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Stability Analysis and Optimal Control for Spreading Typhoid Fever Model with Direct and Indirect Transmissions

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ABSTRACT

This article discusses a model of spreading typhoid fever with direct and indirect transmissions. There are five compartments included in the model, namely susceptible individuals, infected individuals, chronic carrier individuals, recovered individuals, and salmonella typhi bacteria in the environment. As an effort to control and minimize the numbers of infected individuals and chronic carrier individuals, we introduce simultaneously campaign for the susceptible individuals and treatment for the infected individuals and for chronic carrier individuals. The resulting model is a system of non-linear differential equations and quite challenging to analysis globally. Existence of both disease-free equilibrium point and endemic equilibrium point are analysed analytically. Stability of the equilibrium point is analysed locally by determining the eigenvalues of the associated Jacobian matrix, Routh-Hurwitz stability criteria, and basic reproduction number (R_0) via next generation matrix. The minimum Pontryagin principle and Hamiltonian equation are referred to minimize the numbers of infected and chronic carrier individuals. Simulation is carried out using suitable values of parameters. We found that the eigenvalues for endemic equilibrium point are all negative real numbers and $R_0 > 1$. Optimal paths for the state and constate variables are plotted using fourth order forward-backward Runge-Kutta method. In case there are no campaign and treatments, we found $R_0 > 1$ and endemic occurs. When campaign and treatments are included together in the model, we found optimal paths for all compartments that minimize the number of infected and chronic carrier individuals. Giving campaign and treatments increase significantly the susceptible and recovered individuals. At the same time, it reduces significantly the infected, chronic carrier individuals, and salmonella typhi bacteria in the environment. Involving campaign and treatment in the model of spreading typhoid fever can be considered as an effective strategy to minimize the numbers of infected and chronic carrier individuals.

Keywords:
Typhoid fever; health campaign; treatment; optimal control; minimum pontryagin principle; forward-backward sweep

1. Introduction

The prevention and spread of both infectious and non-infectious diseases are still being carried out and remain a concern in the health sector. Some of the diseases that are still of concern on a

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global scale are kidney disease, breast cancer, covid-19, and meningitis [1-4]. In addition to studying the mechanism of disease spread, researchers have also considered various factors as an effort to prevent or inhibit the spread of disease, including vaccination, fogging, treatments, and the like. Wiraningsih, *et al.,* [5] used vaccination and treatment for humans and dogs as an attempt to inhibit and prevent the spread of the disease. A variant of the SIR model has been used by considering various factors such as migration, vaccination, and insecticide spraying as the effort to prevent the spread of malaria [6]. A developed SEIR model has been used to analyze the spread of hepatitis through vaccination and treatment [7]. Mathematical models, as tools and methods that provide a simple analysis, have become an alternative used by many researchers in the study and understanding the spread of infectious diseases.

Typhoid fever is an infectious disease commonly suffered by children caused by Salmonella typhi bacteria [8, 9]. Typhoid symptoms include high fever, weakness, abdominal pain, dizziness, loss of appetite, and rashes on the body [10]. Typhoid fever usually takes 7-14 days to manifest in an infected person. Humans become a place for these bacteria to live and reproduce naturally, and as a place of life [10, 11]. The spread of typhoid fever can occur directly from one individual to another. The spread of typhoid fever can also occur indirectly through the consumption of food or water contaminated by Salmonella typhi bacteria [12, 13]. The World Health Organization (WHO) reported in 2018 that typhoid fever is still widely found in several developing countries. Annually, about 21 million cases and 220,000 deaths worldwide are caused by typhoid, and the pathogen is estimated to cause 9.8 to 13.9 million cases. Most cases occur in South Asia, Southeast Asia, and sub-Saharan Africa, where poor sanitation and inadequate clean water supply are found [14].

Typhoid patients are usually given antibiotic treatment and will improve over the next few days. However, in worse cases, infected patients without proper treatment may develop complications resulting in death [15, 16]. Typhoid fever is a complex problem because it can be a chronic carrier, relapse, or drug resistance, which complicates treatment and prevention efforts. Not all treated patients become completely cured, but there are about 4% of patients who have the potential to become chronic carriers. These patients remain asymptomatic after acute treatment and can excrete Salmonella typhi bacteria for up to one year through feces and urine [17]. Typhoid should be treated quickly and thoroughly, as it can become more serious if not treated promptly. Proper treatment can reduce the patient's chances of becoming a chronic carrier. Therapeutic antimicrobials such as ceftriaxone and floroqinolone are more effective than chloramphenicol [11].

Mathematical models have been widely used in the field of epidemiology to study the mechanism of disease spread as well as a method to make quantitative predictions and control measures [18]. Mathematical models of the spread of typhoid fever have been developed from various perspectives which are taken from the previous studies [19-21]. The direct spread of typhoid disease and its indirect spread have also received attention which are taken from the previous studies [21, 22]. In this study, the direct and indirect spread of typhoid disease is further developed by adding chronic carriers as a compartment and further considering treatment for the infected compartment, treatment for the chronic carrier compartment, and a health campaign as a control. In the model formed, the endemic and disease-free equilibrium points and the basic reproduction number are determined and analyzed. Furthermore, numerical simulations were conducted to determine the effectiveness of providing control as an effort to reduce the spread of typhoid fever.

2. Methodology

The research conducted by the authors in [13] and [21] on the typhoid spread model both direct and indirect spread was developed by adding a chronic carrier compartment. Some disease spread

models have considered chronic carrier as a separate compartment which are taken from the previous studies [19-20]. With the addition of the compartment, the constructed model includes five compartments, namely the susceptible individual compartment (*S*), infected individuals (*I*), chronic carrier individuals (*C*), recovered individuals, and Salmonella typhi bacteria in the environment (*B*). This model includes human populations and bacterial populations and their interactions in the spread of typhoid fever. To inhibit and control the spread of typhoid disease, treatment and campaign about the importance of health are involved in the model as controls. Typhoid fever is transmitted from bacteria to the environment through food or water contaminated with Salmonella typhi bacteria. Typhoid fever can also be transmitted directly through person-to-person contact.

