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Optimal Control Strategies of Non-Pharmaceutical and Pharmaceutical Interventions for COVID-19 Control

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Abstract

In recent, non-pharmaceutical intervention (lockdown, quarantine, expended testing) and the pharmaceutical intervention (use of commonly used drugs) are the only available policy to control the COVID-19 epidemic. But the question is that whether the disease is to be partially or totally eradicated from the human population still remains unsolved. Usually, social distancing, using the mask, etc. are the only available policy to control the pandemic. Uses of common drugs (azithromycin, HCQ, antiprotozoal with Doxycycline) are the most effective treatment for the disease which can only activate the immune system to fight against the disease progression. We have formulated a seven compartmental SEIQR type model describing the spread of the COVID-19 among the human population. We have also apply the optimal control theory to the seven compartmental SEIQR model of ordinary differential equations to reduce the number of the infected population while minimizing the cost associated with the awareness and drug use in a particular time period. Analytical findings along with numerical simulations strongly suggest that the system behavior depends on basic reproduction number and awareness related to social distancing, using the mask and common drug usage are suggested to be maintained at the least possible level.

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1 Introduction

On 31st December 2019, the first case of unknown pneumonia was detected in the WHO country office in Wuhan, China. WHO declared the outbreak a Public Health Emergency on 30th January 2020 [1]. Within a short time, a team of virologists identified and recognized the virus [2]. On 11th February 2020, WHO announced a name for the disease as COVID-19. The infection of COVID -19 associated with the virus SARS-CoV-2 which is a single standard RNA virus genome that is closely related to the severe acute respiratory syndrome SARS-CoV. The infection of COVID-19 is associated with a SARS-CoV.

On March 11, 2020, WHO declared COVID-19 as a global pandemic [1]. As of 31st May 2020, globally more than 6.5 million people are infected and COVID-19 related death have crossed the 0.3 million mark. In India 73 confirmed COVID-19 cases have been observed on March 12, 2020. As per the data from the Ministry of Health and Family Welfare (MHFW), most of the cases were reported from Kerala. After that Union Ministry of Road and Transport and Highways advised states and Union territories to take necessary measures for sanitization of public transport vehicles and terminals were taken by the. All educational institutions, stadiums, and sports clubs were closed from till further orders. On March 24, 2020, the Government of India (GOI) ordered a national wide lockdown for 21 days. After that GOI declared lockdown in three consecutive phases till 30th May 2020. The Government of India divided all the districts into three zones based green, red, and orange [3]. On 17th May, the National Disaster Management Authority extended the lockdown till 31st May 2020 [4].

On 30th May, the lockdown was extended till 30th June 2020 only for containment zones. During the 4th lockdown, it has been observed that the basic reproduction number (R_0) was reduced from 1.83 to 1.23 for all over India [13]. From this measure of basic reproduction number R_0 , we can say that India is controlling COVID -19. The decrease of R_0 is the effect of lockdown. During the lockdown period, social distancing, using masks, wearing long sleeves, frequent hand washing, sanitization played a pivotal role to reduce the basic reproduction number. Also using commonly used drug-like azithromycin, HCQ, antiprotozoal with Doxycycline for the treatment of COVID-19 patients played an effective role to control the disease in

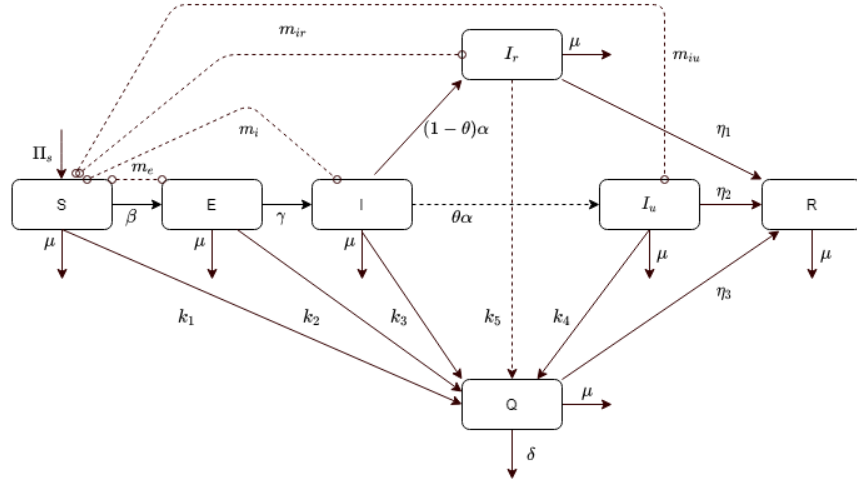


Figure 1: Transmission flowchart of COVID-19

India.

In this article, our main aim is to explore the cost-effective strategies of awareness like social distancing, using mask along with common drug use and its effect on disease transmission and progression. In Section 2, we present the seven compartmental SEIQR model. In section 3, we study the existence and boundedness of the system. In section 4, we study the stability of the system and in section 5 we analyze the sensitivity of R_0 . In section 6, we introduce the objective function and two control variables to minimize the number of infected and exposed populations. In this section, we also develop the adjoint equations and formulate the characterization of optimal control strategies by applying the optimal control theory [10]. In section 7 and 8 we discuss our analytical as well as numerical findings.

2 Mathematical Model Formulation

We propose a seven compartmental SEIQR model (see Figure 1) to describe the transmission of COVID-19 infection in a human population of size $N(t)$.

Here we consider the following seven classes:

- $S(t)$ – the number of susceptible individuals at time t ;
- $E(t)$ – the number of exposed individuals at time t ;

- $I(t)$ – the number of infected individuals at time t ;
- $I_r(t)$ – the number of reported infected individuals and who are in isolation or hospitalised at time t ;
- $I_u(t)$ – the number of asymptomatic infected individuals at time t ;
- $Q(t)$ – the number quarantine individuals at time t ;
- $R(t)$ – the number of recovered individuals at time t .

The total population size $N(t) = S(t) + E(t) + I(t) + I_r(t) + I_u(t) + Q(t) + R(t)$.

In view the above biological consideration, we establish a dynamical mathematical model of *novel coronavirus* following system of non-linear differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi_s - \frac{\beta S}{N}(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - k_1 S - \mu S, \\
\frac{dE}{dt} &= \frac{\beta S}{N}(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - \gamma E - k_2 E - \mu E, \\
\frac{dI}{dt} &= \gamma E - k_3 I - \alpha I - \mu I, \\
\frac{dI_r}{dt} &= \alpha(1 - \theta)I - k_4 I_r - \eta_1 I_r - \mu I_r, \\
\frac{dI_u}{dt} &= \alpha\theta I - k_5 I_u - \eta_2 I_u - \mu I_u, \\
\frac{dQ}{dt} &= k_1 S + k_2 E + k_3 I + k_4 I_r + k_5 I_u - \delta Q - \eta_3 Q - \mu Q, \\
\frac{dR}{dt} &= \eta_1 I_r + \eta_2 I_u + \eta_3 Q - \mu R,
\end{aligned} \tag{1}$$

with this initial conditions

$$S(0) > 0, E(0) \geq 0, I(0) \geq 0, I_r(0) \geq 0, I_u(0) \geq 0, Q(0) \geq 0 \text{ and } R(0) \geq 0. \tag{2}$$

Here, quarantine population refers to the separation of susceptible individuals with travel history, exposed, and infected individuals from the general population. Let Π_s be the net inflow of susceptible individuals into the region per unit time. We assume that μ is the death rate of seven subpopulations of the model irrespective of demographic effect. For four groups of infected population the disease transmission coefficient are βm_e ,

Table 1: Parameters and descriptions used in Model 1

Parameter	Description	value
Π_s	Recruitment rate	-
β	Transmission rate	-
γ	Migration rate of exposed to infected sub class	0.2 (day^{-1})
θ'	Screening/testing rate	0.8 (day^{-1})
δ	Escape rate from quarantine	0.04 (day^{-1})
μ	natural death rate	0.005 (day^{-1})
m_e	Contact factor for exposed individuals	0.3
m_i	Contact factor for infected individuals	0.3
m_{ir}	Contact factor for reported individuals	0.3
m_{iu}	Contact factor for unreported individuals	0.3
α	Modification factor of Screening/testing	0.1
k_1	Quarantine rate of susceptible individual	0.006 (day^{-1})
k_2	Quarantine rate of exposed individual	0.006 (day^{-1})
k_3	Quarantine rate of infected individual	0.006(day^{-1})
k_4	Quarantine rate of reported infected individual	0.006 (day^{-1})
k_5	Quarantine rate of unreported infected individual	0.006 (day^{-1})
η_1	Recovery rate from infected individuals	0.037 (day^{-1})
η_2	Recovery rate from reported infected individuals	0.037 (day^{-1})
η_3	Recovery rate from unreported individuals	0.037 (day^{-1})

βm_i , βm_{ir} , and βm_{iu} respectively where β is the disease transmission rate and m_e , m_i , m_{ir} , m_{iu} are the relative intensity of contact factors. γ is the rate at which the exposed population moves to the infected population. The infected population is reported at a rate of $\alpha(1 - \theta)$ and the infected population moves to the unreported population at a rate of $\alpha\theta$. Here we assume $\theta' = 1 - \theta$, where θ' is the screening/testing rate. Let k_1 , k_2 , k_3 , k_4 , k_5 are quarantine rate of the respective populations and η_1 , η_2 , and η_3 are the rate of recovery of I_r , I_u , and Q respectively. Also, we assume δ is the escape rate of individuals from quarantine.

