

**A MATHEMATICAL MODEL FOR TRANSMISSION DYNAMICS OF
CHOLERA WITH CONTROL STRATEGIES**



**BY
ABU ABEBE**

**A THESIS
SUBMITTED TO APPLIED MATHEMATICS DEPARTMENT
SCHOOL OF APPLIED NATURAL SCIENCE
OFFICE OF GRADUATE STUDIES
ADAMA SCIENCE AND TECHNOLOGY UNIVERSITY**

July, 2019
ADAMA, ETHIOPIA

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Approval Page

This is to certify that the thesis prepared by Abu Abebe, entitled “Mathematical Model for Transmission Dynamics of Cholera with Control Strategies ”and submitted in partial fulfillment of the requirements for the degree of Master’s of Science in Applied Mathematics(Specialization in Differential).

As a member of the board of examiners of the MSc.thesis open defense examination, we certify that we have read and evaluated the thesis prepared by Abu Abbebe and examined the candidate. We recommended that the thesis be accepted as fulfilling the thesis requirement for the degree of Master’s of Science in Applied Mathematics.

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Abstract

Cholera is an epidemic infectious disease caused by the food or water contaminated with the bacterium vibrio cholera. In this thesis we extended and analyzed mathematical model for transmission dynamic of cholera with education, vaccination and treatment as control strategies. We qualitatively analyzed the extended model. In particular, we proved that positivity of solution and its boundedness. The basic reproduction number without control and with control in single and combined control strategies are computed and compared with each other to assess the possible community benefits. Then we studied the stability of disease free and endemic equilibrium points and also we investigated the sensitivity index of the reproduction number with respect to model parameters. Numerical simulation shows that in a unique control strategy, treatment yields the best results followed by vaccination campaign and education being the last. In combination of two controls combination of education with treatment is best followed by combination of treatment and vaccination then combination of education and vaccination is less from combination of two control but it is best than single control strategy. We noted that the control of cholera is very much better when we incorporated more than one strategies.

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Chapter 1

Introduction

1.1 Cholera

Cholera is a critical epidemic infectious disease caused by the ingestion of food or water contaminated with the bacterium *Vibrio cholera*. It is characterized by watery diarrhea, extreme loss of fluid and electrolytes and severe dehydration, vomiting, leg cramps and if untreated, it leads to rapid dehydration, acidosis, circulatory collapse and death within 12–24 hr [28, 35]. The *V. cholera* colonize the intestinal gut, then produce enterotoxin, painless and watery diarrhea that can quickly lead to severe dehydration and death if treatment is not given. Vomiting also occurs in most patients.

As reported in [9] those who recover usually have long-term immunity against re-infection. Cholera can either be transmitted through interaction between humans or through interaction between humans and their environment (i.e., ingestion of contaminated water and food from the environment). Vaccination has been a commonly used method for disease control and works by reducing the number of susceptible individuals in a population [10].

Cholera is a bacterial disease whose primary mode of transmission is indirect other than human-to-human contact; which is caused when individuals ingest fecal-contaminated water containing the bacteria *V. cholera* [34]. Transmission between humans and reservoirs of pathogens implies that disease transmission includes an indirect route. The dynamics of

cholera involve multiple interactions between the human host, the pathogen, and the environment [10], which contribute to both direct human-to-human and indirect environment-to-human transmission pathways.

Due to its huge impact on public health, and social and economic development, cholera has been the subject of extensive studies in clinical, experimental and theoretical fields. It remains an important global cause of mortality and causing periodic epidemic disease [17].

Cholera affects 3 –5 million people and causes 100,000 –130,000 deaths in the world annually and it remains a global threat to public health and a key indicator of lack of social development [36, 25]. Modern sewage and water treatment have virtually eliminated cholera in industrialized countries. The last major outbreak in the United States occurred in 1911 [36]. But cholera is still present in Africa, Southeast Asia and Haiti [43].

The risk of cholera epidemic is highest when poverty, war, migration (immigration) and natural disasters such as earth quack force people to live in crowded conditions without adequate sanitation. Recently, the reemergence of cholera has been noted in parallel with the ever-increasing size of susceptible populations living in unsanitary conditions [36]. Education, which is a key tool in disease control, is often overlooked [8]. It requires investment in people rather than in bio-medical interventions. Conversely, a lack of information can have a severe impact on the spread of the disease. Cholera-specific education includes advising people with symptoms to seek medical care and improving sanitation and hygienic practices [7]. Failures to provide health education can be traced to barriers at one of six sites: to be effective, (1) messages have to reach the intended audience, (2) gain attention, (3) be correctly understood, (4) be accepted, (5) result in changed behavior and (6) result in improvement in health. Radio and word-of-mouth communication were effective educational tools [7].

Water that has been treated with chlorine is effective in preventing the spread of cholera [26]. Understanding the fundamental mechanism in the disease transmission is crucial for effective prevention strategies against a cholera outbreak. For prevention of cholera, if we're traveling to cholera-endemic areas, risk of contracting the disease can be minimized by wash hands with soap and water frequently, drink only safe water, eat

food that's completely cooked and hot. To this effect, mathematical modeling provides a unique approach to gain basic insights into the dynamics of infectious diseases. Therefore, we exploring the potential effects of disease control strategies such as vaccination, education and treatment in our work within mathematical modeling that can show briefly the dynamics of cholera outbreaks.

Mathematical model and simulations are quick and easy to produce, simplify a more complex situation, help us improve our understanding of the real world [13]. It can helps to determine the characteristics and magnitude of epidemic disease transmission, to predict its outbreak and to see which parameters are more influential in the dynamics of the disease etc. The sum of all the above findings are very important for policy makers to implement effective control strategies for cholera outbreak and for researchers to understand the dynamical behaviors of cholera.

Mathematical models are powerful tools for the development of epidemiological theories. Modeling of the dynamic of cholera is process of describing the dynamics of human population and biomass level of vibrio cholerae mathematically with differential equation [1]. The last few years estimated that many cholera outbreaks happened in developing countries namely Ethiopia, Angola, Congo, Haiti, Uganda and Zimbabwe [37, 39, 41].

In an effort to gain deeper understanding of the complex dynamics of cholera, several mathematical models have been published. For example Codeo in 2001 proposed a model [3] that explicitly accounted for the environmental component, i.e., the *V. cholera* concentration in the water supply, into a regular SIR epidemiological model. The incidence (or, the infection force) was modeled by a logistic function to represent the saturation effect. The authors in [9] extended Codeos work by dividing bacteria concentration into a hyper infectious and less infectious state of the pathogen, representing the explosive noneffective of freshly shed *V. cholerae*, based on the laboratory observations [16] and rigorously analyzed in [38]. Modified Codecos model by a threshold pathogen density for infection with a careful discussion on human-environment contact and in-reservoir pathogen dynamics.

In this study we extend the mathematical model proposed in [15] by adding education as control measure of cholera. The modified model is analytically studied. For numerical

simulation, we employed matlab ode45 which is preferable for our highly non-linear system of equation.

The importance of adding education E to this study is to reduce the number of population tends to infection from susceptible and to minimize bacteria concentration in environment that caused for cholera outbreak (cholera disease spread).

The influences of control strategies are to:

- 1) control the susceptible and Infected population increases due to the incoming of immigrants.
- 2) reduce the concentration of vibrio cholerae by creating awareness for community about water sanitation and hygiene.
- 3) increases the recovery rate of infected population
- 4) promote awareness among the communities of causes cholera pandemic.
- 5) instruct, advise and assist a communities, officer, health organization for fast decision making on time to use control measure for minimization of cholera pandemic

1.2 Statement of the problem

Infectious diseases are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi; the diseases can be spread, directly or indirectly, from one person to another. Cholera is an acute diarrhoeal disease that can kill within hours if left untreated.

Cholera pandemic reached the African continent in 1970 in Guinea, sierra Leone, Liberia, Nigeria, then spread into interior of the sub-saharan states. Entering Africa from the eastern countries of Djibouti, Ethiopia frequently affected by cholera 850 cases reported in Ethiopia at 1970, 16 in 2004, 54,070 in 2006 as reported in [22]. In 2019 after some years of absence, cholera re-emerged in Ethiopia as reported in [19] Ethiopia has a low sanitation coverage and has been frequently affected by Acute Watery Diarrhoea and Cholera outbreaks. As of 3rd July 2019 report of ministry of health,

there were at least 871 people affected by the infectious disease with 17 deaths: 1 from Afar, 2 from Oromia and 14 from Amhara region.

More of previous work has been done in the last 2 decades on dynamic of cholera. Most of them so far focus on epidemic dynamic of cholera such as the role of aquatic reservoir of *Vibrio cholerae* [3], transmission way to cause epidemics [9], stability analysis and application of a mathematical model of cholera [38] and few researcher review an epidemic model for cholera with optimal control treatment [14] and mathematical analysis of a cholera model with vaccination and treatment [4] all of them contributed remarkable effort to minimize number of pathogen and infected individual to control the cholera out break, but we are still facing great challenges in the development of effective control and policies to stop the transmission and to avoid global outbreaks. Most of researcher focus on treatment after happen of cholera out break more than prevention. In our study we introduce education and vaccination for cholera as prevention strategies to minimize infected number of susceptible individuals to cholera disease, but after cholera outbreak append treatment is unique control strategy.

Many mathematical models of dynamic of cholera have been developed, but those models have some gaps especially no more model developed for cholera in the literature by including vaccination, education and treatment in well organized way. For example as reported in [18] show that educated individual who may have exposure to be quarantined. Use of quarantine for educated individual can expose them for infection. Quarantine was adopted as a mean of separating persons that may have been infected to a contagious disease and it raises political, ethical and socioeconomic issues and requires a careful balance between public interest and individual rights [33]. We do this work attentively to fill such gap. If vaccination and education had existed from the beginning of cholera outbreaks then the epidemic would have been take out. We believe that the absence of this type of prevention measures was one of the responsible for causing of the cholera outbreak in epidemic areas or countries.

Thus this thesis is intended to answer the following basic questions

1. How modify the model and which parameter more influence the dynamic of cholera?
2. Are the impact of control strategies significant?
3. Are the equilibrium points of the modified model stable?
4. what is the biological interpretation of the solution of the modified mathematical model?

1.3 General objective

The general objective of this study is to investigate the transmission dynamic of cholera with control strategies.

1.4 Specific objective

The specific objective of this study are to:

- modifying mathematical model of cholera disease that describe the impact of education, vaccination and treatment control strategies on cholera outbreak.
- perform local stability of the equilibrium points.
- study the sensitivity of parameters
- Interpret the solution of the extended mathematical model

1.5 Significances of the study

The findings of this study are:

- help health authorities to understand the effect of vaccination and education from beginning of cholera outbreak and treatment for infected group.
- create awareness about the hygiene and water sanitation to minimize spread of cholera epidemic.

- provide useful information for the control strategies which help us to controlling and minimizing of cholera outbreaks.
- give a better insight for mathematicians, researchers, health workers and policy makers about the dynamics of cholera.

Chapter 2

Literature Review

Cholera is one of the main health issue around the world, especially in Africa, where every year thousands of people die due to this enteric disease. International agencies, such as the World Health Organization and the United Nation are making big efforts to help people in need and to stop this infection [37].

Claudia T.C [3] formulated a mathematical model of cholera epidemiology that incorporates an environmental reservoir of *V. cholerae*. Codeco [3] consider only environment to human transmission pathway and for first time they consider explicitly the pathogen concentration in cholera model. The objective of the study was to explore the role of the aquatic reservoir on the persistence of endemic cholera as well as to define conditions for the development of epidemic and endemic cholera.

The mathematical model of their study was formulated as follows

$$\begin{aligned}\frac{ds}{dt} &= \lambda(H - S) - a\lambda(B)S \\ \frac{dI}{dt} &= a\lambda(B)S - \gamma I \\ \frac{dB}{dt} &= B(nb - mb) + eI\end{aligned}$$

where number of susceptible, infected and concentration of toxigenic *V.cholera* in water represented by S , I and B respectively. The first equation describes the dynamics of susceptible in a community of total population H . Susceptible individuals are renewed at a rate n . Renewal may occur as result of birth, immigration and/or

loss of acquired immunity. Susceptible people becomes infected at a rate $a\lambda(B)$, where a is the rate of contact with untreated water and $\lambda(B)$ is the probability of such person to catch cholera.

$$\lambda(B) = \frac{B}{K + B}$$

where K is the concentration of V. cholerae in water that yields half percent chance of catching cholera. Second equation describes the dynamics of infected people in the community. Third equation describes the dynamics of pathogenic V. cholerae in the aquatic reservoir. As reported by authors, if the number of susceptible in this population is greater than a critical number S_C , stability analysis of the model indicates an outbreak will occur. Otherwise, the number of cases will decrease and return to zero, where

$$S_C = \frac{rK(mb - nb)}{e}$$

a critical number S_C threshold increases proportionally with concentration of V. cholerae in water that yields 50 percent(K) and recovery (r) as well as the net mortality rate of V. cholerae in the water. It decreases as contamination of water supplies as well as contact with these waters (e) increase. In other words, the better water quality and sewage treatment are the greater pool of susceptible in order to trigger a cholera outbreak. Where nb growth rate of V. cholerae in the aquatic environment (day-1), mb loss rate of V. cholerae in the aquatic environment (day-1) e contribution of each infected person to the population of V. cholerae in the aquatic environment (cell/ml day-1 person-1).

The result of the study [3] show that the reproduction rate of cholera in a community is defined by the product of social and environmental factors. Variations of contact rates force a cyclical pattern of cholera outbreaks, as observed in some cholera-endemic communities. As the conclusion of authors study further development on cholera modeling requires a better understanding of V. cholerae's ecology and epidemiology.

