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MODELLING AND OPTIMAL CONTROL ANALYSIS OF TYPHOID FEVER

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Abstract: In this paper, we formulate a deterministic mathematical model to describe the transmission dynamics of typhoid fever by incorporating some control strategies. In order to study the impact of these control strategies on the dynamics of typhoid fever, the model captures vaccination and educational campaign as control variables. We show that the model is mathematically and epidemiologically well positioned in a biologically feasible region in human populations. We carry out a detailed analysis to determine the basic reproduction number R_0 necessary for the control of the disease. The optimal control strategies are used to minimize the infected carriers and infected individuals and the adverse side effects of one or more of the control strategies. We derive a control problem and the conditions for optimal control of the disease using Pontryagin's Maximum Principle and it was shown that an optimal control exists for the proposed model. The optimality system is solved numerically, the numerical simulation of the model shows

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that possible optimal control strategies become more effective in the control and containment of typhoid fever when vaccination and educational campaign are combined optimally would reduce the spread of the disease.

Keywords: optimal control; typhoid fever; basic reproduction number.

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1. INTRODUCTION

Typhoid fever is caused by the bacteria Salmonella typhi. Typhoid fever infects 21 million people and kills 200,000 worldwide every year. Asymptomatic carriers are believed to play an essential role in the evolution and global transmission of Typhoid fever, and their presence greatly hinders the eradication of typhoid fever using treatment and vaccination. Typhoid fever is becoming an increasingly common illness worldwide, increasing resistance to various antibiotics is making antibiotic treatment less effective. Anderson and May [1], Hyman [2].

Typhoid fever has continued to be a health problem in developing countries where there is poor sanitation, poor standard of personal hygiene and prevalence of contaminated food. It is endemic in many parts of the developing world, illness do occur around the world in the span of a day. Lifshitz [3].

Typhoid fever treatment is anchored on the blood culture condition of the patients. If the species is sensitive, the oral antibiotic is used. When dealing with large populations, as in the case of Typhoid fever, compartmental mathematical models are used. In the deterministic model, individuals in the population are assigned to different subgroups, each representing a specific stage of the epidemic. Several mathematical models have been developed on the transmission dynamics of typhoid fever these includes, (Adetunde [4]; Lauria et al., [5]; Kalajdzievska [6]; Mushayabasa [7]; Cvjetanovic et al.,[8]; Moffact [9]; Pitzer et al., [10]; Date et al.,[11]; Muhammad, et al.,[12]; Watson and Edmunds [13]; Nthiiri [14]; Moatlhod and Gosaamang [15]; Mushayabasa [16]; Tilahun et al.,[17] Peter and Ibrahim [18]). All of the above studies reveal an important result for typhoid fever dynamics by considering different situation, but we have identified that till now there is no studies that has been done to investigate the typhoid fever dynamics with the application of educational campaign and vaccination as control strategies. In view of the above, we incorporate two control strategies to the proposed model which are educational campaign and vaccination to control the spread of the disease. Many studies have examined optimal control in a good number of models of epidemic diseases [20-25].

2. MATERIALS AND METHOD

2.1 Model formulation

The model compartments consist of the following classes, namely: Susceptible class; $S(t)$; is used to represent the number of people susceptible to the disease or susceptible to the disease at the time. Carrier-class; $I_c(t)$ denote individuals who show no signs of infection and are infectious. Infected class; $I(t)$ the number of people who have been infected with the disease and are able to spread the disease to the susceptible class. Recovered class; $R(t)$ is the compartment used for those infected and have recovered from the disease. Those in this category can not infect or transmit the infection to others again..Recruitment to the susceptible population is either by immigration or birth at the rate θ. It is assumed that the proportion of susceptible class migrate to carrier-class at the rate ρ, while compliment $1-\rho$ migrates to infectious class. We assume that the transmission rate of β for carriers is higher than the transmission rate of γ for individuals who are symptomatically infected because they are more likely to be unaware of their condition and therefore continue their regular activities. Carriers individual can develop symptoms at a rate α. Infectious individuals can be treated and recovered from the infection at a rate δ. Susceptible individuals can be vaccinated at a rate ψ to protect themselves from infection. 1 - ϕ is a parameter that represents awareness that limits the spread of typhoid by carriers and symptoms. This parameter lies between $0 \le \phi \le 1$. When the awareness parameter is set to zero, that is $\phi = 0$, this implies that, there is no awareness so that the entire population in the susceptible class are unaware of typhoid fever and when awareness parameter is equal to unity that is, $\phi = 1$, the entire population in the susceptible class are fully aware of typhoid fever, that is, they are aware of what causes the disease, the mode of transmission and how to avoid contracting the disease. The illustration above is governed by the following set of differential equations.

