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# Transmission dynamics of tuberculosis with multiple re-infections

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ABSTRACT

We propose and analyze an epidemic model describing the transmission dynamics of tuberculosis (TB) with the possibilities of re-infections and fast progression of the disease. The qualitative behavior of the system is studied, covering several distinct aspects of disease transmission. The epidemiological threshold, known as the basic reproduction number, $R_0$, is determined using the next-generation matrix approach. It is observed that the present epidemic system may exhibit a backward bifurcation for $R_0 < 1$. Therefore, we may conclude that reducing $R_0$ to less than unity is not sufficient for eradication of tuberculosis. However, reducing $R_0$ to less than $R_0^*$, the sub-threshold obtained in the absence of recurrent TB, it is possible to eradicate the disease. We notice that a sufficient proportion of newly infected individuals developing a direct progression to the active stage can overcome the possibility of backward bifurcation. We also insight the qualitative nature of backward bifurcation with variation in re-infection level. It is found that increasing the level of re-infections makes the disease eradication more challenging. The theoretical investigations are being supplemented by numerical simulations whenever necessary.



## 1. Introduction

Tuberculosis is a chronic airborne bacterial disease caused by infection with a bacterium called *Mycobacterium tuberculosis (Mtb)*. It is one of the major global health concerns with almost a quarter of the world's population as its reservoir. Moreover, $10-11$ million new active cases of the disease appear each year [37]. It is the most common infection in many developing countries. The South East Asian Region (*SEAR*) including India, Bangladesh, Nepal *etc.* are highly affected by TB infection. In this region, around 4.74 million new TB cases were reported and almost $784,000$ died in 2015. Despite having modern effective clinical therapies for the last two decades, the death toll caused by TB is still extraordinarily high. Hence, to reduce TB incidence globally, more effort is needed.

TB is an airborne disease and transmitted via the respiratory route. When an active TB individual coughs or sneezes, *Mtb* droplets are released in the air, these droplets contain Tubercle bacilli and stay alive for nearly two hours on the air. Inhaling these infectious droplets a susceptible person may be infected, depending on the duration of contact with contagious individuals. The bacteria primarily attacks lungs (pulmonary TB), but severe stages of TB (extra-pulmonary TB) can affect other organs like the central nervous system, bones-joint *etc.* There are various possible outcomes after infection with *Mtb*. In general, after infection, the innate mechanism seizes the bacilli, and the person enters in the period of latency, an asymptotic stage where the person does not suffer from any clinical symptoms and also not infectious. Fundamentally, latent TB can be considered as an equilibrium state between host and *Mtb* bacilli. The duration of the dormant stage can lead from months to decades, depending upon immunity power of the infected individual. The main difference between TB and other infectious diseases is that the disease progression from latent stage to active pulmonary TB is significantly time-consuming. Moreover, a very little proportion (approximately $5-10\%$) of latently infected individuals develop active TB, whereas remaining stays in the non-infectious state for a lifetime. This pattern of developing active TB from the latent stage is known as 'endogenous reactivation' [16]. It mainly classifies the situations when an old infection which was in an asymptotic state becomes symptomatic. Besides the possibility of 'slow progression' to the active stage, there is evidence of 'fast progression' in which, an individual starts manifesting symptomatic active TB within a finite time frame (1 to 3 years). There are some theoretical studies on several aspects of the transmission dynamics of TB [1,4,9,13,19,20]. In [1], the authors proposed an eight compartmental model to study the emergence and propagation of drug-resistant. Bowng and Tewa [2] developed an SEI type model to describe the transmission procedure of TB with general contact rate. They also provide a suitable Lyapunov function to study the global dynamics of their proposed model. In [3], one

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strain and two strain models of TB transmission are investigated. Okuonghae [23] reported a mathematical model incorporating genetic heterogeneity in TB epidemiology and suggests to develop new treatment drug which can reduce disease transmission rates rather than disease progression rates.

The primary purpose of studying infectious disease modelling is to design better health measures to control and ultimately to eradicate the disease. In the last few decades, both mathematicians and biologists have developed many mathematical models to analyze the transmission procedure of several infectious diseases [11,15,18,21,28,31–33]. To determine appropriate public health measures, a threshold quantity called the basic reproduction number $R_0$, plays a significant role [29]. Generally, reducing $R_0$ to less than unity is sufficient to control the disease. However, some studies [4,12,14,15,22] also show the occurrence of a subcritical bifurcation, also known as backward bifurcation. In this scenario, the disease may persist even if the basic reproduction number $R_0 < 1$. This kind of adverse dynamical behavior makes the disease outbreaks less predictable, and hence it is a very significant phenomenon in infectious disease modelling.

In developing countries, re-infection is a major threat, even though it may not be significant in developed countries. In this context, exogenous re-infection [5] and recurrent TB are two essential aspects to be considered. The progression towards the active stage of TB from the latent stage may be accelerated due to exogenous re-infection. Further, Recurrent TB [4,6] is another process through which a recovered person may follow a new episode of TB after the previous infection has been successfully cured. This often happens, as recuperation from TB infection not necessarily ensure permanent immunity from the disease. It has been observed that the person who had TB are at higher risk of developing TB when reinfected. Moreover, chances of re-infection after successful therapy is four times higher than a new infection [8]. Recurrent TB is a severe issue in TB epidemiology as it causes almost $10-30\%$ of the active cases. Thus to design a mathematical model, these re-infections must be incorporated. In these context, two most influential works are described in [12,14]. Considering a TB model with exogenous re-infection, [12] suggest that reducing $R_0$ to less than one may not be adequate to get rid of the disease. On the other hand, considering a data-based model of TB, [14] showed that backward bifurcation should not be a serious concern for a TB eradication process. Thus from the above literature survey, it is found that even though there exists some literature describing re-infections in TB transmission dynamics and existence of backward bifurcation, however, impacts of backward bifurcation are not much clear.

Though TB progression depends on individual immunity level, still there are very few models considering the possibilities of fast progress. In the presence of re-infection, the consequences of rapid progression still are unknown. Existing literature studied only the local dynamics of TB model in the presence of reinfection. It gives no idea about the convergence of a trajectory starting from any arbitrary initial point. Therefore, it is important to analyze the fate of an epidemic process irrespective of the number of individual infectious present in the population. This particular observation motivates us to study the global dynamics of the proposed system. Finally, in the present study, investigations are focused on the substantial effects of re-infection and fast progression of the disease on the transmission dynamics of the disease. We aim to answer: (i) How the re-infection affects the backward bifurcation? (ii) What will be qualitative difference in backward bifurcation if the recurrent TB can be terminated? (iii) What will be the sufficient condition for disease eradication? (iv) How the fast progression of the disease affects the dynamics? (v) Is it possible to establish some parametric conditions for the global stability of the exiting endemic equilibrium point?

Rest of the paper is organized in the following way: In Section 2, a compartmental TB transmission model has been proposed. The qualitative dynamical behaviors of the model in terms of positivity and boundedness of solutions, the existence of equilibria and their stability has been discussed in Section 3. Next, we investigate our model in the absence of recurrent TB in Section 4. The next section is devoted to verifying our analytical results with the help of numerical simulations. Finally, in Section 6 we have discussed the epidemiological significance of our findings with some concluding remarks.

## 2. The mathematical model

In this section, we investigate a mathematical model of TB transmission, which capture the dynamics of exogenous re-infection among the latently infected population. Based on the epidemiological characteristics we categorized the total population into four compartments, namely, susceptible (S), exposed (E, infected but not infectious), infectious (I) and recovered (R, still susceptible). Our TB transmission model has been shown in the following diagram

According to the schematic diagram (Fig. 1), our model system takes the following form

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta IS - \delta S,\\
\frac{dE}{dt} &= (1-c)\beta IS - \alpha\beta EI - kE - \delta E + \gamma\beta RI,\\
\frac{dI}{dt} &= c\beta IS + \alpha\beta EI + kE - hI - \delta I,\\
\frac{dR}{dt} &= hI - \delta R - \gamma\beta RI,
\end{aligned} \tag{1}$$

with initial conditions

$$S(0) \geq 0,\ E(0) \geq 0,\ I(0) \geq 0,\ R(0) \geq 0, \tag{2}$$

where

- $\Lambda$ is a constant recruitment in susceptible class only and $\delta$ is the natural death rate of individuals in each compartment.
- The susceptible class becomes infected through contact with infectious individual at the rate $\beta$. A fraction $c(0<c<1)$ of the newly infected individuals are assumed to undergo a fast progression of the disease due to low resistance power and they directly move to infected class, while remaining are in latent stage.
- There is a chance of exogenous re-infection in the long latency period $\frac{1}{k}$ of an individual. The rate at which exposed population are being re-infected and become infectious is $\alpha\beta EI$, where $\alpha \in [0, 1]$. Here, $\alpha = 0$ refers no exogenous re-infection occur in the system (1).
- $h$ represents the per capita recovery rate.

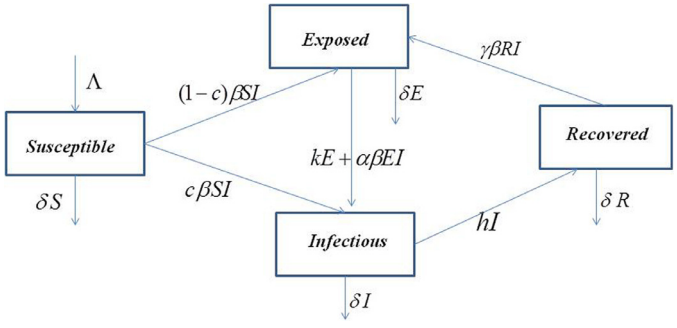


**Fig. 1.** The schematic diagram explaining the dynamics of TB transmission.

- After recovery from the disease an individual is not permanently immune from TB. Therefore, there is a risk to undergo re-infection and repeat the disease. It is assumed that the recovered individual has a certain immunity level to avoid direct progression to active TB. $\gamma\beta RI$ where $0 \leq \gamma \leq 1$, is the rate at which recovered population encounter re-infection and become exposed. Clearly, $\gamma = 0$ represents an ever lasting immunity from TB.

