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Modeling the effect of time delay in controlling the carrier dependent infectious disease – Cholera

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ABSTRACT

A delay mathematical model for the control of cholera epidemic is proposed and analyzed. It is assumed that the disease spreads through carriers, which makes the human food contaminated by transporting bacteria from the environment. It is also assumed that insecticides are used to control the carriers with the rate proportional to the density of carriers. The analysis of model shows that the disease may be controlled by spraying insecticides but a longer delay in spraying insecticides may destabilize the system. Simulation is also carried out to support the analytical results.

1. Introduction

Cholera is an acute infectious disease in which intestine gets infected by the bacterium *Vibrio cholerae* (*V. cholerae*). Generally the infection is mild but sometimes it may be severe and if not treated properly, death may occur within hours. The period of infection of cholera ranges from few hours to 5 days but in general it is of 1–2 days. The main symptoms of cholera are watery diarrhea, vomiting, rapid dehydration, metabolic acidosis, and hypovolemic shock. The world have acquainted and feared cholera for hundreds of years. Several cholera epidemics have occurred worldwide during the 15th–18th centuries. During the 19th and 20th centuries, seven cholera pandemics have ravaged the humankind [1,2]. The seventh cholera pandemic originated from Indonesia in 1961 and thereafter spread around the globe. During the seventh pandemic in 1991, India has been recognized as an endemic zone for cholera due to *V. cholerae* O1 serogroup Ogawa, biotype El Tor, and serogroup O139. In 2005, an outbreak of cholera, dominated by *V. cholerae* O1 Inaba, has also been reported in India [2,3]. The disease is still common in several parts of Asia and Africa.

Prevalence of cholera is closely related to poor environmental conditions and lack of basic infrastructure in developing countries. In earlier times, the main mode of transmission of cholera infection was believed to be the consumption of contaminated water. Therefore, government of various countries made effectual efforts to make drinking water safe for use by means of treatments such as filtration and chlorination. But it is observed that even after the treatment of water, the disease is prevalent in some areas. Some studies reveal that the common housefly, or flies in general, can serve as mechanical vectors of numerous kind of pathogens such as bacteria [4,5], protozoa [6], and helminth eggs [7]. It suggests that, pathogen of cholera may also spread via flies. The increased incidence of dysentery during periods of high density of flies has been reported from various places [5,8,9]. It fortifies the notion that flies are also major transporter of cholera-causing bacteria. Basically,

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the flies transport the bacteria responsible for cholera disease to the human food and make it contaminated [10,11]. Due to the uptake of this contaminated food, people acquire cholera infection [1,12].

In addition to cholera, there are diseases like typhoid fever and other enteric diseases, which spread in human population through carriers. Most of the developing countries are affected by such diseases due to lack of sanitation and wide occurrence of carriers. Various studies have been conducted to understand the role of carriers (e.g., flies, ticks, mites, etc.) and bacteria in the spread of infectious diseases [12–27]. In particular, Hethcote [19] studied a nonlinear mathematical model for communicable diseases by assuming that the carrier population is constant. But, in general the carrier population is not constant and it depends on various environmental factors, like humidity, temperature, etc. Some human-related activities like discharge of household wastes, open sewage drainage, industrial effluents in residential areas, open water storage tanks, ponds, etc., also enhance the growth of carriers. The role of human-related activities on the growth of carrier population has been studied explicitly by some modelers [20–23,25]. Singh et al. [23] proposed and analyzed SIS and SIRS mathematical models for the spread of carrier dependent infectious diseases by assuming that the growth rate and carrying capacity of carrier population are increasing function of total human population density. They have shown that the number of infectives increases as the human-related activities, which makes the environment more conducive for the growth of carriers, increase. Codeco [24] also studied a mathematical model for cholera epidemic by incorporating the role of environmental reservoirs. In this study, the minimum number of conditions for the development of endemicity of cholera have been derived and the persistence of cholera is also discussed. For cholera epidemic it is found that by controlling the environmental fluctuations the severity of the disease can be managed [25].

Although commendable studies have been conducted to explore the role of carriers in the spread of infectious diseases, a little attention is paid to their control. An efficient way to control the spread of carrier dependent infectious diseases may be vaccination of susceptibles [27]. As the spread of diarrheal diseases is closely related to the seasonal increase in abundance of flies, their control helps in declining the cases of enteric diseases. Therefore, generally government uses insecticides, in particular DDT, to control the flies in the environment during cholera outbreaks. But the excessive use of insecticides is harmful for plants and human health, so some people called 'trained squads' are especially trained to perform the fly control in a region. These trained squads are employed by the government to spray DDT in houses as well as in other relevant areas and the amount of insecticides used in fly control depends on the density of carriers [28].

As discussed above, the control of carrier population may be an effective tool for controlling the spread of carrier dependent infectious diseases, especially cholera. So we have concentrated our study on spread of cholera disease due to consumption of food contaminated by carriers present in the environment. Therefore, in this paper, we propose and analyze a mathematical model for the control of cholera disease by controlling the density of carrier population using insecticides. The density of carrier population known to the trained squads may be few days old, thus the rate of change of concentration of insecticides is assumed to be proportional to that density of carrier population, which leads for incorporation of time delay in the rate of spray of insecticides. Furthermore, some amount of insecticides may washout with the passage of time and some may be consumed by the carriers. Hence, the depletion of insecticides has also been considered in the modeling process.

2. Mathematical model

Cholera does not spread directly from one person to another, therefore the casual contacts with an infected person is not a risk for getting infection [29]. Hence, in the modeling process, it is assumed that susceptibles get infected due to the presence of carriers, which contaminate the food. It is also assumed that the carriers grow logistically in their natural environment and human-related activities further enhance their growth rate. We consider that the growth rate of carriers is controlled by spraying insecticides with a rate proportional to the density of carriers, τ time before.