$$\frac{dS}{dt} = \theta - \mu_1 S - S(1-\phi)(\beta I_c + \gamma I) - \psi S$$

$$\frac{dI_c}{dt} = \rho S(1-\phi)(\beta I_c + \gamma I) - \mu_2 I_c - \alpha I_c + \alpha\phi I_c$$

(1)
$$\frac{dI}{dt} = (1-\rho)(1-\phi)S(\beta I_c + \gamma I) + \alpha(1-\phi)I_c - (\mu_3 + \delta)I$$

$$\frac{dR}{dt} = \psi S + \delta I - \mu_4 R$$

2.2 Positivity of Solution

Theorem 1.

Let the initial conditions under consideration be given as $\{S(t),\ I_c(t),\ I(t), R(t) \geq 0\} \in \Omega$ then the solutions of the system of equations are positive for all $t > 0$.

Proof:

From the first equation of the system (1)

$$\frac{dS}{dt} = \theta - \mu_1 S - \lambda S(1-\phi) - \psi S,$$

then,

(2)
$$\frac{dS}{dt} \geq -\{(\mu_1 + \psi) + (1-\phi)\lambda\}S.$$

By separating the variable in (2) and then integrate

$$\int \frac{dS}{S} \geq -\int \{(\mu_1 + \psi) + (1-\phi)\lambda\}dt$$

$$\ln S \geq -\{(\mu_1 + \psi) + (1-\varphi)\lambda\}t + c$$

(3)
$$S(t) \geq Ke^{-\{(\mu_1+\psi)+(1-\phi)\lambda\}t},$$

where

$K = e^c$. At the initial time, t=0 and on substituting into (3)

$K = S(0)$

Thus, inequality (3) becomes

$S(t) \geq S(0)e^{-\{(\mu_1+\psi)+(1-\phi)\lambda\}t} \geq 0$

By repeating the same process for other variables in (1) respectively,

$$I_c(t) \geq I_c(0)e^{-(\mu_2+\alpha(1-\phi))t} \geq 0$$

(4) $$I(t) \geq I(0)e^{-(\mu_3+\delta)t} \geq 0$$

$$R(t) \geq R(0)e^{-\mu_4 \delta t} \geq 0$$

Since $t > 0$ we conclude that the solutions for

$\{S(t),\ I_c(t),\ I(t), R(t)\}$ of the model are non-negative for all $t > 0$.

2.3. The Basic Reproduction Number, $R_\circ$

The size of the basic reproduction number $R_\circ$ can be computed by using the popular technique known as the next generation matrix approach. This approach was formulated by Diekmann et al. [26] but modified by Driessche and Watmough [27] and Peter et al. [28] by constructing $n \times n$ matrix from the system of equations of the model an considering only the infective classes.

$$F_i = \begin{Bmatrix} \rho\beta(1-\phi)S & \rho\gamma(1-\phi)S \\ (1-\rho)\beta(1-\phi)S & (1-\rho)\gamma(1-\phi)S \end{Bmatrix}, \quad V_i = \begin{Bmatrix} \alpha k + \mu_2 & 0 \\ -\alpha k & \mu_3 + \delta \end{Bmatrix}.$$

The inverse of the matrix V is obtained as:

$$\begin{Bmatrix} (\alpha k + \mu_2)^{-1} & 0 \\ \dfrac{\alpha k}{(\alpha k + \mu_2)(\mu_3 + \delta)} & (\mu_3 + \delta)^{-1} \end{Bmatrix}.$$

The product of matrices F and V^{-1} is

$$FV^{-1} = \begin{Bmatrix} \rho\beta(1-\phi)S & \rho\gamma(1-\phi)S \\ (1-\rho)\beta(1-\phi)S & (1-\rho)\gamma(1-\phi)S \end{Bmatrix} \begin{Bmatrix} (\alpha k + \mu_2)^{-1} & 0 \\ \dfrac{\alpha k}{(\alpha k + \mu_2)(\mu_3 + \delta)} & (\mu_3 + \delta)^{-1} \end{Bmatrix}$$

the basic reproduction number which is the highest eigenvector for system (1) is given as

$$R_0 = \frac{k\theta}{\mu_1 + \psi}\left\{\frac{\alpha\gamma k + \beta\rho(\mu_3 + \delta) + \gamma\mu_2(1-\rho)}{(\mu_3 + \delta)(\mu_2 + \alpha k)}\right\}.$$

Where $k = (1-\phi)$.

