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IMPACT OF VACCINATION AND STERILIZATION ON THE TRANSMISSION DYNAMICS OF RABIES

VIJAI SHANKER VERMA, LAXMAN BAHADUR KUNWAR

Abstract. We have constructed a mathematical model by dividing the dog and human populations into eight compartments as the rabies virus is likely to spread in both populations. In the model, disease-controlling strategies such as vaccination, sterilization and culling are taken into consideration, and their impact is studied. The current study assumes that dogs can transmit rabies among dogs as well as to human population. We have applied the next-generation matrix technique to compute the basic reproduction number. Also, each parameters involved are subjected to sensitivity analysis using the approach of normalized sensitivity index. The disease-free (or rabies-free) and endemic-equilibrium points are discovered analytically. The endemic equilibrium point is shown to be locally asymptotically stable. The numerical simulations, which use approximations for parameter values, shows that effective method for controlling rabies transmission is a combination of vaccination, sterilization and culling of infected dogs. The findings indicate that the annual dog birth rate is also a critical factor in affecting the rabies virus spread.

Rabies is a viral zoonotic infectious disease in warm-blooded animals that has huge public significance [26]. The etiological agent is a virus belonging to the genus Lyssavirus. Canine rabies is the form carried by domestic dogs that is overwhelmingly responsible for approximately 59,000 human deaths per year, mostly in Asia and Africa [22]. Among the total death due to the rabies in the world more than 95% of which occur in Asia and Africa [20]. Among the total human death 45% prevails in south Asian Association for Regional Cooperation (SAARC) countries [24]. Despite being a preventable disease, impact of rabies is increasing day by day, which is a worrisome issue in developing and developed countries [16]. The main reservoir hosts for rabies are domestic dogs in low- and middle-income countries, but wild animals including foxes, skunks and raccoon dogs also maintain rabies in some parts of the world [28]. All species of mammals are susceptible to rabies virus infection, but dogs remain the main carrier of rabies and are responsible for most of the human rabies death world wise [6].

Rabies is an invariably fatal, highly pathogenic zoonotic, yet non notifiable viral disease in Nepal [27, 33]. It is one of the major zoonotic threats in Nepal. Each year, several outbreaks and deaths associated with rabies are reported in the animal sector [25]. Likewise, animal bites, more importantly, dog bites are reported in thousands of human individuals leading to the consumption of a large number of

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pre- and post-prophylactic measures. Rabies has been diagnosed in Nepal for a long time, but the information on its epidemiology, impact, and control remains scattered [32]. Official reports show that each year 100-300 livestock and 10 to 100 humans die of rabies in Nepal, but these numbers very likely underestimate the actual rabies burden [14, 27].

Mathematical models offer a relatively inexpensive way to predict and understand future dynamics of the disease and help to predict whether it becomes an epidemic or not [2, 3]. Leung and Davis studied mathematically the rabies vaccination target for stray dog populations. They presented a method to estimate vaccination target for stray dogs when the dog population is made up of stray, free-roaming and confined dogs [22]. Islam et al. derived a high association between the basic reproduction number with environmental carrying capacity and vice versa. They compared different types of control strategies implemented in Dhaka, Bangladesh [18]. Shigui Ruan has constructed a SEIR type model for the spread of rabies virus among dogs and from dogs to humans and use rabies data in China from 1996 to 2010 for the estimations of parameter values [29]. Zhang et al. proposed a deterministic model to study the transmission dynamics of rabies in China and explored effective control and prevention measure [35]. Bornaa et al. proposed mathematical model to study the dynamics of the transmission of rabies, incorporating predation of dogs by humans [5]. Huang (2019) studied transmission dynamics of rabies for dog, Chinese ferret badger and human interactions in Zhejiang province and found that transmission between dogs and Chinese ferret badger, the quantity of dogs, and the vaccination rate of dogs play important roles in the transmission of rabies [17] . Abdulmajid and Hassan formulated and analyzed a delay differential equations model for assessing the effects of controls and time delay as incubation period on the transmission dynamics of rabies in human and dog population [1]. Hailemichael et al. (2022) have developed a mathematical model by dividing the dog population into two categories : stray dogs and domestic dogs and studied the effect of vaccination and culling on the stray dogs to domestic dogs [15]. Our model focuses the transmission of rabies within dogs where the interventions such as vaccination and sterilizations of dogs are not fully on the action [15]. Kunwar and Verma (2022) proposed an SEIV deterministic mathematical model to describe the rabies transmission dynamics within household and stray dogs in the context of Nepal. Their simulation results concluded that the transmission of rabies virus will be controlled effectively when both vaccination and sterilization of dogs are implememted among household and stray dogs [21].

In this study, we construct and analyze a deterministic model to examine the transmission dynamics of dog-to-human and dog-to-dog rabies infection in Nepal .

1. Model formulation

For the mathematical modelling, we divide the population of both animals and humans into four subclasses; susceptible, exposed, infected and vaccinated. The population of dogs in these subclasses at any time t are denoted by $S_d(t), E_d(t), I_d(t)$, and $V_d(t)$ respectively. Similarly, the population of human in these subclasses are denoted by $S(t), E(t), I(t)$, and $V(t)$.

When a susceptible human individual is bitten by an infectious animal or contacted with the saliva having rabies virus, this human individual becomes exposed class. The available data indicates that the incubation period ranges from 5 days

to 3 years, with a median of 41 days and a mean of 70 days. About 15-20% of those bitten by infected progress to illness and becomes infectious since more and more bitten people are seeking post-exposure prophylaxis (PEP), the recovered rate of infected humans has been increasing in Nepal.

In this model, it is assumed that dogs can transmit the rabies virus to themselves and to each other, also the infected dogs can spread the rabies virus to human via contact, and human do not spread the virus further. The flow diagram of proposed model for dynamics of rabies is illustrated in Figure 1. The following set of eight differential equations captures the dynamics of disease in the proposed model:

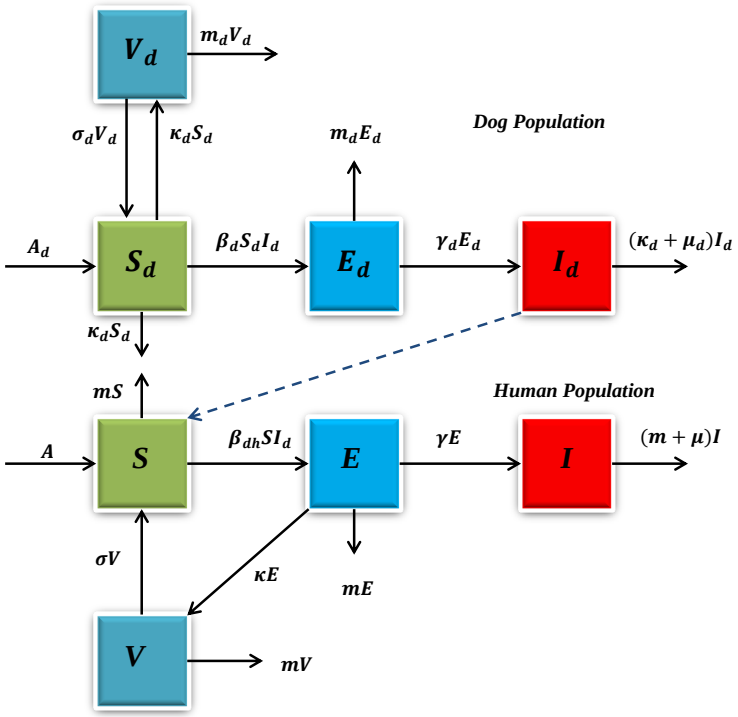

FIGURE 1. Compartmental diagram of the rabies dynamics model of dog-human population

