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Epidemics 41 (2022) 100642

Contents lists available at ScienceDirect

Epidemics

journal homepage: www.elsevier.com/locate/epidemics

Insight into Delta variant dominated second wave of COVID-19 in Nepal

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ARTICLE INFO

Keywords:
Delta variant
COVID-19
Nepal
Hospitalization
Vaccination

ABSTRACT

Objective: To study the spreading nature of Delta variant (B.1.617.2) dominated COVID-19 in Nepal to help the policymakers assess and manage health care facilities and vaccination programs.
Methods: Deterministic mathematical models in the form of systems of ordinary differential equations were developed to describe the COVID-19 transmission in the high- and the low-risk regions of Nepal. The models were validated using the multiple data sets containing daily new cases in the whole country, the high-risk region, the low-risk region, and cases needing medical care, ICU, and ventilator.
Results: We found the reproduction number of $R_t = 4.2$ at the beginning of the second wave, larger than the first wave (~1.8 estimated previously), indicating that the transmissibility of Delta variant is higher than the wild-type circulated during the first wave. Model predicts that ~5% of the COVID-19 cases were reported in Nepal, estimating the seroprevalence of ~63.9% as of July 2021, consistent with the survey conducted by the Government of Nepal. The seroprevalence was expected to reach 94.46% by April 2022, among which ~46% would have both infection and vaccination. The expected cases from September 2021 to April 2022 is 111,300, among which 11,890 people might need medical care, 3590 need ICU, and 953 need ventilators. The COVID-19 cases and medical care needs could be significantly reduced with proper implementation of vaccination and social distancing.
Conclusions: The data-driven mathematical models are useful to assess control programs in resource-limited countries. The appropriate combination of vaccination and social distancing are necessary to keep the pandemic under-control and manage the medical care facilities in Nepal.

1. Introduction

The COVID-19 pandemic caused by the novel coronavirus (SARS-CoV-2) continues with multiple waves worldwide. The pandemic has already generated more than 587 million cases and 6.43 million deaths worldwide as of August 6, 2022 (Worldometer, 2022). Among the several waves of COVID-19 caused by the different variants of the virus, the Delta variant (B.1.617.2) was the dominating strain during the second wave (June 2021 to December 2021 (GISAID, 2022)) until it was suppressed by new Omicron variant. The World Health Organization (WHO) classified the Delta variant as a global concern on May 10, 2021, when it had already spread to more than 30 countries (Nebehay and Farge, 2021). Notably, the Delta variant circulating during the second wave was more infectious (Bolze et al., 2021b; Callaway, 2021; Campbell and Archer, 2021; Jassat et al., 2021; WHO, 2021b) than the wild type, and caused the highest number of cases and deaths compared to other waves in Nepal (MoHP, 2021).

The crisis of Delta variant COVID-19 surge was catastrophic in Nepal, significantly ruining the fragile health care system after the second week of March 2021 (Weissenbach, 2021). With the country's population of

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https://doi.org/10.1016/j.epidem.2022.100642
Received 10 December 2021; Received in revised form 6 September 2022; Accepted 5 October 2022
Available online 6 October 2022
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only 30 million, infections during the second wave soared to over 9000 new cases per day recorded in the first week of May 2020 (MoHP, 2021; Poudel, 2021). As of September 1, 2021, the total COVID-19 related death in Nepal is 10,770, among which more than 7770 were during the second wave (MoHP, 2021). In May 2021, the whole-genome sequencing tests of 35 swab samples confirmed 34 of them as Delta variants (97%) (Poudel, 2021). Note that Alpha variant (B1.1.7) and K417N (AY.1.), a sub-lineage of B.1.617.2, have also been identified in Nepal (MoHP, 2020b).

In response to the second wave of COVID-19, the Government of Nepal implemented the lockdown on April 29, 2021, beginning from Kathmandu, the capital city, and later extending to all parts of the country (ALJAZEERA, 2021). Despite the lockdown for about four months and implemented vaccination, the transmission of the disease was still significantly high (2052 new cases and 20 deaths on September 1, 2021 (MoHP, 2021)). The potential devastation of this pandemic is highly unpredictable, primarily due to significant asymptomatic and undiagnosed cases (Baggett et al., 2020; Li et al., 2020; MoHP, 2020a; Reis et al., 2020). Moreover, the transmission dynamics of the second wave of COVID-19 was quite different from the first wave because of the availability of COVID-19 vaccination, improved treatment strategies, and a higher infectivity of the Delta variant (Hafeez et al., 2021; Ito et al., 2021). During the second wave, a higher reproduction number has been reported (EPH, 2021; WHO, 2021b), and also infected individuals experienced more severe infection resulting in a higher rate of hospitalization (Bager et al., 2021; Funk et al., 2021; Gupta et al., 2021; Sheikh et al., 2021). Different vaccines are found to have varying effects in the community across different regions of the world depending on the variants (Abu-Raddad et al., 2021; Bernal et al., 2021). Therefore, it is critical to gain insight into the unique transmission pattern and potential burden of COVID-19 in Nepal to design policies for the proper management of health care facilities and vaccination.

In this study, we implemented a data-driven modeling approach to study the COVID-19 transmission dynamics focused on two separate regions (high-risk and low-risk). Considering two different regions is essential in the context of Nepal because of the Nepal-India open border and largely populated cities in some regions, making them higher than others. Especially all the districts of the Terai region connected to India and populated cities such as Kathmandu, Surkhet, Pokhara, Lalitpur, Bhaktapur, and Chitwan are taken as a high-risk region. We validated our model by fitting it to the multiple real-time data sets containing new recorded cases from the high- and low-risk regions as well as the hospitalized, Intensive Care Unit (ICU), and Ventilator cases, and estimating key parameters of the model in a realistic range. We estimated the effective reproduction number and predicted the hospital beds, ICU, and Ventilators that would be needed in Nepal until April 2022. Moreover, we extended our model to explore how various vaccination programs would reduce the epidemic burden in Nepal.

2. Methods

2.1. Data

The data used in this study is obtained from the Ministry of Health and Population, Government of Nepal (MoHP, 2021). We used the data from 14 March to 15 September 2021 to fit the model. The six different data sets, the daily new cases of the whole country, the high-risk and low-risk regions, and number of patients in medical care, ICU, and ventilators were used in our model fitting and simulation.

2.2. Transmission dynamics model

In our transmission dynamics model based on the SEIR framework, we incorporated the medical care, ICU, and Ventilator compartments for both high- and low-risk regions to study the second wave of COVID-19 in Nepal. Schematic diagram and short description of the model are provided in Fig. 1, and the detailed description along with model equations is provided in the GitHub public repository (Adhikari, 2021).