In this study, the spread is divided into two parts, namely direct transmission and indirect transmission. Direct transmission is through contact from person to person (direct transmission) with a rate of $\beta_1 I + \beta_2 C$, and indirect transmission is by consuming food or drinks that have been contaminated with Salmonella thypi bacteria (indirect transmission) with a rate of $\beta_3 B$. The constant β_1 is the rate of infection due to contact with the population (I), β_2 is the rate of infection due to contact with the population (*C*), and β_3 is the rate of individuals consuming food and drinks contaminated with Salmonella typhi bacteria (B). It is assumed that the natural mortality rate in each sub-population is the same at μ. Death due to disease only occurs in infected individuals by δ. The rate of transfer of infected individuals into chronic carrier individuals is to θ and ρ is the treatment rate of chronic carrier individuals, while α is the treatment rate of infected individuals. Since the chronic carrier individual (*C*) can excrete bacteria for up to two years, the rate of removal of bacteria to the environment η_1 by the chronic carrier individual (*C*) is greater than the rate of removal of bacteria to the environment η_2 by the infected individual (*I*) so that $\eta_1 > \eta_2$. The natural death rate of Salmonella typhi bacteria in the environment is μ_b.

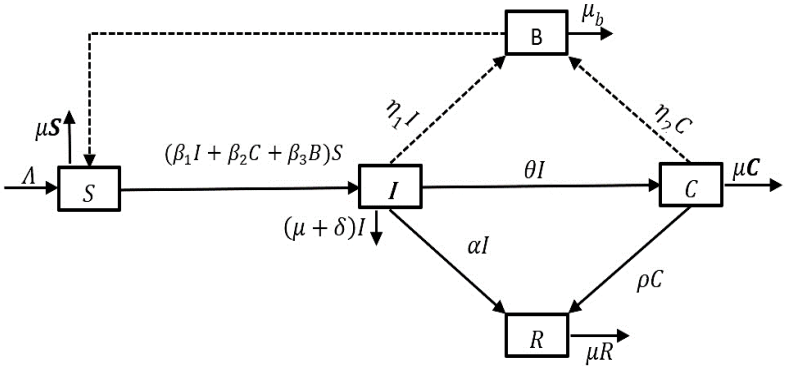


Fig. 1. Flow diagram of the spread of typhoid fever

Based on the above assumptions and the typhoid fever disease spread diagram in Figure 1, the rate of change for each compartment is mathematically expressed in the form of a system of non-linear differential equations as follow:

$$\frac{dS}{dt} = \Lambda - (\beta_1 I + \beta_2 C + \beta_3 B)S - \mu S \quad (1)$$

$$\frac{dI}{dt} = (\beta_1 I + \beta_2 C + \beta_3 B)S - (\alpha + \theta + \eta_1 + \mu + \delta)I \quad (2)$$

$$\frac{dC}{dt} = \theta I - (\rho + \eta_2 + \mu)C \quad (3)$$

$$\frac{dR}{dt} = \alpha I + \rho C - \mu R \tag{4}$$

$$\frac{dB}{dt} = \eta_1 I + \eta_2 C - \mu_b B \tag{5}$$

3. Results

3.1 Basic Reproduction Number

Let $\dot{\boldsymbol{x}} = (I \;\; C \;\; B)^T$ be a matrix whose entries are the compartment of infected individuals. By using the next generation matrix principle, we obtain $\dot{\boldsymbol{x}} = f(\boldsymbol{x}) - v(\boldsymbol{x})$, where:

$$f(\boldsymbol{x}) = \begin{pmatrix} (\beta_1 I + \beta_2 C + \beta_3 B)S \\ 0 \\ 0 \end{pmatrix} \text{ and } v(\boldsymbol{x}) = \begin{pmatrix} L_1 I \\ L_2 C - \theta I \\ \mu_b B - \eta_1 I - \eta_2 C \end{pmatrix} \tag{6}$$

with $L_1 = \alpha + \theta + \eta_1 + \mu + \delta$ and $L_2 = \rho + \eta_2 + \mu$.

The Jacobian matrix for $f(x)$ and $v(x)$ evaluated at the disease-free equilibrium point $\left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right)$ are:

$$F = \begin{pmatrix} \beta_1 \frac{\Lambda}{\mu} & \beta_2 \frac{\Lambda}{\mu} & \beta_3 \frac{\Lambda}{\mu} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} L_1 & 0 & 0 \\ -\theta & L_2 & 0 \\ -\eta_1 & -\eta_2 & \mu_b \end{pmatrix} \tag{7}$$

The inverse of matrix V is:

$$V^{-1} = \begin{pmatrix} \frac{1}{L_1} & 0 & 0 \\ \frac{\theta}{L_1 L_2} & \frac{1}{L_2} & 0 \\ \frac{L_1\eta_1 + \theta\eta_2}{L_1 L_2 \mu_b} & \frac{\eta_2}{L_2 \mu_b} & \frac{1}{\mu_b} \end{pmatrix} \tag{8}$$