For dog population, we have

$$\begin{aligned}
&\frac{dS_d(t)}{dt} A_d + \sigma_d V_d - \beta_d S_d I_d - (m_d + \kappa_d) S_d, \\
&\frac{dE_d(t)}{dt} = \beta_d S_d I_d - (m_d + \gamma_d) E_d, \\
&\frac{dI_d(t)}{dt} = \gamma_d E_d - (m_d + \mu_d) I_d, \\
&\frac{dV_d(t)}{dt} = \kappa_d S_d - (m_d + \sigma_d) V_d
\end{aligned} \tag{1.1}$$

For human population, we have

$$\begin{aligned}
\frac{dS(t)}{dt} &= A + \sigma V - \beta_{dh} S I_d - mS, \\
\frac{dE(t)}{dt} &= \beta_{dh} S I_d - \gamma E - (m+\kappa)E, \\
\frac{dI(t)}{dt} &= \gamma E - (m+\mu)I, \\
\frac{dV(t)}{dt} &= \kappa E - (m+\sigma)V
\end{aligned} \tag{1.2}$$

with initial conditions: $S_d(0) > 0$, $S(0) > 0$, $E_d(0) \geq 0$, $E \geq 0$, $I_d(0) \geq 0$, $I \geq 0$, $V_d(0) \geq 0$, $V \geq 0$.

TABLE 1. Description of the parameters used in the model for dynamics of rabies

param.	description
A_d, A	Annual birth rate of dog and human respectively.
σ_d, σ	Loss of vaccination immunity for dog and human respectively.
γ_d, γ	Risk factor of clinical outcome of exposed dogs and human respectively
m_d, m	Natural death rate of dog and human respectively.
κ_d, κ	Vaccination rate to dog and human respectively.
β_d	Transmission rate of rabies by the interaction between infectious dogs and susceptible dogs.
μ_d, μ	Rate of death due to rabies for dog and human population
β_{dh}	transmission rate of rabies by the interaction between infectious dogs and susceptible human.

2. Model analysis

We shall establish here the various properties of the model solution. First, we show the positivity and boundedness of the solution. Next, we show the existence and stability of equilibrium points of the model system (1.1) and (1.2).

2.1. **Positivity and boundedness.** We assume that the initial populations are chosen such that all the population components remain positive for all time i.e. $t \geq 0$. To ensure the positivity of the solution, we have the following theorem.

Theorem 2.1. *For* $\{S_d(0), S(0) > 0, E_d(0), E(0) > 0, I_d(0), I(0) > 0, V_d, V(0) > 0\}$*, the solution set* $\{S_d(t), E_d(t), I_d(t), V_d(t), S(t), E(t), I(t), V(t)\} \in \mathbb{R}^8_+$ *of the model system is positive for all* $t \geq 0$ *in* $\mathbb{R}^8_+$.

Further, all the solutions of the proposed model with non-negative initial conditions are bounded for all time.

2.2. **Invariant region.** Here, we demonstrate that the proposed model is correctly laid out biologically and mathematically in the invariant set and establish that the closed region is a positively invariant and the result is stated in the following theorem.

Theorem 2.2. *The solution set of the system* (1.1) *and* (1.2) *is a feasible region defined as* $\Omega = \Omega_d \times \Omega_h$*, where*

$$\Omega_d = \{(S_d, E_d, I_d, V_d) \in \mathbb{R}^4_+, N_d \leq \frac{A_d}{m_d}\}, \quad \Omega_h = \{(S, E, I, V) \in \mathbb{R}^4_+, N \leq \frac{A}{m}\}$$

and moreover, the solution set Ω *is positively invariant.*

2.3. **Existence of equilibrium points.** The model represented by system (1.1) and (1.2) has the following two equilibrium points:

(i) a disease-free equilibrium (DFE) point, and
(ii) an endemic equilibrium (EE) point

2.3.1. *Existence of disease-free equilibrium (DFE) point.* Let us denote disease free-equilibrium point by $E_0(S_d^0, E_d^0, I_d^0, V_d^0, S^0, E^0, I^0, V^0)$. In the absence of rabies, we have $E_d = I_d = E = I = V = 0$. For the dog population, V_d cannot be zero in the case of disease-free equilibrium because susceptible dogs which are vaccinated transfer to vaccinated class.

For the disease-free equiibrium point, we have

$$\frac{S_d}{dt} = 0,\ \frac{E_d}{dt} = 0,\ \frac{I_d}{dt} = 0,\ \frac{V_d}{dt} = 0,\ \frac{S}{dt} = 0,\ \frac{E}{dt} = 0,\ \frac{I}{dt} = 0\ \frac{V}{dt} = 0$$

Solving this equations, we obtain the DFE point $E_0(S_d^0, E_d^0, I_d^0, V_d^0, S^0, E^0, I^0, V^0)$, where

$$S_d^0 = \frac{A_d(m_d + \sigma_d)}{m_d(m_d + \kappa_d + \sigma_d)}, \quad E_d^0 = 0, \quad I_d^0 = 0, \quad V_d^0 = \frac{\kappa_d A_d}{m_d(m_d + \kappa_d + \sigma_d)},$$
$$S^0 = \frac{A}{m}, E^0 = 0, I^0 = 0, V^0 = 0\,.$$

2.3.2. *Basic reproduction number.* The basic reproduction number R_0 measures the average number of new rabies infections produced by one rabies infected dog in a completely susceptible (dog and human) population. We have followed the method of Diekmann et al. and Driessche and Watmough to derive the expression for basic reproduction number R_0 [10, 11, 13]. In this model, the compartments E_d, I_d, E and I are the infected compartments. We use the following notation for derivation of the R_0:

$$f_1 = \frac{dE_d(t)}{dt} = \beta_d S_d I_d - (m_d + \gamma_d)E_d,$$
$$f_2 = \frac{dI_d(t)}{dt} = \gamma_d E_d - (m_d + \mu_d)I_d$$
$$f_3 = \frac{dE(t)}{dt} = \beta_{dh} S I_d - (m + \kappa + \gamma)E,$$
$$f_4 = \frac{dI(t)}{dt} = \gamma E - (m + \mu)I$$

The Jacobian matrix for the system f_1, f_2, f_3, f_4 is

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial E_d} & \frac{\partial f_1}{\partial I_d} & \frac{\partial f_1}{\partial E} & \frac{\partial f_1}{\partial I} \\ \frac{\partial f_2}{\partial E_d} & \frac{\partial f_2}{\partial I_d} & \frac{\partial f_2}{\partial E} & \frac{\partial f_2}{\partial I} \\ \frac{\partial f_3}{\partial E_d} & \frac{\partial f_3}{\partial I_d} & \frac{\partial f_3}{\partial E} & \frac{\partial f_3}{\partial I} \\ \frac{\partial f_4}{\partial E_d} & \frac{\partial f_4}{\partial I_d} & \frac{\partial f_4}{\partial E} & \frac{\partial f_4}{\partial I} \end{bmatrix}$$

$$= \begin{bmatrix} -(m_d+\gamma_d) & \beta_d S_d & 0 & 0 \\ \gamma_d & -(m_d+\mu_d) & 0 & 0 \\ 0 & \beta_{dh} S & -(m+\kappa+\gamma) & 0 \\ 0 & 0 & \gamma & -(m+\mu) \end{bmatrix}$$