The total host population is denoted by $N = S + E + I + R$. Then adding all the equations of the system (1), we obtain

$$\frac{dN}{dt} = \Lambda - \delta N. \tag{3}$$

Let, $N^*$ is the positive equilibrium of the system (3), then $\Lambda = \delta N^*$. The total population is assumed in stationary demographic state when the disease is spreading, which gives $N^* = S + E + I + R$. Therefore, $R$ can be replaced by $N^* - S - E - I$. Hence, the system (1) is reduced to a 3-dimensional system

$$\begin{aligned}
\frac{dS}{dt} &= \delta N^* - \beta IS - \delta S,\\
\frac{dE}{dt} &= (1-c)\beta IS - \alpha\beta EI - kE - \delta E + \gamma\beta(N^* - S - E - I)I,\\
\frac{dI}{dt} &= c\beta IS + \alpha\beta EI + kE - hI - \delta I,
\end{aligned} \tag{4}$$

with initial conditions

$$S(0) \geq 0,\ E(0) \geq 0,\ I(0) \geq 0. \tag{5}$$

## 3. Basic properties of the model

### 3.1. Positivity

**Theorem 3.1.** *Every solution of (4) with positive initial conditions (5) defined in $[0, \infty)$, will remain positive for all $t > 0$.*

**Proof.** The system (4) can be written in the vector form

$$\dot{X}(t) = \mathcal{B}X(t), \tag{6}$$

where

$$X(t) = col(S, E, I), \quad X(0) = col(S(0), E(0), I(0)),$$

with

$$\begin{pmatrix} \mathcal{B}_1(X(t)) \\ \mathcal{B}_2(X(t)) \\ \mathcal{B}_3(X(t)) \end{pmatrix} = \begin{pmatrix} \delta N^* - \beta IS - \delta S \\ (1-c)\beta IS - \alpha\beta EI - (k+\delta)E + \gamma\beta(N^* - S - E - I)I \\ c\beta IS + \alpha\beta EI + kE - (\delta + h)I \end{pmatrix},$$

where $\mathcal{B} : \mathbb{R}^3 \to \mathbb{R}^3_+$ and $\mathcal{B} \in C^\infty(\mathbb{R}^3)$. It is obvious that, $\mathcal{B}_i(X_i)|_{X_i=0} \geq 0$ for $i = 1,\ 2,\ 3$. Now using classical theorem by Nagumo [30], one can conclude that, the solutions of (4) with non-negative initial conditions $\mathcal{B}_0 \in \mathbb{R}^3_+$, say $\mathcal{B}(t) = \mathcal{B}(t, \mathcal{B}_0)$ are positive, that is, $\mathcal{B}(t) \in \mathbb{R}^3_+$ for all $t > 0$. □

### 3.2. Boundedness

**Theorem 3.2.** *Every solution of (4) initiating in $\mathbb{R}^4_+$ is bounded.*

**Proof.** From (3), we have

$$N(t) = \frac{\Lambda}{\delta}(1 - e^{-\delta t}) + N(0)e^{-\delta t}.$$

It is observed that, as $t \to \infty$

$$N(t) \to \frac{\Lambda}{\delta}.$$

Hence all solutions of the system (4) initiating from $\{\mathbb{R}^4_+ \setminus 0\}$ are confined in the region

$$\Gamma = \left\{(S, E, I, R) \in \mathbb{R}^4_+ : 0 < S + E + I + R \leq \frac{\Lambda}{\delta} + \epsilon\right\},$$

for any positive number $\epsilon$ and $t \to \infty$. Hence the theorem. □

Therefore, it is convenient to consider the region $\Gamma$ for discussion of the dynamical flow generated by the system (4).

### 3.3. Basic reproduction number

The threshold parameter $R_0$ gives an average number of secondary infection spread by a single infectious individual in a completely susceptible individuals. To find $R_0$, we follow the method of next-generation matrix, illustrated by van den Driessche and Watmough [10].

Let us consider, $\chi = (E, I, S)$ and rewrite the system (4) as

$$\frac{d\chi}{dt} = \mathbb{F} - \mathbb{V},$$

where, $\mathbb{F}$ is the rate at which new infections take place whereas $\mathbb{V}$ is all other flows within and out of each compartments. Therefore, we have

$$\mathbb{F} = \begin{pmatrix} (1-c)\beta IS + \gamma\beta(N^* - S - E - I)I \\ \alpha\beta EI + c\beta IS \\ 0 \end{pmatrix},$$

and

$$\mathbb{V} = \begin{pmatrix} \alpha\beta EI + (k+\delta)E \\ -kE + (\delta + h)I \\ -\delta N^* + \beta IS + \delta S \end{pmatrix}.$$

The system (4) always has an infection free steady state $P_0 = (N^*, 0, 0)$. Then the jacobian matrix of $\mathbb{F}$ and $\mathbb{V}$ at $P_0$ is given by

$$\mathbb{DF}_{P_0} = \begin{pmatrix} F_{2\times 2} & 0 \\ 0 & 0 \end{pmatrix} \text{ and } \mathbb{DV}_{P_0} = \begin{pmatrix} V_{2\times 2} & 0 \\ M_1 & \delta \end{pmatrix},$$

where

$$F = \begin{pmatrix} 0 & (1-c)\beta N^* \\ 0 & c\beta N^* \end{pmatrix},\ V = \begin{pmatrix} k+\delta & 0 \\ -k & h+\delta \end{pmatrix} \text{ and } M_1 = \begin{pmatrix} 0 & \beta N^* \end{pmatrix}.$$

The next generation matrix is of the form

$$FV^{-1} = \frac{\beta N^*}{(k+\delta)(\delta+h)} \begin{pmatrix} (1-c)k & (1-c)(k+\delta) \\ ck & c(k+\delta) \end{pmatrix}.$$

Now according to the Theorem 2 in [10], the spectral radius $\rho$ of matrix $FV^{-1}$, which is the maximum eigenvalue of $FV^{-1}$, gives the basic reproduction number $R_0$ of the system (4). After some algebraic manipulations, we obtain

$$R_0 = \rho(FV^{-1}) = \frac{\beta(c\delta + k)N^*}{(k+\delta)(\delta+h)}. \tag{7}$$

### 3.4. Stability of infection free equilibrium

The infection free steady state of our TB model (4) is $P_0 = (N^*, 0, 0)$. To investigate local asymptotic stability of $P_0$ we compute the variational matrix $J_{P_0}$, given by

$$J_{P_0} = \begin{pmatrix} -\delta & 0 & -\beta N^* \\ 0 & -(\delta+k) & (1-c)\beta N^* \\ 0 & k & c\beta N^* - (\delta + h) \end{pmatrix}.$$

Then the characteristic equation of the matrix $J_{P_0}$ is given by

$$(\lambda + \delta)(\lambda^2 + a_1\lambda + a_0) = 0, \tag{8}$$

where, $a_1 = k + h + 2\delta - c\beta N^*$ and $a_0 = (\delta + k)(\delta + h) - \beta(k + c\delta)N^* = (\delta + k)(\delta + h)(1 - R_0)$.

The Eq. (8) has all its roots with negative real part only when $a_0 > 0$ and $a_1 > 0$. It can be noted that $a_0 > 0$ only when $R_0 < 1$ and $a_1 > 0$ gives $c < \frac{k+h+2\delta}{\beta N^*}$. Therefore, the jacobian $J_{P_0}$ has all its eigenvalue with negative real part if $R_0 < 1$ with $c < \frac{k+h+2\delta}{\beta N^*}$.

The above discussion can be written in the following theorem.

**Theorem 3.3.** *The infection free steady state $P_0$ is locally asymptotically stable whenever $R_0 < 1$ and $c < \frac{k+h+2\delta}{\beta N^*}$, otherwise unstable.*

Biologically it indicates that eradication of the disease when $R_0 < 1$ depends on initial size and proportion of fast progression of the individuals.

### 3.5. Existence and stability of endemic equilibrium

#### 3.5.1. Existence

Now, we investigate the existence of interior steady state $P^*(S^*, E^*, I^*)$ of the system (4). To find the condition for the existence of $P^*$, we solve the following simultaneous equations

$$\begin{aligned} &\delta N^* - \beta I^* S^* - \delta S^* = 0,\\ &\beta(1 - c - \gamma)S^* I^* - \beta(\alpha + \gamma)E^* I^* - (k + \delta)E^* + \gamma\beta I^*(N^* - I^*) = 0,\\ &c\beta S^* I^* + \alpha\beta E^* I^* - (h + \delta)I^* = 0. \end{aligned} \tag{9}$$

Solving the first equation of (9), for $S^*$ and substituting the value of $S^*$ in the third equation of (9), we obtain $S^* = \frac{\delta N^*}{\beta I^* + \delta}$ and $E^* = I^* \frac{(h+\delta)(\beta I^* + \delta) - c\beta\delta N^*}{(\alpha\beta I^* + k)(\beta I^* + \delta)}$. Again, substituting these values in the second equation of (9), we obtain a cubic equation in $I^*$, is given by

$$\eta_3 (I^*)^3 + \eta_2 (I^*)^2 + \eta_1 (I^*) + \eta_0 = 0, \tag{10}$$

where

$$\begin{aligned} \eta_3 &= \alpha\beta^3\gamma,\\ \eta_2 &= \beta^2(h + \delta)(\alpha + \gamma) + \gamma\beta^2(\alpha\delta + k) - \alpha\beta^3\gamma N^*,\\ \eta_1 &= \beta[(h + \delta)\{k + \delta + \delta(\alpha + \gamma)\} - c\beta\delta(\alpha + \gamma)N^*]\\ &\quad - \beta^2 N^*[\alpha\delta(1 - c - \gamma) + \gamma(\alpha\delta + k)] + \gamma\beta\delta k,\\ \eta_0 &= \delta(k + \delta)(\delta + h)(1 - R_0). \end{aligned} \tag{11}$$

Clearly, $I^*$ is a positive real root of the cubic polynomial (10). Now, the number of possible positive real root(s) of the polynomial (10), depend on the signs of $\eta_2$, $\eta_1$ and $\eta_0$. This can be analyzed by applying Descarte's rule of sign. The various possibilities has been shown in the Table 1.

