

APPLICATIONS OF MODELLING AND SIMULATION

Sensitivity Analysis of COVID-19 Transmission Dynamics in Pakistan Using Mathematical Modelling

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Abstract: COVID-19 has profoundly impacted all countries' lives, social habits, and economies, resulting in a swift health system breakdown. This immense effect has caused worldwide research to assess its impact on various healthcare, socioeconomic and demographic factors. This paper focuses on evaluating the impact of COVID-19 in Pakistan by adopting a mathematical model consisting of five population compartments: Susceptible (S), Vaccinated (V), Exposed (E), Infected (I), and Recovered (R) by utilising COVID-19 data specific to Pakistan. The primary objective is to analyse the influence of various parameters within the model. Numerical simulations were obtained using the higher-order Runge-Kutta method for dependent variables and the basic reproduction number by varying the parameters. The sensitivity analysis was then performed to assess the effect of the parameters. From the analysis, it is revealed the key parameters, including death rate, vaccination rate, and vaccine wane rate are more sensitive to the proposed SVEIR model. The simulation of basic reproduction was also carried out by observing the simultaneous effect of the five parameters, which includes the probability of susceptibility to becoming infectious per contact, isolated infectious cases, infectious period, the average number of contacts per day per case and death rate. The simulations show that the death rate produces more variations in almost all classes of the population. Vaccination rate reveals a higher number of recovered populations and reduced infected populations, and vaccine wane rate is suitable for intermediate values of the selected interval. The basic reproduction number also remains significant for the combination of probability of susceptibility to becoming infectious per contact and death rate. These insights contribute to the understanding of the sensitivity of disease dynamics under the influence of various interaction parameters.

Keywords: COVID-19; Disease modelling; SEIVR model; Sensitivity analysis; Transmission in Pakistan.

1. INTRODUCTION

The world health system faces a significant and impending threat from the Coronavirus (COVID-19) pandemic. More than 529 million cases have been confirmed in more than 200 countries since COVID-19 first appeared in December 2019, and more than 6 million people have died as a result [1]. At the onset of 2020, the world has been unprepared to face the unprecedented sanitary emergency of the COVID-19 pandemic. The first cases of the SARS-CoV-2 illness were reported in the Wuhan region of China [2]. As a result of globalisation, the spread of infection along the earth's surface in less than one year, profoundly impacting the lives, social habits, and economies of all countries, resulting in a swift breakdown of their health systems. Sixteen months after the first reported case of COVID-19, the global pandemic has resulted in the death of over 3.8 million individuals and infected more than 175 million people (not including those who have not been tested or diagnosed) [3]. The immense effects of the COVID-19 pandemic sparked an extensive global research effort to gain insight into its transmission and the effectiveness of containment measures [4, 5]. The rapid spread of COVID-19 prompted governments worldwide to implement strict measures such as lockdowns, restrictions on social and economic activities, hygiene standards, and masks to limit the transmission of the virus [6].

Non-pharmaceutical interventions (NPIs) are very successful in limiting the spread of the disease and are the only means of preventing further transmission until effective drugs and vaccines become available [7, 8]. The NPIs play an essential role in controlling the spread of the virus. However, these measures, particularly the restrictions on social and economic interactions, take a significant toll on people's lives, causing heavy financial and psychological burdens [9-11]. NPIs must be carefully planned and optimised for the best possible results with the most negligible negative impact on people's lives. Mathematical models designed to reflect the infection paths and predict how a specific disease will progress in risk populations can be beneficial in recent times. Many papers have addressed the mathematical description of COVID-19. This includes McKendrick

and Kermack [12] which has extended the basic SIR structure (Susceptible, Infected, and Recovered). Multi-compartmental epidemic models have been developed to represent various aspects of COVID-19 mathematically. These models consider the presence of asymptomatic infections, the incubation-latency period, and the challenges associated with contagion tracking [13, 14]. Additionally, quarantine and isolation compartments are included, along with the different severity levels of the disease [15-18].