From which we have:

$$\det(FV^{-1} - \lambda I) = \begin{vmatrix} \frac{\Lambda\beta_1}{\mu L_1} + \frac{\Lambda\beta_2\theta}{\mu L_1 L_2} + \frac{\beta_3\Lambda(\theta\eta_2 + L_2\eta_1)}{\mu L_1 L_2 \mu_b} - \lambda & \frac{\beta_2\Lambda}{\mu L_2} + \frac{\beta_3\Lambda\eta_2}{\mu L_2\mu_b} & \frac{\beta_3\Lambda}{\mu\mu_b} \\ 0 & 0 - \lambda & 0 \\ 0 & 0 & 0 - \lambda \end{vmatrix} \tag{9}$$

Because of the matrix above is a triangular, we have the characteristic equation

$$G(\lambda) = \lambda^2 \left(\frac{\Lambda\beta_1}{\mu L_1} + \frac{\Lambda\beta_2\theta}{\mu L_1 L_2} + \frac{\beta_3\Lambda(\theta\eta_2 + L_2\eta_1)}{\mu L_1 L_2 \mu_b} - \lambda \right) \tag{10}$$

The eigenvalues of $G(\lambda)$ are $\lambda_1 = \lambda_2 = 0$ and $\lambda_3 = \frac{\Lambda\beta_1}{\mu L_1} + \frac{\Lambda\beta_2\theta}{\mu L_1 L_2} + \frac{\beta_3\Lambda(\theta\eta_2 + L_2\eta_1)}{\mu L_1 L_2 \mu_b}$. Therefore, the basic reproduction number obtained from the spectral radius of the next generation matrix FV^{-1} is given by:

$$R_0 = R_m + R_b = \frac{\Lambda\beta_1}{\mu L_1} + \frac{\Lambda\beta_2\theta}{\mu L_1 L_2} + \frac{\beta_3\Lambda(\theta\eta_2 + L_2\eta_1)}{\mu L_1 L_2 \mu_b} \tag{11}$$

The term of $R_m = \frac{\Lambda\beta_1}{\mu L_1} + \frac{\Lambda\beta_2\theta}{\mu L_1 L_2}$ denotes a contribution from direct transmission, that is contact with infected individuals, while $R_b = \frac{\beta_3\Lambda(\theta\eta_2 + L_2\eta_1)}{\mu L_1 L_2 \mu_b}$ is a contribution from bacteria in the environment in the spread of typhoid fever.

3.2 Endemic and Disease-Free Equilibrium Points

The disease-free equilibrium point is a condition where the disease does not spread in the population. This condition occurs when $I = C = B = 0$. By substituting the values of $I = C = B = 0$ into Eq. (1)-(5) we get $R = 0$, and then from Eq. (1) we have $S = \frac{\Lambda}{\mu}$. Therefore, the disease-free equilibrium point is given by:

$$E^0 = (S^0,\ I^0,\ C^0,\ B^0,\ R^0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right) \tag{12}$$

The endemic equilibrium point is a condition where the disease spreads in the population. This condition occurs when $I^* > 0,\ C^* > 0\ , R^* > 0,$ and $B^* > 0$. Therefore, the endemic equilibrium points for model Eq. (1)-(5) is given by:

$$E^* = (S^*,\ I^*,\ C^*,\ R^*,\ B^*) \tag{13}$$

where $S^* = \frac{L_1\mu_b L_2}{M}$, $I^* = \frac{Q}{L_1 M}(R_0 - 1)$, $C^* = \frac{\theta I^*}{L_2}$, $R^* = \frac{1}{\mu}\left(\alpha + \frac{\rho\theta}{L_2}\right)I^*$, $B^* = \frac{1}{\mu_b}\left(\eta_1 + \frac{\eta_2\theta}{L_2}\right)I^*$. Therefore:

$$E^* = \left(\frac{L_1\mu_b L_2}{M}, \frac{Q}{L_1 M}(R_0 - 1), \frac{L_2\theta Q(R_0 - 1)}{L_1 M}, (\alpha L_2 + \rho\theta)\frac{\mu_b}{M}(R_0 - 1), (\eta_1 L_2 + \eta_2\theta)\frac{\mu}{M}(R_0 - 1)\right) \tag{14}$$

where $M = \mu_b L_2\beta_1 + \mu_b\beta_2\theta + L_2\beta_3\eta_1 + \eta_2\theta\beta_3$, $Q = \mu L_1\mu_b L_2$.

3.3 Stability Analysis of Equilibrium Points

Model Eq. (1)-(5) is a non-linear and quite challenging to analyse the global stability of equilibrium points. In this analysis we just consider local stability of the equilibrium points. By linearizing model Eq. (1)-(5) around the equilibrium point, we get the Jacobian matrix as follows:

$$J = \begin{bmatrix} -(\beta_1 I + \beta_2 C + \beta_3 B) - \mu & -\beta_1 S & -\beta_2 S & 0 & -\beta_3 S \\ \beta_1 I + \beta_2 C + \beta_3 B & \beta_1 S - L_1 & \beta_2 S & 0 & \beta_3 S \\ 0 & \theta & -L_2 & 0 & 0 \\ 0 & \alpha & \rho & -\mu & 0 \\ 0 & \eta_1 & \eta_2 & 0 & -\mu_b \end{bmatrix} \tag{15}$$

By evaluating the Jacobian matrix Eq. (15) at the disease-free equilibrium point E^0, we have the characteristic equation $f(\lambda) = det\left(\lambda I - J(E^0)\right)$ as follows:

$$f(\lambda) = (\lambda + \mu)(\lambda + \mu)(\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3) \quad (16)$$

where:
$a_1 = L_2 + \mu_b - \beta_1 S^0 + L_1$
$a_2 = L_2\mu_b - (\beta_1 S^0 - L_1)L_2 - \beta_2 S^0\theta - (\beta_1 S^0 - L_1)\mu_b - \eta_1\beta_3 S^0$
$a_3 = \theta\eta_2\beta_3 S^0 - (\beta_1 S^0 - L_1)\mu_b L_2 - \beta_2 S^0\theta\mu_b - \eta_1\beta_3 S^0 L_2$

The two eigenvalues of Eq. (16) are $\lambda_1 = -\mu$ and $\lambda_2 = -\mu$, while the other three eigenvalues are the roots of the equation $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$.

