Mathematical model of transmission dynamics with mitigation and health measures for SARS-CoV-2 infection in European countries

Shweta Sankhwar

Babasaheb Bhimrao Ambedkar University, Lucknow, India

Narender Kumar

Gargi College, University of Delhi, Delhi, India

Ravins Dohare (✉ ravinsdohare@gmail.com)

Jamia Millia Islamia, New Delhi, India

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Mathematical model of transmission dynamics with mitigation and health measures for SARS-CoV-2 infection in European countries

Shweta Sankhwar · Narender Kumar ·
Ravins Dohare

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Abstract The pandemic of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) continue to pose a serious threat to global health resulting in disease COVID-19. No specific drug or vaccine is available against this infection. Therefore, the prevention is only way to reduce the spread of infection. The pandemic needs an enhanced mathematical model, therefore, we propose a SEIAJR compartmental mathematical model to estimate the basic reproduction number (R_0) and the transmission dynamics of four European countries (Germany, United Kingdom, Switzerland and Spain). The proposed mathematical model incorporates mitigation and healthcare measures as recommended by ECDC (European Centre for Disease Prevention and Control). The simulation of proposed model is done in two phases. First-phase simulation estimates basic reproduction number and mitigation rate according to active infected cases in all four European countries. R_0 estimate 2.82 - 3.3 for considered European countries. Second-phase simulation predicts the dynamics of infection on the estimated R_0 with varying mitigation rate and constant healthcare rate. This study predicts that no more mitigation is required to invade the infection. The current mitigation and healthcare measures are enough to stop the propagation of infection, however, infection would last by end of July 2020. The developed mathematical model would also be applicable

Shweta Sankhwar
Department of Information Technology, Babahaseb Bhimrao Ambedkar University, Lucknow, India
E-mail: shweta.sank@gmail.com

Narender Kumar
Department of Mathematics, Gargi College, Sirifort, New Delhi, India
E-mail: nkumariitd@gmail.com

Ravins Dohare (Corresponding Author)
Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi, India
E-mail: ravinsdohare@gmail.com

to portray the infection transmission dynamics for other geographical regions with varying parameters.

Keywords SARS-CoV-2 · mathematical model · mitigation rate · basic reproduction number

1 Introduction

In early December 2019, a novel coronavirus emerged as an outbreak in the city of Wuhan, Hubei Province, China and rapidly spread to other parts of China. Novel coronavirus causing disease COVID-19 and has progressively expanded to various parts of China and has stretched Internationally including South Korea, Cambodia, Philippines, Russia, United Arab Emirates, Thailand, Vietnam, Malaysia, Singapore, Nepal, Australia, Canada, United States of America and European countries [23]. So far, the novel virus has infected more than 1,843,123 people and died 113,479 of them on 13 April 2020 (source: <https://www.worldometers.info/coronavirus>). Despite recent research efforts in pandemic novel coronavirus there is still no vaccine for coronavirus for use in humans. The world is completely unprepared in order to cope with swiftly and properly to this pandemic. The entire world is suffering from this SARS-CoV-2 infection, and WHO declared pandemic on 11 March 2020. European countries are highly widespread after China [4]. As per the 2nd March 2020, ECDC (European Centre for Disease Prevention and Control) Risk Assessment Report [4] suggested for community mitigation measures for prevention and control such as social distancing, travel-related and screenings of travellers, subsequently, 6th and 7th ECDC Risk Assessment Reports [3], [1] suggested some mitigation measures including social distancing, closing of schools and colleges, social gathering/meeting point etc. Due to the unavailability of vaccine and its control, the mitigation plays important role to stop the infection. Thus, mathematical modelling might be an attempt to understand the infection propagation and it also enables us to know the basic reproduction number (it is an average number of infections one case can generate over the course of the infectious period to uninfected population.), duration of European outbreak. It is observed that many epidemiological (pandemic) scenarios used mathematical modelling with different approaches on different scenarios to estimate basic reproduction number, sensitive parameters and weight of control strategies to stop spreading of infection [17], [18], [19], [8]. The exhaustive literature review throws light that mathematical formulation is widely employed for vector-borne and direct human-to-human contact based viral infection [24], [21], [14], [5], and several researchers also incorporated environmental factors for their studies [22], [13]. In a study, a mathematical model is based on previously reported cases at Wuhan city, Hubei province, China which estimated basic reproduction number $R_0 = 2.82 \pm 0.11$ and suggested the epidemic end in the first week of April 2020 [28]. Another mathematical model was also developed for calculating the transitivity of the infection. Primarily, this model is based on Bats-Hosts-Reservoir-People model, later the model was rebuilt to