3. Extension of the Basic Model into Optimal Control System

In this section, the basic model of typhoid fever is generalized by incorporating two control interventions. These are educational campaign and vaccination u_1 and u_2 respectively.

$$\begin{aligned}
\frac{dS}{dt} &= \theta - \mu_1 S - S(1-\phi)(\beta I_c + \gamma I) - \psi S - u_1 S(t) \\
\frac{dI_c}{dt} &= \rho S(1-\phi)(\beta I_c + \gamma I) - \mu_2 I_c - \alpha I_c + \alpha\phi I_c \\
\frac{dI}{dt} &= (1-\rho)(1-\phi)S(\beta I_c + \gamma I) + \alpha(1-\phi)I_c - (\mu_3 + \delta)I - u_2 I(t) \\
\frac{dR}{dt} &= \psi S + \delta I - \mu_4 R + u_1 S(t) + u_1 S(t)
\end{aligned} \tag{5}$$

with the initial conditions

$S \geq 0,\ I_c \geq 0,\ I \geq 0,\ R \geq 0$

The objective functional is defined as

$$C(u_1, u_2) = \int_0^{t_f}\left(C_1 I_c + C_2 I + C_3\frac{u_1^2}{2} + C_4\frac{u_2^2}{2}\right)dt$$

The goal here is to minimize the total number of carriers and infected individuals and the cost associated with the use of educational campaign and vaccination on $[0, t_t]$

$$C(u_1^*, u_2^*) = \min_{(u_1, u_2)}\int_0^{t_f}\left(C_1 I_c + C_2 I + C_3\frac{u_1^2}{2} + C_4\frac{u_2^2}{2}\right)dt$$

In formulation the optimal problem we consider

$0 \leq u_1^*(t) \leq 1 \quad and \quad 0 \leq u_2^*(t) \ \left| t \in [0, t_t]\right.$.

to minimize $C(u_1^*, u_2^*) = \int_0^{t_f} \left(C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2} \right) dt$

subject to the system in (5) where $u_1(t)$ and $u_2(t)$ are measurable function such that the control constrains is given by

$$U = \{(u_1^*(t), u_2^*(t) \,|\, 0 \le u_1^*(t) \le 1,$$
$$0 \le u_2^*(t) \le 1, t \in [0, t_t]\}.$$

The goal here is to minimize the total number of infected individuals and the cost associated with the use of educational campaign and vaccination of the entire population with the given initial population of all the classes $S(0)$, $I_c(t)$, $I(t), R(t)$ and $C_1 I_c$ from the objective function denote the total number of individuals who are infected but do not show any sign of infection and are infectious and is taken as a measure of death associated with epidemic. $C_2 I$ denote the total number of individuals who have been infected and is taken as a function of death associated with the outbreak. $C_3 \frac{u_1^2}{2}$ represent the cost associated with an educational campaign and $C_4 \frac{u_2^2}{2}$ represent the cost associated with vaccination.

3.1. Existence and Uniqueness of the Control System

Theorem 2

Suppose the objective functional $C(u_1^*, u_2^*) = \int_0^{t_f} \left(C_1 I_c + C_2 I + C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2} \right) dt$

where

$$\{(u_1^*(t), u_2^*(t) \,|\, 0 \le u_1^*(t) \le 1, 0 \le u_2^*(t) \le 1,$$
$$t \in [0, t_t] \in R^+\}$$

there exist an optimal control

$$u^* = (u_1^*, u_2^*)$$

such that

$$\min_{u_1, u_2 \in u} C(u_1, u_2) = C(u_1^*, u_2^*)$$

subject to the control system in (1).

Proof

To prove the existence of an optimal control pair we use the result in [29]. The control and the state variables are non-negative values and are non-empty. In the minimization problem, the necessary convexity of the objective functional in u_1 is satisfied. The control variable u_1, u_2 ∈ U is also convex and closed by definition. The optimal system is bounded which determines compactness needed for the existence of the optimal control. Furthermore, the integrand in the objective functional which is $C_3 \frac{u_1^2}{2} + C_4 \frac{u_2^2}{2}$ is convex on the control set U. There exists constants b_1, $b_2 >$ 0 and β $>$ 1 such that the integrand of the objective functional J is convex and satisfies

$$J(u_1, u_2) \geq b_1 \left(\left| \frac{u_1^2}{2} \right|^2 + \left| \frac{u_2^2}{2} \right|^2 \right)^{\frac{\beta}{2}} - b_2$$