In the case of $R_0 < 1$, i.e. $S^0\frac{\beta_1}{L_1} + S^0\frac{\beta_2\theta}{L_1L_2} + S^0\frac{\beta_3(\theta\eta_2 + L_2\eta_1)}{L_1L_2\mu_b} < 1$, it gives consequences $a_1, a_2, a_3 > 0$. Furthermore, the disease-free equilibrium point E^0 is stable when the Routh-Hurwitz stability criteria are satisfied, i.e. $a_1, a_2, a_3 > 0$ and $a_1a_2 - a_3 > 0$. These criteria result in all the real parts of eigenvalues of the associated Jacobian matrix are negative.

For the stability of endemic equilibrium point E^*, we have the related characteristic equation:

$$g(\lambda) = (\lambda + \mu)(\lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4) \quad (17)$$

where:
$b_1 = (B\beta_3 + C\beta_2 + I\beta_1 - \beta_1 S + \mu + L_1 + L_2 + \mu_b)$
$b_2 = \big((B\beta_3 + C\beta_2 + I\beta_1 - \beta_1 S + \mu + L_1 + L_2)\mu_b + (B\beta_3 + C\beta_2 + I\beta_1 - \beta_1 S + \mu + L_1)L_2 +$
$(B\beta_3 + C\beta_2 + I\beta_1 + \mu)L_1 - S(\mu\beta_1 + \theta\beta_2 + \beta_3\eta_1)\big)$
$b_3 = \big((B\beta_3 + C\beta_2 + I\beta_1 - \beta_1 S + \mu + L_1)L_2 + (B\beta_3 + C\beta_2 + I\beta_1)L_1 - S(\mu\beta_1 + \theta\beta_2)\big)\mu_b +$
$\Big(\big((B\beta_3 + C\beta_2 + I\beta_1 + \mu)L_1 - S(\mu\beta_1 + \beta_3\eta_1)\big)L_2 - \big((\theta\beta_2 + \beta_3\eta_1)\mu + \eta_2\beta_3\theta\big)S\Big)$
$b_4 = \Big(\big((B\beta_3 + C\beta_2 + I\beta_1 + \mu)L_1 - \beta_1 S\mu\big)L_2 - \beta_2 S\mu\theta\Big)\mu_b - \beta_3 S\mu(\theta\eta_2 + L_2\eta_1))$

Therefore, the endemic equilibrium point is locally asymptotically stable when $b_1, b_2, b_3, b_4 > 0$ and $b_1b_2b_3 - b_1^2b_4 - b_3^2 > 0$ are fulfilled.

3.4 Optimal Control Formulation

An optimal control is applied to model Eq. (1)-(5) to obtain the optimal trajectory for control variables. There are three control variables considered in the model, namely health campaign (u_1), treatment for infected individuals (u_2), and treatment for chronic carrier individuals (u_3). The control variable $u_i(t)$ is defined in the region $0 \le u_i(t) \le 1$, for $t \in [t_0, t_f]$ and $i = 1, 2, 3$. Starting time is $t_0 = 0$ and $t_f = 1$ is the end for controlling. The value of $u_1(t) = 0$ indicates that the health campaign is ineffective in reducing the infection rate and the value of $u_1(t) = 1$ indicates that the health campaign is highly effective in reducing the infection rate. The value of $u_2(t) = 0$ indicates that treatment for infected individuals is inefficient in reducing infected individuals (*I*) and the value of $u_2(t) = 1$ indicates that treatment for infected individuals is highly effective in reducing infected individuals (*I*). The value of $u_3(t) = 0$ indicates that treatment for chronic carrier (*C*) individuals is ineffective, while the value of $u_3(t) = 1$ indicates that treatment for chronic carrier (*C*) individuals is highly effective. Based on these assumptions, the control variables are defined in the domain of $U = \{(u_1(t), u_2(t), u_3(t)) |\, 0 \le u_i \le 1, \text{for } t \in [t_0, t_f], i = 1, 2, 3\}$.

To reduce the infection rate, the control variable of health campaign is imposed on the rate of change of susceptible compartment *S* and then the infection rate becomes $(\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1(t))S$. To reduce the number of infected individuals who become chronic carrier individuals, a control variable in the form of treatment for infected individuals is given and then the rate of entry of infected individuals into recovery individuals becomes $(\alpha + u_2(t))I$. To accelerate the recovered of chronic carrier individuals (*C*), the control variable in the form of treatment for chronic carrier individuals is given and then the rate of entry of chronic carriers into recovery individuals becomes $(\rho + u_3(t))C$. Thus, the system of Eq. (1)-(5) becomes:

$$\frac{dS}{dt} = \Lambda - (\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1)S - \mu S \tag{18}$$

$$\frac{dI}{dt} = (\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1)S - (\alpha + \theta + \eta_1 + \mu + \delta)I - u_2 I \tag{19}$$

$$\frac{dC}{dt} = \theta I - (\rho + \eta_2 + \mu)C - u_3 C \tag{20}$$

$$\frac{dR}{dt} = \alpha I + u_2 I + \rho C + u_3 C - \mu R \tag{21}$$

$$\frac{dB}{dt} = \eta_1 I + \eta_2 C - \mu_b B \tag{22}$$

The next step is to form an objective function that minimizes the number of infected individuals and the number of chronic carrier individuals, as well as the costs of health campaign and treatments. The objective function is given by:

$$J = \min_{(u_1, u_2, u_3)} \int_0^{t_f} \left(A_1 I + A_2 C + \frac{1}{2}(w_1 {u_1}^2 + w_2 {u_2}^2 + w_3 {u_3}^2) \right) dt \tag{23}$$

subject to the model Eq. (18)-(22).

