Supplementary Materials

Insight into Delta Variant Dominated Second Wave of COVID-19 in Nepal

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1. Transmission dynamics model

Considering the transmission dynamics model based on the $SEIR$ framework, the whole population is divided into high and low risk regions. The high-risk region consists of 22 districts of terai which are connected to the porous open border with one of the most highly COVID-19 affected country India together with highly populous cities; Kathmandu valley, Kaski, Chitawan, and Surkhet, and the remaining regions are taken as a low-risk region. The population of each region is divided into sixteen distinct compartments: S_H, S_L (susceptible), E_H, E_L (exposed), I_{RH}, I_{RL} (recorded infectious), I_{RH}, 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 for the indication of high and low risk regions respectively. The recruitment rate by birth in high and low-risk regions are Λ_H and Λ_L respectively and the immigrants from abroad to the high-risk region at the rate of $\lambda(t)$. Among the immigrants

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$\lambda(t)$, a portion ϕ is tested by the antigen, and the rest $(1-\phi)$ entered to the community without the antigen test. The ρ portion of immigrants with a positive test is entered to the recorded infectious class (I_{RH}) of the high-risk region and the remaining immigrants (getting negative test) entered to the class of the susceptibles. The immigrants without antigen test are entered to the susceptibles and non-recorded infectious (I_{NH}) with the same portion as that of tested immigrants. Since the low-risk region is not connected with the border, there is no recruitment from immigrantion in low-risk regions.

$\gamma(t)$ be the domestic mobility between two regions with corresponding classes (susceptibles, exposed, non-recorded infectious, and recovered). In the model, the transmission rate of recorded infected individuals of both regions is β_1, whereas the transmission rate from non recorded infectious in high and low-risk regions are $\beta_2(t)$ and $\beta_3(t)$ respectively. The exposed individuals get infectious at the rate of δ among which θ portion is entered to the recorded and $(1-\theta)$ entered to the non-recorded class in both risk regions. Among the recorded infectious in both regions, ω portion of infected entered the medical care class, and the remaining $(1-\omega)$ enter the class without medical care in both regions. From the medical cared group, the severe patients enter to high medical care at the rate ν among them ψ portion enters to the ventilators and $(1-\psi)$ portion to the ICU. The recovery rate of the recorded class without medical care and non-recorded infected class is η and that of medical care, ICU and ventilator are $\alpha_m,\ \alpha_c,$ 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 are k and k' respectively; and that of medical, ICU, and ventilator are $k_1,\ k_2$, and k_3 respectively. The schematic compartmental diagram is shown in the following figure.

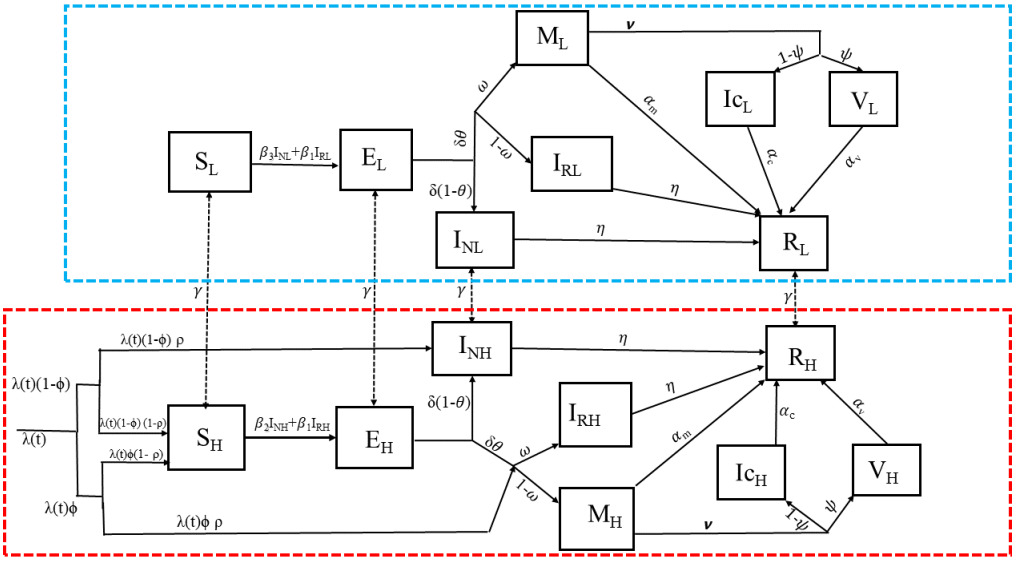

Figure 1: **The compartmental diagram of the model**. The compartments in the red box are of the high-risk region and in blue are of the low-risk region. The arrow represents the transform from one compartment to another. $\lambda(t)$ represents the rate of entering to the high-risk region of the immigratns. There is no entry point in the low-risk region from the border. The natural and diseases induced date rate are not shown in the diagram.

