ANALYTICAL SOLUTION OF TYPHOID FEVER INFECTION VIA HOMOTOPY PERTURBATION METHOD (HPM)

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Abstract
In this paper, a deterministic mathematical model of typhoid fever infection was formulated with a control strategies. We find the analytical solution of the proposed model by Homotopy perturbation method which is one of the best method for finding the solution of the nonlinear problem to obtain the approximate solution of the model. The results are presented graphically and discussed. It is discovered that the epidemic is sustained in the population. Implications of these results indicate that treatment sustain the carrier infectives who in turn sustains the epidemic in the population in the long run.

Keywords: Homotopy Perturbation method, Typhoid fever, model, Simulations

Introduction

Typhoid is a major public health concern in tropical developing countries, especially in areas where access to clean water and other sanitation measures are limited (Crump & Mintz 2010; Mutua, Wang, & Vaidya, 2015; Pitzer et al, 2015). Typhoid fever has complex pathogenesis and manifests as an acute febrile disease, with relatively long incubation period that involves the transmigration of the microorganism through the Peyer's patch, localized multiplication in the mesenteric lymph nodes, and subsequent spread to the liver and spleen prior to showing clinical symptoms (Thompson et al, 2009). It is a serious life-threatening infection characterised by false diagnosis due to similar signs and symptoms with malaria, which leads to improper controls and management of the disease. Despite extensive work on typhoid, not much is understood on the biology of the human-adapted bacterial pathogen and the complexity of the disease in endemic areas, especially in Africa (Wain, et al,2015). Globally, the burden of the disease is estimated at 21 million cases and 222000 deaths annually with high rates reported among children and adolescents in South and Eastern Asia and uncertain in Africa (Date, Bentsi-Enchill, Marks, & Fox, 2015; Mogasale et al, 2014; Qamar, Azmatullah, & Bhutta, 2015). The symptoms are alleviated with antibiotic medications, however, aproportion of people treated for typhoid fever usually experience relapse, after a week of antibiotic treatment with symptoms which are milder and last for a shorter time compared with the original illness, requiring further treatment with antibiotics (Basnyat, 2007; Zaki, 2011). Typhoid fever maybe prevented using vaccines, even though repeated mass vaccinations at intervals of 5 years interval may reduce the disease incidence, small gains re-observed at each subsequent vaccination (Mushayabasa, Bhunu, & Mhlanga, 2014). The dynamics of typhoid fever involve multiple interactions between the human host, pathogen and environment, contributing to both direct human-to-human and indirect environment-to-human transmission pathways (Gonzalez-Guzman, 1989; Pitzer et al,2015). Typhoid fever produces long-term asymptomatic carriers which play a pivotal role in the disease transmission.

In order to gain in-depth understanding of the complex dynamics of typhoid fever a number of studies have been conducted and published. Cvjetanovic et al. (Mushayabasa, Bhunu, & Mhlanga, 2014). Constructed an epidemic model for typhoid fever in a stable population to study the transmission of infection at different levels of endemicity. Mushayabasa et al.

(Gonzalez-Guzman, 1989). Developed and analysed a deterministic mathematical model for assessment of the impact of treatment and educational campaigns on controlling typhoid out-break in Zimbabwe. Date et al. (Date, Bentsi-Enchill, Marks, & Fox, 2015). Reviewed various vaccination strategies using current typhoid vaccines to assess the rationale, acceptability, effectiveness, impact and implementation lessons in order to inform future public health typhoid control strategies. Watson and Edmunds (Mushayabasa, Bhunu, & Mhlanga, 2014). Carried out an intensive review of typhoid fever transmission dynamics models and economic evaluation of vaccination. Clinicians, microbiologists, modellers, and epidemiologists worldwide need full understanding and knowledge of typhoid fever to effectively control and manage the disease (Wain et al,2015).

The Homotopy Analysis Method is one of the well-known methods to solve the linear and non-linear equations. In the last decade, the idea of Homotopy was combined with perturbation. The fundamental work was done by (He 2000). This method involves a free parameter, whose suitable choice results into fast convergence. Homotopy Perturbation Method and its application was introduced by (He, 2000; He, 2006; He, 2008; He, 2009). These methods are independent of the assumption of small parameter as well as they cover all the advantages of the perturbation method. Mohammad *et al.,* (2014) developed a model of SIR by homotopy perturbation method (HPM), the models were solved by non-standard finite difference method (NSFD), Runge-Kutta order 4 (RK4) and compared the HPM solution with NSFD and RK4, it found that the HPM solution have a good agreement with other standard method of NSFD and RK4 (Muhammad, Syed, Sher, Saeed, & Farooq, 2014).