Let $N(t)$ be the total human population at any time t, which is divided into two subclasses, namely (i) susceptible class $X(t)$ and (ii) infective class $Y(t)$. Let $C(t)$ and $C_h(t)$ represent the density of carrier population and the concentration of insecticides respectively at time t. It is assumed that the rate of introduction of insecticides is proportional to $C(t-\tau)$ and its natural depletion rate is proportional to its concentration. It is also assumed that the depletion rate of insecticides due to its uptake by carriers is proportional to the density of carriers as well as the concentration of insecticides. The decline rate of carrier population due to uptake of insecticides is also taken to be proportional to the density of carriers and the concentration of insecticides.

With the above considerations, the model dynamics is governed by the following system of nonlinear delay differential equations:

$$\begin{aligned}
\frac{dX(t)}{dt} &= A - \lambda X(t)C(t) - dX(t) + \nu Y(t),\\
\frac{dY(t)}{dt} &= \lambda X(t)C(t) - (\nu + \alpha + d)Y(t),\\
\frac{dC(t)}{dt} &= rC(t)\left(1 - \frac{C(t)}{K}\right) - s_1 C(t) + r_1 N(t)C(t) - \theta_2 C(t)C_h(t),\\
\frac{dC_h(t)}{dt} &= \theta C(t-\tau) - \theta_0 C_h(t) - \theta_1 C(t)C_h(t),
\end{aligned} \tag{1}$$

where $X(t)+Y(t)=N(t)$ and the initial conditions are given as follows:

$X(0)=X_0>0,\ Y(0)=Y_0\geqslant 0,\ C(\gamma)=C_0>0$ for $\gamma\in[-\tau,0],\ C_h(0)=C_{h0}\geqslant 0$ and $X(0)+Y(0)=N(0)=N_0>0$.

In the above model system (1), A is a constant immigration rate of human population in the region under consideration and constant λ represents the transmission rate of infection due to the presence of carriers in the environment. The constants d, α and ν represent the natural mortality rate, the disease-induced death rate and the recovery rate of human population, respectively. The constants r and K represent the intrinsic growth rate and carrying capacity of carrier population respectively in absence of human-related activities. The constant r_1 represents the growth rate coefficient of carriers due to human-related activities. Constants s_1 and θ_2 represent decline rates of carrier population density due to natural causes and insecticides respectively. The proportionality constants θ,θ_0 and θ_1 represent the spraying rate, natural decay rate and decay rate due to uptake by carriers of the insecticides respectively. All the above constants are assumed to be positive.

Using the fact that $X(t)+Y(t)=N(t)$, the above model system (1) reduces to the following system:

$$\begin{aligned}
\frac{dY(t)}{dt}&=\lambda(N(t)-Y(t))C(t)-(\nu+\alpha+d)Y(t),\\
\frac{dN(t)}{dt}&=A-dN(t)-\alpha Y(t),\\
\frac{dC(t)}{dt}&=rC(t)\left(1-\frac{C(t)}{K}\right)-s_1C(t)+r_1N(t)C(t)-\theta_2C(t)C_h(t),\\
\frac{dC_h(t)}{dt}&=\theta C(t-\tau)-\theta_0C_h(t)-\theta_1C(t)C_h(t).
\end{aligned}\tag{2}$$

As the study of model system (1) is equivalent to the study of model system (2), thus we study model system (2). In the following, we analyze the model system (2) using stability theory of delay differential equations. For the solutions of model system (2), the region of attraction [23,30] is given by the set:

$$\Omega=\left\{(Y,N,C,C_h):0\leqslant Y\leqslant N\leqslant\frac{A}{d},\ 0\leqslant C\leqslant R_d,\ 0\leqslant C_h\leqslant\frac{\theta}{\theta_0}R_d\right\},\tag{3}$$

where $R_d=\frac{K}{r}\left(r+r_1\frac{A}{d}\right)$ and attracts all solutions initiating in the interior of the positive orthant.

3. Equilibrium analysis

The model system (2) has the following two non-negative equilibria, as follows:

(i) The disease-free equilibrium $E_0(0,A/d,0,0)$, which always exist, and
(ii) The endemic equilibrium $E_1(Y^*,N^*,C^*,C_h^*)$, exists under a condition.

The existence of E_0 is obvious. In the following, we show the existence of endemic equilibrium E_1. The endemic equilibrium E_1 may be obtained by solving the following set of algebraic equations:

$$\lambda(N-Y)C-(\nu+\alpha+d)Y=0,\tag{4}$$

$$A-dN-\alpha Y=0,\tag{5}$$

$$r\left(1-\frac{C}{K}\right)-s_1+r_1N-\theta_2C_h=0,\tag{6}$$

$$\theta C-\theta_0C_h-\theta_1CC_h=0.\tag{7}$$

Now using Eq. (5) in Eq. (4), we get the following equation in Y and C

$$(A-(\alpha+d)Y)\lambda C-d(\nu+\alpha+d)Y=0.\tag{8}$$

From Eq. (8) we have

$$Y=\frac{\lambda AC}{\lambda(\alpha+d)C+d(\nu+\alpha+d)}.\tag{9}$$

Again using Eqs. (5) and (7) in Eq. (6), we get another equation in Y and C as follows:

$$r\left(1-\frac{C}{K}\right)-s_1+r_1\left(\frac{A-\alpha Y}{d}\right)-\frac{\theta\theta_2C}{\theta_0+\theta_1C}=0.\tag{10}$$

Now using the value of Y from Eq. (9) in Eq. (10), we get the following equation in C

$$f(C) = r\left(1 - \frac{C}{K}\right) - s_1 + \frac{r_1 A}{d} - \frac{r_1 \alpha}{d}\frac{\lambda AC}{\lambda(\alpha + d)C + d(v + \alpha + d)} - \frac{\theta\theta_2 C}{\theta_0 + \theta_1 C} = 0, \tag{11}$$

From the above Eq. (11), we may easily note that

(i) $f(0) = r - s_1 + \frac{r_1 A}{d}$, which is positive provided

$$r + \frac{r_1 A}{d} > s_1, \tag{12}$$

(ii) $f(R_d)$ is negative, and
(iii) $f'(C)$ is negative.