The dynamical system consisting of ODEs of our model is as follows:

$$\frac{dS_H}{dt} = \Lambda_H + \gamma S_L - \frac{(\beta_2 I_{\mathrm{NH}} + \beta_1 I_{\mathrm{RH}})\, S_H}{N_H} - (\gamma+\mu)S_H + \lambda(1-\rho)(1-\phi) + \lambda(1-\rho)\phi \tag{1}$$

$$\frac{dS_L}{dt} = \Lambda_L + \gamma S_H - \frac{(\beta_3 I_{NL} + \beta_1 I_{\mathrm{RL}})\, S_L}{N_L} - (\gamma+\mu)S_L \tag{2}$$

$$\frac{dE_H}{dt} = \frac{(\beta_2 I_{\mathrm{NH}} + \beta_1 I_{\mathrm{RH}})\, S_H}{N_H} + \gamma E_L - (\gamma+\delta+\mu)E_H \tag{3}$$

$$\frac{dE_L}{dt} = \frac{(\beta_3 I_{NL} + \beta_1 I_{RL})\, S_L}{N_L} + \gamma E_H - (\gamma+\delta+\mu)E_L \tag{4}$$

$$\frac{dI_{NH}}{dt} = \delta(1-\theta)E_H + \gamma I_{NL} - (\eta+k'+\mu)I_{NH} + \lambda\rho(1-\phi) - \gamma I_{NH} \tag{5}$$

$$\frac{dI_{NL}}{dt} = \delta(1-\theta)E_L + \gamma I_{NH} - (\eta+k'+\mu)I_{NL} - \gamma I_{NL} \tag{6}$$

$$\frac{dI_{RH}}{dt} = \delta\theta(1-\omega)E_H + \lambda\rho\phi(1-\omega) - (\eta+k+\mu)I_{\mathrm{RH}} \tag{7}$$

$$\frac{dI_{RL}}{dt} = \delta\theta(1-\omega)E_L - (\eta+k+\mu)I_{RL} \tag{8}$$

$$\frac{dM_H}{dt} = \delta\theta E_H\omega + \lambda\rho\omega\phi - (k_1+\mu+\alpha_m+\nu)\, M_H \tag{9}$$

$$\frac{dM_L}{dt} = \delta\theta\omega E_L - (\alpha_m+k_1+\mu+\nu)\, M_L \tag{10}$$

$$\frac{dI_{cH}}{dt} = \nu(1-\psi)M_H - (\alpha_c+k_2+\mu)\, I_{cH} \tag{11}$$

$$\frac{dI_{cL}}{dt} = \nu(1-\psi)M_L - (\alpha_c+k_2+\mu)\, I_{cL} \tag{12}$$

$$\frac{dV_H}{dt} = \nu\psi M_H - (\alpha_c+k_2+\mu)\, V_H \tag{13}$$

$$\frac{dV_L}{dt} = \nu\psi M_L - (\alpha_c+k_2+\mu)\, V_L \tag{14}$$

$$\frac{dR_H}{dt} = \alpha_c I_{cH} + \alpha_m M_H + \eta(I_{RH}+I_{NH}) + \alpha_v V_H + \gamma R_L - (\mu+\gamma)R_H \tag{15}$$

$$\frac{dR_L}{dt} = \alpha_c I_{cL} + \gamma R_H + \alpha_m M_L + \eta(I_{NL}+I_{RL}) + \alpha_v V_L - (\gamma+\mu)R_L. \tag{16}$$

Here, $N_H = S_H + E_H + I_{RH} + I_{NH} + M_H + I_{cH} + V_H + R_H$ and $N_L = S_L + E_L + I_{RL} + I_{NL} + M_L + I_{cL} + V_L + R_L$.