In this paper, we consider the model presented in (Moatlhodi, & Gosalamang, 2016) by applying the Homotopy perturbation method, to find the approximate solution. First, we formulate our problem and then apply the HPM to find the analytical solution.

Materials and Methods

Following (Moatlhodi, & Gosalamang, 2016), the equations describing typhoid fever epidemics are:

$$\frac{dS}{dt} = \Lambda - \frac{c\beta(I + k_1 I_c + k_2 T)}{N} S - \mu S \quad (1)$$

$$\frac{dI}{dt} = \frac{c\beta\rho(I + k_1 I_c + k_2 T)}{N} S + \alpha I_c - (\mu + \sigma + \delta_1) I \quad (2)$$

$$\frac{dI_c}{dt} = \frac{(1-\rho)c\beta(I + k_1 I_c + k_2 T)}{N} S + \tau T - (\mu + \alpha) I_c \quad (3)$$

$$\frac{dT}{dt} = \sigma I - (\mu + \gamma + \tau + \delta_2) T \quad (4)$$

$$\frac{dR}{dt} = \gamma T - \mu R \quad (5)$$

$$N(t) = S(t) + I(t) + I_c + T(t) + R(t) \quad (6)$$

As initial condition based on our assumptions, we choose

$$S(0) = a_0, I(0) = b_0, I_c(0) = c_0, T(0) = d_0, R(0) = e_0 \quad (7)$$

Where:

Variable	Parameters
$S(t)$ - Susceptible human	Λ - Recruitment rate
$I(t)$ -Infectives human	μ - per capital death rate
$I_c(t)$ - Carriers human	δ_1, δ_2 - Disease-induced deaths
$T(t)$ - Treated infectives	c - effective contacts
$R(t)$ - Recovered human	β - Rate of transmission
	α - Progression to symptomatic state
	γ - Rate of recovery from treatment
	ρ - New infections becoming carriers
	σ - Rate of treatment
	τ - Proportion of treated individuals
	k_1, k_2 - Modification parameters

Method of Solution

Solution of the Model Using Homotopy perturbation Method (HPM)

Homotopy perturbation method (HPM) was developed by [16]. The HPM provides solution to various linear and nonlinear differential equations. The basic ideas of the method are by considering the following nonlinear differential equation:

$$A(U) - f(r) = 0, r \in \Omega \quad (8)$$

With the boundary condition

$$B(u, \frac{\partial u}{\partial n}) = 0, \ r \in \Gamma \quad (9)$$

Where A is the general differential operator, B the boundary operator, $f(r)$ is the analytical function and Γ is the boundary of the domain Ω. The A operator can be divided into two major part L and N been the linear and nonlinear component respectively. Equation (8) can be writtenas follows:

$$L(u) + N(u) = f(r), \ r \in \Omega \quad (10)$$

The HPM is composed as follows:

$$H(V, h) = (1 - p)[L(V) - L(U_o)] + p[A(V) - f(r)] = 0 \quad (11)$$

where $V(r, P) : \Omega \in [0,1] \to R$ (12)

From equation (10), $P \in [0,1]$ is an embedded parameter and U_0 is the approximation that satisfies the boundary condition. The solution to equation (11) can be assumed as power series in h as follows:

$$V = V_0 + p^1 V_1 + p^2 V_2 + \ldots \quad (13)$$

$$U = v_0 + p^1 v_1 + p^2 v_2 + \ldots \quad (14)$$

$$p \to 1$$

The rate of convergence majorly depends on the nonlinear operator $A(V)$

From equation (1) – (5), we have

$$\frac{dS}{dt} = \Lambda - \frac{c\beta(I + k_1 I_c + k_2 T)}{N} S - \mu S \quad (15)$$

$$\frac{dI}{dt} = \frac{c\beta\rho(I + k_1 I_c + k_2 T)}{N} S + \alpha I_c - k_3 I \quad (16)$$

