Research article

Modeling the dynamics of rubella disease with vertical transmission

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ABSTRACT

Rubella is a highly contagious and serious human disease caused by the rubella virus. It affects everyone around the world, but it is especially common in pregnant women and children. In particular, when pregnant women are infected with the rubella virus, it causes Congenital Rubella Syndrome (it transmit vertically from mother to fetus, which causes that the new born baby to inherit birth defect disease). In order to prevent this viral disease, children must receive an MMR (measles, mumps and rubella) vaccine twice. If children receive two doses of the vaccine, then they develop long life immunity (protected against rubella). Based on the biological behavior of rubella disease, the SVPEIRS (susceptible, vaccinated, protected, exposed, infected, recovered) deterministic mathematical model of rubella disease dynamics is proposed. From the perspective of the qualitative behavior of the model, it is bounded in the invariant region and all the solutions of the compartment are positive. In addition, the equilibrium points and the stability of the equilibrium points (local and global) are also analyzed. The basic reproductive number is determined using a next-generation matrix. The results of the sensitivity analysis show that rubella is spread in a community if the values of contact rate, vertical transmission (neonatal infection) rate, exposure rate and rate of waning out of the first vaccinating dose are increase by keeping other parameters constant. On the other hand, increasing the first and second vaccination rate and treatment rate can help to control rubella in the community. Numerical simulation results show that due to the lack of protection for women before pregnancy, the number of infections increases with the birth of infected children, and the two doses of vaccine play a significant role in reducing and eliminating rubella. Therefore, to eliminate rubella in the community, healthcare and policymakers must pay attention to these parameters.

1. Introduction

Rubella, also known as German measles or three-day measles, is a highly contagious and severe human disease caused by the rubella virus (Banatvala and Peckham, 2006). This viral disease spreads from person to person through droplets released from the respiratory secretions of rubella-infected persons, touching tissues contaminated with the rubella virus, touching the urine of children infected with rubella and sharing a cup used by a rubella-infected person (Mawson and Croft, 2019). If pregnant women are affected by this virus, their newborn babies will inherit a birth defect disease called Congenital Rubella Syndrome (CRS). CRS leads to malformations, stillbirths, mental retardation, heart disease, diabetes, encephalitis, low birth weight, and deafness.

Up to 50% of rubella-infected people are asymptomatic, but if they do develop symptoms, they usually start on the face and spread to other parts of the body (WHO, 2012). A pink or red rash appears 14 to 17 days after exposure. Mild fever, fatigue, headache, encephalitis, miscarriage, pruritic, malaise, arthritic, muscular pain, pain in joints, polyarthritis, and loss of appetite are symptoms of this viral disease (Goodson et al., 2011; Mahdy et al., 2021). The MMR (Measles, Mumps, and Chickenpox) vaccine is the most recommended vaccine to prevent this infection and is considered eradicable (WHO, 2012). According to Centers for Disease Control and Prevention recommendations, children should be vaccinated twice with the MMR vaccine. The first dose of the vaccine is recommended between 12 and 15 months of age and provides greater than 95% immunity. The second dose of vaccine is recommended between 4 and 6 years of age and provides permanent immunity to the virus (Grant et al., 2019).

About 12.5 million people were infected with rubella in the United States between 1964 and 1965 during the global rubella epidemic that began in Europe in 1962 (Plotkin, 2006). This complication includes 20,000 children born with CRS, 2000 cases of encephalitis, 11,250 cases of abortions, and 2,100 cases of infant deaths. In Africa, the estimated incidence of CRS is 246 per 100,000 people (Metcalf et al., 2012). According to Tamirat et al. (2017), between 2009 and 2015, about 2,615 people in Ethiopia were affected by rubella; most of them (52.2%) were female, and the ages of confirmed cases ranged from 1 month to 42 years. The highest recorded cases were in the hot and dry season from January to June, and the lowest cases in August and September (Getahun et al., 2016).

In the public health community, mathematical models are useful tools to describe and analyze dynamic behaviors, transmission mechanisms, predictive control strategies, and generate visualizations of infectious disease over time (Li, 2018). The concept of disease transmission and control is based on the mathematical rules used in the research planning process to provide information for the design of infectious diseases (Herzog et al., 2017).

Many authors have studied the public health complications of rubella disease, the dynamics of its transmission, and developed different mathematical models to predict the control mechanisms. For instance, to study the rubella disease transmission with a vaccine, a deterministic mathematical model of rubella disease dynamics was formulated by Prawoto et al. (2020), where the total population was divided into five classes, namely: susceptible S(t), exposed E(t), infected I(t), recovered R(t) and vaccinated V(t) classes (SEIRV deterministic mathematical model). This study pointed out that rubella is a re-infectious viral disease. Al Qurashi (2020) also used fractional differential equations to optimize the sequence and developed mathematical model rubella disease dynamics by dividing the total population into four classes, namely susceptible S(t), exposed E(t), infected I(t), and recovered R(t). Koca (2018) proposed a SEIVR (susceptible-exposed-infected-vaccinated-recovered) model of rubella transmission based on non-singular and non-local fractional derivatives. Baleanu et al. (2020) modified the Koca model by replacing the derivative in time with the new Caputo Fabrizio fractional differential equation. The SEIVR mathematical model was developed by Yang and Freitas (2019) in order to study the biological perspective of vaccination and strategy to eliminate rubella and reduce CRS in the community. Van der Heijden et al. (1998) constructed a deterministic model based on the National Rubella Vaccination Program and the CRS assessment where the total population was divided into six classes: maternal antibody, susceptible S(t), vaccinated V(t), exposed E(t), infected I(t) and recovered R(t) classes.

As far as we know, no studies have been conducted on deterministic mathematical models of rubella disease dynamics under the consideration of vertical transmission and the second vaccine in their model. Therefore, in this study, the vertical transmission of rubella disease from mother to her fetus that occurs during pregnancy and the two-dose vaccine, in which a person who receives two doses of MMR vaccines will have permanent immunity (protected) for the rest of his/her life. The remaining part of this paper is organized as: In Section 2, the formulation and description of the model are discussed. In Section 3, the model analysis and sensitivity analysis are performed. In Section 4, the numerical simulation of the model is discussed. Finally, in Section 5, the discussion and conclusion of the study are presented.

2. Model formulation and description

Based on the behavior of rubella disease, the total population size at a given time t, denoted by N(t), is divided into six classes, namely: susceptible S(t), vaccinated V(t), protected P(t), exposed E(t), infected I(t) and recovered R(t) classes. The susceptible class consists of a group of individuals who have not yet been infected with rubella but are at risk of infection. The first vaccinated class consists of a group of individuals who have received the first dose vaccine. The protected class includes a group of individuals who have received second doses of the MMR vaccine and have active immunity, which means that individuals who have received two doses of the MMR vaccine will not get rubella disease in their lifetime (Grant et al., 2019). The exposed class is the class where susceptible individuals have contact with infected people and those infected but asymptomatic. Individuals classified as infected include a group of individuals who developed symptoms of rubella illness, and individuals classified as recovered are people who have acquired temporary immunity.

