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ORIGINAL ARTICLE

Optimal Intervention Strategies for Transmission Dynamics of Cholera Disease

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Abstract

In this paper, an optimal control model for cholera disease described by a system of first order ordinary differential equations was formulated and examined. The necessary conditions for the attainment of optimum level of control in the dynamical system were derived by employing the Pontryagin's Maximum principle. Numerical studies of the analytical results were conducted to investigate the behaviour of the optimality system and the results were tabulated. The tabular results showed that the combination of the interventions up to 80% was capable of bringing cholera epidemic under control. As the rate of control was directly related to the cost of control, the result of the analysis revealed the control outlay that maintained the optimum balance of interventions with the lowest cost.

Keywords: Optimal control Model, Cholera disease, Pontryagin's Maximum principle

Introduction

While intensive sanitation and availability of potable water have eliminated cholera in advanced countries of the world, the disease still remains a major threat to Africa and the entire less developed countries. The emergence and re-emergence of cholera in the developing countries have resulted in not only the mortality and morbidity of human but also increase in the economic predicaments. Despite the implementation of various intervention strategies towards the eradication of the disease, the disease continues to occur.

On that ground, there is a need to investigate the optimal level of controls required to stem the disease. The standard method for obtaining the solutions of a dynamical optimization problem when the problem is a continuous function of time is termed optimal control. The optimal control theory provides a necessary framework in developing optimal strategies to control various types of diseases with a view to examining the optimal balance in terms of the costs of providing controls in disease management (Laarabi *et al*. 2013).

Investigating the necessary and sufficient conditions required by the interventions to actually prevent or eliminate diseases is not new in modelling. Nana-Kyere *et al.* (2017)

presented an optimal control model of malaria disease with standard incidence rate. They incorporated three control measures and discovered that the optimum interventions considered have total and incompatible results on the limitation of the exposed and infectious humans.

In their work, Laarabi *et al*. (2013) did not examine a particular disease but designed an optimal control problem with respect to epidemic model taking into consideration the saturated incidence rate and the saturated treatment function. The optimal control and no control models were compared and it was discovered that the optimal vaccination was more effective for limiting the population of infectious and susceptible individuals and increasing the population of recovered individuals.

Oke *et al.* (2018) presented a deterministic model of breast cancer defined by a system of first order ordinary differential equations in the presence of chemotherapy treatment and the ketogenic diet. They applied optimal control theory to investigate the optimal drug balance as an essential input control of the system therapy in order to reduce the number of cancerous cells by examining various controlled combinations of administering ketogenic diet and the chemotherapy agents. They discovered that an individual has the tendency of developing breast cancer depending on the number of immune systems, the rate by which ketogenic diet (*d)* is being consumed to resist tumour cells and the potency of the anticancer drug *(k).* Besides, they discovered that the rate of tumour formation can be accelerated if an additional quantity of estrogen is injected into the body already saturated with estrogen quantity either through birth control or hormone replacement therapy (HRT).

Wang and Modnak (2011) developed a cholera model with permanent immunity and incorporated three different control measures into the model. The result obtained showed that the interventions interplayed with one another and concluded that multiple control measures achieve a better result than a single intervention in fighting against the propagation of cholera disease which is in agreement with the outcome of the study conducted by (Sule & Lawal, 2018).

Contrary to the claim by Wang and Modnak (2011), cholera is one of the infectious diseases that do not confer permanent immunity upon recovery. Therefore, it is necessary to examine the effect of providing controls on the population of susceptible and infectious individuals in the SIR-B transmission model where recovered individuals can go back to the susceptible class upon the expiration of the immunity acquired through vaccination.

The implementation of appropriate control strategies could reduce or eliminate disease in a population. Consequently, an optimal control model which takes the form of vaccination, treatment and sanitation is implemented to investigate the extent to which these controls could limit the population of susceptible and infectious individuals and increase the population recovered individuals in a population that is assumed to be fixed.