3 Model Properties

3.1 Positivity and boundedness of solution

In this section, we prove the positivity and boundedness of the system (1) with positive initial condition $(S(0), E(0), I(0), I_r(0), I_u(0), Q(0), R(0))^T \in \mathbb{R}_+^7$. First we state the following lemma.

Lemma 1. Suppose $\Psi \subset \mathbb{R} \times \mathbb{C}$ is open, $h_l \in C(\Psi, \mathbb{R})$, $l = 1, 2, 3, \dots, p$. If $h_i |_{r_l(t)=0, G_t \in \mathbb{C}_{+0}^p} \geq 0$, $G_t = (r_{1t}, r_{2t}, \dots, r_{pt})^T$, then $\mathbb{C}_{+0}^n \{ \varpi = (\varpi_1, \varpi_2, \dots, \varpi_p) : \varpi \in \mathbb{C}([- \tau, 0], \mathbb{R}_{+0}^p) \}$ is the invariant domain of the following equations.

$$\frac{dr_l(t)}{dt} = h_l(t, G_t), t \geq \theta, l = 1, 2, 3, \dots, p,$$

where $\mathbb{R}_{+0}^p = \{(r_1, r_2, r_3, \dots, r_p : r_l \geq 0, l = 1, \dots, p\}$ [11].

Theorem 1. The system (1) with initial condition (2) is invariant with in \mathbb{R}_+^7 .

Proof. We re-write the the system (1), as

$$\frac{dY(t)}{dt} = P(Y(t)), Y(0) = Y_0 \geq 0, \quad (3)$$

$$P(Y(t)) = (P_1(X(t)), \dots, P_7(X(t)))^T.$$

Now, we see that

$$\begin{aligned} \frac{dS}{dt} |_{S=0} &= \Pi_s > 0, \quad \frac{dE}{dt} |_{E=0} = \frac{\beta S}{N} (m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) \geq 0, \\ \frac{dI}{dt} |_{I=0} &= \gamma E \geq 0, \quad \frac{dI_r}{dt} |_{I_r=0} = \alpha(1 - \theta) I \geq 0, \quad \frac{dI_u}{dt} |_{I_u=0} = \alpha \theta I \geq 0, \\ \frac{dQ}{dt} |_{Q=0} &= k_1 S + k_2 E + k_3 I + k_4 I_r + k_5 I_u \geq 0. \\ \frac{dR}{dt} |_{R=0} &= \eta_1 I_r + \eta_2 I_u + \eta_3 Q \geq 0, \end{aligned}$$

So, following this theorem the system (1) is an invariant set \mathbb{R}_+^7 . \square

Theorem 2. All the solution of the system (1) with this initial conditions (2) is uniformly bounded in the region Φ , where feasible regions Φ is defined by

$$\begin{aligned} \Phi = \left\{ (S, E, I, I_r, I_u, Q, R) \in \mathbb{R}_+^7 : S \leq \frac{\Pi_s}{\mu}, \right. \\ \left. S + E + I + I_r + I_u + Q + R \leq \frac{\Pi_s}{\mu} \right\} \quad (4) \end{aligned}$$

with this initial conditions (2).

Proof. Let, time dependent function:

$$N = S + E + I + I_r + I_u + Q + R,$$

Using system (1) in the above expression, we get

$$\begin{aligned} \frac{dN(t)}{dt} &= \Pi_s - [S + E + I + I_r + I_u + Q + R]\mu, \\ &\leq \Pi_s - N\mu, \end{aligned}$$

where, $\mu = \min\{\mu, k_1 + \mu\}$.

Thus,

$$\frac{dN}{dt} + N\mu \leq \Pi_s,$$

using the theorem of Deferential inequality [8], we obtain

$$0 < N \leq N(0)e^{-\mu t} + \frac{\Pi_s}{\mu},$$

where $N(0)$ denotes the initial value of the separate variables, as $t \rightarrow \infty$, we have,

$$0 < S + E + I + I_r + I_u + Q + R \leq \frac{\Pi_s}{\mu}.$$

So, Π_s/μ be an upper bound of N provided that $N(0) \leq \Pi_s/\mu$, if $N(0) \geq \Pi_s/\mu$ then N will decrease to this level. Thus all the solutions of the system (1) are bounded in Φ . \square

4 Model analysis

4.1 Disease-free equilibrium (DFE) and the reproduction number

The system (1) with the initial condition (2) has a DFE point $\Psi_0(S^0, E^0, I^0, I_r^0, I_u^0, Q^0, R^0)$ that is $\Psi_0(\Pi_s/(k_1 + \mu), 0, 0, 0, 0, 0, 0)$ which is always exists, without any condition.

The model reproduction number can be predictable with the next generation operator approach using van den Driessche and Watmough (2002) [9]. The matrices for new infection and transition terms given by F and V respectively, we have

$$F = \begin{pmatrix} \beta m_e & \beta m_i & \beta m_{ir} & \beta m_{iu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} b_2 & 0 & 0 & 0 & 0 & 0 \\ -\gamma & b_3 & 0 & 0 & 0 & 0 \\ 0 & -\alpha(1-\theta) & b_4 & 0 & 0 & 0 \\ 0 & -\alpha\theta & 0 & b_5 & 0 & 0 \\ -k_2 & -k_3 & -k_4 & -k_5 & b_6 & 0 \\ 0 & 0 & -\eta_1 & -\eta_2 & -\eta_3 & \mu \end{pmatrix},$$

where,

$$\begin{aligned} b_1 &= k_1 + \mu, & b_2 &= k_2 + \gamma + \mu, & b_3 &= k_3 + \alpha + \mu, \\ b_4 &= k_4 + \eta_1 + \mu, & b_5 &= k_5 + \eta_2 + \mu, & b_6 &= \delta + \eta_3 + \mu. \end{aligned}$$

The model reproduction number, denoted by R_0 is the spectral radius of next generation matrix given by

$$\begin{aligned} R_0 &= \rho(FV^{-1}) = R_{01} + R_{02} + R_{03} + R_{04} \\ &= \frac{\beta m_e}{(k_2 + \gamma + \mu)} + \frac{\gamma \beta m_i}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)} + \frac{\gamma \beta \alpha (1 - \theta) m_{ir}}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_4 + \eta_1 + \mu)} \\ &\quad + \frac{\gamma \beta \alpha \theta m_{iu}}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_5 + \eta_2 + \mu)} \\ &= \frac{\beta}{(k_2 + \gamma + \mu)} \left[m_e + \frac{\gamma m_i}{(k_3 + \alpha + \mu)} + \frac{\gamma \alpha (1 - \theta) m_{ir}}{(k_3 + \alpha + \mu)(k_4 + \eta_1 + \mu)} \right. \\ &\quad \left. + \frac{\gamma \alpha \theta m_{iu}}{(k_3 + \alpha + \mu)(k_5 + \eta_2 + \mu)} \right]. \end{aligned} \tag{5}$$

4.2 Stability analysis of disease-free equilibrium (DFE)

Theorem 3. *The disease-free equilibrium of the system (1) Ψ_0 , that is exists for all initial condition (2) and is locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$.*

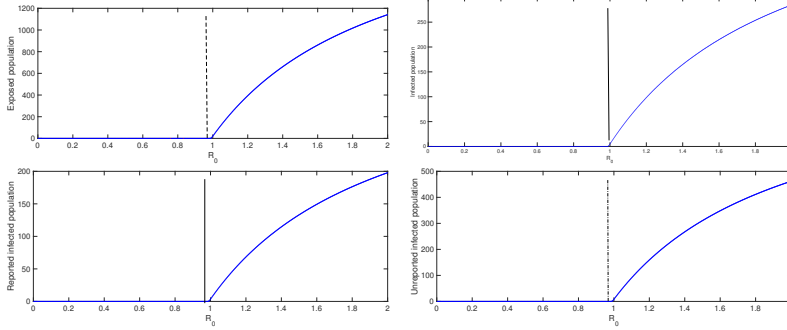


Figure 2: Transcritical bifurcation: steady state value of exposed, infected, reported infected and unreported infected population are plotted versus basic reproduction number R_0 using the set of parameters as given in Table 1 except disease transmission rate β . Endemic steady state feasible when $R_0 > 1$. β is varied in plotting the figure.