Individuals in the susceptible class will increase with the recruitment rate π, rate of the inflow of waning out of the first dose ω and the rate of immunity loss due to recovery of individuals at a rate of ρ. This class will be decreased by contacting infected individuals at a rate of β and administering the first vaccine dose at a rate of α. The exposed class will be increased through contact with infected individuals at a rate of β and decreased by breakthrough into the infected class at a rate of ϑ. Individuals in the infected class will be increases at a rate of ϑ from exposed individuals and at a rate of θ due to the vertical transmission of the disease from mother to fetus. It will be decreased with deaths caused by rubella at a rate of ε and recovery rate at γ which is produced when infected individuals get rest, drink soft drinks, and take treatment under the doctor's advice. When the first dose of vaccine is received at a susceptibility rate α, the number of vaccinated classes will be increased. Since the first dose of vaccine has been reduced, vaccinated individuals are rapidly entering the susceptible population at the rate ω. This class will be decreased by receiving the second vaccine dose at a rate δ. The protected class will be increased with the second dose of vaccine at a rate δ. Due to natural death at a rate of μ, all classes are decreased.

The model was developed under the following assumptions:

➢ If susceptible individuals make contact with the respiratory droplets of rubella-infected individuals, they will become exposed to rubella (Mawson and Croft, 2019).
➢ During pregnancy, vertical transmission occurs from mother to fetus.
➢ Individuals infected with rubella will recover or die due to rubella disease.
➢ The recovered and first-vaccinated individual is susceptible to rubella disease.
➢ An individual who receives the two doses of the MMR vaccine develops active immunity (Grant et al., 2019).
➢ All the parameters to be used in this model are positive.

By considering the above descriptions, assumptions, and interrelationships between compartments and parameters, the dynamics of rubella disease is illustrated in Fig. 1.
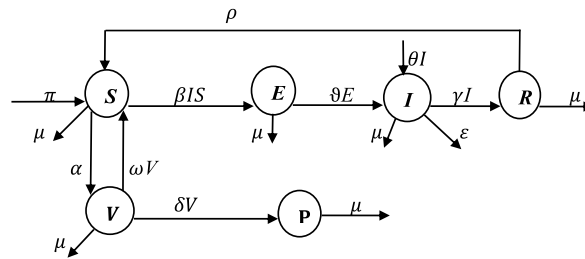
Fig. 1. A diagram of the Rubella disease dynamics.

Table 1. Parameters and their description.

Parameters	Description	Parameters	Description
β	Contact rate	ϑ	Exposed rate
α	First vaccination rate	μ	Natural death rate
δ	Second vaccination rate	π	Recruitment rate
ω	Waning out of first vaccination rate	γ	Treatment rate
θ	Vertical transmission rate	ε	Death rate
ρ	Lose of temporary immunity rate		

From the schematic diagram, the following system of ordinary differential equations is formulated.

$$\begin{cases} \dfrac{dS}{dt} = \pi + \rho R + \omega V - \beta S I - (\alpha + \mu) S \\ \dfrac{dV}{dt} = \alpha S - (\delta + \omega + \mu) V \\ \dfrac{dP}{dt} = \delta V - \mu P \\ \dfrac{dE}{dt} = \beta I S - (\vartheta + \mu) E \\ \dfrac{dI}{dt} = \theta I + \vartheta E - (\mu + \gamma + \varepsilon) I \\ \dfrac{dR}{dt} = \gamma I - (\mu + \rho) R, \end{cases} \tag{1}$$

with the initial conditions $S(0) \geq 0$, $V(0) \geq 0$, $P(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$, $R(0) \geq 0$ (Table 1).

3. Qualitative analysis

This section discusses some basic qualitative behaviors of the model, such as the boundedness of the model, positivity of the solutions, equilibrium points, stability of equilibrium points, basic reproductive number, and sensitivity analysis of the model.

3.1. Positivity of the solutions

Theorem 1. *For all $t > 0$, the solutions of the system of equation (1) are non-negative, with $S(0) \geq 0, V(0) \geq 0, \ P(0) \geq 0, \ E(0) \geq 0, \ I(0) \geq 0, \ R(0) \geq 0$.*

Proof. To prove Theorem 1, let's take the first equation of the system of equations (1):

$$\frac{dS}{dt} = \pi + \rho R + \omega V - \beta S(t)I - (\alpha + \mu) S(t). \tag{2}$$

By considering only the negative part of equation (2), we obtain

$$\frac{dS}{dt} \geq -\beta S(t)I - (\alpha + \mu) S(t). \tag{3}$$

To solve equation (3), let's apply the separation of variables method and integrate both sides of the equation as follows:

$$\int \frac{dS(t)}{S(t)} \geq -\int (\beta I(t) + \alpha + \mu) dt$$

$$ln|S(t)| \geq -\int (\beta I(t) + \alpha + \mu) dt$$

$$exp(ln|S(t)|) \geq exp(-\int (\beta I(t) + \alpha + \mu) dt)$$

$$S(t) \geq S(0) exp(-\int (\beta I(t) + \alpha + \mu) dt). \tag{4}$$

In the same process, the positivity of the other compartments are proved and we get the following solutions: $V(t) \geq V(0) exp(-(\delta + \omega + \mu) t)$, $P(t) \geq P(0) exp(-\mu t)$, $E(t) \geq E(0) exp(-(\vartheta + \mu) t)$, $I(t) \geq I(0) exp(-(\mu + \gamma + \varepsilon) t)$, $R(t) \geq R(0) exp(-(\mu + \rho) t)$. Since the value of the exponential function is positive, then $S(t) > 0$, $V(t) > 0$, $P(t) > 0$, $E(t) > 0$, $I(t) > 0$ and $R(t) > 0$. Therefore, if all solutions to the system equation (1) with positive initial conditions remain positive for all $t > 0$, then the developed model is epidemiologically and mathematically meaningful.

