Bifurcation and Stability Analysis of the Dynamics of Cholera Model with Controls

C. E. Madubueze, S. C. Madubueze, S. Ajama

Abstract—Cholera is a disease that is predominately common in developing countries due to poor sanitation and overcrowding population. In this paper, a deterministic model for the dynamics of cholera is developed and control measures such as health educational message, therapeutic treatment, and vaccination are incorporated in the model. The effective reproduction number is computed in terms of the model parameters. The existence and stability of the equilibrium states, disease free and endemic equilibrium states are established and showed to be locally and globally asymptotically stable when $R_0 < 1$ and $R_0 > 1$ respectively. The existence of backward bifurcation of the model is investigated. Furthermore, numerical simulation of the model developed is carried out to show the impact of the control measures and the result indicates that combined control measures will help to reduce the spread of cholera in the population.

Keywords—Backward bifurcation, cholera, equilibrium, dynamics, stability.

I. INTRODUCTION

CHOLERA continues to be a global threat to public health. It is a major public health problem in many developing countries [1]. Cholera, an acutely dehydrating diarrhoea disease that can rapidly kill its victims, is caused by vibrio cholerae, a gram-negative bacterium [2]. Choleragenic v. cholerae 01 and 0139 are the only causative agents, usually associated with explosive outbreaks and pandemics with propensity to spread across continents [3]. It is a disease associated with poverty and poor environmental sanitation and infects everybody. This is because the medium of transmission is accessible to all [4]. Cholera is transmitted through ingestion of contaminated water and food from sewage or via contact with excretas of an infected person. Infected persons over time have symptoms such as watery diarrhoea accompanied by vomiting which can quickly lead to dehydration. If not treated immediately, it can progress to shock and death within hours. As of 2013 the outbreak of cholera causes about 120,000 deaths annually worldwide of which 43% were reported from Africa [5]. Whilst in Nigeria, it has been endemic with yearly outbreaks since first outbreak was reported in the year 1970. With each outbreak,

epidemiological evidence usually indicates that the entire country is at risk especially children between 1 – 5 years [6]. Improving global access to water, sanitation, and hygiene is a critical step to eliminating African's cholera burden. This will be achieved if there is proper health education and awareness of the infection through radio, word-of-mouth communication, television, social media and posters [7].

Mathematical models are important tools in analysing the spread and control of infectious diseases. This started as far back as 1760 when Daniel Bernoulli developed a model for smallpox [8]. Since then, many mathematical models have been developed for many infectious diseases including cholera. Several researchers have continuously researched on how to reduce cholera infection using mathematical models by incorporating control measures such as hygiene consciousness [9], education and chlorination [10], vaccination [11], vaccination, therapeutic treatment, and water sanitation [12] and so on. All of these researchers in one way or the other have shown that the transmission of cholera could be controlled based on their results.

To this end, this study seeks to investigate analytically the dynamics of cholera by integrating health educational message, therapeutic treatment, and vaccination as controls in order to halt further spread of the infection. This will be accomplishes by extending the work by [12].

II. MODEL FORMULATION

Cholera model classifies the population into human $N_h(t)$ and pathogen populations $N_B(t)$. Human population $N_h(t)$ is subdivided into Susceptible $S(t)$, Infected $I(t)$, and Recovered $R(t)$ classes with natural mortality rate μ in all classes while d is the cholera induced death rate in the infected class. The pathogen population $N_B(t)$ is denoted by $B(t)$ as the concentration of pathogen in the water sources (contaminated water). The model assumed that susceptible individuals are recruited at the rate μN and become infected through contact with stool/faeces of the infected human at the rate $\beta_h SI$ or via contact with environment contaminated by untreated water at the rate $\frac{\beta_e BI}{K+B}$, where β_e and B_h are the contact rates for human to contaminated water and human to human interaction respectively. K is the concentration of pathogen in water that yields 50% chance of getting cholera and μ is taken as the recruitment rate. μ_B is the natural death rate of the pathogen. Furthermore, each infected individual contribute averagely to the pathogen population at the rate $\theta > 0$, while susceptible individuals are vaccinated at the rate v and add to the recovery class. The infected individuals may

C. E. Madubueze is with the Department of Mathematics/Statistics/ Computer Science, University of Agriculture Makurdi, P. M. B. 2373 Nigeria (Corresponding author, phone: +2348039523389; e-mail: ce.madubueze@gmail.com; madubueze.chinwendu@uam.edu.ng).

S. C. Madubueze is with the Department of Family Medicine, Dalhatu Araf Specialist Hospital, P. M. B. 007 Lafia, Nigeria. (E-mail: sc.madubueze13@gmail.com).

S. Ajama is a graduate of Department of Mathematics/Statistics/ Computer Science, University of Agriculture Makurdi, P. M. B. 2373 Nigeria.

recover at the rate γ depending on their immunity, nutrition and age [10]. α is taken as the rate of therapeutic treatment given to the infected individuals in the hospital.

Finally, $0 < \omega_e < 1$ is a constant representing direct education on human terms of public health awareness. This parameter changes the behaviour of humans in order to maintain good sanitation and avoid contact with infected human and contaminated water sources.

Based on the above assumptions, we obtain the following system of nonlinear ordinary differential equations for the dynamics of cholera;

$$
\begin{aligned}
\frac{dS}{dt} &= \mu N - (1 - \omega_e)\left[\frac{\beta_e B}{K + B} + \beta_h I\right]S - \mu S - vS \\
\frac{dI}{dt} &= (1 - \omega_e)\left[\frac{\beta_e B}{K+B} + \beta_h I\right]S - (\alpha + \gamma + d + \mu)I \quad (1) \\
\frac{dR}{dt} &= \gamma I + vS + \alpha I - \mu R \\
\frac{dB}{dt} &= (1 - \omega_e)\theta I - \mu_B B
\end{aligned}
$$

The non-negative initial conditions of the model system (1) are $S(0) > 0, I(0) \geq 0, R(0) \geq 0$, and $B(0) \geq 0$.