The above points (i), (ii) and (iii) imply that there exits a unique positive root (say, C^*) of Eq. (11) in the interval $(0, R_d)$ provided condition (12) is satisfied.

Thus, using this positive value of $C(= C^*)$ in Eq. (9), we get positive value of $Y(= Y^*)$. Finally using these values of Y^* and C^* in Eqs. (5) and (7) respectively, we get the positive values of N^* and C_h^*. Thus the equilibrium $E_1(Y^*, N^*, C^*, C_h^*)$ exists provided condition (12) is satisfied.

Remark 1. From Eqs. (9) and (11) it is easy to see that $\frac{dY^*}{d\theta}$ and $\frac{dC^*}{d\theta}$ are negative. This implies that as the rate of spraying of insecticides in the environment increases, the equilibrium number of infectives and density of carrier population decreases (see Fig. 1).

4. Stability analysis

In this section, we discuss the local stability behavior of both the equilibria without delay as well as with delay. We also perform Hopf-bifurcation analysis by choosing delay τ as a bifurcation parameter.

4.1. Local stability analysis without delay (i.e. $\tau = 0$)

Here we show the local stability behavior of equilibria E_0 and E_1 by finding the eigenvalues of the corresponding variational matrix obtained for model system (2).

The general variational matrix for model system (2) can be obtained as follows:

$$M = \begin{pmatrix} -a_1 & \lambda C & \lambda(N - Y) & 0 \\ -\alpha & -d & 0 & 0 \\ 0 & r_1 C & -a_2 & -\theta_2 C \\ 0 & 0 & \theta - \theta_1 C_h & -a_3 \end{pmatrix},$$

where $a_1 = \lambda C + (v + \alpha + d)$, $a_2 = -r(1 - \frac{2C}{K}) + s_1 - r_1 N + \theta_2 C_h$ and $a_3 = \theta_0 + \theta_1 C$.

Let M_i be the variational matrix M evaluated at the equilibrium $E_i (i = 0, 1)$.

From the matrix M_0, we may easily note that its eigenvalues are $-(v + \alpha + d)$, $-d$, $r - s_1 + \frac{r_1 A}{d}$ and $-\theta_0$. It is easy to see that three eigenvalues of M_0 are clearly negative and one eigenvalue is $r - s_1 + \frac{r_1 A}{d}$, which is positive whenever condition

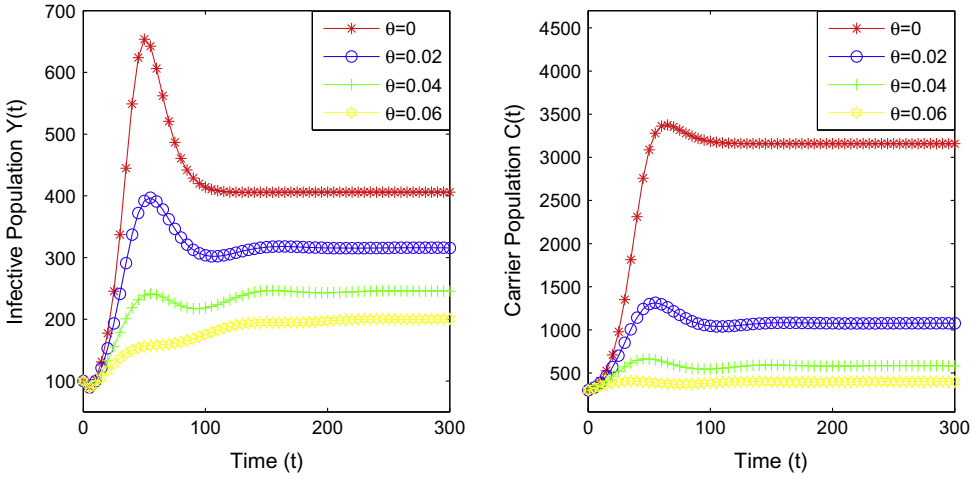

Fig. 1. Variation of Y and C_h with respect to time t for different values of θ.

(12) is satisfied. Thus the equilibrium E_0 has always stable manifold locally in $Y-N-C_h$ space and unstable manifold locally in C-direction whenever endemic equilibrium E_1 exists.

Now we study the local stability behavior of endemic equilibrium E_1 by using Routh–Hurwitz criterion.

The characteristic equation for the matrix M_1 is given by the following equation

$$\Phi^4 + p_1\Phi^3 + p_2\Phi^2 + p_3\Phi + p_4 = 0, \tag{13}$$

where

$$\begin{aligned}
p_1 &= a_1^* + d + a_2^* + a_3^*,\\
p_2 &= (a_1^* + d)(a_2^* + a_3^*) + a_1^* d + a_2^* a_3^* + \alpha\lambda C^* + \theta_0\theta_2 C_h^*,\\
p_3 &= \alpha\lambda C^*(a_2^* + a_3^*) + a_1^* d(a_2^* + a_3^*) + \lambda r_1 \alpha C^*(N^* - Y^*) + (a_1^* + d)(a_2^* a_3^* + \theta_0\theta_2 C_h^*)
\end{aligned}$$

and $p_4 = (a_1^* d + \alpha\lambda C^*)(a_2^* a_3^* + \theta_0\theta_2 C_h^*) + \lambda r_1 \alpha a_3^* C^*(N^* - Y^*)$.