3.2. Invariant region of the model

Theorem 2. *The solution of the system of equations (1) with initial conditions $S(0) \geq 0, V(0), \geq 0,\ P(0) \geq 0,\ E(0) \geq 0,\ I(0) \geq 0$ and $R(0) \geq 0$ is bounded in set $\Omega = \{(S,\ V,\ P,\ E, I,\ R) \in R_+^6 : 0 \leq N(t) \leq \frac{\pi}{\mu}\}$.*

Proof. To prove Theorem 2, let's consider the total population at a given time t by:

$$N(t) = S(t) + V(t) + P(t) + E(t) + I(t) + R(t). \tag{5}$$

Differentiating both sides of equation (5) with respect to time t gives

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dV}{dt} + \frac{dP}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt}. \tag{6}$$

Substitute $\frac{dS}{dt}, \frac{dV}{dt}, \frac{dP}{dt}, \frac{dE}{dt}, \frac{dI}{dt}$ and $\frac{dR}{dt}$ from the system of equation (1) into equation (6):

$$\begin{aligned}
\frac{dN}{dt} &= \pi + \rho R + \omega V - \beta S I - (\alpha + \mu) S + \beta S I - (\vartheta + \mu) E + \theta I + \vartheta E - (\mu + \gamma + \varepsilon) I \\
&\quad + \alpha S - (\delta + \mu) V - \omega V + \delta V - \mu P + \gamma I - \mu R - \rho R \\
&= \pi + \theta I - \varepsilon I - \mu (S + P + V + E + I + R) \\
&= \pi + \theta I - \varepsilon I - \mu N. \tag{7}
\end{aligned}$$

If there is no death due to rubella and no rubella infection in a newly born baby, then

$$\frac{dN}{dt} \leq \pi - \mu N. \tag{8}$$

Use the separation of variables method to solve equation (8) as follows:

$$\pi - \mu N \geq exp(-\mu t + c). \tag{9}$$

Here, $\lim_{t \to \infty} exp(-\mu t + c) = 0$. This means that as $t \to \infty$ in equation (9), the total population size $N \to \frac{\pi}{\mu}$, that is $\lim_{t \to \infty} N(t) = \frac{\pi}{\mu}$. Since the non-negative solution of the model is proved in Theorem 1, then $N(t) \leq \frac{\pi}{\mu}$ for all $t \geq 0$. Therefore, the model is well posed and epidemiologically meaningful in the region $\Omega = \{(S,\ V,\ P,\ E,\ I,\ R) \in R_+^6 : 0 \leq N(t) \leq \frac{\pi}{\mu}\}$.

3.3. Disease-free equilibrium point of the model

In this section, the point at which rubella disease disappears in a community is computed from the system of equation (1). It is determined by setting the right-hand side of the system of equation (1) equal to zero. This can happen when there are no infectious individuals in the population or the epidemic has disappeared from the population.

$$\begin{cases}
\pi + \rho R + \omega V - \beta S I - (\alpha + \mu) S = 0 \\
\alpha S - (\delta + \omega + \mu) V = 0 \\
\delta V - \mu P = 0 \\
\beta I S - (\vartheta + \mu) E = 0 \\
\theta I + \vartheta E - (\mu + \gamma + \varepsilon) I = 0 \\
\gamma I - (\mu + \rho) R = 0. \tag{10}
\end{cases}$$

At the disease-free equilibrium point, $I = E = R = 0$. Then, the system of equation (10) is simplified as follows:

$$\begin{cases}
\pi + \omega V - (\alpha + \mu) S = 0 \\
\alpha S - (\delta + \mu + \omega) V = 0 \\
\delta V - \mu P = 0. \tag{11}
\end{cases}$$

From the second and third equations of the system of equations (11), we get $S = \frac{(\delta + \mu + \omega) V}{\alpha}$ and $V = \frac{\mu P}{\delta}$. Inserting this into the first equation of (11) gives

$$\pi + \frac{\omega \mu P}{\delta} - \frac{(\alpha + \mu)(\delta + \mu + \omega) \mu P}{\alpha \delta} = 0 \qquad \Rightarrow P = \frac{\pi \alpha \delta}{((\alpha + \mu)(\delta + \mu) + \omega \mu) \mu}.$$

Then, by using the value of P we get $V = \frac{\pi \alpha}{(\alpha + \mu)(\delta + \mu) + \omega \mu}$ and $S = \frac{\pi (\delta + \mu + \omega)}{(\alpha + \mu)(\delta + \mu) + \omega \mu}$.

Therefore, the disease-free equilibrium point of the model is: $\{(S^*, V^*, P^*, E^*, I^*, R^*) = (\frac{\pi(\delta + \mu + \omega)}{(\alpha + \mu)(\delta + \mu) + \omega \mu}, \frac{\pi \alpha}{(\alpha + \mu)(\delta + \mu) + \omega \mu}, \frac{\pi \alpha \delta}{((\alpha + \mu)(\delta + \mu) + \omega \mu) \mu}, 0, 0, 0)\}$.

3.4. Endemic equilibrium point the model

In this section, the point at which rubella disease persists in the community is obtained. From the second, third, fourth, and sixth equations of the system of equations (10), we get

$$V = \frac{\mu P}{\delta}. \tag{12}$$

$$S = \frac{(\delta + \omega + \mu)\,\mu P}{\alpha \delta}. \tag{13}$$

$$E = \frac{\beta I S}{(\vartheta + \mu)} = \frac{(\delta + \omega + \mu)\,\beta \mu P I}{\alpha \delta (\mu + \vartheta)}. \tag{14}$$

$$I = \frac{(\mu + \rho)\,R}{\gamma}. \tag{15}$$

Inserting equation (14) into the fifth equation of the system of equations (10), we obtain

$$I\Big(\frac{(\delta + \omega + \mu)\,\vartheta \beta \mu P}{\alpha \delta (\mu + \vartheta)} - (\mu + \gamma + \varepsilon - \theta)\Big) = 0. \tag{16}$$

Since $I \neq 0$, then equation (16) become

$$\frac{(\delta + \omega + \mu)\,\vartheta \beta \mu P}{\alpha \delta (\mu + \vartheta)} - (\mu + \gamma + \varepsilon - \theta) = 0$$

$$\Rightarrow P = \frac{\alpha \delta (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta \mu (\delta + \omega + \mu)}.$$

After substituting P in equations (12), (13) and (14), we get $V = \frac{\alpha(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta (\delta + \omega + \mu)}$, $S = \frac{(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta}$ and $E = \frac{(\delta + \omega + \mu)(\mu + \gamma + \varepsilon - \theta)\mu I}{\vartheta \alpha \delta}$. Next, put S, P and V in the first equation of the system of equation (10).

$$\pi + \rho R + \frac{\alpha \omega (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta (\delta + \omega + \mu)} - \frac{(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)(\mu + \rho)\,R}{\vartheta \gamma} - \frac{(\alpha + \mu)(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta} = 0$$

$$\Rightarrow R = \frac{\gamma [\vartheta \beta \pi (\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega \mu)]}{\vartheta \beta (\delta + \omega + \mu)(\rho \vartheta \gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)(\mu + \rho))}.$$