The minimum Pontryagin principle is applied to get the solution of optimal control $u^*(t)$. The Hamiltonian equation is then formed as:

$$H(t, x, u, \lambda) = f(t, x, u) + \lambda^T(t) g(t, x, u) \tag{24}$$

where $x = (S \ I \ C \ R \ B)^T$ denotes the state variables, $\lambda = (\lambda_1 \ \lambda_2 \ \lambda_3 \ \lambda_4 \ \lambda_5)^T$ denotes the costate variable, and $f(t, x, u) = A_1 I + A_2 C + \frac{1}{2} w_1 {u_1}^2 + \frac{1}{2} w_2 {u_2}^2 + \frac{1}{2} w_3 {u_3}^2$. The Hamiltonian equation is then written as follows:

$$\begin{aligned} H = {} & A_1 I + A_2 C + \frac{1}{2} w_1 {u_1}^2 + \frac{1}{2} w_2 {u_2}^2 + \frac{1}{2} w_3 {u_3}^2 + \lambda_1(\Lambda - (\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1)S - \mu S) \\ & + \lambda_2\big((\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1)S - (\alpha + \theta + \eta_1 + \mu + \delta)I - u_2 I\big) + \lambda_3(\theta I - (\rho + n_2 \\ & \mu + \sigma)C - u_3 C) + \lambda_4(\alpha I + u_2 I + \rho C + u_3 C - \mu R) + \lambda_5(\eta_1 I + \eta_2 C - \mu_b B) \end{aligned} \tag{25}$$

In order to minimize the objective function Eq. (23), the necessary conditions $\dot{\boldsymbol{x}} = \frac{\partial H}{\partial \boldsymbol{\lambda}}$, $\dot{\boldsymbol{\lambda}} = -\frac{\partial H}{\partial \boldsymbol{x}}$, and $\frac{\partial H}{\partial \boldsymbol{u}} = 0$ must be satisfied. Further, we get:

$$\dot{\boldsymbol{x}} = \frac{\partial H}{\partial \boldsymbol{\lambda}} = \left(\frac{\partial H}{\partial \lambda_1} \;\; \frac{\partial H}{\partial \lambda_2} \;\; \frac{\partial H}{\partial \lambda_3} \;\; \frac{\partial H}{\partial \lambda_4} \;\; \frac{\partial H}{\partial \lambda_5}\right)^T \tag{26}$$

where:

$$\frac{\partial H}{\partial \lambda_1} = \Lambda - (\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1)S - \mu S \tag{27}$$

$$\frac{\partial H}{\partial \lambda_2} = (\beta_1 I + \beta_2 C + \beta_3 B)(1 - u_1)S - (\alpha + \theta + \eta_1 + \mu + \delta)I - u_2 I \tag{28}$$

$$\frac{\partial H}{\partial \lambda_3} = \theta I - (\rho + \eta_2 + \mu)C - u_3 C \tag{29}$$

$$\frac{\partial H}{\partial \lambda_4} = \alpha I + u_2 I + \rho C + u_3 C - \mu R \tag{30}$$

$$\frac{\partial H}{\partial \lambda_5} = \eta_1 I + \eta_2 C - \mu_b B \tag{31}$$

For the costate variables, we have:

$$\dot{\lambda} = -\frac{\partial H}{\partial \boldsymbol{x}}, \text{ i.e., } \left(\dot{\lambda}_1 \quad \dot{\lambda}_2 \quad \dot{\lambda}_3 \quad \dot{\lambda}_4 \;\; \dot{\lambda}_5\right)^T = \left(-\frac{\partial H}{\partial S} \quad -\frac{\partial H}{\partial I} \quad -\frac{\partial H}{\partial C} \quad -\frac{\partial H}{\partial R} \;\; -\frac{\partial H}{\partial B}\right)^T \tag{32}$$

where:

$\dot{\lambda}_1 = (\lambda_2 - \lambda_1)\beta_3 u_1 B + (\lambda_2 - \lambda_1)\beta_2 u_1 C + (\lambda_2 - \lambda_1)\beta_1 u_1 I + (\lambda_1 - \lambda_2)\beta_3 B + (\lambda_1 - \lambda_2)\beta_2 C + (\lambda_1 - \lambda_2)\beta_1 I + \mu\lambda_1$

$\dot{\lambda}_2 = (\lambda_2 - \lambda_1)\beta_1 u_1 S + (\lambda_1 - \lambda_2)\beta_1 S + (\lambda_2 - \lambda_4)\alpha + \lambda_2(\delta + \mu) + (\lambda_2 - \lambda_3)\theta + (\lambda_2 - \lambda_5)\eta_1 + (\lambda_2 - \lambda_4)u_2 - A_1$

$\dot{\lambda}_3 = (\lambda_2 - \lambda_1)\beta_2 u_1 S + (\lambda_1 - \lambda_2)\beta_2 S + \lambda_3\mu + (\lambda_3 - \lambda_4)\rho + (\lambda_3 - \lambda_5)\eta_2 + (\lambda_3 - \lambda_4)u_3 - A_2,$

$\dot{\lambda}_4 = \lambda_4\mu$

$\dot{\lambda}_5 = (\lambda_2 - \lambda_1)\beta_3 u_1 S + (\lambda_1 - \lambda_2)\beta_3 S + \lambda_5\mu_b$

