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Dynamics of SEIR model: A case study of COVID-19 in Italy

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A B S T R A C T

COVID-19 takes a gigantic form worldwide in a short time from December, 2019. For this reason, World Health Organization (WHO) declared COVID-19 as a pandemic outbreak. In the early days when this outbreak began, the coronavirus spread rapidly in the community due to a lack of knowledge about the virus and the unavailability of medical facilities. Therefore it becomes a significant challenge to control the influence of the disease outbreak. In this situation, mathematical models are an important tool to employ an effective strategy in order to fight against this pandemic. To study the disease dynamics and their influence among the people, we propose a deterministic mathematical model for the COVID-19 outbreak and validate the model with real data of Italy from 15th Feb 2020 to 14th July 2020. We establish the positivity and boundedness of solutions, local stability of equilibria to examine its epidemiological relevance. Sensitivity analysis has been performed to identify the highly influential parameters which have the most impact on basic reproduction number ($R_0$). We estimate the basic reproduction number ($R_0$) from available data in Italy and also study effective reproduction numbers based on reported data per day from 15th Feb 2020 to 14th July 2020 in Italy. Finally, the disease control policy has been summarized in the conclusion section.

1. Introduction

Several times throughout human history, pandemics and epidemics have ravaged humanity, often resulting in a massive change in the course of history and the end of civilizations. Nevertheless, for the current coronavirus pandemic, the globe is now facing a dangerous and destructive phenomenon which is crucially threatening the humanity [1,2]. First, it was identified in Wuhan city, Hubei Province of China, on December 31, 2019. The World Health Organization (WHO) declared the disease as a pandemic and was named SARS-CoV-2 virus (March 11, 2020) [2]. Scientifically it is proven that COVID-19 is an infectious disease that causes respiratory syndrome and is transmissible from human-to-human [2]. At this stage, more than 210 countries and territories have been reported to have coronavirus patients and increased the infections exponentially [2,3]. The coronavirus is a zoonotic disease, where the primary host was animals and transmitted to humans [4]. The patients face more critical illness, primarily who has other diseases like diabetes, heart disease, asthma, etc. [2].

Till April 20, 2020, according to WHO, COVID-19 infected more than 2.3 million people, and the total death crossed 0.16 million due to the infection [1,2]. Geometrically, the number of new reported cases is growing, and the dynamics of growth are satisfied several mathematical growth functions such that Malthusian, logistic and so on which predict the scenario of COVID-19 outbreak [3,5,6]. Due to the severity, as protection, highly infected counties and territories have announced lockdown, and their administrations, including WHO, are encouraging, advising, and even enforcing (some territories) people to stay at home to
protect their citizens. Experts are suggesting the social distancing to flatten the curve of new cases. As a result, right now, more than one-third of the global population is a lockdown. The WHO is also spreading awareness and advising people to stay at their own habitat without their emergency. Meanwhile WHO is providing instructions on protecting oneself from the virus and any kinds of information regarding the pandemic. The coronavirus pandemic has already started showing immense negative impact on world politics, socio-economics, education, and other important global aspects [7–9]. Moreover, the state of medical emergency is becoming more and more gruesome with every passing day. Therefore, it is an emergency to formulate a mathematical model that effectively describes the transmission of the disease to help policymakers to make important decisions based on the effective assumptions given by the model. Lack of early measures and ineffective decisions have already been attributed to the massive scale destruction that the pandemic is causing, so we cannot afford to be any more ignorant in this matter. In mathematical modeling, some recent studies provided different guidelines introducing basic reproduction number, Education and Socio-Economic Index and Lockdown strategies (see [10–14] and references therein).

In epidemiology, mathematical modeling is widely used to predict an epidemic’s results successfully. The most commonly used epidemic models are SIS, SIR, and SEIR etc. The Kermack–Mckendric’s SIR model is very well-established and used widely for various epidemics [10]. In many cases, there are no visible symptoms of infected individuals such as chickenpox, tuberculosis, etc., and in that case, an SEIR model is mostly used [11]. Therefore, the model with multiple compartments is a valuable tool to predict the nature of the recent most dangerous disease, COVID-19.

We are motivated by the work of Paul et al. in [15]. Our work is an extension of their work. In [15], Paul et al. considered an SEIR model where $S$ stands for susceptible population, $E$ stands for exposed population, $I$ stands for infected population and $R$ stands for recovered population. They studied the positivity and boundedness of solutions then proved the stability of disease-free and endemic equilibrium points. In their work, they considered susceptible peoples infected by only infected peoples. Moreover, they did not consider corona induced death rate in the $I$ class. In this paper, we extend their work by replacing exposed class by exposed & asymptomatic person in same class. Also, we assume susceptible populations are infected by both $E$ and $I$ classes. Moreover, we try to give a new orientation in the SEIR model by considering panic, tension, or anxiety of $S, E, I$ classes. This paper discusses the effect of panic, tension, or anxiety on $S, E, I$ classes. People from these three classes can die of surplus panic, tension, or anxiety. Also, here we consider the corona-induced death rate in the $I$ class.