Then, by inserting R into equations (14) and (15), we get

$$I = \frac{[(\delta + \omega + \mu)\,\vartheta \beta \pi - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega \mu)]}{\vartheta \beta (\delta + \omega + \mu)(\rho \vartheta \gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta))}$$

$$E = \frac{\mu (\mu + \gamma + \varepsilon - \theta)[\vartheta \beta \pi (\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega \mu)]}{\vartheta \beta (\rho \vartheta \gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta))\vartheta \alpha \delta}.$$

Hence, the endemic equilibrium point of the system of equation (1) is $\{(S, V, P,\ E,\ I,\ R) = (\frac{(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta}, \frac{\alpha(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta (\delta + \omega + \mu)}, \frac{\alpha \delta (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta \beta \mu (\delta + \omega + \mu)},$
$\frac{\mu (\mu + \gamma + \varepsilon - \theta)[\vartheta \beta \pi (\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega \mu)]}{\vartheta \beta (\rho \vartheta \gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta))\vartheta \alpha \delta},\ \frac{[\vartheta \beta \pi (\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega \mu)]}{\vartheta \beta (\delta + \omega + \mu)(\rho \vartheta \gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta))},\ \frac{\gamma [\vartheta \beta \pi (\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega \mu)]}{\vartheta \beta (\delta + \omega + \mu)(\rho \vartheta \gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)(\mu + \rho))})\}.$

3.5. Basic reproductive number of the model

In this section, the basic reproductive number denoted by R_0 which is defined as the average number of secondary infections caused by a single infected individual during the entire period of infectiousness (Jones, 2007). It is determined using the next-generation matrix method that mentioned in Heffernan et al. (2005) and considering the infected classes. The infected classes are:

$$\begin{cases} \frac{dE}{dt} = \beta I S - (\vartheta + \mu)\,E \\ \frac{dI}{dt} = \theta I + \vartheta E - (\mu + \gamma + \varepsilon)\,I. \end{cases} \tag{17}$$

By using the next-generation matrix principle mentioned in Heffernan et al. (2005), let f represent the rate of new infectious agents and v represent the transfer of an individual out of the infected compartments. Then, from the system of equations (17), we have

$$f = \begin{bmatrix} \beta I S \\ \theta I \end{bmatrix}. \tag{18}$$

$$v = \begin{bmatrix} (\vartheta + \mu)\,E \\ -\vartheta E + (\mu + \gamma + \varepsilon)\,I \end{bmatrix}. \tag{19}$$

Let F and V be the Jacobian matrices of f and v, with respect to E and I at the disease-free equilibrium point, respectively, then

$$F = \begin{bmatrix} \frac{\partial f}{\partial E} & \frac{\partial f}{\partial I} \\ \frac{\partial f}{\partial E} & \frac{\partial f}{\partial I} \end{bmatrix} = \begin{bmatrix} \frac{\partial(\beta I S)}{\partial E} & \frac{\partial(\beta I S)}{\partial I} \\ \frac{\partial(0)}{\partial E} & \frac{\partial(0)}{\partial I} \end{bmatrix} = \begin{bmatrix} 0 & \beta S \\ 0 & \theta \end{bmatrix}. \tag{20}$$

$$V = \begin{bmatrix} \frac{\partial v_1}{\partial E} & \frac{\partial v_1}{\partial I} \\ \frac{\partial v_2}{\partial E} & \frac{\partial v_2}{\partial I} \end{bmatrix} = \begin{bmatrix} \frac{\partial (\vartheta + \mu)\,E}{\partial E} & \frac{\partial (\vartheta + \mu)\,E}{\partial I} \\ \frac{\partial(-\vartheta E) + (\mu + \gamma + \varepsilon)\,I}{\partial E} & \frac{\partial(-(\vartheta E) + (\mu + \gamma + \varepsilon)\,I)}{\partial I} \end{bmatrix} = \begin{bmatrix} \vartheta + \mu & 0 \\ -\vartheta & \mu + \gamma + \varepsilon \end{bmatrix}. \tag{21}$$

The Jacobian matrices of F and V at the disease-free equilibrium point are

$$F_{DFE} = \begin{bmatrix} 0 & \frac{\pi \beta (\delta + \mu + \omega)}{(\alpha + \mu)(\delta + \mu) + \omega \mu} \\ 0 & \theta \end{bmatrix} \quad \text{and} \quad V_{DFE} = \begin{bmatrix} \vartheta + \mu & 0 \\ -\vartheta & \mu + \gamma + \varepsilon \end{bmatrix}.$$

Next, we find the inverse of V and the product of F and V^{-1}. Then

$$V^{-1} = \frac{adjV}{det(V)} = \frac{\begin{bmatrix} \mu+\gamma+\varepsilon & 0 \\ -\vartheta & \vartheta+\mu \end{bmatrix}}{(\mu+\gamma+\varepsilon)(\vartheta+\mu)} = \begin{bmatrix} \dfrac{1}{\vartheta+\mu} & 0 \\ \dfrac{\vartheta}{(\mu+\gamma+\varepsilon)(\vartheta+\mu)} & \dfrac{1}{(\mu+\gamma+\varepsilon)} \end{bmatrix}. \tag{22}$$

$$FV^{-1} = \begin{bmatrix} \dfrac{(\delta+\mu+\omega)\pi\beta\vartheta}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon-\theta)(\vartheta+\mu)} & \dfrac{(\delta+\mu+\omega)\pi\beta}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon-\theta)} \\ \dfrac{\vartheta\theta}{(\mu+\gamma+\varepsilon)(\vartheta+\mu)} & \dfrac{\theta}{\mu+\gamma+\varepsilon} \end{bmatrix}. \tag{23}$$

The characteristic polynomial formed from FV^{-1} is given by $p(\lambda) = det(FV^{-1} - \lambda I)$, where I is the identity matrix.

$$\Rightarrow p(\lambda) = \begin{vmatrix} \dfrac{(\delta+\mu+\omega)\pi\beta\vartheta}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon)(\vartheta+\mu)} - \lambda & \dfrac{(\delta+\mu+\omega)\pi\beta}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon)} \\ \dfrac{\vartheta\theta}{(\mu+\gamma+\varepsilon)(\vartheta+\mu)} & \dfrac{\theta}{\mu+\gamma+\varepsilon} - \lambda \end{vmatrix}$$

$$= \lambda\left(\lambda - \frac{\pi\beta\vartheta(\delta+\mu+\omega)}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon)(\vartheta+\mu)} - \frac{\theta}{\mu+\gamma+\varepsilon}\right). \tag{24}$$

Roots of the characteristic polynomial (24) are $\lambda_1 = 0$ and $\lambda_2 = \frac{\pi\beta\vartheta(\delta+\mu+\omega)}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon)(\vartheta+\mu)} + \frac{\theta}{\mu+\gamma+\varepsilon}$.