III. MODEL ANALYSIS

We begin by showing that all feasible solutions are uniformly bounded in a proper subset of $\Omega = \Omega_h \times \Omega_B$. The feasible region $\Omega_h = \{(S, I, R) \in R_+^3 : S + I + R \leq k\} \cup \Omega_B = \{(B) \in R_+ : B \leq k\}$ is positively invariant.

Adding all the equations of the model system (1) gives

$$\frac{dN}{dt} = -\alpha I.$$

In the absence of the disease $0 \leq N \leq k$ as $t \to \infty$ where k is a constant. Thus, (1) is both mathematically and epidemiologically well posed in the domain of Ω. We therefore restrict our analysis to the region Ω.

We reduced the model equations (1) since R does not appear in other equations of the model. We have

$$
\begin{aligned}
\frac{dS}{dt} &= \mu N - (1 - \omega_e)\left[\frac{\beta_e B}{K + B} + \beta_h I\right]S - \mu S - vS \\
\frac{dI}{dt} &= (1 - \omega_e)\left[\frac{\beta_e B}{K+B} + \beta_h I\right]S - (\alpha + \gamma + d + \mu)I \quad (2) \\
\frac{dB}{dt} &= (1 - \omega_e)\theta I - \mu_B B
\end{aligned}
$$

where $R = N - S - I$.

A. Disease – Free Equilibrium (DFE)

The disease – free equilibrium is the equilibrium when there is no cholera in the population. At equilibrium point, $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dB}{dt} = 0$. We have the following system of equations (3) to be solved simultaneously for S, I, B,

$$
\begin{aligned}
\mu N - (1 - \omega_e)\left[\frac{\beta_e B}{K + B} + \beta_h I\right]S - \mu S - vS &= 0 \\
(1 - \omega_e)\left[\frac{\beta_e B}{K+B} + \beta_h I\right]S - (\alpha + \gamma + d + \mu)I &= 0 \quad (3) \\
(1 - \omega_e)\theta I - \mu_B B &= 0
\end{aligned}
$$

We have

$$\mu N - (\mu + v)S = 0$$

From which we obtain

$$S = \frac{\mu N}{\mu + v}$$

Thus, the disease – free equilibrium E_0 is given as

$$E_0 = (S_0, I_0, B_0) = \left(\frac{\mu N}{\mu + v}, 0, 0\right) \quad (4)$$

B. Local Stability of the Disease – Free Equilibrium E_0

We first compute the effective reproduction number R_e by using next generation method described by [13] since the stability of DFE will be in terms of R_e.

Here, the associated matrix F is the rate of appearance of new infection in compartment i and matrix V is the transfer of infections from one compartment i to another.

$$F = \begin{bmatrix} (1 - \omega_e)\beta_h S_0 & \dfrac{(1 - \omega_e)\beta_e S_0}{k} \\ 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} \mu + \gamma + \alpha + d & 0 \\ -(1 - \omega_e)\theta & \mu_B \end{bmatrix}$$

It follows that the effective reproduction number R_e is given by;

$$R_e = \rho(FV^{-1}) = \frac{(1 - \omega_e)S_0[\beta_h k \mu_B + (1 - \omega_e)\theta \beta_e]}{k \mu_B(\mu + \alpha + \gamma + d)} \quad (5)$$

where $S_0 = \frac{\mu N}{\mu + v}$ and $\rho(FV^{-1})$ is the spectral radius of the matrix FV^{-1}.

The effective reproduction number is the mean number of new infection generated by a single cholera infected individual in a population where vaccination, therapeutic treatment and education are used as control strategies.

Theorem 1. The disease – free equilibrium E_0 of the reduced model system (2) is locally asymptotically stable if $R_e < 1$ and unstable if $R_e > 1$.

The Theorem 1 is proved using linearization method. The Jaobian matrix associated with the reduced model system (2) at the DFE $E_0 = (S_0, 0, 0)$ is given as

$$J(E_0) = \begin{bmatrix} -(\mu + v) & -(1 - \varphi_e)\beta_h S_0 & -\dfrac{(1 - \varphi_e)\beta_e S_0}{k} \\ 0 & (1 - \varphi_e)\beta_h S_0 - (\mu + \gamma + \alpha + d) & \dfrac{(1 - \varphi_e)\beta_e S_0}{k} \\ 0 & (1 - \varphi_e)\theta & -\mu_B \end{bmatrix} \quad (6)$$

The characteristics equation corresponding to $J(E_0)$ is given as

$$(-(\mu + v) - \lambda)\left[\lambda^2 + (\mu_B - (1 - \varphi_e)\beta_h S_0 + (\mu + \gamma + \alpha + d))\lambda - \mu_B\big((1 - \varphi_e)\beta_h S_0 - (\mu + \gamma + \alpha + d)\big) - \frac{(1 - \varphi_e)^2 \theta \beta_e S_0}{k}\right] = 0$$

This implies that

$$(-(\mu + v) - \lambda) = 0 \ \text{ or } \ P(\lambda) = \lambda^2 + A\lambda + B = 0$$

