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Mathematical Modelling of Tuberculosis and COVID-19 Co-infection in India: A Real Data Analysis on Concomitant Diseases

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Abstract

In this paper, we have proposed an epidemiological model to study the dynamics of concomitant diseases Tuberculosis (TB) and COVID-19. Here, we have formulated a deterministic compartmental model as an extended form of the classical SIS model. First, the basic reproduction number R_0 is derived and then stability analysis of the model is done. It is observed that the disease-free equilibrium is stable when R_0 is less than one and the endemic equilibrium is stable only when R_0 is greater than one. Numerical simulation is carried out to illustrate the theoretical findings and to study the transmission dynamics of both the concomitant diseases during the first and second waves of COVID-19 in India.

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1. Introduction

The word "concomitant" means occurring during the same period of time. As far as concomitant diseases are concerned, they usually refer to secondary symptoms that occur with the main symptom. There are several concomitant diseases such as diabetes and hypertension, diabetes and obesity, TB and HIV, etc. We are interested in the mathematical analysis of recent concomitant diseases TB and COVID-19. The ongoing pandemic COVID-19 emerged in 2019, caused by novel beta coronavirus namely, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which

was first identified in Wuhan (Hubei), China. The disease led to an increase in number of patients throughout the world since December 2019, posing significant threat to global public health and the world economy (Song et al. (2021)). When lockdown becomes a safety measure for extenuating the impact of COVID-19, it is critical to predict the long-term impact of these safety measures on TB and other severe pre-existing infectious diseases. Although there is now digital scanning with artificial intelligence solutions which rapidly screen for both of the diseases TB and COVID-19 (Shrinivasan et al. (2020)), the ongoing several challenges managing TB in the curbing time of COVID-19 is crucial.

Modelling the transmission dynamics of a disease is a technique to formulate known facts about the transmission and to predict all possible outcomes of the disease with mathematical techniques. Mathematical modelling of infectious diseases is done to investigate the exclusive parameters, predict future trends and also to evaluate control measures to provide information for decision-making (Holmdahl and Buckee (2020)).

COVID-19 has significant human-to-human transmission. Maximum cases of COVID-19 infection has minimal symptoms and are self-recovering. Old-aged people as well as people with medical problems like hypertension, cardiovascular diseases, diabetes, chronic respiratory diseases and long incubation period infectious diseases like TB are at significant risk of complications and death due to deadly COVID-19 virus (Kaushik et al. (2020); Chen et al. (2020)).

Both TB and COVID-19 are contagious diseases that are transmitted mainly through close contact. Ongoing researches and clinical evidences reveal that TB is co-related with COVID-19 outcomes, resulting an approximately two to three times increase in fatality and a 25% decrease in the recovery of COVID-19 co-infection with active TB disease (McQuaid et al. (2021)). The statistics about an individual having TB when co-infected with COVID-19 can be at severe risk of poor outcomes (Gupta et al. (2020)).

There have been approximately 34.1 million reported cases and 0.453 million deaths associated with COVID-19 in India until October 22, 2021 (WHO (2020)). Evidences to date reveal that COVID-19 infected population with multiple pre-existing comorbidities such as diabetes, hypertension, and cardiovascular diseases are at greater risk of death, but only a few studies have focused on the involvement of COVID-19 infected population co-infected with other respiratory infectious diseases (Callender et al. (2020)). Over the past several decades, TB incidence and mortality have been gradually declining, showing ongoing improvements in diagnosis, prevention and treatment. When the nationwide lockdown was imposed, the weeks following the imposition on March 24,2020, India reported an 80% drop in daily notifications of TB relative to average pre-lockdown levels. Such declines may be partly due to delays in reporting but are also likely to reflect reductions in access to diagnosis and treatment, potentially having a lasting impact on TB burden at a country-wide level. Missed diagnoses would result an increased opportunities for transmission, while worsened treatment outcomes increase the risk of death from TB (Cilloni et al. (2020)), from which it is concluded that the transmission dynamics of COVID-19 must have affected the transmission dynamics of TB. Study of these two concomitant diseases TB and COVID-19 is very limited to the best of our knowledge and it needs further attention. We, therefore, proposed to study

the disease dynamics of the two concomitant diseases TB and COVID-19 through mathematical modelling. In this paper, we have studied the impact of COVID-19 on TB for both the waves of COVID-19 in India.

2. Mathematical Model

In this paper, we present a deterministic compartmental model for concomitant diseases TB and COVID-19 by assuming a homogeneous mixing of individuals within the population under consideration. To formulate the model, we have divided the total population concerning their disease status into mutually exclusive epidemiological states. Here, we denote the population susceptible to infectious disease TB and COVID-19 by $x(t)$, the population infected with TB only by $y(t)$, the population infected with COVID-19 only by $z(t)$, and the population infected with both TB and COVID-19 diseases by w(t). It is assumed that both the diseases spread via direct contact between susceptible(s) and infected individuals. The individuals who recovered from the infection are also assumed to re-enter the susceptible class. Thus, our model is based on the classical SIS model. Let $N(t)$ be the total population at any time $'t'$ in the region under consideration, which is sum of all the four sub-populations. Thus, we have $N(t) = x(t) + y(t) + z(t) + w(t)$. A schematic representation of our compartmental model is shown in Figure 1.