Various mathematical models have been employed to understand the dynamics of COVID-19 transmission in Pakistan, drawing insights from multiple studies. Shah *et al.* [19] initiated the exploration using the SIR model, followed by Ahmad *et al.* [20], who introduced the SEIR fractional model, providing a more enhanced perspective on the epidemic. Subsequently, Peter *et al.* [21] expanded upon these foundations by developing a new mathematical model based on actual data from Pakistan, contributing to a deeper understanding of the local epidemiological situation. Naik *et al.* [22] further enhanced the modelling framework by integrating treatment dynamics using fractional derivatives, offering valuable insights into the impact of interventions. In parallel, Memon *et al.* [23] conducted a mathematical analysis focusing on measles epidemiology, shedding light on broader regional disease dynamics. Li *et al.* [24] contributed to the discourse with a dynamic study focusing on the third wave of the pandemic, enriching the understanding of temporal patterns. Bhattacharjee *et al.* [25] undertook a comparative analysis of various epidemiological models, providing valuable insights into their respective strengths and limitations. Finally, Gomez *et al.* [26] introduced the SCIR model, incorporating migration dynamics and a non-linear incidence function, representing a significant advancement in epidemic modelling methodologies. These diverse studies collectively contribute to a comprehensive understanding of COVID-19 transmission dynamics, informing effective disease control and mitigation strategies in Pakistan and beyond.

In literature, many studies have been reported to analyse and predict the behaviour of different types of diseases. However, the SVEIR-type model for COVID-19 in Pakistan is not well established. Adopting comprehensive models presents a drawback in that their identification is challenging, particularly during the initial outbreak when prompt decisions must be made. That is the primary motivation for adopting a minimal SVEIR model to describe COVID-19 transmission. It can be unexpectedly diagnosed according to a brief observation interval, and besides, one can benefit from the numerical solutions that can be exploited when designing the control measure policy.

In this paper, some modifications have been made to the proposed model of Gill *et al.* [27] by introducing the vaccination compartment and a few interaction parameters. The problem is formulated based on a time-varying SVEIR model, which facilitates the reproduction of the disease's dynamic evolution with fewer parameters and accounts for the continually changing suppression measures employed by the Pakistani government. To maintain mathematical simplicity in our formulation, we have overlooked significant epidemiological factors that arise over extended periods, such as the loss of immunity following recovery, reinfection, the impact of vaccinations, and virus variations.

2. MATERIALS AND METHODS

2.1 Data Source

The COVID-19 data in Pakistan, covering the period from 18 March 2020 to April 2022, was obtained from reliable sources, including the Countrywide Disaster Control Authority (NDMA) [28], the Ministry of National Health Services Regulations and Coordination [29], and the official website of the Pakistan Bureau of Statistics [30]. The variables consist of active cases, quarantine periods and death rates.

2.2 Data Analysis

The model analysis provides an outbreak simulation that includes the duration of the outbreak, outbreak peak in months and peak active case numbers during the period. These simulations were conducted when no control and movement control measures were taken. Furthermore, the reduction in the percentage of the highest active cases through various controlling measures established was described and analysed.

2.3 Model Formulation

This study introduces an innovative mathematical model considering five variables: Susceptible (S) , Vaccinated (V) , Exposed (E) , Infected (I) and Recovered (R) ; in short (the SVEIR model). The compartmental diagram of the proposed model, which is based on Pakistani data, is shown in Figure 1. By comparing the above compartment model and Gill *et al.* [27], the scenario can be represented as a system of ordinary differential equations as:

$$
\frac{dS}{dt} = (\mu + \omega)V - \frac{\beta \xi SI}{N} - \tau S,\tag{1}
$$

$$
\frac{dV}{dt} = \tau S - (\mu + \omega)V,\tag{2}
$$

$$
\frac{dE}{dt} = \frac{\beta \xi SI}{N} - \varphi E,\tag{3}
$$

$$
\frac{dI}{dt} = \varphi E - \varepsilon I - \delta I - \gamma I,\tag{4}
$$

Figure 1. The extended Susceptible (S), Vaccinated (V), Infected (I), Exposed (E) and Recovered (R) model depicts the control measures taken in Pakistan. The additional compartment is the vaccinated population (V) .

$$
\frac{dR}{dt} = \gamma I. \tag{5}
$$

The description of the different interaction parameters involved in the above SVEIR model and their estimated values (either obtained from reliable sources or calibrated using the Pakistan data) are listed in Table 1.

Parameters	Description	Value	Source	
N	Total human population in Pakistan	235,824,862	Pakistan Bureau of	
			Statistics [30]	
$1/\phi$	Incubation Period	0.1	Estimated using the data	
β	The probability of susceptibility becoming infectious	0.273	Calibrated using data	
	per contact			
$1/\gamma$	Infectious period	1/6.5	Calibrated using data	
ε	The death rate due to COVID-19	0.25	Estimated	
	The average number of contacts per day per case	30	Calibrated using data	
τ	People in the vulnerable groups receiving vaccination rate	1.0	Calibrated using data	
μ	Natural death rate (constant for all classes)	0.8408	Calibrated using data	
ω	Vaccine wane rate	1.0	Calibrated using data	
δ	The mean daily rate at which infectious cases are. isolated	0.039	Fitted	

Table 1. List of the parameters and their corresponding values used in the model simulation.