That is

$$\left[\lambda^2 + \left(\mu_B - (1-\varphi_e)\beta_h S_0 + (\mu+\gamma+\alpha+d)\right)\lambda - \mu_B\left((1-\varphi_e)\beta_h S_0 - (\mu+\gamma+\alpha+d)\right) - \frac{(1-\varphi_e)^2\theta\beta_e S_0}{k}\right] = 0 \quad (7)$$

where

$$A = \left(\mu_B - (1-\varphi_e)\beta_h S_0 + (\mu+\gamma+\alpha+d)\right)$$

$$B = -\left[\mu_B\left((1-\varphi_e)\beta_h S_0 - (\mu+\gamma+\alpha+d)\right) + \frac{(1-\varphi_e)^2\theta\beta_e S_0}{k}\right]$$

Using Routh–Hurwitz criteria, E_0 is locally asymptotically stable if $A > 0$, $AB > 0$ and $AB > 0$ implies that $B > 0$. We have

$$B = -\left[\mu_B\left((1-\varphi_e)\beta_h S_0 - (\mu+\gamma+\alpha+d)\right) + \frac{(1-\varphi_e)^2\theta\beta_e S_0}{k}\right] > 0$$

and this gives

$$\frac{(1-\omega_e)[\beta_h S_0 k\mu_B + (1-\omega_e)\theta\beta_e S_0]}{k\mu_B(\mu+\gamma+\alpha+d)} < 1 \quad (8)$$

Comparing (5) with (8), we have $R_e < 1$. This proves the Theorem 1.

C. Existence of Endemic Equilibrium

The endemic equilibrium point E_1 is a steady state solution where cholera persists in the population. For the existence and uniqueness of endemic equilibrium $E_1 = (S^*, I^*, B^*)$, its coordinates will satisfy the conditions; $E_1 = (S^*, I^*, B^*) \neq 0$, where $S^* > 0, I^* > 0, B^* > 0$. The endemic equilibrium point E_1 is obtained by setting model system equation (2) to zero, and is given as

$$B^* = \frac{(1-\varphi_e)\theta I^*}{\mu_B}, \quad S^* = \frac{(\mu+\alpha+\gamma+d)[k\mu_B + (1-\varphi_e)\theta I^*]}{(1-\varphi_e)[\beta_e(1-\varphi_e)\theta + \beta_h k\mu_B + \beta_h(1-\varphi_e)\theta I^*]} \quad \text{and}$$

$$I^* = \frac{\mu N - (\mu+v)S^*}{(\mu+\alpha+\gamma+d)}.$$

Substituting S^* in I^* and simplify gives I^*, the roots of the following quadratic equation

$$PI^{*2} + QI^* + R = 0 \quad (9)$$

where

$$P = (\mu+\gamma+\alpha+d)(1-\omega_e)^2\theta$$
$$Q = [(\mu+\gamma+\alpha+d)(\beta_e(1-\omega_e)\theta + \beta_h k\mu_B + (\mu+v)\theta) - \mu N(1-\omega_e)\beta_h\theta]$$
$$R = (\mu+\gamma+\alpha+d)(\mu+v)k\mu_B(1-R_e)$$

It is important to note that $P > 0$. Using Descarte's rule of signs to determine the sign of I^* in (9), a unique positive endemic equilibrium I^* exists for any sign of Q if $R_e > 1$. When $R_e < 1$, $Q < 0$, and $Q^2 - 4PR > 0$, we have precisely two endemic equilibria. This may lead to existence of backward bifurcation if we set the discriminate $Q^2 - 4PR = 0$ and solve for the critical value denoted by R_c of R_e. That is

$$R_c = 1 - \frac{Q^2}{4Pk\mu_B(\mu+\gamma+\alpha+d)(\mu+v)}$$

Thus, it can be shown that backward bifurcation would occur for the value of R_e such that $R_c < R_e < 1$.

D. Bifurcation Analysis

Some epidemiological models can be bi-stable due to vaccination or immunity [15], [16] such that $R_e < 1$ is not a sufficient condition to eradicate the disease that is endemic in the population but adequate for avoiding an epidemic caused by few infectives introduced initially in the population [17]. Some models [18], [19] being bi-stable is due to the change of stability that occurs at the bifurcation point (that is, a point where the leading eigenvalue of the Jacobian matrix at the DFE is zero) whenever $R_e = 1$. The bifurcation analysis is use to prove the bi–stable state. There are forward and backward bifurcations depending on the direction of the bifurcation parameter β. When the bifurcation is forward, it implies that disease free equilibrium is locally asymptotically stable for $R_e < 1$ and there is no cholera in the population and also endemic equilibrium is locally asymptotically stable for $R_e > 1$. Backward bifurcation occurs when the endemic equilibrium exists for $R_e < 1$ and disease free equilibrium may exists when $R_e > 1$.

Centre manifold theory [20] is used to analyse the bifurcation condition of the dynamics of cholera (2) and its local asymptotic stability of endemic equilibrium near $R_e = 1$.
Theorem 2. Centre manifold theory [20]. Consider a general system of ODEs with the parameter β:

$$\frac{dx}{dt} = F(x,\beta) \quad (10)$$

$$f: R \to R^n \text{ and } f \in C^2(R^2 \times R)$$

where 0 is an equilibrium point for the system (10) for all values of the parameter β, that is $f(0, \beta) \equiv 0$ for all β and

1. $A = D_x f(0,0) = \left[\frac{df_i}{dx_j}(0,0)\right]$ is the linearization matrix of the system (13) around the equilibrium point 0 with β evaluate at 0. Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts.