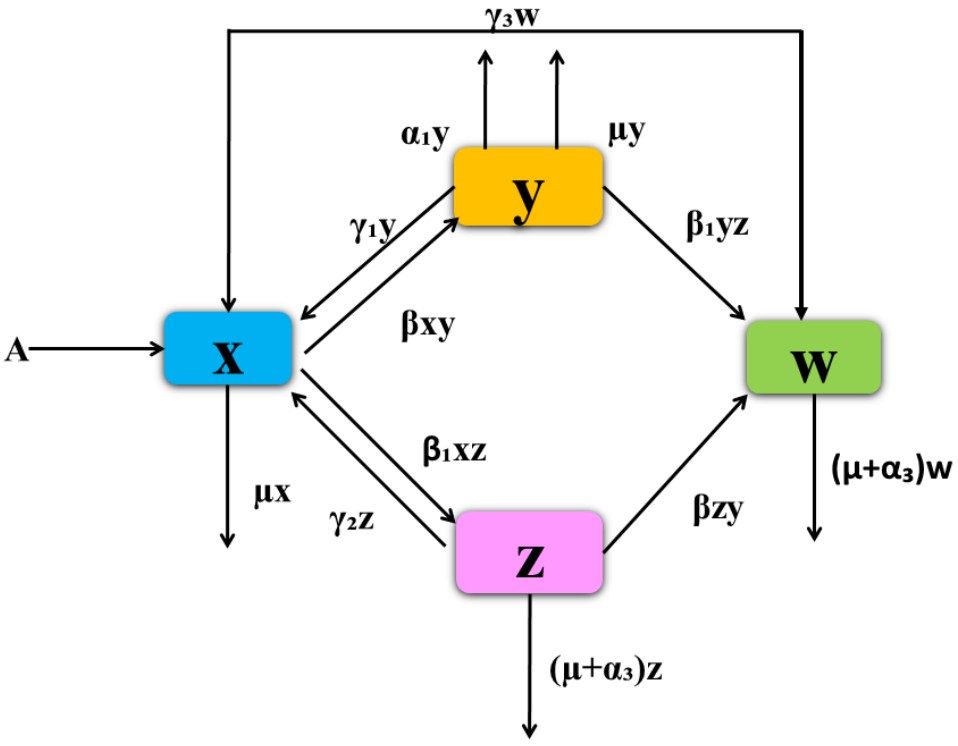

Figure 1. Schematic Representation of Compartmental Model

In the proposed model, let the susceptible population enters the system at constant rate A who moves to the infected class of TB at the transmission rate β_0 and to the infected class of COVID-

19 at the transmission rate β_1. When TB infected population acquires COVID-19, they enter to the class infected with both TB and COVID-19. Also, when COVID-19 acquires infected population with TB, they enter to both TB and COVID-19. In addition, TB infected population recovers at the recovery rate of γ_1, COVID-19 infected population recovers at the recovery rate of γ_2 and population infected with both TB and COVID-19 after recovery re-enter the susceptible population at the recovery rate of γ_3. Further, α_1, α_2 and α_3 are respectively the disease related death rates of TB, COVID-19 and both TB plus COVID-19 infected population and μ is the natural mortality rate of population in each compartment. The description of parameters are defined in Table 1.

Table 1. Description of Parameters

Parameter	Description
A :	Recruitment rate
α_1 :	The disease-related death rate of the TB-infected population
α_2 :	The disease-related death rate of the COVID-19 infected population
α_3 :	The disease-related death rate of both TB and COVID-19 infected population
β_0 :	The transmission coefficient of TB infection from TB population
β_1 :	The transmission coefficient of COVID-19 infection from COVID-19 infected population
γ_1 :	The recovery rate of TB population
γ_2 :	The recovery rate of COVID-19 population
γ_3 :	The recovery rate of both TB and COVID-19 infected population
μ :	Natural mortality rate

The mathematical formulation of our compartmental model is as given below:

$$\left.\begin{aligned} \frac{dx}{dt} &= A + \gamma_1 y + \gamma_2 z + \gamma_3 w - \beta_0 xy - \beta_1 xz - \mu x, \\ \frac{dy}{dt} &= \beta_0 xy - \beta_1 yz - (\gamma_1 + \mu + \alpha_1)\, y, \\ \frac{dz}{dt} &= \beta_1 xz - \beta_0 zy - (\mu + \alpha_2 + \gamma_2)\, z, \\ \frac{dw}{dt} &= \beta_0 zy + \beta_1 yz - (\mu + \alpha_3 + \gamma_3)\, w, \end{aligned}\right\}, \tag{1}$$

with the following initial conditions:

$$x(0) = x_0 > 0, y(0) = y_0 \geq 0, z(0) = z_0 \geq 0, w(0) = w_0 \geq 0. \tag{2}$$

3. Non-Negativity of the Model

Non-negativity conditions are necessary to show that all the state variables remain positive for $t \geq 0$ or the solutions of the system remain positive for all time. Thus, we have the following lemma.

Lemma 3.1.

Under the initial conditions given by (2), all the solutions (x, y, z, w) of the system of equations (1) remain non-negative for $t \geq 0$.

Proof:

From the system of equations (1) and (2), we get

$$\left.\frac{dx}{dt}\right|_{x=0} = A + \gamma_1 y + \gamma_2 z + \gamma_3 w > 0, \tag{3}$$

$$\left.\frac{dy}{dt}\right|_{y=0} = 0, \tag{4}$$

$$\left.\frac{dz}{dt}\right|_{z=0} = 0, \tag{5}$$

$$\left.\frac{dw}{dt}\right|_{w=0} = \beta_0 zy + \beta_1 yz \geq 0. \tag{6}$$

Thus, we conclude that the solution of the system of equations (1) is non-negative for $t \geq 0$. ■

4. Boundedness of the Model

In this section, we show that the solutions of the system of equations (1) are bounded. The boundedness implies the natural restrictions to indefinite growth of infected population due to the various constraints such as natural conditions or preventive habits acquired by the population to protect themselves from acquiring the disease. Now, we prove the following lemma.

Lemma 4.1.

The set $\Omega = \{(x, y, z, w) : 0 \leq x + y + z + w \leq N\}$ is the closed region for the system (1) with non-negative initial conditions for all solutions initiating in the positive octant, where $N_{max} = \frac{A}{\mu}$.