In writing the above values of p_i's, we have used the fact that $\theta - \theta_1 C_h^* = \frac{\theta_0 C_h^*}{C^*}$. Now here we note that

$$a_1^* = \frac{\lambda N^*}{Y^*} > 0, \quad a_2^* = \frac{rC^*}{K} > 0 \quad \text{and} \quad a_3^* = \theta_0 + \theta_1 C^* > 0.$$

Thus, it is clear that all p_i's are positive. Now for the local stability of endemic equilibrium $E_1(Y^*, N^*, C^*, C_h^*)$ of model system (2) without delay, we have the following result.

Theorem 1. *The equilibrium $E_1(Y^*, N^*, C^*, C_h^*)$ if exists, is locally asymptotically stable for $\tau = 0$ iff the following condition is satisfied:*

$$p_3(p_1p_2 - p_3) - p_1^2 p_4 > 0, \tag{14}$$

where p_1, p_2, p_3 and p_4 are defined as above.

Remark 2. Here we can easily show that for $r_1 = 0$, the local stability condition, given in (14) is automatically satisfied. This implies that the growth rate of carriers due to human-related activities has destabilizing effect on the system. This result is similar as obtained by Singh et al. [23].

4.2. Local stability analysis with delay (i.e. $\tau \neq 0$)

In this section, we analyze our model system (2) with delay, i.e., we assume that $\tau \neq 0$. We also derive the stability conditions for the equilibrium E_1 and explore the possibility of Hopf-bifurcation.

Now linearizing the model system (2) about $E_1(Y^*, N^*, C^*, C_h^*)$ by using the following transformations:

$Y = Y^* + y, N = N^* + n,\ C = C^* + c,\ C_h = C_h^* + c_h$, where y, n, c and c_h are small perturbations.

The linearized system around the equilibrium $E_1(Y^*, N^*, C^*, C_h^*)$ is given by:

$$\begin{aligned}
\frac{dy(t)}{dt} &= -(\lambda C^* + v + \alpha + d)y(t) + \lambda C^* n(t) + \lambda(N^* - Y^*)c(t),\\
\frac{dn(t)}{dt} &= -\alpha y(t) - dn(t),\\
\frac{dc(t)}{dt} &= r_1 C^* n(t) - \frac{rC^*}{K}c(t) - \theta_2 C^* c_h(t),\\
\frac{dc_h(t)}{dt} &= -\theta_1 C_h^* c(t) - (\theta_0 + \theta_1 C^*)c_h(t) + \theta c(t-\tau).
\end{aligned} \tag{15}$$

The characteristic equation for the system (15) is given by the following equation

$$P(\psi) + Q(\psi)e^{-\psi\tau} = 0, \tag{16}$$

where $P(\psi) = \psi^4 + A_1\psi^3 + A_2\psi^2 + A_3\psi + A_4$ and $Q(\psi) = B_1\psi^2 + B_2\psi + B_3$.

In the above expressions of $P(\psi)$ and $Q(\psi)$, A_i's and B_i's are given as follows:

$$\begin{aligned}
A_1 &= a_1^* + d + a_2^* + a_3^*,\\
A_2 &= (a_1^* + d)(a_2^* + a_3^*) + a_1^* d + a_2^* a_3^* - \theta_1\theta_2 C^* C_h^* + \alpha\lambda C^*,\\
A_3 &= \alpha\lambda C^*(a_2^* + a_3^*) + a_1^* d(a_2^* + a_3^*) + \lambda r_1 \alpha C^*(N^* - Y^*) + (a_1^* + d)(a_2^* a_3^* - \theta_1\theta_2 C^* C_h^*),\\
A_4 &= (a_1^* d + \alpha\lambda C^*)(a_2^* a_3^* - \theta_1\theta_2 C^* C_h^*) + a_3^* r_1 \lambda\alpha C^*(N^* - Y^*),\\
B_1 &= \theta\theta_2 C^*,\\
B_2 &= \theta\theta_2 C^*(a_1^* + d),\\
B_3 &= \theta\theta_2 C^*(a_1^* d + \alpha\lambda C^*).
\end{aligned}$$

To show the Hopf-bifurcation, we must have a pair of purely imaginary roots of characteristic Eq. (16). For this substituting $\psi = i\omega(\omega > 0)$ into Eq. (16) and separating real and imaginary parts, we get the following transcendental equations

$$\omega^4 - A_2\omega^2 + A_4 = -[(B_3 - B_1\omega^2)\cos\omega\tau + B_2\omega\sin\omega\tau] \tag{17}$$

and

$$-A_3\omega + A_1\omega^3 = B_2\omega\cos\omega\tau - (B_3 - B_1\omega^2)\sin\omega\tau. \tag{18}$$

Now squaring and adding Eqs. (17) and (18) we get the following equation in ω,

$$(\omega^4 - A_2\omega^2 + A_4)^2 + (-A_3\omega + A_1\omega^3)^2 = (B_3 - B_1\omega^2)^2 + (B_2\omega)^2. \tag{19}$$

Substituting $\omega^2 = \eta$ in above Eq. (19), we get the following equation in η

$$(\eta^2 - A_2\eta + A_4)^2 + \eta(A_1\eta - A_3)^2 = (B_3 - B_1\eta)^2 + B_2^2\eta. \tag{20}$$

The above equation may be rewritten as follows

$$h(\eta) = \eta^4 + D_1\eta^3 + D_2\eta^2 + D_3\eta + D_4 = 0, \tag{21}$$

where

$$D_1 = A_1^2 - 2A_2, \quad D_2 = A_2^2 + 2A_4 - 2A_1A_3 - B_1^2,$$

$$D_3 = A_3^2 - 2A_2A_4 + 2B_1B_2 - B_2^2 \quad \text{and} \quad D_4 = A_4^2 - B_3^2.$$