The above model (Equations (1) - (5)) is based on the mathematical modelling theories for disease epidemics [1], whereas, for the endemic equilibrium state, we must have $ds/dt = dE/dt = dI/dt = dR/dt = 0$. Therefore, assuming initially that the population attains disease-free equilibrium as $(S(0), E(0), I(0), R(0)) = (N, 0, 0, 0)$, then $S/N = 1$. For the disease to spread in the population $I > 0$, resulting in $\beta S - (\delta + \gamma + \varepsilon) > 0$. Comparing this inequality with the definition of the basic reproductive number, R_0 , this can be defined as:

$$
R_0 = \frac{\beta \xi}{(\delta + \gamma + \varepsilon)}.\tag{6}
$$

Accordingly, we obtained the vaccinated reproductive number (R_{vac}) through the SVEIR model using the Next Generation Matrix (NGM). The vaccination reproduction number represents the number of secondary cases that can arise from a single infected individual in a completely susceptible population, considering the effect of vaccination. It can be calculated as:

$$
R_{vac} = \frac{\theta \beta (1 - \psi \xi)}{(\theta + \mu)(\alpha I + \delta I + \lambda I + \mu)} (S^* + \omega V^*),
$$
\n(7)

where θ is the duration of quarantine, ψ is vaccine efficacy, α is the vaccine's effectiveness in reducing susceptibility, λ is the force of infection, S^* and V^* are endemic equilibrium points of Susceptible and Vaccinated, respectively. It is also noteworthy to mention that if $R_{vac} > 1$, the epidemic is likely to increase exponentially, indicating a higher transmission potential, and if R_{vac} < 1, the epidemic is expected to reduce over time.

The endemic equilibrium points for the dependent variables exist when $R_0 > 1$. Suppose that $X^* = (S^*, V^*, E^*, I^*, R^*)$ is the endemic equilibrium point of the model (Equations (1) - (5)), then X^* can be computed by taking all derivatives of the equations and equating them to zero as:

$$
(\mu + \omega)V^* - \frac{\beta \xi S^* I^*}{N} - \tau S^* = 0,
$$
\n(8)

$$
\tau S^* - (\mu + \omega)V^* = 0,\tag{9}
$$

$$
\frac{\beta S^* I^*}{N} - \varphi E^* = 0,\tag{10}
$$

$$
\varphi E^* - \varepsilon I^* - \delta I^* - \gamma I^* = 0, \tag{11}
$$

$$
\gamma I^* = 0. \tag{12}
$$

Solving Equations (8) – (12) yields X^* as

$$
S^* = \frac{N(\mu + \omega)V^* - \beta \xi I^* S^*}{N\tau}
$$
\n(13)

$$
V^* = \frac{\tau S^*}{(\mu + \omega)},\tag{14}
$$

$$
E^* = \frac{\beta \xi S^* I^*}{\varphi N},\tag{15}
$$

$$
I^* = \frac{\varphi E^* - \varepsilon I^* - \delta I^*}{\gamma},\tag{16}
$$

$$
R^* = 0.\tag{17}
$$

2.4 Model Simulation

The nonlinear system of ordinary equations (Equations $(1) - (5)$) was solved numerically by writing a user-defined code for the higher-order Runge-Kutta (RK) method on R software. The initial conditions applied were taken from the data, and the values of the other parameters used in the model were chosen, as mentioned in Table 1. It was observed that the death rate (ε) , vaccination rate (τ) and the vaccine wane rate (ω) are the most significant compared to other parameters. Hence, the sensitivity analysis of these three parameters was conducted with varying values. Before sensitivity analysis, a few trials for validation of the active cases were also conducted. For instance, Figure 2 shows the number of active (N_{ac}) cases in Pakistan from 28 December 2021 to 10 March 2022, and Figure 3 compares the active cases data with numerical results for Pakistan for a period of 17 November 2021 to 10 April 2022.

The simulation results in Figure 2 were measured without MCO (Movement control order). Based on this simulation, it is estimated that the number of active cases will exponentially rise and drop after reaching a certain critical point. In addition, the simulation can project the outbreak well over the next few months.

3. RESULTS AND DISCUSSION

The section presents the results of three sensitive parameters and basic reproductive number (R_0) obtained from the numerical solution of the SVEIR.