By standard control arguments involving the bounds on the control, we conclude

$$u_1^* = \begin{cases} 0 & if \quad \frac{\lambda_s - \lambda_R}{C_3} \leq 0 \\ \frac{\lambda_s - \lambda_R}{C_3} & if \;\; 0 < \frac{\lambda_s - \lambda_R}{C_3} < 1 \\ 1 & if \quad \frac{\lambda_s - \lambda_R}{C_3} \geq 1 \end{cases} , \qquad u_1^* = \begin{cases} 0 & if \quad \frac{\lambda_I - \lambda_R}{C_4} \leq 0 \\ \frac{\lambda_I - \lambda_R}{C_4} & if \;\; 0 < \frac{\lambda_I - \lambda_R}{C_4} < 1 \\ 1 & if \quad \frac{\lambda_I - \lambda_R}{C_4} \geq 1 \end{cases}$$

3.2 Necessary conditions of the control

By using Pontryagin's Maximum Principle. Pontryagin's et.al, [30], we give the minimized pointwise Hamiltonian as follows which converts system (1) and (5) objective function into an optimal problem, minimizing pointwise Hamiltonian H with respect to u_1 and u_2.

Theorem 3

There exist an optimal control u_1^* and u_2^* corresponding solution S(t), I_c(t), I(t) and R(t) which minimizes $C(u_1,u_2)$ over U. Furthermore, there exist adjoint variables $J(u_1,u_2)$ satisfying

$$H(S,I_c,I,R)=(C_1I_c+C_2I+C_3\frac{u_1^2}{2}+C_4\frac{u_2^2}{2})+\lambda_1\big(\theta-\mu_1S-S(\beta I_c+\gamma I)(1-\phi)-\psi S-u_1S(t)\big)$$
$$+\lambda_2\big(\rho S(\beta I_c+\gamma I)(1-\phi)-\mu_2I_c-\alpha(1-\phi)I_c\big)+\lambda_3\begin{pmatrix}(1-\rho)(1-\phi)S(\beta I_c+\gamma I)+\\ \alpha(1-\phi)I_c-(\mu_3+\delta)I-u_2I(t)\end{pmatrix}$$
$$+\lambda_4\big(\psi S+\delta I-\mu_4R+u_1S(t)+u_2I(t)\big)$$

We now differentiate the Hamiltonian withrespect to each state variables

$$\frac{d\lambda_1}{dt}=-\frac{dH}{dS}=-\lambda_1\big(-\mu_1-(\beta I_c+\gamma I)(1-\varphi)-\psi-u_1\big)-\lambda_2\big(\rho(\beta I_c+\gamma I)(1-\varphi)\big)-\lambda_3\big((1-\rho)(1-\varphi)(\beta I_c+\gamma I)\big)-\lambda_4\left(\psi+u_1\right)$$
$$\frac{d\lambda_2}{dt}=-\frac{dH}{dI_c}=-\lambda_1\big(-S\beta(1-\phi)\big)-\lambda_2\big(\rho S\beta(1-\phi)-\mu_2-\alpha(1-\phi)\big)-\lambda_3\big((1-\rho)(1-\phi)S\beta+\alpha(1-\phi)\big)-C_1$$
$$\frac{d\lambda_3}{dt}=-\frac{dH}{dI}=-\lambda_1\big(-S\gamma(1-\phi)\big)-\lambda_2\big(\rho S\gamma(1-\phi)\big)-\lambda_3\big((1-\rho)(1-\phi)S\gamma-(u_2+\mu_3+\delta)\big)$$
$$-\lambda_4(\delta+u_2)-C_2$$
$$\frac{d\lambda_4}{dt}=-\frac{dH}{dR}=\lambda_4\mu_4$$

with the transversality conditions

$$\lambda_s(t_f),\lambda_{I_c}(t_f),\lambda_I(t_f),\lambda_R(t_f)=0$$

To find the optimal u_1^* and u_2^*, we use the following partial differential equations $\frac{\partial H}{\partial u_i}=0$

At $u_i=u_i^*$ where i=1, 2

$$\frac{\partial H(S,I_c,I,R)}{\partial u_1}=C_3u_1+\lambda_1(-S)+\lambda_4(S)=0$$
$$\therefore u_1^*=\frac{(\lambda_1-\lambda_4)S}{C_3}$$
$$\frac{\partial H(S,I_c,I,R)}{\partial u_2}=C_4u_2+\lambda_3(-I)+\lambda_4(I)=0$$
$$\therefore u_2^*=\frac{(\lambda_3-\lambda_4)S}{C_4}$$

Therefore,

$$u_1^*=\max\left\{0,\min\left(1,\frac{(\lambda_1-\lambda_4)S}{C_3}\right)\right\}$$

$$u_2^* = \max\left\{0, \min\left(1, \frac{(\lambda_3 - \lambda_4)I}{C_4}\right)\right\}$$

4. NUMERICAL SIMULATIONS OF THE OPTIMAL CONTROL ANALYSIS

Here, we provide the numerical simulations of the model in (5) which describes the theoretical results and predict the evolution of typhoid fever in the population and the dynamical behaviour of the model is studied. We use the forward-backwards sweep method and solved the optimality system numerically. The simulation was carried out by using the values in table 1 and the following initial vales for the simulation of the optimal control. S(0)=60, $I_c(0)$=40, I(0),20, R(0)=10, C_1=1, C_2=1.5, C3=1.5, C_4=0.02.