The results can be summarized in the following theorem

**Theorem 3.4.** *The TB model (4),*

(i) *has a unique endemic equilibrium when $R_0 > 1$ and cases $1 - 3$ are satisfied.*
(ii) *have one or more than one endemic equilibria when $R_0 < 1$ and cases $5 - 7$ are satisfied.*
(iii) *does not have any endemic equilibrium when $R_0 < 1$ and case 8 indicates that all the coefficient are positive.*

#### 3.5.2. Local asymptotic stability

To study the local asymptotic stability of the endemic equilibrium point $P^*$ we compute the following variational matrix $J_{P^*}$, is given by

$$J_{P^*} = \begin{pmatrix} -\delta - \beta I^* & 0 & -\beta S^* \\ (1 - c - \gamma)\beta I^* & -(\alpha + \gamma)\beta I^* - (k + \delta) & (k + \delta)\frac{E^*}{I^*} - \gamma\beta I^* \\ c\beta I^* & \alpha\beta I^* + k & -\frac{kE^*}{I^*} \end{pmatrix}. \tag{12}$$

The characteristic equation of $J_{P^*}$ is

$$\rho^3 + C_1\rho^2 + C_2\rho + C_3 = 0, \tag{13}$$

where

$$\begin{aligned} C_1 &= (\alpha + \gamma)\beta I^* + \frac{kE^*}{I^*} + \delta + \beta I^*,\\ C_2 &= \left(d_1 + \frac{kE^*}{I^*}\right)(\delta + \beta I^*) + c\beta^2 S^* I^* + d_2,\\ C_3 &= (\delta + \beta I^*)d_2 + [(1 - c - \gamma)(\alpha\beta I^* + k) + cd_1]\beta^2 S^* I^*, \end{aligned}$$

with $d_1 = (\alpha + \gamma)\beta I^* + (k + \delta)$, $d_2 = (\alpha\beta I^* + k)\gamma\beta I^* - [\alpha(k + \delta) + k(\alpha + \gamma)]\beta E^*$.

For local asymptotic stability, all eigenvalues of $J_{P^*}$ must have negative real part. Therefore, using well-known Routh–Hurwitz criteria, we obtain a set of parametric conditions for local asymptotic stability of $P^*$, is given by

$$C_2 > 0, \quad C_3 > 0 \quad \text{and} \quad C_1 C_2 - C_3 > 0.$$

#### 3.5.3. Backward bifurcation

Occurrence of backward bifurcation is a significant phenomenon in compartmental epidemiological modelling, especially in TB transmission. This has been studied by many authors [9,14,17,18] in their disease transmission models. In our model (4) existence of multiple TB persistence equilibria $P^*$ for $R_0 < 1$, suggest the possibility of backward bifurcation. Epidemiologically, it recommends that the value of $R_0$ is not enough to determine whether TB will persist or not, rather it depends on the initial size of the individuals when $R_0 < 1$. Our aim is to investigate the existence of backward bifurcation of (4) and set a threshold for it. In order to do so we use the well-known result by Castillo–Chavez and Song [9]. We rewrite our system (4) in a simplified manner by choosing, $S = x_1, E = x_2, I = x_3$. If we set $X = (x_1, x_2, x_3)^T$, then our system (4) can be written in the form $\frac{dX}{dt} = F(X)$ with $F = (f_1, f_2, f_3)^T$.

$$\begin{aligned} &F(X)\\ &= \begin{pmatrix} \delta N^* - \beta x_1 x_2 - \delta x_1 \\ (1 - c)\beta x_1 x_2 - \alpha\beta x_2 x_3 - (k + \delta)x_2 + \gamma\beta(N^* - x_1 - x_2 - x_3)x_3 \\ c\beta x_1 x_3 + \alpha\beta x_2 x_3 + kx_2 - (h + \delta)x_3 \end{pmatrix}\\ &= \begin{pmatrix} f_1 \\ f_2 \\ f_3 \end{pmatrix}. \end{aligned}$$

**Table 1**
Number of possible positive roots of polynomial Eq. (10).

| Cases | $\eta_3$ | $\eta_2$ | $\eta_1$ | $\eta_0$ | $R_0$ | changes in sign | Total possible positive roots |
|---|---|---|---|---|---|---|---|
| 1 | + | − | − | − | $R_0 > 1$ | 1 | 1 |
| 2 | + | + | − | − | $R_0 > 1$ | 1 | 1 |
| 3 | + | + | + | − | $R_0 > 1$ | 1 | 1 |
| 4 | + | − | + | − | $R_0 > 1$ | 3 | 1,3 |
| 5 | + | − | − | + | $R_0 < 1$ | 2 | 0,2 |
| 6 | + | + | − | + | $R_0 < 1$ | 2 | 0,2 |
| 7 | + | − | + | + | $R_0 < 1$ | 2 | 0,2 |
| 8 | + | + | + | + | $R_0 < 1$ | 0 | 0 |

The variational matrix of the system at infection free equilibrium $P_0 = (N^*, 0, 0)$, is

$$J_{P_0} = \begin{pmatrix} -\delta & 0 & -\beta N^* \\ 0 & -(\delta + k) & (1-c)\beta N^* \\ 0 & k & c\beta N^* - (\delta + h) \end{pmatrix}.$$

By choosing $\beta$ as a bifurcation parameter when $R_0 = 1$, we obtain the critical value for $\beta = \beta_c = \frac{(k+\delta)(\delta+h)}{(c\delta+k)N^*}$. At the threshold value, the jacobian matrix $J_{P_0}$ has a simple zero eigenvalue whose left and right eigenvectors are given by $v = (0, 1, \frac{\delta+k}{k})$ and $w = (-\frac{\beta N^*}{\delta}, \frac{(1-c)\beta N^*}{(\delta+k)}, 1)$.

To obtain the following quantities reported in Theorem 4.1, by Castillo–Chavez and Song [9], we have

$$a = \sum_{k,i,j=1}^{3} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0, \beta_c) \quad \text{and} \quad b = \sum_{k,i=1}^{3} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta}(P_0, \beta_c)$$

It can be noted that, the first component of $v$ is zero therefore we do not need to derivative of $f_1$ and the non-zero derivatives of $f_2$ and $f_3$ can be written as

$$\frac{\partial^2 f_2}{\partial x_2 \partial x_3} = -\alpha\beta - \gamma\beta; \quad \frac{\partial^2 f_2}{\partial x_3 \partial x_1} = (1-c)\beta - \gamma\beta; \quad \frac{\partial^2 f_2}{\partial x_3^2} = -2\gamma\beta,$$

$$\frac{\partial^2 f_3}{\partial x_2 \partial x_3} = \alpha\beta; \quad \frac{\partial^2 f_3}{\partial x_1 \partial x_3} = c\beta,$$

and

$$\frac{\partial^2 f_2}{\partial x_3 \partial \beta} = (1-c)N^*; \quad \frac{\partial^2 f_3}{\partial x_3 \partial \beta} = cN^*.$$

Evaluating the quantities $a$ and $b$ at $(P_0, \beta_c)$, we have

$$a = 2w_2w_3\left[\frac{\alpha\beta_c(\delta+k)}{k} - \alpha\beta_c - \gamma\beta_c\right] + 2w_3w_1\left[(1-c)\beta_c - \gamma\beta_c + \frac{c\beta_c(\delta+k)}{k}\right] - 2\gamma\beta_c,$$

$$b = \frac{N^*(c\delta+k)}{k}.$$

According to the result illustrated in [9], our system undergoes backward bifurcation at $\beta = \beta_c$, only when both $a$ and $b$ are positive at $(P_0, \beta_c)$. Clearly, $b$ is always positive. Therefore, the positivity of $a$ gives the threshold condition for backward bifurcation

$$\alpha > \alpha^* = \frac{(c\delta+k)}{\delta^2(1-c)}\left[k + \delta + \frac{\gamma kh}{\delta+h}\right]. \tag{14}$$

*3.5.4. Effects of fast progression TB*

It can be observed that the expression of $\alpha^*$ is dependent on the fraction $c$ of newly infected individuals are subjected to fast progression of TB. This particular parameter has an significant role to avoid backward bifurcation. Differentiating $\alpha^*$ with respect to $c$, we obtain

$$\frac{d\alpha^*}{dc} = \frac{\delta+k}{\delta(1-c)^2}\left[k + \delta + \frac{\gamma kh}{\delta+h}\right].$$

Clearly, $\frac{d\alpha^*}{dc}$ is strictly positive for $0 \le c < 1$. Hence, $\alpha^*$ is an increasing function of $c$. This particular observation is also presented in Fig. 2. Therefore, if we increase $c$ gradually, keeping all other parameters fixed then the threshold value $\alpha^*$ of exogenous re-infection level increases strictly. Therefore, the system (4) becomes unlikely to perform backward bifurcation for higher value of $c$. Moreover, the system (4) undergoes backward bifurcation only when the pair $(c, \alpha)$ lies on the upper portion of the curve. Therefore, for a fixed value of $\alpha$ there exists a sufficiently large value of $c$ by which backward bifurcation may be eliminated.

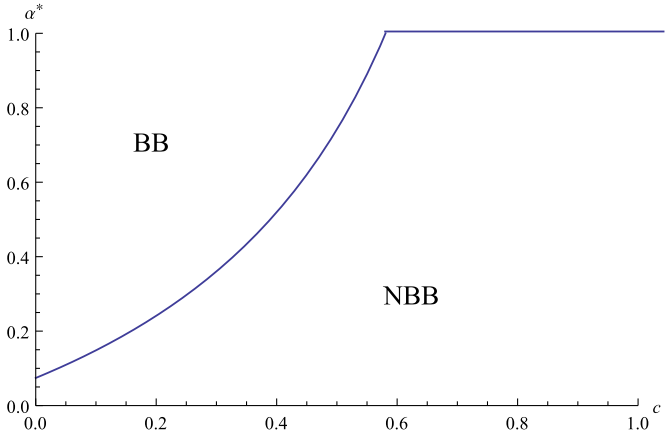


**Fig. 2.** Plot of $\alpha^*$ as a function of c. All the parameter values are mentioned in Table 2. BB and NBB refers backward bifurcation and no backward bifurcation respectively.

*3.5.5. Global asymptotic stability*

In this section, we investigate global asymptotic stability of the endemic equilibrium $P^*$ for the system (4). It can be noted from Theorem 3.4, the system (4) may possess endemic equilibrium points irrespective of the fact $R_0 < 1$ or $R_0 > 1$. Furthermore, in the previous section the occurrence of backward bifurcation is noticed for $R_0 < 1$, which indicates that endemic equilibrium can not be global asymptotically stable in this situation. However, it is worthy to study the global stability of endemic equilibrium for $R_0 > 1$, that is, when case (i) of Theorem 3.4 occurs. To study global asymptotic stability of $P^*$ we shall employ a geometric approach developed by Li and Muldowney [24]. This technique mainly based on higher-dimensional generalizations of Bendixson and Dulac criteria and also used in [25,27]. Now we shall briefly summarize the method developed by Li and Muldowney [24].

Let us consider the mapping $x \to f(x)$, defined on an open set $\Omega \subset \mathbb{R}^n \to \mathbb{R}^n$, such that each solution of the differential equation

$$\frac{dx}{dt} = f(x), \tag{15}$$

is uniquely determined by its initial value $x(0) = x_0$, and the solution be denoted by $x(t, x_0)$. Further, the following assumptions hold

H1) $\Omega$ is simply connected,
H2) there is a compact absorbing set $E \subset \Omega$,
H3) the differential equation has an unique endemic equilibrium $x^*$.