Materials and Methods

SIR-B cholera model was developed where *S(t),* I(t), *R(t)* and *B(t)* are compartments for each state variable and they represent the number of susceptible individuals at time t, the number of infected individuals at time t, the number of recovered individuals at time t and the population of bacteria in the aquatic environment at time t respectively. S(t) is the population of individuals who have not been infected at time t but are capable of being infected, I(t) is the population of individuals who have been infected at time t and are capable of spreading the infection to those in the susceptible category. R(t) is the population of individuals who are temporarily immune to the disease either by the immunity acquired through vaccination or successful treatment after infection. $\pi, \mu, \mu_c, \beta_1, \beta_2, \aleph, \varepsilon, \delta$ *and* γ are parameters representing recruitment rate into susceptibility, human death rate unrelated to the disease, human death rate due to the disease, contact rate between susceptible individuals and contaminated water, contact rate

between susceptible and infectious individuals, pathogen concentration that yields 50% chance of catching cholera, rate at which infectious individuals contributes to the growth of pathogen, natural death rate of the pathogen and human recovery rate unrelated to the treatment respectively

Three intervention strategies which are functions of time with appropriate upper and lower bounds are investigated. The first intervention $\rho(t)$ is in the form of treatment which increases recovery rate and reduces cholera induced death rate. Vaccination, $v(t)$ is also considered as a control strategy and the immunity acquired through it moves susceptible individuals to the recovered class at a rate $v(t)$. Since the best way to limit pathogen concentration and avert bacteria ingestion rates is sanitation then $\omega(t)$ is introduced as a control measure to water supply. Introducing these controls, the following model was developed:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - \left(\mu + v(t)\right)S - \frac{\beta_1 BS}{B+\aleph} - \beta_2 IS + \sigma R \\
\frac{dI}{dt} &= \frac{\beta_1 BS}{B+\aleph} + \beta_2 IS - \left(\mu + \mu_c + \rho(t)\right)I \\
\frac{dR}{dt} &= v(t)S - (\sigma+\mu)R + \rho(t)I \\
\frac{dB}{dt} &= \varepsilon I - (\delta + \omega(t))B
\end{aligned}\right\} \qquad (1)$$

The definition of the model parameters and the sources for their values in the literature are presented in Table 1.

Table 1. Definitions and sources of the model parameters

Parameter	**Symbol**	**Value**	**Unit**	**Source**
Human recruitment rate	π	10	day $^{-1}$	Kadaleka, (2011)
Rate of human contribution to the population of *V.cholerae*	ε	10	cells/ml/day	Isere *et al.,* (2014)
Rate of human exposure to contaminated water	β_1	0.075	day $^{-1}$	Wang & Modnak, (2011)
Pathogen concentration that yields 50% chance of catching cholera	$\aleph$	10^5	cells/ml	Edward & Nyerere, (2015)
Natural death rate for *V.cholerae*	δ	0.4	day $^{-1}$	Isere *et al.,* (2014)
Death rate unrelated to cholera	μ	0.02	day $^{-1}$	Kadaleka, (2011)
Human Death rate due to cholera	μ_c	0.015	day $^{-1}$	Kadaleka, (2011)
Rate of contact between susceptible and infectious individuals	β_2	0.00011	day $^{-1}$	Wang & Modnak, (2011)
Rate of losing immunity	σ	0.01	day $^{-1}$	Al-Arydah *et al.,* (2013)

The control set is given as

$$\Gamma = \left\{ \left(v(t), \rho(t), \omega(t) \right) / 0 \le v(t) \le v_{\max}, 0 \le \rho(t) \le \rho_{\max}, 0 \le \omega(t) \le \omega_{\max} \right\} \quad (2)$$

$v_{\max}, \rho_{\max}$ and $\omega_{\max}$ represent the maximum limits for the impact of vaccination, treatment and sanitation in limiting cholera infection and increasing recovery. Then, the total number of infections and the costs of intervention strategies in a given period of time is minimized subject to objective functional

$$\left(v, \rho, \omega \right) \in \Gamma \int_0^T \left[\begin{array}{l} I(t) + p_{21} v(t) S(t) + p_{22} V(t)^2 + p_{31} \rho(t) \mathrm{I(t)} + \\ p_{32} \rho(t)^2 + p_{41} \omega(t) + p_{42} \omega(t)^2 \end{array} \right] dt \quad (3)$$

The coefficient $p_{i,j} \left(i = 1,2,3,4; j = 1,2 \right)$ in monetary terms gives the cost implications of the intervention strategies while the quadratic terms involved in the objective functional indicate the nonlinear nature of the costs particularly at the high level of intervention which is in agreement with the nonlinear nature of the model. The minimization procedure is based on the models (1) whose equations are regarded as the *state equations* in the optimal control context and the variables S, I, R and B are regarded as the *state variables*. Our main concern is to establish the optimal solutions, $v^*(t), \rho^*(t)$ and $\omega^*(t)$ that minimizes the objective functional (3).