2. Matrix A has a right eigenvector **w** and a left eigenvector **u** corresponding to the zero eigenvalue.

Let f_k be the kth component of f and

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \, \partial x_j}(0,0)$$

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta}(0,0)$$

Then the local dynamics of the system (10) around the equilibrium point 0 is totally determined by the signs of a and b.

i. $a > 0$, $b > 0$ when $\beta < 0$ with $|\beta| \ll 1$, 0 is locally asymptotically stable, and there exists a positive unstable

equilibrium; when $0 < \beta \ll 1$, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium.

ii. $a < 0$, $b < 0$, when $\beta < 0$ with $|\beta| \ll 1$, 0 unstable; when $0 < \beta \ll 1$, asymptotically stable, and there exists a positive unstable equilibrium;

iii. $a > 0$, $b < 0$, when $\beta < 0$ with $|\beta| \ll 1$, 0 unstable; and there exists a locally asymptotically stable negative equilibrium; when $0 < \beta \ll 1$, 0 is stable and a positive unstable equilibrium appears;

iv. $a < 0$, $b > 0$, when $\beta < 0$ changes from negative to positive, 0 changes its stability from stable to unstable. Corresponding to a negative unstable equilibrium becomes positive and locally asymptotically stable.

Particularly, if $a < 0$ and $b > 0$, then a forward bifurcation occurs at $\beta = 0$.

Applying the Theorem 3, we let

$$S = x_1, \quad I = x_2, \quad B = x_3,$$

The reduced model (2) becomes:

$$\frac{dx_1}{dt} = f_1 = \mu N - (1 - \omega_e)\left[\frac{\beta_e x_3}{K + x_3} + \beta_h x_2\right]x_1 - (\mu + v)x_1 \quad (11)$$

$$\frac{dx_2}{dt} = f_2 = (1 - \omega_e)\left[\frac{\beta_e x_3}{K + x_3} + \beta_h x_2\right]x_1 - (\mu + \alpha + \gamma + d)x_2$$

$$\frac{dx_3}{dt} = f_3 = (1 - \omega_e)\theta x_2 - \mu_B x_3$$

The Jacobian matrix $J(E_0)$ of the model (2) at the disease-free equilibrium is defined in (6). Taking $\beta_e = \beta$ and $\beta_h = r\beta$, where β is chosen as the bifurcation parameter that occurs at $R_e = 1$, and solve for β. We have

$$R_e = \frac{(1 - \omega_e)\beta\mu N[rk\mu_B + (1 - \omega_e)\theta]}{k\mu_B(\mu + v)(\mu + \alpha + \gamma + d)} = 1$$

from which we obtain

$$\beta = \frac{k\mu_B(\mu + v)(\mu + \alpha + \gamma + d)}{(1 - \omega_e)\mu N[rk\mu_B + (1 - \omega_e)\theta]}$$

The linearized system of the system (11) with $\beta_e = \beta$ and $\beta_h = r\beta$ at $R_0 = 1$ has a simple zero eigenvalue and all other eigenvalues are negative real part.

Applying the centre Manifold theory, let the right eigenvector of the Jacobian matrix $J(E_0)$ when $R_0 = 1$ be given by $w = (w_1, w_2, w_3)$. We calculate the right eigenvector w by multiplying this vector with the Jacobian Matrix (6) and equating to zero. We have

$$w_1 = -\frac{(\mu + \alpha + \gamma + d)}{(\mu + v)}w_2, \quad w_3 = \frac{(1 - \omega_e)\theta}{\mu_B}w_2$$

The left eigenvector of the Jacobian $J(E_0)$ associated with the zero eigenvalue is given by $u = (u_1, u_2, u_3)$. Transposing Jacobian $J(E_0)$ first and multiply by u, we have

$$u_1 = 0, u_3 = \frac{(1 - \omega_e)\beta\mu N}{k\mu_B(\mu + v)}u_2$$

Using the property $w.u = 1$, we obtain

$$w_2 u_2 = \frac{k\mu_B^2(\mu + v)}{k\mu_B^2(\mu + v) + (1 - \omega_e)^2\theta\beta\mu N} \quad (12)$$

This implies that $w_2 > 0$ if $u_2 > 0$.

E. Computations of a and b

The associated non-zero partial derivatives of $f = (f_1, f_2, f_3)$ at DFE E_0 for model (11) are given by

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_3} = (1 - \omega_e)r\beta, \quad \frac{\partial^2 f_2}{\partial x_3^2} = -\frac{(1 - \omega_e)\beta\mu N}{k^2(\mu + v)}, \quad \frac{\partial^2 f_2}{\partial x_1 \partial x_3} = \frac{(1 - \omega_e)\beta}{k}$$

Since $u_1 = 0$, it follows that

$$a = u_2\left[w_1 w_2 \frac{\partial^2 f_2}{\partial x_1 \partial x_3} + w_1 w_3 \frac{\partial^2 f_2}{\partial x_1 \partial x_3} + w_3^2 \frac{\partial^2 f_2}{\partial x_3^2}\right]$$

$$a = u_2\left[-\frac{(\mu + \alpha + \gamma + d)(1 - \omega_e)r\beta}{(\mu + v)}w_2^2 - \frac{(\mu + \alpha + \gamma + d)(1 - \omega_e)^2\beta\theta}{k\mu_B(\mu + v)}w_2^2 - \frac{(1 - \omega_e)^3\theta^2\beta\mu N}{k^2\mu_B^2(\mu + v)}w_2^2\right]$$

or

$$a = -u_2 w_2^2 \beta \frac{(1 - \omega_e)}{(\mu + v)}\left[(\mu + \alpha + \gamma + d)r + \frac{(\mu + \alpha + \gamma + d)(1 - \omega_e)\theta}{k\mu_B} + \frac{(1 - \omega_e)^2\theta^2\mu N}{k^2\mu_B^2}\right]$$

Using (12), we see that $a < 0$ if $u_2 > 0$ and $a > 0$ if $u_2 < 0$.