2.3. Parameter estimation and model fitting to data

Since the new cases began to increase from March 14, 2021, we took March 14, 2021, as the initial time ($t = 0$) to initiate the second wave. The total population of Nepal in the census year 2011 was 26,494,504, and it is projected to be 29,996,478 at the end of 2020 (CBS, 2011). About 3.5 million Nepalese live in India as migrant workers (Kuwar, 2015; Prasain, 2021), so we did not include this population in our study. Using 14.4% [95% CI: 11.8–17.0] seroprevalence found in the October 2020 (MoHP, 2020a), our previous model (Adhikari et al., 2021) allowed us to estimate the seroprevalence on March 14, 2021, to be 24%. We deducted both seroprevalence and migrant population from the total population and took the initial susceptible population of 19.29 million for this study. Out of these susceptible populations, high and low-risk regions constitute 65% and 35%, respectively (CBS, 2011). The baseline values of all state variables are provided in the GitHub public repository (Adhikari, 2021).

The lockdown in Kathmandu valley was started on March 29, 2021, and gradually extended to almost all parts of the country (ALJAZEERA, 2021). To model this scenario, we defined the transmission rate $\beta_2(t)$ and $\beta_3(t)$ as follows:

$$\beta_2(t) = \begin{cases} \beta_H, & if \quad t \le 47, \\ \beta_H \quad ((1-c_b)exp(-r_H(t-47)) + c_b), & if \quad t > 47, \end{cases}$$

$$\beta_3(t) = \begin{cases} \beta_L, & if \quad t \le 47, \\ \beta_L \quad ((1-c_b)exp(-r_L(t-47)) + c_b), & if \quad t > 47, \end{cases}$$

where β_H and β_L represent the transmission rates before lockdown on the high-risk region and the low-risk region, respectively. Following the lockdown (at day 47), the transmission rates of high-risk and low-risk regions decay at the rates r_H and r_L, respectively. We further estimate the different values of r_H and r_L for different time periods according to the different levels of lockdown. We took $c_b = 0.3$ assuming up to 70% reduction on contacts during the prolonged lockdown period (Coburn et al., 2009). Note that the transmission of diseases by the recorded infectious remains the same regardless of the lockdown situation.

Since the inter-region mobility is quite different during the lockdown period from the pre-lockdown period, we considered two different mobility rates, $\gamma(t) = \gamma_1$, and γ_2, for the period of pre-lockdown and lockdown, respectively. The remaining parameters were estimated from data fitting by using the least square method. The details of data fitting are explained in the GitHub public repository (Adhikari, 2021).

2.4. Calculation of the reproduction number

The reproduction number (R_t) is an average number of secondary infections generated by a single infectious individual (You et al., 2020), which captures the increasing ($R_t > 1$) and decreasing ($R_t < 1$) trend of the infection. We calculated the reproduction number by using our dynamical system model and also using the Maximum Likelihood Method (MLM) from the daily reported incidence using the EpiStem package of R-program (Thompson et al., 2019) (see the GitHub public repository (Adhikari, 2021) for the reproduction number formulation).

2.5. Modeling vaccination program

We assumed the vaccination for individuals in all compartments, except the recorded infectious, medical care, ICU, and ventilator compartments, because the individuals were not vaccinated while they are infected or in medical care. To incorporate the vaccination program into the model, we further divide each vaccination-eligible compartment