$$\frac{dI_c}{dt} = \frac{(1-\rho)c\beta(I + k_1 I_c + k_2 T)}{N} S + \tau T - k_4 I_c \quad (17)$$

$$\frac{dT}{dt} = \sigma I - k_5 T \quad (18)$$

$$\frac{dR}{dt} = \gamma T - \mu R \quad (19)$$

where

$$k_3 = (\mu + \sigma + \delta_1)$$

$$k_4 = (\mu + \alpha)$$

$$k_5 = (\mu + \gamma + \tau + \delta_2)$$

With the following initial conditions $S(0) = a_0, I(0) = b_0, I_c(0) = c_0, T(0) = d_0, R(0) = e_0$

Let

$$S = S_0 + pS_1 + p^2 N_2 + \ldots \quad (20)$$

$$I = I_0 + pI_1 + p^2 I_2 + \ldots \quad (21)$$

$$I_c = I_{c0} + pI_{c1} + p^2 I_{c2} + .. \quad (22)$$

$$T = T_0 + pT_1 + p^2 T_2 + \ldots \quad (23)$$

$$R = R_0 + pR_1 + p^2 R_2 + \ldots \quad (24)$$

Appling Homotopy Perturbation Method (HPM) to equations (15) - (19) using equation (20) - (24), we obtain the orders of p as follows:

$$p^0 : \frac{dS_0}{dt} = 0, \frac{dI_0}{dt} = 0 \; \frac{dI_{c0}}{dt} = 0, \frac{dT_0}{dt} = 0, \frac{dR_0}{dt} = 0 \quad (25)$$

$$p^1 : \frac{dS_1}{dt} = \Lambda - \frac{c\beta}{N_0}(I_0 S_0 + k_1 I_{c0} S_0 - k_2 T_0 S_0) - \mu S_0 \quad (26)$$

$$\frac{dI_1}{dt} = \frac{\rho c\beta}{N_0}(I_0 S_0 + k_1 I_{c0} S_0 - k_2 T_0 S_0) + \alpha I_{c0} + k_3 I_0 \quad (27)$$

$$\frac{dI_{c1}}{dt} = \frac{(1-\rho)c\beta}{N_0}(I_0 S_0 + k_1 I_{c_0} S_0 - k_2 T_0 S_0) + \tau T_0 - k_4 I_{c0} \quad (28)$$

$$\frac{dT}{dt} = \alpha I_o - k_5 T_0 \quad (29)$$

$$\frac{dR}{dt} = \gamma T_0 - \mu R_0 \quad (30)$$

$$p^2 : \frac{dS_2}{dt} = -\frac{c\beta}{N_1}\{(I_0 S_1 + I_1 S_0) + k_1(I_{c0} S_1 + I_{c1} S_0) + k_2(T_0 S_1 + T_1 S_0)\} - \mu S_1 \quad (31)$$

$$\frac{dI_2}{dt} = \frac{c\beta}{N_1}\{(I_0 S_1 + I_1 S_0) + k_1(I_{c0} S_1 + I_{c1} S_0) + k_2(T_0 S_1 + T_1 S_0)\} + \alpha I_{c1} - k_3 I_1 \quad (32)$$

$$\frac{dI_{c2}}{dt} = \frac{c\beta}{N_1}\{(I_0 S_1 + I_1 S_0) + k_1(I_{c0} S_1 + I_{c1} S_0) + k_2(T_0 S_1 + T_1 S_0)\} + \tau T_1 - k_4 I_{c1} \quad (33)$$

$$\frac{dT_2}{dt} = \sigma I_1 - k_5 T_1 \quad (34)$$

$$\frac{dR_2}{dt} = \gamma T_1 - \mu R_1 \quad (35)$$

Solving equation (25) – (35) using the initial condition and collecting the coefficient

of power of p by expansion, we obtain:

$$p^0 : S_0 = a_0, I_0 = b_0, I_{c0} = c_0, T_0 = d_0, and \;\; R_0 = e_0 \tag{36}$$

$$p^1 : S_1 = \{\Lambda - \frac{c\beta}{N_0}[b_0a_0 + k_1c_0a_0 + k_2d_0a_0] - \mu a_0\}t \tag{37}$$

$$I_1 = \{\frac{\rho c\beta}{N_0}[b_0a_0 + k_1c_0a_0 + k_2d_0a_0] + \alpha c_0 - k_3b_0\}t \tag{38}$$