For b, we have the non-zero partial derivatives of $f = (f_1, f_2, f_3)$ at DFE E_0 for model (11) given by

$$\frac{\partial^2 f_2}{\partial x_2 \partial \beta} = \frac{(1 - \omega_e)r\mu N}{(\mu + v)}, \quad \frac{\partial^2 f_2}{\partial x_3 \partial \beta} = \frac{(1 - \omega_e)\mu N}{k(\mu + v)}$$

The value of b can be obtained from

$$b = u_2\left[w_2 \frac{\partial^2 f_2}{\partial x_2 \partial \beta} + w_3 \frac{\partial^2 f_2}{\partial x_3 \partial \beta}\right]$$

Thus,

$$b = u_2 w_2 \frac{(1 - \omega_e)\mu N}{(\mu + v)}\left[\frac{k\mu_B r + (1 - \omega_e)\theta}{k\mu_B}\right] > 0$$

since $b > 0$ and $a < 0$ or $a > 0$ subject to whether $u_2 > 0$ or $u_2 < 0$. We have the following theorem.

Theorem 3. The model (2) exhibits a backward bifurcation at $R_e = 1$ if $u_2 < 0$ and $a > 0$. If $\beta < 0$, there exists a positive unstable endemic equilibrium point and when β changes from negative to positive, a positive stable endemic equilibrium point exists. Therefore, the endemic equilibrium point E_1 is locally asymptotically stable for $R_e > 1$ but close to 1 when $u_2 > 0$ and $a < 0$.

E. Global Stability of Disease – Free Equilibrium

We analyse the global stability of disease-free equilibrium of the model equations (2) when the bifurcation is forward, since global stability does not exist for backward bifurcation.

Using the approach by [14], the model equations (2) can be rewritten as

$$\frac{d\mathbf{x}}{dt} = F(\mathbf{x}, \mathbf{I}), \qquad (13)$$

$$\frac{d\mathbf{I}}{dt} = G(\mathbf{x}, \mathbf{I}), G(\mathbf{x}, \mathbf{0}) = 0 \qquad (14)$$

where $\mathbf{x} \in \mathbb{R} = (S)$ denotes the number of uninfected individuals (susceptible class) and $\mathbf{I} \in \mathbb{R}^2 = (I, B)$ denotes the number of infected compartments (infected and pathogen classes).

The condition for global stability for $E_0 = (S_0, 0, 0)$ is given by

H1. For $\frac{d\mathbf{x}}{dt} = F(\mathbf{x}, \mathbf{0})$, $\mathbf{x}^*$ is globally asymptotically stable,

H2. $G(\mathbf{x}, \mathbf{I}) = W\mathbf{I} - \tilde{G}(\mathbf{x}, \mathbf{I})$, $\tilde{G}(\mathbf{x}, \mathbf{I}) \geq 0$ *for* $(\mathbf{x}, \mathbf{I}) \in \Omega$ where $W = D_I G(\mathbf{x}, 0)$ is an M-matrix (i.e. the off diagonal elements of W are nonnegative) and Ω is the region where the model equations makes epidemiological meaningful.

If the model equations (2) satisfies the conditions (13) and (14) then the Theorem 4. holds:

Theorem 4. The disease-free equilibrium $E_0 = (S_0, 0, 0)$ is globally asymptotically stable if $R_0 < 1$ and that conditions H1 and H2 are satisfied.

From condition H1 $\frac{d\mathbf{x}}{dt}$, we have

$$\frac{dS}{dt} = \mu N - \mu S - vS$$

which gives

$$S(t) = \frac{\mu N}{\mu + v} + \left(S(0) - \frac{\mu N}{\mu + v}\right) e^{-(\mu + v)t}$$

Regardless of the values of initial conditions, (0), $I(0)$, and $B(0)$, $S(t) \to \frac{\mu N}{\mu + v}$ as $t \to \infty$. So E_0 is globally asymptotically stable.

From condition H2, we have

$$W = \begin{bmatrix} (1 - \varphi_e)\beta_h S_0 - (\mu + \gamma + \alpha + d) & \dfrac{(1 - \varphi_e)\beta_e S_0}{k} \\ (1 - \varphi_e)\theta & -\mu_B \end{bmatrix}$$

and $\tilde{G}(\mathbf{x}, \mathbf{I}) = \begin{bmatrix} (1 - \varphi_e)\beta_h I(S_0 - S) + \dfrac{(1 - \varphi_e)\beta_e B(S_0 B + k(S_0 - S))}{k(k+B)} \\ 0 \end{bmatrix}$

We see that matrix W is an $M - matrix$ since all its off – diagonal elements are non – negative and also $\tilde{G}(\mathbf{x}, \mathbf{I}) \geq 0$ since $S_0 \geq S$ for all $(\mathbf{x}, \mathbf{I}) \in \Omega$. Therefore, the condition H2 can be written as

$$\frac{d\mathbf{I}}{dt} \leq W\mathbf{I} \qquad (15.a)$$

The eigenvalues of W is given by solving this characteristics equation (15.b)

$$\left[\lambda^2 + \left(\mu_B - (1 - \varphi_e)\beta_h S_0 + (\mu + \gamma + \alpha + d)\right)\lambda - \mu_B\left((1 - \varphi_e)\beta_h S_0 - (\mu + \gamma + \alpha + d)\right) - \frac{(1 - \varphi_e)^2 \theta \beta_e S_0}{k}\right] = 0 \qquad (15.b)$$

Equation (15.b) is the same as (7).

It follows that for $R_e < 1$, the inequality (15) is stable and it results as $t \to \infty$, $(I, B) \to (0,0)$. Then, the DFE $E_0 = (S_0, 0, 0)$ is globally asymptotically stable if $R_e < 1$ with $u_2 > 0$ *and* $a < 0$.