The main findings in this study are outlined in the following lists:

1. In this paper, we formulate an SEIR model in which susceptible class ($S$) has a constant birth rate and $E$ class is a combination of exposed & asymptomatic classes. The effect of panic, tension, anxiety is included in $S, E, I$ compartments.
2. We analyze the stability of the equilibria of the model using the basic reproduction number to understand the severity.
3. Theoretical results are established using local and global model analysis.
4. During these periods of Quarantine, we have studied human behaviors like panic, anxiety, and tensions which are changing the death rate of individuals.
5. The model is verified considering first wave data of Italy (from 15th Feb 2020 to 14th July 2020) and also first wave data of Spain (from 24th Feb 2020 to 4th July 2020).
6. Numerical illustration ensures the theoretical results are relevant to control the spread of COVID-19.

The paper is organized as follows: Mathematical Model is elaborately discussed in Section 2. Positivity and boundedness of solution including auxiliary results are described in sub Section 2.1. Basic reproduction number and existence of different equilibrium points have been discussed in Section 2.2. Local stability analysis and bifurcation analysis are prescribed in Section 3. Section 4 is accomplished with the real data analysis in comparison with model solution, as a case study in Italy. Sensitivity analysis has been discussed in Section 5. Effects of different sensitive model parameters on infected class are shown in Section 5.1. Estimation of $R_0$ and effective reproduction number are found in Sections 6 and 7, respectively. Finally, Section 8 outlines the summary and discussion of the results.

2. Model formulation

We aim to develop a COVID-19 epidemic model, which is simple but relevant enough to produce effective results upon analysis. The spread of the infection starts with introducing a small group of infected individuals to a large population. The population ($N$) is then divided into four classes; the susceptible ($S$), the exposed & asymptomatic ($E$), the infected ($I$) and the recovered ($R$) at any time $t \geq 0$. An susceptible person may be affected with coronavirus after interacting with corona infected person. After getting infected, that infected person may not transmit disease at that time. He/she can transmit disease to a susceptible person after a few days (normally 2 to 14 days), i.e., when the patient is in the incubation period, he/she does not show any symptoms. These people can affect susceptible people before showing any symptom or even symptom may not appear among them. Therefore, these types of asymptomatic persons can spread disease in the community. Moreover, in the exposed stage, peoples are infected but not infectious. There is no particular time duration when exposed people may be infectious. But after some days, exposed persons can infect the community. For this reason, we take exposed & asymptomatic class in a single compartment for model formulation. Since these peoples move freely in the community, susceptibles may be infected by them [16]. Since as per advisory of WHO [2] the infected persons who show symptom will be isolated in the hospital, and hence they will infect only the medical persons. However, the exposed & asymptomatic class interacts with the common people and spreads disease. To include the above-defined facts, we consider the rate of infection in the form $\beta_1 ES + \beta_2 IS$. Now, in our considered SEIR model, we try to give a new orientation by considering panic, tension, or anxiety in susceptible, exposed & asymptomatic and infected classes. This paper discusses the effect
Table 1

| Notation | Interpretations | Notation | Interpretations |
|----------|-----------------|----------|-----------------|
| $\tau$   | Recruitment rate of $S$ class | $\alpha$ | Panic/tension/anxiety rate of $S$ class |
| $\mu$    | Natural death rate | $\gamma$ | Panic/tension/anxiety rate of $E$ class |
| $k$      | Infected rate of $E$ class | $\eta$  | Panic/tension/anxiety rate of $I$ class |
| $\mu_1$  | Death rate due to infection | $\beta_1$ | Transmission rate of infection from $E$ class |
| $\delta$ | Recovery rate of $I$ class | $\beta_2$ | Transmission rate of infection from $I$ class |

Fig. 1. Diagram of the proposed model.

of panic, tension, or anxiety on these three classes. Panic, tension, or anxiety are injurious to health. Tension or anxiety can increase insulin level, which may affect heart condition, diabetes, blood pressures [17,18]. At the same time, stress can wreak havoc on our immune system. Excessive stress can hamper immunity, and stress lasts for an extended time; it can put in danger a serious health issue, like depression or anxiety. People with panic anxiety are at high risk of infection, and the infected population mortality rate also increases [19,20]. For this reason, we assume some number of susceptibles, exposed & asymptomatic and infected, are reducing, i.e., moving to death for panic, tension, or anxiety. Fig. 1 shows the flow diagram of the proposed model and the corresponding model equations are given below:

$$\begin{align*}
\frac{dS}{dt} &= \tau - (\mu + \alpha)S - (\beta_1 E + \beta_2 I)S \\
\frac{dE}{dt} &= (\beta_1 E + \beta_2 I)S - (k + \mu + \gamma)E \\
\frac{dI}{dt} &= kE - (\mu + \mu_1 + \delta + \eta)I \\
\frac{dR}{dt} &= \delta I - \mu R 
\end{align*}$$

with the initial conditions $S(0) > 0$, $E(0) \geq 0$, $I(0) > 0$, $R(0) \geq 0$, where the interpretation of parameters is presented in Table 1.

2.1. Positivity and boundedness of solutions

An essential feature of an epidemiological model is the positivity and boundedness of the solutions. Therefore, it is important to prove that all the variables are non-negative for all time $t \geq 0$ which implies that any solution with positive initial values will remain positive for all time $t \geq 0$. Biologically, positivity implies the population will survive a long time. Therefore to check the validity of the proposed model biologically, we have to prove the positivity of the proposed model.

Theorem 1. The closed region $\Omega = \{(S, E, I, R) \in \mathbb{R}^4_+ : 0 < N \leq \frac{T}{\mu}\}$ is positively invariant set for the system (2.1).