Now if the coefficients in $h(\eta)$ satisfy the conditions of Routh–Hurwitz criterion, then Eq. (21) will not have any positive real root, thus we may not get any positive value of ω, which satisfy the transcendental Eqs. (17) and (18). In this case the result may be written in the form of following theorem:

Theorem 2. *If the coefficients in $h(\eta)$ (i.e. D_i's) satisfy the conditions of Routh–Hurwitz criterion, then the endemic equilibrium E_1 of model system (2) is locally asymptotically stable for all delay $\tau > 0$ provided it is locally asymptotically stable in absence of delay.*

Assuming contrary that the values of D_i's, $(i = 1, 2, 3, 4)$ in Eq. (21) do not satisfy the Routh–Hurwitz criterion. In this case a simple assumption for the existence of a positive root of Eq. (21) is $D_4 < 0$, which gives

$$A_4 - B_3 < 0. \tag{22}$$

Now if condition (22) holds, then Eq. (21) has a positive root η_0, and Eq. (16) has a pair of purely imaginary roots of the form $\pm i\omega_0$. From transcendental Eqs. (17) and (18), we may obtain

$$\tan\omega\tau = \frac{B_2\omega_0(\omega_0^4 - A_2\omega_0^2 + A_4) + \omega_0(A_1\omega_0^2 - A_3)(B_3 - B_1\omega_0^2)}{(B_3 - B_1\omega_0^2)(\omega_0^4 - A_2\omega_0^2 + A_4) - B_2\omega_0^2(A_1\omega_0^2 - A_3)}. \tag{23}$$

Now τ_k corresponding to this positive value of ω_0 is given as follows

$$\tau_k = \frac{k\pi}{\omega_0} + \frac{1}{\omega_0}\arctan\frac{B_2\omega_0(\omega_0^4 - A_2\omega_0^2 + A_4) + \omega_0(A_1\omega_0^2 - A_3)(B_3 - B_1\omega_0^2)}{(B_3 - B_1\omega_0^2)(\omega_0^4 - A_2\omega_0^2 + A_4) - B_2\omega_0^2(A_1\omega_0^2 - A_3)}, \tag{24}$$

where $k = 0, 1, 2, 3, \ldots$

By using Butler's lemma [31], we can say that the endemic equilibrium of model system (2) remains stable for $\tau < \tau_0$.

Now we investigate whether there is a phenomenon of Hopf-bifurcation as τ increases through τ_0. For this we will make use of the following lemma.

Lemma 1. *The following transversality condition is satisfied:*

$$sgn\left[\frac{d(Re(\psi))}{d\tau}\right]_{\tau=\tau_0} > 0. \tag{25}$$

Proof. Differentiating Eq. (16) with respect to τ, we get

$$\begin{aligned}\left(\frac{d\psi}{d\tau}\right)^{-1} &= \frac{(4\psi^3 + 3A_1\psi^2 + 2A_2\psi + A_3) + (2B_1\psi + B_2)e^{-\psi\tau}}{\psi(B_1\psi^2 + B_2\psi + B_3)e^{-\psi\tau}} - \frac{\tau}{\psi} \\ &= \frac{4\psi^3 + 3A_1\psi^2 + 2A_2\psi + A_3}{\psi(B_1\psi^2 + B_2\psi + B_3)e^{-\psi\tau}} + \frac{2B_1\psi + B_2}{\psi(B_1\psi^2 + B_2\psi + B_3)} - \frac{\tau}{\psi}.\end{aligned} \tag{26}$$

Now using Eqs. (16)–(18) in above Eq. (26) and after a simple algebraic manipulation, we get

$$\left[\frac{d(Re(\psi))}{d\tau}\right]^{-1}_{\psi=i\omega_0} = \left[Re\left(\frac{d\psi}{d\tau}\right)^{-1}\right]_{\psi=i\omega_0} = \frac{4\omega_0^6 + 3D_1\omega_0^4 + 2D_2\omega_0^2 + D_3}{\Lambda} = \frac{h'(\omega_0^2)}{\Lambda}. \tag{27}$$

where $\Lambda = B_2\omega_0^2 + (B_3 - B_1\omega_0^2)^2 = (A_3 - A_1\omega_0^2)\omega_0^2 + (\omega_0^4 - A_2\omega_0^2 + A_4)^2$. Here it may be noted that $h'(\omega_0^2) > 0$, if the condition (22) is satisfied. This proves the Lemma 1. Thus the results obtained are stated in the form of following theorem. □

Theorem 3. *If the condition (22) is satisfied then the endemic equilibrium E_1 of model system (2) is locally asymptotically stable for $\tau < \tau_0$ and becomes unstable for $\tau > \tau_0$. The condition for Hopf-bifurcation is also satisfied yielding the required periodic solutions from the endemic equilibrium E_1 as τ passes through τ_0, i.e. Hopf-bifurcation occurs at $\tau = \tau_0$ [32].*

5. Numerical simulation

In the previous sections, we have presented qualitative analysis of the model system (2) and obtained some results about the stability of disease-free equilibrium and endemic equilibrium of the system. In this section, we present a numerical simulation of the model system (2) using MATLAB 7.0.1. For numerical simulation, we choose the following set of parameter values in model system (2).

$$A = 100,\quad \lambda = 0.00002,\quad \nu = 0.02,\quad \alpha = 0.2,\quad d = 0.01,\quad r = 0.065,\quad s_1 = 0.00001,$$
$$r_1 = 0.00002,\quad K = 2000,\quad \theta = 0.04,\quad \theta_0 = 0.02,\quad \theta_1 = 0.00002,\quad \theta_2 = 0.0002.$$

We have chosen above parameter values to illustrate the validity of theoretical results for Hopf-bifurcation rather than as an application to a specific region of cholera disease.