F. Global Stability of the Endemic Equilibrium E_1

In this section, we study the global stability of the endemic equilibrium state of the cholera model (2) if the bifurcation is forward. The following theorem provides the global property of the endemic equilibrium of the cholera model (2) when $u_2 > 0$ *and* $a < 0$

Theorem 5. The endemic equilibrium $E_1 = (S^*, I^*, B^*)$ of the model (2) is globally asymptotically stable if $R_e > 1$.

Proof. To prove global stability of E_1, we apply [21] approach by constructing the following Lyapunov function

$$L = (S - S^* \ln S) + P(I - I^* \ln I) + Q(B - B^* \ln B)$$

The time derivative of L is given by

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)S' + P\left(1 - \frac{I^*}{I}\right)I' + Q\left(1 - \frac{B^*}{B}\right)B'$$

$$= \left(1 - \frac{S^*}{S}\right)\left(\mu N - (1 - \omega_e)\left[\frac{\beta_e B}{K + B} + \beta_h I\right]S - (\mu + v)S\right)$$

$$+ P\left(1 - \frac{I^*}{I}\right)\left((1 - \omega_e)\left[\frac{\beta_e B}{K + B} + \beta_h I\right]S - (\alpha + \gamma + d + \mu)I\right)$$

$$+ Q\left(1 - \frac{B^*}{B}\right)\left((1 - \omega_e)\theta I - \mu_B B\right) \qquad (16)$$

The model (2) satisfy the following relations at the equilibrium point $E_1 = (S^*, I^*, B^*) \neq 0$:

$$\mu N = (1 - \omega_e)\left[\frac{\beta_e B^*}{K + B^*} + \beta_h I^*\right]S^* - (\mu + v)S^*$$

$$(\alpha + \gamma + d + \mu) = \frac{(1 - \omega_e)}{I^*}\left[\frac{\beta_e B}{K + B} + \beta_h I\right]S \qquad (17)$$

$$\mu_B = \frac{(1 - \omega_e)\theta I^*}{B^*}$$

Substituting system (17) in (16), we obtain

$$\frac{dL}{dt} = \left(1 - \frac{S^*}{S}\right)\left[(1 - \omega_e)\left(\left(\frac{\beta_e BS}{K + B} + \beta_h IS\right) - \frac{I}{I^*}\left(\frac{\beta_e B^* S^*}{K + B^*} + \beta_h I^* S^*\right)\right) - (\mu + v)(S - S^*)\right]$$

$$+ P\left(1 - \frac{I^*}{I}\right)(1 - \omega_e)\left[\left(\frac{\beta_e BS}{K + B} + \beta_h IS\right) - \frac{I}{I^*}\left(\frac{\beta_e B^* S^*}{K + B^*} + \beta_h I^* S^*\right)\right]$$

$$+ Q(1 - \omega_e)\theta(I - I^*)\left(1 - \frac{B^*}{B}\right)$$

Upon simplification, we get

$$\frac{dL}{dt} = -(\mu + v)\frac{(S - S^*)^2}{S} + (1 - \omega_e)f(x, y, z) \qquad (18)$$

where $\frac{S}{S^*} = x, \frac{I}{I^*} = y, \frac{B}{B^*} = z$ and

$$f(x,y,z) = \frac{\beta_e S^* B^* k}{(k+B^*)(k+B^*z)}\left(1 - zx - \frac{1}{x} + z\right) + B^*\left(2z - xz - \frac{z}{x}\right) +$$

$$\beta_h S^* I^*(1-xy) + P\left[\frac{\beta_e S^* B^* k\left(1+zx-y-\frac{xz}{y}\right)}{(k+B^*)(k+B^*z)} + B^*\left(z + xz - yz - \frac{xz}{y}\right) + \beta_h I^* S^*(xy-1)\right] + Q\theta I^*\left(1 + y - \frac{y}{z} - z\right) \quad (19)$$

In order to determine P and Q, we set the coefficients of xy and y of (19) equal to zero and solve the result equations. We obtain,

$$P = 1, \quad Q = \frac{\beta_e S^* B^* k}{(k+B^*)(k+B^*z)\theta I^*}.$$

Substituting P and Q in (19) and simplifying, we have

$$f(x,y,z) = \frac{\beta_e S^* B^* k}{(k+B^*)(k+B^*z)}\left(3 - \frac{1}{x} - \frac{y}{z} - \frac{xz}{y}\right)$$
$$+ B^* z\left(3 - y - \frac{x}{y} - \frac{1}{x}\right) \quad (20)$$

Using arithmetic and geometric mean inequality, we have

$$\frac{1}{x} + \frac{y}{z} + \frac{xz}{y} > 3 \quad \text{and} \quad y + \frac{x}{y} + \frac{1}{x} > 3.$$

This implies that $f(x,y,z) \le 0$. Therefore, $\frac{dL}{dt} \le 0$ in Ω. The equality $\frac{dL}{dt} = 0$ holds only for $x = y = z = 1$ for which $S = S^*$, $I = I^*$, $B = B^*$. Thus, the model system (2) has a unique endemic equilibrium point E_1 which is globally asymptotically stable if $R_e > 1$ as well as $u_2 > 0$ *and* $a < 0$ using the LaSalles invariance principle [22].

IV. NUMERICAL SIMULATIONS

In this section, we carry out numerical simulations for model equations (2) in order to validate our analytical results. This is achieved by using a set of model parameters whose values are mainly from literature along with assumed values so as to have realistic numerical results. Table I presents the model parameter values and respective sources.