$$I_{c1} = \{\frac{(1-\rho)c\beta}{N_0}[b_0a_0 + k_1c_0a_0 + k_2d_0a_0] + \tau d_0 - k_3c_0\}t \tag{39}$$

$$T_1 = \{\sigma b_0 - k_5d_0\}t \tag{40}$$

$$R_1 = \{\gamma d_0 - \mu e_0\}t \tag{41}$$

$$p^2 : S_2 = \frac{1}{2}t^2\{-\frac{c\beta}{N1}[(b_0a_1 + b_1a_0) + k_1(c_0a_1 + c_1a_0) + k_2(d_0a_1 + d_1a_0)] - \mu a_1\} \tag{42}$$

$$I_2 = \frac{1}{2}t^2\{\frac{\rho c\beta}{N1}[(b_0a_1 + b_1a_0) + k_1(c_0a_1 + c_1a_0) + k_2(d_0a_1 + d_1a_0)] + \alpha c_1 - k_3b_1\} \tag{43}$$

$$I_{c2} = \frac{1}{2}t^2\{\frac{(1-\rho)c\beta}{N1}[(b_0a_1 + b_1a_0) + k_1(c_0a_1 + c_1a_0) + k_2(d_0a_1 + d_1a_0)] + \tau d_1 - k_3c_1\} \tag{44}$$

$$T_2 = \frac{1}{2}t^2\{\sigma b_1 - k_5d_1\} \tag{45}$$

$$R_2 = \frac{1}{2}t^2\{\gamma d_1 - \mu e_1\} \tag{46}$$

Substituting the values above into the series in equation (20) - (24) taking the limit as $p \to 1$, we obtained the result as follows:

$$S(t) = a_0 + \{\Lambda - \frac{c\beta}{N_0}[b_0a_0 + k_1c_0a_0 + k_2d_0a_0] - \mu a_0\}t + \frac{1}{2}t^2\{-\frac{c\beta}{N1}[(b_0a_1 + b_1a_0) + k_1(c_0a_1 + c_1a_0) + k_2(d_0a_1 + d_1a_0)] - \mu a_1\} \tag{47}$$

$$I(t) = b_0 + \{\frac{\rho c\beta}{N_0}[b_0a_0 + k_1c_0a_0 + k_2d_0a_0] + \alpha c_0 - k_3b_0\}t + \frac{1}{2}t^2\{\frac{\rho c\beta}{N1}[(b_0a_1 + b_1a_0) + k_1(c_0a_1 + c_1a_0) + k_2(d_0a_1 + d_1a_0)] + \alpha c_1 - k_3b_1\} \tag{48}$$

$$I_c(t) = c_0 + \{\frac{(1-\rho)c\beta}{N_0}[b_0a_0 + k_1c_0a_0 + k_2d_0a_0] + \tau d_0 - k_3c_0\}t + \frac{1}{2}t^2\{\frac{(1-\rho)c\beta}{N1}[(b_0a_1 + b_1a_0) + k_1(c_0a_1 + c_1a_0) + k_2(d_0a_1 + d_1a_0)] + \tau d_1 - k_3c_1\} \tag{49}$$

$$T(t) = d_0 + \{\sigma b_0 - k_5d_0\}t + \frac{1}{2}t^2\{\sigma b_1 - k_5d_1\} \tag{50}$$

$$R(t) = e_0 + \{\gamma d_0 - \mu e_0\}t + \frac{1}{2}t^2\{\gamma d_1 - \mu e_1\} \quad (51)$$

Numerical Simulations

The simulations were carried out using the following variables and parameters in the table below for initial conditions at time (t). Computations were run in maple 17 software for investigation. Here we investigate the analytical solution of the model equation (1) to (6), using data from table below. We consider various treatment scenarios to investigate the effect of treatment in reducing the burden of the disease and evolution of carriers. We provide the graphs of our solutions to the problem under consideration. The discussions are presented after the graphs