3.1 Sensitivity Analysis of the Death Rate of COVID-19

Figures 4-8 exhibit the variations in *S, V, E, I* and *R* under the influence of ε , respectively. The behaviour of the trends demonstrates that the *S, E, I* and *R* pose more variations to ε while *V* has less effect towards ε . The average values of all five dependent variables under the varied values of ε are listed in Table 2. Furthermore, increasing the values of ε , the trends of *S*, *E, I* and *R* also increased simultaneously. Figure 4 shows that the susceptible population (*S*) tends to decrease for the number of days to some extent and then marginally increase or asymptotically decrease for some fixed values of *ε.* It appears that the values of ε can control the behaviour of (*S*) significantly. In contrast, the vaccinated population (*V*) is not significantly affected by ε , as depicted in Figure 5. Figure 6 reveals that the exposed population (E) tends to behave like normally distributed data where the *E* shows the normal curves to the number of days. When ε is increased, the peak of curves is reduced. In Figure 7, the infected population (*I*) also exhibits normal behaviour concerning time, but as the values of *ε* are reduced, the peak of normal curves reaches an upward direction significantly. This suggests that to reduce the infection, *ε* should be set to high values to reduce the infection. The behaviour of the recovered population (R) under the influence of ε is shown in Figure 8. It can be seen from the results that for the intermediate values of *ε,* more recovery is expected as compared to other smaller or larger values. The analysis presented in Figures 4-8 may help to select any feasibility value of ε for which the infection can be put into any desired range.

Figure 2. SVEIR model simulation of COVID-19 active cases in Pakistan (28 December 2021 to 10 March 2022).

Figure 3. Comparison of actual data with numerical results of the SVEIR model for Pakistan.

ε	Susceptible, S	Vaccinated, V	Exposed, E	Infected, I	Recovered, R
0.25	34,040,504	1,942,888	39,778,580	19,847,416	237,972,173
0.50	276,704,574	1.942.909	16,860,919	8,649,101	83,091,958
0.75	193,244,161	1.942.902	28,644,037	14,314,555	132, 116, 353
.00.	136,015,435	1.942.897	34,474,716	17,208,178	168, 138, 651

Table 2. Effect of the ε on the S, V, E, I, R population of Pakistan.

Figure 4. Behaviour of Susceptible (S) class for different death rates due to COVID-19 (ε) values.

Figure 6. Behaviour of Exposed (E) class for different death

Figure 5. Behaviour of Vaccinated (V) class for different death rates due to COVID-19 (ε) values.

rates due to COVID-19 (ε) values.
Figure 7. Behaviour of Infected (I) class for different death
rates due to COVID-19 (ε) values. rates due to COVID-19 (ε) values.

Figure 8. Behaviour of Recovered (R) class for different death rates due to COVID-19 (ε) values.

3.2 Sensitivity Analysis of the Vaccination Rate

Similarly, to study the relation between the vaccination rate and the behaviour of the *S*, *E*, *I*, *V* and *R* populations, the SVEIR model was run for the different values. $\tau = 0.001$, $\tau = 0.01$, $\tau = 0.1$ and $\tau = 1$ while all other parameters were set, as mentioned in Table 1. The average values of all five dependent variables under the varied values of τ are listed in Table 3. Figures 9-13 exhibit the variations in *S*, *E*, *I*, *V* and *R* under the influence of respectively. The behaviour of the trends demonstrates that the *S*, *E*, *I*, *V* and *R* do not pose more variations towards τ . It appears that only for a higher value of $\tau = 1$ the trends of *S*, *E*, *I*, *V* and *R* abruptly increase while for other small values of τ the slight variations in the dependent variables are observed. The analysis also suggests that the time duration for the *S* and *V* is too small to be affected by the τ while for other classes, *E*, *I* and *R*, the time to reach the asymptotic value is significant.

Table 3. Effect of the τ on the *S, V, E, I, R* population of Pakistan.

	Susceptible, S	Vaccinated, V	Exposed, E	Infected, I	Recovered, R
0.001	136,015,434	1.942.897	34,474,716	17,208,178	168, 138, 651
0.010	35,459,887	2,129,359	43,222,250	21,509,527	257,036,309
0.100	48,819,740	4,532,697	87,446,014	42,855,197	505,030,569
1.000	212,478,655	116,797,869	2,157,338,841	1,041,959,426	12,731,433,504

Figure 9. The behaviour of the Susceptible (S) class for different vaccination rate (τ) values.

Figure 10. The behaviour of the Vaccinated (V) class for different vaccination rate (τ) values.

Figure 11. Behaviour of the Exposed (E) class for different vaccination rate (τ) values.

Figure 13. Behavior of the Recovered (R) class for different vaccination rate (τ) values.

