# MATHEMATICAL MODEL OF FOOT AND MOUTH DISEASE CONSIDERING VACCINATION DISINFECTION AND EARLY QUARANTINE

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Abstrak: Penyakit Mulut dan Kuku (PMK) adalah penyakit yang sangat menular yang dapat menginfeksi semua hewan berkuku terbelah. PMK adalah salah satu penyakit virus menular yang paling penting di dunia. Penyakit ini bertanggung jawab atas kerugian internasional dalam produksi dan perdagangan ternak. Pada artikel ini, kami merumuskan model matematika untuk penyebaran PMK di peternakan kambing yang mempertimbangkan intervensi karantina dini, vaksinasi, dan desinfeksi. Model yang dibangun dinyatakan sebagai sistem persamaan diferensial biasa yang terdiri dari delapan variabel keadaan. Kami menentukan bilangan reproduksi dasar menggunakan metode matriks generasi berikutnya. Hasil simulasi numerik kami menunjukkan bahwa vaksinasi memiliki peran yang sangat penting dalam mengendalikan penyebaran PMK dan mengurangi angka reproduksi dasar. Selain itu, intervensi karantina pada kambing laten dan infeksius juga efektif dalam mengendalikan penyebaran PMK. Angka reproduksi dasar juga dapat ditekan dengan intervensi disinfeksi dan karantina. Oleh karena itu, kami merekomendasikan untuk melaksanakan program vaksinasi, skrining dan disinfeksi secara rutin. Selain itu, peternak sebaiknya diberikan edukasi agar memiliki kemampuan untuk mengidentifikasi kambing yang terpapar PMK sehingga karantina dapat dilakukan sejak dini.

*Kata Kunci:* model matematika, penyakit mulut dan kuku, vaksinasi, desinfeksi, karantina dini.

**Abstract:** Foot and Mouth Disease (FMD) is a highly contagious disease that can infect all cloven hoofed animals. FMD is one of the most important infectious viral diseases in the world. This disease is responsible for international losses in livestock production and trade. In this article, we formulate a mathematical model for the spread of FMD in goat farms that considers early quarantine, vaccination, and disinfection interventions. The model constructed is expressed as a system of ordinary differential

equations consisting of eight state variables. We determine the basic reproduction number using the next-generation matrix method. Our numerical simulation results show that vaccination has a very crucial role in controlling the spread of FMD and reducing the basic reproduction number. In addition, quarantine interventions for latent and infectious goats are also effective in controlling the spread of FMD. The basic reproduction number can also be suppressed by disinfection and quarantine interventions. Therefore, we recommend implementing routine vaccination, screening and disinfection programs. In addition, farmer should be given education so that they have the ability to identify goats exposed to FMDV so that quarantine can be carried out early.

*Keywords:* mathematical models, foot and mouth disease, vaccination, disinfection, early quarantine.

#### PENDAHULUAN

There are more than 100 species that have been infected with the FMD virus (Weaver et al. 2013). Livestock including cattle, buffalo (*Bubalus bubalis*), pigs, sheep, and goats are susceptible to infection and can spread disease (Tesfaye 2020). The cause of FMD is a virus that belongs to the Aphthovirus genus of the Picornaviridae family (Dabasa and Abunna 2021). It is known that there are seven serotypes of the Foot and Mouth Disease Virus (FMDV), namely O, A, C, Asia1, SAT1, SAT2, and SAT3 (Tesfaye 2020). The most widely distributed serotypes are serotypes O and A. The SAT 1, SAT 2, and SAT 3 serotypes are usually specified to Africa, while the Asia 1 serotype is only found in Asia. Presently, the spread of FMD caused by serotype C infection has decreased and its distribution has become very limited (Dabasa and Abunna 2021). In Southeast Asia, Serotype O is the main cause of FMD cases, although serotypes A and Asia 1 have driven outbreaks in most nations in the region but Indonesia (Blacksell et al. 2019).

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The most typical ways of spreading FMD are through direct contact between infectious and susceptible animals, providing of contaminated animal products to susceptible livestock, and indirect contact, including contact with the virus from infected animals attached to persons, livestock vehicles, fomites, or wild animals. Another spread mechanism is the transport of the virus by the wind which has the potential to cause spread over considerable distances (Alexandersen et al. 2003). In known, infection happens via aerosolization of the virus. Nevertheless. Transmission can also occur through mucous membranes. This transmission needs 10,000 times more virus (Weaver et al. 2013).