Table 1: Typhoid Model Parameter and their Interpretations

Description	Parameter	Value	Citation
Recruitment rate	Λ	31.3-55/100	[Pitzer, *et al* (2014)]
Per capital death rate	μ	7.7-27.8/1000	[Pitzer, *et al* (2014)]
Disease-induced deaths	δ_1, δ_2	0.03-0.02-0.001	[Pitzer, *et al* (2014)]
Effective contacts	c	10	[Ghosh, *et al* (2004)]
Rate of transmission	β	0.000197/day	[Mushayabasa, (2011)]
Progression to symptomatic state	α	1/90	[Cvjetanovic, *et al* (1971)]
Rate of recovery from treatment	γ	0.002485/day	
New infections becoming carriers	ρ	0.003-0.80	[Pitzer, *et al* (2014)]
Rate of treatment	σ	0.19-0.8	Varied
Proportion of treated individuals	τ	1/18	[Cvjetanovic, *et al* (1971)]
Modification parameters	k_1, k_2	1-1.2	Varied

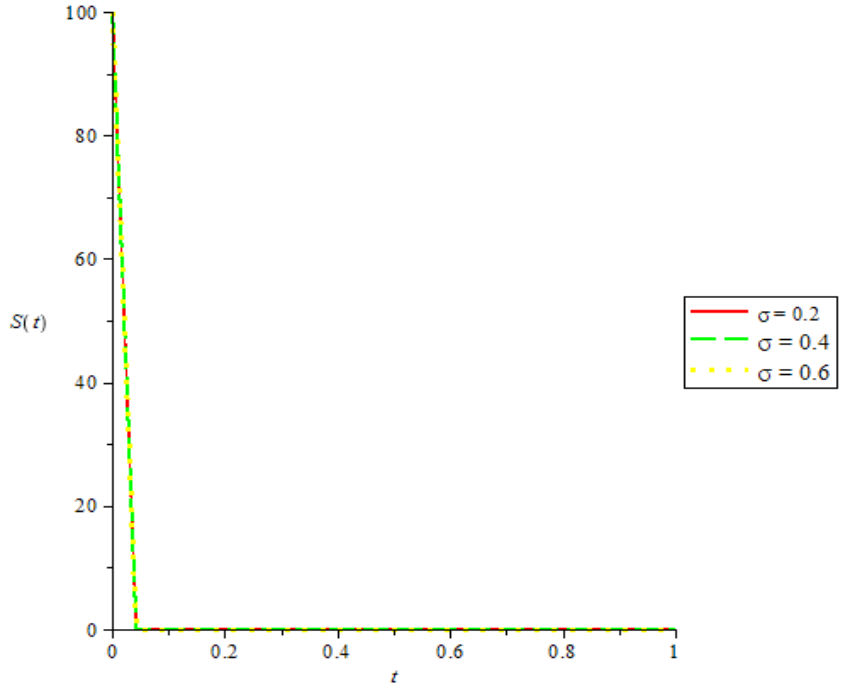

Figure 1: $S(t)$ versus time t for various value of σ at Λ=55/1000, $\delta_1 = 0.001, \delta_2 = 0.000247, \beta = 0.125, \gamma = 0.01, \rho = 0.8, \mu = 0.02, \alpha = 0.45, \tau = 0.056, k_2 = 1, k_1 = 1.2$,