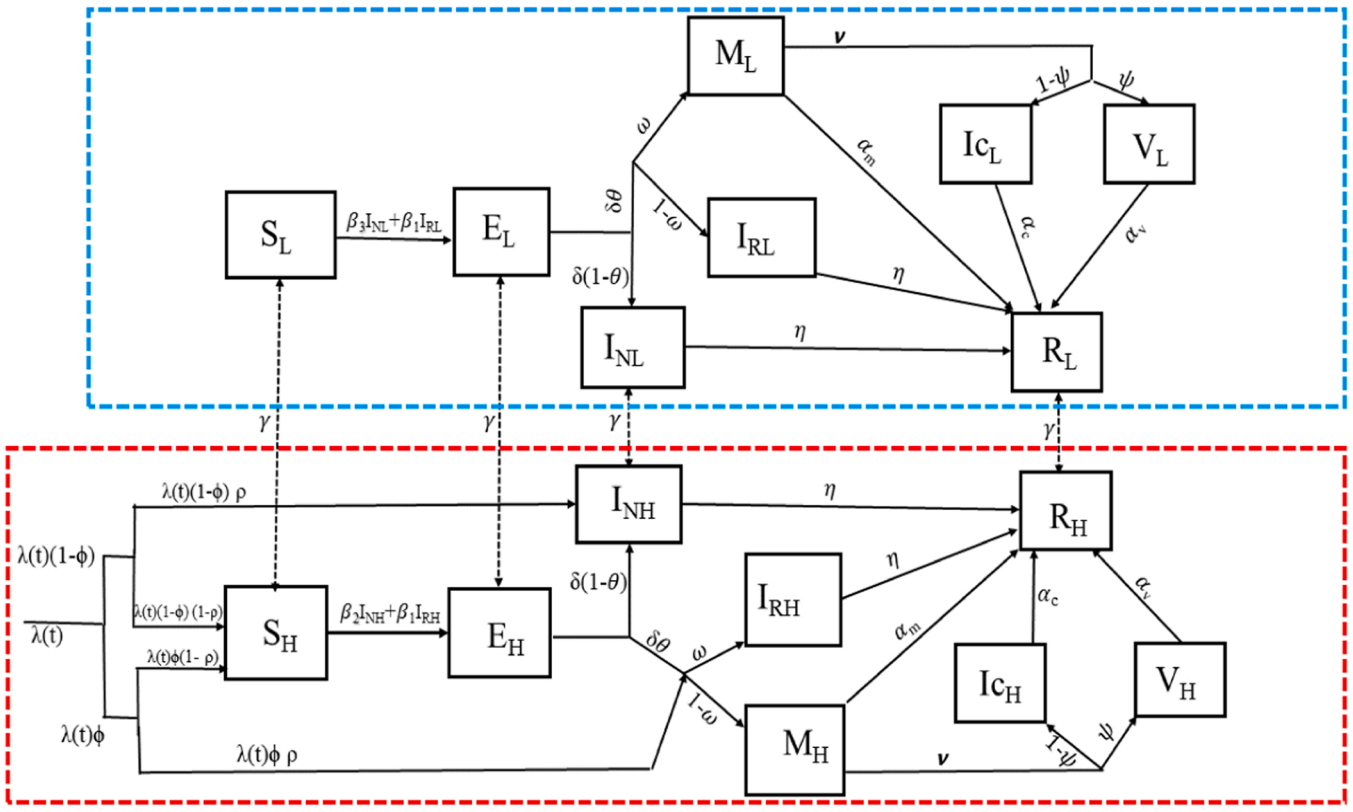

Fig. 1. Compartmental diagram of the Model. The red box denotes the high-risk region and blue the low-risk region. Here we divided the population into sixteen distinct compartments: S_H, S_L (susceptible), E_H, E_L (exposed), I_{RH}, I_{RL} (recorded infectious), I_{NH}, I_{NL}, (non-recorded infectious), M_H, M_L (Medical care), I_{CH}, I_{CL} (ICU), V_H, V_L (Ventilator) and R_H, R_L (recovered), where the suffixes H and L are used to indicate the high- and low-risk regions, respectively. $\wedge_H$ and $\wedge_L$ represent the recruitment rates due to birth and $\lambda(t)$ is the rate of entry of the immigrants from abroad to the high-risk region. Among the immigrants, a portion ϕ is tested by the antigen, and the rest $(1-\phi)$ entered the community without the antigen test. The ρ portion of immigrants with a positive test enter I_{RH} class and the remaining with a negative test enters S_H class. The immigrants without antigen test are entered to S_H and I_{NH} with the same portion $1-\rho$ and ρ, respectively. There is no recruitment from immigration in the low-risk region as it does not have a border with India. γ is the mobility rate between two regions. The transmission rate from the recorded infectious classes are β_1 for both regions, and that from non-recorded infectious classes in high- and low-risk regions are β_2 and β_3, respectively. The incubation period is represented by $\frac{1}{\delta}$. θ is the rate of being recorded, among which a portion ω enter M_H and M_L, and a portion $(1-\omega)$ enter I_{RH}, and I_{RL}, respectively. From M_H and M_L classes, the severe patients enter high medical care at the rate υ among them $(1-\psi)$ portion enter I_{CH}, I_{CL}, and ψ portion enter V_H, and V_L at the rate ν. The recovery rate of I_{RH}, I_{NH}, I_{RL}, and I_{NL} classes is η and that of (M_H, M_L), (I_{CH}, I_{CL}), and (V_H, V_L) are α_m, α_c, and α_v, respectively. The natural death rate of all the classes is μ and the disease-induced death rate for recorded and non-recorded infectious individuals are k and k', respectively, and that of individuals in medical care, ICU, and ventilator are k_1, k_2 and k_3, respectively. A detailed description of the model and system of differential equations are provided in the GitHub public repository (Adhikari, 2021).

into vaccinated and unvaccinated sub-compartments and transfer individuals from unvaccinated to vaccinated compartment upon receiving vaccinations. We assumed that the vaccinated individuals are less susceptible to infection, less vulnerable for medical care, and immune during the study period. The extended model diagram with the vaccination program is presented in the GitHub public repository (Adhikari, 2021).

3. Results

3.1. Pattern of the second wave of COVID-19 in Nepal and model validation

We used the extended model to fit the data and future predictions. The model was fitted to the multiple data sets consisting altogether 1116 data points simultaneously (186 data points of each of the daily recorded new cases in the whole country, the high-risk region, and the low-risk region, and cases in medical care, ICU, and ventilator) (Fig. 2). The large number of 6 different kinds of data points allowed us to estimate the unique parameters. In the beginning, the vaccination level in Nepal was negligible, but from middle of July 2021, the vaccination rate was significantly increased. So, we also incorporated the realistic vaccination program in our basic model fitting. The model is in excellent agreement with each data set, asserting the validation of our model.

The second wave increased rapidly until the 1st week of May 2021, hitting the highest new cases of 9070 on May 6, 2021. The implementation of lockdown reduces the new cases in both the high- and low-risk regions, but the effect observed in the low-risk region was one month delayed compared to the high-risk region. After the relaxation in lockdown in some places of the high- and low-risk regions, the COVID-19 cases resurged from mid-July of 2021, forcing these places to impose the second lockdown (For example, Jhapa district imposed the second lockdown from the last week of July 2021 and then relaxed from the second week of August 2021 (The Himalayan, 2021)). As revealed in Fig. 2, during the first peak of the second wave, the hospital beds, ICUs, and ventilators needed were below the capacity allocated by the government. The estimated parameters are given in Table 1.

3.2. Forecasting of the second wave of COVID-19 in Nepal

The long-term prediction of the disease dynamics using the dynamical system model is widely accepted. There are many mathematical models (Chowdhury et al., 2020; Goscé et al., 2020; Hachtel et al., 2022; Putra et al., 2020; Shankar et al., 2021; Tuite et al., 2020), which have