Reservoir-People model and estimated basic reproduction number [11]. Several researchers are involved continuously on the development of mathematical modelling for pandemic COVID-19 [12].

In this research, a enhanced mathematical model for coronavirus dynamics and transmission is devised for prediction of infection scenerio with incorporation of all possible parameters which is suggested by ECDC in 5th, 6th and 7th Risk Assesment Reports [4], [3], [1]. Prediction of infection dynamics aims to estimate the basic reproduction number R_0 , dynamics of active infected cases and outbreak period. In addition, the proposed mathematical model is developed for better understanding of disease transmission among people, the peak of infectiousness among population during the outbreak of novel coronavirus, severity of the infection and to sketch the effective interventions have been and ought to be. This model suggests to strictly impliment mitigation measures. However, available severe acute respiratory illness data could be inaccurate, contain substantial uncertainty, for instance, the precise timing and natural history of cases. It is well-known that the estimation of this number may vary due to several methodological issues, including different assumptions and choice of parameters, utilized models, used datasets and estimation period.

2 Materials and Methods

2.1 Mathematical Model Construction

In this section, we construct a mathematical model of SARS-CoV-2 infection dynamics that is based on the SARS-CoV-2 Reservoir-People model (RP model) [11] and 2009 A/H1N1 influenza SEIAR mathematical model [20]. RP model does not include transmission from asymptomatic population to symptomatic but a research showed that about 82.5% population geting symptoms from asytmomatic [26]. As per the ECDC report mitigation measuress is only way to prevent and control the infection. Therefore, we also include isolation of infected people who do not involve in the further infection propagation and other population is directly cut-off from susceptible due to the other mitigation measures as suggested by ECDC. Here, the total population N is sub-divided in 6 comparmental population : susceptible for infection (S), latent infected such that a population which is involved in the transmission of infection but not infected (E), infected (symtomatic) population (I), asytmomatic population (A), Isolated from infected (the population which does not have role in the further transmission of infection) (J), recoverd/death population (R). Although $I+J$ is total population is active infected case.

It is assumed here, that the population is homogeneous-mixed and people have equal probability of acquiring the infection. Proposed Model does not consider the migration from one country to other country and new births or deaths by natural process. It considers only human-to-human transmission.

Fig. 1 SEIAJR compartment structure for SARS-CoV-2.

The proposed mathematical model is represented for SARS-CoV-2 based on SEIAJR compartmental structure as shown in Figure 1. The model is formulated for European countries for SARS-CoV-2 infection scenerio in the system non-linear ordinary differential equations (1-6).

$$\frac{dS}{dt} = -\alpha \frac{(E + I + A)}{N} S - \sigma S \quad (1)$$

$$\frac{dE}{dt} = \alpha \frac{(E + I + A)}{N} S - \beta_1 E \quad (2)$$

$$\frac{dI}{dt} = \beta_1 h E + \beta_2 r A - \psi q I - \gamma(1 - q) I \quad (3)$$