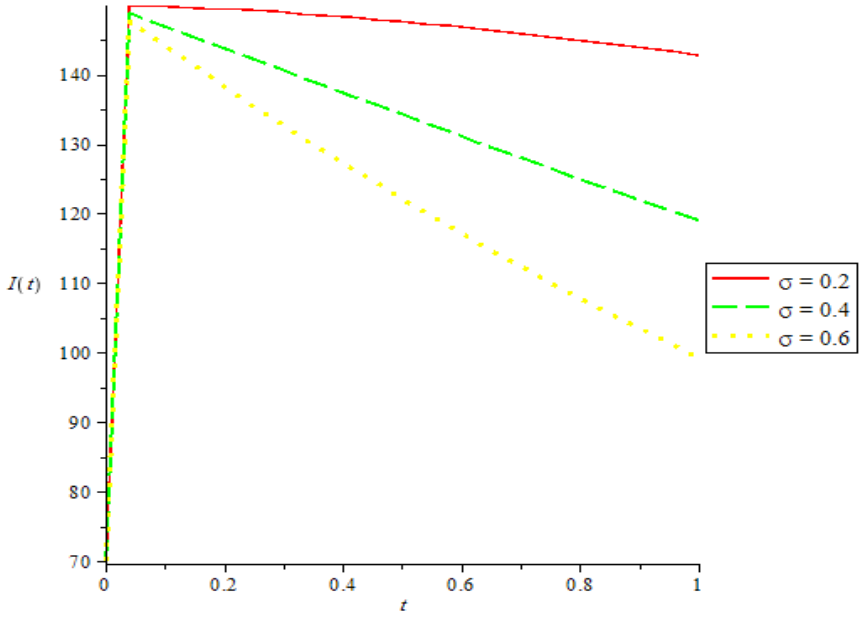

Figure 2: I(t) versus time t for various value of σ at Λ=55/1000, $\delta_1 = 0.001$, $\delta_2 = 0.000247$, $\beta = 0.125$, $\gamma = 0.01$, $\rho = 0.8$, $\mu = 0.02$, $\alpha = 0.45$, $\tau = 0.056$, $k_2 = 1$, $k_1 = 1.2$,

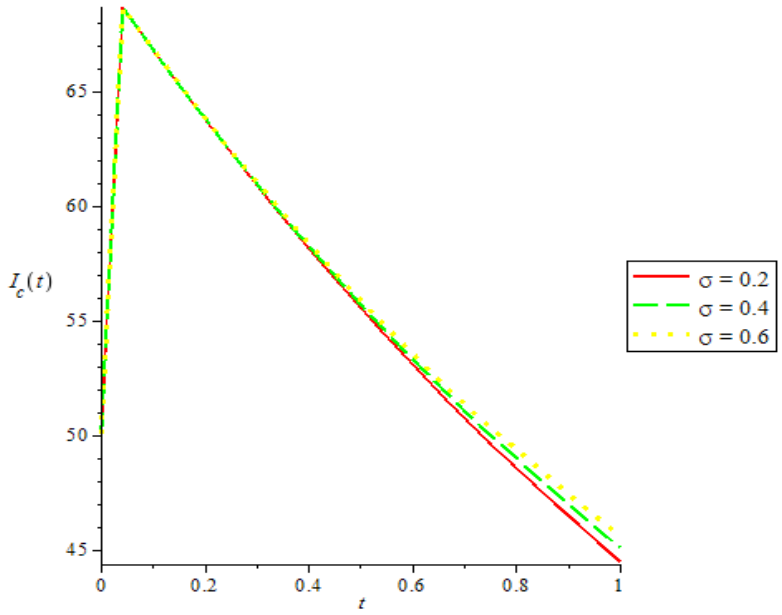

Figure 3: I_C(t) versus time t for various value of σ at Λ=55/1000, $\delta_1 = 0.001$, $\delta_2 = 0.000247$, $\beta = 0.125$, $\gamma = 0.01$, $\rho = 0.8$, $\mu = 0.02$, $\alpha = 0.45$, $\tau = 0.056$, $k_2 = 1$, $k_1 = 1.2$,