By applying the Pontryaging's Maximum Principle as in (Akande & Ibrahim, 2017; Neilan *et al.,* 2010; Agusto *et al*. 2012; Isere, 2014; Lashari *et al*., 2013), the necessary conditions for the optimality of the controls are derived. The Pontryaging's Maximum Principle which is based on the introduction of adjoint functions shall be applied to obtain the solutions of the optimal control problem. The Principle uses the state and adjoint functions to represent the optimal control problem. The method transforms the problem of minimizing the objective functional (under the constraint of state equations) into minimizing the Hamiltonian with respect to the intervention strategies.

The Hamiltonian Adjoint Equations

Suppose the adjoint functions introduced are λ_1, λ_2, λ_3 and λ_4. Since there are four state variables, S, I, R and B then, λ_1, λ_2, λ_3 and λ_4 correspond to *S*, *I*, *R* and *B* respectively. The Hamiltonian, *H* can then be derived by finding the product of each adjoint function with its corresponding state equation and adding each of these products to the integrand of the objective functional. Hence,

$$
\left.\begin{aligned}
H = {} & I(t) + p_{21}v(t)S(t) + p_{22}v(t)^2 + p_{31}\rho(t)I(t) + p_{32}\rho(t)^2 + p_{41}\omega(t) + p_{42}\omega(t)^2 \\
& + \lambda_1\left[\pi - (\mu + v)S - \frac{\beta_1 BS}{B+\aleph} - \beta_2 IS + \sigma R\right] \\
& + \lambda_2\left[\frac{\beta_1 BS}{B+\aleph} + \beta_2 IS - (\mu + \mu_c + \rho)\mathrm{I}\right] \\
& + \lambda_3\left[vS - (\mu + \sigma)\mathrm{R} + \rho\,\mathrm{I}\right] \\
& + \lambda_4\left[\varepsilon I - (\delta + \omega)\mathrm{B}\right]
\end{aligned}\right\} \quad (4)
$$

The adjoint function (4) is characterized as:

$$
\left.\begin{aligned}
\frac{\partial\lambda_1}{\partial t} &= \frac{-\partial H}{\partial S} = -p_{21}v(t) + \lambda_1\left[\mu + v(t) + \frac{\beta_1 B}{B+\aleph} + \beta_2 I\right] - \lambda_2\left[\frac{\beta_1 B}{B+\aleph} + \beta_2 I\right] - \lambda_3[v(t)] \\
\frac{\partial\lambda_2}{\partial t} &= \frac{-\partial H}{\partial I} = -1 - p_{31}\rho(t) + \lambda_1\left[\beta_2 S\right] - \lambda_2\left[\beta_2 S - (\mu + \mu_c) - \rho(\mathrm{t})\right] - \lambda_3[\rho(t)] - \lambda_4[\varepsilon] \\
\frac{\partial\lambda_3}{\partial t} &= \frac{-\partial H}{\partial R} = -\lambda_1[\sigma] + \lambda_3[\sigma + \mu] \\
\frac{\partial\lambda_4}{\partial t} &= \frac{-\partial H}{\partial B} = \lambda_1\left[\frac{\beta_1 \aleph S}{(B+\aleph)^2}\right] - \lambda_2\left[\frac{\beta_1 \aleph S}{(B+\aleph)^2}\right] + \lambda_4[\delta + \omega(t)]
\end{aligned}\right\} \quad (5)
$$

Subject to the following conditions of transversality (i.e, when time becomes zero):

$$
\lambda_1(\mathrm{T}) = 0, \quad \lambda_2(\mathrm{T}) = 0, \quad \lambda_3(\mathrm{T}) = 0, \quad \lambda_4(\mathrm{T}) = 0 \quad (6)
$$

The Optimality Equation/ Optimality Condition

We may wish to minimize or maximize in optimal control theory depending on our intention. Controls was used to minimize infections and susceptibility or to maximize efforts directed to limit infections and susceptibility. Controls can also be used to maximize recovery. The optimal control is minimal if the second derivative of the Hamiltonian equation with respect to a control variable is negative otherwise it is maxima. i.e

$$
\frac{\partial^2}{\partial u^2} < 0 \; - \; \max imum \quad (7)
$$

$$
\frac{\partial^2}{\partial u^2} > 0 \; - \; \text{minimum} \quad (8)
$$

In respect to the present study, the optimality equations are derived by determining the differential coefficients of the Hamiltonian equation (4) with respect to the control variables.