$$\frac{dA}{dt} = \beta_1 (1 - h) E - \beta_2 r A - \gamma(1 - r) A \quad (4)$$

$$\frac{dJ}{dt} = \psi q I - \gamma J \quad (5)$$

$$\frac{dR}{dt} = \gamma(1 - q) I + \gamma(1 - r) A + \gamma J \quad (6)$$

The α is the transmission rate of infection, β_1 is the rate of latent infection, β_2 is the rate of appearance the symptoms in the asymptomatic population, ψ is the rate of isolation for infected population, σ is the mitigation rate for susceptible individuals. Further, $\gamma_1, \gamma_2, \gamma_3$ (all are assumed to be same level say γ) are the recovery rates from asymptomatic, symptomatic and isolated infected population, respectively, because period of infection is similar in symptomatic and asymptomatic SARS-CoV-2 infected population [10], [16].

The symbol h represents proportion of exposed population which shows symptoms in individuals those are at exposed stage, r shows proportion of population to get symptomatic infection from asymptomatic stage, q represents proportion of isolated population in infected individuals.

2.2 Basic Reproduction Number

Basic reproduction number (R_0) provides an average measure of infected population by single infected individual when whole population has been treated as susceptible [15]. It is an important threshold parameter which indicates the progression characteristic of the infection in a given population. The infection will spread if the value of R_0 is greater than one otherwise infection it will not be able to spread in the given population. In this section, we drive the formula of R_0 for the proposed model. For this purpose, we observed that at infection free stage $E = A = I = R = 0$ which imply $S = N$. Then the above system of equation can be reduced into the following linearized subsystem of equations:

$$\frac{dE}{dt} = \alpha(E + I + A) - \beta_1 E \quad (7)$$

$$\frac{dI}{dt} = \beta_1 h E + \beta_2 r A - \psi q I - \gamma(1 - q)I \quad (8)$$

$$\frac{dA}{dt} = \beta_1(1 - h)E - \beta_2 r A - \gamma(1 - r)A \quad (9)$$

$$\frac{dJ}{dt} = \psi q I - \gamma J \quad (10)$$

Above system of equations can be written in the matrix form as follow:

$$\frac{d\mathbf{X}}{dt} = (\mathbf{T} + \mathbf{\Sigma})\mathbf{X}$$

$$\text{where } \mathbf{X} = \begin{bmatrix} E \\ I \\ A \\ J \end{bmatrix}, \mathbf{T} = \begin{bmatrix} \alpha & \alpha & \alpha & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

$$\text{and } \mathbf{\Sigma} = \begin{bmatrix} -\beta_1 & 0 & 0 & 0 \\ \beta_1 h & -\psi q - \gamma(1 - q) & \beta_2 & 0 \\ \beta_1(1 - h) & 0 & -\beta_2 r - \gamma(1 - r) & 0 \\ 0 & \psi q & 0 & -\gamma \end{bmatrix}.$$

Then we can compute the next-generation matrix:

$$\mathbf{G} = -\mathbf{T}\mathbf{\Sigma}^{-1} = \begin{bmatrix} \frac{\alpha}{\beta_1} + \frac{\alpha(1-h)}{D_1} + \frac{\alpha(\gamma h + \beta_2 r - \gamma h r)}{D_2} & \frac{\alpha}{\gamma - \gamma q + \psi q} & \frac{\alpha}{D_1} + \frac{\alpha \beta_2 r}{D_2} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

where $D_1 = \gamma + \beta_2 r - \gamma r$ and $D_2 = D_1(\gamma - \gamma q + \psi q)$. The basic reproduction number of this modified model is given by spectral radius of matrix $\mathbf{G}$, and computed as:

$$R_0 = \frac{\alpha}{\beta_1} + \frac{\alpha(1-h)}{D_1} - \frac{\alpha(\gamma h + \beta_2 r - \gamma h r)}{D_2} \quad (11)$$