Proof:

Adding all the four equations of the system (1), we get

$$\frac{dN}{dt} = A - \mu x - \mu y - \alpha_1 y - \mu z - \alpha_2 z - \mu w - \alpha_3 w. \tag{7}$$

Using the relation $N = x + y + z + w$, the equation (7) can be re-written as

$$\frac{dN}{dt} = A - \mu N - \alpha_1 y - \alpha_2 z - \alpha_3 w.$$

Thus, we conclude the following:

$$\frac{dN}{dt} \leq A - \mu N.$$

Now, by using comparison principle, we can write

$$0 < N \leq \frac{A}{\mu}. \tag{8}$$

Thus, the set $\Omega = \{(x, y, z, w) : 0 \leq x + y + z + w \leq N\}$ is the closed region for the system (1) and all the solutions of the model enter in the set Ω. Thus, our proposed model is well-defined biologically and mathematically. ■

5. Existence of Equilibrium Points

In this section, we shall show the existence of equilibrium points. In a dynamical system, an equilibrium point is a state of the system that does not change with respect to time. Thus, if the system begins at an equilibrium point, the state will try to remain at an equilibrium point forever. The system (1) has two equilibrium points: one disease-free equilibrium point $E_0(\frac{A}{\mu}, 0, 0, 0)$ and the other endemic equilibrium point $E^*(x^*, y^*, z^*, w^*)$.

The endemic equilibrium point must satisfy the following equations:

$$A + \gamma_1 y^* + \gamma_2 z^* + \gamma_3 w^* - \beta_0 x^* y^* - \beta_1 x^* z^* - \mu x^* = 0, \tag{9}$$

$$\beta_0 x^* - \beta_1 z^* - (\gamma_1 + \mu + \alpha_1) = 0, \tag{10}$$

$$\beta_1 x^* - \beta_0 y^* - (\mu + \alpha_2 + \gamma_2) = 0, \tag{11}$$

$$\beta_0 z^* y^* + \beta_1 y^* z^* - (\mu + \alpha_3 + \gamma_3) = 0. \tag{12}$$

Now, from Equation (10), we have

$$z^* = \frac{\beta_0 x^* - (\gamma_1 + \mu + \alpha_1)}{\beta_1} = f_1(x^*). \tag{13}$$

Again, from Equation (11), we have

$$y^* = \frac{\beta_1 x^* - (\gamma_2 + \mu + \alpha_2)}{\beta_0} = f_2(x^*), \tag{14}$$

and from Equation (12), we have

$$w^* = \frac{(\beta_0 + \beta_1) y^* z^*}{(\gamma_3 + \mu + \alpha_3)} = \frac{(\beta_0 + \beta_1)\, f_1(x^*) f_2(x^*)}{\gamma_3 + \mu + \alpha_3}. \tag{15}$$

Using (13), (14) and (15) in Equation (9), we have

$$\begin{aligned} g(x) = A + \frac{\gamma_1}{\beta_0}\{\beta_1 x^* - (\gamma_2 + \mu + \alpha_2)\} + \frac{\gamma_2}{\beta_1}\{\beta_0 x^* - (\gamma_1 + \mu + \alpha_1)\} + \frac{\gamma_3(\beta_0 + \beta_1)}{(\gamma_3 + \mu + \alpha_3)} \\ \left[\{\frac{1}{\beta_0 \beta_1}\beta_0 x^* - (\gamma_1 + \mu + \alpha_1)\}\{\beta_1 x^* - (\gamma_2 + \mu + \alpha_2)\}\right] \\ - \beta_1 x^{*2} + (\gamma_2 + \mu + \alpha_2)x^* - \beta_0 x^{*2} + (\gamma_1 + \mu + \alpha_1)x^* - \mu x^* \end{aligned} \tag{16}$$

Therefore, we have

$$g(0) = A - \frac{\gamma_1}{\beta_0}(\gamma_2+\mu+\alpha_2) - \frac{\gamma_2}{\beta_1}(\gamma_1+\mu+\alpha_1) - \frac{\gamma_3(\beta_0+\beta_1)}{(\gamma_3+\mu+\alpha_3)\beta_0\beta_1}\left[(\gamma_1+\mu+\alpha_1)(\gamma_2+\mu+\alpha_2)\right], \quad (17)$$

and

$$g\left(\frac{A}{\mu}\right) = \frac{\gamma_1}{\beta_0}\left\{\beta_1\left(\frac{A}{\mu}\right) - (\gamma_2+\mu+\alpha_2)\right\} + \frac{\gamma_2}{\beta_1}\left\{\beta_0\left(\frac{A}{\mu}\right) - (\gamma_1+\mu+\alpha_1)\right\} + \frac{\gamma_3(\beta_0+\beta_1)}{(\gamma_3+\mu+\alpha_3)\beta_0\beta_1}\left[\left\{\beta_0\left(\frac{A}{\mu}\right) - (\gamma_1+\mu+\alpha_1)\right\}\left\{\beta_1\left(\frac{A}{\mu}\right) - (\gamma_2+\mu+\alpha_2)\right\}\right] - \beta_1\left(\frac{A}{\mu}\right)^2 + (\gamma_2+\mu+\alpha_2)\left(\frac{A}{\mu}\right) - \beta_0\left(\frac{A}{\mu}\right)^2 - (\gamma_1+\mu+\alpha_1)\left(\frac{A}{\mu}\right). \quad (18)$$

Now, from Equation (16), we find

$$g^{'}(x) = \frac{\gamma_1\beta_1}{\beta_0} + \frac{\gamma_2\beta_0}{\beta_1} + \frac{\gamma_3(\beta_0+\beta_1)}{(\gamma_3+\mu+\alpha_3)}\left[\frac{-2\beta_1\beta_0x^* + -(\gamma_1+\mu+\alpha_1)\beta_1 - (\gamma_2+\mu+\alpha_2)\beta_0}{\beta_0\beta_1}\right] - 2\beta_1x^* + (\gamma_2+\mu+\alpha_2) - 2\beta_0x^* + (\gamma_1+\mu+\alpha_1). \quad (19)$$

Clearly, $g(\frac{A}{\mu}) > 0$. Thus, a unique value x^* of x exists if $g(0) < 0$ and $g^{'}(x) > 0$; $\forall\ 0 < x < \frac{A}{\mu}$. Then, the values y^*, z^* and w^* can be obtained respectively from Equations (14), (13) and (15).