Proof. For determine the local stability of Ψ_0 , the Jacobian matrix of the system (1) is calculated at DFE as:

$$J_{\Psi_0} = \begin{pmatrix} -b_1 & -\beta m_e & -\beta m_i & -\beta m_{ir} & -\beta m_{iu} & 0 & 0 \\ 0 & -b_{16} & \beta m_i & \beta m_{ir} & \beta m_{iu} & 0 & 0 \\ 0 & \gamma & -b_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha(1-\theta) & -b_4 & 0 & 0 & 0 \\ 0 & 0 & \alpha\theta & 0 & -b_5 & 0 & 0 \\ k_1 & k_2 & k_3 & k_4 & k_5 & -b_6 & 0 \\ 0 & 0 & 0 & \eta_1 & \eta_2 & \eta_3 & -\mu \end{pmatrix},$$

where, $b_{16} = b_2 - \beta m_e$.

Let us consider ϑ is a eigenvalue of the matrix J_{Ψ_0} . The characteristic equation is $\det(J_{\Psi_0} - \vartheta I_7) = 0$. From this characteristics equation, three eigenvalues of J_{Ψ_0} are $-\mu$, $-(k_1 + \mu)$ and $-(\delta + \eta_3 + \mu)$, these are real, negative and the other four eigenvalues is expressed in the form

$$\begin{aligned} & \gamma\beta m_i(\vartheta + b_4)(\vartheta + b_5) + \gamma\alpha(1-\theta)\beta m_{ir}(\vartheta + b_5) \\ & + \gamma\alpha\theta\beta m_{iu}(\vartheta + b_4) + \beta m_e(\vartheta + b_3)(\vartheta + b_4)(\vartheta + b_5) \\ & - (\vartheta + b_2)(\vartheta + b_3)(\vartheta + b_4)(\vartheta + b_5) = 0. \end{aligned}$$

We can rewrite the above equation:

$$\begin{aligned} \frac{\beta m_e}{(\vartheta + b_2)} + \frac{\gamma \beta m_i}{(\vartheta + b_2)(\vartheta + b_3)} + \frac{\gamma \alpha (1 - \theta) \beta m_{ir}}{(\vartheta + b_2)(\vartheta + b_3)(\vartheta + b_4)} \\ + \frac{\gamma \alpha \theta \beta m_{iu}}{(\vartheta + b_2)(\vartheta + b_3)(\vartheta + b_5)} = 1. \end{aligned} \quad (6)$$

Let

$$R_1(\vartheta) = \frac{\beta m_e}{(\vartheta + b_2)} + \frac{\gamma \beta m_i}{(\vartheta + b_2)(\vartheta + b_3)} + \frac{\gamma \alpha (1 - \theta) \beta m_{ir}}{(\vartheta + b_2)(\vartheta + b_3)(\vartheta + b_4)} \quad (7)$$

$$+ \frac{\gamma \alpha \theta \beta m_{iu}}{(\vartheta + b_2)(\vartheta + b_3)(\vartheta + b_5)}. \quad (8)$$

Rewrite the equation (7) $R_1(\vartheta)$ as

$$R_1(\vartheta) = R_{01}(\vartheta) + R_{02}(\vartheta) + R_{03}(\vartheta) + R_{04}(\vartheta).$$

Now if $Re(\vartheta) \geq 0$, $\vartheta = v + iw$, we get

$$\begin{aligned} |R_{01}(\vartheta)| &\leq \frac{\beta m_e}{|\vartheta + b_2|} \leq R_{01}(v) \leq R_{01}(0), \\ |R_{02}(\vartheta)| &\leq \frac{\gamma \beta m_i}{|\vartheta + b_2||\vartheta + b_3|} \leq R_{02}(v) \leq R_{02}(0), \\ |R_{03}(\vartheta)| &\leq \frac{\gamma \alpha (1 - \theta) \beta m_{ir}}{|\vartheta + b_2||\vartheta + b_3||\vartheta + b_4|} \leq R_{03}(v) \leq R_{03}(0), \\ |R_{04}(\vartheta)| &\leq \frac{\gamma \alpha \theta \beta m_{iu}}{|\vartheta + b_2||\vartheta + b_3||\vartheta + b_5|} \leq R_{04}(v) \leq R_{04}(0). \end{aligned}$$

Then

$$R_{01}(0) + R_{02}(0) + R_{03}(0) + R_{04}(0) = R_1(0) = R_0 < 1,$$

which means; $|R_1(\vartheta)| \leq 1$. If $R_0 < 1$, then all the eigenvalues of the above characteristic equation $R_1(\vartheta) = 1$ has negative real part.

Therefore, for $R_0 < 1$, all eigenvalue are negative. Hence, DFE Ψ_0 is locally asymptotically stable.

Again, if we consider $R_0 > 1$, that is $R_1(0) > 1$, then

$$\lim_{\vartheta \rightarrow \infty} R_1(\vartheta) = 0.$$

If there exist $\vartheta_1 > 0$, such that $R_1(\vartheta_1) = 1$. This means that there exist positive eigenvalue $\vartheta_1 > 0$ of the matrix J_{Ψ_0} .

Hence, the disease-free equilibrium $\Psi_0(\Pi_s/(k_1 + \mu), 0, 0, 0, 0, 0, 0)$ is unstable when $R_0 > 1$. \square

4.3 Existence of the endemic equilibrium

The model system (1) with initial condition (2) also exhibits an endemic equilibrium $\Psi^*(S^*, E^*, I^*, I_r^*, I_u^*, Q^*, R^*)$ with positive components provided, $R_0 > 1$. Equating the derivatives in the system (1) to zero and solving the resulting equations, we get;

$$\begin{aligned} S^* &= \frac{N^*}{R_0}, \quad E^* = \frac{k_3 + \alpha + \mu}{\gamma} I^*, \quad I_r^* = \frac{\alpha(1 - \theta)}{k_4 + \eta_1 + \mu} I^*, \\ I^* &= \frac{\gamma[(R_0 - 1)\Pi_s + (\Pi_s - N^*(k_1 + \mu))]}{N^*(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)}, \quad I_u^* = \frac{\alpha\theta}{k_5 + \eta_2 + \mu} I^*, \\ Q^* &= \frac{k_1 N^*}{(\delta + \eta_3 + \mu)R_0} + \left(k_3 + \frac{k_2(k_3 + \alpha + \mu)}{\gamma} + \frac{k_4\alpha(1 - \theta)}{k_4 + \eta_1 + \mu} + \frac{k_5\alpha\theta}{k_5 + \eta_2 + \mu} \right) I^*, \\ R^* &= \left(\frac{\eta_1\alpha(1 - \theta)}{k_4 + \eta_1 + \mu} + \frac{\eta_2\alpha\theta}{k_5 + \eta_2 + \mu} \right) I^* + \eta_3 Q^*, \end{aligned}$$

if, (i) $R_0 > 1$, (ii) $\Pi_s/(k_1 + \mu) > N^*$.

5 Sensitivity analysis

To determine the best way to reduce infection and mortality due to COVID-19, it is necessary to know which parameters play a pivotal role in its transmission and disease progression. Initial disease transmission is directly related to the basic reproduction number of the system which is a function of model parameters.

Here we calculate the sensitivity indices of the reproductive number, R_0 , to the parameters in the model. From these outcomes, we can determine which parameters are most crucial for controlling the disease transmission. We know that sensitivity analysis is mainly used to determine the parameter that has a high impact on the model dynamics.