The clinical manifestation of FMD can look like other diseases. This causes the case of misdiagnosis (Weaver et al. 2013). Clinical signs of FMD are fever for several days, lack of appetite, and lesions in the mouth and four legs. Lesions are in the form of blisters on the surface of the mucous membranes of the mouth, including the tongue, gums, inner cheeks, and lips. Lesions can also be seen in the nostrils and their surroundings. On the feet, the lesions are visible on the heels, nail gaps, and along the coronary bands of the nails. In some cases, the symptoms of FMD can be confused with foot rot (Adjid 2020). In general, animals showing acute infection recover within 7-14 days (Weaver et al. 2013).

There are several efforts to control FMD disease, including increasing the use of vaccines and improving livestock management practices (Weaver et al. 2013). Nowadays, the procedure for diagnosing FMD is progressing towards a cellular version, which seeks at the on-site diagnosis of FMDV. In addition, another diagnostic specifically designed for on-site diagnosis is the lateral flow test immunochromatographic test strip. This technique is considered to have several benefits, including on-site diagnostic tests can be easily carried out by untrained personnel including farmers, and results can be obtained in a few minutes (Wong et al. 2020). In this article, we develop a mathematical model to study the impact of several interventions on the spread of FMD, including disinfection, early detection and quarantine, and vaccination.

#### **RESEARCH METHODS**

This research was carried out according to the following stages:

### **Specify Model Assumptions**

The following are the assumptions of the model used.

- 1. In this article, we consider the case of FMD in livestock, especially goats.
- 2. We divided the goat population into seven compartments, namely susceptible goats

(S), exposed goats (L) (infected but not yet infectious), quarantined exposed

goats  $(E_q)$ , infectious goats (I), quarantined infectious goats  $(I_q)$ , immune goats (R), and quarantined immune goats  $(R_q)$ . To accommodate the indirect transmission, we include virus compartment (O) in our model. The virus compartment represents the virus on the surface of the object.

- 3. The recruitment rate of the goats is constant.
- 4. Vaccination and recovery from FMD only provide temporary immunity.
- 5. Susceptible goats can become infected after contact with infectious goats and viruses on object surfaces.
- 6. Natural deaths and deaths due to FMD are ignored.
- 7. Quarantine is carried out strictly so that the no viruses produced by the quarantined infectious goats comes out of the quarantine area.

### **Mathematical Model Formulation**

Based on the assumptions used, we constructed a compartment diagram as shown in Figure 1.

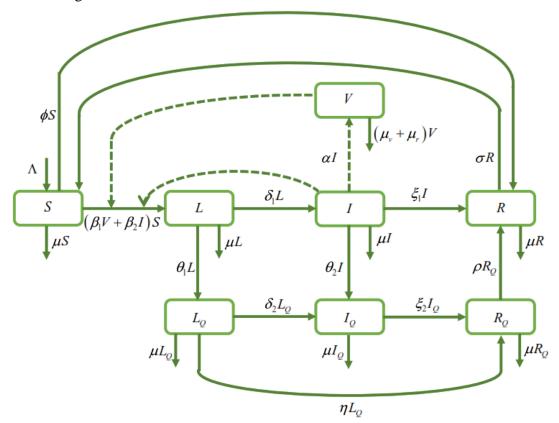


Figure 1. Compartment Diagram

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Based on assumptions and compartment diagrams, we construct a mathematical model as follows.

$$\begin{aligned} \frac{dS}{dt} &= \Lambda + \sigma R - \left(\beta_1 V + \beta_2 I\right) S - \left(\mu + \phi\right) S, \\ \frac{dL}{dt} &= \left(\beta_1 V + \beta_2 I\right) S - \left(\mu + \theta_1 + \delta_1\right) L, \\ \frac{dI}{dt} &= \delta_1 L - \left(\mu + \theta_2 + \xi_1\right) I, \\ \frac{dR}{dt} &= \phi S + \xi_1 I + \rho R_{\varrho} - \left(\mu + \sigma\right) R, \\ \frac{dL_{\varrho}}{dt} &= \theta_1 L - \left(\mu + \eta + \delta_2\right) L_{\varrho}, \\ \frac{dI_{\varrho}}{dt} &= \delta_2 L_{\varrho} + \theta_2 I - \left(\mu + \xi_2\right) I_{\varrho}, \\ \frac{dR_{\varrho}}{dt} &= \eta L_{\varrho} + \xi_2 I_{\varrho} - \left(\mu + \rho\right) R_{\varrho}, \\ \frac{dV}{dt} &= \alpha I - \left(\mu_V + \mu_r\right) V, \end{aligned}$$
(1)

where the definition of all parameters of system (1) corresponds to those given in Table 1.