5.1. Basic Reproduction Number

The basic reproduction number R_0 is a dimensionless number and plays an important role in analysing any epidemiological model. It is defined as the number of secondary infections spread by an infected individual during one's complete infectious period in a population in which each individual is susceptible. It can be analytically determined if the disease-free equilibrium of the given system exists. We use the generalized approach, i.e., next generation matrix approach to determine the basic reproduction number as proposed by Van den Driessche and Watmough (2002). For the system (1), the disease-free equilibrium point is $E_0(\frac{A}{\mu},0,0,0)$ and hence to determine the basic reproduction number of the proposed model. We decompose the right hand side of the system(1) corresponding to the infected compartments as $R_1 - R_2$, where

$$R_1 = \begin{bmatrix} \beta_0xy - \beta_1yz \\ \beta_1xz - \beta_0zy \\ \beta_0zy + \beta_1yz \\ 0 \end{bmatrix},$$

and

$$R_2 = \begin{bmatrix} (\gamma_1+\mu+\alpha_1)y \\ (\gamma_2+\mu+\alpha_2)z \\ (\gamma_3+\mu+\alpha_3)w \\ (\ -A - \gamma_1y - \gamma_2z - \gamma_3w + \beta_0xy + \beta_1xz + \mu x) \end{bmatrix}.$$

Now, we have

$$X = \left[\frac{dx}{dt}, \frac{dy}{dt}, \frac{dz}{dt}, \frac{dw}{dt}\right].$$

Let us define $\tilde{R_1} = \left[\frac{\partial(R_1)_i}{\partial x_j}\right]$, and $\tilde{R_2} = \left[\frac{\partial(R_2)_i}{\partial x_j}\right]$, for $i, j = 1, 2, 3$ at disease-free equilibrium point.

Thus, differentiating R_1 with respect to y, z, and w, we get

$$\tilde{R_1} = \begin{bmatrix} \beta_0 x - \beta_1 z & -\beta_1 y & 0 \\ \beta_1 z & \beta_1 x - \beta_0 y & 0 \\ \beta_0 z + \beta_1 z & \beta_0 y + \beta_1 y & 0 \end{bmatrix}.$$

Now, at the disease-free equilibrium E_0, (where $x = \frac{A}{\mu}$, $y = 0$, $z = 0$, and $w = 0$), we have

$$\tilde{R_1} = \begin{bmatrix} \beta_0 \frac{A}{\mu} & 0 & 0 \\ 0 & \beta_1 \frac{A}{\mu} & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

Similarly, differentiating R_2 with respect to y, z, and w, we get

$$\tilde{R_2} = \begin{bmatrix} (\gamma_1 + \mu + \alpha_1) & 0 & 0 \\ 0 & (\gamma_2 + \mu + \alpha_2) & 0 \\ 0 & 0 & (\gamma_3 + \mu + \alpha_3) \end{bmatrix}.$$

Note that $\tilde{R_1}$ is non-negative and $\tilde{R_2}$ is a non-singular M-matrix, whose inverse $\tilde{R_2^{-1}}$ is non-negative and, therefore, $R_1 R_2^{-1}$ is non-negative. Thus, we have

$$\tilde{R_1}\tilde{R_2}^{-1} = \begin{bmatrix} \beta_0 \frac{A}{\mu} & 0 & 0 \\ 0 & \beta_1 \frac{A}{\mu} & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\gamma_1+\mu+\alpha_1} & 0 & 0 \\ 0 & \frac{1}{\gamma_2+\mu+\alpha_2} & 0 \\ 0 & 0 & \frac{1}{\gamma_3+\mu+\alpha_3} \end{bmatrix},$$

$$\text{i.e.,} \qquad \tilde{R_1}\tilde{R_2}^{-1} = \begin{bmatrix} \frac{\beta_0 A}{\mu(\gamma_1+\mu+\alpha_1)} & 0 & 0 \\ 0 & \frac{\beta_1 A}{\mu(\gamma_2+\mu+\alpha_2)} & 0 \\ 0 & 0 & 0 \end{bmatrix}. \tag{20}$$

Therefore, we have

$$R_0 = max\left[\beta_0 \frac{A}{\mu(\gamma_1 + \mu + \alpha_1)}, \beta_1 \frac{A}{\mu(\gamma_2 + \mu + \alpha_2)}, 0\right] = max(R_1, R_2, 0), \tag{21}$$

where $R_1 = \beta_0 \frac{A}{\mu(\gamma_1+\mu+\alpha_1)}$ corresponds to the reproduction number of TB infection and $R_2 = \beta_1 \frac{A}{\mu(\gamma_2+\mu+\alpha_2)}$ corresponds to that of COVID-19 infection. Since the infection rate of TB is very small as compared to COVID-19 infection, therefore, the basic reproduction number for our system is given by

$$R_0 = R_2. \tag{22}$$

Thus, in case of concomitant diseases TB and COVID-19, COVID-19 infection contributes to the basic reproduction number of the system.