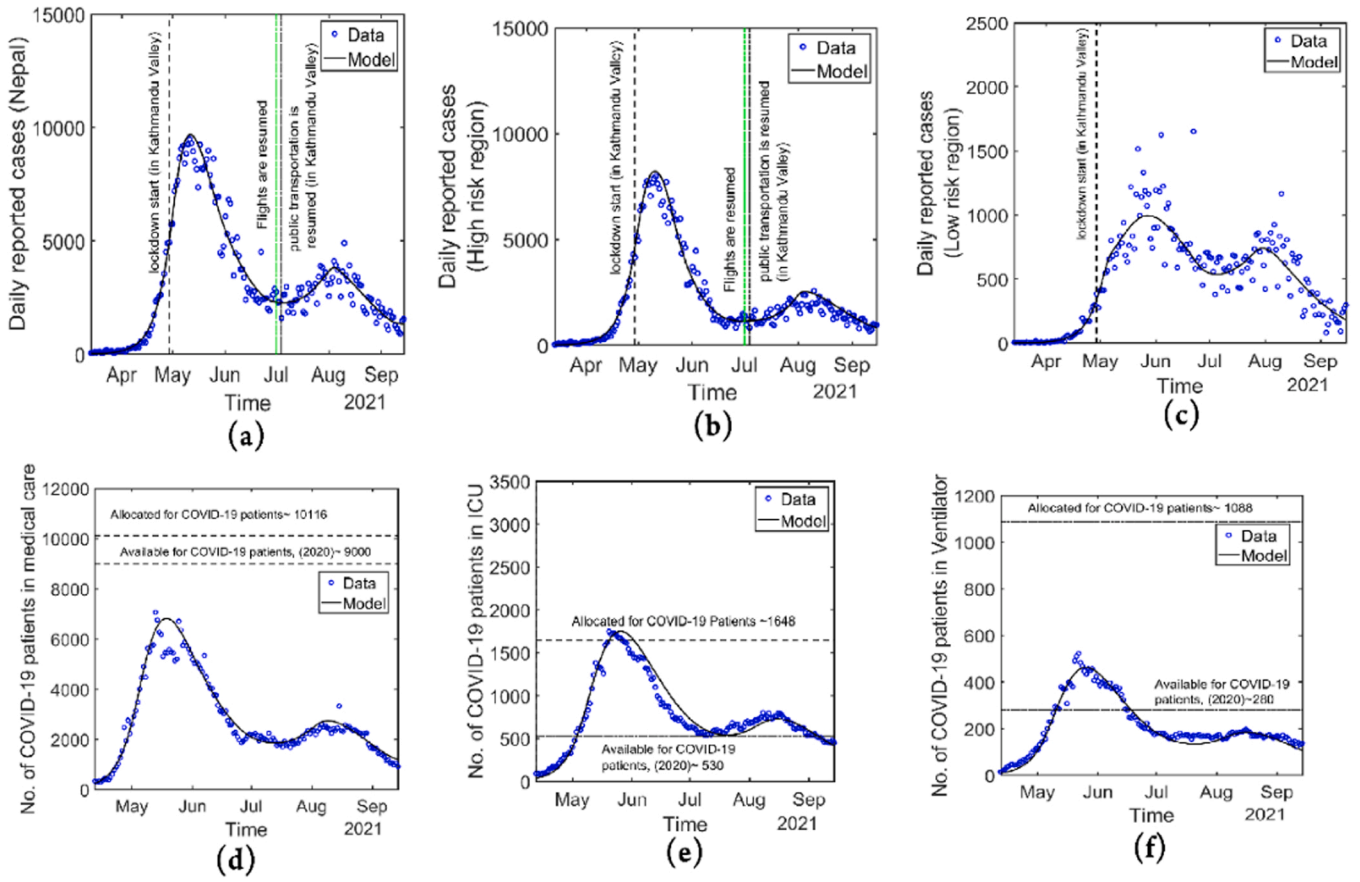

Fig. 2. Model Fitting to Multiple Data Sets. Daily reported cases of the whole country Nepal (a), the high-risk region (b), and the low-risk region (c), and cases in medical care (d), ICU (e), and ventilator (f). Solid lines represent the model prediction, and the circles represent the data. We take different decay rates r_H and r_L of transmission to address the different level of lockdown in different parts as follows: $r_H = 0$ ($0 \le t$ 47, Pre lockdown time), 0.082 ($47 \le t$ 95, Lockdown to all regions), −0.05 ($95 \le t$ 193 186, Partial relockdown in some parts), and $r_L = 0$ ($0 \le t < 47$, Pre lockdown time), 0.033 ($47 \le t < 105$, Lockdown starts and extend to other parts), −0.038 ($105 \le t < 135$, Relaxation of lockdown), 0.038 ($135 \le t < 185$ Partial relockdown in some places).

been used to predict the long-term behavior of pandemic in different places of the world. Here, we used our extended model to predict the long-term trend of the epidemic from 16 September 2021 to the end of April 2022 with the scenario of gradual relaxation of lockdown to reach the pre-lockdown phase. We would like to mention our long-term prediction includes short-term predictions as in some previous studies (Dahal et al., 2021; IHME, 2021). We also used our model to evaluate the various vaccination programs that the Nepal Government could implement. The trend of the epidemic with the level of vaccination implemented by the government (Fig. 3) shows a steady decrease to an almost extinct level with no cases of hospitalization at the end of April 2022. However, we note that our prediction was for the scenario in which no novel strain of SARS-CoV-2 would dominate the transmission. As per model estimations, 111,300 new cases would be reported, with 11,890 people needing medical care, 3590 needing ICU, and 950 needing ventilators, from September 16, 2021, to April 30, 2022.

3.3. Estimation of reproduction number in Nepal

We first estimated the reproduction number (R_t) from the data using the Maximum Likelihood Method (MLM). As mentioned earlier, the April 14 was the starting date of the second wave of COVID-19 in Nepal. Taking the 7 day-window for the calculation of R_t (see method section), we estimated the reproduction number from 21 April 2021–15 September 2021 (the last data considered). We observed that before the lockdown, R_t reached up to 2 in both the high- and low-risk regions as well as in the whole country (around the 3rd week of April), indicating that the significant community transmission of the disease had already occurred before the lockdown.

While R_t estimated from the data provides valuable information regarding the disease trend, it lacks the asymptomatic cases, which may be the dominating spreader of the disease. To overcome this limitation, we also estimated the time-dependent reproduction number (R_t) by using our model. As expected, the model predicted a higher value of the reproduction number of 4.2 due to the asymptomatic cases. R_t decreases rapidly after the implementation of the lockdown (Fig. 4). Around the 1st week of June, it fell below 1 and again raised following the partial relaxation of lockdown. This trend of R_t well-describes the trends of new cases in both high-and low-risk regions.

Under the complete national-level lockdown, it took one month longer in the low-risk region to bring R_t below 1 compared to the high-risk region. Our model also allowed us to predict a long-term R_t up until 30 April 2022. According to our model prediction, R_t remained less than the threshold value 1, indicating the decreasing trends of new cases in both regions (Fig. 4) throughout the pandemic until April 2022.

3.4. Estimates of seroprevalence

The antibody of COVID-19 forms in the body due to the viral infection and/or vaccination. Estimating the seroprevalence is practically essential for COVID-19, mainly because of a large portion of unreported infected individuals. We assumed that recovered and/or vaccinated people remain immune during the simulation period. We estimated 63.9% seroprevalence (Fig. 5) as of the end of July. We also used our model to predict the expected seroprevalence during the pandemic until April 2022 (Fig. 5). As predicted by our model, the seroprevalence

Table 1
Parameters of the model.