## **Determination of Disease-free Equilibrium Point**

The equilibrium point is obtained by solving system (1) when the left-hand side is equal to zero. Therefore, the equilibrium point is the solution of system (2).

$$0 = \Lambda + \sigma R - (\beta_{1}V + \beta_{2}I)S - (\mu + \phi)S,$$
  

$$0 = (\beta_{1}V + \beta_{2}I)S - (\mu + \theta_{1} + \delta_{1})L,$$
  

$$0 = \delta_{1}L - (\mu + \theta_{2} + \xi_{1})I,$$
  

$$0 = \phi S + \xi_{1}I + \rho R_{\varrho} - (\mu + \sigma)R,$$
  

$$0 = \theta_{1}L - (\mu + \eta + \delta_{2})L_{\varrho},$$
  

$$0 = \delta_{2}L_{\varrho} + \theta_{2}I - (\mu + \xi_{2})I_{\varrho},$$
  

$$0 = \eta L_{\varrho} + \xi_{2}I_{\varrho} - (\mu + \rho)R_{\varrho},$$
  

$$0 = \alpha I - (\mu_{V} + \mu_{r})V.$$
(2)

After substituting I = 0 into system (2), we get a FMD-free equilibrium point which is expressed as

$$E_{0} = \left(S^{*}, L^{*}, I^{*}, R^{*}, L_{Q}^{*}, I_{Q}^{*}, R_{Q}^{*}, V^{*}\right) = \left(\frac{(\sigma + \mu)\Lambda}{(\phi + \sigma + \mu)\mu}, 0, 0, \frac{\phi\Lambda}{(\phi + \sigma + \mu)\mu}, 0, 0, 0, 0\right).$$

#### **Determination of The Basic reproduction number**

We use the next-generation matrix method as described in (van den Driessche and Watmough 2002) to determine the basic reproduction number. In system (1), there are seven infected compartments, namely L, E, I, R,  $L_Q$ ,  $E_Q$ ,  $R_Q$ , and V. Therefore, two column matrices are obtained, i.e., one matrix is related to new infections while the other column matrix is related to transitions that occur in the infected compartment. These matrices are as follows.

$$H = \begin{pmatrix} (\beta_{1}V + \beta_{2}I)S \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \text{ and } K = \begin{pmatrix} (\mu + \theta_{1} + \delta_{1})L \\ (\mu + \theta_{2} + \xi_{1})I - \delta_{1}L \\ (\mu + \theta_{2} + \xi_{1})I - \delta_{1}L \\ (\mu + \theta_{2} + \xi_{2})L_{0} - \theta_{1}L \\ (\mu + \eta + \xi_{2})L_{0} - \theta_{1}L \\ (\mu + \xi_{2})I_{0} - \delta_{2}L_{0} - \theta_{2}I \\ (\mu + \rho)R_{0} - \eta L_{0} - \xi_{2}I_{0} \\ (\mu_{V} + \mu_{r})V - \alpha I \end{pmatrix}.$$

The Jacobian matrices of H and K at FMD-free equilibrium point  $E_0$  are respectively given by

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and

$$J_{K} = \begin{pmatrix} \left(\mu + \theta_{1} + \delta_{1}\right) & 0 & 0 & 0 & 0 & 0 & 0 \\ -\delta_{1} & \left(\mu + \theta_{2} + \xi_{1}\right) & 0 & 0 & 0 & 0 & 0 \\ 0 & -\xi_{1} & \left(\mu + \sigma\right) & 0 & 0 & -\rho & 0 \\ -\theta_{1} & 0 & 0 & \left(\mu + \eta + \delta_{2}\right) & 0 & 0 & 0 \\ 0 & -\theta_{2} & 0 & -\delta_{2} & \left(\mu + \xi_{2}\right) & 0 & 0 \\ 0 & 0 & 0 & -\eta & -\xi_{2} & \left(\mu + \rho\right) & 0 \\ 0 & -\alpha & 0 & 0 & 0 & 0 & \left(\mu_{V} + \mu_{r}\right) \end{pmatrix}.$$