The vaccination rate in Nepal is very low till the end of the June, 2021 (2601316 people take the 1st dose and only 755019 people complte the doses) [1]. But after the Auguest, the vaccination rate was increased, so we extended our model for the simulation including the impact of vaccination. This exteded

model allows us to assess the impact of vaccination on the future epidemic trend.

2. Modeling vaccination program

We extended our model to incorporate the vaccination program by further dividing each compartment into vaccinated and non-vaccinated compartments except the recorded infectious compartments and medical compartments. For our study period, we assumed that there is no loss of immunity of vaccinated and recovered people. We also assumed that due to the vaccination,there is 50% reduction in infection and 90% reduction in medical cases.The schematic compartmental diagram is shown in the following figure.

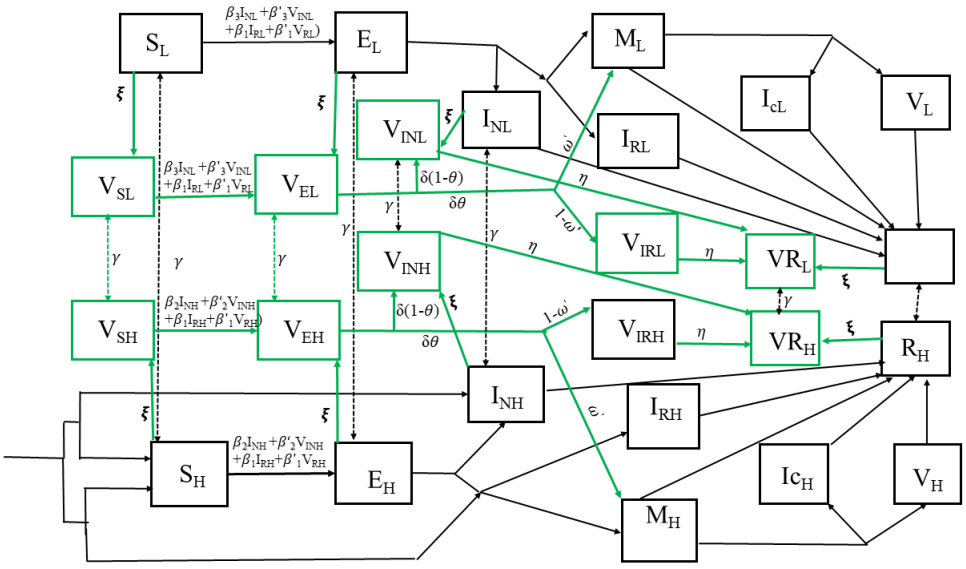

Figure 2: **The compartmental diagram of the model with vaccination**.The green boxes represents the vaccination compartments respect to the non vaccinationed compartment of each region. All othe rates of transform between compartments are same as in Figure 1 except transmission rates and hospitalization rate ($\beta_i' = 0.5\beta_i, i = 1, 2, 3$, and $\omega' = 0.1\omega$)

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3. Computation of reproduction number

3.1. Next generation method on the model

3.1.1. Reproduction number (Nepal)

For the calculation of basic reproduction number, first we calculate the diseases free equilibrium point. At the disease free equilibrium point the portion of positive antigen test must be zero i.e $\rho = 0$ and we use at the prepandemic condition $\lambda = \lambda(0)$ and $E_H = E_L = I_{RH} = I_{RL} = I_{NH} = I_{NL} = M_H = M_L = I_{cH} = I_{cL} = V_H = V_L = 0$ then we get the following disease free equilibrium point: $E^* = (S_H^*, S_L^*, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0)$ where,

$$S_H^* = \frac{\lambda(0)(\gamma+\mu) + (\gamma+\mu)\Lambda_H + \gamma\Lambda_L}{\mu(2\gamma+\mu)},\ S_L^* = \frac{\gamma\lambda(0) + \gamma\Lambda_H + (\gamma+\mu)\Lambda_L}{\mu(2\gamma+\mu)}.$$

Using the next generation matrix method, we divide the compartments used in the model into two groups: infected $\vec{x} = (x_i, i = 1, 2, ..., 12) = (E_H, E_L, I_{RH}, I_{RL}, I_{NH}, I_{NL}, M_H, M_L, I_{cH}, I_{cL}, V_H, V_L)$ and non-infected group $\vec{y} = (y_j, j = 1, 2, 3, 4) = (S_H, S_L, R_H, R_L)$. Then the system (1-16) can be written as:

$$x_i' = f_i(\vec{x}, \vec{y}) \text{ and } y_j' = g_j(\vec{x}, \vec{y}) \text{ for } i = 1, 2, ..., 12, j = 1, 2, 3, 4.$$