The normalized forward sensitivity index of a variable to a parameter is defined below:

Definition: The normalized forward sensitivity index of a variable B , that depends differentiable on a parameter x , is defined as:

$$\Upsilon_x^B := \frac{\partial B}{\partial x} \times \frac{x}{B} \quad (9)$$

Table 2: Sensitivity indices of R_0 to parameters for the seven compartmental SEIQR model, evaluated at the parameter values given in Table 1. The parameters are ordered from most sensitive to least. Here the most sensitive parameter is disease transmission rate β and least sensitive parameter is k_3

Parameter	β	m_{iu}	θ	m_{ir}	α	m_i	m_e	k_2
Sensitivity index	1	0.571	0.191	0.163	0.157	0.144	0.121	0.025
Parameter	k_4	μ	γ	η_1	k_5	η_2	k_3	
Sensitivity index	-0.043	-0.071	-0.0843	-0.1106	-0.1506	-0.3872	-0.7896	

5.1 Sensitivity indices of R_0

We have already found out the explicit formula of R_0 in (5), we can derive the analytical expression for sensitivity of R_0 defined as $\Upsilon_x^{R_0} = \frac{\partial R_0}{\partial x} \times \frac{x}{R_0}$ for each of fifteen parameters. The sensitivity index of R_0 with respect to the system parameters are as follows:

$$\begin{aligned}
\Upsilon_{\beta}^{R_0} &= \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1, \\
\Upsilon_{m_e}^{R_0} &= \frac{\partial R_0}{\partial m_e} \times \frac{m_e}{R_0} = \frac{\beta}{(k_2 + \gamma + \mu)} \times \frac{m_e}{R_0}, \\
\Upsilon_{m_i}^{R_0} &= \frac{\partial R_0}{\partial m_i} \times \frac{m_i}{R_0} = \frac{\gamma\beta}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)} \times \frac{m_i}{R_0}, \\
\Upsilon_{m_{ir}}^{R_0} &= \frac{\partial R_0}{\partial m_{ir}} \times \frac{m_{ir}}{R_0} = \frac{(1 - \theta)\gamma\beta\alpha}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_4 + \eta_1 + \mu)} \times \frac{m_{ir}}{R_0}, \\
\Upsilon_{m_{iu}}^{R_0} &= \frac{\partial R_0}{\partial m_{iu}} \times \frac{m_{iu}}{R_0} = \frac{\theta\gamma\beta\alpha}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_5 + \eta_2 + \mu)} \times \frac{m_{iu}}{R_0}, \\
\Upsilon_{k_2}^{R_0} &= \frac{\partial R_0}{\partial k_2} \times \frac{k_2}{R_0} = -\frac{R_0}{(k_2 + \gamma + \mu)} \times \frac{k_2}{R_0}, \\
\Upsilon_{k_3}^{R_0} &= \frac{\partial R_0}{\partial k_3} \times \frac{k_3}{R_0} = -\frac{\gamma\beta}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)^2} \left[m_i + \frac{(1 - \theta)\alpha m_{ir}}{(k_4 + \eta_1 + \mu)} \right. \\
&\quad \left. + \frac{\theta\alpha m_{iu}}{(k_5 + \eta_2 + \mu)} \right] \times \frac{k_3}{R_0}, \\
\Upsilon_{k_4}^{R_0} &= \frac{\partial R_0}{\partial k_4} \times \frac{k_4}{R_0} = -\frac{\gamma\beta(1 - \theta)\alpha m_{ir}}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_4 + \eta_1 + \mu)^2} \times \frac{k_4}{R_0},
\end{aligned}$$

$$\begin{aligned}
\Upsilon_{\eta_1}^{R_0} &= \frac{\partial R_0}{\partial \eta_1} \times \frac{\eta_1}{R_0} = -\frac{\gamma\beta(1-\theta)\alpha m_{ir}}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_4 + \eta_1 + \mu)^2} \times \frac{\eta_1}{R_0}, \\
\Upsilon_{k_5}^{R_0} &= \frac{\partial R_0}{\partial k_5} \times \frac{k_5}{R_0} = -\frac{\gamma\beta\alpha\theta m_{iu}}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_5 + \eta_2 + \mu)^2} \times \frac{k_5}{R_0}, \\
\Upsilon_{\eta_2}^{R_0} &= \frac{\partial R_0}{\partial \eta_2} \times \frac{\eta_2}{R_0} = -\frac{\gamma\beta\alpha\theta m_{iu}}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)(k_5 + \eta_2 + \mu)^2} \times \frac{\eta_2}{R_0}, \\
\Upsilon_{\theta}^{R_0} &= \frac{\partial R_0}{\partial \theta} \times \frac{\theta}{R_0} = \frac{\gamma\beta\alpha}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)} \left[\frac{m_{iu}}{(k_5 + \eta_2 + \mu)} \right. \\
&\quad \left. - \frac{m_{ir}}{(k_4 + \eta_1 + \mu)} \right] \times \frac{\theta}{R_0}, \\
\Upsilon_{\alpha}^{R_0} &= \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0} = \frac{\gamma\beta}{(k_2 + \gamma + \mu)(k_3 + \alpha + \mu)^2} \left[m_i + \frac{(k_3 + \mu)(1-\theta)\alpha m_{ir}}{(k_4 + \eta_1 + \mu)} \right. \\
&\quad \left. + \frac{(k_3 + \mu)\theta\alpha m_{iu}}{(k_5 + \eta_2 + \mu)} \right] \times \frac{\alpha}{R_0}, \\
\Upsilon_{\gamma}^{R_0} &= \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = \frac{1}{(k_2 + \gamma + \mu)} \left[\frac{\beta}{(k_3 + \alpha + \mu)} \left(m_i + \frac{(1-\theta)\alpha m_{ir}}{(k_4 + \eta_1 + \mu)} \right. \right. \\
&\quad \left. \left. + \frac{\theta\alpha m_{iu}}{(k_5 + \eta_2 + \mu)} \right) - R_0 \right] \times \frac{\gamma}{R_0}, \\
\Upsilon_{\mu}^{R_0} &= \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{1}{(k_2 + \gamma + \mu)} \left[\frac{\beta}{(k_3 + \alpha + \mu)^2} \left(m_i \right. \right. \\
&\quad \left. \left. + \frac{(k_3 + k_4 + \eta_1 + \alpha + 2\mu)(1-\theta)\alpha m_{ir}}{(k_4 + \eta_1 + \mu)^2} \right. \right. \\
&\quad \left. \left. + \frac{(k_3 + k_5 + \eta_2 + \alpha + 2\mu)\theta\alpha m_{iu}}{(k_5 + \eta_2 + \mu)^2} \right) + R_0 \right] \times \frac{\mu}{R_0}.
\end{aligned}$$

Here $\Upsilon_{\beta}^{R_0} = 1$ is the largest sensitivity index and $\Upsilon_{k_3}^{R_0} = -0.7896$ is the least sensitivity index. If disease transmission rate β reduces 1% then R_0 also reduces 1%. Similarly R_0 is increasing function of the parameters m_{iu} , m_{ir} , m_e , m_i , k_2 , θ , α . From this finding we have also observed that R_0 increases as the unreported rate θ increases. Hence if we increase the rate of testing R_0 decreases and thus disease can be controlled.

The reproduction number R_0 is a decreasing function of the quarantine parameters k_3 , k_4 , k_5 , η_1 , η_2 , γ and μ respectively. As the quarantine rate of infected, unreported, and reported infected individuals increases, the basic reproduction number decreases. Hence high quarantine rate plays a pivotal role to control the disease spread. We obtained the results from our theoretical (see Figure 3) as well as numerical findings (see Figure 2).

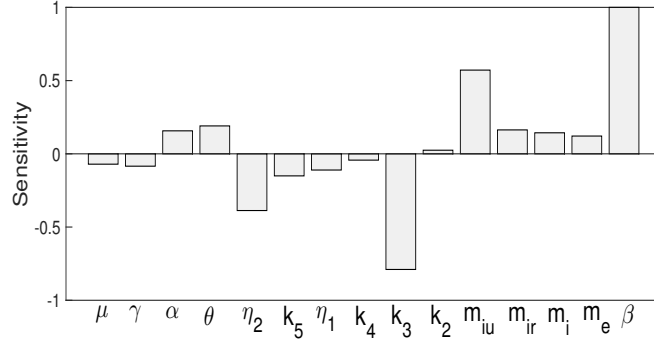


Figure 3: Tornado plot of sensitivity analysis of all fifteen parameters that influence R_0 .

6 *Optimal control*

In this section, we apply an optimal control technique; this is one of the most powerful mathematical tools which make the result involving infectious disease dynamical systems ([5]- [7]). By using this mathematical tool we trying to reduce the spread of coronavirus infection in our community. Our main objective is to minimize the infected population and to maximize the recovered population [10]. In the model (1) we have seven state variables i.e. $S, E, I, I_r, I_u, Q,$ and R . In this optimal control problem, we introduce two control variables.

(i). The first control $u_1(t)$ represents that when susceptible persons handling the coronavirus infected persons then they should cover all cuts, wear full cover shoes, gloves, use the shirts with long sleeves, mask, hygiene, and maintain distancing.