5.2. Stability Analysis of Equilibrium Points

5.2.1. *Local Stability Analysis of Disease Free Equilibrium Point E_0*

To analyze the stability of an equilibrium point, we compute variational matrix V(E) of system of equations (1), which is obtained as follows:

$$V(E) = \begin{bmatrix} -\beta_0 y - \beta_1 z - \mu & \gamma_1 - \beta_0 x & \gamma_2 - \beta_1 x & \gamma_3 \\ \beta_0 y & \beta_0 x - \beta_1 z - (\gamma_1 + \mu + \alpha_1) & -\beta_1 y & 0 \\ \beta_1 z & -\beta_0 z & \beta_1 x - \beta_0 y - (\mu + \alpha_2 + \gamma_2) & 0 \\ 0 & \beta_0 z + \beta_1 z & \beta_1 y + \beta_0 y & -(\mu + \alpha_3 + \gamma_3) \end{bmatrix},$$

For the disease-free equilibrium point E_0, the variational matrix $V(E_0)$ is given by

$$V(E_0) = \begin{bmatrix} -\mu & \gamma_1 - \beta_0 \frac{A}{\mu} & \gamma_2 - \beta_1 \frac{A}{\mu} & \gamma_3 \\ 0 & \beta_0 \frac{A}{\mu} - (\gamma_1 + \mu + \alpha_1) & 0 & 0 \\ 0 & 0 & \beta_1 \frac{A}{\mu} - (\mu + \alpha_2 + \gamma_2) & 0 \\ 0 & 0 & 0 & -(\mu + \alpha_3 + \gamma_3) \end{bmatrix}.$$

The eigenvalues of the variational matrix corresponding to disease-free equlibrium point are:
$\lambda_1 = -\mu$,
$\lambda_2 = \frac{\beta_0 A}{\mu} - (\gamma_1 + \mu + \alpha_1), = -(\gamma_1 + \mu + \alpha_1)(1 - R_1)$,
$\lambda_3 = \frac{\beta_1 A}{\mu} - (\gamma_2 + \mu + \alpha_2), = -(\gamma_2 + \mu + \alpha_2)(1 - R_2)$,
$\lambda_4 = -(\mu + \alpha_3 + \gamma_3)$.

Clearly, the two eigenvalues λ_1 and λ_4 of the variational matrix of the disease free equilibrium point are negative and the remaining two eigenvalues λ_2 and λ_3 have negative real parts if $R_1 < 1$, and $R_2 < 1$ respectively. Hence, the disease-free equilibrium point is locally asymptotically stable by Routh-Hurwitz Criteria (Routh (1877)), if $R_1 < 1, R_2 < 1$ and unstable if $R_1 > 1, R_2 > 1$.

5.2.2. *Local Stability Analysis of Endemic Equilibrium Point E^**

To determine local stability of endemic equilibrium point E^*, we linearize the system about it by setting $x = x_1 + x^*$, $y = y_1 + y^*$, $z = z_1 + z^*$ and $w = w_1 + w^*$. After linearization, the system

of equations (1) can be written as follows:

$$\begin{aligned}
\frac{dx_1}{dt} &= \gamma y_1 + \gamma_2 z_1 + \gamma_3 w_1 - \beta_0 x_1 y^* - \beta_0 x^* y_1 - \beta_1 x^* z_1 - \beta_1 x_1 z^* - \mu x_1, \\
\frac{dy_1}{dt} &= \beta_0 x^* y_1 + \beta_0 x_1 y^* - \beta_1 y_1 z^* - \beta_1 y^* z_1 - (\gamma_1 + \mu + \alpha_1)\, y_1, \\
\frac{dz_1}{dt} &= \beta_1 x^* z_1 + \beta_1 x_1 z^* - \beta_0 z^* y_1 - \beta_0 z_1 y^* - (\mu + \alpha_2 + \gamma_2)\, z_1, \\
\frac{dw_1}{dt} &= \beta_0 z^* y_1 + \beta_0 z_1 y^* + \beta_1 y^* z_1 + \beta_1 y_1 z^* - (\mu + \alpha_3 + \gamma_3)\, w_1.
\end{aligned}$$

Now, let us consider the Lyapunov function

$$V = \frac{1}{2}x_1^2 + \frac{1}{2}y_1^2 + \frac{1}{2}z_1^2 + \frac{1}{2}w_1^2. \tag{23}$$

Differentiating Equation (23) with respect to 't', we have

$$\left.\begin{aligned}
\dot{V} = &-\frac{1}{3}a_{11}x_1^2 + a_{12}x_1y_1 - \frac{1}{3}a_{22}y_1^2, -\frac{1}{3}a_{11}x_1^2 + a_{13}x_1z_1 - \frac{1}{3}a_{33}z_1^2, \\
&-\frac{1}{3}a_{11}x_1^2 + a_{14}x_1w_1 - \frac{1}{3}a_{44}w_1^2, -\frac{1}{3}a_{22}y_1^2 + a_{23}y_1z_1 - \frac{1}{3}a_{33}z_1^2, \\
&-\frac{1}{3}a_{22}y_1^2 + a_{24}y_1w_1 - \frac{1}{3}a_{44}w_1^2, -\frac{1}{3}a_{33}z_1^2 + a_{34}z_1w_1 - \frac{1}{3}a_{44}w_1^2,
\end{aligned}\right\}, \tag{24}$$

where

$$\left.\begin{aligned}
a_{11} &= (-\beta_0 y^* - \beta_1 z^* - \mu), \\
a_{22} &= \{\beta_0 x^* - \beta_1 z^* - (\gamma_1 + \mu + \alpha_1)\}, \\
a_{33} &= \{\beta_1 x^* - \beta_0 y^* - (\mu + \alpha_2 + \gamma_2)\}, \\
a_{44} &= \{-(\mu + \alpha_3 + \gamma_3)\}, \\
a_{12} &= \{\gamma_1 - \beta_0 x^* + \beta_0 y^*\}, \\
a_{13} &= \{\gamma_2 - \beta_1 x^* + \beta_1 z^*\}, \\
a_{14} &= \gamma_3, \\
a_{23} &= \{-\beta_1 y^* - \beta_0 z^*\}, \\
a_{24} &= \{\beta_0 z^* + \beta_1 z^*\}, \\
a_{34} &= \{\beta_0 y^* + \beta_1 y^*\}.
\end{aligned}\right\}. \tag{25}$$