For the next-generation matrix method, the Jacobian matrix at the disease free equilibrium point is put into two submatries F and W, where F is the new non-negative infectious matrix and W matrix consists of death, increase state, and other transmissions. Thus, we have

$$J(E_0) = \begin{bmatrix} -(m_d+\gamma_d) & \beta_d S_d^0 & 0 & 0 \\ \gamma_d & -(m_d+\mu_d) & 0 & 0 \\ 0 & \beta_{dh} S^0 & -(m+\kappa+\gamma) & 0 \\ 0 & 0 & \gamma & -(m+\mu) \end{bmatrix} = F - W,$$

where

$$F = \begin{bmatrix} 0 & \beta_d S_d^0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & \beta_{dh} S^0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \quad W = \begin{bmatrix} (m_d+\gamma_d) & 0 & 0 & 0 \\ -\gamma_d & (m_d+\mu_d) & 0 & 0 \\ 0 & 0 & (m+\kappa+\gamma) & 0 \\ 0 & 0 & -\gamma & (m+\mu) \end{bmatrix}.$$

The next generation matrix is

$$G = F\,W^{-1} = \begin{bmatrix} \frac{\beta_d \gamma_d S_d^0}{(m_d+\gamma_d)(m_d+\mu_d)} & \frac{\beta_d S_d^0}{(m_d+\mu_d)} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ \frac{\beta_{dh} \gamma_d S^0}{(m_d+\gamma_d)(m_d+\mu_d)} & \frac{\beta_{dh} S^0}{(m_d+\mu_d)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The basic reproduction number (R_0) is the spectral radius, denoted by $\rho(FW^{-1})$, defined as the largest eigenvalue of FW^{-1}; which is also called the dominant eigenvalue of FW^{-1}. Therefore, the spectral radius FW^{-1} of the next generation matrix is R_0 for the proposed model, and is given by

$$R_0 = \frac{\beta_d \gamma_d S_d^0}{(m_d+\gamma_d)(m_d+\mu_d)}, \quad \text{where} \quad S_d^0 = \frac{A_d(m_d+\sigma_d)}{m_d(m_d+\kappa_d+\sigma_d)}.$$

Therefore,

$$R_0 = \frac{\beta_d A_d \gamma_d (m_d+\sigma_d)}{m_d(m_d+\gamma_d)(m_d+\mu_d)(m_d+\kappa_d+\sigma_d)} \tag{2.1}$$

2.3.3. *Existence of endemic equilibrium (EE) point.* At the endemic equilibrium point, infection is always present in the system. The endemic equilibrium point is determined by solving the system of equations obtained by equating the right-hand side of the equations in (1.1) and (1.2) to zero. If R_0 is greater than unity, then the system has an endemic infection because of the introduction of those with secondary infection. Let $E^*(S_d^*, E_d^*, I_d^*, V_d^*, S^*, E^*, I^*, V^*)$ be the endemic equilibrium point of system (1.1)-(1.2). Thus, for dog population, we find the following expressions: From $\frac{dE_d^*}{dt}\big|_{E^*} = 0$, we obtain

$$\beta_d S_d^* I_d^* = (m_d+\gamma_d) E_d^* \tag{2.2}$$

From $\frac{dI_d^*}{dt}\big|_{E^*} = 0$, we obtain

$$E_d^* = \frac{(m_d+\mu_d)}{\gamma_d} I_d^* \tag{2.3}$$

From $\frac{dV_d^*}{dt}\big|_{E^*} = 0$, we obtain

$$V_d^* = \frac{\kappa_d S_d^*}{(m_d + \sigma_d)}\,. \tag{2.4}$$

From (2.2), we obtain $\beta_d S_d^* I_d^* = (m_d + \gamma_d)E_d^*$ which implies

$$S_d^* = \frac{(m_d + \gamma_d)}{\beta_d I_d^*} E_d^* = \frac{(m_d + \gamma_d)}{\beta_d I_d^*}\big[\frac{(m_d + \mu_d)}{\gamma_d} I_d^*\big].$$

Therefore,

$$S_d^* = \frac{(m_d + \gamma_d)(m_d + \mu_d)}{\beta_d \gamma_d} \tag{2.5}$$

From equation (2.4), we obtain

$$V_d^* = \frac{\kappa_d S_d^*}{(m_d + \sigma_d)} = \frac{\kappa_d}{(m_d + \sigma_d)}\big[\frac{(m_d + \gamma_d)(m_d + \mu_d)}{\beta_d \gamma_d}\big].$$

Therefore,

$$V_d^* = \frac{\kappa_d (m_d + \gamma_d)(m_d + \mu_d)}{\beta_d \gamma_d (m_d + \sigma_d)} \tag{2.6}$$

Again, using the equilibrium condition of endemic equilibrium point for the human population, equating the left hand side of the equations of the system (1.2) to zero, we find the following expressions: From $\frac{dS}{dt}\big|_{E^*} = 0$, we obtain

$$A + \sigma V^* - \beta_{dh} S^* I_d^* - m S^* = 0 \tag{2.7}$$

From $\frac{dE}{dt}\big|_{E^*} = 0$, we obtain

$$\beta_{dh} S^* I_d^* - (m + \kappa + \gamma)E^* = 0 \tag{2.8}$$

From $\frac{dI}{dt}\big|_{E^*} = 0$, we obtain

$$\gamma E^* - (m + \mu)I^* = 0 \tag{2.9}$$

From $\frac{dV}{dt}\big|_{E^*} = 0$, we obtain

$$\kappa E^* - (m + \sigma)V^* = 0 \tag{2.10}$$

Now, from equation (2.9), we obtain $\gamma E^* - (m + \mu)I^* = 0$; therefore,

$$E^* = \frac{(m + \mu)}{\gamma} I^* \tag{2.11}$$

Again, from equation (2.10), we obtain $(m + \sigma)V^* = \kappa E^*$, which implies

$$V^* = \frac{\kappa E^*}{(m + \sigma)} = \frac{\kappa}{(m + \sigma)}\big[\frac{(m + \mu)}{\gamma} I^*\big].$$

Therefore,

$$V^* = \frac{\kappa (m + \mu)}{\gamma (m + \sigma)} I^* \tag{2.12}$$

Next, from equation (2.8), we obtain $\beta_{dh} S^* I_d^* - (m + \kappa + \gamma)E^* = 0$, which implies

$$S^* = \frac{(m + \kappa + \gamma)}{\beta_{dh} I_d^*} E^* = \frac{(m + \kappa + \gamma)}{\beta_{dh} I_d^*}\big[\frac{(m + \mu)}{\gamma} I^*\big].$$

Therefore,

$$S^* = \frac{(m + \mu)(m + \kappa + \gamma)}{\beta_{dh} \gamma I_d^*} I^* \tag{2.13}$$

Again, we derive an expression to calculate I_d^* and I^* using the values of parameters as follows:

From $\frac{dS_d}{dt} = 0$, we obtain

$$\beta_d S_d^* I_d^* = A_d + \sigma_d V_d^* - (m_d + \kappa_d) S_d^* \implies I_d^* = \frac{A_d + \sigma_d V_d^* - (m_d + \kappa_d) S_d^*}{\beta_d S_d^*}$$

which implies

$$I_d^* = \frac{A_d + \sigma_d \frac{\kappa_d (m_d+\gamma_d)(m_d+\mu_d)}{\beta_d \gamma_d (m_d+\sigma_d)} - (m_d + \kappa_d) \frac{(m_d+\gamma_d)(m_d+\mu_d)}{\beta_d \gamma_d}}{\beta_d \frac{(m_d+\gamma_d)(m_d+\mu_d)}{\beta_d \gamma_d}}.$$

Therefore,

$$\begin{aligned} I_d^* = &\Big[A_d \beta_d \gamma_d (m_d + \sigma_d) + \sigma_d \kappa_d (m_d + \gamma_d)(m_d + \mu_d) \\ &- (m_d + \kappa_d)(m_d + \sigma_d)(m_d + \gamma_d)(m_d + \mu_d)\Big] \\ &\div \Big[\beta_d (m_d + \gamma_d)(m_d + \mu_d)(m_d + \sigma_d)\Big] \end{aligned}$$