Table 1: Parameter values of the model

Parameter	Initial Value	Source
μ_2	0.2	Assumed
ψ	0.3	Assumed
μ_1	0.142	[16]
μ_3	0.2	Assumed
μ_4	0.142	[16]
α	0.3	Assumed
ρ	0.5	Assumed
β	0.02	Assumed
γ	0.01	[16]
δ	0.75	Assumed
ϕ	0.3	Estimated
θ	10^6	[30]

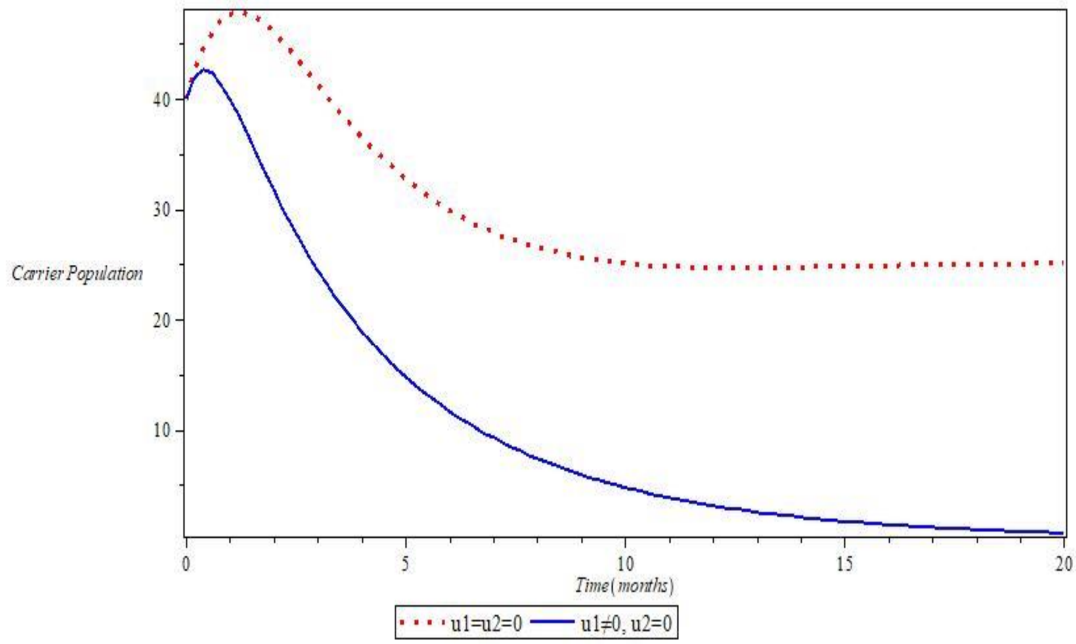

FIGURE 1: Simulation Result Showing Effect of Using Optimal Vaccination as the Only Control Strategies on Carriers Population