The Lozinskii measure for an $n \times n$ matrix $B$ with respect to induced matrix norm $|.|$ is defined as

$$\eta(B) = \lim_{h \to 0^+} \frac{|I + hB| - 1}{h}$$

Let us consider the map $x \to P(x)$ where $P(x)$ is a nonsingular ${}^nC_2 \times {}^nC_2$ matrix-valued $C^1$ function on $\Omega$. The matrix $B$ is defined as $B = P_f P^{-1} + PV^{[2]}P^{-1}$; where, $P_f$ is obtained by replacing each entry $p_{ij}$ of $P$ by its derivative in the direction of $f$ and $V^{[2]}$ is the second additive compound matrix corresponding to the variational matrix $V$ of the system (15). For the Lozinskii measure $\eta$ on $\mathbb{R}^{{}^nC_2 \times {}^nC_2}$, a quantity is defined as

$$q = \lim_{t \to \infty} \sup \sup_{x_0 \in E} \frac{1}{t} \int_0^T \eta(Bx(s, x_0))ds.$$

The following result has been established in Theorem 3.5 of [24].

**Table 2**
Parameter values with description for the model (4).

| Descriptions | Symbol used | Taken value | Admissible range | Sources |
|---|---|---|---|---|
| Total population | $N^*$ | 100 | – | – |
| Transmission rate | $\beta$ | 0.12 | 0 – 1 | – |
| Level of exogenous re-infection | $\alpha$ | 0.26 | 0.25 – 1 | [34] |
| Re-infection level of recovered individuals | $\gamma$ | 0.5 | 0.25 – 1 | [34] |
| Endogenous reactivation rate | $k$ | 0.002 $yr^{-1}$ | – | [4,35,36] |
| Fast route to active TB | $c$ | 0.06 | 0.03 – 1 | [4,36] |
| Per capita recovery rate | $h$ | 2 $yr^{-1}$ | – | [34] |
| Natural death rate | $\delta$ | $\frac{1}{62.5}$ $yr^{-1}$ | – | Assumed |

**Theorem 3.5.** *If the system (15) satisfies the assumptions (H1), (H2) and (H3) then the unique equilibrium $x^*$ is globally asymptotically stable in $\Omega$ when $q<0$, for a function $P(x)$ and Lozinskii measure $\eta$.*

Now, we apply Theorem 3.5, to investigate the global asymptotic stability of the infected equilibrium $P^*$ for $R_0>1$. Before we start the proof, we will establish that the system (4) is uniformly persistent, by using the result demonstrated by Freedman et al. [26].

**Definition 3.1.** The system (4) is said to be uniformly persistent if there exists a constant $m>0$ such that any solution $(S(t), E(t), I(t))$ starting from $(S(0), E(0), I(0))\in\Gamma$ satisfies $min\{\liminf_{t\to\infty} S(t), \liminf_{t\to\infty} E(t), \liminf_{t\to\infty} I(t)\}\geq m$.

**Lemma 3.1.** *The system (4) is uniformly persistent if and only if $R_0>1$.*

**Proof.** The infection free equilibrium point $P_0$ is not local asymptotic stable when $R_0>1$, which serves the necessity condition $R_0>1$. To prove that $R_0>1$ is sufficient for uniform persistent, we shall follow the approach described **by** Freedman in [26]. To confirm that system (4) satisfies all the conditions of Theorem 4.3 in [26], we consider $X=\mathbb{R}^3$ and $E=\Gamma$. The maximal invariant set $N$ on the boundary $\partial\Gamma$ is the disease free equilibrium $P_0$, which is isolated. Therefore, we may conclude from Theorem 4.3 in [26], the uniform persistence of (4) when $R_0>1$ is equivalent to instability $P_0$. □

Now on the shed of above discussion, we shall proceed to establish the following Theorem.

**Theorem 3.6.** *An unique endemic equilibrium $P^*$ is globally asymptotically stable for $R_0>1$.*

**Proof.** Since the system (4) is uniformly persistent in the interior of simply connected domain $\Gamma$ when $R_0>1$. Therefore, there exits a compact absorbing set $E\subset int\,\Gamma$. Hence, the system (4) satisfies the assumption $(H2)$.

Again, from the first case of the Theorem 3.4 gives the condition for existence of an unique endemic equilibrium when $R_0>1$. Therefore, the assumption $(H3)$ is also satisfied.

The variational matrix $V(S, E, I)$ corresponding to the system (4) is

$$V=\begin{pmatrix} -\delta-\beta I & 0 & -\beta S \\ (1-c-\gamma)\beta I & -(\alpha+\gamma)\beta I-(k+\delta) & (1-c-\gamma)\beta S-(\alpha+\gamma)\beta E-2\gamma\beta I+\gamma\beta N^* \\ c\beta I & \alpha\beta I+k & c\beta S+\alpha\beta E-(\delta+h) \end{pmatrix}. \tag{16}$$

The associated second additive compound matrix is

$$V^{[2]}=\begin{pmatrix} -\beta I-(\alpha+\gamma)\beta I-k-2\delta & (1-c-\gamma)\beta S-(\alpha+\gamma)\beta E-2\gamma\beta I+\gamma\beta N^* & \beta S \\ \alpha\beta I+k & -\beta I+c\beta S+\alpha\beta E-h-2\delta & 0 \\ -c\beta I & (1-c-\gamma)\beta I & -(\alpha+\gamma)\beta I+c\beta S+\alpha\beta E-h-k-2\delta \end{pmatrix}. \tag{17}$$

Let us assume that the function $x\to P(x)$ as

$$P(S,E,I)=diag\left(1,\frac{E}{I},\frac{E}{I}\right).$$

Therefore, we have

$$P^{-1}(S,E,I)=diag\left(1,\frac{I}{E},\frac{I}{E}\right);\quad P_f=diag\left(0,\frac{\dot{E}}{I}-\frac{E}{I^2}\dot{I},\frac{\dot{E}}{I}-\frac{E}{I^2}\dot{I}\right),$$

$$P_fP^{-1}=diag\left(0,\frac{\dot{E}}{E}-\frac{\dot{I}}{I},\frac{\dot{E}}{E}-\frac{\dot{I}}{I}\right),$$

$$B=P_fP^{-1}+PV^{[2]}P^{-1}=P_fP+V^{[2]}=\begin{pmatrix} B_{11} & B_{12} \\ B_{21} & B_{22}\end{pmatrix},$$

where

$$B_{11}=\left[-\beta I-(\alpha+\gamma)\beta I-k-2\delta\right],$$
$$B_{12}=\left[(1-c-\gamma)\beta S-(\alpha+\gamma)\beta E-2\gamma\beta I+\gamma\beta N^*,\ \beta S\right],$$
$$B_{21}=\left[\alpha\beta I+k,-c\beta I\right]^T,$$
$$B_{22}=\begin{pmatrix} \frac{\dot{E}}{E}-\frac{\dot{I}}{I}-\beta I+c\beta S+\alpha\beta E-h-2\delta & 0 \\ (1-c-\gamma)\beta I & \frac{\dot{E}}{E}-\frac{\dot{I}}{I}-(\alpha+\gamma)\beta I+c\beta S+\alpha\beta E-h-k-2\delta\end{pmatrix}.$$

Now, we consider the norm on $\mathbb{R}^3$ as

$$|(u,v,w)|=max\{|u|,|v|+|w|\},\quad \forall\ \ (u,v,w)\in\mathbb{R}^3.$$

Again, the Lozinskii measure is defined as

$$\eta(B)\leq max\{g_1,g_2\},$$

with, $g_1=\eta_1(B_{11})+|B_{12}|$ and $g_2=\eta_1(B_{22})+|B_{21}|$, where $\eta_1$ is the Lozinskii measure of matrix with respect to the $L^1$ norm and

$|B_{12}|, |B_{21}|$ are matrix norms with respect to $L^1$ vector norm. Therefore, we obtain

$$\begin{aligned}\eta_1(B_{11}) &= -\beta I - (\alpha+\gamma)\beta I - k - 2\delta,\\ |B_{12}| &= \max\{(1-c-\gamma)\beta S - (\alpha+\gamma)\beta E - 2\gamma\beta I + \gamma\beta N^*,\ \beta S\}|,\\ |B_{21}| &= \max\{\alpha\beta I + k, -c\beta I\} = \alpha\beta I + k,\\ \eta_1(B_{22}) &= \frac{\dot{E}}{E} - \frac{\dot{I}}{I} + c\beta S + \alpha\beta E - h - 2\delta\\ &\quad - \min\{(c+\gamma)\beta I, k + (\alpha+\gamma)\beta I\}. \end{aligned} \tag{18}$$

Now from the third equation of the system (4), we obtain

$$\frac{\dot{I}}{I} = c\beta S + \alpha\beta E - (h+\delta) + \frac{kE}{I}. \tag{19}$$

Therefore, we obtain from (18) and (19)

$$\eta_1(B_{22}) = \frac{\dot{E}}{E} - \frac{kE}{I} - \delta - \min\{(c+\gamma)\beta I, k + (\alpha+\gamma)\beta I\}. \tag{20}$$

Hence using the relations (20) and (18), we get

$$g_2 = \frac{\dot{E}}{E} + \alpha\beta I + k - \frac{kE}{I} - \delta - min\{(c+\gamma)\beta I, k + (\alpha+\gamma)\beta I\}. \tag{21}$$

Again from the second equation of system (4), we get

$$\frac{\dot{E}}{E} = (1-c)\beta\frac{IS}{E} - \alpha\beta I - (k+\delta) - \gamma\beta I + \gamma\beta(N^* - S - I)\frac{I}{E}. \tag{22}$$

Therefore, using this relations (22) and (18), we can write $g_1$ as

$$g_1 = \frac{\dot{E}}{E} + \beta I - (1-c)\beta\frac{IS}{E} - \gamma\beta(N^* - S - I)\frac{I}{E} - \delta + |B_{12}|. \tag{23}$$

Finally,

$$\eta(B) \le max\{g_1, g_2\} = \frac{\dot{E}}{E} - (\delta - \theta),$$

where

$\theta = max\{\theta_1 - \beta I - (1-c)\beta\frac{IS}{E} - \gamma\beta(N^* - S - I)\frac{I}{E}, \alpha\beta I + k - \frac{kE}{I} - \theta_2\}$, with $\theta_1 = max\{(1-c-\gamma)\beta S - (\alpha+\gamma)\beta E - \gamma\beta(N^* - I), \beta S\}$ and $\theta_2 = \min\{(c+\gamma)\beta I, k + (\alpha+\gamma)\beta I\}$. Finally we obtain

$$q = \frac{1}{t}\int_0^T \eta(Bx(s,x_0))ds \le \frac{1}{t}log\frac{E(t)}{E(0)} - (\delta - \theta),$$

$$\Rightarrow \lim_{t\to\infty}\sup\sup_{x_0\in E}\frac{1}{t}\int_0^T \eta(Bx(s,x_0))ds \le 0$$

provided, $\delta > \theta$.