The resulting equations are equated to zero and the control variables are solved for from which the optimal solutions, $v^*(t), \rho^*(t)$ and $\omega^*(t)$ are obtained subject to the lower and upper constraints $0 \le v \le v_{\max}, \quad 0 \le \rho \le \rho_{\max}, \quad 0 \le \omega \le \omega_{\max}$. So when $\frac{\partial H}{\partial v} = 0, \frac{\partial H}{\partial \rho} = 0$ and $\frac{\partial H}{\partial \omega} = 0$ in (4) then,

$$\left.\begin{aligned} \frac{\partial H}{\partial v} &= p_{21} S(t) + 2 p_{22} \mathrm{v}(t) + \lambda_1 [-S(t)] + \lambda_3 [S(t)] = 0 \\ \frac{\partial H}{\partial \rho} &= p_{31} \mathrm{I}(t) + 2 p_{32} \rho(t) - \lambda_2 [\mathrm{I}(t)] + \lambda_3 [\mathrm{I}(t)] = 0 \\ \frac{\partial H}{\partial \omega} &= p_{41} + 2 p_{42} \omega(t) + \lambda_4 [-B(t)] = 0 \end{aligned}\right\} \quad (9)$$

From which the optimal values for $v^*(t), \rho^*(t)$ and $\omega^*(t)$ are obtained as

$$\left.\begin{aligned} v(t)^* &= \frac{(\lambda_1 - \lambda_3 - p_{22})}{2 p_{22}} S(t) \\ \rho(t)^* &= \frac{(\lambda_2 - \lambda_3 - p_{31})}{2 p_{32}} \mathrm{I}(t) \\ \omega(t)^* &= \frac{(\lambda_4 B(t) - p_{41})}{2 p_{42}} \end{aligned}\right\} \quad (10)$$

To distinguish between the *minima* and *maxima*, we find the second derivative of (9) and each of $\frac{\partial^2 H}{\partial v^2}$, $\frac{\partial^2 H}{\partial \rho^2}$ and $\frac{\partial^2 H}{\partial \omega^2}$ is greater than zero. Hence, the optimality is minimum. That is our objective is achieved under minimum cost.

Numerical Simulation of the Optimal Control Analysis and Discussion

The solutions for the systems (1), (4), and (5) can be obtained numerically when there are initial conditions for (1) and transversality conditions for (4) and (5) at the point where $\frac{\partial H}{\partial v} = \frac{\partial H}{\partial \rho} = \frac{\partial H}{\partial \omega} = 0$

The forward-backwards method as in Wang and Modnak (2011) is applied to solve the optimality system (1), (4) and (5) in an iterative manner. Equations (1) are solved forward in time by the classical fourth-order Runge-Kutta method using initial guess for the intervention variables. Equations (4) and (5) are solved backwards in time by the solutions of equations (1). The values of the controls are varied with the new solutions of equations (1), (4) and (5) and the process is repeated until the solutions converge.

To achieve the numerical simulation, the values assigned to the model parameters in Table 1 are adopted. The cost parameters values in Wang and Modnak (2011) are also adopted so that p_{21} =2, p_{22} =10, p_{31} =10, p_{32} =10, p_{41} =10 and p_{42} =20. The initial values assumed for the state variables are: $S(0)=70,\ I(0)=5,\ R(0)=25,\ B(0)=3$ while the overall period of infection time is assumed to be $T=70$ days. The initial values assumed for the adjoint functions are given in eqn. (6) as : $\lambda_1(T)$= 0, $\lambda_2(T)$ = 0, $\lambda_3(T)$= 0, $\lambda_4(T)$= 0. We use mathematical software (Maple 18) to determine the numerical values of the variables *S(t), I(t), R(t)* and *B(t)* when the values of the controls $v(t), \rho(t)$ and $\omega(t)$ are varied from 0 to 1and the results are depicted in Tables 2 - 8.