Symbol	Description	Value	References
β_1	transmission rate of recorded infectious people of high and low risk region	0.005	Data fitting
β_H	transmission rate of non-recorded infectious people of high region	0.525	Data fitting
β_L	transmission rate of non-recorded infectious people of low-risk region	0.235	Data fitting
θ	detection rate	0.05	Data fitting
ϕ	border screening rate	0.1	Data fitting
ρ	positivity rate of migrant workers at border	0.1	(MoHP, 2021)
k	disease induced death rate of reported non- hospitalized infected	0.0002	Data fitting
k'	disease induced death rate of non-reported non-hospitalized infected	0.00002	Data fitting
k_1, k_2, k_3	disease induced death rate in medical care, ICU, and ventilator	0.001,0.041,0.071	Data fitting
γ_1, γ_2	mobility rate between high and low risk regions before and after lockdown	0.015, 0.0001	Data fitting
ω	proportion of infected who need medical care	0.1125	Data fitting
τ	rate of admission on ICU from medical care	0.1	Data fitting
ν	rate of admission on high medical care (ventilator and ICU)	0.05	Data fitting
Ψ	proportion of infected who need ventilator	0.21	Data fitting
$\alpha_m, \alpha_c, \alpha_v$	recovery rate from medical care, ICU, and ventilator	0.092,0.1,0.0625	Data fitting
η	recovery rate of infectious without medical care	0.0588	(WHO, 2021a)
δ	incubation period	0.1923	(Linton et al., 2020)

reached ~89% in December 2021 and ~95% in April 2022.

Moreover, our model allows us to identify whether the seroprevalence achieved is due to vaccination, actual infection, or both. Among the ~89% seroprevalence achieved by December 31, 2021, ~7% are from vaccination, ~52% are from infection, and ~30% are from both vaccination and infection. Similarly, ~7%, ~42%, and ~46% are expected contributions from vaccination, infection, and both, respectively, towards the total seroprevalence of ~95% by April 30, 2022.

3.5. Role of vaccination in the mitigation of COVID-19 in Nepal

Here, we considered different vaccination scenarios under the complete relaxation of non-pharmaceutical interventions and used the model to predict the outcome of the pandemic under these vaccination programs. Based on the literature, we modeled the effectiveness of vaccination using a 50% reduction in infection and a 90% reduction in hospitalization for vaccinated people. While we used this level of effectiveness for demonstration purposes, the simulations with other values produce a similar qualitative behavior with a slight quantitative difference.

The Government of Nepal had set the target to vaccinate 71.6% of the people from the eligible age groups (MoHP, 2021). Therefore, we focus on vaccination programs targeting 71.6% of the eligible population by a specific timeframe. The vaccination rate (ζ), in our model with the target to cover 71.6% eligible population by vaccination timeframe, T, can be calculated using $\zeta = \frac{-\ln(1-\frac{71.6}{100})}{T}$ (Pantha et al., 2021a). For varying vaccination timeframes from October 31, 2021, to April 30, 2022, and the varying level of lockdown from 0% to 80%, we simulated our model to predict maximum daily cases, the total cases, the total deaths, the total medical cares, the total ICUs, and the total ventilators, during the pandemic until April 2022 (Fig. 6).

With the level of vaccination implemented and complete relaxation of the lockdown, the peak value of new cases is 2232 per day. However, the peak could be reduced to ~ 1726, 1966, 2070 and 2134 per day, respectively, when the vaccination timeframe is set to the end of October 2021, December 2021, February 2022, and April 2022. Our model simulations show that the total number of cases by the end of April 2022 could be reduced from 154,000 to 62,000, 94,000, 119,000, and 132,000 by setting the vaccination timeframe at the end of October 2021, December 2021, February 2022, and April 2022, respectively. With these vaccination programs, i.e., the time frame of the end of October 2021, December 2021, February 2022, and April 2022, the number of recorded deaths could be reduced from 1509 to 686, 1017, 1196, and 1316, respectively. Similarly, these vaccination timeframes could reduce the total medical patients from 16,610 to 5885, 9965, 12,150, and 14,080, respectively. In this case, the total ICU patients could be reduced from 4941 to 1964, 3147, 3790, and 4220, respectively, and ventilator patients could be reduced from 1305 to 522, 836, 1007, and 1122, respectively (Fig. 6).

4. Discussion

The timely characterization of the COVID-19 wave is essential for policy intervention to overcome the devastating impacts of the pandemic. Here, we developed a data-driven mathematical model to describe Nepal's unique delta variant-dominated second wave of COVID-19. Using multiple data sets simultaneously and considering two distinct high- and low-risk regions are unique features with more practical applications in our model. Our results provide a great insight into some relevant scenarios of COVID-19 in Nepal and predict the impact of potential vaccination programs on mitigating the burden of the pandemic, helping policymakers design proper health care facilities and vaccination strategies.

We identified the distinct pattern of the Delta wave in high- and low-risk regions regarding its magnitude and time period. As expected, most of the cases (>80%) were recorded in high-risk region and it peaked about one month earlier than low-risk region. Such spatial disparity on the pandemic trend was also found in the previous study (Pantha et al., 2021b), which performed the province-wise analysis of the first wave of COVID-19 in Nepal. The increasing trend of the epidemics remained for the period of April-May 2021 in high-risk region and for the period of May-June 2021 in low-risk region.

The delta variant was the dominant variant during the second wave of COVID-19 in Nepal. As per our model estimates, the reproduction number of $R_t = 4.2$ at the beginning of the Delta variant dominated second wave is higher than the first wave (~1.8) (Adhikari et al., 2021), indicating a significantly higher virus transmission during the second wave than the first wave. The maximum likelihood method gives a relatively low effective reproduction number (~2) at the peak time of epidemic that is similar to the other study (Dahal et al., 2021). The higher transmissibility of the Delta variant observed in our study is supported by the previous studies in different parts of the world (Campbell and Archer, 2021; Funk et al., 2021; Saito et al., 2021; Bolze et al., 2022; Li et al., 2021) and higher reproduction numbers in many other reports and studies (Campbell and Archer, 2021; Ito et al., 2021; WHO, 2021b). While the national implementation of lockdown caused the reproduction number to decrease to below the threshold value 1, the effect seen in the low-risk region was about a month delayed compared to the high-risk region. Such inter-regional disparity highlights that regional level policy, and thus regional level modeling, is needed for more effective control of the local-level outbreak. The inter-region discrepancy overserved in our estimated R_t is consistent with the inter-provincial disparity identified in Pantha et al. (Pantha et al.,