Figs. 1 and 2 show the impact of vaccination, therapeutic treatment, and education on the infected and pathogen populations. The infected and pathogen populations decrease as the controls are implemented together. Combined implementation of therapeutic treatment and vaccination substantially reduces both infected and pathogen populations but still leave residues with potential to cause frequent new outbreaks. This may explain why cholera is endemic in many developing countries. It is only when the three controls are carried out together that a disease free equilibrium may be achieved.

Figs. 3 and 4 reveal how education can reduce the infected and pathogen populations. As the rate of education increases, the infected and pathogen population reduce. This simply means that vaccination and therapeutic treatment are not enough to eliminate the cholera infection in the population. People need to be aware of the infection especially those in rural areas and urban slums. This can be achieved through

education of the populace on hygiene consciousness [9], through radio, word-of-mouth communication, television, social media and posters [7].

TABLE I
MODEL PARAMETER VALUES

Parameter	Value	Source
N	10000	[12]
μ	$(43.5yr)^{-1}$	,,
β_e	$0.15/day$	,,
β_h	$0.0005/day$	,,
θ	$\frac{10 cells}{ml} - day$	,,
γ	$(5day)^{-1}$	,,
k	$1000000 cells/ml$	,,
μ_B	$0.02\ day^{-1}$	[23]
d	0.015	,,
v	0.2	Assumed
ω_e	$0.3/day$	[10]
α	0.2	Assumed

V. CONCLUSION

In this study, a mathematical model of cholera has been proposed in order to assess the impact of vaccination, therapeutic treatment, and health educational message on the transmission dynamics of cholera infection in a varying population. The disease free and endemic equilibria are proved to be locally and globally asymptotically stable if $R_e < 1$ and $R_e > 1$ respectively provided $u_2 > 0$ and $a < 0$. In addition, a backward bifurcation exists where the effective reproduction number is equal to unity, $R_e = 1$ if $u_2 < 0$ and $a > 0$. Numerical simulation is carried out to support the analytical results. The result shows that the disease free equilibrium may be attain if the controls are implemented together.
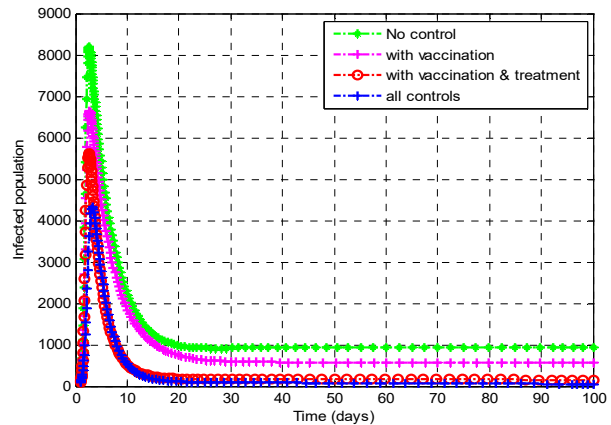

Fig. 1 The impact of vaccination, therapeutic treatment and health educational message on infected population
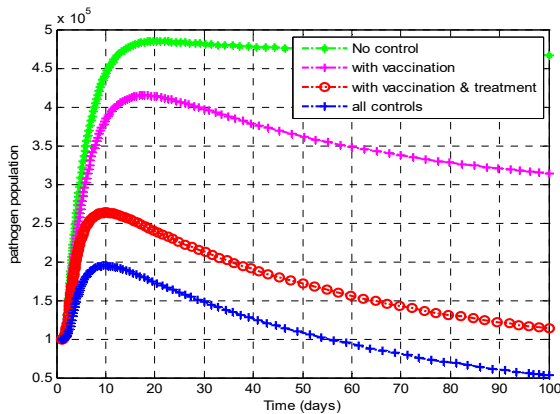
Fig. 2 The impact of vaccination, therapeutic treatment and health educational message on pathogen population
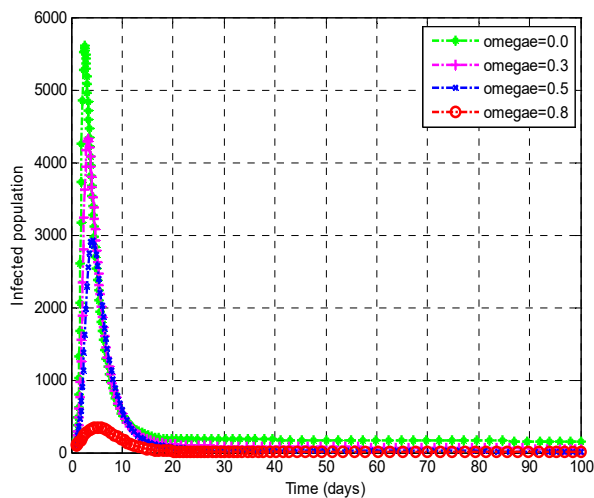

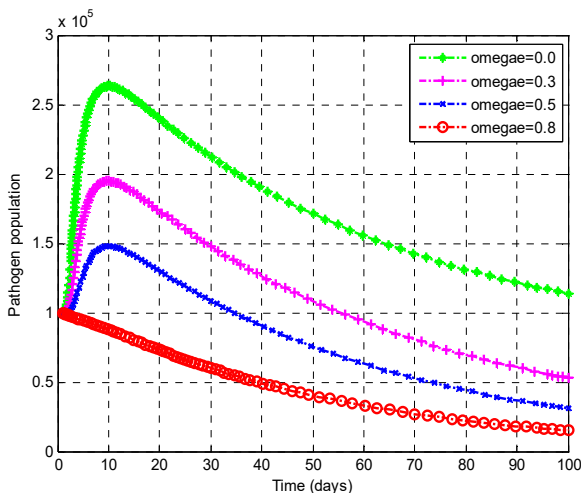Fig. 3 The impact of health educational message on infected population

Fig. 4 The impact of health educational message on infected population

REFERENCES

[1] O.A. Adagbada, S.A. Adesida, F.O. Nwaokorie, M. Niemogha, and A.O. Coker, "Cholera epidemiology in Nigeria: An overview", *Pan African Medical Journal*, vol. 12, no. 59, 2012.