The right hand side of the system of infected compartments can be written as: $f_i(\vec{x}, \vec{y}) = F_i(\vec{x}, \vec{y}) - V_i(\vec{x}, \vec{y})$, where $F_i(\vec{x}, \vec{y})$ contains the terms representing the new infections in compartment i and $V_i(\vec{x}, \vec{y})$ contains the terms containing the difference between the transfer of individuals out of and into the compartment i. Then we construct the following two matrices using $F = \left(\frac{\partial F_i}{\partial x_i}\right)$ and $V = \left(\frac{\partial V_i}{\partial x_i}\right)$

$$F = \begin{pmatrix} A_{6\times6} & 0_{6\times6} \\ 0_{6\times6} & 0_{6\times6} \end{pmatrix},\ V = \begin{pmatrix} B_{8\times6} & 0_{6\times6} \\ 0_{4\times6} & C_{6\times6} \end{pmatrix},$$

where

$$A = \begin{pmatrix} 0 & 0 & \frac{\beta_1 S_H^*}{N_L^*} & 0 & \frac{\beta_H S_H^*}{N_H^*} & 0 \\ 0 & 0 & 0 & \frac{\beta_1 S_L^*}{N_L} & 0 & \frac{\beta_L S_L^*}{N_L^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$B = \begin{pmatrix} \gamma+\delta+\mu & -\gamma & 0 & 0 & 0 & 0 \\ -\gamma & \gamma+\delta+\mu & 0 & 0 & 0 & 0 \\ -\delta\theta(1-\omega) & 0 & k+\eta+\mu & 0 & 0 & 0 \\ 0 & -\delta\theta(1-\omega) & 0 & k+\eta+\mu & 0 & 0 \\ -\delta(1-\theta) & 0 & 0 & 0 & \gamma+\eta+\mu+k' & -\gamma \\ 0 & -\delta(1-\theta) & 0 & 0 & -\gamma & \gamma+\eta+\mu+k' \\ -\delta\theta\omega & 0 & 0 & 0 & 0 & 0 \\ 0 & -\delta\theta\omega & 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$C = \begin{pmatrix} p & 0 & 0 & 0 & 0 & 0 \\ 0 & p & 0 & 0 & 0 & 0 \\ -\nu(1-\psi) & 0 & q & 0 & 0 & 0 \\ 0 & -\nu(1-\psi) & 0 & q & 0 & 0 \\ -\nu\psi & 0 & 0 & 0 & r & 0 \\ 0 & -\nu\psi & 0 & 0 & 0 & r \end{pmatrix},$$

where $p = k_1 + \mu + \alpha_m, \quad q = \alpha_c + k_2 + \mu$ and $r = k_3 + \mu + \alpha_v$.

Let a be eigen values of FV^{-1} then the characteristic polynomial is $P(a) = a^{10}Q(a)$. Then the charastrictic polynomial equation gives 10 zero eigen values and two positive real eigen values obtained from

$$X = \begin{pmatrix} \frac{S_H^* T_1 \beta_1}{N_H^*} + \frac{S_H^* T_3 \beta_2}{N_H^*} & \frac{S_H^* T_2 \beta_1}{N_H^*} + \frac{S_H^* T_4 \beta_2}{N_H^*} \\ \frac{S_L^* T_2 \beta_1}{N_L^*} + \frac{S_L^* T_4 \beta_3}{N_L^*} & \frac{S_L^* T_1 \beta_1}{N_L^*} + \frac{S_L^* T_3 \beta_3}{N_L^*} \end{pmatrix}$$

where

$$T_1 = \frac{\delta\theta(1-\omega)(\gamma+\delta+\mu)}{(\delta+\mu)(2\gamma+\delta+\mu)(\eta+k+\mu)}, \qquad T_2 = \frac{\gamma\delta\theta(1-\omega)}{(\delta+\mu)(2\gamma+\delta+\mu)(\eta+k+\mu)},$$