This work is an effort towards the formulation of a cholera theory mathematically that incorporates a V. cholerae environmental reservoir and serve as initial for some

researcher. The model proposed is very simple, but does not include any intervention and many features of this complex system

Jing'an Cui et al.[4], Modify the Codeco's [3] model by adding vaccination and consider $SVR - B$ type of cholera model. Also [4] consider both environment to human and human to human transmission pathway and develop a cholera model with an additional equation for the vaccinated of susceptible individuals in their mathematical model as follows.

$$\begin{aligned}\frac{dS(t)}{dt} &= \mu_1 - \frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} - \frac{\beta_2 S(t)I(t)}{1+\alpha_2 I(t)} - \phi S(t) - \mu_1 S(t) + \theta V(t) \\ \frac{dV(t)}{dt} &= \phi S(t) - \theta V(t) - \mu_1 V(t) \\ \frac{dI(t)}{dt} &= \frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} + \frac{\beta_2 S(t)I(t)}{1+\alpha_2 I(t)} - (\delta + \alpha + \mu_1)I(t) \\ \frac{dB(t)}{dt} &= \eta I(t) - \mu_2 B(t)\end{aligned}$$

Here, S, V, I and B refer to the susceptible individuals, vaccinated individuals, infected individuals and pathogen population at time t respectively. In their study they analysis and determine local and global stability of a disease-free-equilibrium and endemic equilibrium based on the value of reproductive number.

The result of the study of Jing'an Cui et al in [4] show that the vaccine reduce the reproduction number of the disease, and in the absence of the vaccination, the disease transmission will be high. The vaccinated rate ϕ and the wanning rate θ play equal important roles in reducing the control reproduction number. The disease can be controlled if and only if the reproduction number is reduced to values less than unity if the vaccinated rate ϕ exceed the threshold and the wanning rate θ less than the threshold simultaneously and they conclude that vaccination is a good way to control cholera.

David M. H [9], also extended the Codeo model by incorporate hyper-infectious B_H and lower-infectious B_L of bacteria concentration. Higher and lower infectious quantity of vibrio cholera probably varies from place to place, depending on sanitation, population density, and hygiene standards. In this modified model, infections, I , are caused by ingesting water contaminated with B_H of vibrios per ml or B_L of vibrios per ml. Ingestion of hyper and less infectious of vibrio's occur at the rate β_H and

β_L respectively. Hyper and less infectious of vibrio cholerae added into aquatic environment at rate of ξ and δ_L respectively. The relationship between infection rates and the density of cholera is described by function $\frac{\beta B}{K+B}$ where K is the probability of V. cholerae infectious concentration and β is rate of drinking contaminated water. All idea of the work in [9] are expressed by the following mathematical model:

$$\begin{aligned}\frac{dS}{dt} &= bN - \beta_L S \frac{B_L}{K_L+B_L} - B_H S \frac{B_H}{K_H+B_H} - bS \\ \frac{dI}{dt} &= \beta_L S \frac{B_L}{K_L+B_L} + \beta_H S \frac{B_H}{K_H+B_H} - (\gamma + b)I \\ \frac{dR}{dt} &= \gamma I - bR \\ \frac{dB_H}{dt} &= \xi I - \chi B_H \\ \frac{dB_L}{dt} &= \chi B_H - \delta_L B_L\end{aligned}$$

Representation of all parameter in the model are given in the study [9]

The expression for basic reproductive number for this model is associated with the number of new infections caused by hyper-infectious (HI) and less-infectious of vibrio. In this model analysis the disease die out or more spread estimated based on basic reproductive number of model.

Neilan, R. L. M [20] in 2010 modified the cholera model proposed by Hartley, et al. [9] by divided infected individual into symptomatic and asymptomatic in their model and consequently analyzed the optimal control and conducted numerical simulation of their model, but no human-to-human transmission route is considered in their work. This model consider that hyper-infectious B_H and less-infectious B_L of bacteria concentration, additionally they consider symptomatic (I_S) and asymptomatic I_A infectious of infected individual which is not considered in [9]. Bacteria concentration transmitted from high to less infectious by rate of χ and δ is mortality rate of less-infectious bacteria. Susceptible individuals become infected asymptotically I_A and symptomatically I_S with cholera by rate of p and $1 - p$ respectively through hyper or less ingestion of contaminated water by rate of β_H and β_L respectively. As their assumption the asymptomatic class will have smaller rates of cholera-related

death (e_1) see the remain parameters in [20]

$$\begin{aligned}
\frac{dS}{dt} &= -(1 - m(t))[\beta_L \frac{B_L(t)}{K_L + B_L(t)} + \beta_H \frac{B_H(t)}{K_H + B_H(t)}]S(t) + \omega R(t) - \nu(t)S(t) \\
\frac{dI_A}{dt} &= p(1 - m(t))[\beta_L \frac{B_L(t)}{K_L + B_L(t)} + \beta_H \frac{B_H(t)}{K_H + B_H(t)}]S(t) - (e_1 + \gamma_1)I_A(t) \\
\frac{dI_S}{dt} &= (p - 1)(1 - m(t))[\beta_L \frac{B_L(t)}{K_L + B_L(t)} + \beta_H \frac{B_H(t)}{K_H + B_H(t)}]S(t) - (1 - u(t))(e_2 + \gamma_2)I_S(t) - u(t)(e_3 + \gamma_3)I_S(t) \\
\frac{dR}{dt} &= \nu(t)S(t) + \gamma_1 I_A(t) + \gamma_2(1 - u(t))I_S(t) - \omega R(t) \\
\frac{dB_H}{dt} &= \eta_1 I_A(t) + \eta_2 I_S(t) - \chi B_H(t) \\
\frac{dB_L}{dt} &= \chi B_H - \delta B_L
\end{aligned}$$

To determine the role of their model parameters in dynamics of cholera outbreak the authors conduct a sensitivity analysis. According to their model the basic reproductive number is calculated. [20] use optimal control to reduce cholera related deaths with minimal cost. The result of Neilan, R. L. M in [20] show that rehydration and antibiotic treatment of severe infections greatly reduces death due to disease. In combination with other controls, high levels of sanitation are most beneficial at the beginning of an outbreak to decrease the explosiveness of infection, providing more time to effectively implement the other treatments

Jing Wang [38] considered three types of control strategies such as vaccination, therapeutic treatment (including hydration therapy, antibiotics, etc.), and water sanitation, but the author did not incorporate the role of education control strategy in their model and they have no equation for vaccination, treatment and sanitation. Simply used only vaccination rate, treatment rate and water sanitation rate in the model as parameter. As their result shows the infection level has been significantly reduced due to the incorporation of the three types of controls vaccination, sanitation and treatment.

Torres, D.F. et al. [14] proposed a mathematical model for cholera with treatment through quarantine. The model is shown to be both epidemiologically and mathematically well posed. In their study they proved positivity of solutions of the model and boundedness; and that every solution with initial conditions in a certain meaningful set remains in that domain for all time. The existence of unique disease-free and endemic equilibrium points is proved and the basic reproduction number is computed. Then study the local asymptotic stability of DFE and endemic equilibrium points. An optimal control problem is proposed and analyzed, whose goal is to

obtain a successful treatment through quarantine by minimizing infected individual and bacteria concentration, as well as the costs associated with the quarantine in their study. Finally, a numerical simulation of the cholera outbreak in the Department of Artibonite (Haiti), in 2010, is carried out. All these concepts are concluded by the following mathematical model:

$$\begin{aligned} S'(t) &= \Lambda - \frac{\beta B(t)}{k+B(t)} S(t) + \omega R(t) - \mu S(t) \\ I'(t) &= \frac{\beta B(t)}{k+B(t)} S(t) - (\delta + \alpha_1 + \mu) I(t) \\ Q'(t) &= \delta I(t) - (\epsilon + \alpha_2 + \mu) Q(t) \\ R'(t) &= \epsilon Q(t) - (\omega + \mu) R(t) \\ B'(t) &= \eta I(t) - dB(t) \end{aligned}$$

This is a SIQRB model type for cholera transmission dynamics. The model of this study is differs from the other mathematical models for cholera dynamics transmission in the literature, because it assumes that infectious individuals subject to treatment stay in quarantine during that period. The numerical simulations show that after approximately three months (87 days) the optimal strategy implies a gradual reduction of the fraction of infectious individuals that stay in quarantine. The result of the study show that introducing treatment through quarantine reduces the number of infected individuals reported by WHO [40],but their work have some gap such as absence of vaccination and education even if use of quarantine for controlling epidemic diseases has always been controversial, because such strategy raises political, ethical and socioeconomic issues and requires a careful balance between public interest and individual rights [33]which is considered in [15]

Torres, D.F. et al. [15] modify the model studied in [14] which is consider treatment in quarantine. In the study of [15] a mathematical model proposed and analyzed for cholera by considering vaccination and treatment out of quarantine. It is epidemiologically and mathematically well posed and prove the existence and uniqueness of disease-free and endemic equilibrium points. This paper is done based on the biggest cholera outbreak of happened in Yemen between 27th April 2017 and 15th April 2018 [32]. A vaccination campaign began on 6th May 2018 and ended on 15th May 2018 that means the vaccination is given after long period of cholera outbreak. The basic reproduction number is determined and the local asymptotic stability of

equilibrium is studied.

As reported in [15] a SITRV(Susceptible–Infectious –Treated –Recovered –Vaccinated) type model is developed, which includes a class of bacterial concentration. The sensitivity of the basic reproduction number with respect to all parameters of the model is analyzed. The total human population $N(t)$ is divided into five classes: susceptible $S(t)$, infectious with symptoms $I(t)$, in treatment $T(t)$, recovered $R(t)$ and vaccinated $V(t)$ at time t , for $t \geq 0$ and consider a class $B(t)$ that reflects the bacterial concentration at time t .

Λ assumed as positive recruitment rate and μ is a natural death rate for time t . Susceptible individuals can be vaccinated at rate $\varphi \geq 0$ and become infected with cholera at rate $\frac{\beta B(t)}{k+B(t)} \geq 0$ which is dependent on time t . $\beta > 0$ is the ingestion rate of the bacterium through contaminated sources. $k > 0$ is the half saturation constant of the bacterial population, and $\frac{B(t)}{k+B(t)}$ measures the possibility of an infected individual to have the disease. In most of the study recovered and vaccinated individual can lose the immunity at rate $\omega_1 > 0$ and $\omega_2 > 0$ respectively and can be susceptible again. The infected individuals can get a proper treatment, at rate $\delta \geq 0$ and the individuals in treatment can recover at rate $\varepsilon \geq 0$. Disease-related death rates associated with the individuals that are infected and in treatment are α_1, α_2 respectively. Each infected individual contributes to the increase of the bacterial concentration at rate $\eta > 0$ the mathematical model depicting the interactions between all those assumption are translated into the following mathematical model

$$\begin{aligned}
 S'(t) &= \Lambda - \frac{\beta B(t)}{k+B(t)} S(t) + \omega_1 R(t) + \omega_2 V(t) - (\varphi + \mu) S(t) \\
 I'(t) &= \frac{\beta B(t)}{k+B(t)} S(t) - (\delta + \alpha_1 + \mu) I(t) \\
 T'(t) &= \delta I(t) - (\varepsilon + \alpha_2 + \mu) T(t) \\
 R'(t) &= \varepsilon T(t) - (\omega_1 + \mu) R(t) \\
 V'(t) &= \varphi S(t) - (\omega_2 + \mu) V(t) \\
 B'(t) &= \eta I(t) - dB(t)
 \end{aligned} \tag{2.0.1}$$

Simulations of their mathematical model, with and without vaccination are shown, but in their study contributions of education are not considered and our work is to fill this gap, we now modify this model by adding education and in addition we

have the equation for education E :

$E'(t) = \psi S(t) - (\mu + \gamma + \epsilon)E(t)$ and all parameters are positive, where ψ , μ , γ , ϵ are educated rate of susceptible, natural death rate of human, infected rate of educated, susceptible rate of educated respectively. Education include creating awareness about water sanitation, hygiene and symptoms of cholera. Education is used for prevention of community from infection of cholera.

Chapter 3

Methodology of the study

This section consists of methods used to undertake the study. These are study design, source of information and procedure of the study.

3.1 Study Design

The aim of this study is to modify a mathematical model for prevention and treatment of cholera with control strategies. The first task is understanding the control strategies used in reviewed literature then we find their gap and the effect of control strategies we used to fill that gap has been studied in detail in order to show its effect. We modify mathematical model and we solve the modified model then we show numerical simulation of the modified model and understand the biological interpretation of the result.

3.2 Source of information

Our study depends on various sources of information, Such as mathematical modeling, differential and numerical reference books, journals and different related studies published/unpublished and downloaded documents from Internet.

3.3 Procedures of the study

To attain the objective of the study, the following procedures are undertaken:

- defining the problem
- modifying the model
- analysis of the model and solving the model using numerical methods
- check the models by comparing the solution with previously developed model simulation result.

Chapter 4

Model formulation

In this thesis we modify a mathematical model introduced in [15] by incorporating education. Where contribution of education is not considered in model of Torres, D.F. et al [15], but education is decisive control strategy for prevention of cholera disease that will shown in next section of our work significantly. By considering the contribution of education in reducing number of infectious individual and bacteria concentration by creating awareness about water sanitation and hygiene, so that we add education in our work as control strategy. Then in our study total human population divided into six compartments depending on the epidemiological status of individuals. These compartments include: susceptible S , educated E , vaccinated V , infected I , treated T and recovered R individuals . The susceptible S are those who are at risk of contracting cholera. At initial all compartments are susceptible.

4.1 Model Assumption

Our model mainly based on the following assumption

- (a) The total human population of community are not constant
- (b) Education and Vaccination is introduced for newly embedded and all susceptible human population in community assumed as epidemic.