3.3 Sensitivity Analysis of the Vaccine Wane Rate

To analyse the effect of the vaccine vane rate ω on the behaviour of the *S*, *E*, *I*, *V* and *R* population, the SVEIR model was run for the different values such as $\omega = 0.25$, $\omega = 0.5$, $\omega = 0.75$ and $\omega = 1$ while all other parameters were set, as mentioned in Table 1. The average values of all five dependent variables under the varied values of ω are listed in Table 4. Figures 14-17 show the variations in *S*, *E*, *I*, *V* and *R* under the influence of ω respectively. It is revealed that the *S* and *V* do not pose significant variations towards ω , whereas the E and I trend increase and then decrease after reaching the peak point; their period to reach an asymptote is more significant than *S* and *V*. The recovered class *R* is exposed under an abrupt change of $\omega = 1$.

ω	Susceptible, S	Vaccinated, V	Exposed, E	Infected, I	Recovered, R
0.25	34,150,079	2,461,229	39,778,361	19,847,161	237,506,191
0.5	34,112,990	2,213,656	39,778,508	19,847,279	237,717,403
0.75	34,076,145	2,052,794	39,778,567	19,847,359	237,864,132
1.0	34,040,504	1,942,888	39,778,580	19,847,416	237,972,173

Table 4. Effect of the ω on the *S*, *E*, *I*, *V* and *R* population of Pakistan.

Figure 16. Behaviour of Exposed (E) class for different vaccine wane rate (ω) values.

Figure18. Behaviour of Recovered (R) class for different vaccine wane rate (ω) values.

3.4 Basic Reproductive Number

More specifically, the sensitivity analysis of the Basic Reproduction Number (R_0) is performed under the simultaneous effect of β , δ , γ , ξ and ε values, respectively. In this regard, Figure 19 shows the changes in the reproduction number based on the mean daily rate of isolated infectious cases δ and the probability of susceptibility β . It is revealed that with a simultaneous increase in β and δ , the values of reproductive number decrease. Moreover, Figure 20 depicts the changes in the reproduction number according to the infectious period $1/\gamma$ versus the average number of contacts per day per case, ξ . The figure shows that with a simultaneous increase in ξ and $1/\gamma$ decreases the values of the basic reproductive number. Further, Figure 21 depicts the changes in the reproduction number according to the mean daily rate at which infectious cases are isolated *δ* versus the infectious period $1/\gamma$. It can be observed that an increase in δ leads to a decrease in R_0 . At the same time, the increase in γ also increases the value of *R*0. Figure 22 depicts the changes in the reproduction number according to the death rate due to COVID-19, ε versus the probability of susceptibility becoming infectious per contact β . It can be observed that the simultaneous increase in the values of β and ε decreases the values of R_0 whereas the magnitude of R_0 is much higher at β and ε . In summary, the R_0 remains more significant than 1 for the combination of β and ε and for other parameters, it remains less than 1.

4. CONCLUSION

The mathematical modelling of COVID-19, specifically in Pakistan, has been the focus of this paper. First, a SVEIR mathematical model was obtained by incorporating the vaccination variable and other interaction parameters. Then, the numerical solution was obtained on R by writing a systematic user-defined code. Different simulation trials were run to validate the data, and the most appropriate values for the interaction parameters were examined. Since the main objective was to analyse the sensitivity of the most significant parameters on the dynamics of *S*, *V*, *E*, *I* and *R* classes, the sensitivity of the key parameters, including death, vaccination, and vaccine wane rates, was analyzed. In addition to these parameters, the other parameters, such as the probability of susceptibility becoming infectious per contact isolated infectious cases, infectious period, the average number of contacts per day per case, and death rate, were assessed for the sensitivity of the Basic Reproduction Number R_0 . The analysis reveals that the death rate is more sensitive as it produces more variations in almost all population classes. The vaccination rate reveals a higher number of recovered and reduced infected populations, and the vaccine wane rate performs better for intermediate values of the selected interval. Also, the R_0 remains more significant than 1 for the probability of susceptibility becoming infectious per contact and death rate, and for other parameters, it remains less than 1. The results of this study may be quite helpful in understanding and predicting the behaviour of COVID-19. They may also provide insight into the control measures and the policy-making to mitigate the infection of such diseases that may probably appear in the future.

Figure19. Sensitivity analysis of basic reproduction number R_0 under simultaneous variation in the parameters β and δ .

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DECLARATION OF CONFLICTING INTERESTS

The authors declare no potential conflicts of interest with respect to the research and publication of this article.

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Figure 20. Sensitivity analysis of basic reproduction number R_0 under simultaneous variation in the parameters ζ and γ .

Figure 22. Sensitivity analysis of basic reproduction number R_0 under simultaneous variation in the parameters β and ε .

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