Table 1 Initial value of state variables during the simulation

State variable	Description	Initial value
S	Susceptible	90 % of total population
E	Exposed (Latent)/ The population which is infectious but not infected	$9 \times (I + A)$
I	Confirmed Infected	Number of infected case (First day of infection)
A	Asymptomatic Infected	Infected case $\times f$, where f is a multiple factor, adjusted according to outbreak data.
J	Isolated Infected	0
R	Recovered	0

Table 2 Parameters with definitions and values with their range

Symbol	Description	Value	References
h	Proportion of exposed population showing symptoms from exposed directly	0.1	Note: We assumed here that very few are showing symptoms directly from exposed individuals
β_1	1/latent period of infection (symptomatic or asymptomatic)	1/7	one week[1]
β_2	Rate of change to get symptoms (1/incubation period)	1/14	[1], [6]
α	Transmission rate	-	Varying as per the state
r	Proportion of population to get symptomatic infection from asymptomatic	17.5%	[26]
ψ	Rate of isolation from infected	0.9	Note: we assumed that most of the infected population is in isolation at everywhere due to the WHO intervention
q	Proportion of population for isolation	0.9	Note: we assumed that most of the infected population is in isolation at everywhere due to the WHO intervention
$\gamma_1/\gamma_2/\gamma_3$	recovery rate in asymptomatic, symptomatic, isolated (1/ Infection periods)	1/14	[29]

2.3 Sensitivity analysis of R_0

To use the model as predictive tool, a knowledge about change in model output is required when the values of parameters involved in the model changes. This crucial knowledge may be obtained via the sensitivity tool. If alteration in the value of parameters gives a small change in the model output then parameters are less sensitive for model output. But, when the model output changes in a great magnitude with respect to the small perturbation in input parameters then model is known as highly sensitive with respect to these parameters. Sensitivity has been defined in several ways by many researchers and scientists [9, 27, 7]. Normalized sensitivity index (elasticity index; Γ) of a output variable y with respect to the input parameter p may be defined as:

$$\Gamma_p^y = \frac{\partial y}{\partial p} \times \frac{p}{y} \quad (12)$$

We discussed in section 2.2, basic reproduction number is an important quantity which provide the information about the progression of the infection in the given population. Therefore, we did the sensitivity analysis of R_0 with respect to different parameters involved in its expression and listed in Table 4.

3 Results and Discussion

The heft of a mathematical model is only significant when the developed solution correlates with realistic data. In this research, we simulate a proposed SEIAJR mathematical model for four European countries including UK. At time of simulation, initial values for the compartmental population is assumed as per country current scenario according to ECDC database as listed in Table. 1 and parameters are obtained from literature. The aforesaid parameters are based on physiological characteristics of SARS-CoV-2 in human, the values of the parameters are listed in Table. 2. In Addition, few parameters are estimated which varies as per the geographical reasons, human-to-human interaction behavior and mitigation strategies as enumerated in Table. 3.

The proposed model is simulated in two phase with respect to time. In first phase, the model is deployed and best fitted with outbreak real data (Source: on 05 April 2020, <https://www.worldometers.info/coronavirus>). Through this simulation, we estimated infection transmission rate (α), mitigation rate of susceptible population (σ) and basic reproduction number (R_0), as mentioned in Table. 3. In second phase, simulation predicts the infection dynamics on different rate of infection mitigation by assuming estimated basic reproduction number (same as estimated in first phase). The whole simulation as shown in detail in Figure. 2a-2d for all 4 countries.

The simulation result showed R_0 of SARS-COV-2 was estimated 2.815, 2.981, 3.326 and 2.943 for Germany, United Kingdom, Switzerland and Spain respectively. In addition to this, R_0 was also similar in recent research studies [1], [25]. A small variation in R_0 values might be due to different method and assumption of modelling. It is also similar to China outbreak where it is commonly accepted $R_0 = 2.9$ [11]. Aforesaid, simulated results also showed mitigation rates 0.15, 0.135, 0.218 and 0.186 for Germany, United Kingdom, Switzerland and Spain. The mitigation rate was estimated almost similar to all countries, however, it is highest in Switzerland. High mitigation rate means that they were following quickly implementation of mitigation measures. It could be easily visible through simulation that the impact is decreasing rapidly in Switzerland due to their high mitigation measures implementation as shown in Figure. 2c.