(ii). The second control $u_2(t)$ is to use common effective antibiotic use.

The above control variables in the model (1) are adjusted in the following form

$$\begin{aligned}
\frac{dS}{dt} &= \Pi_s - \frac{\beta S}{N}(1 - u_1(t))(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - k_1 S - \mu S, \\
\frac{dE}{dt} &= \frac{\beta S}{N}(1 - u_1(t))(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - \gamma E - k_2 E - \mu E, \\
\frac{dI}{dt} &= \gamma E - k_3 I - \alpha I - \mu I - u_2(t)I, \\
\frac{dI_r}{dt} &= \alpha(1 - \theta)I - k_4 I_r - \eta_1 I_r - \mu I_r, \\
\frac{dI_u}{dt} &= \alpha\theta I - k_5 I_u - \eta_2 I_u - \mu I_u, \\
\frac{dQ}{dt} &= k_1 S + k_2 E + k_3 I + k_4 I_r + k_5 I_u - \delta Q - \eta_3 Q - \mu Q, \\
\frac{dR}{dt} &= \eta_1 I_r + \eta_2 I_u + \eta_3 Q + u_2(t)I - \mu R.
\end{aligned} \tag{10}$$

The control set for the control variables is defined as,

$$U = \{u = (u_1(t), u_2(t)) \mid 0 \leq u_1, u_2 \leq 1, \text{ is Lebesgue measurable.}\} \tag{11}$$

Our aim is to minimize the objective functional:

$$\mathcal{K}(u) = \int_0^T \left[\sigma_1 E + \sigma_2 I + \sigma_3 I_r + \sigma_4 I_u + \frac{1}{2} (\nu_1 u_1^2 + \nu_2 u_2^2) \right] dt. \tag{12}$$

All the coefficients $\sigma_1, \sigma_2, \sigma_3, \sigma_4, \nu_1$, and ν_2 are nonnegative, its represents weights on the different terms of objective functional.

Theorem 4. Define an optimal control vector $u^* = (u_1^*, u_2^*) \in U$ and the corresponding state solutions $p^* = (S^*, E^*, I^*, I_r^*, I_u^*, Q^*, R^*)$ in the model (10), there exist adjoint variables $\varphi_j(t), j=1, \dots, 7$, satisfying

$$\begin{aligned}
\varphi_1' &= - \left[(\varphi_2 - \varphi_1) \frac{\beta(1 - u_1)}{N} (m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - (k_1 - \mu) \varphi_1 \right. \\
&\quad \left. + k_1 \varphi_6 \right], \\
\varphi_2' &= - \left[\sigma_1 + (\varphi_2 - \varphi_1) \frac{\beta(1 - u_1) S}{N} m_e - (\mu + k_2 + \gamma) \varphi_2 + \gamma \varphi_3 + k_2 \varphi_6 \right], \\
\varphi_3' &= - \left[\sigma_2 + (\varphi_2 - \varphi_1) \frac{\beta(1 - u_1) S}{N} m_i + (\mu + k_3 + \alpha + u_2) \varphi_3 + (1 - \theta) \alpha \varphi_4 \right. \\
&\quad \left. + \theta \alpha \varphi_5 + k_3 \varphi_6 + u_2 \varphi_7 \right],
\end{aligned}$$

$$\begin{aligned}\varphi'_4 &= -\left[\sigma_3 + (\varphi_2 - \varphi_1)\frac{\beta(1-u_1)S}{N}m_{ir} - (\mu + k_4 + \eta_1)\varphi_4 + k_4\varphi_6 + \eta_1\varphi_7\right], \\ \varphi'_5 &= -\left[\sigma_3 + (\varphi_2 - \varphi_1)\frac{\beta(1-u_1)S}{N}m_{ir} - (\mu + k_5 + \eta_2)\varphi_5 + k_5\varphi_6 + \eta_2\varphi_7\right], \\ \varphi'_6 &= (\mu + \delta + \eta_3)\varphi_6 - \eta_3\varphi_7, \quad \varphi'_7 = \mu\varphi_7,\end{aligned}$$

with the transversality conditions: $\varphi_j(T) = 0, j = 1, \dots, 7$.

Additionally, the optimal control vector is given by $u^* = (u_1^*, u_2^*)$, where

$$\begin{aligned}u_1^* &= \min \left\{ \max \left\{ 0, \frac{(\varphi_2 - \varphi_1)\beta S(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u)}{\nu_1 N} \right\}, 1 \right\}, \\ u_2^* &= \min \left\{ \max \left\{ 0, \frac{(\varphi_3 - \varphi_7)I}{\nu_2} \right\}, 1 \right\}.\end{aligned}$$

Proof. Following the Pontryagin's Minimum Principle [10], we can obtain the Hamiltonian as we get:

$$\begin{aligned}\mathcal{H} &= \sigma_1 E + \sigma_2 I + \sigma_3 I_r + \sigma_4 I_u + \frac{1}{2}(\nu_1 u_1^2 + \nu_2 u_2^2) \\ &+ \varphi_1 \left[\Pi_s - \frac{\beta S}{N}(1-u_1(t))(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - (k_1 + \mu)S \right] \\ &+ \varphi_2 \left[\frac{\beta S}{N}(1-u_1(t))(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u) - (\gamma + k_2 + \mu)E \right] \\ &+ \varphi_3 \left[\gamma E - (k_3 + \alpha + \mu + u_2(t))I \right] + \varphi_4 \left[\alpha(1-\theta)I - (k_4 + \eta_1 + \mu)I_r \right] \\ &+ \varphi_5 \left[\alpha\theta I - (k_5 + \eta_2 + \mu)I_u \right] \\ &+ \varphi_6 \left[k_1 S + k_2 E + k_3 I + k_4 I_r + k_5 I_u - (\delta + \eta_3 + \mu)Q \right] \\ &+ \varphi_7 \left[\eta_1 I_r + \eta_2 I_u + \eta_3 Q + u_2(t)I - \mu R \right].\end{aligned}$$

Now, adjoint variables $\varphi_j(t) = 0, j = 1, \dots, 7$, by:

$$\begin{aligned}\varphi'_1 &= -\frac{\partial \mathcal{H}}{\partial S}, \quad \varphi'_2 = -\frac{\partial \mathcal{H}}{\partial E}, \quad \varphi'_3 = -\frac{\partial \mathcal{H}}{\partial I}, \quad \varphi'_4 = -\frac{\partial \mathcal{H}}{\partial I_r}, \\ \varphi'_5 &= -\frac{\partial \mathcal{H}}{\partial I_u}, \quad \varphi'_6 = -\frac{\partial \mathcal{H}}{\partial Q}, \quad \varphi'_7 = -\frac{\partial \mathcal{H}}{\partial R},\end{aligned}$$

with the transversality conditions $\varphi_j(T) = 0, j = 1, \dots, 7$. We get the characterization of optimal controls by saying

$$\frac{\partial \mathcal{H}}{\partial u_1} = 0, \quad \frac{\partial \mathcal{H}}{\partial u_2} = 0.$$

From $\frac{\partial \mathcal{H}}{\partial u_1} = 0$ and $\frac{\partial \mathcal{H}}{\partial u_2} = 0$, we get

$$\begin{aligned} u_1 &= \frac{(\varphi_2 - \varphi_1)\beta S(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u)}{\nu_1 N}, \\ u_2 &= \frac{(\varphi_3 - \varphi_7)I}{\nu_2}. \end{aligned}$$

By holding the upper and lower bounds for u_1 and u_2 into account, we are following the characterization of optimal controls:

$$\begin{aligned} u_1^* &= \min \left\{ \max \left\{ 0, \frac{(\varphi_2 - \varphi_1)\beta S(m_e E + m_i I + m_{ir} I_r + m_{iu} I_u)}{\nu_1 N} \right\}, 1 \right\} \\ u_2^* &= \min \left\{ \max \left\{ 0, \frac{(\varphi_3 - \varphi_7)I}{\nu_2} \right\}, 1 \right\} \end{aligned}$$

This proof is completes. \square

7 Numerical Study

From the estimated value of R_0 of different states ([13]) during 4th lockdown and recovery rate of different state ([14]), we focused our seven compartmental SEIQR model (1) to the daily new COVID-19 cases for the six states of India namely Tamil Nadu, Punjab, Uttar Pradesh, Karnataka, Bihar, and West Bengal. Daily COVID-19 cases are collected for the period of 4th lockdown (18th May 2020 to 31st May 2020) from the National Information Centre, Ministry of Electronics and Information Technology, Government of India. Figure 4 shows the graphical representation of the state-wise COVID-19 effective reproduction rate R_0 and the recovery rate of six major states in India during 4th lockdown in India. From these figures, it is clearly observed that during 4th lock down the basic reproduction number is maximum for Bihar. But there is a hope that the recovery rate of Bihar is maximum compared to other major states in India. Comparing the R_0 and recovery rate from Figure 4, we have studied the optimal control strategies for these states. For the parameter values of Table 1, we have $R_0 = 10.3514\beta$. Table 3 shows the relation between R_0 and disease transmission rate β for the six-state of India.