For the control variables, we have $\frac{\partial H}{\partial \boldsymbol{u}} = \left(\frac{\partial H}{\partial u_1} \;\; \frac{\partial H}{\partial u_2} \;\; \frac{\partial H}{\partial u_3}\right)^T = (0 \quad 0 \quad 0)^T$, where $u_1 = \frac{(\lambda_2 - \lambda_1)\beta_3 BS + (\lambda_2 - \lambda_1)\beta_2 CS + (\lambda_2 - \lambda_1)\beta_1 IS}{w_1}, u_2 = \frac{(\lambda_2 - \lambda_4)I}{w_2}$, and $u_3 = \frac{(\lambda_3 - \lambda_4)C}{w_3}$. The boundary conditions for the control variables are given by $0 \leq u_i \leq 1$. Further, the optimal controls for ${u_i}^*(t)$ are obtained as follows:

$${u_1}^*(t) = \min\left[1, max\left[0, \frac{(\lambda_2 - \lambda_1)\beta_3 BS + (\lambda_2 - \lambda_1)\beta_2 CS + (\lambda_2 - \lambda_1)\beta_1 IS}{w_1}\right]\right] \tag{33}$$

$${u_2}^*(t) = \min\left[1, max\left[0, \frac{(\lambda_2 - \lambda_4)I}{w_2}\right]\right] \tag{34}$$

$${u_3}^*(t) = \min\left[1, \max\left[0, \frac{(\lambda_3 - \lambda_4)C}{w_3}\right]\right] \tag{35}$$

4. Numerical Simulation

The parameter values with suitable units used in the simulation are given in Table 1.

Table 1
Parameter values used for the model

Parameter	Description	Value	References
$\boldsymbol{\Lambda}$	Human birth rate	100	[23]
$\boldsymbol{\mu}$	Natural death rate in humans	0.0005	[23]
$\boldsymbol{\beta_1}$	The rate of infection from compartment (I) to compartment (S)	0.02	[13]
$\boldsymbol{\beta_2}$	The rate of infection from compartment (C) to compartment (S)	0.0001	Assumed
$\boldsymbol{\beta_3}$	The rate of individuals consuming food and drinks contaminated with salmonella thypi bacteria (B)	0.01	[13, 21]
$\boldsymbol{\alpha}$	Treatment rate of infected compartment (I)	0.002	[23]
$\boldsymbol{\rho}$	Treatment rate of chronic carrier compartment (C)	0.000315	[19]
$\boldsymbol{\theta}$	Rate of movement from compartment (I) to compartment (C) due to treatment failure	0.0004	[24]
$\boldsymbol{\delta}$	Death rate due to disease	0.002	[19, 25]
$\boldsymbol{\eta_1}$	Rate of removal of salmonella typhi bacteria from the compartment (I)	0.4	[13]
$\boldsymbol{\eta_2}$	Rate of removal of salmonella typhi bacteria from the compartment (C)	0.2	[13]
$\boldsymbol{\mu_b}$	Natural death rate of the Salmonella thypi bacteria compartment	0.3	Assumed

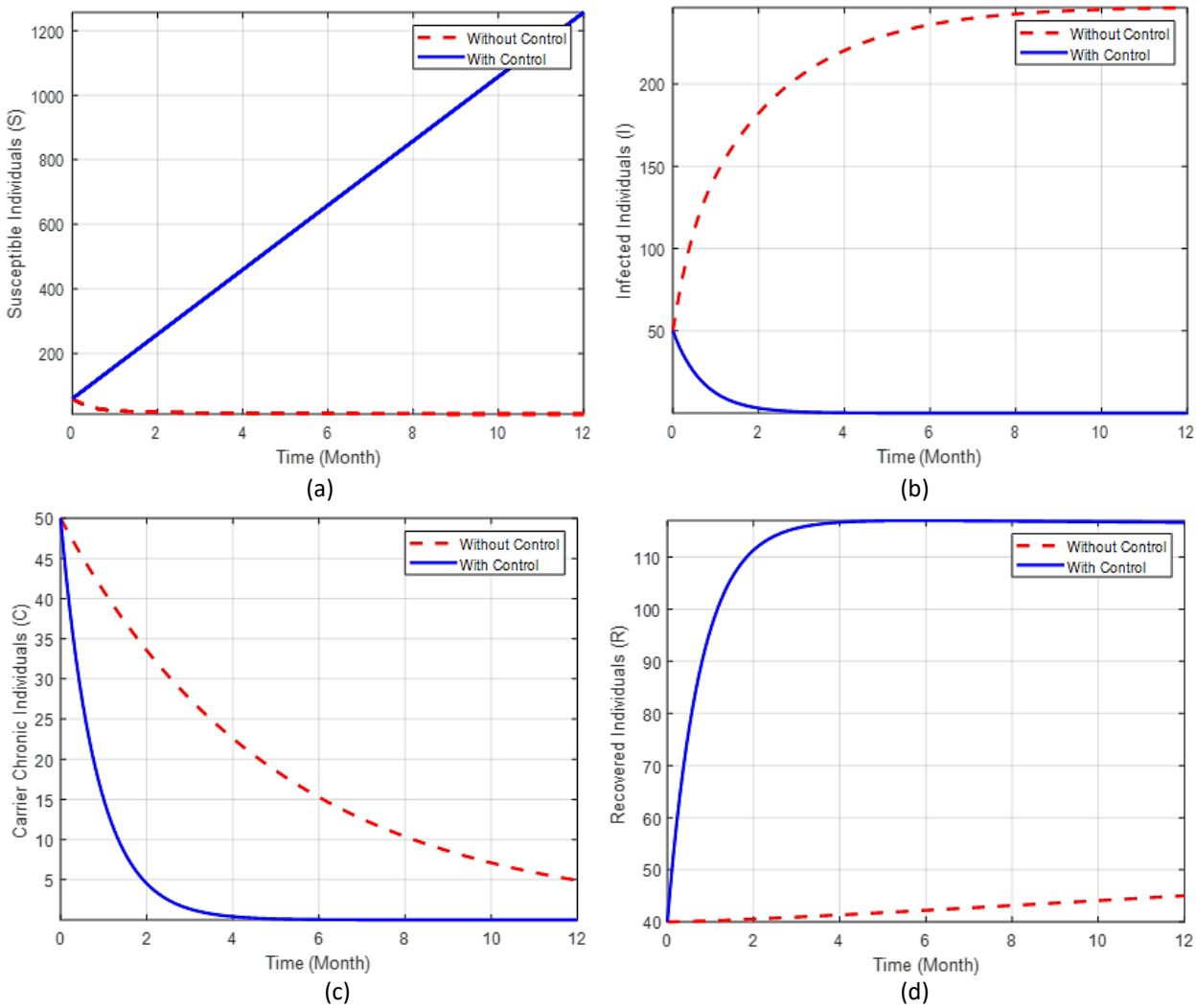
Model Eq. (18)-(22) with the parameter values given as in Table 1 without controls $(u_1 = u_2 = u_3 = 0)$ gives disease-free equilibrium point $E^0 = (20{,}000, 0, 0, 0, 0)$ and endemic equilibrium point $E^* = (12.1421, 246.9596, 0.4919, 988.1482, 329.7074)$. The eigenvalues associated with the disease-free equilibrium point are $\lambda_1 = -0.0005$, $\lambda_2 = -0.0005$, $\lambda_3 = -0.2009$, $\lambda_4 = -0.4998$, and $\lambda_5 = 3{,}999.7951$. The eigenvalues associated with the endemic equilibrium point are $\lambda_1 = -0.0005$, $\lambda_2 = -0.3209$, $\lambda_3 = -0.3209$, $\lambda_4 = -0.2008$, and $\lambda_5 = -7.9867$. The parameter values also give $R_m = 9{,}879$, $R_b = 6{,}592$. Thus, we have basic reproduction number $R_0 = 16{,}471$. From the basic reproduction number and eigenvalues, we know that the endemic equilibrium point becomes stable. This means that the numbers of infected individuals, chronic carrier individuals, and salmonella typhi bacteria are always positive.