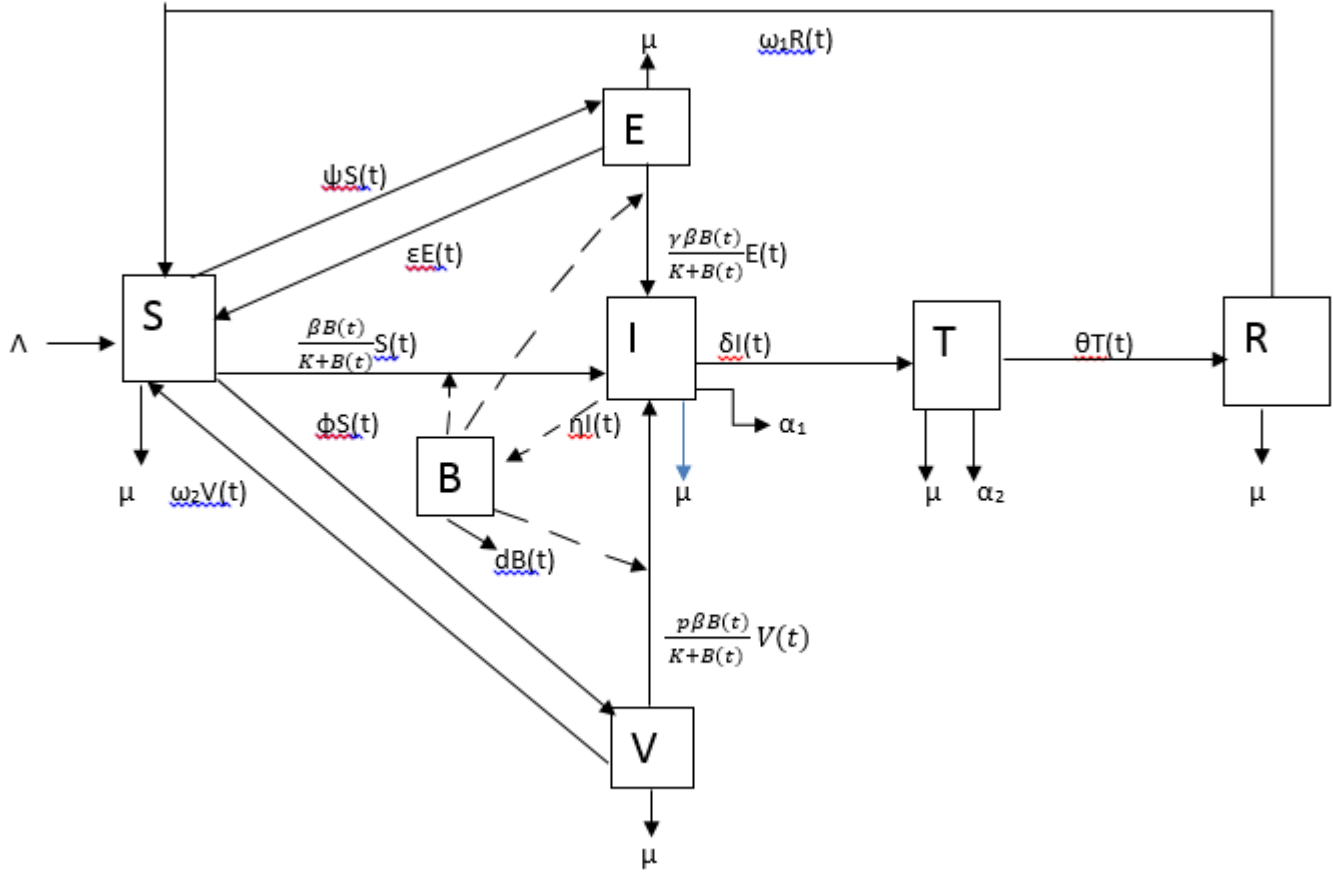


Figure 4.1: Compartmental diagram of cholera's dynamics with Education, Vaccination and Treatment.

- (c) Therapeutic treatment is applied to the infected individuals then come into treated compartment T
- (d) Education is giving awareness about sanitation and hygiene but unsaved individual become infected.
- (e) Water sanitation leads to the death of vibrios
- (f) The time delay between consumption of vibrio infected food or water and the commencement of infectiousness is negligible

The above assumption and disease progression in community leads the compartmental diagram in Figure (4.1).

There are two routes of transmission. By consumption of *Vibrio* infected water from aquatic sources and by consumption of food that may be contaminated with vibrios from fecal matter that referred to as person-to-person transmission. We assume that at any moment in time, there are inflow of immigrants into epidemic community come into susceptible compartment S

Table 4.1: Parameters and their description

Symbol	Description
Λ	inflow of newly embedded including new born into susceptible class
μ	natural Mortality rate of human
ω_2	immunity loss of vaccinated individual
ϕ	vaccinated rate of susceptible
β	contact (ingestion) rate of bacteria
$\frac{\beta B(t)}{K+B(t)}$	probability of susceptible catching cholera at time depend.
ϵ	Precaution of education
ψ	effectively educated rate of susceptible
γ	infected rate of educated individuals
p	inefficacy of the vaccine or vaccine failure
$\frac{\gamma\beta B(t)}{K+B(t)}$	probability of educated individual catching cholera at time depend.
$\frac{p\beta B(t)}{K+B(t)}$	probability of vaccinated individual catching cholera at time depend .
α_1	disease related death rate of infected individual
α_2	disease related death rate of individual in treatment
η	contribution rate of infected individual to bacteria concentration
δ	treatment rate of infected individual
θ	recovery rate of treated individual
ω_1	immunity lose rate of recovered individual

4.2 The Model Equation

The susceptible population increases due to recovered individuals come back to susceptible by losing their immunity at rate of ω_1 and due to the immigrants (renewed) individuals Λ , due to precaution of education ϵ and due to failure of immunity of vaccinated individuals those can be susceptible at rate of ω_2 and decreases due to natural death,

vaccinated, educated and infected which is time dependent of individual at rate of μ, ϕ, ψ and $\frac{\beta B(t)}{K+B(t)}$ respectively. where K is concentration of *Vibrio Cholerae* in food and water that yields 50 percent chance of catching cholera disease. Infected individuals move into compartment I and their numbers increases as vaccinated, educated and susceptible individual become infected at rate of $\frac{p\beta B(t)}{K+B(t)}, \frac{\gamma B(t)}{K+B(t)}$ and $\frac{\beta B(t)}{K+B(t)}$ which is dependent on time respectively. Infected individual become treated at rate of δ . Recovered individuals come from treated at rate of θ and it may come back to susceptible by losing immunity at rate of ω_1 .

There are short period of time between consumption of vibrio infected food or contaminated water and the beginning of infectiousness, so there are no exposed period. From the assumptions, descriptions and the compartmental diagram in Figure (4.1), we formulate the following system of differential equations. The model system of our study with control strategies is as follows

$$\begin{aligned}
S'(t) &= \Lambda - (\mu + \phi + \Psi + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_2 V(t) + \epsilon E(t) + \omega_1 R(t) \\
E'(t) &= \psi S(t) - (\mu + \epsilon + \frac{\gamma \beta B(t)}{K+B(t)})E(t) \\
V'(t) &= \phi S(t) - (\mu + \omega_2 + \frac{p\beta B(t)}{K+B(t)})V(t) \\
I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \frac{p\beta B(t)}{K+B(t)}V(t) + \frac{\gamma \beta B(t)}{K+B(t)}E(t) - (\mu + \alpha_1 + \delta)I(t) \\
T'(t) &= \delta I(t) - (\mu + \alpha_2 + \theta)T(t) \\
R'(t) &= \theta T(t) - (\mu + \omega_1)R(t) \\
B'(t) &= \eta I(t) - dB(t)
\end{aligned} \tag{4.2.1}$$

With initial condition

$$\begin{aligned}
S(0) &= \frac{\Lambda a_1 a_2}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)}, E(0) = \frac{\Lambda \psi a_2}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)}, V(0) = \frac{\Lambda \phi a_1}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)}, I(0) = 0, T(0) = 0, \\
R(0) &= 0, B(0) = 0
\end{aligned} \tag{4.2.2}$$

We obtain this initial condition by making right hand side of model (4.2.1) equal to zero and express E_0 and V_0 in terms of S_0 then substitute E_0 and V_0 in first equation of model (4.2.1) by making right hand side equal to zero and initially no bacteria concentration, infection, treatment and recovered.

Let us assume the following throughout our work.

$$\begin{cases} a_0 = (\mu + \phi + \psi), a_1 = (\mu + \epsilon), a_2 = (\mu + \omega_2), a_3 = (\mu + \alpha_1 + \delta), a_4 = (\mu + \alpha_2 + \theta), \\ a_5 = (\mu + \omega_1) \end{cases} \quad (4.2.3)$$

Then

$$\begin{cases} a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2) = (\mu + \phi + \psi)(\mu + \epsilon)(\mu + \omega_2) - (\omega_2 \phi(\mu + \epsilon) + \epsilon \psi(\mu + \omega_2)) \\ = \mu^3 + \mu^2 \omega_2 + \mu^2 + \mu \epsilon \omega_2 + \phi \mu^2 + \phi \mu \omega_2 + \phi \epsilon \mu + \phi \epsilon \omega_2 + \mu^2 \psi + \psi \mu \omega_2 + \psi \epsilon \mu + \mu \epsilon \omega_2 - \omega_2 \phi \mu \\ - \omega_2 \phi \epsilon - \epsilon \psi \mu - \epsilon \psi \omega_2 \\ = \mu^3 + \mu^2 \omega_2 + \mu^2 \epsilon + \mu \epsilon \omega_2 + \phi \mu^2 + \phi \epsilon \mu + \mu^2 \psi + \psi \mu \omega_2 > 0 \end{cases} \quad (4.2.4)$$

Because of the model system (4.2.1) describes the dynamics of human population and biomass level of *Vibrio cholerae*, so all the model variables and parameters are non-negative.

The first equation of (4.2.1) describes the dynamics of susceptible in the total human population $N = S + E + V + I + T + R$. The death rate of human population is represented by μ in every compartment. Note that $\beta > 0$ is the ingestion rate of the bacterium through contaminated sources. $K > 0$ is the half saturation constant of the bacterial population. All the other parameters used in our model described in table (4.1). Second equation of (4.2.1) describes the dynamics of educated people in the community, their number increases as susceptible become educated and decreases as the educated become susceptible by failure rate of education ϵ and by infected rate of educated individual γ . Third equation of (4.2.1) describe about dynamic of vaccinated individual. Their number decreases at susceptible rate of vaccinated ω_2 and at infected rate of vaccinated individual $\frac{p\beta B(t)}{K+B(t)}$ by losing immunity, their number increases at vaccinated rate of susceptible ϕ . Forth equation of (4.2.1) describes the dynamics of infected people in the community, their number increases as susceptible, educated and vaccinated become infected and decreases as the infected come to treated or with disease related death or by natural death. Fifth equation of (4.2.1) describe the dynamic of treated individuals where increased by treated rate of infected individual δ and decreased by recovered rate of treated individuals θ . The sixth equation of (4.2.1) describe dynamic of recover individual those increased by recovered rate of treated individuals and decreased by immunity lose rate ω_1 of recovered individual and all human population compartment decreases by natural death rate

μ the last equation show the dynamic of pathogen that increased by contribution rate of infected individual to bacteria concentration η and decreased by its death rate d . All of the above concept describe the dynamic of human and pathogen population are given briefly in mathematical model which we modify (4.2.1)

4.3 Basic Property of the Model

4.3.1 Positivity of Solution

Since model (4.2.1) describes the dynamics of human population and biomass level of *V. cholerae* (bacteria population), so throughout this thesis we assume that the initial condition of system (4.2.1) are non-negative.

$$\begin{aligned} S(0) = S_0 > 0, E(0) = E_0 \geq 0, V(0) = V_0 \geq 0, I(0) = I_0 \geq 0, T(0) = T_0 \geq 0, R(0) = R_0 \geq 0, \\ B(0) = B_0 \geq 0 \end{aligned} \quad (4.3.1)$$

Lemma 4.3.1. *The solution $(S(t), E(t), V(t), I(t), T(t), R(t), B(t))$ of system (4.2.1) are non-negative for all $t \geq 0$ with non-negative initial conditions given in equations (4.3.1).*

Proof. Consider the second equation of the system (4.2.1)

$$\begin{aligned} E'(t) &= \psi S(t) - (\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})E(t) \\ E'(t) &\geq -(\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})E(t) \text{ if } S(t) \text{ is positive.} \end{aligned}$$

Now we can solve this by separation of variables method.

$$\frac{dE(t)}{E(t)} \geq -(\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})dt$$

Then integrate both side to obtain

$$\begin{aligned} \ln E(t) &\geq -(\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})t + c \\ \Rightarrow E(t) &\geq e^{-(\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})t + c} = C e^{-(\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})t} \text{ where } C \text{ is any arbitrary constant.} \end{aligned}$$

Using initial condition

$$E(0) = E_0 = C \Rightarrow E(t) = E_0 e^{-(\mu + \epsilon + \frac{\gamma\beta B(t)}{K+B(t)})t} \geq 0$$

By the same procedure we can show that

$$\begin{aligned} V(t) &= V(0)e^{-(\mu + \omega_2 + \frac{p\beta\beta B(t)}{K+B(t)})t} \geq 0, I(t) = I_0 e^{-(\mu + \alpha_1 + \delta)t} \geq 0, \\ T(t) &= T_0 e^{-(\mu + \alpha_2 + \theta)t} \geq 0, R(t) = R_0 e^{-(\mu + \omega_1)t} \geq 0 \text{ and } B(t) = B_0 e^{-dt} \geq 0 \\ S'(t) &= \Lambda - (\mu + \phi + \psi + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_2 V(t) + \epsilon E(t) + \omega_1 R(t) \end{aligned}$$

$$S'(t) \geq -(\mu + \phi + \frac{\beta B(t)}{K+B(t)})S(t)$$

By separation of variable method

$$\frac{dS(t)}{S(t)} \geq -(\mu + \phi + \frac{\beta B(t)}{K+B(t)})dt$$

Then integrate both side and obtain

$$\ln S(t) \geq -(\mu + \phi + \frac{\beta B(t)}{K+B(t)})t + c$$

$$S(t) \geq e^{-(\mu + \phi + \frac{\beta B(t)}{K+B(t)})t + c} = Ce^{-(\mu + \phi + \lambda^*)t}$$

Using initial condition

$$S(0) = S_0 = C \Rightarrow S(t) = S_0 e^{-(\mu + \phi + \frac{\beta B(t)}{K+B(t)})t} > 0$$

Therefore any solution of system (4.2.1) is such that $\{S(t), E(t), V(t), I(t), T(t), R(t), B(t)\} \in (R_0^+)^7$ for all $t \geq 0$ $\square$

The next Lemma (4.3.2) shows that it is sufficient to consider the dynamics of the flow generated by equation (4.2.1) and (4.3.1) in a certain region Ω .