Therefore, we can conclude that the infected equilibrium, when it exits uniquely, is globally asymptotically stable for $R_0 > 1$. □

## 4. Absence of recurrent TB

Our aim of this section is to analyze the system (4) without recurrent TB, that is, for $\gamma = 0$. It can be observed that the expression for basic reproduction number $R_0$ remains unaltered as $\gamma$ does not appear in $R_0$. To investigate the existence of endemic equilibrium point $P^*$ we observe, for $\gamma = 0$, the cubic polynomial (10) reduces into a quadratic equation

$$\eta_2(I^*)^2 + \eta_1(I^*) + \eta_0 = 0, \tag{24}$$

where

$$\eta_2 = \alpha\beta^2(h+\delta);\quad \eta_1 = \beta(h+\delta)(k+\delta+\alpha\delta) - \alpha\beta^2\delta N^*;$$
$$\eta_0 = \delta(k+\delta)(\delta+h)(1-R_0).$$

Here, we observe that $\eta_2 > 0$ and $\eta_0 > 0$ when $R_0 < 1$ and vice versa. Therefore, using the Descarte's rule of sign and the theory of quadratic equation we derive the following theorem.

**Theorem 4.1.** *The system (4) with $\gamma = 0$ has*

*(i) a unique endemic equilibrium for $R_0 > 1$;*
*(ii) two positive endemic equilibria when $R_0 < 1$, $\eta_1 < 0$ and the discriminant $\Delta = \eta_1^2 - 4\eta_2\eta_0 > 0$;*
*(iii) a unique endemic equilibrium point when $R_0 > 1$ and $\eta_1 = 0$;*
*(iv) no endemic equilibrium for $R_0 \le 1$ and $\eta_1 > 0$.*

The case (*ii*) of the Theorem 4.1 suggest that the possibility of backward bifurcation as well as multiple TB persistent equilibria exits in spite of $R_0 < 1$. Note that, the condition $\Delta = \eta_1^2 - 4\eta_2\eta_0 > 0$ is necessary for the existence of two positive equilibria. In fact, these two equilibria collied when the quadratic polynomial (24) has repeated roots, that is, when $\Delta = 0$. Further, if $\Delta < 0$, the polynomial (4) has no positive roots and consequently the system (4) has no endemic equilibrium point. Therefore, the critical condition for backward bifurcation can be obtained where $\Delta$ changes sign.

Now, by setting $\Delta(\beta) = 0$, we will find a critical value $\beta^*$ of the transmission rate $\beta$ for backward bifurcation. We choose

$$\eta_1 = \beta\phi_1 - \beta^2\phi_2;\ \ \eta_2\eta_0 = \beta^2\phi_3 - \beta^3\phi_4; \phi_1 = (h+\delta)(k+\delta+\alpha\delta); \tag{25}$$

$$\phi_2 = \alpha\delta N^*;\ \ \phi_3 = \alpha\delta^2 k(h+\delta)^2;\ \ \phi_4 = \alpha\delta N^*(h+\delta)(c\delta+k). \tag{26}$$

After some algebraic manipulation, $\Delta(\beta^*) = 0$ leads the following expression of $\beta^*$

$$\beta^* = \frac{1}{\phi_2^2}\left[(\phi_1\phi_2 - 2\phi_4) + 2\sqrt{\phi_4^2 + \phi_2^2\phi_3 + \phi_1\phi_2\phi_4}\right]. \tag{27}$$

The critical value $R_0^*$, of the basic reproduction number $R_0$ is obtained by substituting $\beta$ at $\beta^*$ in the expression (7), which leads to

$$R_0^* = \frac{(c\delta+k)N^*}{(k+\delta)(\delta+h)}\left(\frac{(\phi_1\phi_2 - 2\phi_4) + 2\sqrt{\phi_4^2 + \phi_2^2\phi_3 + \phi_1\phi_2\phi_4}}{\phi_2^2}\right). \tag{28}$$

The quantity $R_0^*$ determines a sub-threshold regarding the occurrence of backward bifurcation for the system (4). The system possess two endemic equilibrium points for $R_0^* < R_0 < 1$. As a result it undergoes backward bifurcation when basic reproduction number $R_0$ lies in the domain $(R_0^*, 1)$. Further, endemic equilibria are vanished for $R_0 < R_0^*$ and hence it discards the possibility of backward bifurcation. This discussion clearly gives a sufficient condition for disease eradication from the system (4) which is $R_0 < R_0^*$. These remarks are summarized as the following theorem

**Theorem 4.2.** *Our model system (4) with $\gamma = 0$*

*(i) has a unique endemic equilibrium point when $R_0 > 1$;*
*(ii) has two endemic equilibrium points if $R_0^* < R_0 < 1$ and hence undergo backward bifurcation;*
*(iii) has no endemic equilibrium point for $R_0 < R_0^*$.*

Again, from the expression (22) it can be observed that, $R_0^*$ increases as the level of exogenous re-infection $\alpha$ decreases, that is, $R_0^* \propto \frac{1}{\alpha}$. This observation is approved by Fig. 3 where, $R_0^*$ has been plotted as a function of $\alpha$. This measurement signifies that high value of exogenous re-infection in TB, makes the disease eradication more challenging as it extends the backward regime of the bifurcation curve (see Fig. 10).

#### 4.0.1. Effect of fast progression in absence of recurrent TB

It is clear from (7) that basic reproduction number $R_0$ increases linearly with $c$, the proportion of newly infected individuals endure fast progression. Again, expression in (28) shows that $R_0^*$ is a

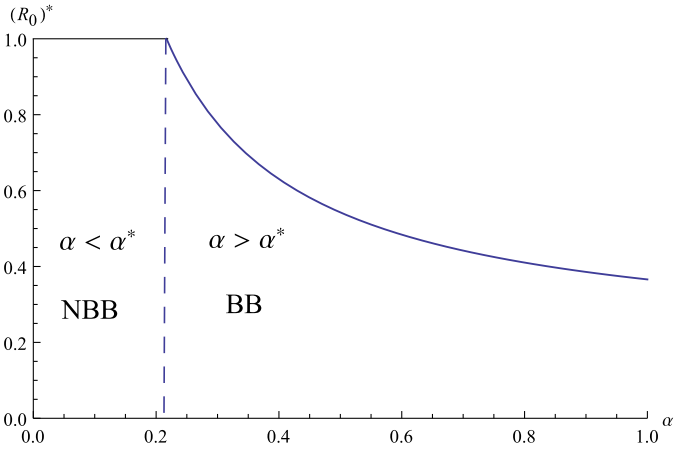


**Fig. 3.** Plot of $R_0^*$ as a function of exogenous re-infection level $\alpha$, other parameter values are specified in Table 2. The dotted vertical line depicts the straight line $\alpha = \alpha^*$. NBB and BB represent the regions of no backward bifurcation and backward bifurcation respectively.

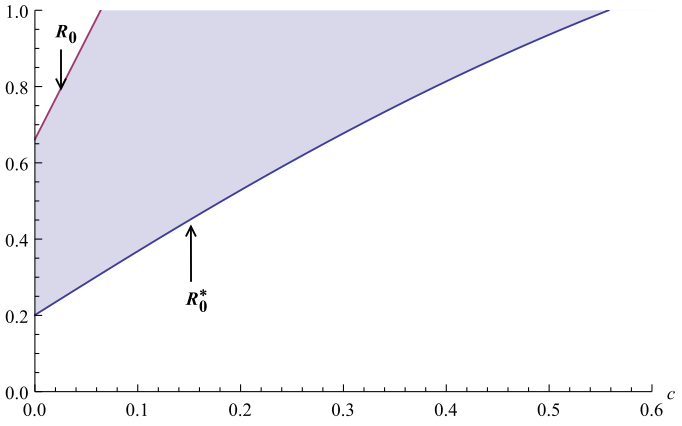


**Fig. 4.** Plot of $R_0$ and $R_0^*$ as a function of $c$. All the parameter values are mentioned in Table 2.

function of $c$. since the expression is too complicated to determine whether $R_0^*$ is increasing or decreasing function of $c$, we plot $R_0^*$ as a function of $c$ in Fig. 4 with other parameter values specified in Table 2. The plot shows (i) the value of $R_0$ and $R_0^*$ increases with $c$, (ii) $R_0$ is always bigger than $R_0^*$ and (iii) the difference between $R_0$ and $R_0^*$ extends gradually with $c$. Though higher value of $c$ increases $R_0^*$ and looses disease eradication criterion but simultaneously it increases the difference between $R_0$ and $R_0^*$ which impose another challenge on TB elimination programme.

## 5. Numerical simulations

In this section some numerical simulations are performed mainly to visualize obtained analytical results. The parameter values chosen for simulation are displayed in Table 2. Presented ranges or values of parameters are biologically feasible and most of them are taken from relevant literature of tuberculosis epidemic model.