The Lyapunov function $\dot{V}$ is negative definite, if the following conditions hold:

$$(i)\ (\gamma_1 - \beta_0 x^* + \beta_0 y^*)^2 < \frac{4}{9}(-\beta_0 y^* - \beta_1 z^* - \mu)\left\{\beta_0 x^* - \beta_1 z^* - (\gamma_1 + \mu + \alpha_1)\right\},$$

$$(ii)\ (\gamma_2 - \beta_1 x^* + \beta_1 z^*)^2 < \frac{4}{9}(-\beta_0 y^* - \beta_1 z^* - \mu)\left\{\beta_1 x^* - \beta_0 y^* - (\gamma_2 + \mu + \alpha_2)\right\},$$

$$(iii)\ \gamma_3^2 < \frac{4}{9}(\beta_0 y^* + \beta_1 z^* + \mu)(\mu + \alpha_3 + \gamma_3),$$

$$(iv)\ (\beta_1 y^* + \beta_0 z^*)^2 < \frac{4}{9}\left\{-\beta_0 x^* + \beta_1 z^* + (\gamma_1 + \mu + \alpha_1)\right\}\left\{-\beta_1 x^* + \beta_0 y^* + (\mu + \alpha_2 + \gamma_2)\right\},$$

$$(v)\ (\beta_0 + \beta_1)^2 z^{*2} < \frac{4}{9}\frac{\gamma_1 - \beta x^*}{\beta y^*} - \beta_0 x^* + \beta_1 z^* + (\gamma_1 + \mu + \alpha_1)(\mu + \alpha_3 + \gamma_3),$$

$$(vi)\ (\beta_0 + \beta_1)^2 y^{*2} < \frac{4}{9}\frac{\gamma_1 - \beta_1 x^*}{\beta_1 z^*} - \beta_1 x^* + \beta_0 y^* + (\gamma_2 + \mu + \alpha_2)(\mu + \alpha_3 + \gamma_3).$$

Thus, if all the conditions (i) through (vi) are satisfied, the endemic equilibrium point E^* is locally asymptotically stable.

6. Sensitivity Analysis

In this section, we analyze the sensitive parameters of the model. For example, for a parameter c, the sensitivity of c is defined as how the model behaves to a small change in any parameter value according to the following definition:

$$K_c = \frac{\partial R_0}{\partial c}\frac{c}{R_0},$$

where

$$R_0 = \frac{\beta_1 A}{\mu(\gamma_2 + \mu + \alpha_2)}.$$

The sensitivity analysis for each of the parameters with respect to R_0 is given by:

$$K_{\beta_1} = \frac{\partial R_0}{\partial \beta_1}\frac{\beta_1}{R_0} = 1,$$

$$K_A = \frac{\partial R_0}{\partial A}\frac{A}{R_0} = 1,$$

$$K_\mu = \frac{\partial R_0}{\partial \mu}\frac{\mu}{R_0} = -2.895,$$

$$K_{\gamma_2} = \frac{\partial R_0}{\partial \gamma_2}\frac{\gamma_2}{R_0} = -0.2067,$$

$$K_{\alpha_2} = \frac{\partial R_0}{\partial \alpha_2}\frac{\alpha_2}{R_0} = -0.7932.$$

The sensitivity analysis of the concomitant model reveals that the contact rate β_1, and the recruitment rate A have a high positive impact on the spread of the virus. The analysis recommends that the magnitudes of impact of A and β_1 are the same. The other parameters μ,γ_2,α_2 have negative impact. A graphical representation of sensitivity indices of R_0 is shown in Figure 2.

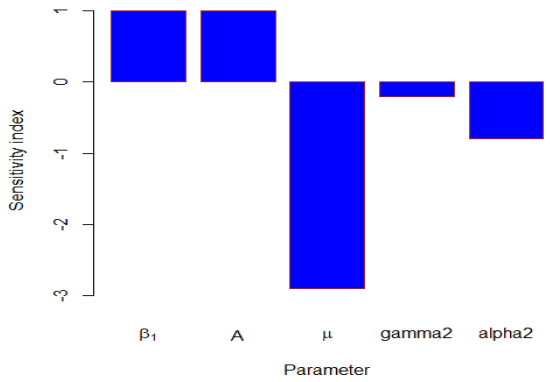

Figure 2. Sensitivity Analysis of Parameters

7. Numerical Simulation

In this section, we have discussed the quantitative behaviour of the transmission dynamics of concomitant diseases TB and COVID-19 in India. We justify the analytical findings of the impact of COVID-19 on the TB-infected population and vice-versa using MATLAB software. Table 2 gives the parameter values used to perform numerical simulation of the model. Most of the parameter values have been taken from health sites of the Indian Government and some of them are assumed. Numerical simulation is done for the first wave of COVID-19 in India from June 1, 2020, to September 2, 2020, and for the second wave from March 1, 2021, to June 1, 2021, by the same parameter values except transmission coefficient rates β_0 and β_1. The basic reproduction number R_0 is computed and is found to be 2.55 for the first wave and 2.65 for the second wave.