Lemma 4.3.2. *Let*

$$\Omega_H = \left\{ (S, E, V, I, T, R) \in (R_0^+)^6 \mid 0 \leq S(t) + E(t) + V(t) + I(t) + T(t) + R(t) = N(t) \leq \frac{\Lambda}{\mu} \right\} \quad (4.3.2)$$

and

$$\Omega_B = \left\{ B \in R_0^+ \mid 0 \leq B \leq \frac{\Lambda \eta}{\mu d} \right\} \quad (4.3.3)$$

Define

$$\Omega = \Omega_H \times \Omega_B \quad (4.3.4)$$

If $N(0) \leq \frac{\Lambda}{\mu}$ and $B(0) \leq \frac{\Lambda \eta}{\mu d}$, then the region Ω is positively invariant for model (4.2.1) with non-negative initial conditions (4.3.1) in $(R_0^+)^7$

Proof. Let us split system (4.2.1) into two parts: the human population, i.e., $S(t), E(t), V(t), I(t), T(t), R(t)$ and the pathogen population, i.e., $B(t)$. Adding the first six equations of system (4.2.1) gives

$$N'(t) = S'(t) + E'(t) + V'(t) + I'(t) + T'(t) + R'(t) = \Lambda - \mu N(t) - \alpha_1 I(t) - \alpha_2 T(t) \leq \Lambda - \mu N(t)$$

$$\Rightarrow \frac{dN}{dt} \leq \Lambda - \mu N(t)$$

$$\frac{dN}{\Lambda - \mu N} \leq dt, \text{ then integrate both side to obtain}$$

$\frac{-1}{\mu} \ln(\Lambda - \mu N) \leq t + c$ then multiply both side by $-\mu$

$$\ln(\Lambda - \mu N) \geq -\mu(t + c)$$

$$\Lambda - \mu N \geq e^{-\mu(t+c)}$$

$\Lambda - \mu N \geq Ce^{-\mu(t)}$, then by applying initial condition we find C, where C is arbitrary constant.

$$\Lambda - \mu N(0) \geq C$$

$$\Rightarrow \Lambda - \mu N \geq (\Lambda - \mu N_0)e^{-\mu t}, \text{ then multiply both side by } -1$$

$$-\Lambda + \mu N \leq -(\Lambda - \mu N_0)e^{-\mu t}$$

$$\Rightarrow \mu N \leq \Lambda - (\Lambda - \mu N_0)e^{-\mu t}$$

$$N \leq \frac{\Lambda}{\mu} - \frac{(\Lambda - \mu N_0)e^{-\mu t}}{\mu}$$

As $t \rightarrow \infty$ the total population size $N \rightarrow \frac{\Lambda}{\mu}$

$\Rightarrow 0 < N \leq \frac{\Lambda}{\mu}$ then we conclude that $N(t) \leq \frac{\Lambda}{\mu}$ within the given initial value problem, the right hand side is Lipschitz and hence the solution exist and unique. Hence (4.3.2) is mathematically well-posed and biologically (epidemiologically) in the closed set Ω_H for the human population. For the pathogen population we have

$$B'(t) = \eta I(t) - dB(t) \leq \eta \frac{\Lambda}{\mu} - dB(t)$$

$$\Rightarrow \frac{dB}{dt} \leq \frac{\eta \Lambda}{\mu} - dB(t)$$

$$\frac{\frac{\eta \Lambda}{\mu} - dB(t)}{\frac{\eta \Lambda}{\mu} - dB(t)} \leq dt \text{ then integrating both side}$$

$$\Rightarrow \frac{-1}{d} \ln(\frac{\eta \Lambda}{\mu} - dB) \leq t + c \text{ then multiply both side by } -d$$

$$\Rightarrow \ln(\frac{\eta \Lambda}{\mu} - dB) \geq -d(t + c)$$

$$\Rightarrow \frac{\eta \Lambda}{\mu} - dB \geq e^{-d(t+c)} \text{ by multiply both side by } -1$$

$$-\frac{\eta \Lambda}{\mu} + dB \leq -e^{-d(t+c)} \text{ by rearranging}$$

$$dB(t) \leq \frac{\eta \Lambda}{\mu} - e^{-d(t+c)} \text{ divided both side by } d$$

$$B(t) \leq \frac{\eta \Lambda}{\mu d} - e^{-d(t+c)}$$

Then as $t \rightarrow \infty$ $B(t) \rightarrow \frac{\eta \Lambda}{\mu d}$, and $B(t) \leq \frac{\eta \Lambda}{\mu d}$ so that (4.3.3) defines the biologically feasible region for the pathogen population. From (4.3.2) and (4.3.3) we know that $N(t)$ and $B(t)$ are bounded for all $t \geq 0$. Therefore, every solution of system (4.2.1) with initial condition in Ω remains in Ω . In region Ω defined by (4.3.4), our model is epidemiologically and mathematically well posed in Ω for all $t \geq 0$. $\square$

4.4 Model Analysis

The model of system (4.2.1) is analyzed qualitatively to get better understanding of the impact of control strategies on the transmission of vibrio cholera virus.

4.4.1 Disease Free Equilibrium Point(DFE)

The most important equilibrium dynamic of disease is the disease-free equilibrium (DFE) and its linear stability is governed by the basic reproduction number (R_0) [11], which is mathematically defined as the spectral radius (largest eigen value) of the next generation matrix ($F_0V_0^{-1}$).

The disease free equilibrium of model system (4.2.1) is obtained by setting $S'(t) = E'(t) = V'(t) = I'(t) = T'(t) = R'(t) = B'(t) = 0$ and in the absence of disease $I = B = T = R = 0$ so that

$$\begin{aligned} S_0 &= \frac{\Lambda a_1 a_2}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)} \\ E_0 &= \frac{\psi \Lambda a_2}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)} \\ V_0 &= \frac{\phi \Lambda a_1}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)} \end{aligned}$$

Hence DFE is

$$\begin{aligned} \bar{E} = (S_0, E_0, V_0, I_0, T_0, R_0, B_0) &= \left(\frac{\Lambda a_1 a_2}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)}, \frac{\psi \Lambda a_2}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)}, \frac{\phi \Lambda a_1}{a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2)}, \right. \\ &\quad \left. 0, 0, 0, 0 \right) \end{aligned} \tag{4.4.1}$$

Note that $a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2) > 0$ as shown in (4.2.4)

4.4.2 Basic reproduction number, R_0

The basic reproduction number denoted by R_0 is the average number of secondary infections caused by an infectious individual [5]. For model (4.2.1) basic reproduction number with control is:

$$R_0^c = \frac{\beta\eta\Lambda a_1(a_2 + p\phi)}{Kda_3(a_0a_1a_2 - (a_1\omega_2\phi + a_2\psi\epsilon))} \quad (4.4.2)$$

When there is no any control strategy model (4.2.1) reduce to:

$$\begin{aligned} S'(t) &= \Lambda - (\mu + \frac{\beta B(t)}{K+B(t)})S(t) \\ I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) - (\mu + \alpha_1)I(t) \\ B'(t) &= \eta I(t) - dB(t) \end{aligned}$$

Where $\psi = \epsilon = \phi = \omega_1 = \omega_2 = p = \alpha_2 = \gamma = \delta = \theta = 0$ then we obtain the basic reproduction number with out control is:

$$R_0 = \frac{\Lambda\beta\eta}{Kd\mu(\mu + \alpha_1)}$$

To find R_0^c Consider that $F_i(t)$ is the rate of appearance of new infections in the compartment associated with index i , $\nu_i^+(t)$ is the rate of transfer of individuals into the compartment associated with index i and $\nu_i^-(t)$ is the rate of transfer of individuals out of compartment associated with index i . By this manner from the matrices $F(t)$, $\nu^+(t)$ and $\nu^-(t)$ associated with model (4.2.1) are given by

$$F(t) = \begin{bmatrix} 0 \\ 0 \\ 0 \\ \frac{\beta B(t)S(t)}{K+B(t)} + \frac{p\beta B(t)V(t)}{K+B(t)} + \frac{\gamma\beta B(t)}{K+B(t)}E(t) \\ 0 \\ 0 \\ 0 \end{bmatrix}, V^+(t) = \begin{bmatrix} \Lambda + \omega_2 V(t) + \epsilon E(t) + \omega_1 R(t) \\ \psi S(t) \\ \phi S(t) \\ 0 \\ \delta I(t) \\ \theta T(t) \\ \eta I(t) \end{bmatrix}$$

and

$$V^-(t) = \begin{bmatrix} (a_0 + \frac{\beta B(t)}{K+B(t)})S(t) \\ (a_1 + \frac{\gamma\beta B(t)}{K+B(t)})E(t) \\ (a_2 + \frac{p\beta B(t)}{K+B(t)})V(t) \\ a_3 I(t) \\ a_4 T(t) \\ a_5 R(t) \\ dB(t) \end{bmatrix}$$

Therefore by considering that $V(t) = V^-(t) - V^+(t)$, we have that

$$V(t) = \begin{bmatrix} (a_0 + \frac{\beta B(t)}{K+B(t)})S(t) - (\Lambda + \omega_2 V(t) + \epsilon E(t) + \omega_1 R(t)) \\ a_1 E(t) - \psi S(t) \\ (a_2 + \frac{p\beta B(t)}{K+B(t)})V(t) - \phi S(t) \\ a_3 I(t) \\ a_4 T(t) - \delta I(t) \\ a_5 R(t) - \theta T(t) \\ dB(t) - \eta I(t) \end{bmatrix}$$

$$\begin{bmatrix} S'(t) & E'(t) & V'(t) & I'(t) & T'(t) & R'(t) & B'(t) \end{bmatrix}^T = F(t) - V(t)$$

The Jacobian matrices of $F(t)$ and $V(t)$ are respectively given by

$$J(F(t)) = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta B(t)}{K+B(t)} & \frac{\gamma\beta B(t)}{K+B(t)} & \frac{p\beta B(t)}{K+B(t)} & 0 & 0 & 0 & \frac{\beta K S(t) + pK\beta V(t)}{(K+B(t))^2} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$J(V(t)) = \begin{bmatrix} a_0 + \frac{\beta B(t)}{K+B(t)} & -\epsilon & -\omega_2 & 0 & 0 & -\omega_1 & \frac{\beta K}{(K+B(t))^2} \\ -\psi & (a_1 + \frac{\gamma\beta B(t)}{K+B(t)}) & 0 & 0 & 0 & 0 & 0 \\ -\phi & 0 & a_2 + \frac{p\beta B(t)}{K+B(t)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & a_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\delta & a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\theta & a_5 & 0 \\ 0 & 0 & 0 & -\eta & 0 & 0 & d \end{bmatrix}$$

By using disease free equilibrium (DFE) $\bar{E}$ defined by (4.4.2), we obtain the Jacobian matrices of F_0 and V_0 as follows

$$J(F_0) = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta\Lambda a_1(a_2+p\phi)}{K(a_0a_1a_2-(\omega_2\phi a_1+\epsilon\psi a_2))} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \text{ and } J(V_0) = \begin{bmatrix} a_0 & -\epsilon & -\omega_2 & 0 & 0 & -\omega_1 & \frac{\beta}{K} \\ -\psi & a_1 & 0 & 0 & 0 & 0 & 0 \\ -\phi & 0 & a_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & a_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\delta & a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\theta & a_5 & 0 \\ 0 & 0 & 0 & -\eta & 0 & 0 & d \end{bmatrix}$$

The basic reproduction number of model (4.2.1) is then given by $R_0^c = \rho(F_0V_0^{-1})$. The matrix FV^{-1} is known as the next-generation matrix. Inverse of V_0 is:

$$V_0^{-1} = \begin{bmatrix} \frac{a_1a_2}{\chi} & \frac{a_2}{\chi} & \frac{a_1}{\chi} & \frac{-\beta\eta a_1a_2}{Kda_3\chi} & 0 & \frac{\omega_1a_1a_2}{a_5\chi} & \frac{-\beta a_1a_2}{Kd\chi} \\ \frac{a_2\psi}{\chi} & \frac{\psi a_1+\chi}{a_1\chi} & \frac{\psi}{\chi} & \frac{-\beta\eta a_2\psi}{Kda_3\chi} & 0 & \frac{\psi\omega_1a_2}{a_5\chi} & \frac{-\beta a_2}{Kd\chi} \\ \frac{a_1\phi}{\chi} & \frac{\phi}{\chi} & \frac{a_1\phi+\chi}{a_2\chi} & \frac{-\beta\eta a_1\phi}{Kda_3\chi} & 0 & \frac{\omega_1a_1\phi}{a_5\chi} & \frac{-\beta a_1\phi}{Kd\chi} \\ 0 & 0 & 0 & \frac{1}{a_3} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\delta}{a_3a_4} & \frac{1}{a_4} & 0 & 0 \\ 0 & 0 & 0 & \frac{\theta\delta}{a_3a_4a_5} & \frac{\theta}{a_4a_5} & \frac{1}{a_5} & 0 \\ 0 & 0 & 0 & \frac{\eta}{a_3d} & 0 & 0 & \frac{1}{d} \end{bmatrix}$$

assume that $\chi = a_0a_1a_2 - (a_1\omega_2\phi + a_2\psi\epsilon) > 0$, see (4.2.4) then

$$F_0V_0^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\beta\eta\Lambda a_1(a_2+p\phi)}{Kda_3\chi} & 0 & 0 & \frac{\beta\Lambda a_1(a_2+p\phi)}{Kd\chi} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

By calculating eigen-value for matrix $F_0V_0^{-1}$ the maximum eigen value is basic reproduction number of model (4.2.1) given as:

$$R_0^c = \rho(F_0V_0^{-1}) = \frac{\beta\eta\Lambda a_1(a_2+p\phi)}{Kda_3(a_0a_1a_2 - (a_1\omega_2\phi + a_2\psi\epsilon))}$$

The basic reproduction number is non-dimensional quantity. It is important in the study of epidemic disease for evaluation of effective control strategies. We can assure whether a disease become persistent or dies out in a community depends on the value of the reproduction number R_0^c . A large number of R_0^c may indicate the possibility of a major epidemic. Further more stability of DFE point and endemic equilibrium point can be analyzed using R_0^c .