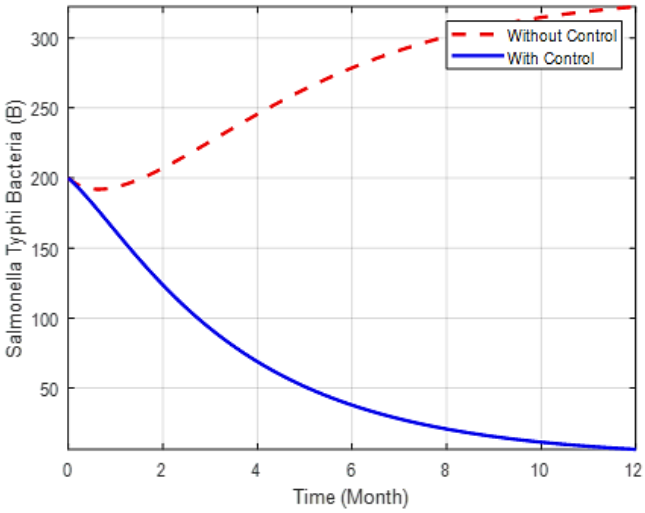
For simulation, the initial values for each compartment are given by $S(0) = 60$, $I(0) = 50$, $C(0) = 50$, $R(0) = 40$, and $B(0) = 200$. It is assumed that the controls carried out are limited, which $u_{1_{max}} = u_{2_{max}} = u_{3_{max}} = 1$ means that the controls can be applied up to 100%, whereas $u_{1_{min}} = u_{2_{min}} = u_{3_{min}} = 0$ means that the controls are completely ineffective. We apply individual weights given by $A_1 = A_2 = 50$ because the interests in minimizing each infected subpopulation are the same. The constant w_1 is the weight of costs for health campaign, w_2 is the weight of medical costs for infected individuals and w_3 is the weight of medical costs for chronic carrier individuals. The cost weights required for each control in controlling the spread of typhoid fever are given by $w_1 = 12$, $w_2 = 2$, and $w_3 = 2$. The fourth order Forward-Backward Sweep Runge-Kutta method is applied to plot the solution curves for compartments *S, I, C, R,* and *B* with and without control, as given in Figure 2.

Figure 2(a) shows that sustainable individual without controls decreasing as time goes. By applying controls, sustainable individuals significantly increase. Contrary in Figure 2(b), the infected individual without control increases while the infected individual with control decreases as time goes.

Figure 2(c) shows that, with and without controls, the chronic carrier individual decreases as time goes. Trajectory of chronic carrier individuals with controls decreases more quickly compared to the compartment without controls. Figure 2(d) shows that, with and without controls, the recovered individual increases. Trajectory of recovered individuals with controls more quickly increases compared with the trajectory without controls. Figure 2(e) shows that salmonella typhi bacteria without control increases while salmonella typhi bacteria without control decreases as time goes.

Figures 2(b), 2(c), and 2(e) show that by implementing controls in the form of health campaign (u_1), treatment of infected individuals (u_2), and treatment of chronic carrier individuals (u_3), the number of infected individuals (I), chronic carrier individuals (C), and Salmonella typhi bacteria decrease from the beginning of the observation to the end of the observation. Figures 2(a) and 2(d) show that the number of susceptible individuals (S) and recovered individuals (R) increase from the beginning of the observation to the end of the observation. From the simulations we know that providing health campaigns (u_1) can reduce the occurrence new infections, while treatment of infected individuals (u_2) can reduce infected individuals (I) and treatment of chronic carrier individuals (u_3) can reduce the number of chronic carrier individuals (C). The control variables reduce effectively the level of salmonella typhi bacteria in the environment.