For the optimal control problem (10, 11) and (12) the value of R_0 becomes

Table 3: State wise values of β and recovery rate depending on R_0

State	R_0	β	Recovery rate (%)
Bihar	2.10	0.21	33.61
Karnataka	1.62	0.1565	11.52
West Bengal	1.22	0.1179	10.99
Punjab	1.32	0.1275	0.92
Uttar Pradesh	1.33	0.1285	3.91
Tamil Nadu	2.01	0.1941	6.01

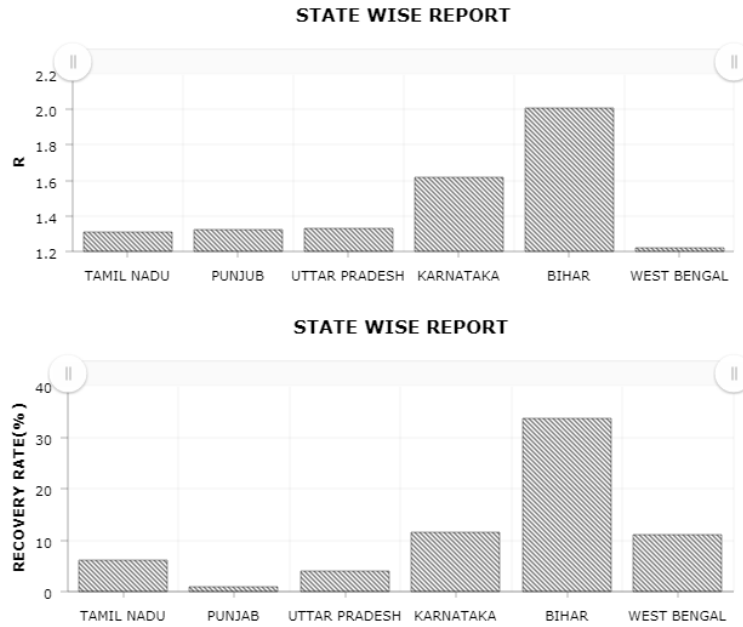


Figure 4: Top Panel: State-level COVID-19 effective reproduction rate in major six state of India [13]. Bottom Panel: State-level COVID-19 effective recovery rate in major six state of India [14].

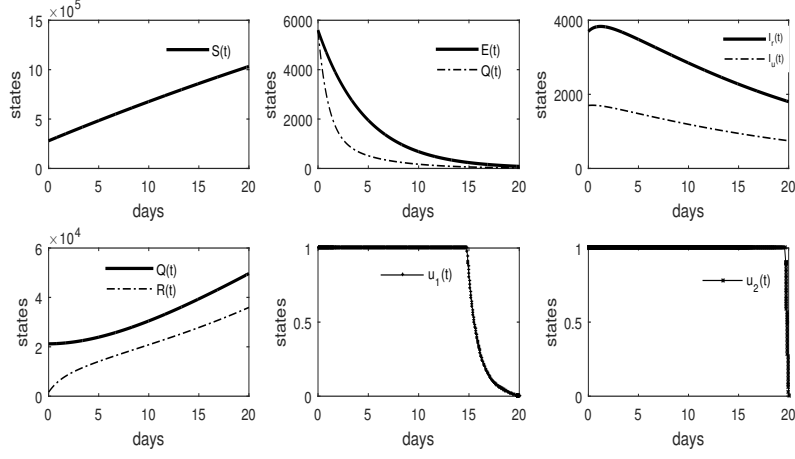


Figure 5: Optimal solution and optimal control for Bihar when $R_0 = 2.10$ and $T = 20$ days with recovery rate 33.16%.

$$\begin{aligned}
R_0^c(u_1, u_2) = & \frac{(1 - u_1)\beta}{(k_2 + \gamma + \mu)} \left[m_e + \frac{\gamma m_i}{(k_3 + \alpha + \mu + u_2)} \right. \\
& + \frac{\gamma \alpha (1 - \theta) m_{ir}}{(k_3 + \alpha + \mu + u_2)(k_4 + \eta_1 + \mu)} \\
& \left. + \frac{\gamma \alpha \theta m_{iu}}{(k_3 + \alpha + \mu + u_2)(k_5 + \eta_2 + \mu)} \right].
\end{aligned}$$

Assuming $u_1(\max) = 0.9$ and $u_2(\max) = 0.9$ we get $R_0^c(u_{1\max}, u_{2\max}) = 3.7681\beta$.

It is clear that for any possible value of β , $R_0^c(u_{1\max}, u_{2\max}) < 1$ holds.

This means that the maximum implementation of social awareness and adequate common drug use should control the epidemic. It is also clear that $u_{1\max}$ and $u_{2\max}$ can be reduced when the disease progression is under control.

The following figures (Figure 5 - Figure 16) represents the outcomes of this seven compartmental SEIQR model for different states in India for 20 days and 40 days control respectively.

Figure 5 and Figure 6 show the results of Bihar COVID-19 cases in computations for optimal control strategies for the upcoming 20 days and 40 days respectively. These figures demonstrate that during 20 days time period the recovery rate increases and new infection number reduces to less

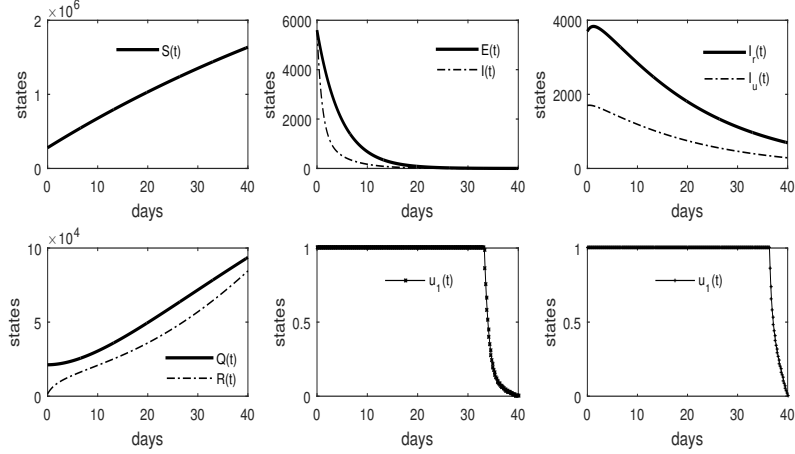


Figure 6: Optimal solution and optimal control for Bihar when $R_0 = 2.10$ and $T = 40$ days with recovery rate 33.16%.

than 100. If we extend the time period to 40 days the newly reported cases reduce below 10.

Figure 7 and Figure 8 are show the results of Karnataka COVID-19 cases in computations for optimal control strategies for upcoming 20 days and 40 days respectively. Figure 7 and Figure 8 are reveals the recovery rate increases during 20 days time period and new infection number reduces to less than 250. But the time period of control is to be extended 40 days then the newly reported cases reduce below 5.

For the COVID-19 cases of West Bengal, computations for optimal control strategies for approaching 20 days and 40 days respectively are shown in Figure 9 and Figure 10. These figures are demonstrate that during 20 days time period the recovery rate increases and new infection number reduces to less than 400. When we draw out the time period of control to 40 days the newly reported cases reduce below 10.

Figure 11 and Figure 12 are show the results of Punjab COVID-19 cases in computations for optimal control strategies for upcoming 20 days and 40 days respectively. These figures demonstrate that during 20 days time period the recovery rate increases and new infection number reduces to less than 20. If we extend the time period of control to 40 days the newly reported cases reduce below 3.