[2] C. Chin, J. Sorenson, J.B. Harris, W.R. Robins, R.C. Charles, R.R. Jean-Charles, *et al*, "The origin of the Haitian cholera outbreak strain", *The New England Journal of Medicine*, vol. 364, pp. 33 – 42, 2011.

[3] F.J. Luquero, L. Grout, I. Ciglenecki, K. Sakoba, B. Traore, M. Helie, et al, "Use of vibrio cholerae vaccine in an outbreak in Guinea", *The New England Journal of Medicine*, vol. 370, pp. 2111 – 2120, 2014.

[4] H.D.N. Nyamogoba, A. A. Obala, and R. Kakai, "Combating cholera epidemics by targeting reservoirs of infection and transmission routes: A review", *East African Medical Journal*, vol. 79, no. 3, pp. 150 – 155, March 2002.

[5] World Health Organisation, "Cholera 2013", *Weekly epidemiological record*, vol. 89, no. 31, pp. 345 -356, 2014.

[6] S.M. Farugue, M.J. Albert, and J.J. Mekalanos, "Epidemiology, genetics, and ecology of toxigenic vibrio cholerae", *Microbiology and Molecular Biology Reviews*, vol. 62, no. 4, pp. 1301 – 1314, 1998.

[7] J. Einardóttir, A. Passa, and G. Gunnlaugsson, "Health education and cholera in rural Guinea-bissau", *Int. J. Infect. Dis.*, vol. 5, no. 3, pp. 133 – 138, 2001.

[8] H. W. Hethcote, "The Mathematics of Infectious Diseases", *SIAM REVIEW*, vol. 42, no. 4, pp. 599-653, 2000.

[9] M.J. Ochoche, C.E. Madubueze, and T.B. Akaabo, "A mathematical model on the control of cholera: hygiene consciousness as a strategy", *J. Math. Comput. Sci.*, vol. 5, no. 2, pp. 172 – 187.

[10] M. Al-arydah, A. Mwasa, J.M. Tchuenche, and R.J. Smith, "Modelling cholera disease with education and chlorination", *Journal of Biological System*, Vol. 21, no. 4, 1340007 (20 pp.), 2013.

[11] J. Cui, Z. Wu, and X. Zhou, "Mathematical analysis of a cholera model with vaccination", *Journal of Applied Mathematics*, vol. 2014, article ID324767, 16 pp., 2014.

[12] J. Wang and C. "Modnak, Modeling cholera dynamics with controls," *Canadian Applied Mathematics Quarterly*, vol. 19, no. 3, pp. 255 – 273, 2011.

[13] P. Van Den Driessche, and J. Watmough, "Reproduction numbers and sub-thresholds endemic equilibrium for compartmental models of disease transmission", *Mathematical Bioscience*, vol. 180, no. 2002, pp. 29 – 48, 2002.

[14] C. Castillo-Chavez, Z. Feng, and W. Huang, "On the computation of R_0 and its role on global stability", In: Mathematical Approaches for Emerging and Re-emerging Infectious Diseases: An Introduction, IMA, vol. 125, pp. 229 – 250, 2002.

[15] S.M. Garba, A.B. Gumel, and M.R.A. Bakar, "Backward bifurcations in dengue transmission dynamics", *Mathematical Biosciences*, vol. 15, no. 1, pp. 11-25, 2008.

[16] N. Chitnis, J.M. Cushing, and J.M. Hyman, "Bifurcation analysis of a mathematical model for malaria transmission", *SIAM J. APPL. MATH.*, vol. 67, no. 1, pp. 24-45, 2006.

[17] N. Piazza, and W. Hao, "Bifurcation and sensitivity analysis of immunity duration in a Epidemic", *International Journal of Numerical Analysis and Modelling*, Series B, vol. 4, no. 2, pp. 179-202, 2013.

[18] J. Arion, C.C. Mccluskey, and P. Van Den Driessche, "Global results for an epidemic model with vaccination that exhibits backward bifurcation", *SIAM. J. APPL. MATH.*, vol. 64, no. 1, pp. 260-276, 2003.

[19] W. Huang, K.L. Cooke, and C. Carlos, "Stability and bifurcation for a multiple-group model for the dynamics of HIV/AIDS transmission", *SIAM. J. APPL. MATH.*, vol. 52, no. 3, pp. 835-854, 1992.

[20] C. Castillo – Chavez, and B. Song, "Dynamical models of tuberculosis and their applications", *Mathematical Biosciences and Engineering*, vol. 1, no. 2, pp. 361-404, 2004.

[21] N. Kaur, M. Ghosh, and S.S. Bhatia, "Mathematical analysis of the transmission dynamics of HIV/AIDS: Role of female sex workers", *Appl. Math. Inf. Sci., Vol.* 8, no. 5, pp. 2491 – 2501, 2014.

[22] J.P. LaSalle, "The stability of dynamical systems", Regional Conference Series in Applied Mathematics, SIAM, Philadelphia, PA.

[23] S. Edward, and N. Nyerere, "A mathematical model for the dynamics of cholera with control measures", *Applied and Computation Mathematics*, vol. 4, no. 2, pp. 53 – 63, 2015.