The set of parameter values as specified in Table 2 with $\beta = 0.12$, gives the basic reproduction number $R_0 \approx 0.978863 < 1$ and both the quantities $\eta_2$ and $\eta_1$ obtained in (11) are negative. Therefore, according to the case 5 of Table 1 there is a possibility that the system (4) possess two endemic equilibrium points and they are respectively (4.45221, 62.1946, 2.86143) and (89.991, 8.23813, 0.01483). The system also possess an infection free equilibrium point $P_0 = (100, 0, 0)$. Now, the eigenvalues corresponding to the Jacobian matrix $J_{P_0}$ are $-1.313$, $-0.016$, $-0.0006$ that is, all are negative. Therefore, disease free steady state $P_0$ is locally asymptotically stable (Fig. 6). Again, the eigenvalues corresponding to two endemic equilibria are $-0.458$, $-0.112 \pm 0.064i$ and $-1.13$, $-0.017$, $0.0006$ respectively. The first set of eigenvalues are all with negative real part whereas the other set contains a positive value. As a result the first endemic equilibrium is locally stable and the other one is unstable. This shows the

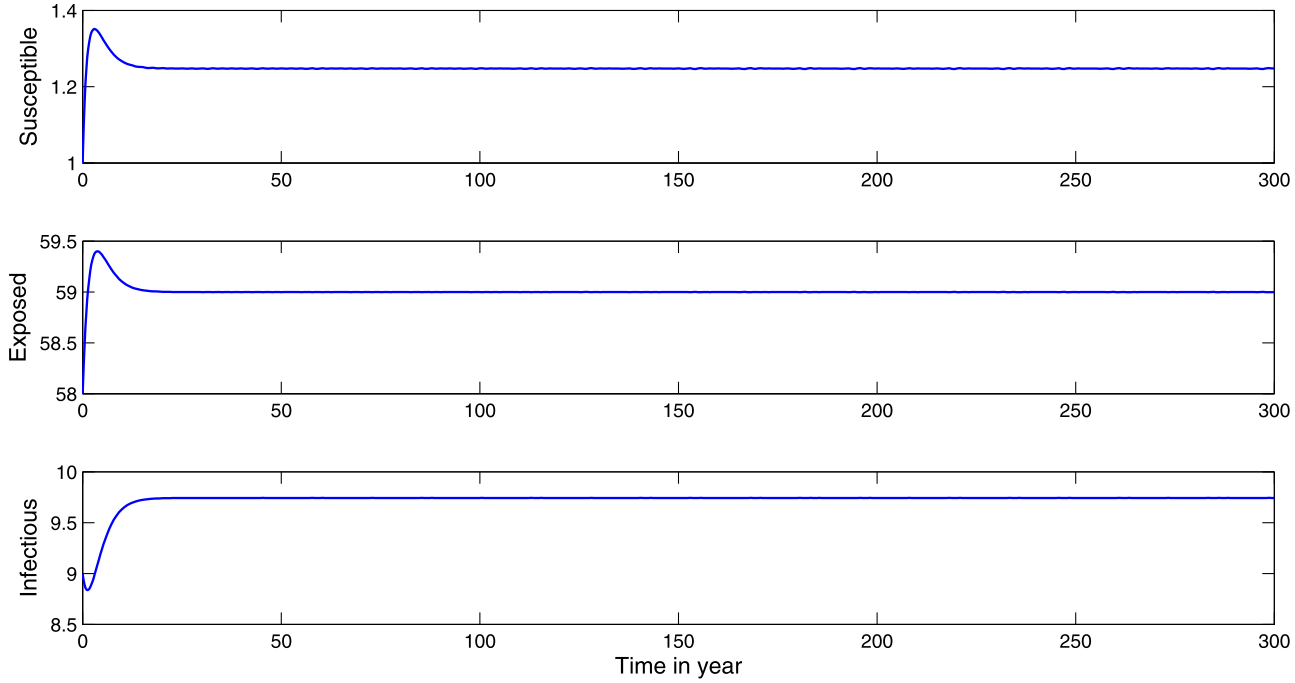


**Fig. 5.** Solution trajectories of the system (4) for $\alpha = 0.26$, $\beta = 0.13$ and all other parameter values as specified in the Table 2. Here $R_0 = 1.06041 > 1$ and the initial size of individuals are taken as (1,58,9).

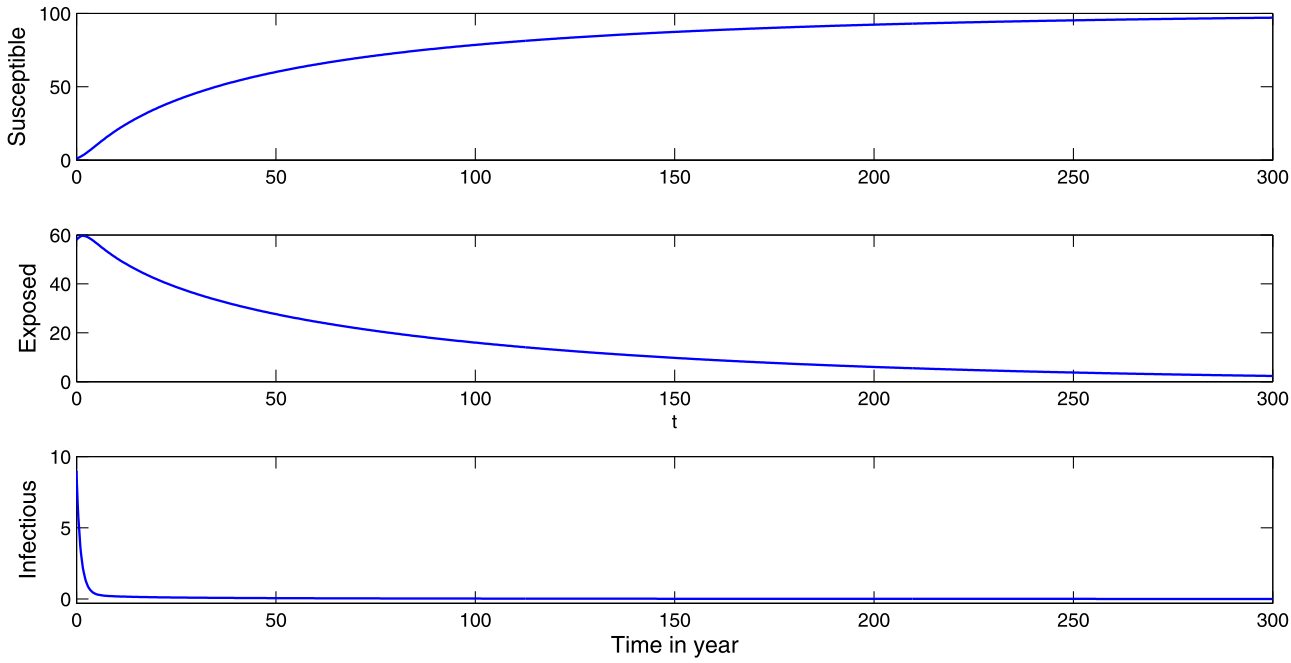


**Fig. 6.** Solution trajectories for the system (4) when $\alpha = 0.26, \beta = 0.1$ and all other parameter values same as the Table 2. Here, $R_0 = 0.815679 < 1$ and initial size of individuals are (1,58,9).

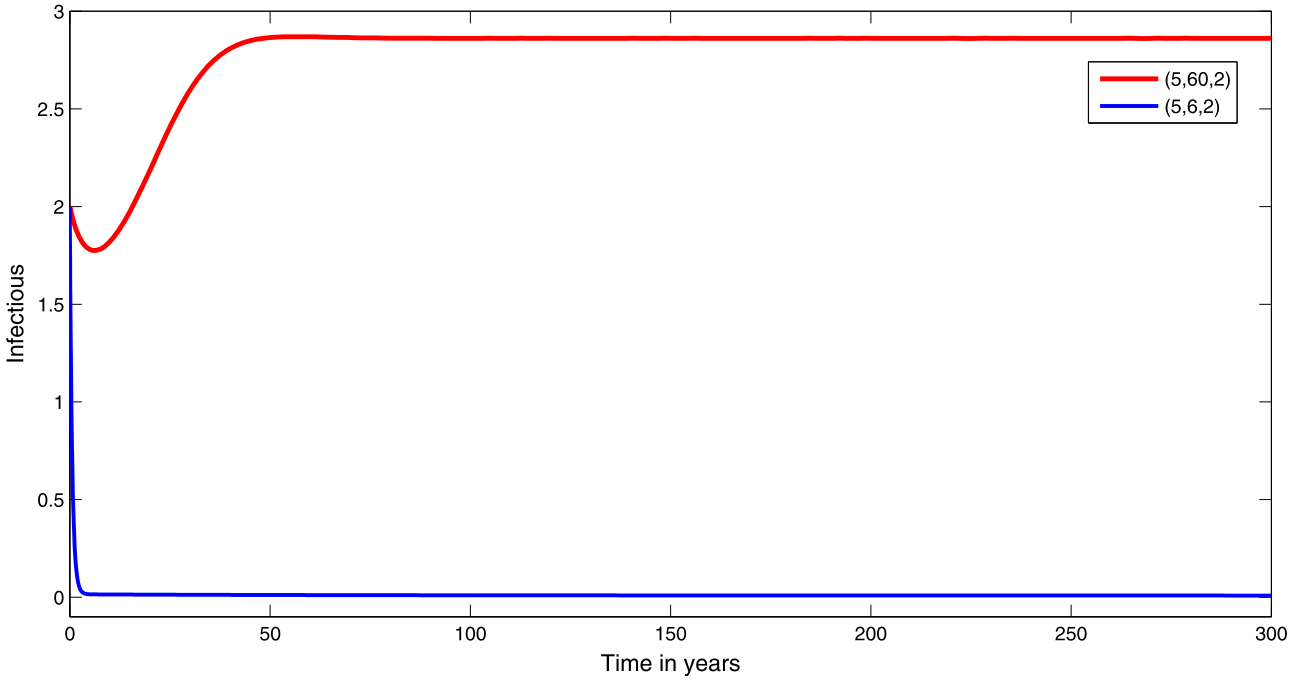


**Fig. 7.** Time series solution for infectious class (I) for $\alpha = 0.26, \beta = 0.12$ and all other parameter values same as specified in Table 2. The red curve converges to endemic equilibrium $P^*$ whereas the black curve converges to disease free equilibrium point $P_0$ with two different initial sizes of the individuals. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

existence of TB persistent stable steady state in-spite of $R_0 < 1$ and hence the convergence of trajectory depends on initial size of the population. To illustrate this graphically, solution trajectories are plotted in Fig. 7 with two different initial sizes of the population.

It can be observed that, the value of $R_0$ is highly sensitive to disease transmission rate $\beta$ moreover, $R_0$ is an increasing function of $\beta$. Choosing $\beta = 0.13$ and $\alpha = 0.26$ with all other parameters same as in Table 2, we obtain $R_0 = 1.06041 > 1$ and both $\eta_2, \eta_1$ are negative. Therefore, as claimed in case 1 of Table 1, the system (4) possess a unique endemic equilibrium point which is $P^* = (1.2475, 58.9988, 9.7427)$ together with a disease free equilibrium $P_0 = (100, 0, 0)$. The eigenvalues of corresponding Jacobian matrices evaluated at $P_0$ and $P^*$ are respectively, $-1.26, -0.016, 0.002$ and $-1.32, -0.6, -0.35$. Clearly, signs of eigenvalues reveal that $P_0$ is unstable and $P^*$ is stable (see Fig. 5).