$$T_3 = \frac{\gamma\delta(1-\theta)\left(2\gamma+\delta+\eta+k'+2\mu\right)}{(\delta+\mu)N_L(2\gamma+\delta+\mu)\left(\eta+k'+\mu\right)\left(2\gamma+\eta+k'+\mu\right)},$$

$$T_4 = \frac{\delta(1-\theta)\left(\delta\eta+\delta\mu+\eta\mu+\gamma\left(2\gamma+\delta+\eta+k'+2\mu\right)+\delta k'+\mu k'+\mu^2\right)}{(\delta+\mu)(2\gamma+\delta+\mu)\left(\eta+k'+\mu\right)\left(2\gamma+\eta+k'+\mu\right)}$$

. The largest eigen value of the above matrix X is the basic reproduction number, which we obtain as

$$R_0 = \frac{1}{2}\left(D + \sqrt{D^2-4E}\right), \tag{17}$$

where

$$D = \frac{\beta_1 T_1 S_H N_L + \beta_1 T_1 N_H S_L + \beta_2 T_3 S_H N_L + \beta_3 T_3 N_H S_L}{N_H N_L}$$

, and

$$E = \frac{S_H S_L\left(\beta_1^2 T_1^2 - \beta_1^2 T_2^2 + \left(\beta_2+\beta_3\right)\beta_1 T_1 T_3 - \left(\beta_2+\beta_3\right)\beta_1 T_2 T_4 + \beta_2\beta_3\left(T_3^2 - T_4^2\right)\right)}{N_H N_L}.$$

At the diseases free eqilibrium point, $S_H = S_H^*$, and $S_L = S_L^*$, $N_H = N_H^*$, $N_L = N_L^*$ $S_H^* = N_H^*$, and $S_L^* = N_L^*$ then the basic reproduction number is

$$R_0 = \frac{1}{2}\left(2\beta_1 T_1 + \beta_2 T_3 + \beta_3 T_3 + \sqrt{4\beta_2\beta_3 T_4^2 + 4\beta_1\beta_3 T_2 T_4 + 4\beta_1^2 T_2^2 + \left(\beta_2-\beta_3\right)^2 T_3^2 + 4\beta_1\beta_2 T_2 T_3}\right). \tag{18}$$

The corresponding effective reproduction number is obtained by making the respective state variables of 17 as function of t.

3.1.2. Reproduction number (high risk region)

Then we construct the following two matrices using $F = \left(\frac{\partial F_i}{\partial x_i}\right)$ and $V = \left(\frac{\partial V_i}{\partial x_i}\right)$ for high risk region

$$F_H = \begin{pmatrix} 0 & \frac{\beta_1 S_H^*}{N_H^*} & \frac{\beta_2 S_H^*}{N_H^*} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V_H = \begin{pmatrix} \gamma+\delta+\mu & 0 & 0 & 0 & 0 & 0 \\ -\delta\theta(1-\omega) & k+\eta+\mu & 0 & 0 & 0 & 0 \\ -\delta(1-\theta) & 0 & k'+\gamma+\eta+\mu & 0 & 0 & 0 \\ -\delta\theta\omega & 0 & 0 & \mu+\nu+k_1+\alpha_m & 0 & 0 \\ 0 & 0 & 0 & -\nu(1-\psi) & \mu+k_2+\alpha_c & 0 \\ 0 & 0 & 0 & -\nu\psi & 0 & \mu+k_3+\alpha_v \end{pmatrix}$$

and, futhermore,

$$F_H V_H^{-1} = \begin{pmatrix} \frac{\delta\theta(1-\omega)S_H^*\beta_1}{(\gamma+\delta+\mu)(k+\eta+\mu)N_H^*} + \frac{\delta(1-\theta)S_H^*\beta_2}{(\gamma+\delta+\mu)(k'+\gamma+\eta+\mu)N_H^*} & \frac{S_H^*\beta_1}{(k+\eta+\mu)N_H^*} & \frac{S_H^*\beta_2}{(k'+\gamma+\eta+\mu)N_H^*} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

The dominated Eigenvalue of $F_H V_H^{-1}$ is the basic reproduction number obtained as;

$$R_{H0} = \frac{\delta S_H^* \left(\beta_2(1-\theta)(\eta+k+\mu) + \theta\beta_1(1-\omega)(\gamma+\eta+k'+\mu)\right)}{N_H^*(\gamma+\delta+\mu)(\eta+k+\mu)(\gamma+\eta+k'+\mu)}. \qquad (19)$$

