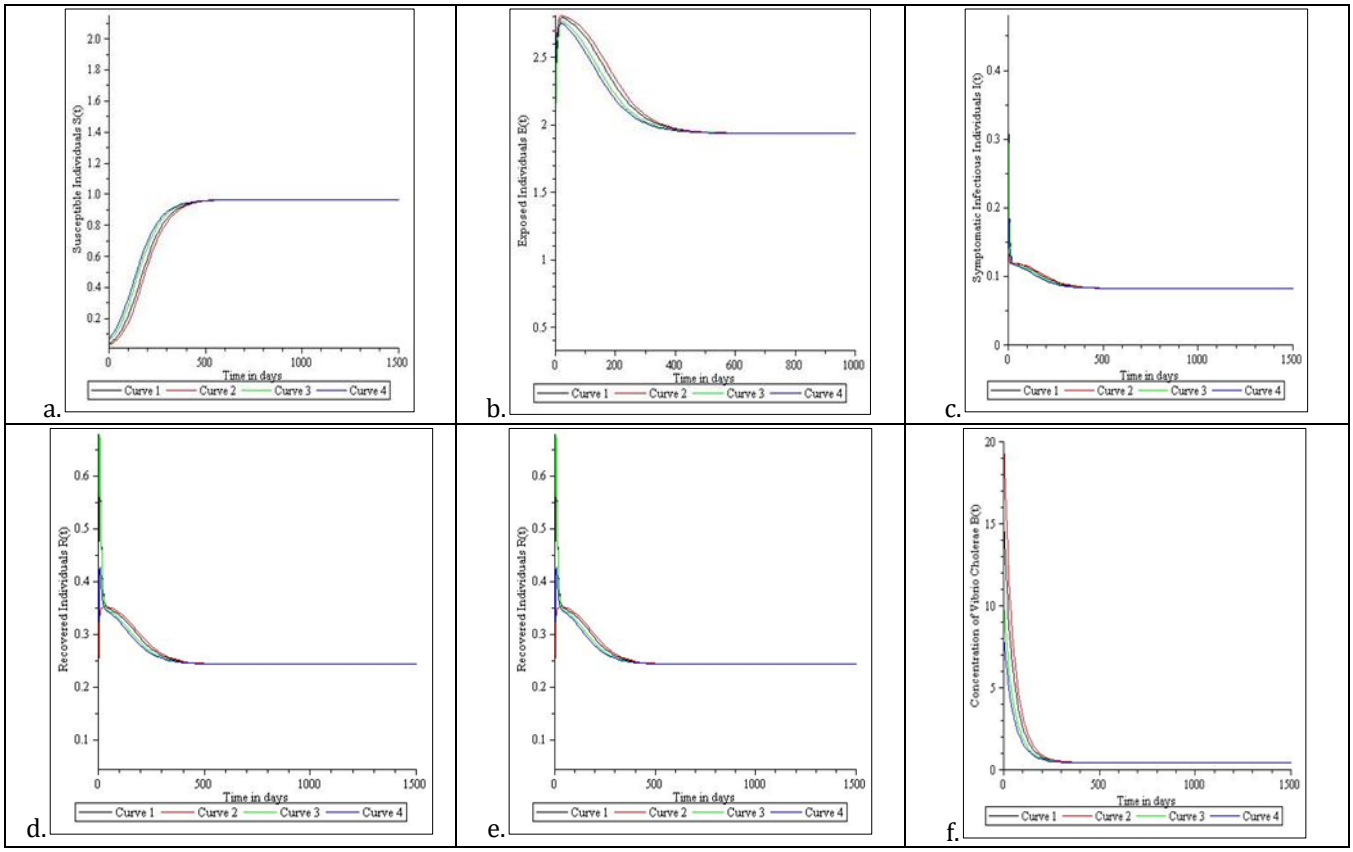

Figure 2 Time series simulations of the models (1-6), showing the total number of populations as a function of time, with different initial conditions. Parameter values used are as given in table 1, with $R_0 > 1$. (a) $S(t)$ for $R_0 > 1$ (b) $E(t)$ for $R_0 > 1$ (c) $I(t)$ for $R_0 > 1$ (d) $V(t)$ for $R_0 > 1$ (e) $R(t)$ for $R_0 > 1$ (f) $B(t)$ for $R_0 > 1$.

6. Conclusion

The study is a six dimensional compartmental model designed to analyze the vaccination models for cholera transmission dynamics in a population. The model was rigorously studied and analyzed to understand the disease transmission dynamical features. The following results were established:

- The model basic properties for positivity of solution and the invariant region are tested and were found to be epidemiologically and mathematically well posed.
- A threshold level of vaccine coverage necessary for controlling or eradicating the disease has been determined using the next generation matrix approach. It has shown that higher values of vaccine coverage that are lower than the threshold value significantly reduces the number of infected individuals, but never lead to disease eradication. Disease eradication is only feasible if the vaccination coverage level exceeds the threshold value when the vaccination function is decreasing i.e. $R_0 < 1$.
- The stability behavior of the models was investigated using Lyapunov function approach and the models at the cholera free equilibrium were found to be asymptotically stable, whenever basic reproduction number, is less than unity and the cholera endemic equilibrium point occurred whenever reproduction number exceeds unity.
- Lastly, the theoretical findings have been verified numerically, accuracy of results and the plots for simulations of the models were found to be in good agreement with analytical results.

Therefore, to curtail the spread of cholera in communities, it is recommended that public health campaigns be conducted frequently as well as basic health services be provided and the vaccination against cholera should complement other preventive and control measures.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors declare that they have no conflicts of interest. The contents of the paper have been reviewed and approved by each co-author, and there are no competing financial interests to disclose. We attest that the submission is unique and is not already being considered by another publisher.

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