Proof. Let $N(t) = S(t) + E(t) + I(t) + R(t)$ then

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt}$$

So, from model (2.1):

$$\frac{dN}{dt} = \tau - \mu N - (\mu_1 + \eta)I - \alpha S - \gamma E$$

which yields

$$\frac{dN}{dt} \leq \tau - \mu N$$

It implies that $\frac{dN}{dt} < 0$ whenever $N(t) > \frac{T}{\mu}$. Thus, the right-hand side of Eq. (2.2) implies that $\frac{dN}{dt}$ is bounded by $-\frac{T}{\mu}$.

Integrating the inequality (2.3), using initial condition, we obtain

$$N(t) \leq N(0)e^{-\mu t} + \frac{T}{\mu} \left[1 - e^{-\mu t}\right].$$

Letting $t$ tends to infinity, asymptotically we get $N(t) \leq \frac{T}{\mu}$. We can also prove this result using comparison lemma [21]. □
Therefore, \( \Omega \) is positively invariant set of the model (2.1) so that no solution path leaves through any boundary of \( \Omega \). This proves that the formulated model is relevant both mathematically and epidemiologically.

The model is considered in the biologically feasible region i.e. the proposed model is defined in positively bounded region. We need to show that any phase trajectory that started anywhere in the non-negative region \( \mathbb{R}^4_+ \) of the phase space eventually enters the feasible region \( \Omega \) and remains in \( \Omega \) thereafter. It can be done by proving that \( \Omega \) is a positively invariant set and global attractor of the system.

2.2. Basic reproduction number, DFE and EE

The basic reproduction number is an important threshold quantity for analyzing an infectious disease. It determines whether the disease will die out or persist in the population as time increases. It is defined as the number of secondary infections produced by one primary infection in a population where everyone is susceptible and is denoted by \( R_0 \). Suppose \( R_0 > 1 \), and one primary infection can produce more than one secondary infection. This implies that the disease-free equilibrium (DFE) is unstable. As a result, an epidemic breaks out. If \( R_0 < 1 \), the situation is under control. In this case, the disease-free equilibrium (DFE) will be locally asymptotically stable, and the disease cannot persist in the population. So, when a pandemic breaks out, an effective strategy should be developed so that the reproduction number reduces to less than one as soon as possible [13,16,22,23].

Since the considered model has DFE \( (E_0) = \left( \frac{\tau}{\mu + \alpha}, 0,0,0 \right) \) (see Appendix A), hence \( R_0 \) can be found analytically. Using next generation matrix method [22], the reproduction number for the COVID-19 model given by (2.1) can be calculated from the relation \( R_0 = \rho(FV^{-1}) \), that is the spectral radius of \( FV^{-1} \) [22] where

\[
F = \begin{bmatrix}
\frac{\beta_1 \tau}{\mu + \alpha} & \frac{\beta_2 \tau}{\mu + \alpha} & 0 & 0 \\
0 & 0 & 0 & 0
\end{bmatrix}
\]

and

\[
V = \begin{bmatrix}
k + \mu + \gamma & 0 & -k & \mu + \mu_1 + \delta + \eta \\
-\frac{k}{\mu} & \frac{\mu}{\mu_1} & \frac{\mu}{\mu_1} & \frac{\mu}{\mu_1} + \frac{\mu}{\mu_1}
\end{bmatrix}.
\]

Therefore, the basic reproduction number is the spectral radius of \( FV^{-1} \) which is given by

\[
R_0 = \rho(FV^{-1}) = \frac{\tau \beta_1 (\mu + \delta + \mu_1 + \eta) + \tau \beta_2 k}{(\mu + \alpha)(k + \mu + \gamma)(\mu + \delta + \mu_1 + \eta)}. \tag{2.4}
\]

For disease free equilibrium point, we have \( E = 0, I = 0 \). But for endemic equilibrium point both \( E \neq 0, I \neq 0 \).

To find the endemic equilibrium state of the model we set

\[
\frac{dS}{dt} = 0, \frac{dE}{dt} = 0, \frac{dI}{dt} = 0, \frac{dR}{dt} = 0.
\]

Solving the above system, we get the endemic equilibrium (EE) state

\[
E^* = (S_1, E_1, I_1, R_1)
\]

where

\[
S_1 = \frac{\tau (\mu + \delta + \mu_1 + \eta)}{k \beta_1 E_1 + (\mu + \alpha + \beta_1 E_1)(\mu + \delta + \mu_1 + \eta)}, I_1 = \frac{k E_1}{\mu + \delta + \mu_1}
\]

\[
E_1 = \frac{(\mu + \delta + \mu_1 + \eta)(\mu + \alpha)(R_0 - 1)}{(\beta_1 \mu + \delta + \mu_1 + \eta + k \beta_2)}, R_1 = \frac{\delta k E_1}{\mu (\mu + \delta + \mu_1 + \eta)}.
\]

It is obvious from the expressions of the \( E_1 \) the endemic equilibrium point EE will exists only when \( R_0 > 1 \). For further analysis, the Jacobian matrix of the system (2.1) at any equilibrium point \((S, E, I, R)\) is given by

\[
J = \begin{bmatrix}
-\mu - \beta_1 E - \beta_2 I - \alpha & -\beta_1 S & -\beta_2 S & 0 \\
\beta_1 E + \beta_1 I & \beta_1 S - (k + \mu + \gamma) & \beta_2 S & 0 \\
0 & k & (\mu + \delta + \mu_1 + \eta) & 0 \\
0 & 0 & -\mu & \delta
\end{bmatrix}.
\]

3. Stability and bifurcation of the equilibrium states

In this section we shall establish the stability and bifurcation condition if the equilibrium point exists. In Theorem 2, we shall establish nature of the disease free equilibrium point \( E_0 \) and in Theorem 4 nature of endemic equilibrium point \( E^* \).