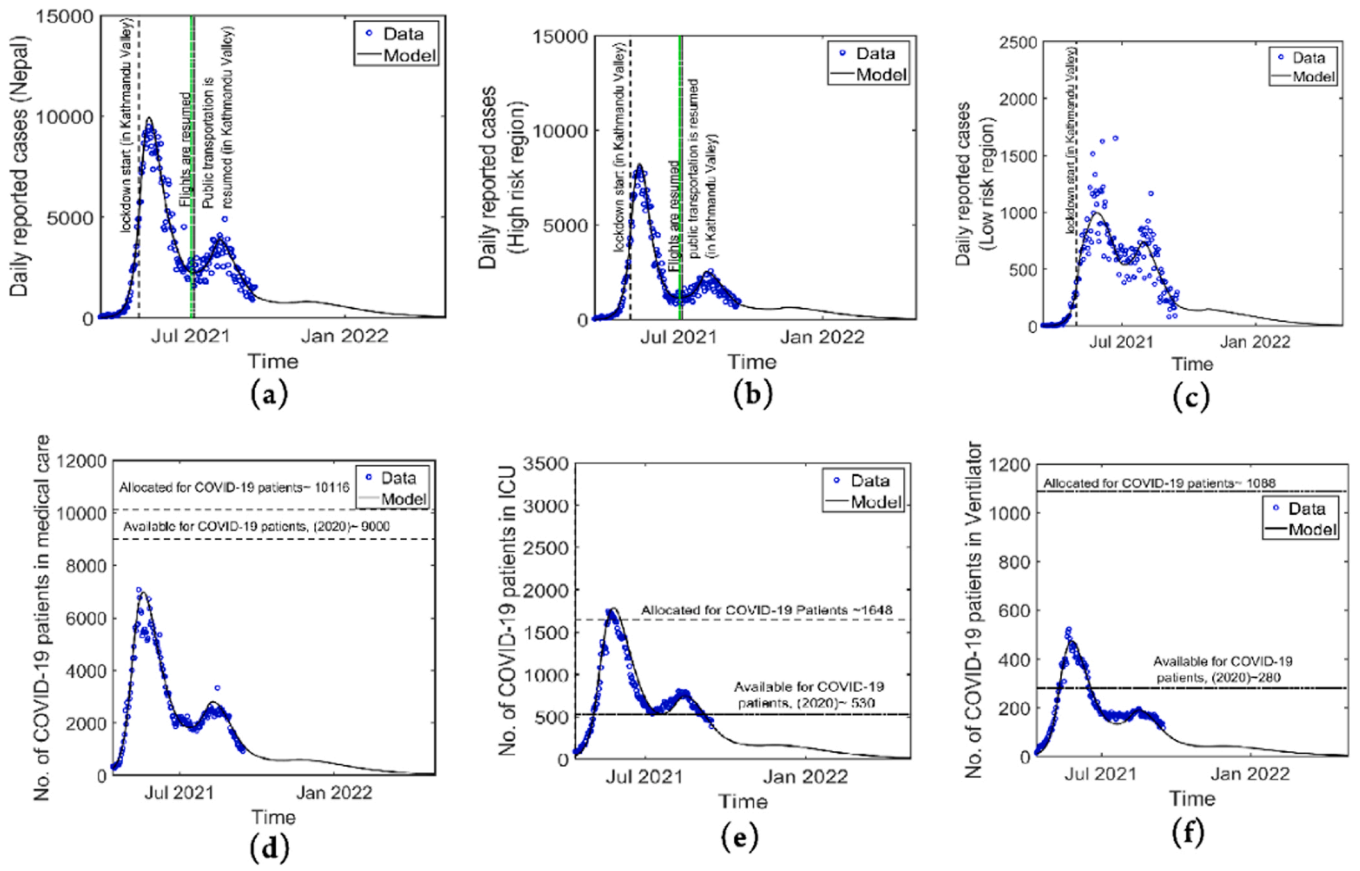

Fig. 3. Long term Prediction of the Model. Prediction of daily reported cases of the whole country Nepal (a), the high-risk region (b), and the low-risk region (c), and cases in medical care (d), ICU (e), and ventilator (f), predicted by the model until April 30, 2022.

2021b) during the first wave of COVID-19 in Nepal.

The potential transmission from the undiagnosed cases is one of the most contributing factors to the uncertainty of the COVID-19 pandemic, causing extreme difficulty for its control. Estimating this critical transmission rate from undiagnosed cases requires a large-scale seroprevalence survey, which is often limited by resources in developing countries like Nepal. We implemented our data-driven dynamical system-based model to estimate this transmission rate. We found a significantly high transmission rate from undiagnosed cases (~95%), consistent with the seroprevalence survey of the Government of Nepal (MoHP). Our model predicts ~63% seroprevalence in Nepal at the end of July 2021, consistent with the result (~68.6%) from the Nepal Government's survey (MoHP). With the level of vaccination implemented, the model predicts that ~95% of people were immune to the circulating strains of COVID-19 by the end of April 2022. Among these immune people, about 46% had experienced both vaccination and actual infection.

For developing countries like Nepal, timely assessment of expected burden is critical to avoid an overwhelming situation in hospitals and medical facilities. Our simulation results identified the duration of hospitalization of the COVID-19 patients in Nepal (7 days in normal medical care, 7.2 days in ICU, and 7.5 days in ventilators) shorter than that noted in other studies (Ben, 2021; Li et al., 2020; Twohig et al., 2022; Gupta et al., 2021). As in many other studies (Saito et al., 2021; Twohig et al., 2022; Verity et al., 2020; Jassat et al., 2021), Nepal faced a significant increase in the hospitalization burden due to the delta-variant compared to the wild-type. Based on our model analysis, we found the hospitalization of ~11.25% of recorded cases in Nepal, similar to the rates identified in other countries (~9.2%–25%) (Bager et al., 2021; Gupta et al., 2021). Among the hospitalized patients, ~35% of them needed extensive medical care, such as ICU and ventilator. According to the report on May 2020 (MoHP, 2020b), Nepal had 26,930 hospital beds, 1595 ICU beds, and 840 ventilators, including the government and private sectors. The Government of Nepal planned to allocate one-third of these facilities for COVID-19 patients. Later, the Government of Nepal extended its capacity to 10,116 hospital beds, 1648 ICUs, and 1088 ventilators for COVID-19 patients (MoHP, 2021). Interestingly, these data show that the predicted total hospitalization burden remains below the total capacity of Nepal even though the country is expected to have limited medical resources and prevention programs. However, we note that during the peak time (last of May 2021), many national and international media (Ben, 2021; Bhandari and Hannah Peterse, 2021; Prasain, 2021; ReliefWeb, 2021) covered the news about a shortage of hospital beds, ICU, ventilators, and oxygen cylinders. This discrepancy may be attributed to mismanagement of the hospital infrastructure and/or underreporting of patients. We also note that the low hospital rate may partially be attributable to the hospitalization of only complicated cases or scarcity of the hospital beds at the time of peak (Ben, 2021; Prasain, 2021; ReliefWeb, 2021).