The eigenvalues of the next generation matrix  $(J_H)(J_K^{-1})$  are the roots of the characteristic equation (3).

$$P(\lambda) = \lambda^{6} \left( \lambda - \left( \frac{\beta_{2} \delta_{1} S^{*}}{\left(\mu + \theta_{1} + \delta_{1}\right) \left(\mu + \theta_{2} + \xi_{1}\right)} + \frac{\beta_{1} \delta_{1} S^{*} \alpha}{\left(\mu + \theta_{1} + \delta_{1}\right) \left(\mu + \theta_{2} + \xi_{1}\right) \left(\mu_{V} + \mu_{r}\right)} \right) \right).$$
(3)

According to (van den Driessche and Watmough 2002), the basic reproduction number is the dominant eigenvalue of the next-generation matrix. Therefore, we obtain  $R_0$  as follows.

$$\begin{split} R_0 &= \frac{\beta_2 \delta_1 S^*}{\left(\mu + \theta_1 + \delta_1\right) \left(\mu + \theta_2 + \xi_1\right)} + \frac{\beta_1 \delta_1 S^* \alpha}{\left(\mu + \theta_1 + \delta_1\right) \left(\mu + \theta_2 + \xi_1\right) \left(\mu_V + \mu_r\right)} \\ &= \frac{\beta_2 \delta_1 \left(\sigma + \mu\right) \Lambda}{\left(\mu + \theta_1 + \delta_1\right) \left(\mu + \theta_2 + \xi_1\right) \left(\phi + \sigma + \mu\right) \mu} + \frac{\beta_1 \delta_1 \alpha \left(\sigma + \mu\right) \Lambda}{\left(\mu + \theta_1 + \delta_1\right) \left(\mu + \theta_2 + \xi_1\right) \left(\phi + \sigma + \mu\right) \mu}. \end{split}$$

## **Conducting numerical experiment**

Numerical experiments were conducted using the parameter values listed in Table 1. Some parameter values were collected from various scientific sources. For parameters whose values are not found in various scientific sources, we use assumed values but still consider the biological aspects.

| Symbol  | Definition   | Values           | Unit                                    | Source                    |  |  |
|---------|--|------------------|---|---------------------------|--|--|
| Λ       | Recruitment rate of the Goats                                    | 1                | Goat<br>day                             | Assumptions               |  |  |
| $eta_1$ | FMD transmission rate from infectious goats to susceptible goats | 10 <sup>-6</sup> | $\frac{1}{\text{Goat}\times\text{day}}$ | (Gashirai et<br>al. 2020) |  |  |