Figure 13 and Figure 14 show the results of Uttar Pradesh COVID-19 cases in computations for optimal control strategies for upcoming 20 days

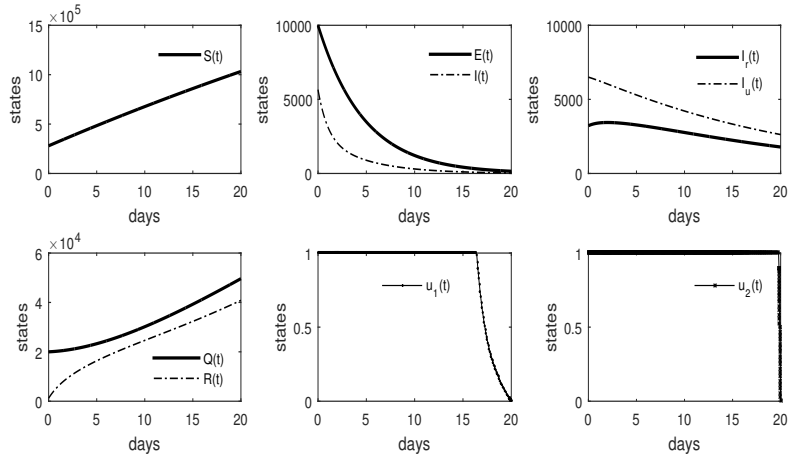


Figure 7: Optimal solution and optimal control for Karnataka when $R_0 = 1.62$ and $T = 20$ days with recovery rate 11.52%.

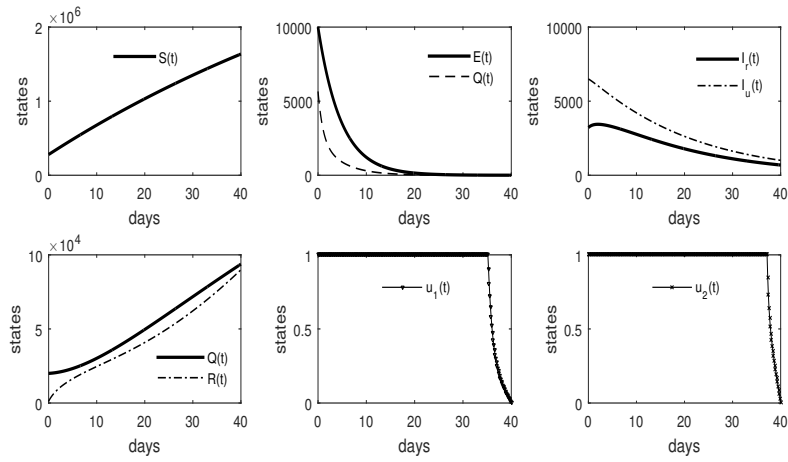


Figure 8: Optimal solution and optimal control for Karnataka when $R_0 = 1.62$ and $T = 40$ days with recovery rate 11.52%.

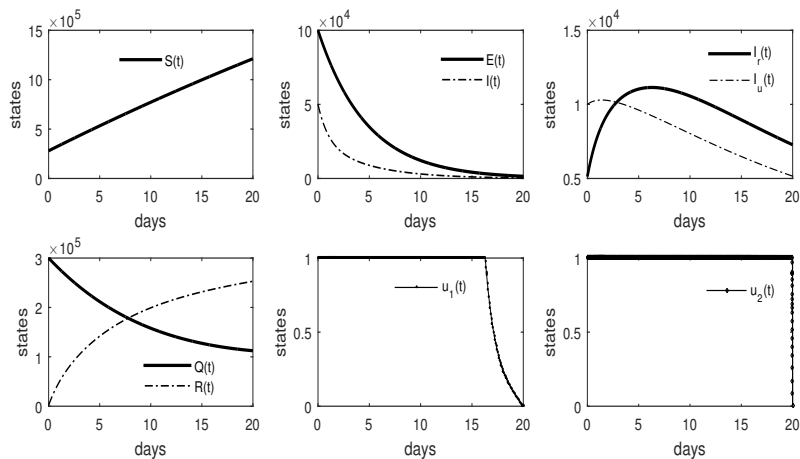


Figure 9: Optimal solution and optimal control for West Bengal when $R_0 = 1.22$ and $T = 20$ days with recovery rate 10.99%.

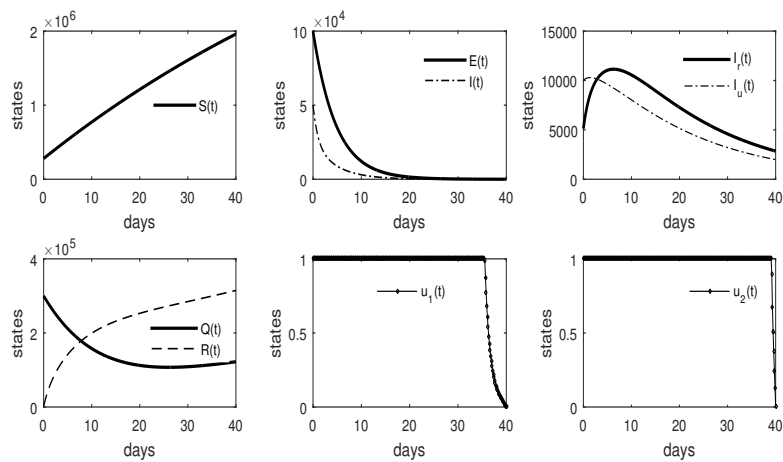


Figure 10: Optimal solution and optimal control for West Bengal when $R_0 = 1.22$ and $T = 40$ days with recovery rate 10.99%.

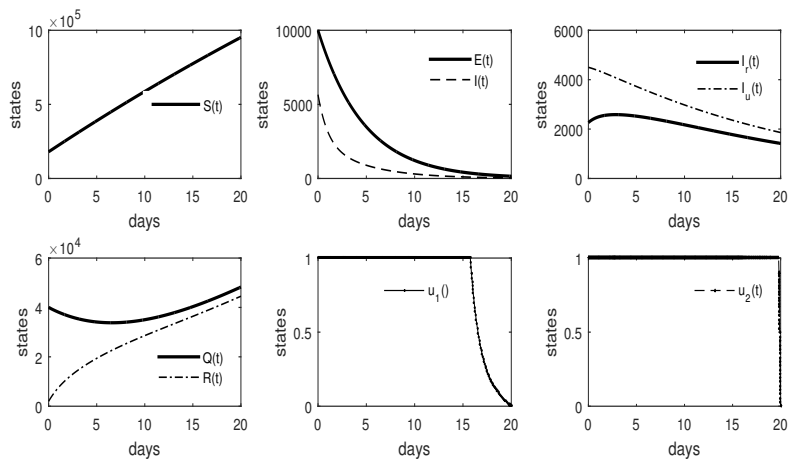


Figure 11: Optimal solution and optimal control for Punjab when $R_0 = 1.32$ and $T = 20$ days with recovery rate 0.92%.

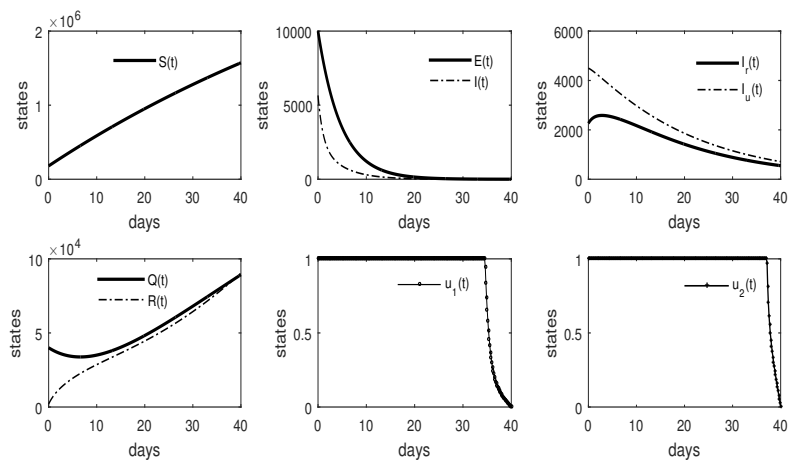


Figure 12: Optimal solution and optimal control for Punjab when $R_0 = 1.32$ and $T = 40$ days with recovery rate 0.92%.

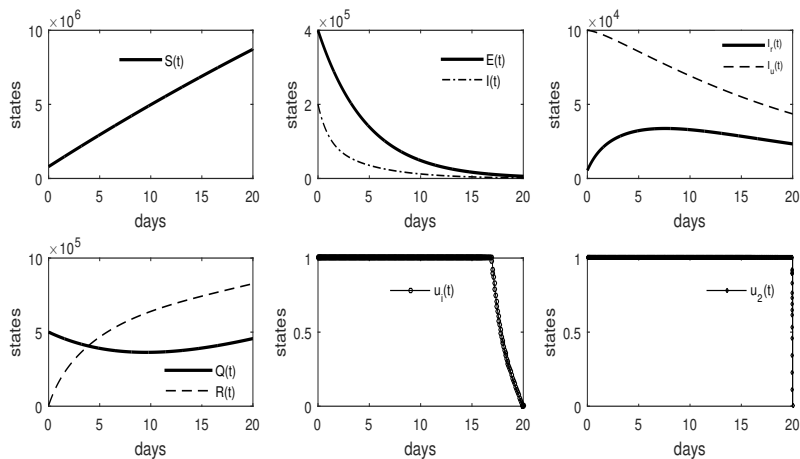


Figure 13: Optimal solution and optimal control for Uttar Pradesh when $R_0 = 1.33$ and $T = 20$ days with recovery rate 3.91%.