The significant impact of the vaccination, including against the new variants, has been reported (Abu-Raddad et al., 2021; Bernal et al., 2021). Both vaccination programs and the relaxation of lockdown were ongoing in Nepal after the September 2021. We implemented our model to predict the potential epidemic trends and medical care needed (hospital bed, ICU, ventilator) for various coverage rates of vaccination programs and levels of lockdown during the pandemic until April 2022 (Fig. 6). Our model predictions of 111,300 cases, 11,890 hospitalizations, 3590 ICUs, and 950 ventilators by the end of April 2022 is also compatible with the prediction of IHME model (IHME, 2021). The results on vaccination and lockdown provide information on suitable strategies for Nepal to manage medical care and the pandemic burden.

We acknowledge some limitations of our study. Daily new cases may be affected by the number of tests and the positivity rate, which were not

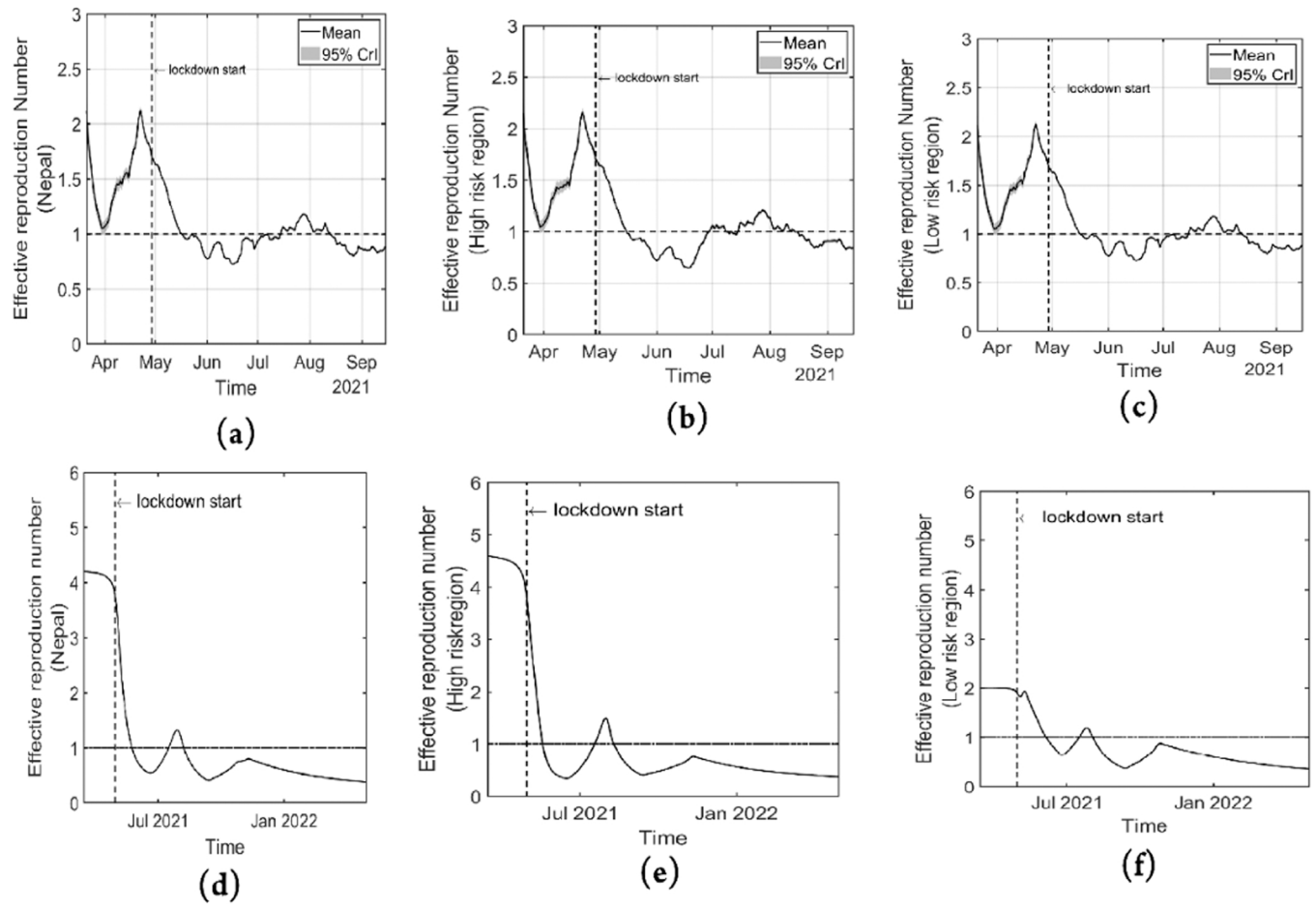

Fig. 4. Reproduction number. Time-dependent reproduction number of COVID-19 estimated from the recorded data for the whole country Nepal (a), the high-risk region (b), and the low-risk region (c). Time-dependent reproduction number of COVID-19 estimated from the model for the whole country Nepal (d), the high-risk region (e), and the low-risk region (f). Note that the higher reproduction number estimated from the model is presumably due to the unreported cases. The horizontal lines indicate the threshold value, $R_t = 1$, above (below) which shows an increasing (decreasing) trend of the disease spread. The model allowed us to predict R_t for the longer time up until April 2022.

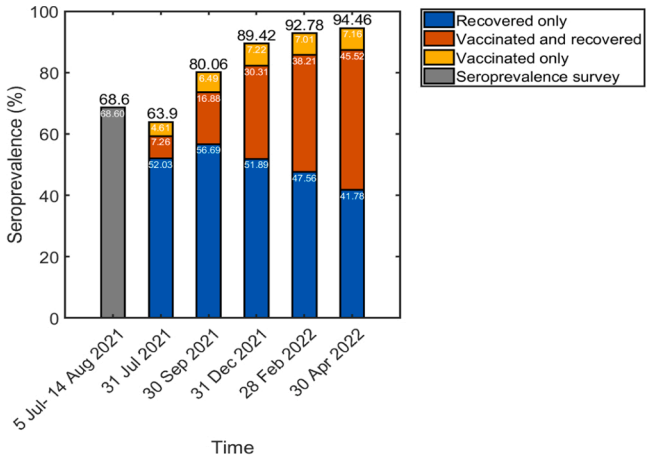

Fig. 5. Estimation of seroprevalence. The predicted seroprevalence achieved due to actual infection only, vaccination only, and both. The first bar represents the survey data by the Government of Nepal.