Tabel 1. Definition of Parameters

| $eta_2$                         | FMDV infection rate   | 2×10 <sup>-7</sup>              | $\frac{1}{\text{Virus} \times \text{day}}$ | Assumptions                                     |
|---------------------------------|---|---------------------------------|--|---|
| $\phi$                          | Vaccination rate  | $\frac{1}{4 \times 4 \times 7}$ | $\frac{1}{day}$                            | Assumptions                                     |
| $\sigma$                        | The rate of loss of immunity to FMD   | $\frac{1}{6 \times 4 \times 7}$ | $\frac{1}{day}$                            | (Ringa and<br>Bauch 2014)                       |
| μ                               | Goat harvesting rate  | $\frac{1}{365 \times 1.5}$      | $\frac{1}{day}$                            | Assumptions                                     |
| $	heta_1$                       | Latent goat quarantine rate   | $\frac{1}{7}$                   | $\frac{1}{day}$                            | Assumptions                                     |
| $\delta_{\scriptscriptstyle 1}$ | Transition rate from latent goat to infectious goat                               | 0.25                            | $\frac{1}{day}$                            | (Ringa and<br>Bauch 2014)                       |
| $	heta_2$                       | Infectious goat quarantine rate   | $\frac{1}{7}$                   | $\frac{1}{day}$                            | Assumptions                                     |
| $\xi_1$                         | Infectious goat recovery rate   | 0.143                           | $\frac{1}{day}$                            | (Ringa and<br>Bauch 2014)                       |
| ρ                               | The rate of releasing the quarantined immune goat                                 | $\frac{1}{2}$                   | $\frac{1}{day}$                            | Assumptions                                     |
| η                               | Quarantined latent goat recovery rate   | $\frac{1}{1 \times 7}$          | $\frac{1}{day}$                            | Assumptions                                     |
| $\delta_2$                      | Transition rate from quarantined<br>latent goat to quarantined<br>infectious goat | 0.25                            | $\frac{1}{day}$                            | (Ringa and<br>Bauch 2014)                       |
| $\xi_2$                         | Quarantined infectious goat recovery rate   | 0.143                           | $\frac{1}{day}$                            | (Ringa and<br>Bauch 2014)                       |
| $\mu_{_V}$                      | FMDV natural death rate   | $\frac{1}{4}$                   | $\frac{1}{day}$                            | (Bartley,<br>Donnelly, and<br>Anderson<br>2002) |
| $\mu_r$                         | FMDV mortality rate due to disinfection   | $\frac{1}{3}$                   | $\frac{1}{day}$                            | Assumptions                                     |
| α                               | FMDV excretion rate   | $10^4$                          | $\frac{FMDV}{\text{Goat}\times\text{day}}$ | (Gashirai et<br>al. 2020)                       |

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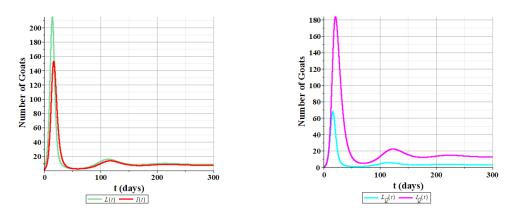
#### **RESULTS AND DISCUSSION**

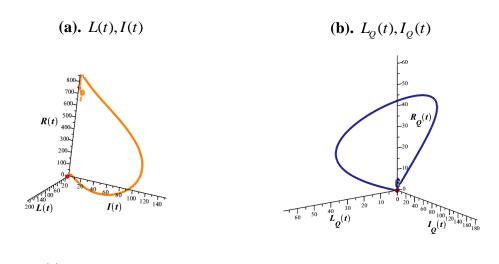
We have determined the basic reproduction number employing the nextgeneration matrix. Based on Theorem 2 in (van den Driessche and Watmough 2002), we obtain the following theorem.

**Theorem 1.** The FMD -free equilibrium point is stable if  $R_0 < 1$ . If  $R_0 > 1$ , then the FMD-free equilibrium point is unstable.

The first numerical simulation is carried out using the parameter values delivered in Table 1. After substituting the parameter values into  $R_0$ , we obtain  $R_0 = 1.92 > 1$ . According to Theorem 1, the FMD-free equilibrium point is unstable. This result is supported by the numerical solution shown in Figure 2. The solution curve of L(t) shown in Figure 2(a) indicates that the number of goats that are still in the latent period reaches 230 before day 50. Meanwhile, the number of infectious goats reaches 150 when the number of goats that are still in the latent period begins to decline as shown by the solution curve of I(t) displayed in Figure 2(a). Besides, the solution curve of  $L_Q(t)$  displays the number of goats that are still in the latent period. It is clear that its peak is around 70. This number is much lower than the peak of the number of quarantined infectious goats as indicated by the solution curve of  $I_Q(t)$  and  $I_Q(t)$  shown in Figure 2(b). It is clear that the solution curves of L(t), I(t),  $L_Q(t)$  and  $I_Q(t)$  do not go to zero.

Figure 2(c) illustrates the trajectory of the solution in the LIR space with the red dot being the initial value. It is clear that the solution trajectory does not go to I(t) = 0 and L(t) = 0. In addition, Figure 2(d) displays that the trajectory of the solution does not go to the point (0,0,0). The results shown in Figure 2 indicates that FMD will not be successfully eradicated.