Table 2. Values and Sources of Parameters

Parameter	Value	Source
A	65937.74 day^{-1}	(worldbank (2022))
α_1	0.004 day^{-1}	(Nikshay.in (2020))
α_2	0.274 day^{-1}	(COVID-19 (2020))
α_3	0.272 day^{-1}	Assumed
β_0	1.345399 $\times 10^{-11}$	Assumed
β_1	2.675 $\times 10^{-10}$	Assumed
γ_1	0.0166 day^{-1}	(medicinenet (2020))
γ_2	0.0714 day^{-1}	(mohfw.gov (2022))
γ_3	0.0222 day^{-1}	Assumed
μ	0.00002 day^{-1}	(Knoema (2020))

Here, we have plotted the Figures for both the waves of a COVID-19 in India and compared them. In Figure 3, we have plotted the variations of TB-infected population with time for different rates of transmission coefficient β_1 of COVID-19 infection for first and second wave of COVID-19. We observe that as β_1 increases, TB-infected population decreases during both the waves. But the

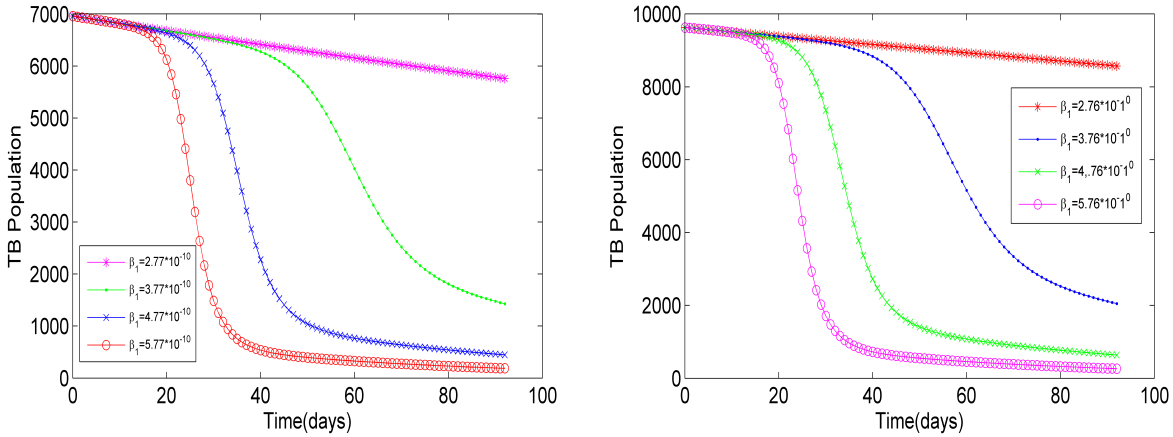

Figure 3. Variation of TB population for different values of β_1 during first and second waves of COVID-19

number of TB-infected population reported during the second wave was slightly higher than that during the first wave.

In Figure 4, we have drawn variation of TB infected population with time in the presence of COVID-19 infection. From the figure, we observe that number of TB infected population reported in this situation decline drastically. This decrement in number of infected TB population may be due to diagnosing TB as COVID-19 and treating TB infected population as COVID-19 infected population. Figures 5 and 6 display the variation of R_0 with parameters α_2, γ_2 and β_1 for both the waves of COVID-19 infection. It is observed that the qualitative nature of the graph is same in both the waves. For both the waves, it is observed that R_0 increases linearly for transmission coefficient β_1 of COVID-19 infection. However, R_0 decreases approaches to zero with the increase in death rate α_2 due to COVID-19 infection. Moreover, as recovery rate γ_2 of COVID-19 infected population increases, then R_0 decreases linearly. The graph illustrates that the most sensitive parameter is β_1 while the least sensitive parameter is found to be γ_2. Also, the sensitivity of the parameters in descending order is β_1, α_2, γ_2. It is also observed that R_0 increases linearly as A increases.

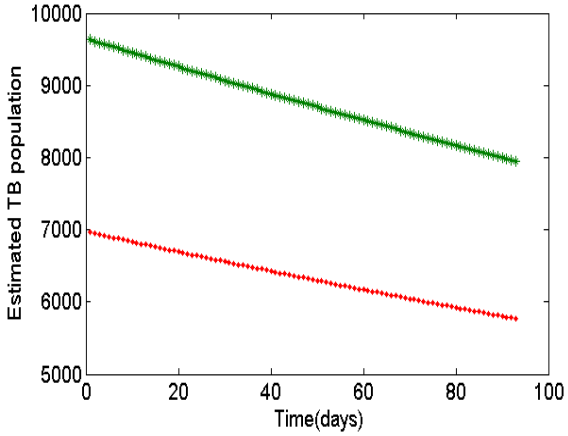

Figure 4. Variation of TB population with time during the first and second wave of COVID-19