Table 2. Solutions for $v=\rho=\omega=0$

Variables	Solutions
S(t)	111.837579
I(t)	4.376176
R(t)	21.517670
B(t)	99.452444

Table 3. Solutions for $v=\rho=\omega=0.2$

Variables	Solutions
S(t)	55.327145
I(t)	1.658802
R(t)	80.866229
B(t)	37.083681

Table 4. Solutions for $v=\rho=\omega=0.5$

Variables	Solutions
S(t)	24.616507
I(t)	0.412408
R(t)	112.910952
B(t)	8.636379

Table 5. Solutions for $v=\rho=\omega=0.7$

Variables	Solutions
S(t)	16.821730
I(t)	0.178463
R(t)	120.969778
B(t)	3.374444

Table 6: Solutions for $v=\rho=\omega=0.8$

Variables	Solutions
S(t)	14.339035
I(t)	0.122864
R(t)	114.470338
B(t)	2.145826

Table 7: Solutions for $v=\rho=\omega=0.9$

Variables	Solutions
S(t)	12.663374
I(t)	0.879498
R(t)	125.237576
B(t)	1.387464

Table 8: Solutions for $v = \rho = \omega$ =1.0

Variables	**Solutions**
S(t)	11.283978
I(t)	0.657491
R(t)	126.646675
B(t)	0.916652

Tables 2-8 are provided in order to give numerical and quantitative pictures of our analysis. Considering table 2 – table 8, it is observed that increase in the values of the controls from 0 to 1 results in increase in the population of the recovered individuals but decrease in the population of other state variables which is the aim of disease control in epidemiology. With controls, we expect the population of the recovered individuals to increase but that of the susceptible, infectious and pathogen to decrease. In fact, the population of the infectious individuals and pathogen need to be reduced to zero for the disease to be completely eradicated.

However, as disease control is cost-oriented, rates of controls which give the best result in terms of cost management need to be determined, either 0.5, 0.7, 0.8, 0.9 or 1.0 from Tables 2 - 8. Even though, the populations of the infectious individuals and the pathogen are reduced to zero when the rate of control is maintained at 1.0 in table 8 yet, the population of infectious individuals is about to take off in table 8 compared to table 6 where the population of the infectious individuals is the least. As the rate of controls is directly related to the cost of control therefore, optimum balance with the lowest cost is achieved when the rate of controls is 80% (i.e. 0.8) in table 6. The combination of controls at this level is capable of driving cholera outbreak into extinction. We only need to raise the control $\omega(t)$ that has impact on *B(t)* in order to reduce the pathogen population to zero but keep both the treatment rate $\rho(t)$ and vaccination rate $v(t)$ at 0.8. Graphical profiles of the above numerical results (Tables 2 - 8) are presented in Figure 2 - 8.