According to the principle of the next-generation matrix, the largest solution of a characteristic polynomial (i.e. the largest eigenvalue of the Jacobian matrix) is the basic reproductive number. Therefore, $R_0 = \frac{\pi\beta\vartheta(\delta+\mu+\omega)}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\mu+\gamma+\varepsilon)(\vartheta+\mu)} + \frac{\theta}{\mu+\gamma+\varepsilon}$.

3.6. Local stability of disease-free equilibrium point

As cited in the study by Nurhasen (2017), the stability analysis of the disease-free equilibrium point of the model is performed by linearizing the non-linear system of equations. Thus, the stability of this point in the system of equation (1) is done by calculating the characteristic equation of the Jacobian matrix J. This is examined by using the eigenvalues of the corresponding Jacobian matrix, which depends on the model parameters.

Theorem 3. *The disease-free equilibrium point of the system of equation (1) is locally asymptotically stable if $R_0 < 1$, unless unstable if $R_0 > 1$.*

Proof. To prove Theorem 3, we have to construct the Jacobian matrix of the system of equations (1) as follows:

$$J(S,V,P,E,I,R) = \begin{bmatrix} \frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial V} & \frac{\partial f_1}{\partial P} & \frac{\partial f_1}{\partial E} & \frac{\partial f_1}{\partial I} & \frac{\partial f_1}{\partial R} \\ \frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial V} & \frac{\partial f_2}{\partial P} & \frac{\partial f_2}{\partial E} & \frac{\partial f_2}{\partial I} & \frac{\partial f_2}{\partial R} \\ \frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial V} & \frac{\partial f_3}{\partial P} & \frac{\partial f_3}{\partial E} & \frac{\partial f_3}{\partial I} & \frac{\partial f_3}{\partial R} \\ \frac{\partial f_4}{\partial S} & \frac{\partial f_4}{\partial V} & \frac{\partial f_4}{\partial P} & \frac{\partial f_4}{\partial E} & \frac{\partial f_4}{\partial I} & \frac{\partial f_4}{\partial R} \\ \frac{\partial f_5}{\partial S} & \frac{\partial f_5}{\partial V} & \frac{\partial f_5}{\partial P} & \frac{\partial f_5}{\partial E} & \frac{\partial f_5}{\partial I} & \frac{\partial f_5}{\partial R} \\ \frac{\partial f_6}{\partial S} & \frac{\partial f_6}{\partial V} & \frac{\partial f_6}{\partial P} & \frac{\partial f_6}{\partial E} & \frac{\partial f_6}{\partial I} & \frac{\partial f_6}{\partial R} \end{bmatrix},$$

where $f_1 = \pi + \rho R + \omega V - \beta S(t)I(t) - (\alpha+\mu)S$, $f_2 = \alpha S - (\delta+\omega+\mu)V$, $f_3 = \delta V - \mu P$, $f_4 = \beta S(t)I(t) - (\vartheta+\mu)E$, $f_5 = \theta I + \vartheta E - (\mu+\gamma+\varepsilon)I$ and $f_6 = \gamma I - (\mu+\rho)R$. Then

$$J = \begin{bmatrix} -(\beta I(t)+\alpha+\mu) & \omega & 0 & 0 & -\beta S(t) & \rho \\ \alpha & -(\delta+\omega+\mu) & 0 & 0 & 0 & 0 \\ 0 & \delta & -\mu & 0 & 0 & 0 \\ \beta I(t) & 0 & 0 & -(\vartheta+\mu) & \beta S(t) & 0 \\ 0 & 0 & 0 & \vartheta & -(\mu+\gamma+\varepsilon-\theta) & 0 \\ 0 & 0 & 0 & 0 & \gamma & -(\mu+\rho) \end{bmatrix}$$

The Jacobian matrix at the disease-free equilibrium point J_{DFEP} becomes

$$J_{DFEP} = \begin{bmatrix} -(\alpha+\mu) & \omega & 0 & 0 & \dfrac{\pi\beta(\delta+\mu+\omega)}{(\alpha+\mu)(\delta+\mu)+\omega\mu} & \rho \\ \alpha & (\delta+\omega+\mu) & 0 & 0 & 0 & 0 \\ 0 & \delta & -\mu & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\vartheta+\mu) & -\dfrac{\pi\beta(\delta+\mu+\omega)}{(\alpha+\mu)(\delta+\mu)+\omega\mu} & 0 \\ 0 & 0 & 0 & \vartheta & \theta-(\mu+\gamma+\varepsilon) & 0 \\ 0 & 0 & 0 & 0 & \gamma & -(\mu+\rho) \end{bmatrix}$$

Let $A = \alpha+\mu$, $B = \delta+\omega+\mu$, $C = \vartheta+\mu$, $D = \frac{\pi\beta(\delta+\mu+\omega)}{(\alpha+\mu)(\delta+\mu)+\omega\mu}$, $E = \mu+\gamma+\varepsilon-\theta$, $F = \mu+\rho$. Then, the characteristic polynomial of J_{DFEP} is computed from $det(J_{DFEP} - \lambda I)$, where I is the identity matrix.

$$\Rightarrow p(\lambda) = \begin{vmatrix} -(A+\lambda) & \omega & 0 & 0 & D & \rho \\ \alpha & -(B+\lambda) & 0 & 0 & 0 & 0 \\ 0 & \delta & -(\mu+\lambda) & 0 & 0 & 0 \\ 0 & 0 & 0 & -(C+\lambda) & -D & 0 \\ 0 & 0 & 0 & \vartheta & -(E+\lambda) & 0 \\ 0 & 0 & 0 & 0 & \gamma & -(F+\lambda) \end{vmatrix}$$

$$= (\mu+\lambda)(F+\lambda)((C+\lambda)(E+\lambda) - D\vartheta)[(A+\lambda)(B+\lambda) - \alpha\omega]. \tag{25}$$

Next, we have to compute the corresponding eigenvalues of J_{DFEP} which is the same as the roots of $p(\lambda)$.

$$\Rightarrow (\mu+\lambda)(F+\lambda)((C+\lambda)(E+\lambda) - D\vartheta)[(A+\lambda)(B+\lambda) - \alpha\omega] = 0$$

$$(\mu+\lambda)(F+\lambda) = 0 \quad \text{or} (C+\lambda)(E+\lambda) - D\vartheta = 0 \quad \text{or} (A+\lambda)(B+\lambda) - \alpha\omega = 0$$

$$\Rightarrow \lambda = -\mu \quad \text{or} \lambda = -F \quad \text{or} \lambda^2 + (C+E)\lambda + CE - D\vartheta = 0 \quad \text{or} \lambda^2 + (A+B)\lambda + AB - \alpha\omega.$$