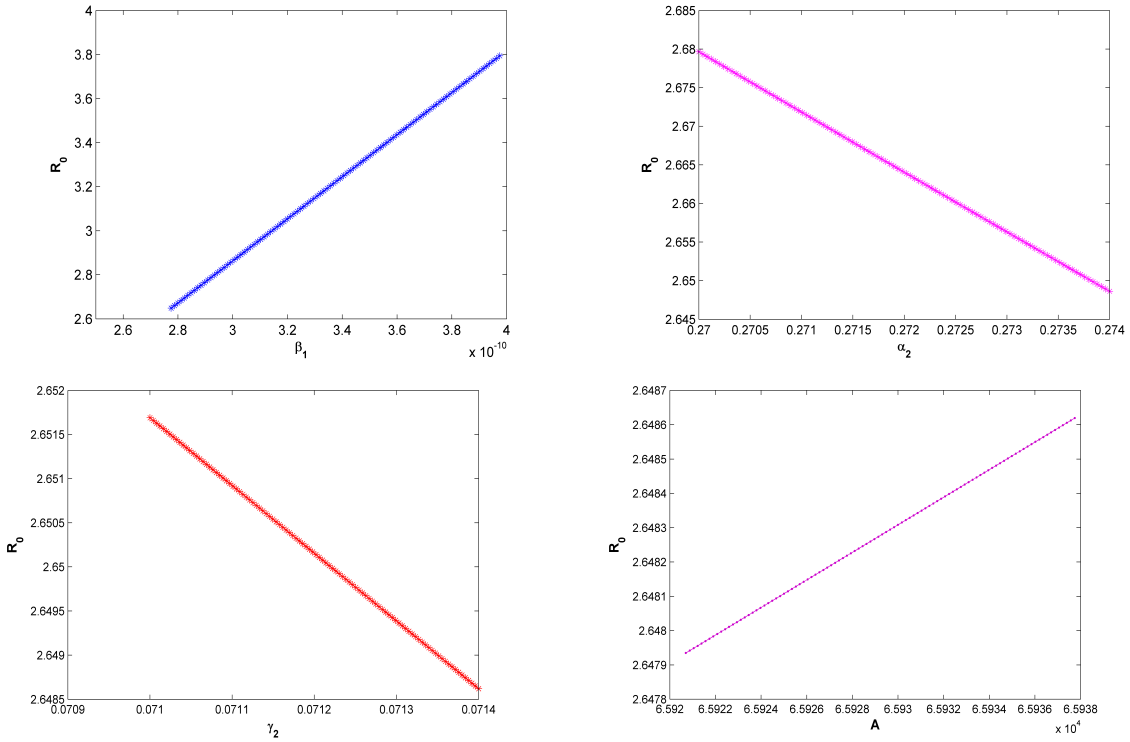

Figure 5. Variation of the R_0 with β_1, α_2, γ_2 and A during the first wave of COVID-19

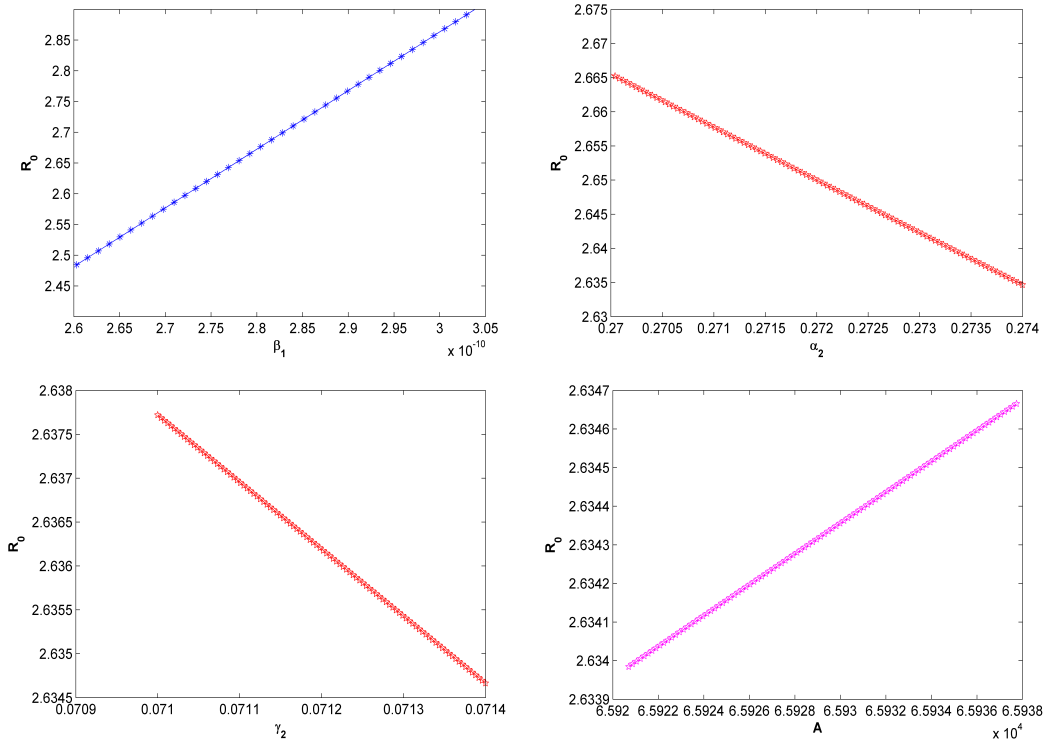

Figure 6. Variation of the R_0 with β_1, α_2, γ_2 and A during the second wave of COVID-19

8. Conclusion

In this study, a non-linear deterministic mathematical model for the co-infection of two concomitant diseases TB and COVID-19 is proposed to examine the dynamics of spread of these diseases. The biological meaningfulness of the model is proved by showing the existence, uniqueness, non-negativity, and boundedness of solutions in a given region. Then, the equilibrium points are computed. The stability analysis of the equilibrium points is also presented with the help of the basic reproduction number. The analytical study of the model reveals that the disease-free equilibrium point is stable if the basic reproduction number is less than unity otherwise unstable. Further, there exist a stable endemic equilibrium point for the basic reproduction number greater than one. Different numerical simulation cases were performed to supplement the analytical results and it is observed to be in good agreement. Furthermore, the simulation result reveals that there is drastic decrease in number of TB patient during COVID-19 situation.

Once the model parameter has been estimated on the basis of the available data on WHO and Nikshay Portal, the model enables us to find out the decrement in the statistics of TB. COVID-19 being the most dangerous disease is much harmful for the TB-infected population, because of the similar symptoms of TB and COVID-19, the TB-infected population face problems in medical facilities due to which number of TB infected population are expected to rise but decrement in notified cases is the matter of major concern and must be taken seriously with proper arrangements of screening and supplying medical facilities to the TB-infected population, so that we do not get an abrupt rise in TB notified patients once COVID-19 situations are normed. Disease-related death rate of COVID-19 is also high when compared to disease-related death of TB. As per the literature, decrease in number of TB-infected population interprets, the impact of immediate lockdown to control the COVID-19 infection. But it causes heavy risk to TB population due to the disruption in health services. Thus, our model is an attempt to draw attention of the policymakers towards the TB population infected with COVID-19 and actual number of notified cases of TB during the spread of COVID-19 as any false interpretation in the actual number of TB-infected cases may lead to another health hazard in the community.

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