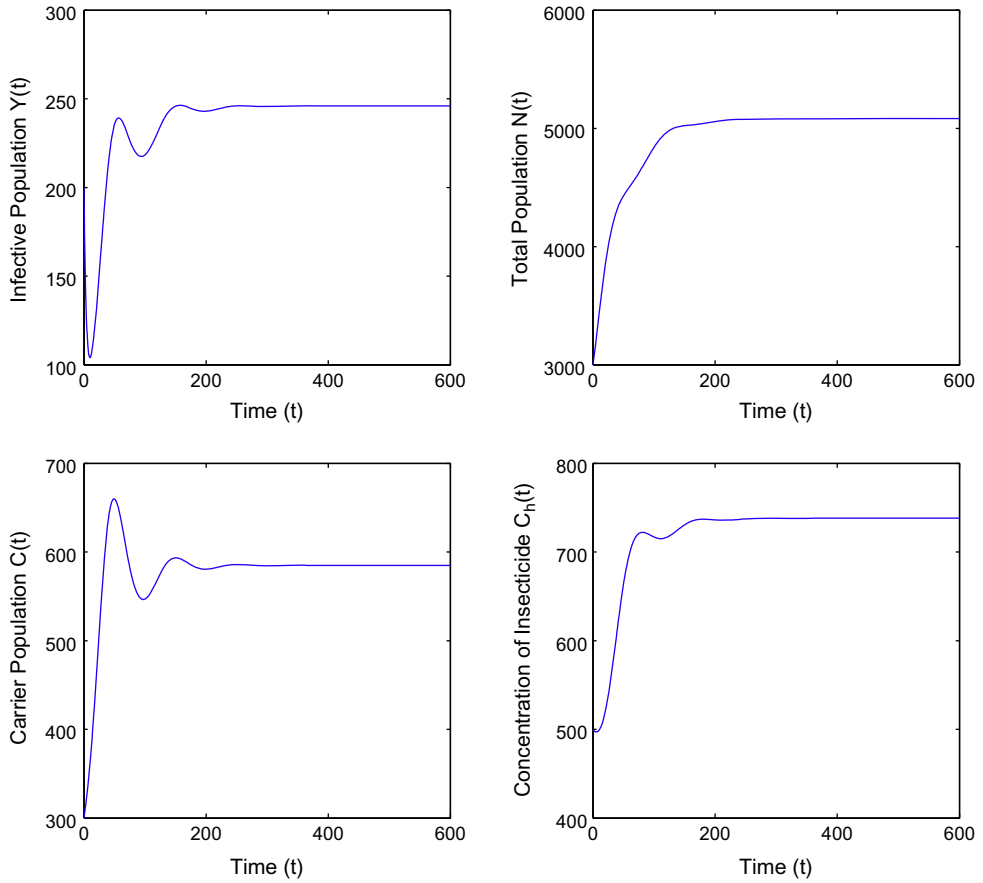

Fig. 2. Variation of Y, N, C and C_h with respect to time t in absence of delay.

The equilibrium values in the endemic equilibrium E_1 for this data are obtained as

$$Y^* = 245.93, \quad N^* = 5081.50, \quad C^* = 584.86, \quad C_h^* = 738.06.$$

For $\tau = 0$, the eigenvalues of the variational matrix corresponding to the equilibrium E_1 for the model system (2) are -0.0236, -0.2356, -0.0215 $-0.0621\,i$ and -0.0215 $+0.0621\,i$. We note that two eigenvalues of variational matrix M_1 are negative whereas the remaining two eigenvalues are with negative real part. Hence, the endemic equilibrium E_1 is locally asymptotically stable in absence of delay (i.e. $\tau = 0$).

For non-delay model, the variation of infective population $Y(t)$, total population $N(t)$, density of carrier population $C(t)$ and concentration of insecticides $C_h(t)$ with respect to time t is presented in Fig. 2. From this figure, it is clear that all the variables are approaching to their equilibrium values as time approaches infinity, which shows the stability of endemic equilibrium E_1 of model system (2).

Further, it may be noted that for the above set of parameter values, the condition (22) for existence of a pair of purely imaginary roots of characteristic Eq. (16) is also satisfied. The numerical value of τ_0, computed using Eq. (24), is found to be 10.

Now applying Theorem 3, we can say that the endemic equilibrium E_1 of model system (2) is stable for $\tau < 10$ and unstable for $\tau > 10$. This result has been shown in Figs. 3 and 4, for $\tau = 8$ and $\tau = 13$ respectively. From Fig. 3, it is clear that all the variables are approaching to their equilibrium values, showing the stability of endemic equilibrium E_1 for $\tau < \tau_0$. However, from Fig. 4, we may note that the behavior of all the variables is oscillatory, this implies that the endemic equilibrium E_1 is unstable for $\tau > \tau_0$.

The nonlinear stability results for the above set of data in $Y - C_h$ plane and $C - C_h$ plane of model system (2) for $\tau = 8$ and $\tau = 13$ are presented in Figs. 5 and 6 respectively. In Fig. 5, we can see that solution trajectories are reaching to their equilibrium values, which shows that the endemic equilibria E_1 is nonlinearly stable in $Y - C_h$ plane and $C - C_h$ plane for $\tau = 8$. However, in Fig. 6, it can be seen that the solution trajectories are moving away from the equilibrium values and forming a limit cycle. This implies that the endemic equilibrium is unstable for $\tau = 13$.