According to the Routh-Hurwitz stability criterion of the quadratic function, the system of characteristic equations is stable if and only if both coefficients are greater than zero (Nurhasen, 2017). Then

  i. $A + B > 0 \Rightarrow \alpha + \mu + \delta + \omega + \mu = \alpha + \delta + \omega + 2\mu > 0.$
 ii. $C + E > 0 \Rightarrow \vartheta + \mu + \mu + \gamma + \varepsilon - \theta = \vartheta + 2\mu + \gamma + \varepsilon - \theta > 0.$
iii. $AB - \alpha\omega > 0 \Rightarrow (\alpha + \mu)(\delta + \mu) + \omega\mu > 0.$
 iv.

$$CE - D\vartheta > 0 \Rightarrow (\mu + \gamma + \varepsilon)(\vartheta + \mu) - \theta(\vartheta + \mu) - \frac{\pi\beta\vartheta(\delta + \mu + \omega)}{(\alpha + \mu)(\delta + \mu) + \omega\mu} > 0$$

$$\Rightarrow -\frac{\pi\beta\vartheta(\delta + \mu + \omega)}{(\alpha + \mu)(\delta + \mu) + \omega\mu} - \theta(\vartheta + \mu) > -(\mu + \gamma + \varepsilon)(\vartheta + \mu)$$

$$\Rightarrow \frac{\pi\beta\vartheta(\delta + \mu + \omega)}{(\alpha + \mu)(\delta + \mu) + \omega\mu} + \theta(\vartheta + \mu) < (\mu + \gamma + \varepsilon)(\vartheta + \mu) \quad \Rightarrow$$

$$\frac{\pi\beta\vartheta(\delta + \mu + \omega)}{((\alpha + \mu)(\delta + \mu) + \omega\mu)(\mu + \gamma + \varepsilon)(\vartheta + \mu)} + \frac{\theta}{(\mu + \gamma + \varepsilon)} < 1.$$

Since $R_0 = \frac{\pi\beta\vartheta(\delta + \mu + \omega)}{((\alpha + \mu)(\delta + \mu) + \omega\mu)(\mu + \gamma + \varepsilon)(\vartheta + \mu)} + \frac{\theta}{\mu + \gamma + \varepsilon}$, then the disease-free equilibrium point of system of equation is locally asymptotically stable, if $R_0 < 1$.

3.7. Global stability of disease-free equilibrium point

Theorem 4. *The disease-free equilibrium point of the system of equation (1) is globally asymptotically stable, if $R_0 < 1$.*

Proof. Considering the infected classes of system of equation (1), let's construct the Lyapunov function technically as follows:

$$L = uE + vI, \tag{26}$$

where u and v are positive constants.

By differentiating both sides of the equation (26) with respect to time t, we get

$$\frac{dL}{dt} = u\frac{dE}{dt} + v\frac{dI}{dt}. \tag{27}$$

Next, substituting $\frac{dE}{dt}$ and $\frac{dI}{dt}$ from system of equation (1) into equation (27) gives

$$\frac{dL}{dt} = u\beta IS - v(\mu + \gamma + \varepsilon - \theta)I - u(\vartheta + \mu)E + v\vartheta E. \tag{28}$$

Let's take $v = (\frac{\vartheta + \mu}{\vartheta})u$, then

$$\frac{dL}{dt} = u\beta IS - (\frac{\vartheta + \mu}{\vartheta})u(\mu + \gamma + \varepsilon - \theta)I - u(\vartheta + \mu)E + (\frac{\vartheta + \mu}{\vartheta})u\vartheta E$$

$$= (\frac{\vartheta\beta S + \theta(\vartheta + \mu) - (\vartheta + \mu)(\mu + \gamma + \varepsilon)}{\vartheta})uI - u(\vartheta + \mu)E + (\vartheta + \mu)uE$$

$$= (\frac{\vartheta\beta S + \theta(\vartheta + \mu) - (\vartheta + \mu)(\mu + \gamma + \varepsilon)}{\vartheta})uI. \tag{29}$$

At disease-free equilibrium point, then equation (29) become

$$\Rightarrow \frac{dL}{dt} = \left(\frac{(\delta + \mu + \omega)\pi\beta}{(\alpha + \mu)(\delta + \mu) + \omega\mu} + \frac{\theta(\vartheta + \mu)}{\vartheta} - \frac{(\vartheta + \mu)(\mu + \gamma + \varepsilon)}{\vartheta} \right)uI$$

$$= \frac{(\vartheta + \mu)(\mu + \gamma + \varepsilon)}{\vartheta} \left(\frac{(\delta + \mu + \omega)\pi\beta\vartheta}{((\vartheta + \mu)(\alpha + \mu)(\delta + \mu) + \omega\mu)(\mu + \gamma + \varepsilon)} + \frac{\theta}{(\mu + \gamma + \varepsilon)} - 1 \right)uI$$

$$= \frac{(\vartheta + \mu)(\mu + \gamma + \varepsilon)}{\vartheta}(R_0 - 1)uI. \tag{30}$$

Here, $\frac{dL}{dt} < 0$, if $R_0 < 1$. This implies that the disease-free equilibrium point of the system of equation (1) is globally asymptotically stable if $R_0 < 1$.

3.8. Local stability of endemic equilibrium point of the model

To verify the stability of an endemic equilibrium point, we have to verify the existence and uniqueness of this point.

Theorem 5. *The model has a unique endemic equilibrium point, if $R_0 > 1$.*

Proof. Since the disease is persisting at this point, then both I and E are greater than zero.

i. $\Rightarrow I = \dfrac{(\mu + \rho)\left[\vartheta\beta\pi(\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega\mu)\right]}{\vartheta\beta(\delta + \omega + \mu)(\rho\vartheta\gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)(\mu + \rho))} > 0$

$\Rightarrow \vartheta\beta\pi(\delta + \omega + \mu) + ((\alpha + \mu)(\delta + \mu) + \omega\mu)(\mu + \vartheta)\theta - (\mu + \vartheta)(\mu + \gamma + \varepsilon)((\alpha + \mu)(\delta + \mu) + \omega\mu) > 0$

$\dfrac{\vartheta\beta\pi(\delta + \omega + \mu)}{(\mu + \vartheta)(\mu + \gamma + \varepsilon)((\alpha + \mu)(\delta + \mu) + \omega\mu)} + \dfrac{\theta}{\mu + \gamma + \varepsilon} > 1$

$\Rightarrow R_0 > 1$.