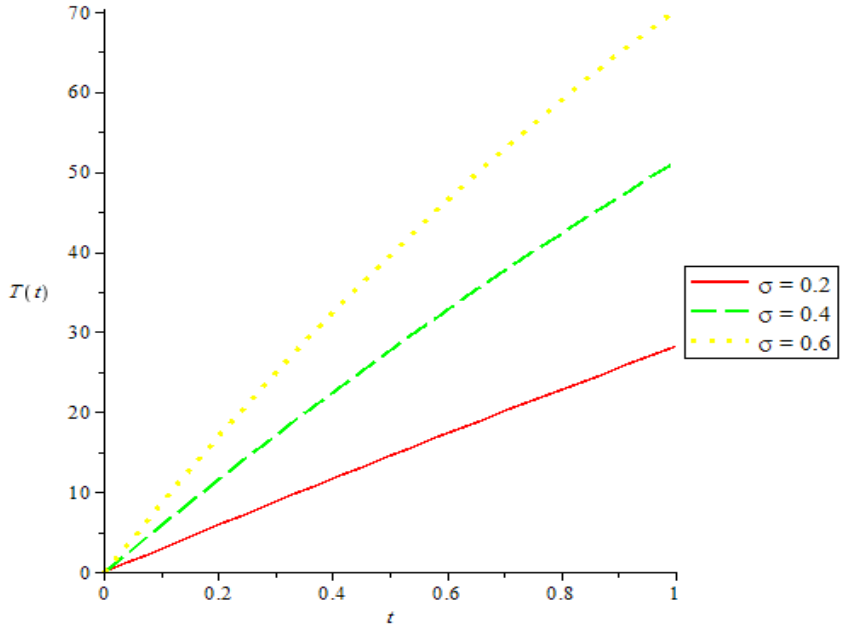

Figure 4: T(t) versus time t for various value of σ at Λ=55/1000, $\delta_1 = 0.001$, $\delta_2 = 0.000247$, $\beta = 0.125$, $\gamma = 0.01$, $\rho = 0.8$, $\mu = 0.02$, $\alpha = 0.45$, $\tau = 0.056$, $k_2 = 1$, $k_1 = 1.2$,

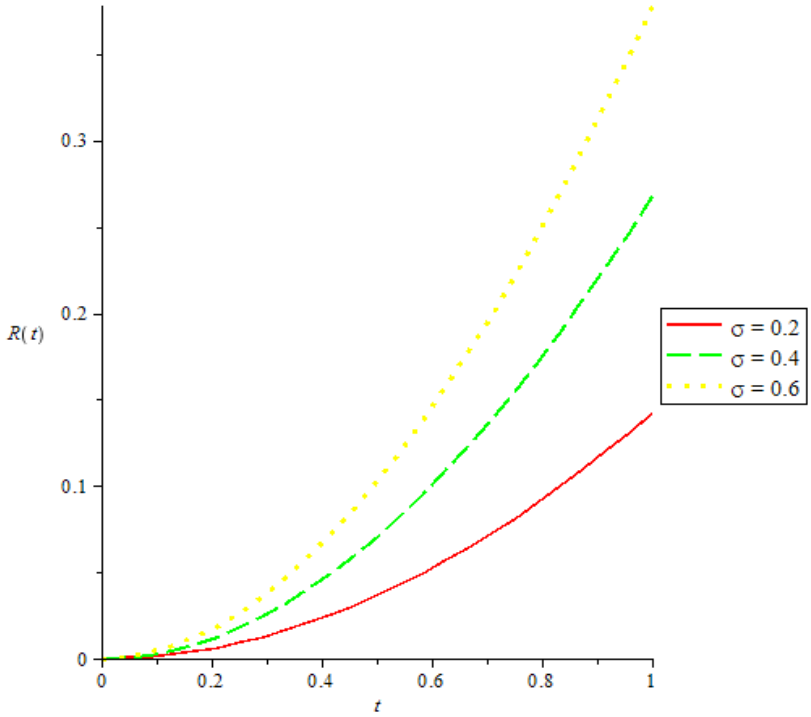

Figure 5: R (t) versus time t for various value of σ at Λ=55/1000, $\delta_1 = 0.001$, $\delta_2 = 0.000247$, $\beta = 0.125$, $\gamma = 0.01$, $\rho = 0.8$, $\mu = 0.02$, $\alpha = 0.45$, $\tau = 0.056$, $k_2 = 1$, $k_1 = 1.2$,

Results and Discussion

Numerical simulations suggested that increasing treatment sustains the typhoid epidemic in the population. Implications of this result points to an added effect from carriers evolving from treatment relapse. The dependence of modification transmission parameter k_2 on

treated population provides insight in the role of treatment in the transmission dynamics of the disease. Due to complexity of the model closed form solutions of the population density dependent transmission rate could not be obtained. The study suggest development and implementation of preventive and treatment strategies which can reduce the burden of carriers in the population. Sensitive algorithms for case detection of infectives, especially carriers will play a critical role in reducing the burden of typhoid disease. Epidemic trends guide allocation of resources, targeted design of control strategies and surveillance or improved techniques for data collection. Even though, this study provides insight on the transmission dynamics of typhoid infection. The dependence of infection parameters in the state variables seemed to suggest crucial dynamics appropriate to describe realistic behaviour of diseases.

Conclusion

We presented a deterministic model for typhoid fever transmission model with treatment. The study revealed through simulations that the epidemic is sustained in the population. Implications of these results indicate that treatment sustain the carrier infectives who in turn sustains the epidemic in the population in the long run. Our paper is hypothetical and requires detailed study involving sensitivity analysis and parameter estimations to improve model predictions.

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