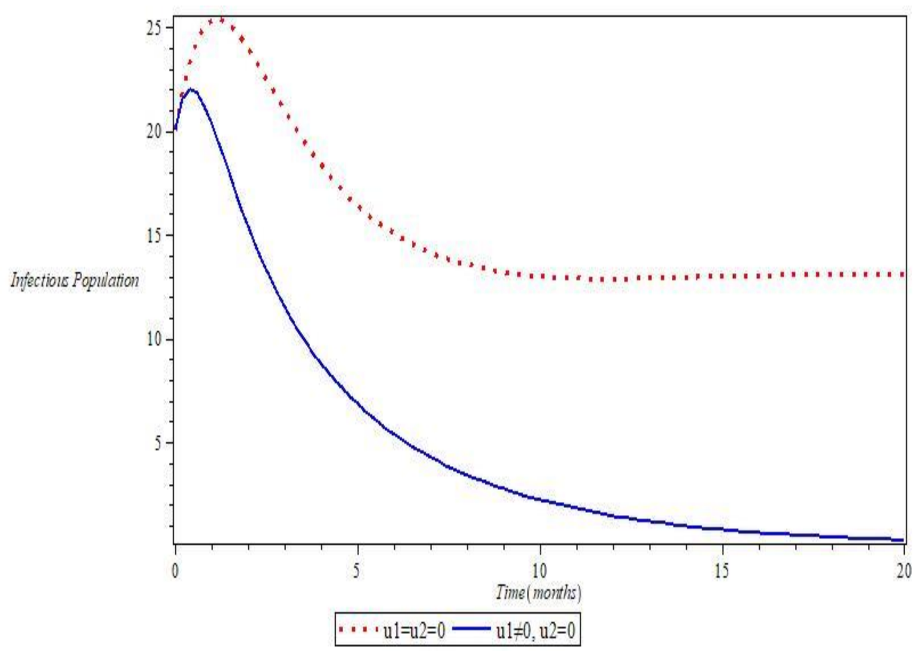

FIGURE 2: Simulation Result Showing Effect of Using Optimal Vaccination as the Only Control Strategies on Infectious Population

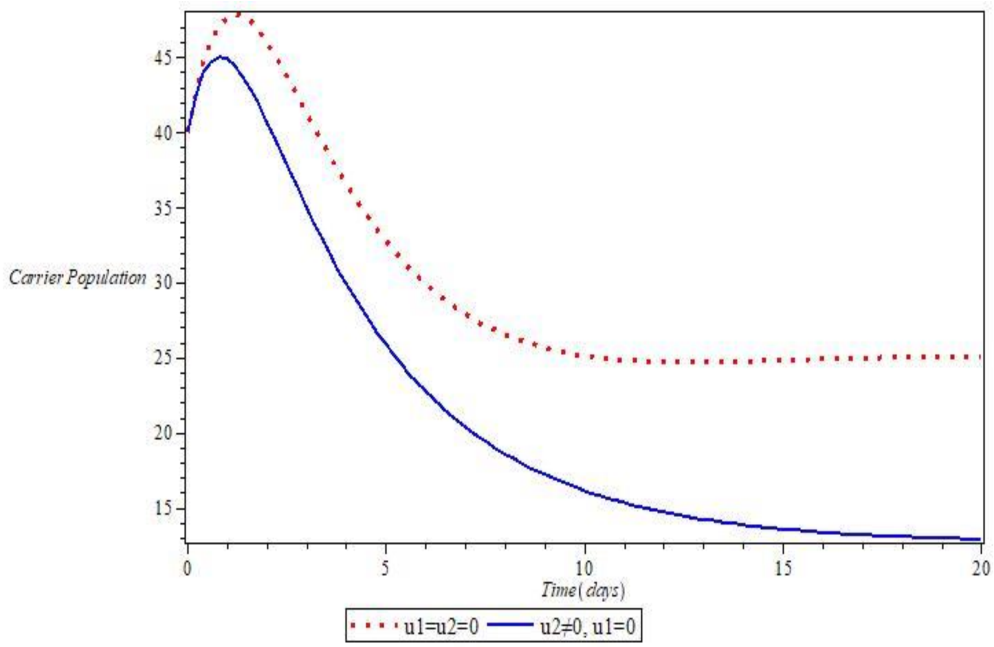

FIGURE 3: Simulation Result Showing Effect of Using Optimal Educational Campaign as the Only Control Strategies on Carriers Population

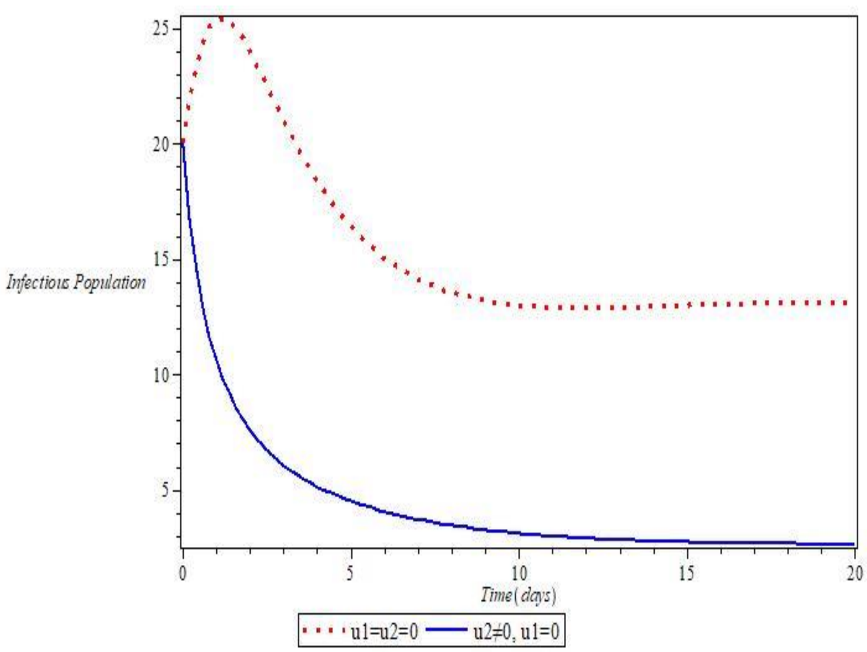

FIGURE 4: Simulation Result Showing Effect of Using Optimal Educational Campaign as the Only Control Strategies on Infected Population