By (2.7), we obtain

$$A + \sigma\big[\frac{\kappa(m+\mu)}{\gamma(m+\sigma)} I^*\big] - (\beta_{dh} I_d^* + m)\big[\frac{(m+\mu)(m+\kappa+\gamma)}{\beta_{dh}\gamma I_d^*} I^*\big] = 0$$

which implies

$$\Big[\frac{(\beta_{dh} I_d^* + m)(m+\mu)(m+\kappa+\gamma)(m+\sigma) - \sigma\kappa(m+\mu)\beta_{dh} I_d^*}{\beta_{dh}\gamma I_d^* (m+\sigma)}\Big] I^* = A.$$

Therefore,

$$I^* = \frac{A\beta_{dh}\gamma(m+\sigma) I_d^*}{(\beta_{dh} I_d^* + m)(m+\mu)(m+\sigma)(m+\kappa+\gamma) - \sigma\kappa\beta_{dh}(m+\mu) I_d^*}$$

Hence, the unique endemic equilibrium point is $E^*(S_d^*, E_d^*, I_d^*, V_d^*, S^*, E^*, I^*, V^*)$, such that

$$\begin{gathered} S_d^* = \frac{(m_d+\gamma_d)(m_d+\mu_d)}{\beta_d\gamma_d}, \quad E_d^* = \frac{(m_d+\mu_d)}{\gamma_d} I_d^*, \quad V_d^* = \frac{\kappa_d(m_d+\gamma_d)(m_d+\mu_d)}{\beta_d\gamma_d(m_d+\sigma_d)}, \\ S^* = \frac{(m+\mu)(m+\kappa+\gamma)}{\beta_{dh}\gamma I_d^*} I^*, \quad E^* = \frac{(m+\mu)}{\gamma} I^*, \quad V^* = \frac{\kappa(m+\mu)}{\gamma(m+\sigma)} I^*, \end{gathered}$$

where

$$\begin{aligned} I_d^* = &\Big[A_d \beta_d \gamma_d (m_d + \sigma_d) + \sigma_d \kappa_d (m_d + \gamma_d)(m_d + \mu_d) \\ &- (m_d + \kappa_d)(m_d + \sigma_d)(m_d + \gamma_d)(m_d + \mu_d)\Big] \\ &\div \Big[\beta_d (m_d + \gamma_d)(m_d + \mu_d)(m_d + \sigma_d)\Big], \\ I^* = &\frac{A\beta_{dh}\gamma(m+\sigma) I_d^*}{(\beta_{dh} I_d^* + m)(m+\mu)(m+\sigma)(m+\kappa+\gamma) - \sigma\kappa\beta_{dh}(m+\mu) I_d^*} \end{aligned}$$

2.4. **Stability analysis of disease-free equilibrium (DFE) point.**

Theorem 2.3. *The disease-free equilibrium point E_0 of the model represented by (1.1) and (1.2) is locally asymptotically stable if $R_0 < 1$, otherwise unstable.*

Proof. For analyzing local stability of the disease-free equilibrium point, the Jacobian matrix of the model system (1.1)-(1.2) at E_0 is evaluated first. Then, stability is ensured based on the trace's indication and the determinant of the Jacobian matrix at the disease-free equilibrium point. For this, we first derive the Jacobian matrix (J) of the system (1.1)-(1.2) by differentiating each of the equations of the system in terms of the state variables $S_d, E_d, I_d, V_d, S, E, I, V$. We denote the right-hand sides of the equations of the system as $D_S, D_E, D_I, D_V, H_S, H_E, H_I, H_V$ respectively.

We use the following notation for convenience:

$$\begin{aligned}
D_S: &\quad \frac{dS_d(t)}{dt} = A_d + \sigma_d V_d - \beta_d S_d I_d - (m_d + \kappa_d) S_d,\\
D_E: &\quad \frac{dE_d(t)}{dt} = \beta_d S_d I_d - (m_d + \gamma_d) E_d,\\
D_I: &\quad \frac{dI_d(t)}{dt} = \gamma_d E_d - (m_d + \mu_d) I_d,\\
D_V: &\quad \frac{dV_d(t)}{dt} = \kappa_d S_d - (m_d + \sigma_d) V_d\\
H_S: &\quad \frac{dS(t)}{dt} = A + \sigma V - \beta_{dh} S I_d - mS,\\
H_E: &\quad \frac{dE(t)}{dt} = \beta_{dh} S I_d - \gamma E - (m + \kappa) E,\\
H_I: &\quad \frac{dI(t)}{dt} = \gamma E - (m + \mu) I,\\
H_V: &\quad \frac{dV(t)}{dt} = \kappa E - (m + \sigma) V
\end{aligned}$$

Again, using the notation: $a_1 = (m_d + \kappa_d) > 0$, $a_2 = (m_d + \gamma_d) > 0$, $a_3 = (m_d + \mu_d) > 0$, $a_4 = (m_d + \sigma_d) > 0$, $a_5 = (m + \kappa + \gamma) > 0$, $a_6 = (m + \mu) > 0$, and $a_7 = (m + \sigma) > 0$, the system of equations (1.1)-(1.2) reduces to the form

$$\begin{aligned}
D_S: &\quad \frac{dS_d(t)}{dt} = A_d + \sigma_d V_d - \beta_d S_d I_d - a_1 S_d,\\
D_E: &\quad \frac{dE_d(t)}{dt} = \beta_d S_d I_d - a_2 E_d,\\
D_I: &\quad \frac{dI_d(t)}{dt} = \gamma_d E_d - a_3 I_d,\\
D_V: &\quad \frac{dV_d(t)}{dt} = \kappa_d S_d - a_4 V_d\\
H_S: &\quad \frac{dS(t)}{dt} = A + \sigma V - \beta_{dh} S I_d - mS,\\
H_E: &\quad \frac{dE(t)}{dt} = \beta_{dh} S I_d - (a_5 + \gamma) E,\\
H_I: &\quad \frac{dI(t)}{dt} = \gamma E - a_6 I,
\end{aligned}$$

$$H_V: \quad \frac{dV(t)}{dt} = \kappa E - a_7 V$$

To point out the stability condition at DEF point, we first find the Jacobian matrix of the system as follows:

$$J = \begin{bmatrix} -\beta_d I_d - a_1 & 0 & -\beta_d S_d & \sigma_d & 0 & 0 & 0 & 0 \\ \beta_d I_d & -a_2 & \beta_d S_d & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_d & -a_3 & 0 & 0 & 0 & 0 & 0 \\ \kappa_d & 0 & 0 & -a_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_{dh} S & 0 & -\beta_{dh} I_d - m & 0 & 0 & \sigma \\ 0 & 0 & \beta_{dh} S & 0 & \beta_{dh} I_d & -a_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -a_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & \kappa & 0 & -a_7 \end{bmatrix}$$

Now, the Jacobian matrix at disease-free equilibrium point E_0 is

$$J(E_0) = \begin{bmatrix} -a_1 & 0 & -\beta_d S_d^0 & \sigma_d & 0 & 0 & 0 & 0 \\ 0 & -a_2 & \beta_d S_d^0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_d & -a_3 & 0 & 0 & 0 & 0 & 0 \\ \kappa_d & 0 & 0 & -a_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_{dh} S^0 & 0 & -m & 0 & 0 & \sigma \\ 0 & 0 & \beta_{dh} S^0 & 0 & 0 & -a_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -a_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & \kappa & 0 & -a_7 \end{bmatrix} \tag{2.14}$$