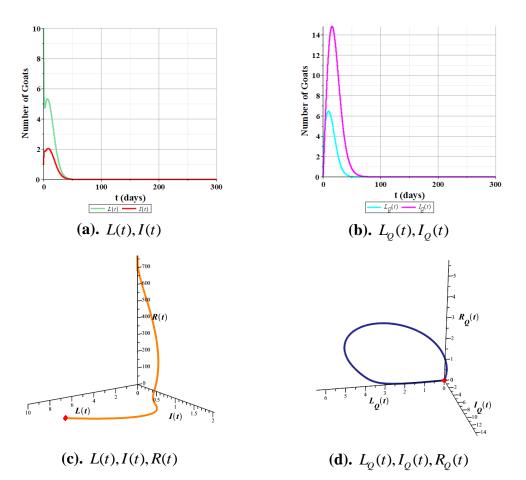


(c). L(t), I(t), R(t) (d).  $L_Q(t), I_Q(t), R_Q(t)$ Figure 2. The Trajectory and Solution Curves of System (1) for  $R_0 = 1.92 > 1$ 

Next, we conduct numerical simulations by adjusting the values of several parameters, namely  $\theta_1, \theta_2, \phi, \mu_r$ . The values used for these four parameters are greater than those used in the first simulation, i.e.,  $\theta_1 = \frac{1}{2}, \theta_2 = \frac{1}{2}, \phi = \frac{1}{4 \times 7}, \mu_r = \frac{1}{2}$ . Increasing the value of the parameters describes the improvement in quarantine, vaccination, and disinfection interventions. In the second simulation, we get  $R_0 = 0.13 < 1$ . Therefore, the FMD-free equilibrium point is stable. This result is consistent with the numerical solution shown in Figure 3. It can be seen that the peak of the number of latent goats and the peak of the number of infectious goats are much lower than the result obtained in the first simulation. Actually, the solution curves of L(t) and I(t) shown in Figure 3(a) touched zero on day 50. Meanwhile, the same thing is seen in the peak number of the quarantined latent goats and the peak number of quarantined infectious goats. The peak of the  $L_Q(t)$  and  $I_Q(t)$  displayed in Figure 3(b) is far below the peak of the  $L_Q(t)$  and  $I_Q(t)$  solution curves are toward zero.

Figure 3(c) shows the solution trajectory in *LIR* space. It can easily be identified that the solution trajectory leads to I = 0 and L = 0. Meanwhile, Figure 3(d) shows that the solution trajectory goes to the point (0,0,0). The results of the second simulation show a situation where FMD will be successfully eradicated.

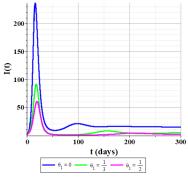
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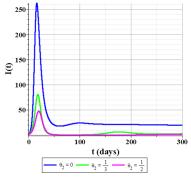
**Figure 3.** The Trajectory and Solution Curves of System (1) for  $R_0 = 0.13 < 1$ 

## **Impact of control measures**

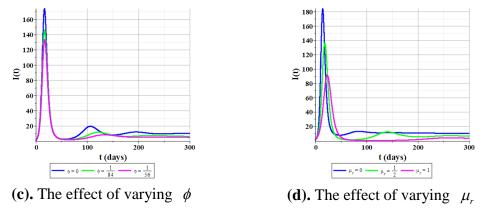
In this subsection, we perform several numerical simulations by varying the value of one parameter while the other parameters are as given in Table 1.



(a). The effect of varying  $\theta_1$ 



**(b).** The effect of varying  $\theta_2$ 



**Figure 4.** The Solution Curves of System (1) with Varying  $\theta_1, \theta_2, \phi, \mu_r$ 

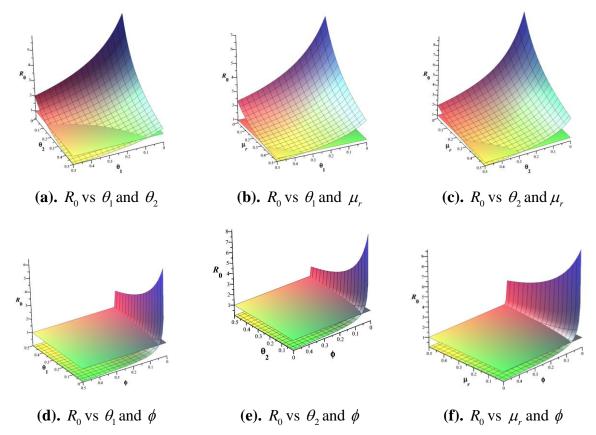
Firstly we vary the value of  $\theta_1$  to investigate the impact of early quarantine of the goats that are still in the latency period. There are three values of  $\theta_1$ , i.e.,  $0, \frac{1}{3}, \frac{1}{2}$ , which give  $R_0 = 3.01, 1.29, 1.01$ , respectively. It is clear that the larger the  $\theta_1$ , the smaller the  $R_0$ . Figure 4(a) shows the higher the  $\theta_1$ , the lower the number of infectious goats. These results indicate that early detection and quarantine can reduce the basic reproduction number and the number of infectious goats.