Second-phase analysis depicts the peak of the infection found in the mid and last week of April 2020 in all 4 European countries and outbreak would last by end of July 2020. Although, simulation suggests that there is no more additional mitigation measures are required. The peak would reach on 9th-10th week of outbreak and it is again similar to China outbreak [28].

Furthermore, we have also done sensitivity analysis of R_0 with respect to other considered parameters. The basic reproduction number is directly correlated with transmission rate. It is observed through this analysis that there are two more parameters which are also sensitive for R_0 namely β_1 and β_2 . The absolute value of index for $\beta_1 = 0.49$ and for $\beta_2 = 0.39$. This value implies that β_1 (based latent period) is second most sensitive parameter for propagation of infection. The proposed model as well as the literature both states that the latent period plays crucial role in terms of infection propagation [2]. The plot R_0 versus parameters can be seen in Figure 3a-3c. Blue and Yellow solid line in Figure 3a depict that R_0 would decrease by less than 1 only at values of α and β_1 . Other all the parameters are cannot decrease R_0 by less than 1 (see Figure 3a and 3b). Thus, the combined three dimension plot of R_0 versus α and β_1 is shown in Figure 3c.

The proposed mathematical model might be applicable for other European countries too by tuning only two parameters (i.e. transmission rate and mitigation rate). Apparently, the analysis could highlight the dynamical behavior of infection and estimates reproduction number, peak, infectious cases, the

Fig. 2 Two phase infectious dynamics in different regions of Europeans Countries (a)) in Germany, (b) in United Kingdom, (c) in Switzerland, (d) in Spain

estimated mitigation rate is suggested about the future preparedness to stop the invasion of infection.

Conclusions

We proposed SEIAJR mathematical model is develope to estimate the basic reproduction number and infection transmission dynamics with incorporation of mitigation measures for SARS-CoV-2. The model is deployed and fitted in 4 European countries outbreak real data with fixing infection transmission and mitigation rate . The basic reproduction number is estimated and lies between 2.8 to 3.3 for considered all 4 European countries, as noted by other

Fig. 3 Graphical sensitivity of R_0 with respect to involved parameters.

research studies and also reported in 7th rapid risk assesment report released by ECDC. Apparntly, this could be said that aforesaid report is validating the proposed mathematical model. Futhermore, the infection would last by end of July 2020 on the basis of estimated R_0 even though if no more ad-ditinal mitigation measures implemented. The model predicts that the peak of infection reaches in the mid and last week of April 2020 which meets the other research studies hypothesis. The simulation of model suggests that the latent period is another highly sensitive parameter for infection transmission.

Table 3 Calculated value of reproduction number R_0 at best fitted parameters for different geographical regions .

Symbol	Description	Germany	U. K.	Switzerland	Spain
α	infection transmission rate	0.22	0.233	0.26	0.23
σ	mitigation rate for susceptibles	0.15	0.135	0.218	0.186
R_0	basic reproduction number	2.815	2.981	3.326	2.943

Table 4 Sensitivity elasticity expression and its value for basic reproduction number R_0 with respect to involved parameters ($h = 0.1, \beta_1 = 1/10, \beta_2 = 1/10, r = 1-0.175(0.825), \psi = 0.9, q = 0.9, \gamma = 1/14, \alpha = 0.22$).