Theorem 4.4.1. (*Stability of the DFE $\bar{E}$*)

The disease-free equilibrium $\bar{E}$ of model (4.2.1) is locally asymptotic stable, if $R_0^c < 1$ and unstable if $R_0^c > 1$

Proof. The Jacobian matrix of model (4.2.1) at DFE ($\bar{E}$) is:

$$\begin{bmatrix} -a_0 & \epsilon & \omega_2 & 0 & 0 & \omega_1 & \frac{\beta a_1 a_2}{K(a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2))} \\ \psi & -a_1 & 0 & 0 & 0 & 0 & \frac{\gamma \beta (\psi \Lambda a_2)}{K(a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2))} \\ \phi & 0 & -a_2 & 0 & 0 & 0 & \frac{p \beta \phi \Lambda a_1}{K(a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2))} \\ 0 & 0 & 0 & -a_3 & 0 & 0 & \frac{\beta a_1 a_2 + \gamma \beta \psi \Lambda a_2 + p \beta \phi \Lambda a_1}{K(a_0 a_1 a_2 - (\omega_2 \phi a_1 + \epsilon \psi a_2))} \\ 0 & 0 & 0 & \delta & -a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & \theta & -a_5 & 0 \\ 0 & 0 & 0 & \eta & 0 & 0 & -d \end{bmatrix}$$

By transferring this matrix to triangular matrix by elementary row and column transformation we obtain

$$\begin{bmatrix} -a_0 & \epsilon & \omega_2 & 0 & 0 & \omega_1 & \frac{\beta a_1 a_2}{K\chi} \\ 0 & -a_1 a_0 & \omega_2 \psi - \epsilon \psi & -\epsilon \psi & -\epsilon \psi & \omega_1 \psi - \epsilon \psi & \frac{\psi \beta a_1 a_2 + \gamma \beta \psi \Lambda a_2 a_0}{K\chi} - \epsilon \psi \\ 0 & 0 & -a_2 & 0 & 0 & 0 & \frac{p \beta \phi \Lambda a_1}{K\chi} \\ 0 & 0 & 0 & -a_3 & 0 & 0 & \frac{\beta \Lambda (a_1 a_2 + \gamma \psi a_2 + p \phi a_1)}{K\chi} \\ 0 & 0 & 0 & 0 & -(a_3 a_4) & 0 & \frac{\delta (\beta a_1 a_2 + \gamma \beta \psi \Lambda a_2 + p \beta \phi \Lambda a_1)}{K\chi} \\ 0 & 0 & 0 & 0 & 0 & -a_5 a_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{\eta \beta \Lambda (a_1 a_2 + \gamma \psi a_2 + p \phi a_1) - d a_3 K \chi}{K\chi} \end{bmatrix}$$

where $\chi = a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon) > 0$,

The characteristic equation of Jacobian matrix of model (4.2.1) at DFE ($\bar{E}$) is given by $P(\lambda) = \det(F_0 - V_0 - \lambda I_7)$. We obtain root of $P(\lambda)$ from diagonal of triangular matrix

of Jacobian of the model (4.2.1), that we have

$$\begin{bmatrix} -a_0 - \lambda & \epsilon & \omega_2 & 0 & 0 & \omega_1 & \frac{\beta a_1 a_2}{K\chi} \\ 0 & -a_1 a_0 - \lambda & \omega_2 \psi - \epsilon \psi & -\epsilon \psi & -\epsilon \psi & \omega_1 \psi - \epsilon \psi & \frac{\psi \beta a_1 a_2 + \gamma \beta \psi \Lambda a_2 a_0}{K\chi} - \epsilon \psi \\ 0 & 0 & -a_2 - \lambda & 0 & 0 & 0 & \frac{p\phi \beta \Lambda a_1}{K\chi} \\ 0 & 0 & 0 & -a_3 - \lambda & 0 & 0 & \frac{\beta a_1 (a_2 + \gamma \beta \psi \Lambda a_2 + p\beta \phi \Lambda a_1)}{K\chi} \\ 0 & 0 & 0 & 0 & -a_3 a_4 - \lambda & 0 & \frac{\delta(\beta a_1 a_2 + \gamma \beta \psi \Lambda a_2 + p\beta \phi \Lambda a_1)}{K\chi} \\ 0 & 0 & 0 & 0 & 0 & -a_5 a_4 - \lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{\eta \beta (\Lambda(a_1 a_2 + \gamma \psi a_2 + p\phi a_1)) - da_3 K\chi}{K\chi} - \lambda \end{bmatrix}$$

roots of $P(\lambda)$ are: $\lambda_1 = -a_0$, $\lambda_2 = -a_1 a_0$, $\lambda_3 = -a_2$, $\lambda_4 = -a_3$, $\lambda_5 = -a_3 a_4$, $\lambda_6 = -a_5 a_4$ and

$$\lambda_7 = \frac{\eta \beta \Lambda a_1 a_2 + \gamma \eta \beta \psi \Lambda a_2 + p \beta \eta \phi \Lambda a_1 - K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))}{K(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))}$$

λ_7 can be express in terms of R_0^c . where

$$R_0^c = \frac{\beta \eta \Lambda a_1 (a_2 + p\phi)}{K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))}$$

$$R_0^c (K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))) = \beta \eta \Lambda a_1 a_2 + \beta \eta \Lambda a_1 p\phi$$

Subtract $K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))$ from both side

$$\Rightarrow (R_0^c - 1) K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)) = \beta \eta \Lambda a_1 a_2 + \beta \eta \Lambda a_1 p\phi - K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))$$

Therefore

$$\lambda_7 = \frac{(R_0^c - 1) K d a_3 (a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)) + \gamma \eta \beta \Lambda a_2}{K(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))}$$

now we can conclude that all roots of the characteristic equation $P(\lambda)$ are negative if and only if $(R_0^c - 1) < 0$

$\Rightarrow R_0^c < 1$ this show that DFE point $(\bar{E})$ of model (4.2.1) is locally asymptotically stable if $R_0^c < 1$, other wise if at list one of the root of $P(\lambda)$ positive or if $R_0^c > 1$ disease free equilibrium $(\bar{E})$ is unstable.

Theorem 4.4.2. (Global stability of disease free equilibrium (DFE) point If $R_0^c < 1$, then the disease free equilibrium $\bar{E}$ of model (4.2.1) is globally asymptotically stable in Ω .

Proof. The variable S does not appear in the first term of susceptible compartment. Dropping this term ([29]) then equation (4.2.1) reduces to

$$\begin{aligned}
S'(t) &= -(\mu + \phi + \Psi + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_2 V(t) + \epsilon E(t) + \omega_1 R(t) \\
E'(t) &= \psi S(t) - (\mu + \gamma + \epsilon)E(t) \\
V'(t) &= \phi S(t) - (\mu + \omega_2 + \frac{p\beta B(t)}{K+B(t)})V(t) \\
I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \frac{p\beta B(t)}{K+B(t)}V(t) + \gamma E(t) - (\mu + \alpha_1 + \delta)I(t) \\
T'(t) &= \delta I(t) - (\mu + \alpha_2 + \theta)T(t) \\
R'(t) &= \theta T(t) - (\mu + \omega_1)R(t) \\
B'(t) &= \eta I(t) - dB(t)
\end{aligned} \tag{4.4.3}$$

At disease free equation (4.4.4) reduced to

$$\begin{aligned}
S'(t) &= -(\mu + \phi + \psi)S + \omega_2 V + \epsilon E \\
E'(t) &= \psi S - (\mu + \epsilon)E \\
V'(t) &= \phi S - (\mu + \omega_2)V
\end{aligned} \tag{4.4.4}$$

Define a Lyapunov function L as

$$L(S, E, V,) = b_1 S + b_2 E + b_3 V \tag{4.4.5}$$

Where $b_1 > 0$, $b_2 > 0$, $b_3 > 0$,

Then the derivative of L in (4.4.6) with respect to t is

$$\frac{dL}{dt} = b_1 S' + b_2 E' + b_3 V' \tag{4.4.6}$$

Have to obtain $\frac{dL}{dt} < 0$ in Ω to establish that $R_0^c < 1$

Substitute equation (4.4.4) into equation (4.4.6) and use (4.2.3) then collecting terms in terms of each variable then.

$$\begin{aligned}
\frac{dL}{dt} &= b_1 S' + b_2 E' + b_3 V' \\
&= b_1(-a_0 S + \omega_2 V + \epsilon E) + b_2(\psi S - (\mu + \epsilon)E) + b_3(\phi S - a_2 V) \\
&= [-b_1 a_0 + b_2 \psi + b_3 \phi]S + [b_1 \epsilon - b_2(\mu + \epsilon)]E + [b_1 \omega_2 - b_3 a_2]V
\end{aligned} \tag{4.4.7}$$

Then express ψ , ϕ , ϵ , ω_2 in terms of R_0^c (4.4.3) and put the result in (4.4.8) then

$$\begin{aligned}
\frac{dL}{dt} &= [-b_1 a_0 + b_2 \psi + b_3 \phi]S + [b_1 \epsilon - b_2(\mu + \epsilon)]E + [b_1 \omega_2 - b_3 a_2]V \\
&= [-b_1 a_0 + b_2(\frac{kda_3(R_0^c(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)) + \beta \eta(\Lambda a_1(a_2 + p\phi)))}{kda_3 a_2 \epsilon(R_0^c - 1)}) \\
&\quad + b_3(\frac{kda_3(R_0^c(a_0 a_1 a_2 - a_2 \psi \epsilon) - a_1 \omega_2 \phi) + \beta \eta(\Lambda a_1(a_2 + p\phi))}{kda_3 a_1 \omega_2(R_0^c - 1)})]S \\
&\quad + [b_1(\frac{kda_3(R_0^c(a_0 a_1 a_2 - a_1 \omega_2 \phi) - a_2 \psi \epsilon) + \beta \eta \Lambda a_1(a_2 + p\phi))}{kda_3 a_2 \psi(R_0^c - 1)}) - b_2(\mu + \epsilon)]E \\
&\quad + [b_1(\frac{kda_3(R_0^c(a_0 a_1 a_2 - a_2 \psi \epsilon) - a_1 \omega_2 \phi) + \beta \eta \Lambda a_1(a_2 + p\phi))}{kda_3 a_1 \phi(R_0^c - 1)}) - b_3 a_2]V
\end{aligned} \tag{4.4.8}$$

Since model (4.2.1) monitors human and bacteria population then all the parameters as well as variables are non- negative and the coefficient of each state variable in (4.4.8) is negative that is

$$\begin{aligned} & [-b_1 a_0 + b_2 \left(\frac{kda_3(R_0^c(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)) + \beta \eta (\Lambda a_1 (a_2 + p \phi)))}{kda_3 a_2 \epsilon (R_0^c - 1)} \right) \\ & + b_3 \left(\frac{kda_3(R_0^c(a_0 a_1 a_2 - a_2 \psi \epsilon) - a_1 \omega_2 \phi) + \beta \eta (\Lambda a_1 (a_2 + p \phi))}{kda_3 a_1 \omega_2 (R_0^c - 1)} \right)] < 0 \end{aligned} \quad (4.4.9)$$

$$[b_1 \left(\frac{kda_3(R_0^c(a_0 a_1 a_2 - a_1 \omega_2 \phi) - a_2 \psi \epsilon) + \beta \eta \Lambda a_1 (a_2 + p \phi)}{kda_3 a_2 \psi (R_0^c - 1)} \right) - b_2 (\mu + \epsilon)] < 0 \quad (4.4.10)$$

$$[b_1 \left(\frac{kda_3(R_0^c(a_0 a_1 a_2 - a_2 \psi \epsilon) - a_1 \omega_2 \phi) + \beta \eta \Lambda a_1 (a_2 + p \phi)}{kda_3 a_1 \phi (R_0^c - 1)} \right) - b_3 a_2] < 0 \quad (4.4.11)$$

Equation (4.4.9 - 4.4.11) establish $\frac{dL}{dt} < 0$ in Ω if $R_0^c < 1$. This show that $\bar{E}$ is globally asymptotically stable in invariant region Ω if $R_0^c < 1$ where $\bar{E}$ is disease free equilibrium of the model (4.2.1) $\square$

Proposition 4.4.3. (*Endemic equilibrium*). *If the basic reproduction number $R_0^c > 1$ (4.4.3) then the model (4.2.1) has an endemic equilibrium given by*

$$\varepsilon^* = (S^*, E^*, V^*, I^*, T^*, R^*, B^*) \quad (4.4.12)$$

Where

$$\left\{ \begin{array}{l} S^* = \frac{\Lambda a_5 a_4 a_3 a_1 (a_2 + p \lambda^*)}{M} \\ E^* = \frac{\Lambda a_5 a_4 a_3 \psi (a_2 + p \lambda^*)}{M} \\ V^* = \frac{\Lambda a_5 a_4 a_3 a_1 \phi}{M} \\ I^* = \frac{\Lambda a_5 a_4 [(a_1 \lambda^* + \gamma \psi)(a_2 + p \lambda^*) + a_1 p \lambda^* \phi]}{M} \\ T^* = \frac{\Lambda a_5 \delta [(a_1 \lambda^* + \gamma \psi)(a_2 + p \lambda^*) + a_1 p \lambda^* \phi]}{M} \\ R^* = \frac{\Lambda \delta \theta [(a_1 \lambda^* + \gamma \psi)(a_2 + p \lambda^*) + a_1 p \lambda^* \phi]}{M} \\ B^* = \frac{\Lambda a_5 a_4 \eta [(a_1 \lambda^* + \gamma \psi)(a_2 + p \lambda^*) + a_1 p \lambda^* \phi]}{dM} \end{array} \right.$$

by using assumption in (4.2.3), Let $M = (a_2 + p \lambda^*)[a_5 a_4 a_3 a_1 (a_0 + \lambda^*) - a_5 a_4 a_3 \epsilon \psi - \omega_2 \theta \delta a_1 \lambda^* - \omega_2 \theta \delta \gamma \psi] - \phi \omega_2 a_1 (\theta \delta p \lambda^* + a_5 a_4 a_3)$ and $\lambda^* = \frac{\beta B^*}{K + B^*} = \frac{\beta \Lambda a_5 a_4 \eta [(a_1 \lambda^* + \gamma \psi)(a_2 + p \lambda^*) + a_1 p \lambda^* \phi]}{K + \beta \Lambda a_5 a_4 \eta [(a_1 \lambda^* + \gamma \psi)(a_2 + p \lambda^*) + a_1 p \lambda^* \phi]}$