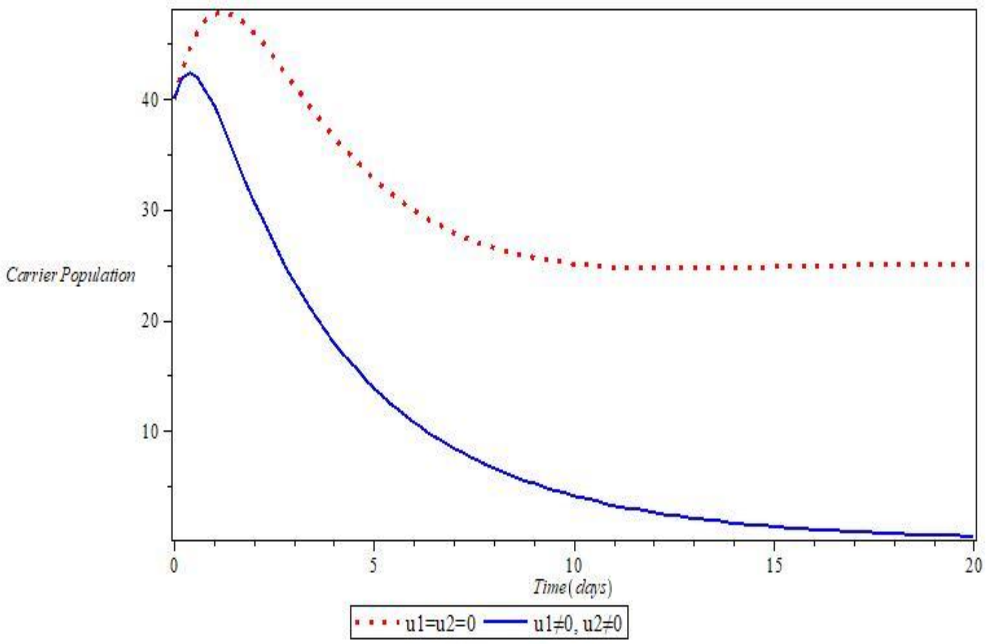

FIGURE 5: Simulation Result Showing Effect of Using Optimal Vaccination and Educational Campaign on Carriers Population

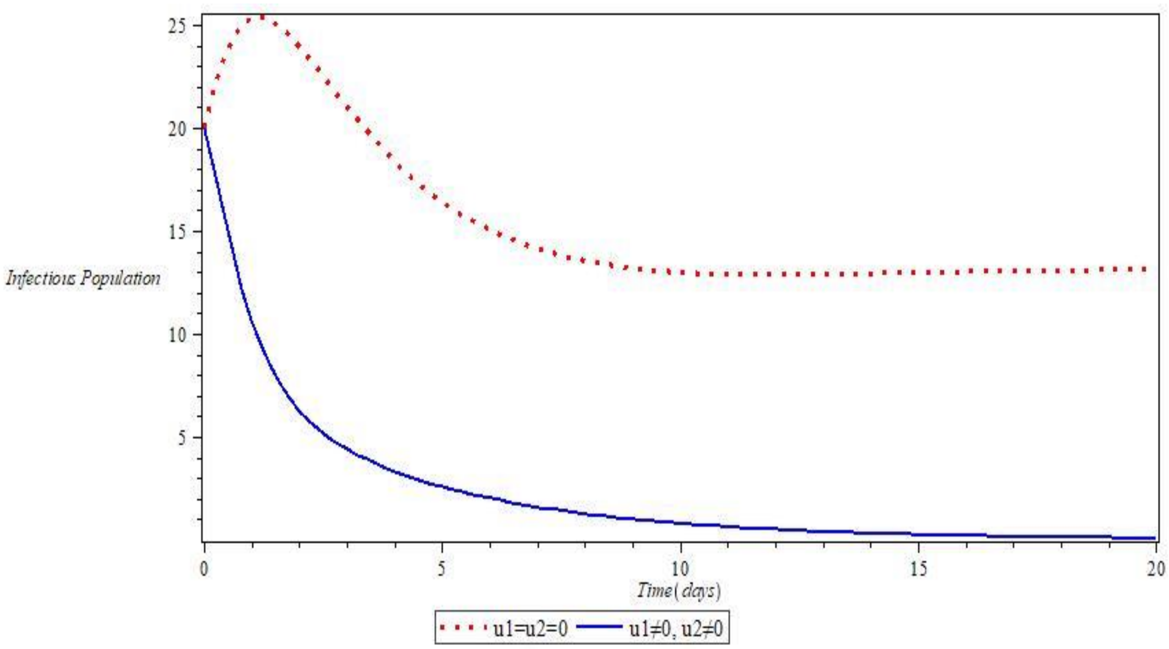

FIGURE 6: Simulation Result Showing Effect of Using Optimal Vaccination and Educational Campaign on Infectious Population