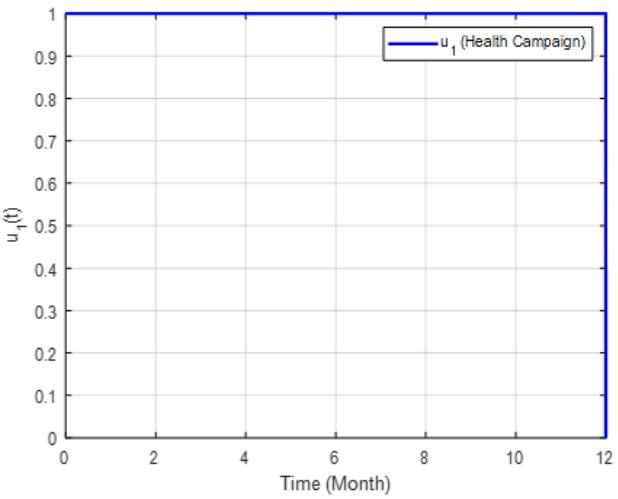




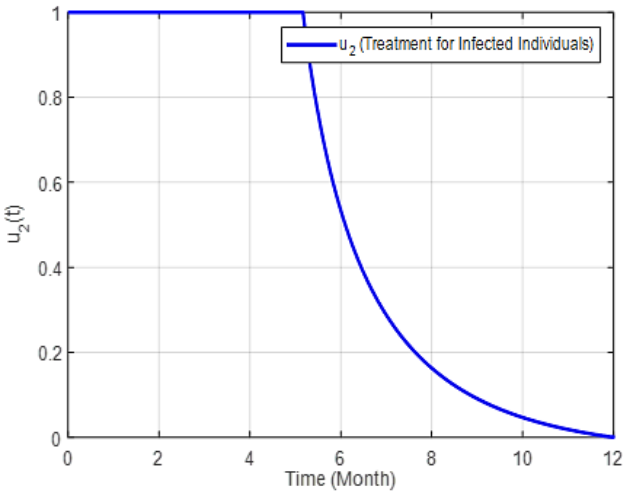
(e)

Fig. 2. Plots of trajectories with and without control (a) *S* (b) *I* (c) *C* (d) *R* (e) *B*

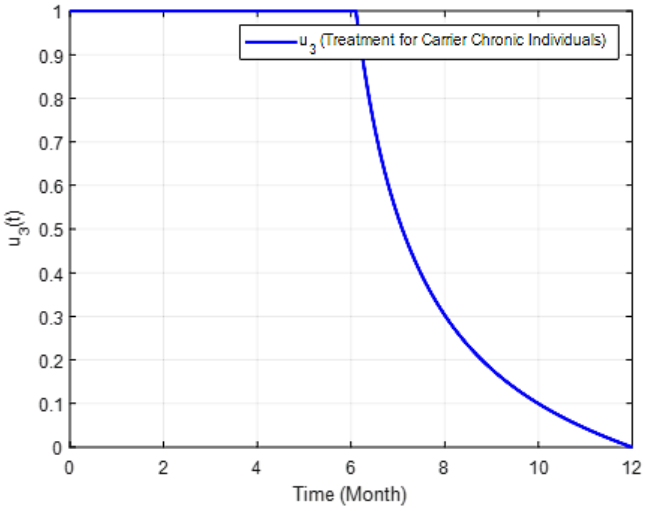
Figure 3(a) shows that the health campaign (u_1) must be applied maximally from the beginning of the observation until the end of the observation. Treatment for infected individuals (u_2) must be applied maximally from the beginning until the fifth month and in the following months the control (u_2) can be reduced slowly, Figure 3(b). The treatment for chronic carrier individuals (u_3) must be applied maximally from the beginning of observation until the sixth month of observation and then it can be reduced gradually until the end of observation, Figure 3(c).



(a)



(b)



(c)

Fig. 3. Trajectories for control variables (a) u_1 (b) u_2 (c) u_3

5. Conclusions

Model on spreading typhoid fever with direct and indirect transmissions and also without campaign and treatments results susceptible individuals decrease slowly, infected individuals increase rapidly, chronic carrier individuals decrease rapidly, recovered individuals increase slowly, and salmonella typhi bacteria increases rapidly. Simulation with parameter values as given in Table 1 gives disease-free equilibrium point $E^0 = (20{,}000, 0, 0, 0, 0)$ and endemic equilibrium point $E^* = (12.1421, 246.9596, 0.4919, 988.1482, 329.7074)$ with basic reproduction number $R_0 = 16{,}471$. Without providing campaign for the susceptible individuals and treatments for the infected individuals, endemic situation occurs in the population. The number of infected individuals grows rapidly and tends to the endemic equilibrium point.

By implementing campaign for the susceptible individuals, treatments for the infected individuals and for the chronic carrier individuals simultaneously, the minimum numbers of infected and chronic carrier individuals are obtained. These conditions are achieved when the campaign is applied effectively while treatments are initially given effectively and then gradually reduced, Figure 3. At the same time, the number of susceptible individuals become increasing. The number of infected individuals, chronic carrier individuals, and salmonella typhi bacteria decreases and then tends to zero. The number of recovered individuals increase rapidly. Giving campaign and treatments simultaneously as controls to the model of spreading typhoid fever with direct and indirect transmission reduce effectively the number of infected individuals, chronic carrier individuals, and salmonella typhi bacteria. This strategy maybe considered as an efective control to reduce transmission of typhoid fever in the population.

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