Proof. In existence of disease, infection rate $\lambda^* = \frac{\beta B^*}{K + B^*} > 0$, by making the left hand side of 4.2.1 equal to zero we get the endemic equilibrium point 4.4.12 then we can note that by using 4.2.3 and 4.4.12

$$1 . a_0 = \mu + \phi + \psi > 0$$

$$2 . a_1 = \mu + \epsilon > 0$$

$$3 . a_2 = \mu + \omega_2 > 0$$

$$4 . a_3 = \mu + \alpha_1 + \delta > 0$$

$$5 . a_4 = \mu + \alpha_2 + \theta > 0$$

$$6 . a_5 = \mu + \omega_1 > 0$$

$$7 . \beta, K, d, p, \eta > 0$$

$$8 . a_2 + p\lambda^* > 0$$

$$9 . a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon) > 0 , \text{as shown in (4.2.4)}$$

$$10 . \Lambda a_5 a_4 \eta > 0, \text{ because } \Lambda, a_5, a_4, \eta > 0$$

with the above inequalities we can conclude that $M > 0$ and consequently $S^* > 0, E^* \geq 0, V^* \geq 0$. The basic reproduction number given by $R_0^c = \frac{\beta\eta(\Lambda a_1(a_2+p\phi))}{Kda_3(a_0a_1a_2-(a_1\omega_2\phi+a_2\psi\epsilon))}$. Thus it follows that

$$\beta\eta(\Lambda a_1(a_2+p\phi)) = R_0^c Kda_3(a_0a_1a_2 - (a_1\omega_2\phi + a_2\psi\epsilon))$$

$$\beta\eta(\Lambda a_1(a_2+p\phi)) - Kda_3(a_0a_1a_2 - (a_1\omega_2\phi + a_2\psi\epsilon)) = (R_0^c - 1)Kda_3(a_0a_1a_2 - (a_1\omega_2\phi + a_2\psi\epsilon))$$

Therefore we have that

$$\begin{aligned} I^* &= \frac{\Lambda a_5 a_4 [(a_1 \lambda^* + \gamma \psi)(a_2 + p\lambda^*) + a_1 p \lambda^* \phi] Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))(R_0^c - 1)}{M(\beta\eta(\Lambda a_1(a_2 + p\phi)) - Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)))} \\ T^* &= \frac{\Lambda a_5 \delta [(a_1 \lambda^* + \gamma \psi)(a_2 + p\lambda^*) + a_1 p \lambda^* \phi] Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))(R_0^c - 1)}{M(\beta\eta(\Lambda a_1(a_2 + p\phi)) - Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)))} \\ R^* &= \frac{\Lambda \delta \theta [(a_1 \lambda^* + \gamma \psi)(a_2 + p\lambda^*) + a_1 p \lambda^* \phi] Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))(R_0^c - 1)}{M(\beta\eta(\Lambda a_1(a_2 + p\phi)) - Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)))} \\ B^* &= \frac{\Lambda a_5 a_4 \eta [(a_1 \lambda^* + \gamma \psi)(a_2 + p\lambda^*) + a_1 p \lambda^* \phi] Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))(R_0^c - 1)}{dM(\beta\eta(\Lambda a_1(a_2 + p\phi)) - Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon)))} \end{aligned}$$

We obtain an endemic equilibrium $I^*, B^* > 0$ if $R_c - 1 > 0$ then $R_c > 1$ this show that $\beta\eta(\Lambda a_1(a_2 + p\phi)) > Kda_3(a_0 a_1 a_2 - (a_1 \omega_2 \phi + a_2 \psi \epsilon))$ $\square$

Theorem 4.4.4. (Local asymptotic stability of endemic equilibrium (4.4.12)). The endemic equilibrium ε^* of our model (4.2.1) is locally asymptotically stable.

Proof. by using $\lambda^* = \frac{\beta B}{K+B}$ and (??)

let

$$L_1 = \frac{-\beta SK}{(K+B)^2}, L_2 = \frac{-p\beta VK}{(K+B)^2} \text{ and } L_3 = \frac{-(\beta SK + p\beta VK)}{(K+B)^2} \quad (4.4.13)$$

The Jacobian of the system (4.2.1) evaluated at $\varepsilon^*(S^*, E^*, V^*, I^*, T^*, R^*, B^*)$ is

$$J(\varepsilon^*) = \begin{bmatrix} -(a_0 + \lambda^*) & \varepsilon & \omega_2 & 0 & 0 & \omega_1 & -L_1 \\ \psi & -a_1 & 0 & 0 & 0 & 0 & 0 \\ \phi & 0 & -(a_2 + p\lambda^*) & 0 & 0 & 0 & -L_2 \\ \lambda^* & \gamma & p\lambda^* & -a_3 & 0 & 0 & -L_3 \\ 0 & 0 & 0 & \delta & -a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & \theta & -a_5 & 0 \\ 0 & 0 & 0 & \eta & 0 & 0 & -d \end{bmatrix}$$

By using matlab characteristic equation of the matrix $J(\varepsilon^*)$ is given by

$\det(\lambda I_7 - J(\varepsilon^*)) = P(\lambda) = c_6\lambda^6 + c_5\lambda^5 + c_4\lambda^4 + c_3\lambda^3 + c_2\lambda^2 + c_1\lambda + c_0$ where $c_6 > 0$, $c_5 > 0$, $c_4 > 0$, $c_3 > 0$, $c_2 > 0$, $c_1 > 0$, $c_0 > 0$, $c_5c_4 - c_6c_3 > 0$, $(c_3c_5c_4 - c_6c_3^2) - (c_5^2c_2 - c_1c_5c_6) > 0$, $c_5c_2 - c_6c_1 > 0$ and using tabular routh's criterion.

By Routh's stability criterion [23, 44] If the degree of the resulting polynomial is at list two and all coefficient of the polynomial $p(\lambda)$ have the same sign then all roots of $p(\lambda)$ have negative real part then the endemic equilibrium (EE) ε^* is locally asymptotically stable. But if a coefficient is negative or zero and the other coefficients is positive, then a root exists which is in the right half-plane or imaginary then the system is known as unstable. so according to Routh's criterion characteristic equation of $P(\lambda)$ show that EE (ε^*) is locally asymptotically stable. $\square$

4.4.3 Sensitivity Analysis

Sensitivity analysis is used to determine which parameters have a high impact on R_c . If the calculation of a parameter result is negative, then the relationship between that parameters and R_c is inversely proportional. If the result of sensitivity of a parameter is positive, the relation between that parameter and disease spread is directly proportional. The expression of R_c that is given in (4.4.3) depend on fourteen parameters. To carry out sensitivity analysis, we followed the technique outlined in [2]. We derive an analytical

expression for its sensitivity to each parameters as follows

$$\Upsilon_p^{R_c} = \left(\frac{\partial R_c}{\partial p}\right)\left(\frac{p}{R_c}\right)$$

for p substituted by each basic parameters in expression of R_c . From an explicit formula for equation (4.4.3), we derive an analytical expression for the sensitivity of parameters involved in R_c . For example, the sensitivity index of R_c with respect to Λ , β , k is

$$\Upsilon_{\Lambda}^{R_c} = \frac{\partial R_c}{\partial \Lambda} * \frac{\Lambda}{R_c} = +1.0002$$

$$\Upsilon_{\psi}^{R_c} = \frac{\partial R_c}{\partial \beta} * \frac{\beta}{R_c} = +1$$

$$\Upsilon_k^{R_c} = \frac{\partial R_c}{\partial k} * \frac{k}{R_c} = -1$$

respectively. And remaining parameters, are obtained and evaluated with respect to $\eta = 10$, $\mu = 0.000016$, $\phi = 0.005$, $\psi = 0.008$, $\epsilon = 0.003$, $\gamma = 0.005$, $p = 0.15$, $d = 0.33$, $\omega_2 = 0.00068$, $\alpha_1 = 0.000006$, $\alpha_2 = 0.000003$. Their sensitivity indices were written in table in the following.

Table 4.2: Sensitivity indices table

Symbol of parameters	sensitivity indices
η	+ve
μ	-ve
ϕ	+ve
ψ	-ve
ϵ	-ve
γ	+ve
p	+ve
d	-ve
ω_2	-ve
α_1	-ve

Interpretation of sensitivity analysis

The sensitivity indices of the basic reproductive number with respect to main parameters are given in table (4.2). Those parameters that have positive indices show that they have great impact on expanding the disease in the community if their values are increasing.

Due to the reason that the basic reproduction number increases as their values increase, it means that the average number of secondary cases of infection increases in the community. And also those parameters in which their sensitivity indices are negative have an influence of minimizing the burden of the disease in the community as their values increase while the others are left constant. And also as their values increase, the basic reproduction number decreases, which leads to minimizing the endemicity of the disease in the community.

4.5 Numerical Simulation

In this section, we present the numerical simulation of our models. In model (4.2.1) we used $S(0) = 28249670$, $E(0) = 0$, $V(0) = 0$, $I(0) = 750$, $T(0) = 0$, $R(0) = 0$, $B(0) = 275000$, as initial values and parameter values in Table (4.3) [15]

Note that the numerical simulation for the models that focus on recruitment rate of human Λ and contact rate β for model (4.2.1). Because those parameters have great impact on the basic reproduction number as their values increases the endemicity of the disease also increases. Numerical simulations were conducted using Matlab.

Analysis of R_0^c with single control strategy

In this subsection we analyze reproduction number of each control strategies.

If education is the only control strategy, $\psi \neq 0$, $\epsilon \neq 0$, $\gamma \neq 0$, $\alpha_1 \neq 0$, $\phi = \omega_1 = \omega_2 = p = \alpha_2 = \theta = 0$ then our model (4.2.1) reduced to

$$\begin{aligned} S'(t) &= \Lambda - (\mu + \Psi + \frac{\beta B(t)}{K+B(t)})S(t) + \epsilon E(t) \\ E'(t) &= \psi S(t) - (\mu + \gamma + \epsilon)E(t) \\ I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \gamma E(t) - (\mu + \alpha_1)I(t) \\ B'(t) &= \eta I(t) - dB(t) \end{aligned} \tag{4.5.1}$$

then from this reduced model we obtain the basic reproduction number with education only denoted by (R_E) which is given by:

$$R_E = \frac{\beta \eta [\Lambda(\mu + \epsilon)\mu]}{kd(\mu + \alpha_1)[(\mu + \psi)(\mu + \epsilon)\mu - \mu\psi\epsilon]}$$

Table 4.3: Sensitivity indices table

Symbol of parameters	description indices	Value	Source
k	Half saturation constant	10^7	Assumed
Λ	Recruitment rate	$28.4N(0)/365000$ (day1)	[15]
ϕ	Vaccination rate	$5/1\ 000$ (day1)	Assumed
η	Shedding rate (infected)	10 (cell/ml day1 person1)	[15]
ω_2	Efficacy vaccination waning rate	$1/1\ 460$ (day1)	[15]
θ	Recovery rate	0.2 (day1)	[15]
δ	Treatment rate	1.15 (day1)	Assumed
α_1	Death rate (infected)	6106 (day1)	[15]
μ	Natural death rate	1.6105 (day1)	[15]
ω_1	Immunity waning rate	$0.4/365$ (day1)	[15]
α_2	Death rate (in treatment)	3106 (day1)	Assumed
β	Contact (ingestion) rate of vibrio	$0.2143/\text{day}$	[9]
p	Inefficacy of the vaccine or vaccine failure	$0.2143/\text{day}$	[18]
γ	Infected rate of educated	$0.005/\text{day}$	Assumed
ψ	Educated rate of susceptible	$0.008/\text{day}$	[18]
ϵ	Inefficacy of the education	$0.003/\text{day}$	Assumed
$S(0)$	Susceptible individual at $t = 0$	28249670 (Person)	[15]
$E(0)$	Educated individual at $t = 0$	0 (Person)	[15]
$V(0)$	Vaccinated individual at $t = 0$	0 (Person)	[15]
$I(0)$	Infected individual at $t = 0$	750 (Person)	[15]
$T(0)$	Treated individual at $t = 0$	0 (Person)	[15]
$R(0)$	Recovered individual at $t = 0$	0 (Person)	[15]

The numerical result for only education is introduced as control strategy shown in Figure (4.2)(a)

If vaccination is the only control strategy $\phi \neq 0$, $\omega_2 \neq 0$, $p \neq 0$, $\alpha_1 \neq 0$, $\psi = \epsilon = \psi = \epsilon = \omega_1 = \alpha_2 = \gamma = \delta = \theta = 0$ then model (4.2.1) reduced to

$$\begin{aligned}
S'(t) &= \Lambda - (\mu + \phi + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_2 V(t) \\
V'(t) &= \phi S(t) - (\mu + \omega_2 + \frac{p\beta B(t)}{K+B(t)})V(t) \\
I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \frac{p\beta B(t)}{K+B(t)}V(t) - (\mu + \alpha_1)I(t) \\
B'(t) &= \eta I(t) - dB(t)
\end{aligned}$$

then from reduced model we obtain basic reproduction number with vaccination only denoted by (R_V) is given by

$$R_V = \frac{\beta\eta\Lambda\mu(\mu + \omega_2 + p\phi)}{kd(\mu + \alpha_1)[\mu(\mu + \phi)(\mu + \omega_2) - \mu\omega_2\phi]}$$

The numerical result for only vaccination is introduced as control strategy shown in Figure (4.2)(b)

Our result show that when we introducing both education and vaccination control strategy separately we obtain almost similar result but, if we use only treatment as control strategy of cholera disease the numerical result shown in figure (4.3) and we have $\delta \neq 0$, $\alpha_2 \neq 0$, $\alpha_1 \neq 0$, $\theta \neq 0$, $\omega_1 \neq 0$, $\psi = \epsilon = \phi = \omega_2 = p = \gamma = 0$ then the model (4.2.1) reduced to

$$\begin{aligned} S'(t) &= \Lambda - (\mu + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_1 R(t) \\ I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) - (\mu + \alpha_1 + \delta)I(t) \\ T'(t) &= \delta I(t) - (\mu + \alpha_2 + \theta)T(t) \\ R'(t) &= \theta T(t) - (\mu + \omega_1)R(t) \\ B'(t) &= \eta I(t) - dB(t) \end{aligned}$$

from reduced model when treatment is introduced as control strategy we obtain basic reproduction number with only treatment that denoted by (R_T) is given by:

$$R_T = \frac{\beta\eta\Lambda}{kd\mu(\mu + \alpha_1 + \delta)}$$

The numerical result for single control strategy show that treatment is effective than education and vaccination when introduced separately. See figure (4.2-4.3) when only treatment is introduced bacteria concentration and infected individuals are reduced and number of recovered population are increased.