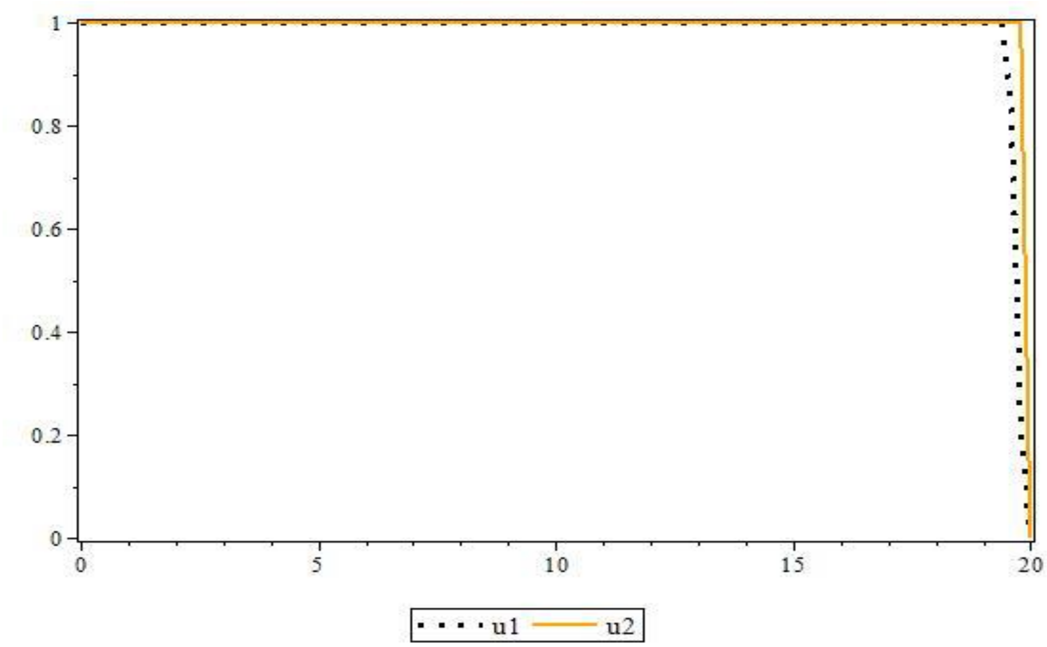

FIGURE 7: Control Profiles for u_1 and u_2

5. Discussion of Results

In figure 1 and 2 when a single intervention strategy is implemented that is, vaccination, there is a decrease in the population of the infected carrier and the infected individuals. Also when [[[vaccination is intensified to bring the disease under control there is a noticeable decrease in the population of the infected individuals and the infected carrier individuals. The implication of this is that vaccination timing, efficacy and coverage must be high enough before it can have a desirable impact on typhoid propagation and eradication.

In figure 3 and 4 when an educational campaign is implemented as a single intervention the population of infected carrier individuals and infected individuals fall continuously. The implication of this is that education campaign as a control strategy has more influence in reducing the population of both the infected individuals and the infected carrier individuals

In figure 5 and 6 when both interventions, vaccination and education campaign are implemented at an optimum level the population of the infected individuals and infected carrier individuals falls rapidly. Figure 7 shows the control profile, that is, the effectiveness of the two controls when combined together.

In all, each of the interventions is capable of influencing typhoid outbreak but the combination of the two strategies that is, vaccination and educational campaign are more efficient in limiting the spread and propagation of the disease and should be implemented in every typhoid prone community.

6. CONCLUSION

We showed that the model is mathematically and epidemiologically well positioned in a biologically feasible region in human populations. We also carried out a detailed analysis to determine the basic reproduction number R_0 necessary for the control of the disease. The optimal control strategies are used to minimize the infected carriers and infected individuals and the adverse side effects of one or more of the control strategies. In order to achieve control of the disease. The study concluded that possible optimal control strategies become more effective in the control and elimination of typhoid fever when vaccination and educational campaign are combined. It is therefore recommended that any measure directed towards achieving typhoid fever-free society should include vaccination and educational campaign.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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