To investigate the backward bifurcation numerically, we first find out the quantities $a$ and $b$, which are reported in Section 3.5.3. The specified set of parameter values in Table 2 with $\alpha = 0.26$ and $\beta = 0.12$ gives $a = 61.112$ and $b = 148$. Since both $a$ and $b$ are

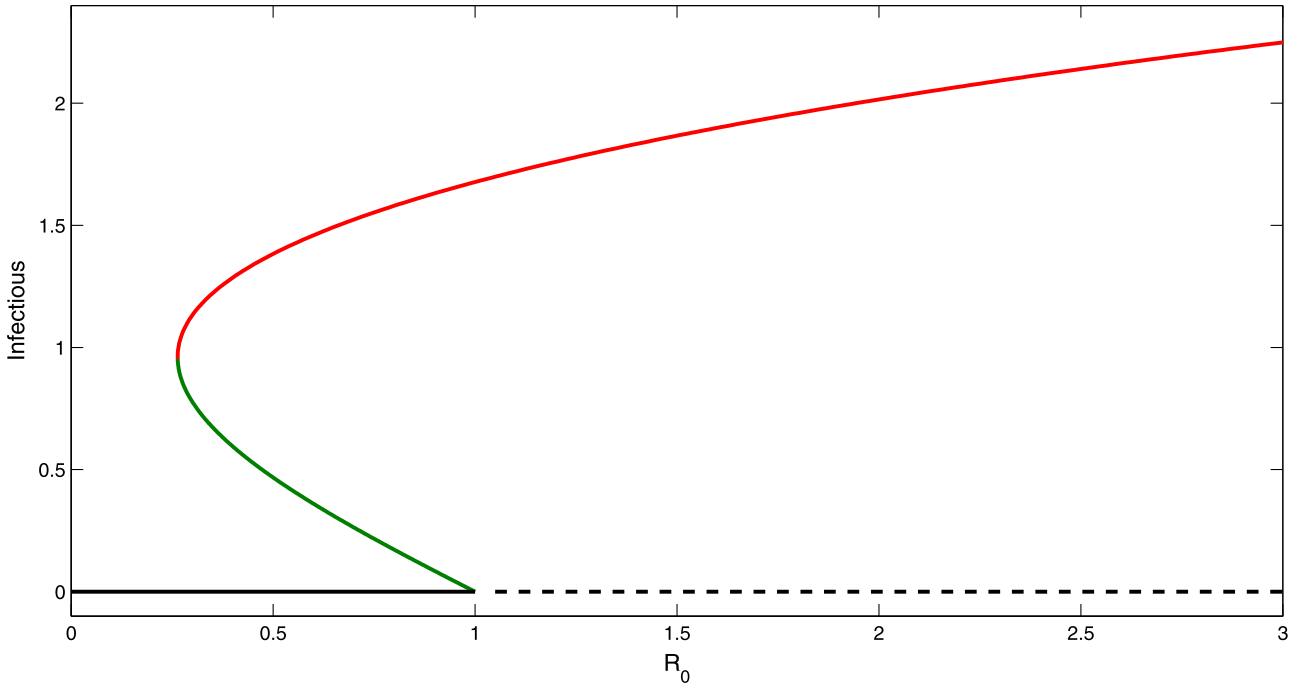


**Fig. 8.** The figure shows the backward bifurcation of the system (1) for $\alpha = 0.26, \beta = 0.12$ and all other parameters as specified in Table 2. Here, solid red and black line depicts the stability of endemic equilibrium and disease free equilibrium for $R_0 < 1$, Whereas dotted black curve shows the instability of disease free steady state for $R_0 > 1$ and solid green curve represents instability of another endemic equilibrium when $R_0 < 1$. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

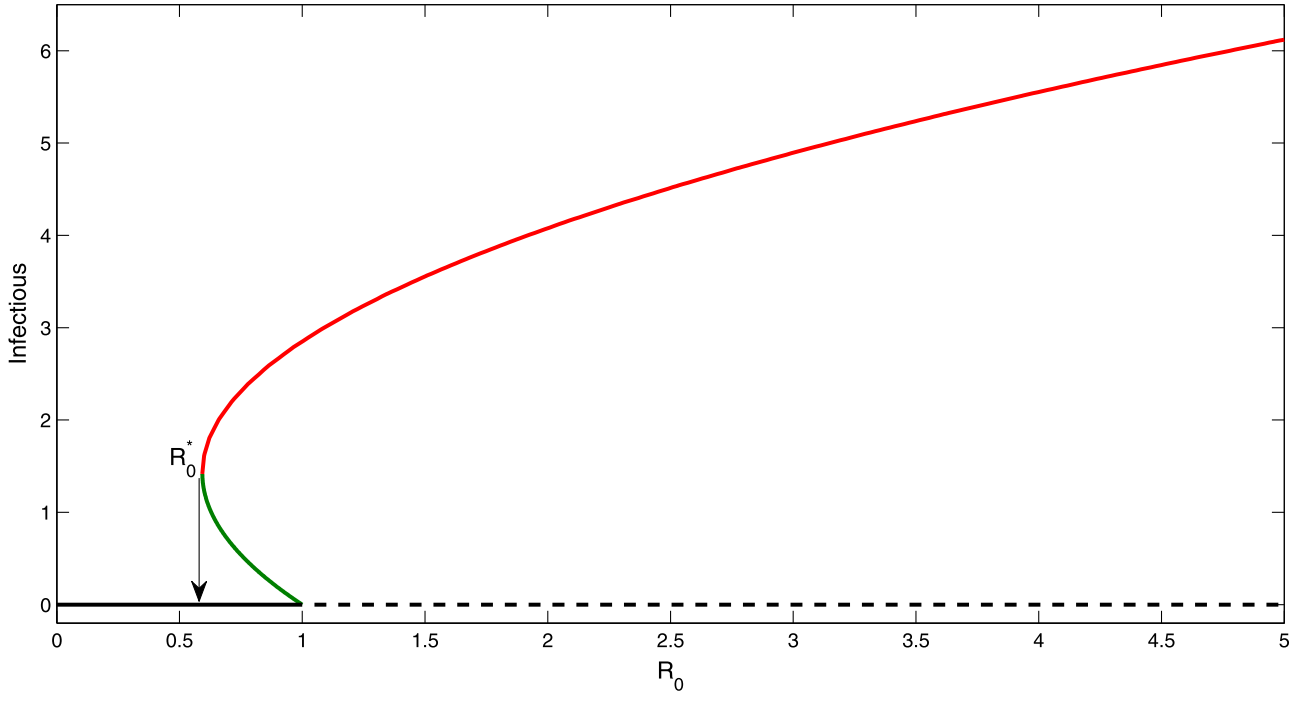


**Fig. 9.** The figure shows the backward bifurcation of the system (4) without recurrent TB ($\gamma = 0$) for $\alpha = 0.26, \beta = 0.12$ and all other parameter values as specified in Table 2. The solid red line depicts the local stability of one of the bifurcating endemic equilibrium whereas solid black line depicts that of infection free equilibrium point $P_0$. The green curve represents instability of another endemic equilibrium when $R_0 < 1$ and dashed black line represents that of $P_0$ when $R_0 > 1$. Two endemic equilibria collied when $R_0 = R_0^* = 0.593$, as a result there is no endemic equilibrium for $R_0 < R_0^*$. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

non-negative, our system undergoes backward bifurcation. Fig. 8 depicts that, a branch of infected equilibrium point bifurcating backwards at $R_0 = 1$. From Fig. 8, it is clear that the system (4) has two disease persistent equilibrium points for $R_0 < 1$. The solid red line depicts stable endemic equilibrium point whereas green curve describes unstable endemic equilibrium point. Also the disease free equilibrium point is locally asymptotically stable whenever $R_0 < 1$, which is represented by solid black line.

Again, the quantities $a$ and $b$ of Section 3.5.3 in absent of recurrent TB are calculated as $a = 46.432$ and $b = 148$. Both are again positive and hence the system (4) undergoes backward bifurcation. The bifurcation curve is shown in Fig. 9 with specified

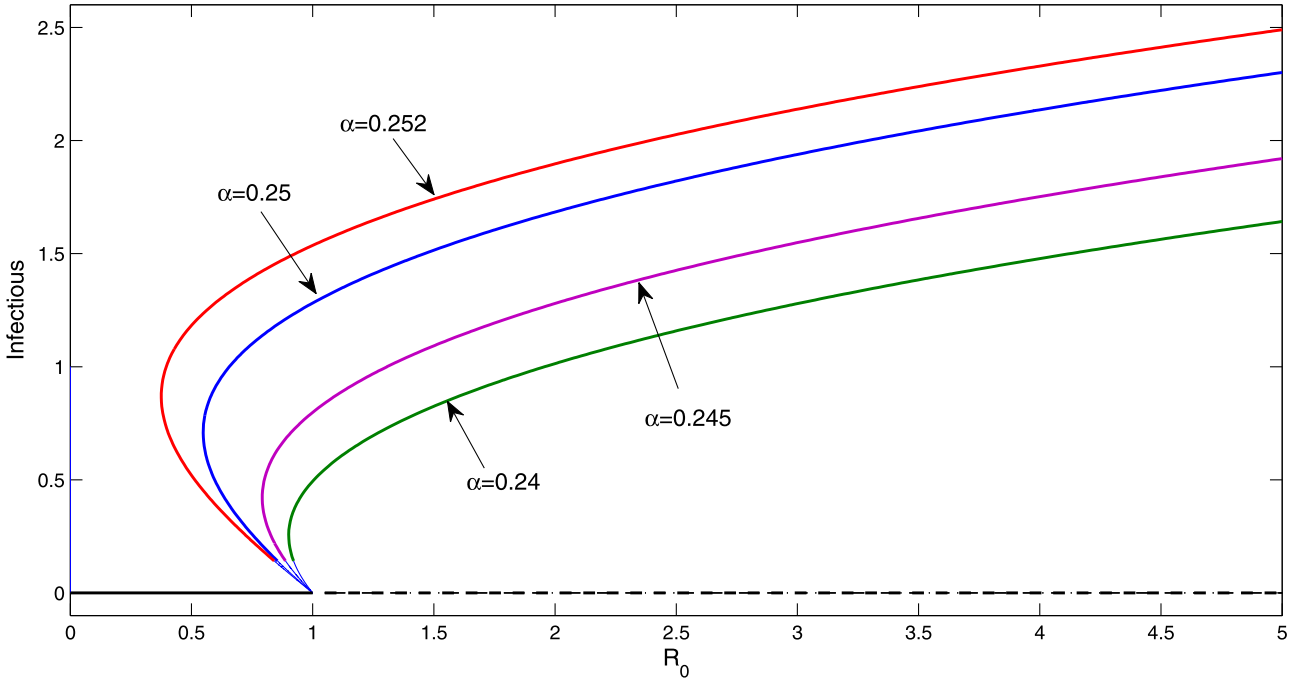


**Fig. 10.** Effects of variation of exogenous re-infection level $\alpha$, on backward bifurcation, keeping all other parameters value same as in Table 2. The diagram shows that the extent of backward bifurcation regime increases gradually with increasing $\alpha$.