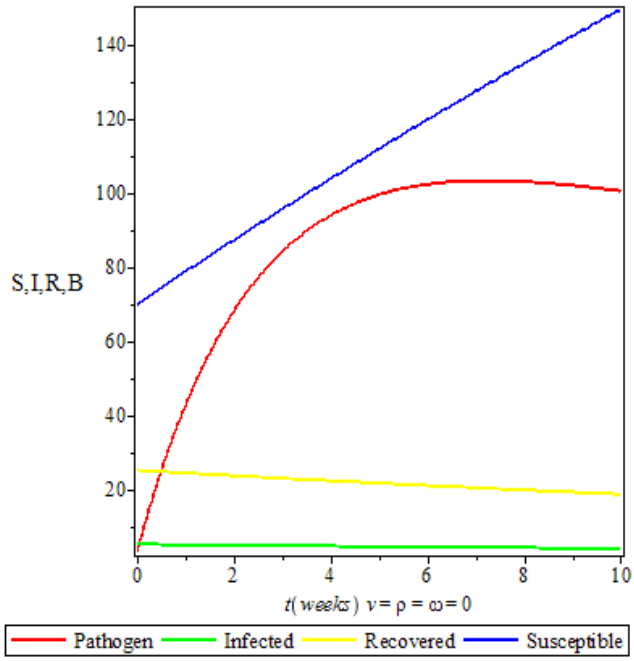

Figure 2. Effect of controls at zero

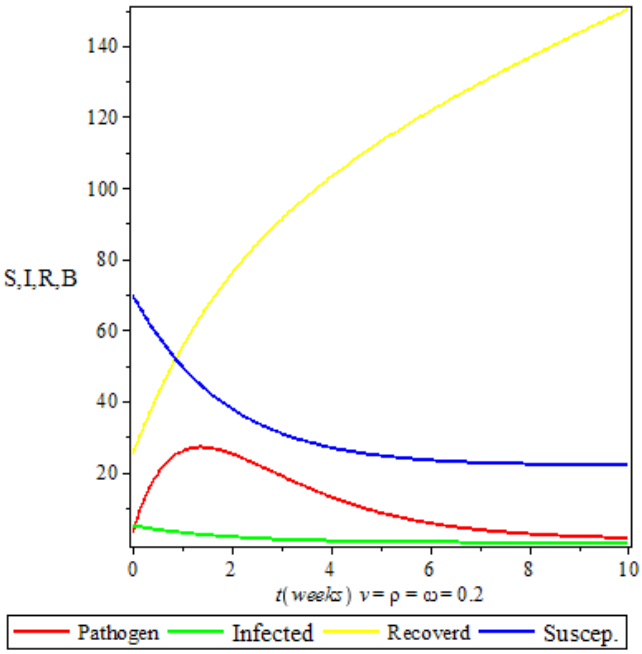

Figure 3. Effect of controls at 0.2

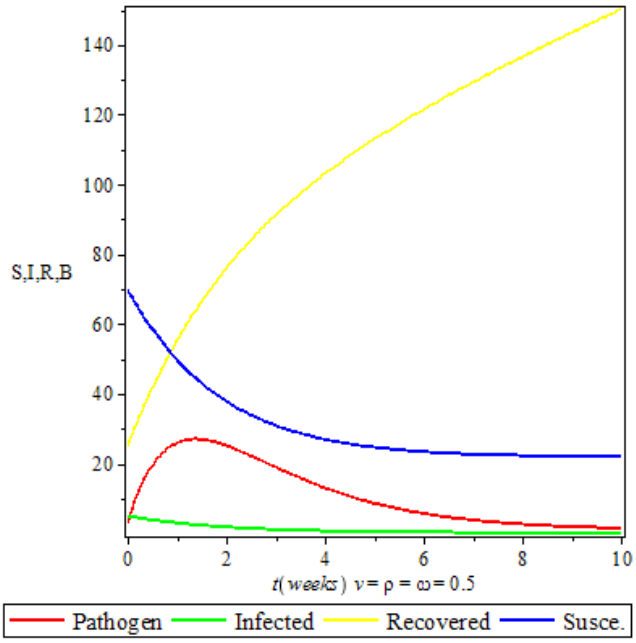

Figure 4. Effect of controls at 0.5

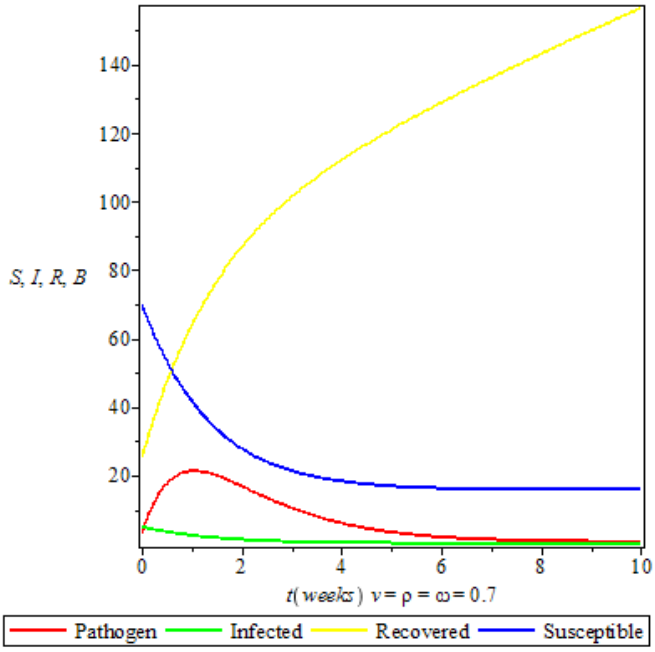

Figure 5. Effect of controls at 0.7

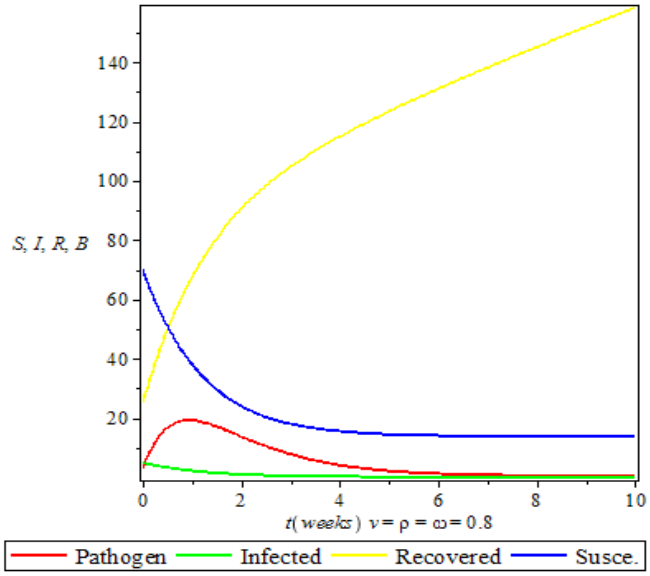

Figure 6. Effect of controls at 0.8

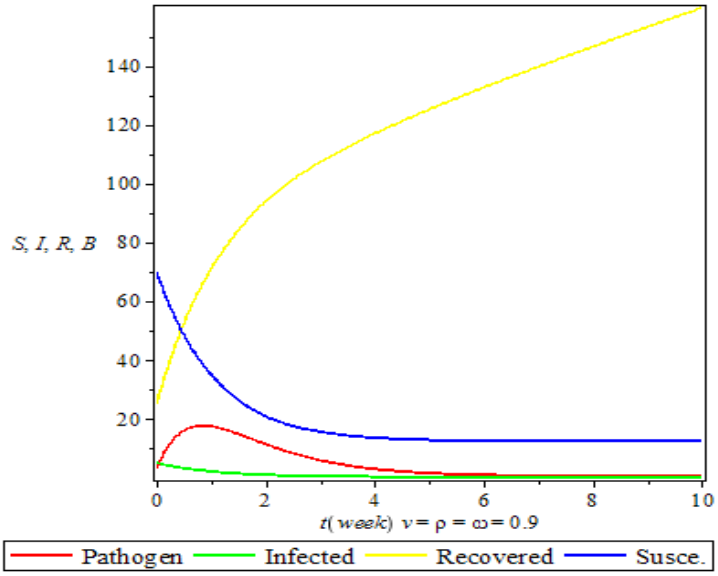

Figure 7. Effect of controls at 0.9

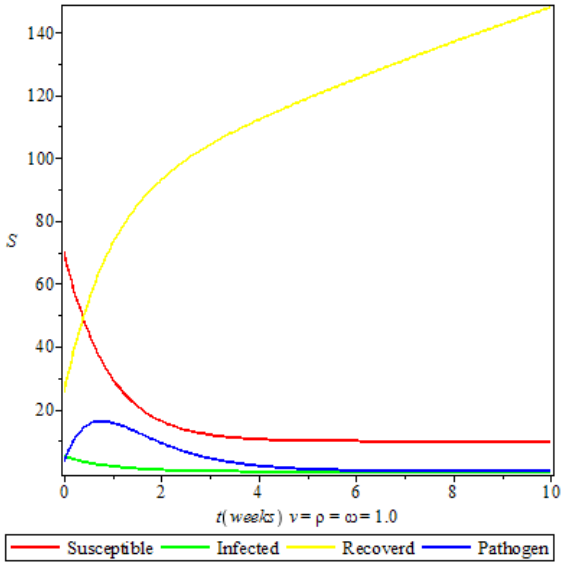

Figure 8. Effect of controls at 1.0

Conclusion

In this work, an optimal control model for cholera disease described by a system of first-order nonlinear ordinary differential equations was developed. The necessary and sufficient conditions for the attainment of the optimum level of control in the dynamical system are derived by employing the popular Pontryagin's Maximum Principle. Based on the outcome of the study, society is bound to exist cholera outbreak and maintain cholera-free atmosphere if it can keep the cholera vaccination and cholera treatment rates at 80% and at the same time, raise the rate of sanitation above 80%. This has been working for developed countries like the US, Great Britain, France, etc. where cholera outbreak has become history.

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