Parameter	Expression for elasticity index	Index value
h	$-\frac{h \left(\frac{a}{\gamma + \beta_2 r - \gamma r} - \frac{a(\gamma - \gamma r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)}}$	-0.05043314754
β_1	$-\frac{b_1 \left(\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{a \beta_2 r (h-1) (\gamma r - \gamma q + \psi q)}$	-0.4865578761
β_2	$\frac{(\gamma + \beta_2 r - \gamma r)^2 (\gamma - \gamma q + \psi q) \left(\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{a r (h-1) (\gamma^2 - \gamma^2 q + \beta_2 \gamma q - \beta_2 \psi q + \gamma \psi q)}$	-0.3941748637
r	$-\frac{(\gamma + \beta_2 r - \gamma r)^2 (\gamma - \gamma q + \psi q) \left(\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{a \psi q (\gamma h + \beta_2 r - \gamma h r)}$	-0.07937983431
ψ	$-\frac{(\gamma + \beta_2 r - \gamma r) (\gamma - \gamma q + \psi q)^2 \left(\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{a q (\gamma - \psi) (\gamma h + \beta_2 r - \gamma h r)}$	-0.052033706
q	$\frac{(\gamma + \beta_2 r - \gamma r) (\gamma - \gamma q + \psi q)^2 \left(\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{a q (\gamma - \psi) (\gamma h + \beta_2 r - \gamma h r)}$	-0.0479040468
γ	$-\frac{\gamma \left(\frac{a(h-1)(r-1)}{(\gamma + \beta_2 r - \gamma r)^2} - \frac{a(q-1)(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)^2} - \frac{a(r-1)(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)^2 (\gamma - \gamma q + \psi q)} + \frac{a h (r-1)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)} \right)}{\frac{a}{b_1} - \frac{a(h-1)}{\gamma + \beta_2 r - \gamma r} + \frac{a(\gamma h + \beta_2 r - \gamma h r)}{(\gamma + \beta_2 r - \gamma r)(\gamma - \gamma q + \psi q)}}$	-0.4865578761
α	1	1

It means the untraced infected population could extend the outbreak as untraced infected population seems to spreading infection, which is also stated by the WHO situation report-73 on COVID-19. Thus, the model might be key role to understand European outbreak of SARS-CoV-2 and also for other geographical reasons with varying certain parameters. In addition, the deployment of proposed mathematical model would also helpful to evaluate the basic reproduction number which would suggest the weight of community mitigation measures implementation in near future.

Declaration

Availability of data and material

Not Applicable

Competing interests

The authors declare that they have no conflict of interest.

Funding

No funding for this project.

Authors' contributions

Dr. Shweta Sankhwar completed her M. Sc. And Ph.D. from Department of Information Technology, Babasaheb Bhimrao Ambedkar University (BBAU), Lucknow, India. Dr. Sankhwar has an outstanding academic background with a very sound academic and research experience. She has a research expertise in the areas of cyber security and internet security. She has published more than 15 research papers in international and national journals. She contributed as framing and writing the manuscript.

Mr. Narender Kumar received his MSc in Mathematics from the Indian Institute of Technology Delhi, New Delhi, India. Presently, he is a Research Scholar at the Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi. He is also a faculty in the Department of Mathematics, Gargi College, University of Delhi. His research interest is in the field of mathematical modelling of viral infectious diseases. Kumar contributed in methodology part and simulation.

Dr. Ravins Dohare, M.Sc., Ph.D. is an Assistant Professor of Mathematics at the Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi, India. Dr. Dohare completed his M.Sc. (Mathematics) from Indian Institute of Technology Delhi (IIT Delhi) and Ph.D. from Jamia Millia Islamia, New Delhi, India. He has a research expertise in the areas of mathematical modelling for dynamics of infectious populations and algorithm development for network community detection and their application to gene expression data. He has published more than 35 research papers in international and national journals. Dohare developed the model, write, framed and done simulation.

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Figures

Figure 1

SEIAJR compartment structure for SARS-CoV-2.

Figure 2

Two phase infectious dynamics in different regions of Europeans Countries (a)) in Germany, (b) in United Kingdom, (c) in Switzerland, (d) in Spain

Figure 3

Graphical sensitivity of R_0 with respect to involved parameters.