3.1. Stability of disease-free equilibrium state \((E_0)\)

In this section, first, we prove the local stability of disease-free equilibrium point \((E_0)\) for \( R_0 < 1 \). Biologically, the disease will die out from the population when the basic reproduction number is less than unity.
Theorem 2. The disease free equilibrium point \((E_0)\) is locally asymptotically stable if \(R_0 < 1\) and unstable if \(R_0 > 1\).

Proof. The Jacobian of the system at the disease free equilibrium point is

\[
J(E_0) = \begin{pmatrix}
-\mu - \alpha & -\beta_0 \frac{\tau}{\mu + \eta} & -\beta_0 \frac{\tau}{\mu + \eta} & 0 \\
0 & \frac{\beta_0 \tau}{\mu + \alpha} - (k + \mu + \gamma) & \frac{\beta_0 \tau}{\mu + \alpha} & 0 \\
0 & k & -(\mu + \delta + \mu_1 + \eta) & 0 \\
0 & 0 & \delta & -\mu
\end{pmatrix}
\]

The characteristic roots of the Jacobian matrix at \(J(E_0)\) are \(-\mu - \alpha, -\mu,\) and other two roots are roots of the following equation

\[
\lambda^2 + a_1 \lambda + a_2(1 - R_0) = 0
\]

where \(a_1 = (\mu + \delta + \mu_1 + \eta) + (\mu + k + \gamma)\left(\frac{\tau \beta_0 k}{k \mu + \alpha + k + \gamma + \mu + \mu_1 + \eta}\right) + 1 - R_0\) and \(a_2 = (\mu + \delta + \mu_1 + \eta)(k + \mu + \gamma)\). If \(R_0 < 1\) then \(a_1 > 0, a_2 > 0\), therefore no positive root exists in this case. Hence all the roots will be negative if \(R_0 < 1\). If \(R_0 > 1\), then \(a_2 < 0\) and hence one root must be positive for \(R_0 > 1\). Therefore, the disease-free equilibrium state \((E_0)\) is locally asymptotically stable if \(R_0 < 1\) and unstable if \(R_0 > 1\). □

It is clear from the above analysis when \(R_0 = 1\) then above analysis fails. The term \(R_0 = 1\) is equivalent to \(\beta_2 = \beta_2^{(TC)} = \frac{(\mu + \alpha)(k + \mu + \gamma) - \beta_1}{k \mu + \alpha}\), in the next theorem we shall show model system \((2.1)\) experiences Transcritical bifurcation at disease free equilibrium point \((E_0)\) when model parameter \(\beta_2\) passes through its critical value \(\beta_2 = \beta_2^{(TC)}\).

Theorem 3. Model \((2.1)\) undergoes through Transcritical bifurcation at disease free equilibrium point \((E_0)\) when model parameter \(\beta_2\) passes through its critical value \(\beta_2 = \beta_2^{(TC)}\).

Proof. At \(\beta_2 = \beta_2^{(TC)}\), one of the eigenvalue vanishes and classical eigenmethod analysis fails. Then we have to use the Sotomayer theorem [24–26] to investigate the nature of the disease free equilibrium point. Let \(V\) and \(W\) be the eigenvector corresponding to the zero eigenvalue of \(J(E_0)\) and \([J(E_0)]^{-1}\) respectively then

\[
V = \begin{pmatrix}
\frac{-\delta + \mu + \mu_1 + \eta}{\mu + \delta + \mu_1 + \eta} \\
\frac{k}{\mu + \delta + \mu_1 + \eta} \\
\frac{1}{\delta} \\
\frac{\mu}{\delta}
\end{pmatrix}, \quad W = \begin{pmatrix}
0 \\
2(\mu + \delta + \mu_1 + \eta) \\
\frac{k(\mu + \alpha)}{\mu + \alpha} \\
0
\end{pmatrix}
\]

Let \(F = \begin{pmatrix}
\tau - (\mu + \alpha)S - (\beta_1 E + \beta_2 I)S \\
(\beta_1 E + \beta_2 I)S - (k + \mu + \gamma)E \\
kE - (\mu + \delta + \mu_1 + \eta)I \\
\delta I - \mu R
\end{pmatrix}\) then

\[
W^T F_{\beta_2}^{(1)} \big|_{E_0, \beta_2 = \beta_2^{(TC)}} = 0, \\
W^T D F_{\beta_2}^{(1)} \big|_{E_0, \beta_2 = \beta_2^{(TC)}} V = -\frac{\tau(\mu + \delta + \mu_1 + \eta)}{k(\mu + \alpha)} \neq 0, \\
W^T D^2 F_{\beta_2}^{(1)} \big|_{E_0, \beta_2 = \beta_2^{(TC)}} (V, V) = -\frac{2(\mu + \delta + \mu_1 + \eta)^2(\gamma + k + \mu)\beta_1}{k^2(\mu + \alpha)} \neq 0.
\]

Hence the system experiences Transcritical bifurcation when the rate of infection by the \(I\) class \(\beta_2\) crosses the critical value \(\beta_2 = \beta_2^{(TC)}\). There is a critical value of the rate of infection by the \(I\) class below which the disease is easy to control but above of which the society will experience endemic disease spreading. □

It is clear from Fig. 2 that for \(R_0 < 1\), the system \((2.1)\) has only stable disease-free equilibrium point and for \(R_0 > 1\) a stable endemic equilibrium point arises, the disease free equilibrium (DFE) becomes unstable i.e. here exchange of stability of the disease free equilibrium points occurs with the endemic equilibrium point at \(R_0 = 1\). Therefore if model parameter \(\beta_2\) passes through its critical value \(\beta_2^{(TC)}\), then disease free equilibrium changes its stability from stable to unstable i.e. Transcritical bifurcation occurs at disease free equilibrium points occurs for \(R_0 = 1\).