considered into our model. The inherent complexities of an unfolding epidemic, human behavior, implementation timing, and governmental policy change may have some impact on our predictions. We ignored the spatial heterogeneity in the dynamics within each region, the high- and low-risk regions. Furthermore, the inhomogeneity of the age structures of the study population was ignored. These questions can be addressed by heterogeneous and/or age-structured models, but more granular data is required. We considered high- and low-risk districts based on interconnections with India, a highly affected country by Delta variant, population density, and mobility pattern. The lack of data and information might have caused some uncertainty in categorizing districts into high- or low-risk regions. For example, our model classified the Makawanpur district, which is connected to high-risk districts (Chitwan, Lalitpur, and three Tarai districts), as low-risk due to its low density, low mobility pattern (a hilly district), and low infected cases. Moreover, because of the lockdown implemented during the second wave, there was less mobility across the districts, making Makawanpur a low-risk district despite its high-risk neighboring districts. Our long-term predictions were under the assumption that a novel strain would not appear for the study period. Therefore, the results need to be interpreted when the viral evolution and emergence of more severe strains are absent.

In summary, our data-driven model reveals some essential and insightful facts regarding the Delta-dominated second wave of COVID-19 in Nepal. In-depth exploration of the potential discrepancy between the actual epidemic burden and the recorded data suggests the policymakers revisit the gaps between the plan and practice of management of the pandemic. Estimated seroprevalence, new COVID-19 cases, and the hospitalization burdens under vaccination can provide helpful information for designing plans to control the pandemic in Nepal.

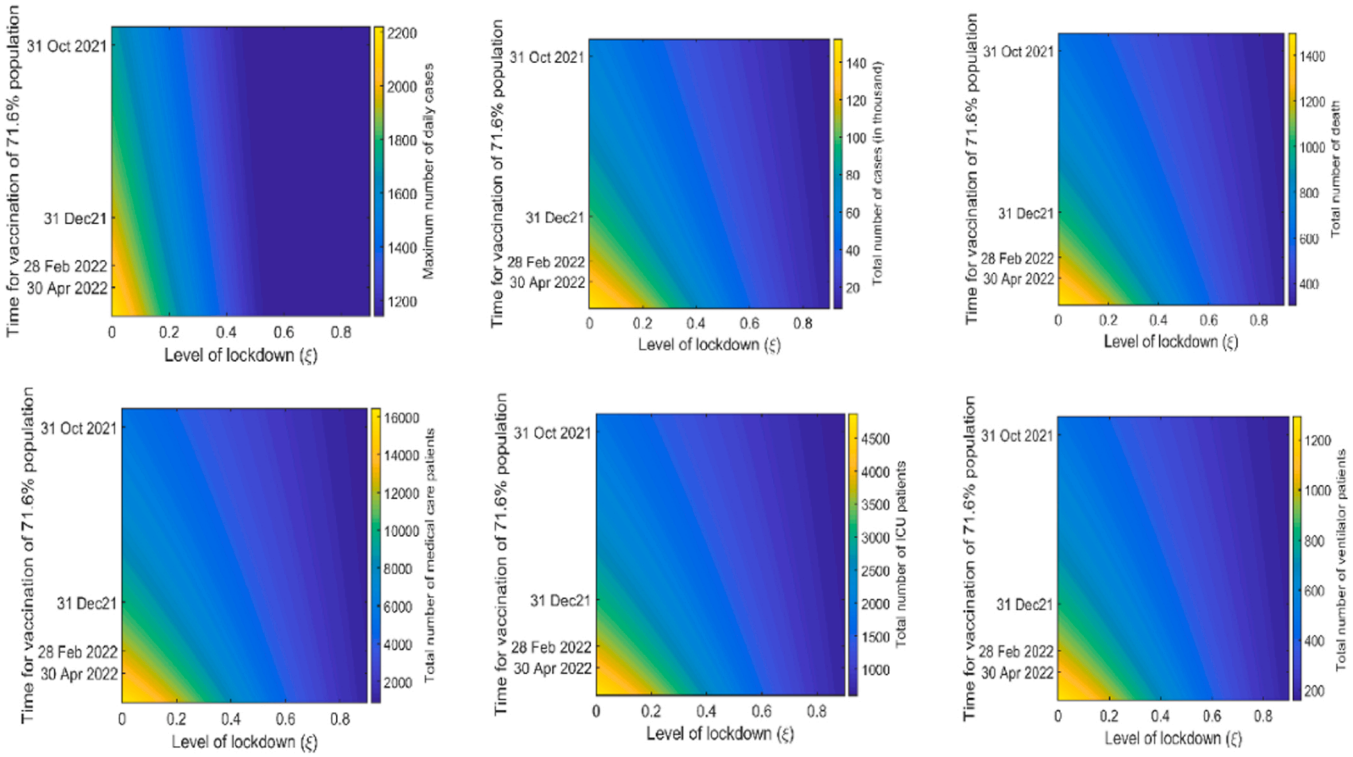

Fig. 6. Assessment of vaccination and lockdown program combined. The predicted peak value of the daily cases (a), total cases (b), total death (c), medical care cases (d), ICU cases (e), and ventilator cases (f) during the period from September 01, 2021, to April 30, 2022, for varying vaccination target timeframe and lockdown level.

CRediT authorship contribution statement

Khagendra Adhikari: Formal analysis, Investigation, Methodology, Writing – original draft. **Ramesh Gautam**: Formal analysis, Investigation, Methodology, Writing – original draft. **Anjana Pokharel**: Formal analysis, Investigation, Methodology, Writing – original draft. **Meghnath Dhimal**: Formal analysis, Writing – review & editing. **Kedar Nath Uprety**: Formal analysis, Supervision, Writing – review & editing. **Naveen K. Vaidya**: Conceptualization, Formal analysis, Supervision, Writing – review & editing.

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.

Acknowledgments

This research is supported by the GRAID (Graduate Research Assistantships in Developing Countries) awards from the International Mathematical Union (IMU). KA acknowledges the Nepal Academy of Science and Technology (NAST) for Ph.D. Fellowship. RG acknowledges the University Grants Commission (UGC) Nepal for Ph.D. Fellowship 2021. The work of NKV was supported by NSF grants DMS-1951793 and DEB-2030479 from the National Science Foundation of USA and UGP award from San Diego State University.

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