Analysis of R_0^c with combination of two control strategies

In this subsection, we analyze further the effective control strategy in combination by computing reproduction numbers for the combination of two control strategies. If the combination of education and vaccination campaign is the only intervention we have that $\psi \neq 0$, $\epsilon \neq 0$, $\gamma \neq 0$, $\phi \neq 0$, $\omega_2 \neq 0$, $p \neq 0$, $\alpha_1 \neq 0$, $\omega_1 = \alpha_2 = \delta = \theta = 0$ then model

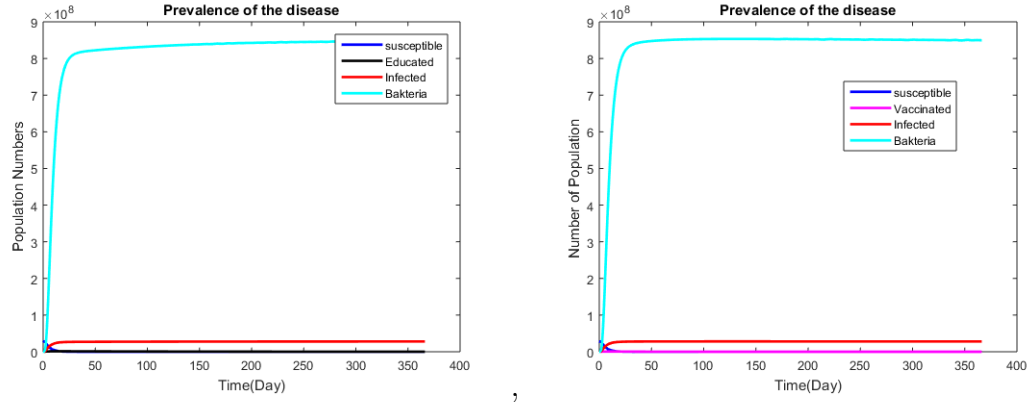


Figure 4.2: Numerical solution of model (4.2.1) when only education and vaccination introduced as control strategy separately

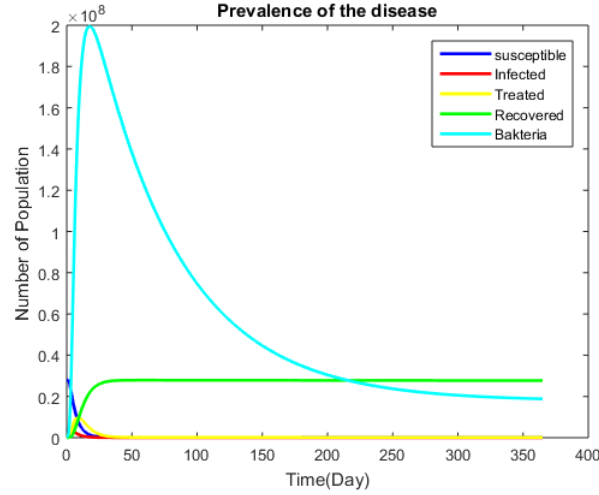


Figure 4.3: Numerical solution of model (4.2.1) when only treatment introduced as control strategy

(4.2.1) reduced to

$$\begin{aligned}
 S'(t) &= \Lambda - (\mu + \phi + \Psi + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_2 V(t) + \epsilon E(t) \\
 E'(t) &= \psi S(t) - (\mu + \gamma + \epsilon)E(t) \\
 V'(t) &= \phi S(t) - (\mu + \omega_2 + \frac{p\beta B(t)}{K+B(t)})V(t) \\
 I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \frac{p\beta B(t)}{K+B(t)}V(t) + \gamma E(t) - (\mu + \alpha_1 + \delta)I(t) \\
 B'(t) &= \eta I(t) - dB(t)
 \end{aligned}$$

their numerical solution is given in Figure (4.4) (a) and basic reproduction number in combination of education and vaccination are introduced as control strategies denoted by

R_{EV} is given by:

$$R_{EV} = \frac{\beta\eta\Lambda(\mu + \epsilon)(\mu + \omega_2 + p\phi)}{kd(\mu + \alpha_1)[(\mu + \phi + \psi)(\mu + \epsilon)(\mu + \omega_2) - ((\mu + \epsilon)\omega_2\phi + (\mu + \omega_2)\psi\epsilon)]}$$

As shown in (4.2.4) $kd(\mu + \alpha_1)[(\mu + \phi + \psi)(\mu + \gamma + \epsilon)(\mu + \omega_2) - ((\mu + \gamma + \epsilon)\omega_2\phi + (\mu + \omega_2)\psi\epsilon)] > 0$.

If the combination of treatment and education campaign are introduced as control strategy we have: $\psi \neq 0$, $\epsilon \neq 0$, $\gamma \neq 0$, $\delta \neq 0$, $\theta \neq 0$, $\omega_1 \neq 0$, $\alpha_1 \neq 0$, $\alpha_2 \neq 0$, $\phi = \omega_2 = p = 0$ then the model (4.2.1) reduced to

$$\begin{aligned} S'(t) &= \Lambda - (\mu + \Psi + \frac{\beta B(t)}{K+B(t)})S(t) + \epsilon E(t) + \omega_1 R(t) \\ E'(t) &= \psi S(t) - (\mu + \gamma + \epsilon)E(t) \\ I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \gamma E(t) - (\mu + \alpha_1 + \delta)I(t) \\ T'(t) &= \delta I(t) - (\mu + \alpha_2 + \theta)T(t) \\ R'(t) &= \theta T(t) - (\mu + \omega_1)R(t) \\ B'(t) &= \eta I(t) - dB(t) \end{aligned}$$

Their numerical solution is given in Figure (4.4)(b) and basic reproduction number in combination of education and treatment are introduced as control strategies is denoted by R_{ET} computed as follows

$$R_{ET} = \frac{\beta\eta\Lambda(\mu + \epsilon)\mu}{kd(\mu + \alpha_1 + \delta)[(\mu + \psi)(\mu + \epsilon)\mu - \mu\psi\epsilon]}$$

If the combination of vaccination and treatment taken as control strategy $\omega_2 \neq 0$, $\phi \neq 0$, $p \neq 0$, $\alpha_1 \neq 0$, $\delta \neq 0$, $\theta \neq 0$, $\omega_1 \neq 0$, $\psi = \epsilon = \gamma = 0$ then model (4.2.1) reduced to

$$\begin{aligned} S'(t) &= \Lambda - (\mu + \phi + \frac{\beta B(t)}{K+B(t)})S(t) + \omega_2 V(t) + \omega_1 R(t) \\ V'(t) &= \phi S(t) - (\mu + \omega_2 + \frac{p\beta B(t)}{K+B(t)})V(t) \\ I'(t) &= \frac{\beta B(t)}{K+B(t)}S(t) + \frac{p\beta B(t)}{K+B(t)}V(t) - (\mu + \alpha_1 + \delta)I(t) \\ T'(t) &= \delta I(t) - (\mu + \alpha_2 + \theta)T(t) \\ R'(t) &= \theta T(t) - (\mu + \omega_1)R(t) \\ B'(t) &= \eta I(t) - dB(t) \end{aligned}$$

Their numerical solution is given in Figure (4.5) and basic reproduction number in combination of vaccination and treatment are introduced as control strategies denoted by R_{VT}

is computed as follows:

$$R_{VT} = \frac{\beta\eta\Lambda\mu(\mu + \omega_2 + p\phi)}{kd(\mu + \alpha_1 + \delta)[(\mu + \phi)\mu(\mu + \omega_2) - \mu\omega_2\phi]}$$

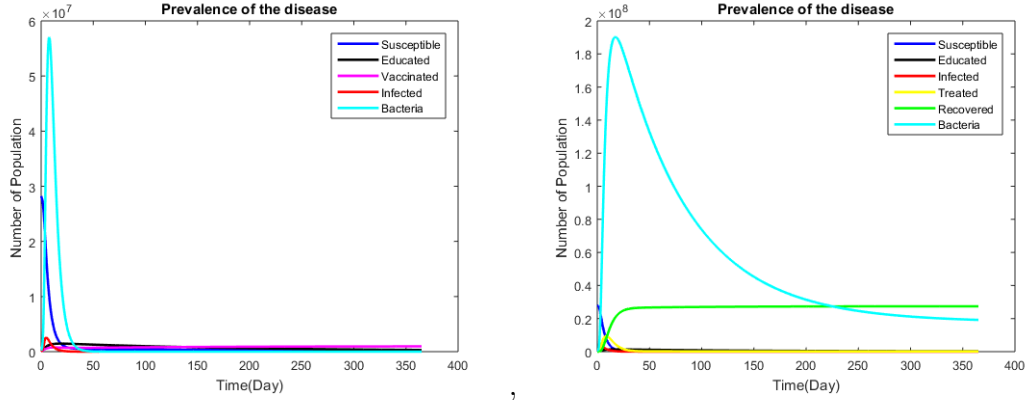


Figure 4.4: Numerical result of model (4.2.1) when only education and vaccination introduced in combination as control strategy in figure (a) and for combination of education with treatment in (b)

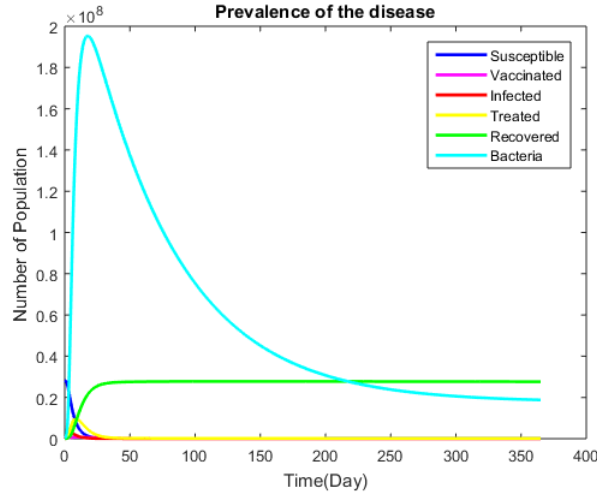


Figure 4.5: Numerical result of model (4.2.1) when only vaccination with treatment introduced in combination as control strategy

Generally we conclude that $R_0^c < R_{ET} < R_{VT} < R_{EV} < R_T < R_V < R_E$ When we apply all our control strategies (education, vaccination and treatment) all parameters are different from zero then we obtain reproductive number with all control strategies R_0^c that is in (4.4.3) and the numerical solution is shown in figure(4.7)

When we compare numerical result of model (2.0.1) with modified model (4.2.1) show that bacteria concentration within model (4.2.1) reduced in short period of time or day and accelerate number of recovered individuals more than within model (2.0.1) as shown by numerical result in figure (4.6 and 4.7).

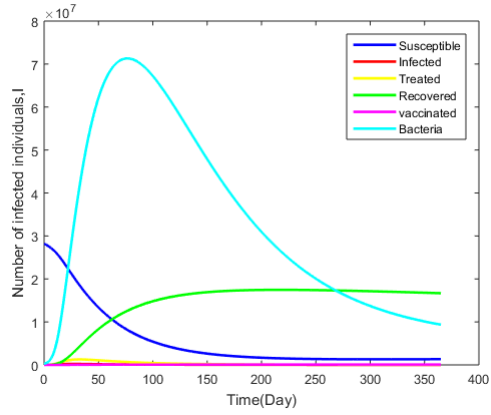


Figure 4.6: Numerical solution of model (2.0.1) when vaccination and treatment introduced in combination

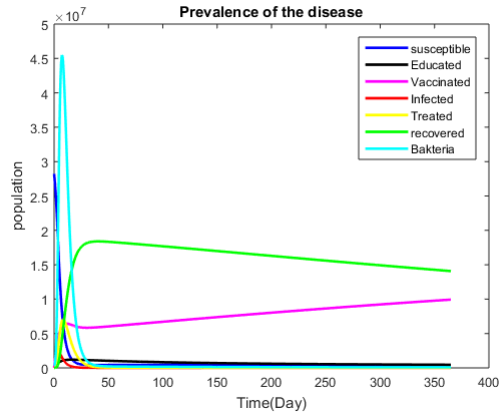


Figure 4.7: Numerical solution of model (4.2.1) when education, vaccination and treatment introduced in combination with parameter values given in Table 4.3

Chapter 5

Conclusion

In this thesis we modify and analyzed the cholera model introduced in [15] with control strategies and evaluate the impact of education, vaccination and treatment to control the spread of cholera in short period of time. We derived the basic reproduction number with control strategies. The existence of disease free equilibrium (DFE) point and stability of (DFE) and endemic equilibrium (EE) point of the modified model (4.2.1) presented in section (4.4). We proved the locally asymptotically stability of disease free equilibrium point depend on root of characteristic equation of Jacobian matrix of modified model and by showing that all eigenvalue of the Jacobian matrix of model (4.2.1) are negative.