3.2. Stability of endemic equilibrium state

Now we prove local stability of endemic equilibrium point if \(R_0 > 1\). Biologically, the disease will persist in the population if the basic reproduction number is greater than unity.

Theorem 4. The endemic equilibrium state \(E^*(S_1, E_1, I_1, R_1)\) is stable if \(R_0 > 1\).
Fig. 2. Transcritical bifurcation analysis using the dynamics of $R_0$: The blue line corresponds the stable branch and the red line corresponds to unstable branch.

**Proof.** Recall the Jacobian of the system (2.1) at any equilibrium point $(S, E, I, R)$ and we have

$$J = \begin{bmatrix}
-\mu - \beta_1E - \beta_2I - \alpha & -\beta_1S & -\beta_2S & 0 \\
\beta_1E + \beta_2I & \beta_1S - (k + \mu + \gamma) & \beta_2S & 0 \\
0 & k & -(\mu + \delta + \mu_1 + \eta) & 0 \\
0 & 0 & \delta & -\mu
\end{bmatrix}.$$  

At the endemic equilibrium point $E^*$, calculating the Jacobian matrix $J(E^*)$ and then solving $det(J - \lambda I) = 0$, we get one roots of the characteristic equations corresponding to $J(E^*)$ is $\lambda_1 = -\mu < 0$ and other three satisfies the following quadratic equation

$$\lambda^3 + C_1\lambda^2 + C_2\lambda + C_3 = 0 \quad (3.1)$$

where

$$C_1 = -(c_3 + b_2 + a_1), C_2 = -(-a_1b_2 - a_1c_3 + a_2b_1 - b_2c_3 + c_2k), C_3 = -a_1b_2c_3 + kc_2a_1 + a_2b_1c_3 - a_2c_1k$$

and $a_1 = -\mu - \beta_1E_1 - \beta_2I_1 - \alpha, b_1 = -\beta_1S_1, c_1 = -\beta_2S_1, a_2 = \beta_1E_1 + \beta_2I_1, b_2 = \beta_1S_1 - (k + \mu + \gamma), c_2 = \beta_2S_1, c_3 = -(\mu + \delta + \mu_1 + \eta)$.  

It can be easily shown that for $R_0 > 1$ coefficients of (3.1) will satisfy the Routh–Hurwitz criterion [24] and hence all the roots of Eq. (3.1) will have negative real part. Thus for $R_0 > 1$ endemic equilibrium point will be locally asymptotically stable.  

In the following section, we will estimate the parametric values to illustrate the numerical results for further applications.

4. **Parameter estimation, model validation**

The nonlinear system in (2.1) can be fitted to the real infected data of Covid-19 using the numerical methods and then we can give proper predictions about the disease spreading from the model. To numerically solve the data we estimate the parameters using the methodology as described in [24,27].

4.1. **Case study: Italy**

The best way to fit the proposed model with real reported data is least squares method [24]. The principle of the least square method is to fit the model with real infected data with minimum sum of square error. The fitness of the model is good if the sum of squares of vertical distances among real data and model predicted data is as smaller as possible. To fit the model, we consider the formula of sum of the squares error as

$$f(\phi, n) = \sum_{j=1}^{n} (Y_j - I(t_j))^2,$$

where $\phi$ represents set of all model parameters, $Y_j$ represents cumulative number of the real reported data for $j$th observation, $I(t_j)$ represents model predicted cumulative data for $j$th observation and $n$ represents total number of available data. The number of cumulative model predicted infected data satisfies the formula

$$\frac{dI(t_j)}{dt} = kE.$$
Table 2
Parameters estimation for Italy.

| Parameter | Value | References |
|-----------|-------|------------|
| $\tau$   | 0.05812 | [28]       |
| $\beta_1$| $3.565207228818550 \times 10^{-09}$ | Estimated |
| $\beta_2$| $1.042634849127262 \times 10^{-07}$ | Estimated |
| $\mu$    | 0.01  | [28]       |
| $k$      | $1/14$ | Assumed   |
| $\gamma$ | $8.658193552394484 \times 10^{-04}$ | Estimated |
| $\mu_1$  | 0.12  | [1]        |
| $\delta$ | $0.515825936950256$ | Estimated |
| $\alpha$ | $0.031441013505254$ | Estimated |
| $\eta$   | $0.808967250951627$ | Estimated |

Fig. 3. (a) Fitting model to cumulative cases in Italy (b) Residuals of the fit (c) Bar diagram for 151 days from 15th February to 14th July.