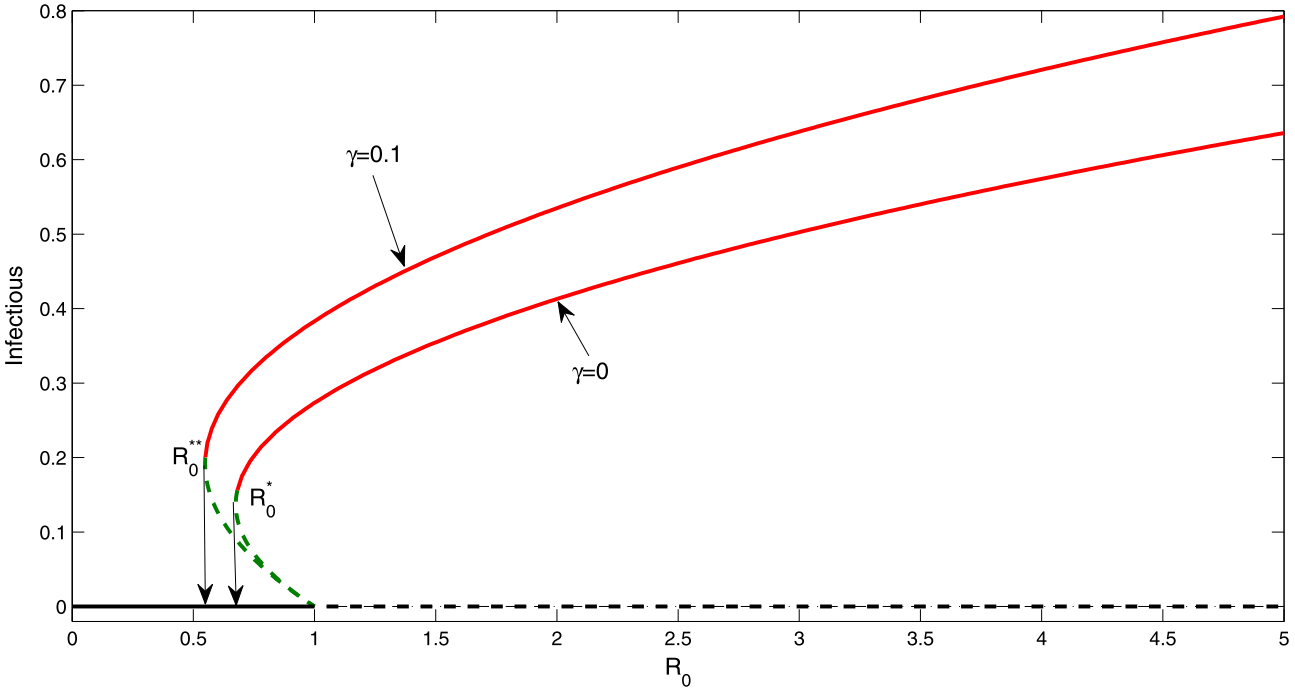


**Fig. 11.** The figure shows the backward bifurcation of the system (4) with recurrent TB ($\gamma > 0$) and without recurrent TB ($\gamma = 0$) for $\alpha = 0.5, \beta = 0.1$ and all other parameters as specified in Table 2. Here, solid red line depicts the local asymptotic stability of one endemic equilibrium whereas dotted green line shows instability of other infected equilibrium when $R_0 < 1$. Moreover, stability and instability of disease free steady state shown by solid and dotted black line respectively as $R_0$ passes through 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

parameter values in Table 2 and $\alpha = 0.26,\ \beta = 0.12$. In this diagram, when $R_0$ crosses through 1, a branch of endemic equilibria bifurcates backward from $R_0 = 1$. The solid red line depicts local asymptotic stable branch of endemic equilibrium point which persists in spite of $R_0 < 1$, whereas solid black line illustrate the local stability of disease free equilibrium point whenever $R_0 < 1$. From the expression in (28), we obtain the value of sub-threshold as $R_0^* = 0.593$ whereas that of basic reproduction number $R_0 = 0.978836$. Fig. 9 shows that for $R_0^* < R_0 < 1$, the system (4) possesses two TB persistence equilibrium, one is stable and another one is unstable. However, if $R_0 < R_0^*$, then there exist only infection free steady state which is locally asymptotically stable. Therefore, sufficient condition for eradication of the disease from the system (4) is $R_0 < R_0^*$.

The presence of backward bifurcation with multiple co-existing equilibria makes the system dynamics more complicated and

demands special control strategies. For example, in Fig. 8 or in Fig. 9, suppose the system is in equilibrium around $P_0$ and we slightly increase the value of $R_0$ through 1. The figures suggest that if $R_0$ crosses 1 then, there is a sudden bounce in number of infectious cases and the system (4) stabilize around endemic steady state. On the other hand, if the system is at an endemic level and $R_0$ being reduced slowly through the critical value 1. After $R_0$ reduced just below 1, the system does not come back to disease free level rather the population converges to an endemic level. Therefore, reduction of $R_0$ below 1 can not ensure the disease eradication. However, in Fig. 9 if $R_0$ being reduced below $R_0^*$ then the endemic branch disappears and the system become stable around infection free steady state $P_0$.

It has been observed that $R_0^*$ is a decreasing function of exogenous re-infection level $\alpha$ (see Fig. 3). Therefore, with increasing value of $\alpha$, disease eradication becomes more challenging. Graphically it can be observed in Fig. 10. The figure illustrates that, with bigger values of $\alpha$ the extent of the backward bifurcation regime increases gradually. As a result, the basic reproduction number $R_0$ has to be reduced appropriately to ensure disease eradication. Whereas, for smaller value of $\alpha$, sub-threshold $R_0^*$ is closer to 1.

Further, the effect of recurrent TB in backward bifurcation is examined in Fig. 11 which shows two bifurcation curves, one is in presence of recurrent TB ($\gamma \neq 0$) and another one is in absence of recurrent TB ($\gamma = 0$). Fig. 11 shows that incorporation of recurrent TB enlarges the extent of backward regime of the curve. Therefore, reducing $R_0$ below the quantity $R_0^*$ is not sufficient to omit multiple endemic equilibrium point in presence of recurrent TB. Here, another sub threshold $R_0^{**}$ is indicated in the Fig. 11 to achieve the desire state. It can be noted in Fig. 11 that when $R_0 < R_0^{**} < R_0^*$, then our system (4) has only disease free equilibrium $P_0$ which is locally asymptotically stable.

## 6. Discussion and conclusions

The evidence of re-infection through exogenous re-infection both in immunocompetent and immunosuppressed people have been reported in [7]. Also, Chaisson et al. [6] suggest the possibility of re-infection after recovery, which is known as recurrent TB. In this investigation, a compartmental model of TB transmission is formulated considering the role of both exogenous re-infection and recurrent TB. The basic reproduction number $R_0$ is obtained by the method of the next-generation matrix. The system (4) possess two equilibrium points one is disease free and another one endemic. The infection free equilibrium is locally asymptotically stable for $R_0 < 1$ with a parametric condition $c < \frac{k+h+2\delta}{\beta N^*}$, otherwise unstable. Further, existence criteria of endemic equilibrium show that the system (4) possess multiple TB persistent equilibria for $R_0 < 1$ and hence gives rise the possibility of backward bifurcation. In this situation, a stable endemic equilibrium persists with stable disease free equilibrium in-spite of $R_0 < 1$. This bi-stability makes the dynamics of TB transmission more complex in nature, as reducing $R_0$ less than one is not sufficient to eradicate TB, rather the initial size of the population determine the condition (see Fig. 7). To avoid this unfavorable situation a threshold criterion on exogenous re-infection level ($\alpha$) is established in Section 3.5.3. It has been observed that the system (4) undergoes backward bifurcation only when $\alpha > \alpha_c$. It is observed that the endemic equilibrium point is globally asymptotically stable for $R_0 > 1$.

Further, the model system (4) is analyzed in the absence of recurrent TB, that is when the recovered individual can resist the possibility of re-infection. The investigation shows that the system (4) undergoes backward bifurcation in this situation too. The comparison of the qualitative nature of the backward bifurcation with the previous system is shown in Fig. 11. It is observed that (i) in the presence of recurrent TB the backward extent of the bifurcation curve is larger than that of in the absence of recurrent TB, (ii) the number of infectious individuals in the presence of recurrent infection is higher than that of in the absence of recurrent infection. These observations need to be implemented in TB control strategy, as the presence of recurrent TB makes the situation more challenging. In order to find a sufficient condition for disease elimination in the absence of recurrent TB, a sub-threshold quantity $R_0^*$ is investigated. It is observed that the endemic equilibrium points disappear when $R_0 < R_0^* < 1$. Therefore, reducing basic reproduction number $R_0$ below the sub-threshold $R_0^*$ discards the possibility of bi-stability, as the only equilibrium point in this situation is disease free which is stable (see Fig. 9). The value of exogenous re-infection level ($\alpha$) plays an important role to determine the value of sub-threshold $R_0^*$. It is noted that $R_0^*$ is inversely proportional to $\alpha$, that is, $R_0^* \propto \frac{1}{\alpha}$. The assertion is verified by Fig. 3. Further, effects of re-infection level $\alpha$ in presence of recurrent TB are shown in Fig. 10. A higher value of $\alpha$ bends the curve on the left also increases the infected population. As a result, disease elimination becomes more challenging, with a higher value of $\alpha$.

The proportion $c$ of newly infected individuals developing fast active TB plays a significant role in disease dynamics. The possibility of backward bifurcation is reduced with the increasing proportion possessing fast progression. It has been observed that if the pool of susceptible directly to infectious class is sufficiently large, then the system may not perform backward bifurcation. Therefore, a population with less innate immunity response unlikely exhibits backward bifurcation. Further, in the absence of recurrent TB higher value of $c$ has both advantages and disadvantages from the epidemiological point of view. It is observed that $c$ increases the value of $R_0^*$, but it also increases the quantity $|R_0 - R_0^*|$. An optimum situation from a public health point of view is a higher value of $R_0^*$ with minimum $|R_0 - R_0^*|$. It is clear that the value of $c$ must be observed to design effective control strategies.

In summary, the re-infection parameters $\alpha$ and $\gamma$, though they do not occur in the expression of basic reproduction number $R_0$ but still, play a pivotal role to determine the stability of the existing equilibrium points. Recent developments of various clinical techniques are capable of detecting TB in several stages of the disease. Identification of re-infections both in exposed and recovered stages and their successful treatment enhance the possibility of TB eradication.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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