Here, the trace of the matrix $J(E_0)$ is

$$\begin{aligned} \text{trace}[J_{E_0}] &= -a_1 - a_2 - a_3 - a_4 - a_5 - a_6 - a_7 - m \\ &= -(m_d + \kappa_d) - (m_d + \gamma_d) - (m_d + \mu_d) - (m_d + \sigma_d) \\ &\quad - (m + \kappa + \gamma) - (m + \mu) - (m + \sigma) - m \\ &= -(4m_d + \kappa_d + \gamma_d + \mu_d + \sigma_d + 4m + \kappa + \gamma + \mu + \sigma) < 0 \end{aligned}$$

Now, the determinant of the Jacobian matrix $J(E_0)$ after expanding and simplifying yields

$$\det[J(E_0)] = m m_d a_5 a_6 a_7 (m_d + \sigma_d + \kappa_d)(m_d + \gamma_d)(m_d + \mu_d)(1 - R_0) \tag{2.15}$$

From (2.15), we note that $\det[J(E_0)] > 0$ when $R_0 < 1$. Consequently, when $R_0 < 1$, then $\text{trace}[J(E_0)] < 0$ and $\det[J(E_0)] > 0$, so that the disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$, otherwise it is unstable. □

2.5. **Stability analysis of endemic equilibrium (EE) point.**

Theorem 2.4. *The endemic equilibrium point E^* of the epidemic model, if exists, it is locally asymptotically stable.*

Proof. The stability of the endemic equilibrium point of the model is established by finding the sign of the eigenvalues of the Jacobian matrix of the model (1.1)-(1.2) at E^*. The Jacobian matrix $J(E^*)$ of the model is evaluated at E^* and is given as

follows:

$$J(E^*) = \begin{bmatrix} -\beta_d I_d^* - a_1 & 0 & -\beta_d S_d^* & \sigma_d & 0 & 0 & 0 & 0 \\ \beta_d I_d^* & -a_2 & \beta_d S_d^* & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_d & -a_3 & 0 & 0 & 0 & 0 & 0 \\ \kappa_d & 0 & 0 & -a_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_{dh} S^* & 0 & -\beta_{dh} I_d^* - m & 0 & 0 & \sigma \\ 0 & 0 & \beta_{dh} S^* & 0 & \beta_{dh} I_d^* & -a_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -a_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & \kappa & 0 & -a_7 \end{bmatrix}$$

$$= \begin{bmatrix} -x_1 - a_1 & 0 & -x_2 & \sigma_d & 0 & 0 & 0 & 0 \\ x_1 & -a_2 & x_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_d & -a_3 & 0 & 0 & 0 & 0 & 0 \\ \kappa_d & 0 & 0 & -a_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & -x_3 & 0 & -x_4 - m & 0 & 0 & \sigma \\ 0 & 0 & x_3 & 0 & x_4 & -a_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -a_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & \kappa & 0 & -a_7 \end{bmatrix}$$

where $x_1 = \beta_d I_d^*$, $x_2 = \beta_d S_d^*$, $x_3 = \beta_{dh} S^*$, $x_4 = \beta_{dh} I_d^*$

The characteristic equation of the Jacobian matrix $J(E^*)$ is $|J(E^*) - \lambda I| = 0$. One root of this characteristic equation is $\lambda = -a_6 = -(m + \mu)$. The next three roots of the characteristic equation are given by $\lambda^3 + \{(a_5 + a_7) + x_5\}\lambda^2 + \{(a_5 + a_7)x_5 + a_5 a_7\}\lambda + (m^2 + m\sigma + m\kappa + m\gamma + \sigma\gamma)x_4 + a_5 a_7 m = 0$ or

$$\lambda^3 + C_1\lambda^2 + C_2\lambda + C_3 = 0 \tag{2.16}$$

where $C_1 = a_5 + a_7 + x_5 > 0$, $C_2 = (a_5 + a_7)x_5 + a_5 a_7 > 0$, and $C_3 = (m^2 + m\sigma + m\kappa + m\gamma + \sigma\gamma)x_4 + a_5 a_7 m > 0$.

The remaining four characteristic roots are given by:

$$\lambda^4 + D_1\lambda^3 + D_2\lambda^2 + D_3\lambda + D_4 = 0 \tag{2.17}$$

where

$$\begin{aligned} D_1 &= \{a_2 + a_3 + a_4 + x_6\} > 0 \\ D_2 &= \{(a_2 a_3 + \gamma_d x_2)(a_2 + a_3)(a_4 + a_7) + a_4 x_1 + m_d(m_d + \sigma_d + \kappa_d)\} > 0 \\ D_3 &= \big\{(a_4 + x_6)(a_2 a_3 + \gamma_d x_2) + (a_2 + a_3)\{a_4 x_1 + m_d(m_d + \sigma_d + \kappa_d)\} \\ &\quad + x_1 x_2 \gamma_d\big\} > 0 \\ D_4 &= \big\{\{a_4 x_1 + m_d(m_d + \sigma_d + \kappa_d)\}(a_2 a_3 + \gamma_d x_2) + x_1 x_2 a_4 \gamma_d\big\} > 0 \end{aligned}$$

Thus, one root of the characteristic equation of the Jacobian matrix $J(E^*)$ is $\lambda = -a_6$ and other seven characteristic roots are given by the equation

$$\{\lambda^3 + C_1\lambda^2 + C_2\lambda + C_3\}\{\lambda^4 + D_1\lambda^3 + D_2\lambda^2 + D_3\lambda + D_4\} = 0,$$

or

$$\phi_7\lambda^7 + \phi_6\lambda^6 + \phi_5\lambda^5 + \phi_4\lambda^4 + \phi_3\lambda^3 + \phi_2\lambda^2 + \phi_1\lambda + \phi_0 = 0 \tag{2.18}$$

which may also be put in the form $\sum_{i=0}^{i=7} \phi_i\lambda^i = 0$, where $\phi_7 = 1$, $\phi_6 = C_1 + D_1$, $\phi_5 = C_2 + C_1 D_1 + D_2$, $\phi_4 = C_3 + C_1 D_2 + C_2 D_1 + D_3$, $\phi_3 = C_1 D_3 + C_2 D_2 + C_3 D_1 + D_4$, $\phi_2 = C_1 D_4 + C_2 D_3 + C_3 D_2 + D_2$, $\phi_1 = C_2 D_4 + C_3 D_3$, $\phi_0 = C_3 D_4$. Since $\phi_i > 0$ for $i = 0, 1, 2, \ldots, 7$, by utilizing the Descartes' rule of sign of roots of polynomial

equation, all the roots of the equation (2.16) have negative real parts. Hence, the endemic equilibrium point E^* is locally asymptotically stable. □

3. Numerical simulation, results and discussion

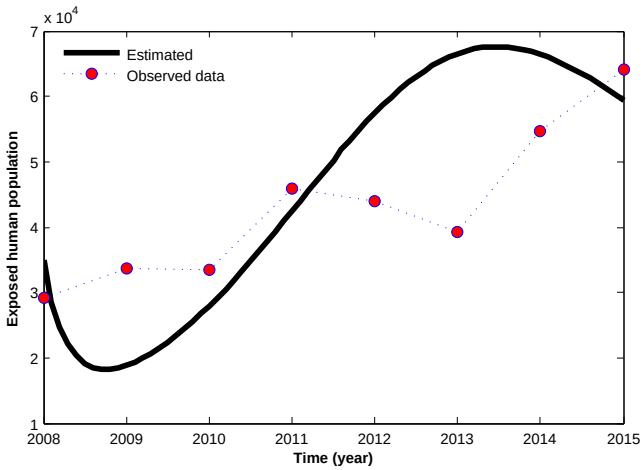

Figure 2. Comparison between the reported human rabies exposed cases in Nepal from 2008 to 2015 and the simulation from the model. The value of parameters are given in the table 2

.