Analytically minimization of $f(\phi, n)$ is very difficult, here we use matlab minimization software fmincon package to estimate the important model parameters using the Italy infection cases from 15th February to 14th July 2020, which are given in Table 2. To execute the Matlab package, we have considered the initial population size as

$S(0) = 60461826, E(0) = 150, I(0) = 3, \text{ and } R(0) = 0$

where $E(0)$ is estimated and rest of them are collected from [1]. Another way to verify the fitness of the model can be justified by finding residuals. Therefore here the fitness of the model with the real data is verified computing the residuals. The residuals are defined as

$residuals = \{Y_j - I(t_j)\ j = 1, 2, 3, ..., n\}$

where $Y_j$ is the $j$th day cumulative infection data and $I(t_j)$ model predicted cumulative infected data of same day. If the residuals are randomly distributed them we can say that the fitness is reasonably good [24].

The estimated model parameters are given in Table 3. To validate the model, we consider the actual case of COVID-19 infection of Italy from 15th February to 14th July 2020, i.e., the real cases for 151 days. The model is fitted to the cumulative number of infected cases, presented in Fig. 3(a). The fit residuals are presented in Fig. 3(b), which shows that the residuals are small and random. In Fig. 3(c), we plot a bar diagram of the infected population for 151 days. The randomness of the residuals shows that the fitness is best.

We have also verified the proposed model for the first wave (from 24th February 2020 to 4th July 2020) in Spain (see Appendix B). From the model fitting, it is obvious that our model is well fitted i.e. the proposition of the model is well defined as we observe that the considered model is verified by real reported data of first wave (from 24th February 2020 to 4th July 2020) in Spain. Also, we have seen that residuals are randomly distributed. From the residuals, we can conclude that the fit of the proposed model is good.

In the next section, first we shall perform sensitivity analysis for finding most influential model parameters to control the corona outbreak considering the estimated values of the parameters as given in Table 2. Here, we also show the effect of different model parameters on the model dynamics. Further we shall estimate the value of basic reproduction number ($R_0$) from actual data in Section 6. To estimate basic reproduction number from actual data, we shall use the methodology as described in [29]. Finally, we shall find per day basis reproduction number i.e. effective reproduction number from the real infected data and considering the same estimated model parameters.

5. Sensitivity analysis

Sensitivity analysis reveals the influence of the model parameters, which have the most significant impact on the basic reproduction number of the COVID-19 model system. By such analysis, epidemiologists can predict the critical parameters playing
a crucial role in disease-spread dynamics. To prevent or control the influence of the disease, we need to determine the values of sensitivity indices by which we have a clue about the model parameters which should be maintained or checked.

In the present scenario, the Novel coronavirus spreads worldwide gigantically at a high rate of infection, and this dangerous virus highly threatens the human population. In order to dominate the spreading of the infection, we need to identify which model parameters play a vital role in disease spreading. In order to identify such model parameters, we need to estimate the variation of the basic reproduction number $R_0$ concerning different model parameters; in other words, we need to determine normalized forward sensitivity index of the basic reproduction number $R_0$ concerning different model parameters. Using sensitivity index, we can calculate the changing rate of variables when the parameter changes. Here our objective is to estimate significant model parameters controlling basic reproduction number $R_0$. For studying sensitivity analysis here we use normalized forward sensitivity index [30] of basic reproduction number $R_0$ with respect to model parameter $\phi$ which is denoted by $I_{R_0} = \frac{\partial R_0}{\partial \phi} \cdot \frac{\phi}{R_0}$.

The parameter with higher sensitive index is the more sensitive parameter on basic reproduction number $R_0$. The positive sign of sensitive index of the model parameter implies basic reproduction number $R_0$ increases with parameter increases and vice-versa. We put sensitive index on $R_0$ with respect to each parameter in Table 3. In our findings, most significant model parameters are recruitment rate of susceptible population ($\mu$), disease transmission rate due to infected population ($\beta_1$), disease transmission rate due to infected population ($\beta_2$), disease induced death rate ($\mu_1$), panic/tension/anxiety of susceptible class ($\alpha$), disease induced death rate ($\mu$) and panic/tension/anxiety of infected class ($\eta$). Sensitivity index of each parameter is given in the Table 3.

### 5.1. Effect of the different sensitive parameters on infected population

For realizing the sensitive effect of the different model parameters on the proposed model numerically, we plot time series of infected population $(I(t))$ at any time $t$ for different values of the model parameter as given in Table-2 with initial condition $S(0) = 60461826$, $E(t) = 150$, $I(t) = 3$, $R(t) = 0$. In the following we will discuss the effect of the different sensitive model parameters on the infected population $I(t)$.

#### 5.1.1. Effect of disease transmission rate of both exposed & asymptomatic and infected population ($\beta_1$ & $\beta_2$) on the infected population

From Fig. 4(a) it is clear that the number of infected population $(I(t))$ increases with the rate of disease transmission rate of exposed & asymptomatic class ($\beta_1$) increases and vice-versa. On the other hand from Fig. 4(b) it is clear that the number of infected population $(I(t))$ increases when rate of disease transmission of infected class ($\beta_2$) increases and vice-versa. Therefore we observe that infected population increases with increase of disease transmission rate $\beta_1$ and $\beta_2$ which means infected population is highly affected by increasing the rate of disease transmission rate $\beta_1$ and $\beta_2$.

#### 5.1.2. Effect of natural death rate and disease induced death rate ($\mu$ & $\mu_1$) on disease spreading

Figs. 5(a) and 5(b) show that the disease is spreading decreases when the natural death rate $\mu$ and disease-induced death rate $\mu_1$ increases. From the discussion, it is clear that the number of infected decreases if the natural death rate $\mu$ and disease-induced death rate $\mu_1$ increases. Therefore, we have seen that the density of the infected population is highly affected by both parameters $\mu$ & $\mu_1$.