For endemic equilibrium point, we proved the locally asymptotically stability by using Routhz criteria and global stability of disease free equilibrium point is shown by using Lyapunov function. Accordingly if $R_0 < 1$, the disease free equilibrium point (DFE) is globally asymptotically stable and unstable when $R_0 > 1$.

Our sensitivity analysis confirmed that the most effective parameters in this study are contact rate, recruitment rate as well as shedding rate (infected rate). The numerical simulation of modified model shows the possible communities benefits when education, vaccination and treatments are used in combination as control strategies to restrict the epidemic spread of cholera disease.

Comparing the control strategies we observed that treatment is the best in single case while education and vaccination is take rank in respective order. This is depend on

their reproduction number that already shown $R_T < R_E < R_V$,but it is dependent of parameters it can be changed based on the variation of parameter values. As our numerical result shows that effective control of the cholera epidemic can easily be achieved when education,vaccination and treatment are implemented together.

5.1 Recommendation

Therefore the researcher recommended to all stack holder to use education,vaccination and treatment in combination to control the cholera transmission.

Appendices

Appendix 1

Matlab code for simulation of ODE system.

1). For simulation result of model (2.0.1)

```
function dydt = tores(t,y) dydt = zeros(6,1); global beta k p Lambda phi eta gamma
alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon l beta =0.01694; k=10000000;
p = 0.15; Lambda = 0.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006;
alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.015; delta =1.15; omega2
= 0.00068; omega1 = 0.00111; epsilon=0.2; l=0.5;
dydt(1) = Lambda -(beta*y(6))/(k+y(6))*y(1) + omega1*y(4)+omega2*y(5)-(phi+mu)*y(1);
dydt(2) = (beta*y(6))/(k+y(6))*y(1)-(delta+alpha1+mu)*y(2); dydt(3) = delta*y(2)-
(epsilon+alpha2+mu)*y(3); dydt(4) = epsilon*y(3)-(omega1+mu)*y(4); dydt(5)= phi*y(2)-
(omega2+mu)*y(5); dydt(6) = eta*y(2)-d*y(6);
clear all close all clc tspan = [0 365]; y0 = [28249670 750 0 0 0 275000]; [t,y] = ode45('tores',tspan,y0);
plot(t,y(:,1),'b',t, y(:,2),'r',t, y(:,3),'y',t,y(:,4),'g',t,y(:,5),'m',t,y(:,6),'c','Linewidth',2) xla-
bel('Time(Day)') ylabel('Number of infected individuals,I') legend('Susceptible','Infected','Treated','Re
```

2) Simulation result of Modified model (4.2.1)

```
function dydt = abu1(t,y) dydt = zeros(7,1); global beta k p Lambda phi eta gamma
alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon beta =10.2143; k=10000000;
p = 0.15; Lambda = 28.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006;
alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.33; delta =1.15; omega2
= 0.00068; omega1 = 0.00111; epsilon=0.003;
```

```

dydt(1) = Lambda -(mu+phi+psi+(beta*y(7))/(k+y(7)))*y(1) + omega2*y(3)+ epsilon*y(2)+omega1*y(6); dydt(2) = psi*y(1)-(mu+gamma+epsilon)*y(2); dydt(3) = phi*y(1)-(mu+omega2+(p*beta*y(7))/(k+y(7)))*y(3); dydt(4) = ((beta*y(7))/(k+y(7)))*y(1)+(p*beta*y(7))/(mu+alpha1+delta)*y(4); dydt(5) = delta*y(4)-(mu+alpha2+theta)*y(5); dydt(6) = theta*y(5)-(mu+omega1)*y(6); dydt(7) = eta*y(4)-d*y(7);

```

```

clear all close all clc tspan = [0 365]; y0 = [28249670 0 0 750 0 0 275000]; [t,y] = ode45('abu1',tspan,y0); plot(t,y(:,1),'b',t,y(:,2),'black',t,y(:,3),'m',t,y(:,4),'r',t,y(:,5),'y',t,y(:,6),'g',t,y(:,7),'c'); xlabel('Time(Day)') ylabel('population') title('Prevalence of the disease') legend('susceptible','Educated','Infected','Recovered')

```

3) For Education only function dydt = abue1(t,y) dydt = zeros(4,1); global beta k p Lambda phi eta gamma alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon beta =0.2143; k=10000000; p = 0.15; Lambda = 28.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006; alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.33; delta =1.15; omega2 = 0.00068; omega1 = 0.00111; epsilon=0.003;

```

dydt(1) = Lambda-(mu+psi+(beta*y(4))/(k+y(4)))*y(1)+epsilon*y(2); dydt(2) = psi*y(1) - (mu+gamma+epsilon)*y(2); dydt(3) = (beta*y(4)/(k+y(4)))*y(1)+gamma*y(2)-(mu+alpha1)*y(3); dydt(4) = eta*y(3)-d*y(4);

```

```

clear all close all clc tspan = [0 365]; y0 = [28249670 0 750 275000]; [t,y] = ode45('abue1',tspan,y0); plot(t,y(:,1),'b',t,y(:,2),'black',t,y(:,3),'r',t,y(:,4),'c','Linewidth',2) xlabel('Time(Day)') ylabel('Population Numbers') title('Prevalence of the disease') legend('susceptible','Educated','Infected','Recovered')

```

4)for vaccination only

```

function dydt = abuv1(t,y) dydt = zeros(4,1); global beta k p Lambda phi eta gamma alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon beta =0.2143; k=10000000; p = 0.15; Lambda = 28.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006; alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.33; delta =1.15; omega2 = 0.00068; omega1 = 0.00111; epsilon=0.003;

```

```

dydt(1) = Lambda-(mu+phi+(beta*y(4))/(k+y(4)))*y(1)+omega2*y(2); dydt(2) = phi*y(1) - (mu+omega2+p*beta*y(4)/(k+y(4)))*y(2); dydt(3) = (beta*y(4)/(k+y(4)))*y(1)+p*beta*y(4)-(mu+alpha1)*y(3); dydt(4) = eta*y(3)-d*y(4);

```

```
clear all close all clc tspan = [0 365]; y0 = [28249670 0 750 275000]; [t,y] = ode45('abuv1',tspan,y0);
plot(t,y(:,1),'b',t, y(:,2),'m',t,y(:,3),'r',t,y(:,4),'c','Linewidth',2) xlabel('Time(Day)') yla-
bel('Number of Population ') title('Prevalence of the disease') legend('susceptible','Vaccinated','Infected'
)
```

5) for treatment only

```
function dydt = abut1(t,y) dydt = zeros(5,1); global beta k p Lambda phi eta gamma
alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon l beta =0.2143; k=10000000;
p = 0.15; Lambda = 0.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006; al-
pha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.015; delta =1.15; omega2 =
0.00068; omega1 = 0.00111; epsilon=0.003; l=0.5; dydt(1) = Lambda -(mu+(beta*y(5))/(k+y(5)))*y(1
+ omega1*y(4); dydt(2) = ((beta*y(5))/(k+y(5)))*y(1)-(mu+alpha1+delta)*y(2); dydt(3)
= delta*y(2)-(mu+alpha2+theta)*y(3); dydt(4) = theta*y(3)-(mu+omega1)*y(4); dydt(5)
= eta*y(2)-d*y(5);
```

```
clear all close all clc tspan = [0 365]; y0 = [28249670 750 0 0 275000]; [t,y] =
ode45('abut1',tspan,y0); plot(t,y(:,1),'b',t, y(:,2),'r',t,y(:,3),'y',t,y(:,4),'g',t,y(:,5),'c','Linewidth',2)
xlabel('Time(Day)') ylabel('Number of Population ') title('Prevalence of the disease') leg-
end('susceptible','Infected','Treated','Recovered','Bakteria' )
```

6) For Education and Vaccination

```
function dydt = abul(t,y) dydt = zeros(5,1); global beta k p Lambda phi eta gamma
alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon beta =0.2143; k=10000000;
p = 0.15; Lambda = 28.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006;
alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.33; delta =1.15; omega2
= 0.00068; omega1 = 0.00111; epsilon=0.003;
```

```
dydt(1) = Lambda-(mu+phi+psi+(beta*y(5))/(k+y(5)))*y(1)+omega2*y(3)+epsilon*y(2);
dydt(2) = psi*y(1) - (mu+gamma+epsilon)*y(2); dydt(3) = phi*y(1)-(mu+omega2+(p*beta*y(5)))/(k-
dydt(4) = (beta*y(5)/(k+y(5)))*y(1)+(p*beta*y(5))/(k+y(5))*y(3)+gamma-(mu+alpha1+delta)*y(4)
dydt(5) = eta*y(4)-d*y(5);
```

```
clear all close all clc tspan = [0 365]; y0 = [28249670 0 0 750 275000]; [t,y] =
ode45('abuev',tspan,y0); plot(t,y(:,1),'b',t, y(:,2),'black',t, y(:,3),'m',t,y(:,4),'r',t,y(:,5),'c','Linewidth',2)
xlabel('Time(Day)') ylabel('Number of Population ') title('Prevalence of the disease') leg-
end('Susceptible','Educated','Vaccinated','Infected','Bacteria')
```

7) For Education and Treatment

```
function dydt = abuet(t,y) dydt = zeros(6,1); global beta k p Lambda phi eta gamma
alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon l beta =0.2143; k=10000000;
p = 0.15; Lambda = 0.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006;
alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.015; delta =1.15; omega2
= 0.00068; omega1 = 0.00111; epsilon=0.003; l=0.5;
```

```
dydt(1) = Lambda -(mu+psi+(beta*y(6))/(k+y(6)))*y(1) + epsilon*y(2)+omega1*y(5);
dydt(2) = psi*y(1)-(mu+gamma+epsilon)*y(2); dydt(3) = ((beta*y(6))/(k+y(6)))*y(1)+
gamma*y(2)-(mu+alpha1+delta)*y(3); dydt(4) = delta*y(3)-(mu+alpha2+theta)*y(4);
dydt(5) = theta*y(4)-(mu+omega1)*y(5); dydt(6) = eta*y(3)-d*y(6);
```

```
clear all close all clc tspan = [0 365]; y0 = [28249670 0 750 0 0 275000]; [t,y] =
ode45('abuet',tspan,y0); plot(t,y(:,1),'b',t, y(:,2),'black',t, y(:,3),'r',t,y(:,4),'y',t,y(:,5),'g',t,y(:,6),'c','Lin
xlabel('Time(Day)') ylabel('Number of Population ') title('Prevalence of the disease') leg-
end('Susceptible','Educated','Infected','Treated','Recovered','Bacteria')
```

8) For Vaccination and Treatment

```
function dydt = abuvt(t,y) dydt = zeros(6,1); global beta k p Lambda phi eta gamma
alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon l beta =0.2143; k=10000000;
p = 0.15; Lambda = 0.4853; phi=0.005; eta = 10; gamma= 0.005; alpha1 = 0.000006;
alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2; d=0.015; delta =1.15; omega2
= 0.00068; omega1 = 0.00111; epsilon=0.003; l=0.5;
```

```
dydt(1) = Lambda -(mu+phi+(beta*y(6))/(k+y(6)))*y(1) + omega2*y(2)+omega1*y(5);
dydt(2) = phi*y(1)-(mu+omega2+(p*beta*y(6))/(k+y(6)))*y(2); dydt(3) = ((beta*y(6))/(k+y(6)))*y
(mu+alpha1+delta)*y(3); dydt(4) = delta*y(3)-(mu+alpha2+theta)*y(4); dydt(5) = theta*y(4)-
(mu+omega1)*y(5); dydt(6) = eta*y(3)-d*y(6);
```

```
clear all close all clc tspan = [0 365]; y0 = [28249670 0 750 0 0 275000]; [t,y] =
ode45('abuvt',tspan,y0); plot(t,y(:,1),'b',t, y(:,2),'m',t, y(:,3),'r',t,y(:,4),'y',t,y(:,5),'g',t,y(:,6),'c','Linew
xlabel('Time(Day)') ylabel('Number of Population ') title('Prevalence of the disease') leg-
end('Susceptible','Vaccinated','Infected','Treated','Recovered','Bacteria')
```

Matlab code for Figure (??) is:- function dydt = abu1(t,y) dydt = zeros(7,1); global beta k p Lambda phi eta gamma alpha1 alpha2 mu psi theta d delta omega2 omega1 epsilon
beta =0.2143; k=10000000; p = 0.15; Lambda = 28.4853; phi=0.05; eta = 10; gamma= 0.005; alpha1 = 0.000006; alpha2 = 0.000003; mu = 0.000016; psi=0.008; theta=0.2;
d=0.33; delta =1.15; omega2 = 0.00068; omega1 = 0.00111; epsilon=0.003;

```

dydt(1) = Lambda -(mu+phi+psi+(beta*y(7))/(k+y(7)))*y(1) + omega2*y(3)+ epsilon*y(2)+omega1*y(6); dydt(2) = psi*y(1)-(mu+gamma+epsilon)*y(2); dydt(3) = phi*y(1)-(mu+omega2+(p*beta*y(7))/(k+y(7)))*y(3); dydt(4) = ((beta*y(7))/(k+y(7)))*y(1)+(p*beta*y(7))/(mu+alpha1+delta)*y(4); dydt(5) = delta*y(4)-(mu+alpha2+theta)*y(5); dydt(6) = theta*y(5)-(mu+omega1)*y(6); dydt(7) = eta*y(4)-d*y(7);

clear all close all clc tspan = [0 365]; y0 = [28249670 0 0 750 0 0 275000]; [t,y] = ode45('abul',tspan,y0); plot(t,y(:,1),'b',t, y(:,2),'black',t,y(:,3),'m',t,y(:,4),'r',t,y(:,5),'y',t,y(:,6),'g',t,y(:,7),'k'); xlabel('Time(Day)') ylabel('population') title('Prevalence of the disease') legend('susceptible','Educated').

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