There is currently no fixed database of rabies in Nepal. Therefore, the data in this paper are obtained from previously published literature and reports. We set the beginning of year 2008 as the initial time of our model dynamics. In Nepal, there are approximately 2 million dogs [9]. As we do not have dog vaccination data available for the year of 2008, we assume that about 20% (4×10^5) of the dog population were vaccinated in 2008. In addition for our base case, we assume that about 0.5% dogs were exposed to rabies and 0.01% dogs were infected by rabies.

Number of vials of anti-rabies vaccine consumed in 2008 by human in Nepal is recorded 145,978. Considering the 7 dose per person including wastage and damages, the exposed number of human population is $145978/7 = 20,854$. So, it is reasonable to take the number of exposed human population as 20,000 [31]. The human population of Nepal in 2008 is about 26,882,000 (Country Economy, 2018) [8]. Based on the data, we assume that about 20,000 human population were exposed, 1000 human were infected and about 15,000 vaccinated.

3.1. **Model fitting and validation of the model.** Based on the parameter values listed in the Table 2, we have used model (1.1)-(1.2) to simulate the data and we predicted the trend of exposed to rabies human population in Nepal. For model fitting, we have used exposed rabies cases data of Nepal from 2008 to 2015 for the simulation. However, the availability of observed data of exposed to rabies of human cases is inadequate, the predicted data obtained from the simulation of our model seems to match to the observed data with reasonable parameter values from

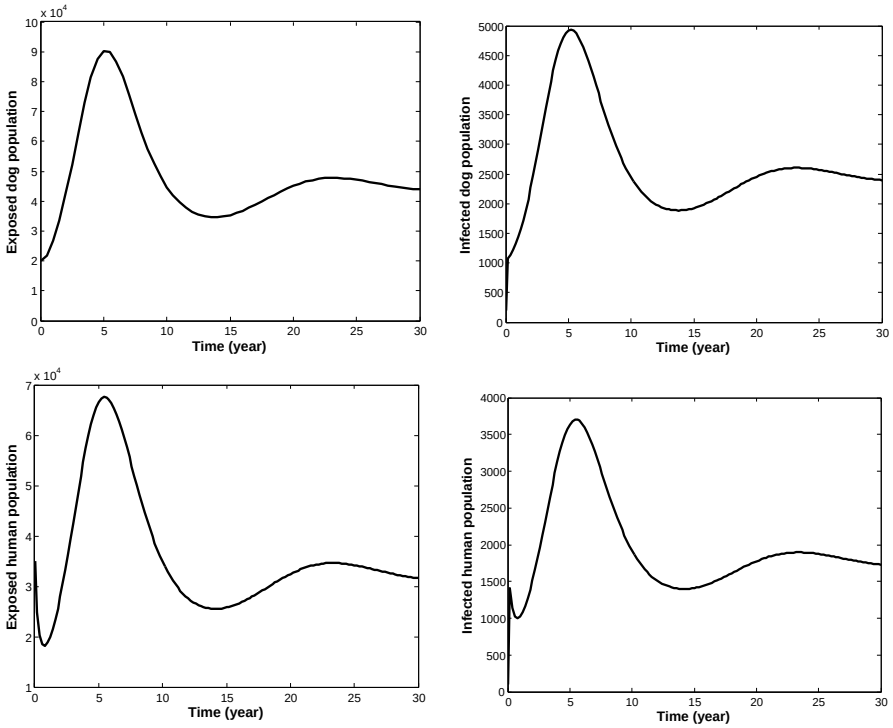

FIGURE 3. Simulation of the model illustrating the endemic equilibrium for baseline parameter values in table 2 for which $R_0 > 1$.

2008 to 2015. Figure 2 indicates that our model provides a good match to the recorded data with reasonable parameter values in Nepal from 2008 to 2015.

Figure 3 demonstrates the trend of epidemic (exposed and infected dog and human cases) with the current control and prevention measures for next 30 years. The nature of graph indicates that the human rabies infection will level off in the next couple of years and then with increase to next 8 years under the current measures. Using the simulated parameter values in Table 2, we compute the value of basic reproduction number as $R_0 = 1.324$ in Nepal. Thus, with the current control and prevention measures, dog and human rabies will persist endemically, which is also justified in Figure 3.

3.2. **Sensitivity analysis for R_0.** We study the impact of model parameter values on the output estimation of the basic reproduction number using the sensitivity analysis. Here, the normalized forward sensitivity index of a variable to a parameter is applied [30]. The normalized forward sensitivity index of a variable to a parameter is defined as the ratio of relative change in the variable to relative change in the parameter.

The normalized forward sensitivity index of a variable U, with respect to parameter p is defined as follows [7]:

$$C_p^U = \frac{p}{U} \times \frac{\partial U}{\partial p}$$

TABLE 2. Parameters used in the simulation of model for dynamics of rabies

parameter value	source
$A_d = 400,000$	[19]
$A = 3,82,934$	Estimated
$\sigma_d = 1$	[29]
$\sigma = 0.08$	Estimated
$\kappa_d = 0.03$	[25]
$\kappa = 1.25$	Estimated
$m_d = 0.2$	[22]
$m = 0.01423$	[33]
$\mu_d = 36.5$	[22]
$\mu = 36.5$	[7]
$\gamma_d = 2$	[32]
$\gamma = 2$	[33]
$\beta_d = 0.0000274$	[25]
$\beta_{dh} = 0.00000171$	[25]
initial dog population	initial human population
$N_d(0) = 20,00,000$	$N_h(0) = 2,68,82,000$
$S_d = 15,89,800$	$S = 2,52,65,000$
$E_d = 0.1\% of N_d(0) = 20,000$	$E = 35,000$
$I_d = 0.01\% of N_d(0) = 200$	$I = 100$
$V_d = 20\% of 20,00,000 = 400,000$	$V = 34,900$

From the model, the sensitivity index of R_0 concerning β_d, γ_d, μ_d, σ_d, m_d, κ_d, and A_d are

$$C_{\beta_d}^{R_0} = +1, \quad C_{\gamma_d}^{R_0} = -\frac{m_d}{(m_d+\gamma_d)}, \quad C_{\mu_d}^{R_0} = -\frac{\mu_d}{(m_d+\mu_d)},$$
$$C_{\sigma_d}^{R_0} = \frac{\sigma_d\kappa_d}{(m_d+\sigma_d)(m_d+\kappa_d+\sigma_d)}, \quad C_{\kappa_d}^{R_0} = -\frac{\kappa_d}{(m_d+\kappa_d+\sigma_d)}, \quad C_{A_d}^{R_0} = +1,$$
$$C_{m_d}^{R_0} = \frac{m_d}{(m_d+\sigma_d)} - \frac{4m_d^3+3(\kappa_d+\sigma_d+\gamma_d)m_d^2+2(\kappa_d+\sigma_d+\mu_d\sigma_d)m_d+\gamma_d\mu_d\sigma_d}{(m_d+\gamma_d)(m_d+\mu_d)(m_d+\kappa_d+\sigma_d)}.$$

The normalized sensitivity indices of R_0 related to the parameters for the rabies model, evaluated at the baseline parameter values are tabulated in Table 3. The parameters are ordered from most sensitive to least. The most sensitive parameters are the transmission rate β_d and dog recruitment rate A_d of the susceptible in Nepal. These are followed by the natural death rate μ_d. The least sensitive parameter is the anti-rabies vaccine inefficiency σ_d. In general, from the Table 3, it can be seen, parameters that have positive sensitivity indices, namely β_d, A_d, σ_d has a positive impact on R_0 in the condition that other parameters remain constant. That is, increase in the values of β_d and A_d can increase in the R_0 value in the same direction or cause an outbreak. In contrast, the increase of parameters whose sensitivity indices is negative $\gamma_d, m_d, \mu_d, \kappa_d$ have negative impact on R_0, minimizing the effect of spread of disease. Therefore, control strategies must focus on a decrease in the parameters β_d and A_d.