### 6. Estimation of $R_0$ from actual data

In this part of the manuscript, we shall find the estimated value of $R_0$ from the reported data up to which time series of the infected data stay exponential. To estimate $R_0$ from the initial growth phase of the disease, we have used the methodology used in [29]. We assume at the beginning of disease, cumulative case $(Q(t))$ varies as $exp(At)$ that means $Q(t) \propto exp(At)$. Similarly number of exposed & asymptomatic, infected population varies as $exp(At)$. Therefore

$$
\begin{align*}
E & \sim E_0 \exp(At) \\
I & \sim I_0 \exp(At)
\end{align*}
$$

(6.1)

where $E_0$ and $I_0$ are constants.

---

**Table 3**

| Parameter | Sensitivity index |
|-----------|------------------|
| $\tau$   | 1.000000000     |
| $\beta_1$| 0.4105292448    |
| $\beta_2$| 0.5894707555    |
| $\mu$    | -0.3668737257   |
| $k$      | -0.2784932788   |
| $\gamma$ | -0.1052100085   |
| $\mu_1$  | -0.4862305599   |
| $\delta$ | -0.2090086119   |
| $\alpha$ | -0.7586931608   |
| $\eta$   | -0.3277871661   |
The constant number of susceptible population is given by $S_0 = \frac{r}{\mu}$. Substituting (6.1) in Eq. (2.1), we get

$$\left( A + k + \mu + \gamma - \frac{\beta_1 r}{\mu} \right) E_0 = \frac{\beta_1 r}{\mu} I_0$$

(6.2)

Putting the value of $\beta_2$ from (6.2) in Eq. (2.4), we obtain the expression of basic reproduction number $R_0$ as in the form

$$R_0 = \frac{\tau \beta_1}{(\mu + \alpha)(k + \mu + \gamma)} + \frac{k \mu \left( A + k + \mu + \gamma - \frac{\beta_1 r}{\mu} \right) (A + \mu + \mu_1 + \delta + \eta)}{(\mu + \alpha)(k + \mu + \gamma)(\mu + \mu_1 + \delta + \eta)}$$

(6.3)

For estimating $R_0$, first we have to estimate force of infection ($A$). Number of new cases per day ($q(t)$) varies with number of cumulative cases per day ($Q(t)$) as $q(t) \sim A Q(t)$.

Plotting daily new cases with daily cumulative cases, we estimate the force of infection ($A$). From the diagram (Fig. 6) we get the threshold value of the cumulative case for which a new number of cases shows exponential growth. By the least square method, the linear regression curve is fitted [31,32]. The force of infection ($A$) is the slope of the regression line. Based on slope of regression line, we have $A = 0.1232352602014$ day$^{-1}$. Using the expression (6.3) with the estimated value of $A$ and other estimated parameters enlisted in Table 2, we get estimated value of basic reproduction number $R_0 = 1.4669387723$ with lower value 1.3581601558 and upper value 1.5757511687.

Thus we get a range of $R_0$ from the initial phase of the corona infection. From the range of $R_0$, we see that the values of $R_0$ lies always greater than unity. But to eradicate corona virus from the community, we should keep its value less than unity. Therefore, it is clear from the range of $R_0$, corona virus emerges among the population. Moreover corona virus persists in the community since value of $R_0$ lies greater than unity always.
7. Effective reproduction number $R(t)$

Basic reproduction number is an important factor in spreading disease dynamics. Basic reproduction number is the average number of secondary infections produced by an infected person as an infected host during its lifespan. At the beginning stage, the disease spreads quickly among the population but after attending peak position, it starts to decrease. Therefore reproduction is not always constant. Now we aim to study time-varying reproduction numbers, which means reproduction number per day basis. This type of reproduction number is known as adequate reproduction number $R(t)$ [33–35]. Depending on effective reproduction numbers, researchers can give information about the disease and provide suitable preventive measures to control the disease. We use the formula

$$R(t) = \lim_{\lambda \to 0} \frac{c(t)}{\int_{0}^{\infty} c(t-\lambda)h(\lambda)\,d\lambda}$$

(7.1)

for estimating effective reproduction number where $c(t)$ denotes new cases at $t$th day and $h(\lambda)$ denotes generation interval distribution. Let exposed & asymptomatic, infected class leave at the rate $b_1 = k + \mu + \gamma$, $b_2 = \mu + \mu_1 + \delta + \eta$ respectively. Let $b_1 e^{-b_1 t}$, $b_2 e^{-b_2 t}$ be the combination of generation interval distribution, then formula is given by

$$h(t) = \sum_{i=1}^{2} \frac{b_1 b_2 e^{b_j t}}{\prod_{j=1, j\neq i}^{2} (b_j - b_i)}$$

(7.2)

with mean $T = \frac{1}{b_1} + \frac{1}{b_2}$. The above formula is valid when $A > \min \{-b_1, -b_2\}$. Using new cases and Eq. (7.1), effective reproduction number can be estimated using formula (7.2). The value of effective reproduction number is presented by Fig. 7. From the figure, value of $R(t)$ oscillates around unity. $R(t)$ is dropped from 5.354 to 0.4934. Thus we have obtained the basic reproduction number for per day. At the initial stage, the reproduction number was very high and with the increase of time, the values of reproduction number per day basis decrease. After 80 days the value of reproduction number lies around unity. To control the spread of corona virus, we have to keep its value less than unity.