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At the diseases free eqilibrium point, $N_H^* = S_H^*$ then finally the basic repro-

duction number is

$$R_{H0} = \frac{\delta\left(\beta_2(1-\theta)(\eta+k+\mu)+\theta\beta_1(1-\omega)(\gamma+\eta+k'+\mu)\right)}{(\gamma+\delta+\mu)(\eta+k+\mu)(\gamma+\eta+k'+\mu)}. \qquad (20)$$

The corresponding effective reproduction number is obtained by making the respective state variables of 19 as function of t.

3.1.3. Reproduction number (low risk region)

Here we construct the following two matrices using $F_L = \left(\frac{\partial F_i}{\partial x_i}\right)$ and $V_L = \left(\frac{\partial V_i}{\partial x_i}\right)$ for low risk region as as follow:

$$F_L = \begin{pmatrix} 0 & \frac{\beta_1 S_L^*}{N_L^*} & \frac{\beta_3 S_L^*}{N_L^*} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V_L = \begin{pmatrix} \gamma+\delta+\mu & 0 & 0 & 0 & 0 & 0 \\ -\delta\theta(1-\omega) & k+\eta+\mu & 0 & 0 & 0 & 0 \\ -\delta(1-\theta) & 0 & k'+\gamma+\eta+\mu & 0 & 0 & 0 \\ -\delta\theta\omega & 0 & 0 & \mu+\nu+k_1+\alpha_m & 0 & 0 \\ 0 & 0 & 0 & -\nu(1-\psi) & \mu+k_2+\alpha_c & 0 \\ 0 & 0 & 0 & -\nu\psi & 0 & \mu+k_3+\alpha_v \end{pmatrix}.$$

Now, we have

$$F_L V_L^{-1} = \begin{pmatrix} \frac{\delta\theta(1-\omega)S_L^*\beta_1}{(\gamma+\delta+\mu)(k+\eta+\mu)N_L^*} + \frac{\delta(1-\theta)S_L^*\beta_3}{(\gamma+\delta+\mu)(k'+\gamma+\eta+\mu)N_L^*} & \frac{S_L^*\beta_1}{(k+\eta+\mu)N_L^*} & \frac{S_L^*\beta_3}{(k'+\gamma+\eta+\mu)N_L^*} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

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The dominated Eigenvalue of $F_H V_H^{-1}$ is the basic reproduction number obtained as;

$$R_{L0} = \frac{S_L^* \delta \left(\beta_1 \theta (1-\omega)(\gamma+\eta+k'+\mu) + \beta_3 (1-\theta)(\eta+k+\mu)\right)}{N_L^* (\gamma+\delta+\mu)(\eta+k+\mu)(\gamma+\eta+k'+\mu)} \tag{21}$$

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At the diseases free eqilibrium point, $N_L^* = S_L^*$ then finally the basic reproduction number is

$$R_{L0} = \frac{\delta \left(\beta_1 \theta (1-\omega)(\gamma+\eta+k'+\mu) + \beta_3 (1-\theta)(\eta+k+\mu)\right)}{(\gamma+\delta+\mu)(\eta+k+\mu)(\gamma+\eta+k'+\mu)}. \tag{22}$$

The corresponding effective reproduction number is obtained by making the respective state variables of 22 as function of t.

3.1.4. Maximum likelihood method on data

There are number of methods to estimate the basic reproduction number from the disease incidence data. Among them, the method proposed by White and Pagano [6, 7] known as the maximum likelihood method (MLM), is widely used in many studies.

We also calculate the effective Reproduction number (R_t) from the daily incidence data as a marker for the decrease or surge in infections from the real-time data. Time-varying R_t can be calculated using the time series of the infections and generation time distribution [4]. We use the approach developed by Thompson et al [3] for the estimation of effective reproduction numbers using the EpiEstem package of the R program. We take the mean serial interval as 4.7 days (95% CrI: 3.7, 6.0) days, with an SD of 2.9 days (95% CrI: 1.9, 4.9) days based on the previous study [5].