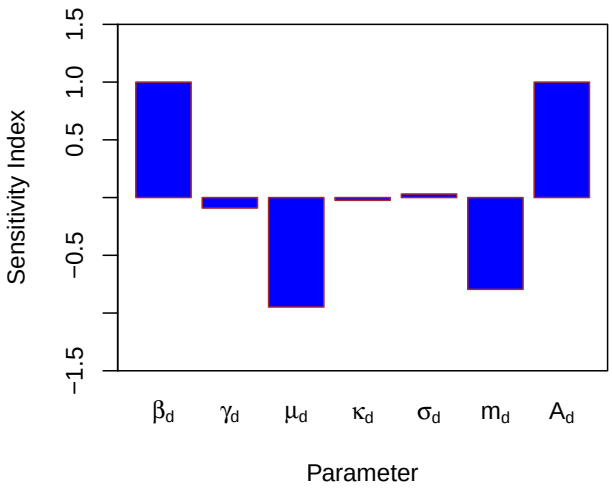

FIGURE 4. Bar diagram of sensitivity indices taking parameter values in table 2 for $R_0 > 1$.

TABLE 3. Sensitivity indices of R_0

Parameter	β_d	γ_d	μ_d	κ_d	σ_d	m_d	A_d
Sensitivity index	1	-0.091	-0.948	-0.024	0.031	-0.795	1

3.3. **Impact of control measures on disease dynamics.**

Dog sterilization. Sterilization refers to the surgical removal of a dog's reproductive organs (spaying for females and neutering for males), does not have a direct impact on rabies transmission in the human population but decreases the recruitment rate effectively to reduces transmission of rabies indirectly. The primary method for preventing rabies in humans is through vaccination, not sterilization. By reducing the population of stray and unowned dogs by sterilization, it can reduce the overall risk of rabies transmission because stray dogs are more likely to be unvaccinated and have limited access to medical care. Figure 7 demonstrates the population dynamics of exposed and infected dog and human population for the different levels of sterilization of dog population. The graph indicates that steriization is effective measure to some extent.

Dog vaccination. The model is simulated taking the different vaccination rates for dogs as variable (Figure 8). Trends of the graph shows that increased dog vaccination rate have an important effect in regard to the rate of rabies exposed and infected dogs and human population. Furthermore, increasing the vaccination rate (κ_d) of dogs within the model decreased the number of exposed and infected dogs and human.

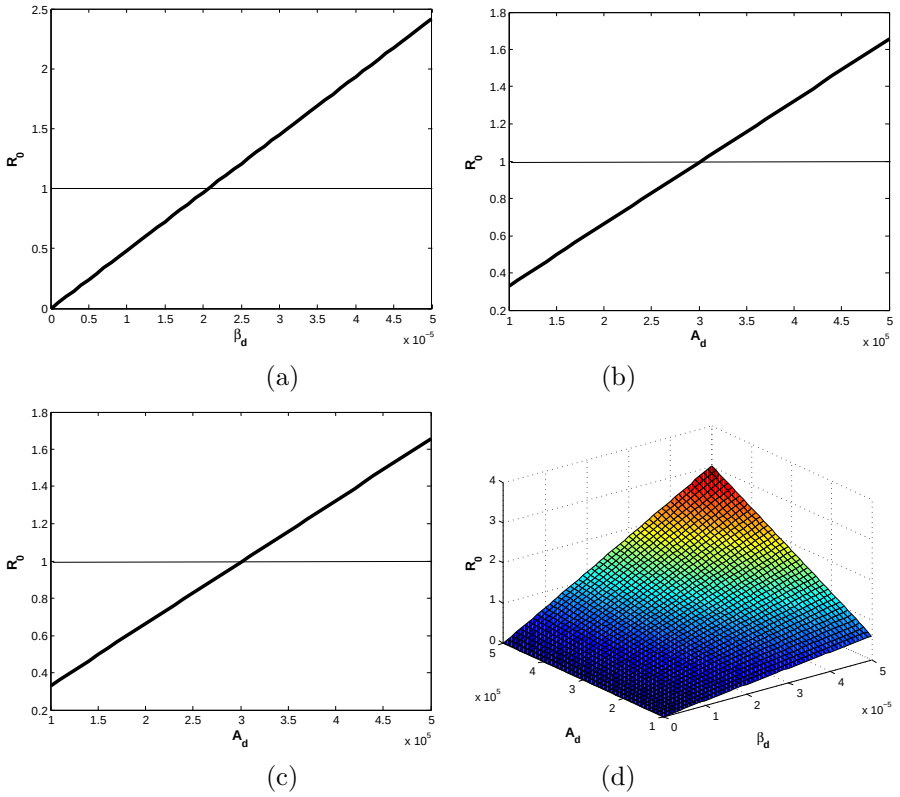

FIGURE 5. Influence of parameters on R_0 (a) versus β_d; (b) versus dog recruitment rate A_d; (c) versus β_d and σ_d; (d) versus β_d and A_d.

3.4. **Culling.** Culling involves the systemic and deliberate killing of dogs to reduce the spread of rabies virus. In our model, the per capita rate of dog culling, c_d can be introduced taking $m_d \to m_d + c_d$ and $\mu_d \to \mu_d + c_d$. In Figure **??**, we present the impact of change in m_d and μ_d as $m_d + c_d$ and $\mu_d + c_d$ in the basic reproduction number R_0. The plot of figure indicates that there is a great impact of culling. Hence, coverage of dog culling significantly decreases the rabies dog population as well as human rabies cases.

While culling has been practiced as a method of control rabies in Nepal, it is often met with opposition from animal welfare and conservation groups. Additionally, controversy arises due to ethical concerns and the potential ecological impacts of culling. Reducing the population subsequent number of dog population (either stray or pet) can disrupt ecosystems and may not be a humane method of rabies control. So, we perfer to focus on other measure as well simultaneously such as public education and other non-lethal methods to prevent the spread of rabies virus.

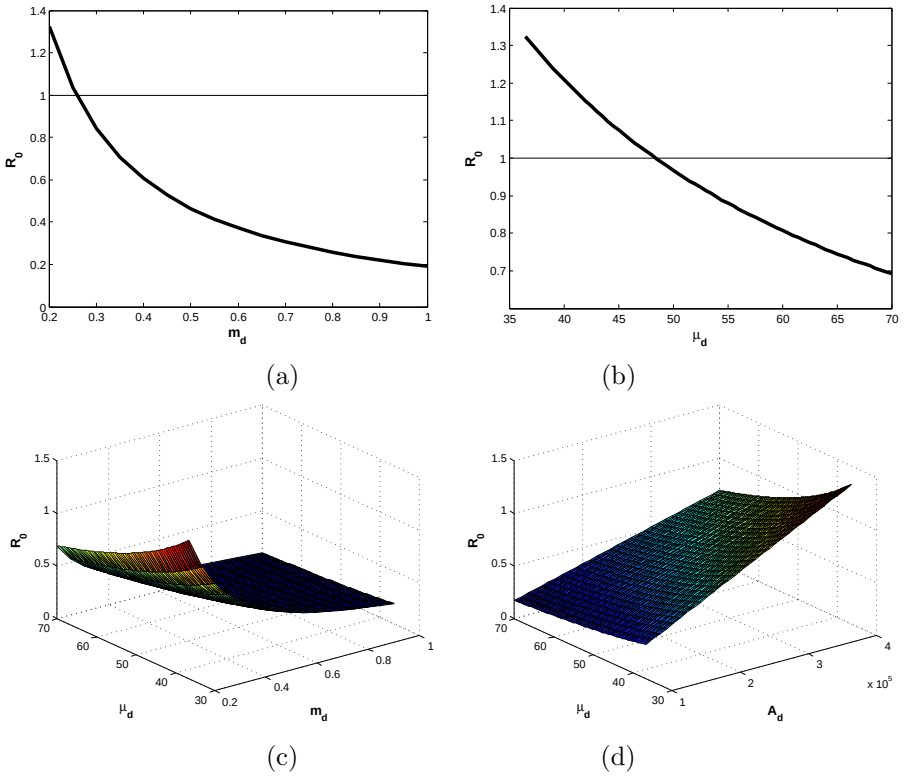

FIGURE 6. Influence of parameters on R_0 (a) versus m_d; (b) versus μ_d; (c) versus m_d and μ_d; (d) versus A_d and μ_d.