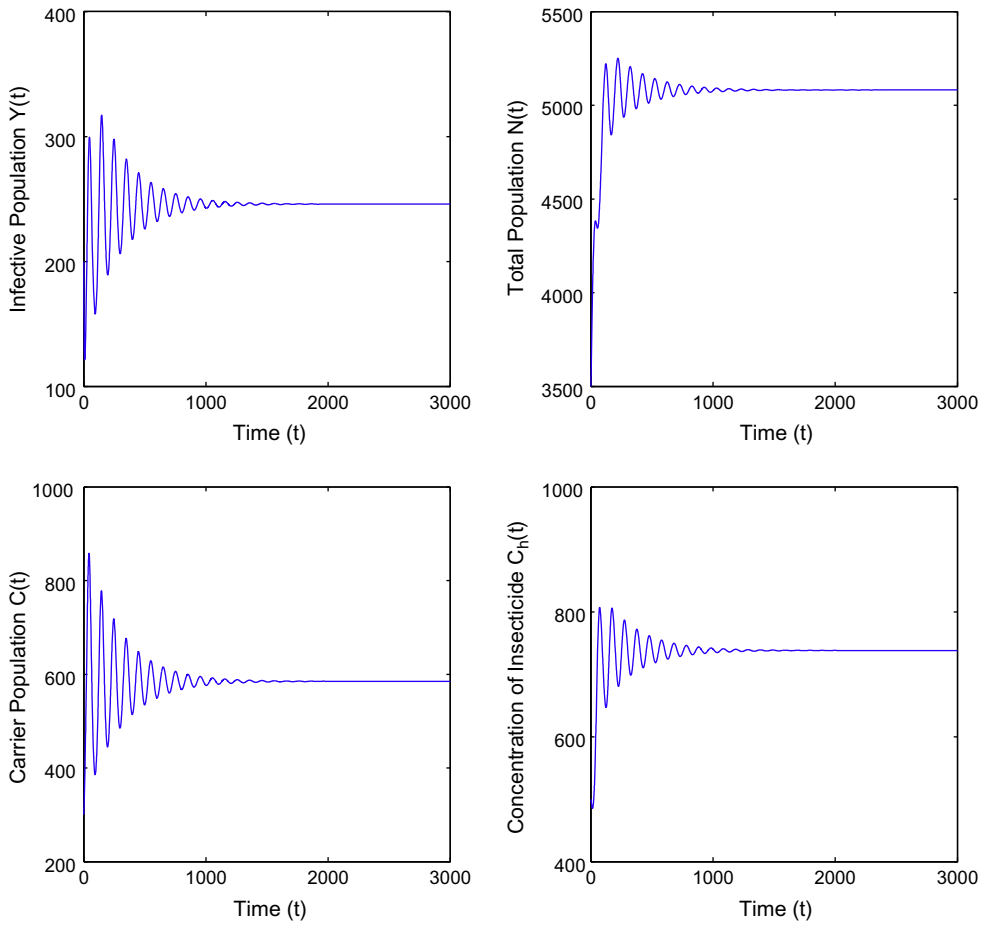

Fig. 3. Variation of Y, N, C and C_h with respect to time t for $\tau = 8$.

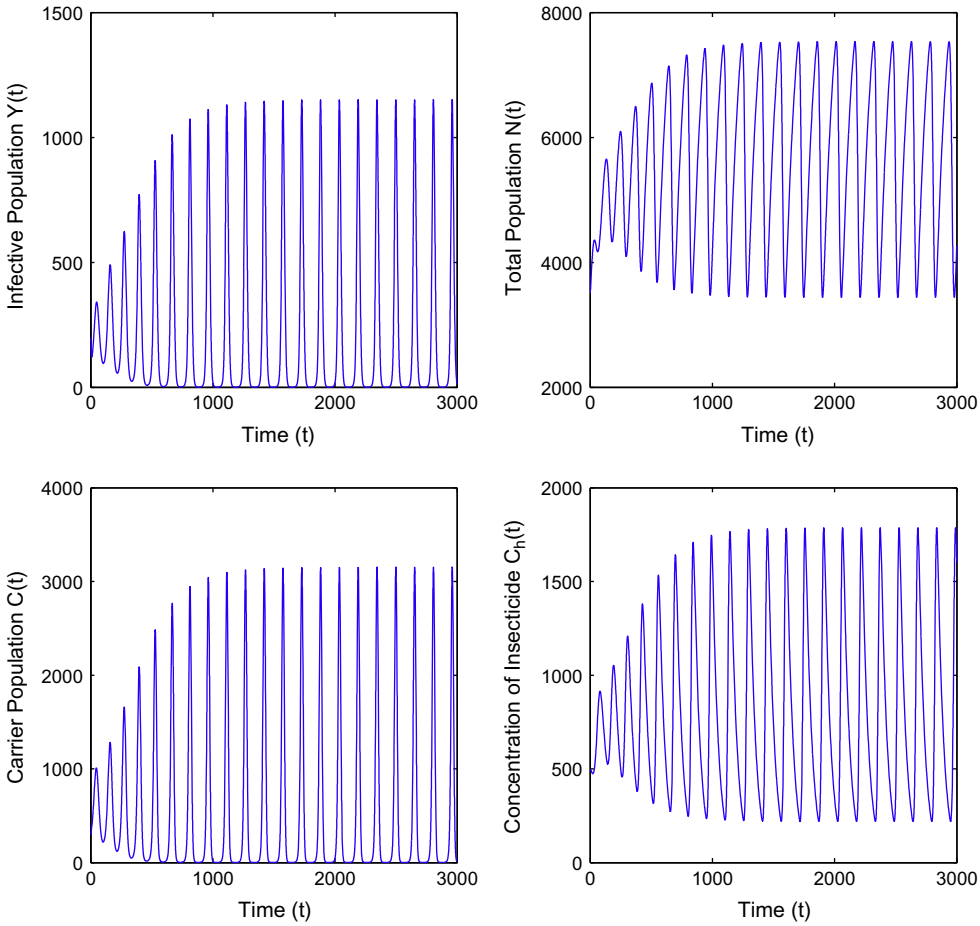

Fig. 4. Variation of Y, N, C and C_h with respect to time t for $\tau = 13$.