3.2. Parameter estimation and model fitting to data

3.2.1. Data fitting

The model is fitted with the datas: daily new cases of recorded infectious people of: Nepal, high risk region, low risk region; number of patients who

need medical care, ICU, and ventilator simultaneously. Using our model, the recorded new infections in Nepal, high risk rgion and low risk region, the number of patients who are in medical care, ICU and ventilator generated at time t, can be computed using the following respective equations:

$$L_r(t) = \delta\theta E_H + \lambda(t)\phi\rho + \delta\theta E_L, \tag{23}$$

$$L_{rh}(t) = \delta\theta E_H + \lambda(t)\phi\rho, \tag{24}$$

$$L_{rl}(t) = \delta\theta E_L, \tag{25}$$

$$L_m(t) = \delta\omega\theta(E_H+E_L)+\lambda(t)\phi\rho\omega-\alpha_m(M_H+M_L)-k_1(M_H+M_L)-\nu(M_H+M_L), \tag{26}$$

$$L_c(t) = \nu(1-\psi)(M_H+M_L) - (k_2+\alpha_c)(M_H+M_L), \tag{27}$$

$$L_v(t) = \nu\psi(M_H+M_L) - (k_3+\alpha_v)(V_H+V_L). \tag{28}$$

We solve the system of differential equations numerically by using a fourth-order Runge-Kutta method. We use the solutions to obtain the best-fit parameters via a nonlinear least-squares regression method that minimizes the following sum of the squared residuals:

$$J(\beta_1,\beta_H,\beta_L,\theta,r_H,r_L,\gamma_1,\gamma_2,\omega,\nu,\psi,\alpha_m,\alpha_c,\alpha_v,\nu,k,k',k_1,k_2,k_3) = \sum_{i=1}^{n}\big[\big(L_r(t_i)-\bar{L_r}(t_i)\big)^2 + \big(L_{rh}(t_i)-\bar{L_{rh}}(t_i)\big)^2+\big(L_{rl}(t_i)-\bar{L_{rl}}(t_i)\big)^2+\big(L_m(t_i)-\bar{L_m}(t_i)\big)^2+\big(L_c(t_i)-\bar{L_c}(t_i)\big)^2 + \big(L_v(t_i)-\bar{L_v}(t_i)\big)^2\big]$$

where $\beta_1,\beta_H,\beta_L,\theta,r_H,r_L,\gamma_1,\gamma_2,\omega,\nu,\psi,\alpha_m,\alpha_c,\alpha_v,\nu,k,k',k_1,k_2,k_3$, and k_3 are parameters to be estimated, and $L_r(t_k), L_{rh}(t_i), L_{rl}(t_i), L_m(t_i), L_c(t_i), L_v(t_i)$

and
$\bar{L_r}(t_i), \bar{L_{rh}}(t_i), \bar{L_{rl}}(t_i), \bar{L_m}(t_i), \bar{L_c}(t_i), \bar{L_v}(t_i)$ are the model values and those given in the available data of the respective classes. Here, n represents the total number of data points used for the model fitting.

In our study, all computations were carried out in MATLAB 2020a (The MathWorks, Inc.).

3.2.2. Initial values of the state variables

Description	State variables	Base Value	Reference
Susceptible population in high risk region	$S_H(0)$	12,818,000	Calculated
Susceptible population in low risk region	$S_L(0)$	6,479,000	Calculated
Exposed population in high risk region	$E_H(0)$	100	Assumed
Exposed population in low risk region	$E_L(0)$	80	Assumed
Recorded infectious population in high risk region	$I_{RH}(0)$	200	Assumed
Recorded infectious population in low risk region	$I_{RL}(0)$	100	Assumed
Non-Recorded infectious population in high risk region	$I_{NH}(0)$	1000	Assumed
Non-Recorded infectious population in low risk region	$I_{NL}(0)$	800	Assumed
Patients in medical care in high risk region	$M_H(0)$	0	Assumed
Patients in medical care in low risk region	$M_L(0)$	0	Assumed
Patients in medical care in high risk region	$I_{cH}(0)$	0	Assumed
Patients in medical care in low risk region	$M_{cL}(0)$	0	Assumed
Patients in medical care in high risk region	$V_H(0)$	0	Assumed
Patients in medical care in low risk region	$V_L(0)$	0	Assumed
Recovered population in high risk region	$R_H(0)$	460,8000	Calculated
Recovered population in low risk region	$R_L(0)$	256,8000	Calculated

References

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