8. Conclusion

In this paper, we have proposed a $SEIR$ epidemic model for pandemic COVID-19 in Italy where $S$, $E$, $I$, $R$ represent susceptible population, exposed & asymptomatic population, infected and recovered population respectively. First, we study the proposed model’s basic properties, i.e., positivity and boundedness of the model. Then we compute the basic reproduction number $R_0$ of the considered model. From our theoretical analysis, it is clear that there are two types of equilibrium points of the model: disease-free equilibrium point and endemic equilibrium point. We prove that the disease-free equilibrium point is stable if basic reproduction number is less than unity which means the disease is eradicated from the population. On the other hand, for basic reproduction numbers greater than unity, the endemic equilibrium point is stable, which implies disease persists in this case. We observe that the model system has a Transcritical bifurcation at disease-free equilibrium point for the critical value of the bifurcation parameter $\beta_2$, disease transmission rate of the infected class.

Our study considers the data from 15th February 2020 to 14th July 2020 in Italy. At the early stage, the disease spread rapidly in a short period due to the inattention of the people about the infection. In Italy, lockdown is started from 9th March 2020 and is continued up to 18th May 2020. But before 9th March, 2020 many exposed & asymptomatic and infected peoples moved all over the country. At the same time, many infected people came into Italy from outside of the country. For this reason, before 9th March 2020, disease spread rapidly among the people. Maintaining lockdown, home quarantine, hand wash, musk wearing, the influence of the disease is started to decrease day by day.
To check the validity of the proposed model, we perform data fitting of the model from the reported data from 15th February to 14th July 2020 in Italy. We observe that our proposed model is well fitted for the reported data from data fitting. We have done sensitivity analysis to find out the most influential model parameter. For sensitivity analysis, we have used the normalized forward sensitivity index method. By sensitivity analysis we observe that most sensitive model parameters are disease transmission rate for both exposed & asymptomatic and also infected compartment namely $\beta_1$ and $\beta_2$ respectively, panic/tension/ anxiety of the susceptible and infected class namely $\alpha$ and $\eta$ respectively, natural death rate ($\mu$), disease-induced death rate ($\mu_1$). Our analysis shows that the number of infected populations increases when $\beta_1$ and $\beta_2$ increase. On the other hand, the infected population decreases when $\alpha$ and $\eta$ increase. Thus, we observe that the spread of the infection increases rapidly, and after taking proper preventive measures, it decreases gradually. Then we estimate the basic reproduction number $R_0$ from actual data in Italy. From the estimation of basic reproduction number, we have seen that the value of the initial reproduction number is 0.1232352602014, and the value of the basic reproduction number lies between 1.3581601558 and 1.5757511687. Finally, we find out the adequate reproduction number of the proposed model; the value of effective reproduction number lies near unity. The value of the adequate reproduction number is dropped from 5.354 to 0.4934. Based on our theoretical and numerical analysis, we can conclude that mathematical modeling is an efficient method to estimate the situation of global pandemic COVID-19 if the parameters can be appropriately estimated.

CRediT authorship contribution statement

Md. Kamrujjaman: Model formulation, Computation. Pritam Saha: Computation, Numerical simulation. Md. Shahidul Islam: Supervision, Review and editing. Uttam Ghosh: Model formulation, Computation, Numerical simulation.

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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Appendix A. Proof of disease-free equilibrium point ($E_0$)

To find disease-free equilibrium point ($E_0$), we have $E = 0, I = 0$. Then from first equation of model (2.1), we have $S = \frac{r}{\mu + \alpha}$ and from fourth equation, we have $R = 0$. Therefore, disease-free equilibrium point ($E_0$) is given by $\left( \frac{r}{\mu + \alpha}, 0, 0, 0 \right)$. 

Fig. 7. Effective reproduction number.
### Table 4
Parameters estimation for Spain.

| Parameter | Value | References |
|-----------|-------|------------|
| $\tau$    | 0.00814 | [28] |
| $\beta_1$ | $1.1721405503047 \times 10^{-9}$ | Estimated |
| $\beta_2$ | $1.49478835847718 \times 10^{-7}$ | Estimated |
| $\mu$     | 0.0093  | [28] |
| $k$       | $1/14$  | Assumed   |
| $\gamma$  | $0.0063966888479989$ | Estimated |
| $\mu_1$   | 0.009   | [1]       |
| $\delta$  | $0.357592168378645$ | Estimated |
| $\alpha$  | $0.038717882508566$ | Estimated |
| $\eta$    | $0.484591866531165$ | Estimated |

### Appendix B. Validation of the proposed model for Spain

In Section 4, we have already shown that the model is well fitted for the first wave (from 15th Feb 2020 to 14th July 2020) in Italy. We will show that our proposed model is also well fitted for the first wave (from 24th Feb 2020 to 4th July 2020) in Spain. We have considered initial values

$$ S(0) = 46784213, \ E(0) = 350, \ I(0) = 3, \text{ and } R(0) = 0. $$

The estimated model parameters are given in Table 4. To validate the model, we consider the actual case of COVID-19 infection of Spain from 24th February to 4th July 2020, i.e., the real cases for 132 days. The model is fitted to the cumulative number of infected cases, presented in Fig. 8(a), and the residuals of the fit are presented in Fig. 8(b), which shows that the residuals are small and random. In Fig. 8(c), we plot a bar diagram of the infected population for 132 days. The randomness of the residuals shows that the fitness is best. Therefore proposition of our model is well defined.

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