4. Conclusion

We employed a mathematical compartmental deterministic approach to investigate the dynamics of rabies transmission from dogs to humans and from dogs to dogs. The model was created to illustrate how rabies spreads from dogs to human beings. In this investigation, only susceptible animals and exposed human populations were considered to have undergone immunizations. Because of the challenges involved in identifying affected dogs, it is not currently feasible to immunize them.

We examine the fundamental properties of the epidemic model in terms of boundedness and positivity of the solution of the model, and we conclude that the solution of the state variables is positive at all times for any positive values of the initial condition. Analytically, we determine expressions for both the disease-free and endemic-equilibrium points, and we analyze their stability. The numerical simulation using acceptable parameter values confirmed the results. We demonstrate that the endemic-equilibrium and disease-free equilibrium points are both locally asymptotically stable.

Our research demonstrates that vaccination, along with the culling of infected dogs, sterilization of dogs to reduce the number of puppies born each year, are the most effective methods for reducing the spread of rabies among dogs and humans. Additionally, the dogs may receive vaccination together when they are captured

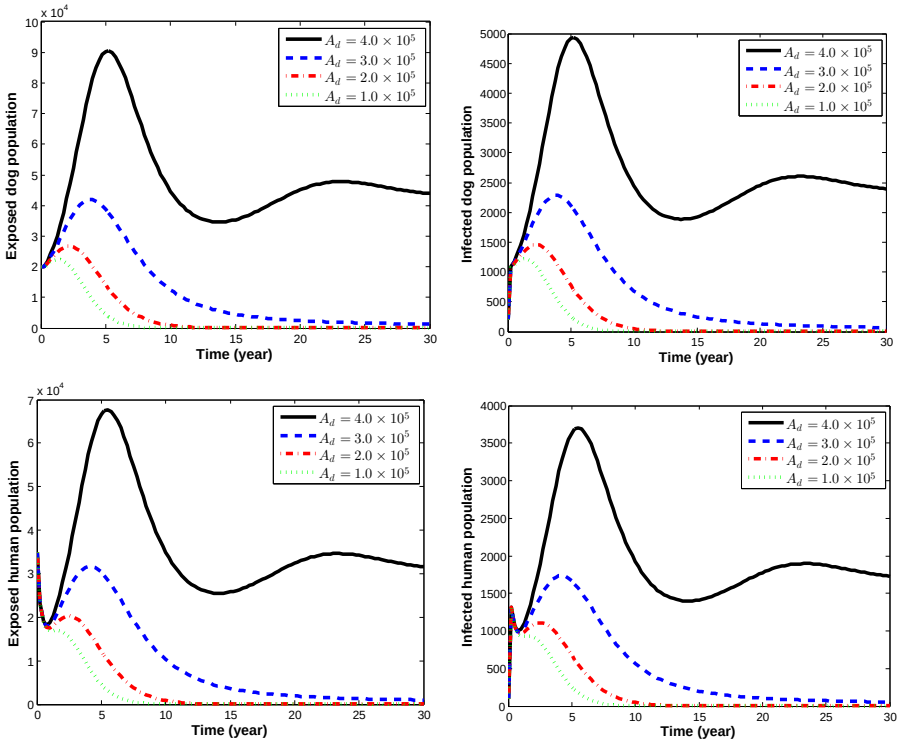

FIGURE 7. Simulation of the effect of dog sterilization on the exposed and infected dog and human population

for sterilization, delivering a dual-pronged approach for rabies management. Based on the results of our research study, we expect that the government may create a program to eradicate rabies. We strongly advise estimating the accurate dog population in order to determine the annual dog birth rate and sterilization levels. The development of a sustainable vaccination, culling, and sterilization plan for the dog population is dependent upon accurate data.

Future modelling exercise may consider the potential role of habitat heterogeneity and its effect on the territorial size and configuration, group size and composition, and the potential indirect effect on transmission dynamics. Our model is limited to the modelling of rabies dynamics regarding vaccination of dog population alone, and not both dog and cattle population. The interventions that proved to reduce rabies prevalence in dog population is not necessarily reduce transmission from dogs to cattle.

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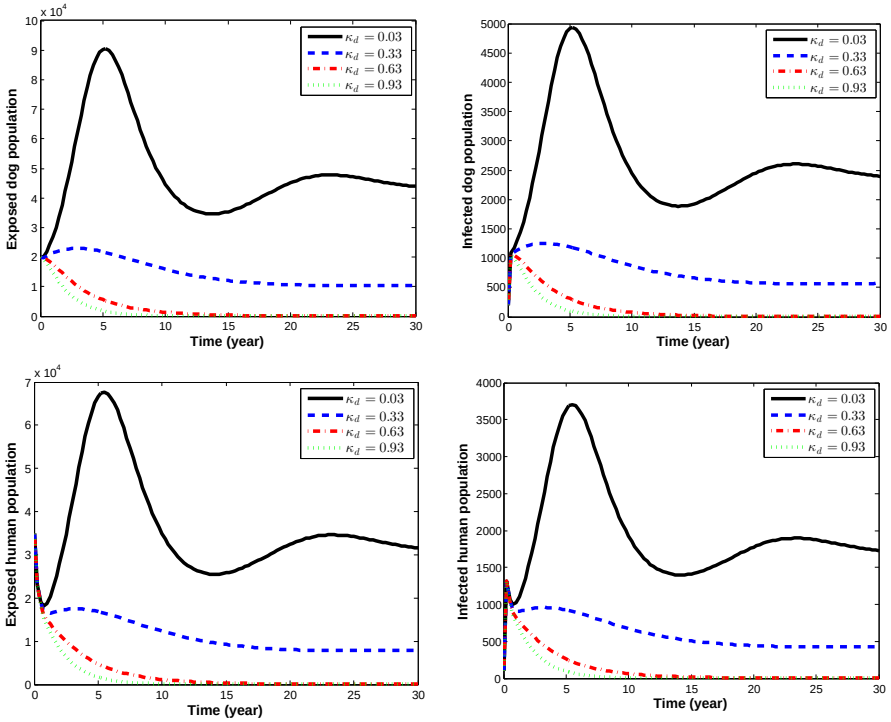

FIGURE 8. Simulation of effect of vaccination on the exposed and infected dog and human population.

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Vijai Shanker Verma
Department of Mathematics & Statistics, Deen Dayal Upadhyaya Gorakhpur University, India
Email address: vsverma.mathstat@ddugu.ac.in, drvsverma01@gmail.com

Laxman Bahadur Kunwar
Department of Mathematics, Thakur Ram Multiple Campus, Tribhuvan University, Birgunj, Nepal
Email address: laxman.kunwar@trmc.tu.edu.np