$E = \dfrac{\left[\vartheta\beta\pi(\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega\mu)\right]}{\vartheta\beta(\delta + \omega + \mu)(\rho\vartheta\gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)} > 0$

$\Rightarrow \vartheta\beta\pi(\delta + \omega + \mu) + ((\alpha + \mu)(\delta + \mu) + \omega\mu)(\mu + \vartheta)\theta - (\mu + \vartheta)(\mu + \gamma + \varepsilon)((\alpha + \mu)(\delta + \mu) + \omega\mu) > 0$

$\dfrac{\vartheta\beta\pi(\delta + \omega + \mu)}{(\mu + \vartheta)(\mu + \gamma + \varepsilon)((\alpha + \mu)(\delta + \mu) + \omega\mu)} + \dfrac{\theta}{\mu + \gamma + \varepsilon} > 1$

$\Rightarrow R_0 > 1$.

Hence, the endemic equilibrium point of the model exists and is unique if $R_0 > 1$.

Theorem 6. *A unique endemic equilibrium point of equation (1) is locally asymptotically stable, if $R_0 > 1$.*

Proof. The Jacobian matrix J of the system of equations (1) at the endemic equilibrium point J_{EEP} is given by:

$$\begin{bmatrix} -(\beta I^*(t) + \alpha + \mu) & \omega & 0 & 0 & -\beta S^*(t) & \rho \\ \alpha & -(\delta + \omega + \mu) & 0 & 0 & 0 & 0 \\ 0 & \delta & -\mu & 0 & 0 & 0 \\ \beta I^*(t) & 0 & 0 & -(\vartheta + \mu) & \beta S^*(t) & 0 \\ 0 & 0 & 0 & \vartheta & -(\mu + \gamma = \varepsilon - \theta) & 0 \\ 0 & 0 & 0 & 0 & \gamma & -(\mu + \rho) \end{bmatrix}$$

Let $A = (\beta I(t) + \alpha + \mu)$, $B = \delta + \omega + \mu$, $C = \vartheta + \mu$, $D = \beta S(t)$, $E = -(\mu + \gamma + \varepsilon - \theta)$, $F = \mu + \rho$, $G = \beta I(t)$. Now, let's compute the characteristic polynomial.

$$\Rightarrow p(\lambda) = \begin{vmatrix} -(A + \lambda) & \omega & 0 & 0 & D & \rho \\ \alpha & -(B + \lambda) & 0 & 0 & 0 & 0 \\ 0 & \delta & -(\mu + \lambda) & 0 & 0 & 0 \\ 0 & 0 & 0 & -(C + \lambda) & -D & 0 \\ 0 & 0 & 0 & \vartheta & -(E + \lambda) & 0 \\ 0 & 0 & 0 & 0 & \gamma & -(F + \lambda) \end{vmatrix}$$

The following characteristic polynomial is obtained by following the same method and formula used in subsection 3.6.

$$p(\lambda) = (\mu + \lambda)\big[\lambda^5 + (A + B + C + E + F)\lambda^4 + (AB + C(E + F + A + B) + EF + (E + F)(B + A) + D\vartheta - \omega\alpha)\lambda^3$$

$$+ ((C + E + F)AB - \omega\alpha) + (CE + CF + D\vartheta)(A + B) + F(CE + D\vartheta) + GD\vartheta)\lambda^2$$

$$+ [(CE + D\vartheta + CF + EF)(AB - \omega\alpha) + F(CE + D\vartheta)(B + A) + DG\vartheta(B + F) - \rho\gamma G\vartheta]\lambda$$

$$+ F(CE + D\vartheta)(AB - \alpha\omega) + G\vartheta B(DF - \rho\gamma)\big]. \tag{31}$$

Let

$x_1 = A + B + C + E + F$.

$x_2 = AB + C(E + F + A + B) + EF + (E + F)(B + A) + D\vartheta - \omega\alpha$.

$x_3 = (C + E + F)(AB - \omega\alpha) + (CE + D\vartheta)(B + A + F) + (CF + EF)(B + A) + DG\vartheta$.

$x_4 = (CE + D\vartheta + CF + EF)(AB - \omega\alpha) + F(CE + D\vartheta)(B + A) + DG\vartheta(B + F) - \rho\gamma G\vartheta$.

$x_5 = F(CE + D\vartheta)(AB - \alpha\omega) + G\vartheta B(DF - \rho\gamma)$.

Thus, equation (31) become:

$$p(\lambda) = -(\mu - \lambda)(\lambda^5 + x_1\lambda^4 + x_2\lambda^3 + x_3\lambda^2 + x_4\lambda + x_5). \tag{32}$$

Next, we find the eigenvalues of J_{EEp} from $p(\lambda) = 0$.

$$\Rightarrow \lambda = -\mu \quad \text{or} \lambda^5 + x_1\lambda^4 + x_2\lambda^3 + x_3\lambda^2 + x_4\lambda + x_5 = 0$$

Let

$$f(\lambda) = \lambda^5 + x_1\lambda^4 + x_2\lambda^3 + x_3\lambda^2 + x_4\lambda + x_5 \tag{33}$$

According to Routh-Hurwitz stability, the characteristic equation (33) has a negative real root if the following conditions are satisfied:

i. $x_1 > 0, \ x_2 > 0, \ x_3 > 0, \ x_4 > 0, \ x_5 > 0$
ii. $x_1 x_2 - x_3 > 0, \ x_1 x_2 x_3 - x_1^2 x_4 - x_3^2 > 0$
iii. $x_5^2 x_3 x_1 - x_5^3 - x_5^2 x_2^2 x_1 - x_5^2 x_3^2 x_2^2 + x_5^2 x_4 x_1 - x_1^2 x_4^2 x_5 - x_1 x_2 x_3 x_4 x_5 - x_4 x_5 x_3^2 > 0.$