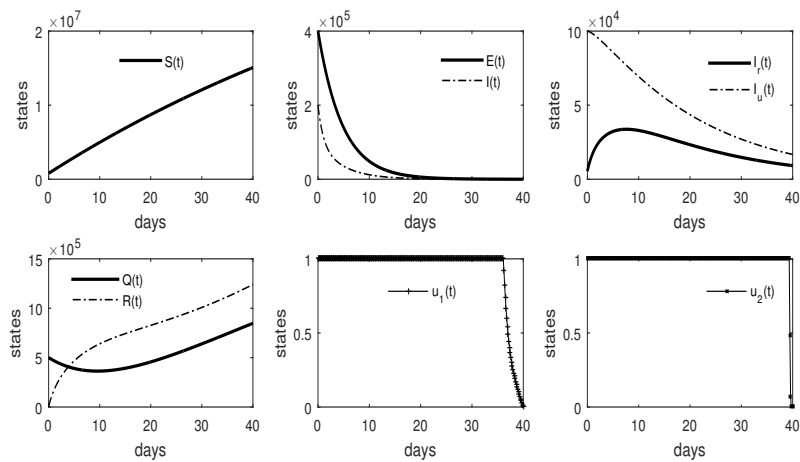


Figure 14: Optimal solution and optimal control for Uttar Pradesh when $R_0 = 1.33$ and $T = 40$ days with recovery rate 3.91%.

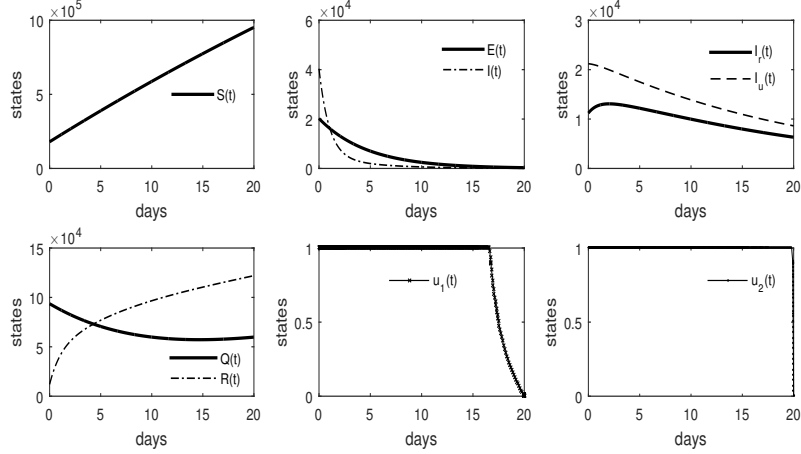


Figure 15: Optimal solution and optimal control for Tamil Nadu when $R_0 = 2.01$ and $T = 20$ days with recovery rate 6.01%.

and 40 days respectively. These figures demonstrate that during 20 days time period the recovery rate increases and new infection number reduces to less than 150. But we extend the time period of control to 40 days the newly reported cases reduce below 5.

Figure 15 and Figure 16 show the results of Tamil Nadu COVID-19 cases in computations for optimal control strategies for upcoming 20 days and 40 days respectively. These figures demonstrate that during 20 days time period the recovery rate increases and new infection number reduces to less than 300. If we extend the time period of control to 40 days the newly reported cases reduce below 10.

Comparing the numerical outcomes in Figure 5 to Figure 16 it is clearly observed that the basic reproduction number R_0 and the recovery rate has a great impact to control the disease. From these findings, we can conclude that for a lower R_0 the outcomes would be considerably better, and our computation confirms this assumption. For all cases, the optimal control u_1^* and u_2^* should be kept as high as possible during the control period. We should keep the optimal control u_1^* and u_2^* at its high from starting of the control policy until a considerable decrease of the infection level is reached. After that, we can reduce its level to its minimum value to avoid other complications. In the case of 20 days time period the optimal control u_1^* should be maximum during the first 2 weeks and then it is slowly decreasing. However, the case of 40 days the optimal control u_1^* should be maximum for

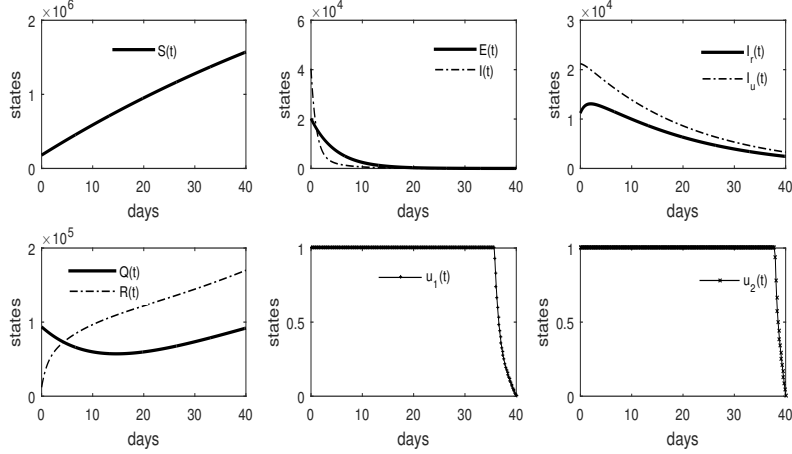


Figure 16: Optimal solution and optimal control for Tamil Nadu when $R_0 = 2.01$ and $T = 40$ days with recovery rate 6.01%.

one month. But in both cases the optimal control u_2^* should be maximum during the total control period.

8 Discussion and Conclusions

In the present scenario, there is neither vaccine nor COVID-19 specific drug available. A non-pharmaceutical intervention like lockdown, quarantine, maintain social distancing are indirect protective measures during this time period. In view of this, we have proposed a seven compartmental SEIQR type model that describes the spread of COVID-19 virus in a human population of variable size are considered. The models differ by the infection rates that describe virus transmission.

In our analytical finding shows that if the basic reproduction number $R_0 < 1$ the system attains its disease-free state and if $R_0 > 1$ the system moves towards its endemic state. We have derived the sensitivity index of the model parameters. From these findings, we have observed that R_0 reduces as the screening/testing along with the quarantine rate of infected individuals increases. Thus screening/testing along with quarantine effect plays a major role to control the disease progression.

To understand the non-pharmaceutical and pharmaceutical effect to control COVID-19 infection, we applied the optimal control theory to a seven

compartmental system of differential equations. Our main objective is to reduce the number of new infections and increase the recovery in the regions while the cost associated with the non-pharmaceutical (lockdown, quarantine, and distribution of mask, gloves, and other necessary arrangements) and pharmaceutical use in a particular time period. In view of that, we have formulated the characterizations of optimal control strategies. We have considered the first control $u_1(t)$ which represents the non-pharmaceutical intervention like social awareness in form of social distancing, cover all cuts, wear full cover shoes, gloves, use the shirts with long sleeves, masks, hygiene, sensitization process. The second control $u_2(t)$ represents the pharmaceutical intervention like use common effective drugs (azithromycin, HCQ, antiprotozoal with Doxycycline).

Our simulation considered 20 days and 40 days time period since we want to observe the quarantine effect. Numerical simulation showed that with our control strategies the percentage of new infection along with reported and unreported infection reduced dramatically. Also, the percentage of recovery increases exceptionally during the control period. However, the results very much dependent on the basic reproduction number of the region. If the basic reproduction number is greater than 1.5, then a minimum of 40 days control should be maintained. Otherwise, 15 days to 20 days control is sufficient for controlling the disease. Therefore, social awareness, using gloves and mask, sensitization is key for the control of COVID-19 infections.

We also studied the impact of quarantine and screening/testing factors over the control strategies and outcomes. Quarantine of migrant individuals, isolation of undiagnosed individuals, door to door screening, and testing also plays a critical role in optimal strategy making.

It is essential to have reported infected individuals under pharmaceutical control through hospitalization for the purpose of quick healing. Thus rapid screening and testing are beneficial for these control strategies and give a better outcome.

Real data on the cost of screening, testing, quarantine arrangement, as well as penalties on overdosing drugs will be helpful to provide the optimal cost-effectiveness analysis for this pandemic.

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