Next we examined the impact of quarantining infectious goats by changing the  $\theta_2$  while other parameters as given in Table 1. The  $\theta_2$  used are  $0, \frac{1}{3}, \frac{1}{2}$ . Meanwhile, the basic reproduction number obtained is 3.82,1.15,0.85. These results show that  $R_0$  is inversely proportional to  $\theta_2$ . Figure 4(b) shows that the number of infectious goats decreased as the  $\theta_2$  increased. These results imply that the higher the  $\theta_2$ , the lower the basic reproduction number  $R_0$  and the lower the number of infectious goats. Hence, it is necessary to quarantine the infected goats early.

Figure 4(c) displays the numerical simulation results when  $\phi$  is varied. It can be seen that the number of infectious goats decreased as  $\phi$  increased. A similar phenomenon is also obtained after calculating  $R_0$ . We get  $R_0 = 4.13, 1.63, 1.25$  for  $\phi = 0, \frac{1}{84}, \frac{1}{56}$ , respectively, which suggest that  $R_0$  decreases as  $\phi$  increases. These results indicate that routine vaccination should be carried out on animals potentially infected with FMD.

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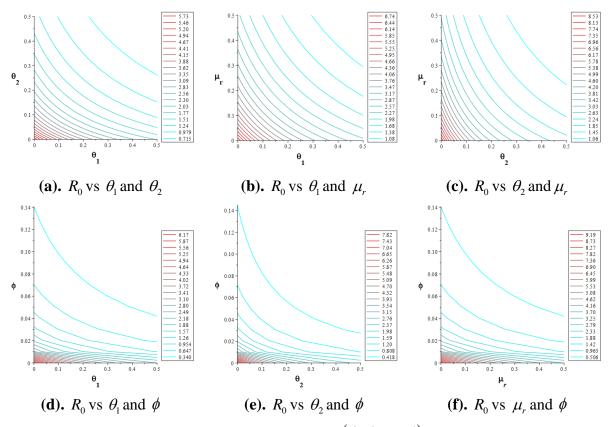
The impact of varying the value of  $\mu_r$  on the spread of FMD can be seen in Figure 4(d). The figure indicates that the larger the  $\mu_r$ , the less the number of infectious goats. We use three values of  $\mu_r$ , i.e.,  $0, \frac{1}{2}, 1$ , that yield  $R_0 = 4.49, 1.49, 0.89$ , respectively. It is clear that the larger the value of the  $\mu_r$ , the smaller the basic reproduction number  $R_0$ . Therefore, it is advisable to carry out routine disinfection around the farm area.



**Figure 5.** Relationship between control parameter  $(\theta_1, \theta_2, \mu_r, \phi)$  and  $R_0$  in three-dimensional

space

Figure 5 illustrates the surface plot of  $R_0$ . It is clear that vaccination has an important role in suppressing the basic reproduction number. This can be seen from the breadth of the  $R_0$  field which is under the  $R_0 = 1$ . Based on the contour plots presented in Figure 6, it is clear that the basic reproduction number is more sensitive to vaccination rate.



**Figure 6.** Relationship between control parameter  $(\theta_1, \theta_2, \mu_r, \phi)$  and  $R_0$  in two dimensional space

#### CONCLUSIONS

In this article, we develop a mathematical model of the spread of foot and mouth disease taking into account vaccination, disinfection, and early quarantine. The results of our study show that vaccination has an important role in controlling the spread of FMD. In addition, routine vaccination programs can also reduce the basic reproduction number. In addition to vaccination, quarantine and disinfection measures also have a positive impact on controlling the spread of FMD because they can reduce the basic reproduction number. Because of that, we recommend implementing routine vaccination, screening and disinfection programs.

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