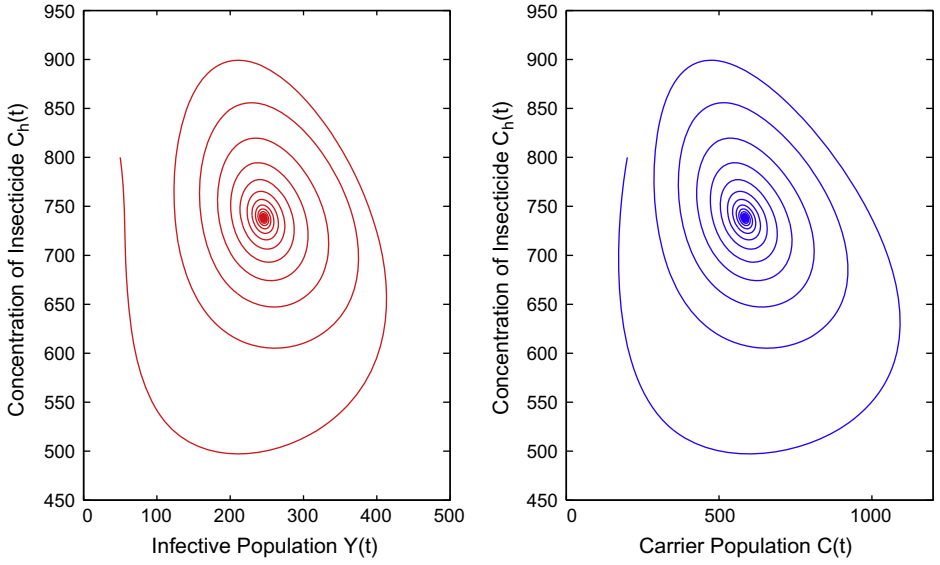

Fig. 5. Nonlinear stability in $Y - C_h$ plane and $C - C_h$ plane for $\tau = 8$.

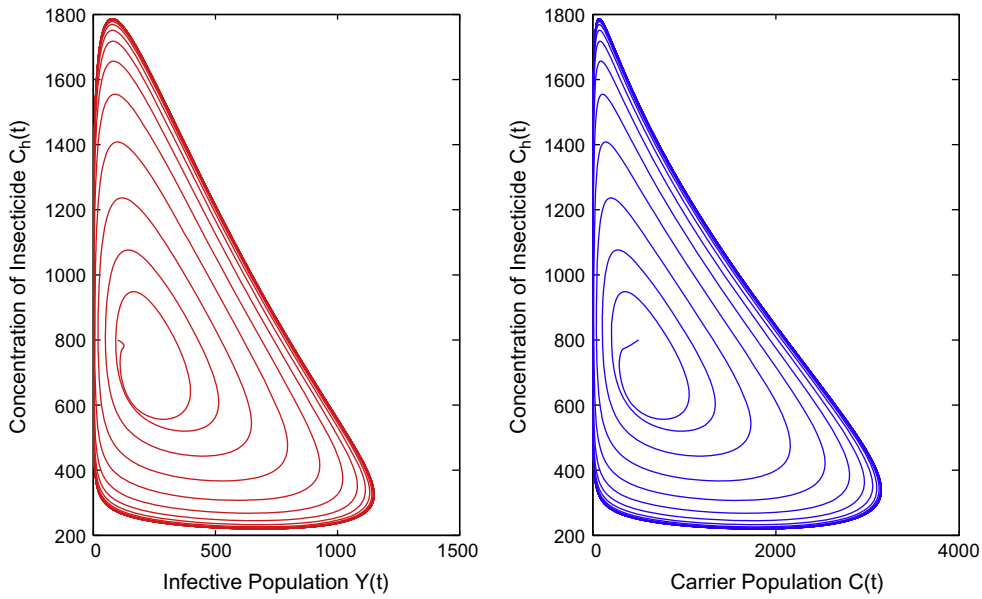

Fig. 6. Limit cycle in $Y - C_h$ plane and $C - C_h$ plane for $\tau = 13$.

The epidemiological meaning of the above discussion is that if the measured data for the density of carriers is older than τ_0 time then the number of infective will fluctuate and in this case one cannot predict the size and severity of cholera epidemic. If one wants to predict the size of cholera epidemic then the measured density of carrier population should not be older than τ_0 time.

6. Conclusions

In this paper, a nonlinear delay mathematical model for the control of cholera disease, using insecticides to control the growth of carriers in the environment, is proposed and analyzed. The model exhibits two equilibria, namely disease-free equilibrium (DFE) and endemic equilibrium. The DFE exists without any condition however the endemic equilibrium exists whenever DFE is unstable. In the absence of delay (i.e. $\tau = 0$), the endemic equilibrium, if exists, is locally asymptotically stable under condition stated in Theorem 1. It is found that the growth rate of carrier population due to human-related activities has destabilizing effect on the system. The analysis of the model shows that the density of carrier population decreases as the rate of spray of insecticides increases, which leads to reduction in the number of cholera infectives. We have determined the conditions for Hopf-bifurcation using time delay as a bifurcation parameter. It is shown that stability of endemic equilibrium does not change when time delay is suitably small, while a loss of stability by a Hopf-bifurcation can occur as the delay crosses some critical value τ_0. This critical value of τ_0 has been obtained analytically and is given by Eq. (24). In terms of epidemiology, Hopf-bifurcation analysis suggests that cholera disease may be controlled by spraying insecticides in the environment but a longer delay (more than τ_0) in spraying it may lead to difficulty in controlling the disease. In the latter case, sometimes the number of infectives will be low and sometimes their number may be higher. These fluctuations in the number of infectives will make it difficult to predict the future course of epidemic.

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