This implies

$$x_1 = A + B + C + E + F = 3\mu + \delta + \beta I + \alpha + \vartheta + \theta + \rho - \varepsilon - \gamma > 0$$

$$x_2 = AB + C(E + F + A + B) + EF + (E + F)(B + A) + D\vartheta - \omega\alpha > 0.$$

$$x_3 = (C + E + F)(AB - \omega\alpha) + (CE + D\vartheta)(B + A + F) + (CF + EF)(B + A) + DG\vartheta$$

$$= (\vartheta + \mu + \rho - \gamma - \varepsilon - \theta)((\beta I + \alpha + \mu)(\delta + \omega + \mu - \omega\alpha) - ((\vartheta + \mu)(\mu + \gamma + \varepsilon - \theta) - \beta\vartheta S)((\beta I + \alpha + 3\mu + \delta + \omega + \rho)$$

$$+ [(\mu + \rho)(2\vartheta - \gamma - \varepsilon][\beta I + \alpha + 2\mu + \delta + \omega] + \beta^2\vartheta S I > 0.$$

$$x_4 = (CE + D\vartheta + CF + EF)(AB - \omega\alpha) + F(CE + D\vartheta)(B + A) + DG\vartheta(B + F) - \rho\gamma G\vartheta > 0.$$

$$x_5 = F(CE + D\vartheta)(AB - \alpha\omega) + G\vartheta B(DF - \rho\gamma) > 0$$

$$= (\mu + \rho)[(\vartheta + \mu)(-\mu - \gamma - \varepsilon + \theta) + \beta\vartheta S][(\beta I + \alpha + \mu)(\delta + \omega + \mu) - \alpha\omega]$$

$$+ \beta\vartheta I(\delta + \omega + \mu)[(\beta S(\mu + \rho) - \rho\gamma) > 0.$$

By substituting I and S in the above inequality (condition $x_5 > 0$), we obtain

$$(\mu + \rho)((\vartheta + \mu)(-\mu - \gamma - \varepsilon + \theta) + (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)) *$$

$$[(\frac{[\vartheta\beta\pi(\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega\mu)]}{\vartheta(\delta + \omega + \mu)(\rho\vartheta\gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)} + \alpha + \mu)(\delta + \omega + \mu) - \alpha\omega]$$

$$+ \frac{[\vartheta\beta\pi(\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega\mu)]}{(\delta + \omega + \mu)(\rho\vartheta\gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}(\delta + \omega + \mu)[(\frac{(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)}{\vartheta}(\mu + \rho) - \rho\gamma] > 0$$

$$\Rightarrow \frac{[\vartheta\beta\pi(\delta + \omega + \mu) - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)((\alpha + \mu)(\delta + \mu) + \omega\mu)]}{(\rho\vartheta\gamma - (\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)} * (\frac{(\mu + \vartheta)(\mu + \gamma + \varepsilon - \theta)(\mu + \rho) - \vartheta\rho\gamma}{\vartheta}) > 0$$

$$\Rightarrow \vartheta\beta\pi(\delta + \omega + \mu) + \theta(\mu + \vartheta)((\alpha + \mu)(\delta + \mu) + \omega\mu)$$

$$> (\mu + \gamma + \varepsilon)((\alpha + \mu)(\delta + \mu) + \omega\mu)(\mu + \vartheta)$$

$$\Rightarrow \frac{\vartheta\beta\pi(\delta + \omega + \mu)}{(\mu + \vartheta)(\mu + \gamma + \varepsilon)((\alpha + \mu)(\delta + \mu) + \omega\mu)} + \frac{\theta}{\mu + \gamma + \varepsilon} > 1$$

$$\Rightarrow R_0 > 1.$$

This indicates that the endemic equilibrium point is locally asymptotically state if $R_0 > 1$.

3.9. Global stability of endemic equilibrium point

Theorem 7. *The unique endemic equilibrium point of the system of equation (1) is globally asymptotically stable, if $R_0 > 1$.*

Proof. To prove this theorem, let's consider the following Lyapunov function L that is constructed technically:

$$L\left(S^*, V^*, P^*, E^*, I^*, R^*\right) = \left(S - S^* - S^*\ln S\right) + \left(V - V^* - V^*lnV\right) + \left(P - P^* - P^*lnP\right)$$

$$+ \left(E - E^* - E^*lnE\right) + \left(I - I^* - I^*lnI\right) + \left(R - R^* - R^*lnR\right). \tag{34}$$

By differentiating both sides of equation (34) with respect to t, we get

$$\frac{dL}{dt} = \left(\frac{dS}{dt} - \frac{S^*}{S}\frac{dS}{dt}\right) + \left(\frac{dV}{dt} - \frac{V^*}{V}\frac{dV}{dt}\right) + \left(\frac{dP}{dt} - \frac{P^*}{P}\frac{dP}{dt}\right) + \left(\frac{dE}{dt} - \frac{E^*}{E}\frac{dE}{dt}\right) + \left(\frac{dI}{dt} - \frac{I^*}{I}\frac{dI}{dt}\right) + \left(\frac{dR}{dt} - \frac{R^*}{R}\frac{dR}{dt}\right)$$

$$= \left(\frac{S - S^*}{S}\right)\frac{dS}{dt} + \left(\frac{V - V^*}{V}\right)\frac{dV}{dt} + \left(\frac{P - P^*}{P}\right)\frac{dP}{dt} + \left(\frac{E - E^*}{E}\right)\frac{dE}{dt} + \left(\frac{I - I^*}{I}\right)\frac{dI}{dt} + \left(\frac{R - R^*}{R}\right)\frac{dR}{dt}$$

$$= \left(1 - \frac{S^*}{S}\right)(\pi + \rho R + \omega V - \beta S I - (\alpha + \mu)S) + \left(1 - \frac{V^*}{V}\right)(\alpha S - (\delta + \omega + \mu)V) + \left(1 - \frac{P^*}{P}\right)(\delta V - \mu P) + \left(1 - \frac{E^*}{E}\right)(\beta I S - (\vartheta + \mu)E)$$

Table 2. Parameters and their sensitivity indicators of the model.

Parameters	Description	Sensitivity indicators
π	recruitment rate	Positive
β	contact rate	Positive
ϑ	exposure rate	Positive
ω	rate of waning out of the first vaccination dose	Positive
θ	vertical transmission rate	Positive
δ	rate of the second vaccination dose	Negative
γ	treatment rate	Negative
α	first vaccination dose	Negative

$$+ \left(1 - \frac{I^*}{I}\right)(\theta I + \vartheta E - (\mu + \gamma + \varepsilon)I) + \left(1 - \frac{R^*}{R}\right)(\gamma I - (\mu + \rho)R)$$

$$= \pi + S^*(\beta I + \alpha + \mu) + V^*(\delta + \mu + \omega) + P^*\mu + E^*(\vartheta + \mu) + \theta I + I^*(\mu + \gamma + \varepsilon) + R^*(\mu + \rho) - (\mu S + \frac{S^*}{S}(\pi + \rho R + \omega V)$$

$$+ \mu V + \frac{V^*\alpha S}{V} + \mu P + \frac{P^*\delta V}{P} + \mu E + \frac{E^*\beta I S}{E} + (\mu + \varepsilon)I + I^*\theta + \frac{I^*}{I}\vartheta E + \mu R + \frac{R^*\gamma I}{R}). \tag{35}$$

Let

$$X = \pi + S^*(\beta I + \alpha + \mu) + V^*(\delta + \omega + \mu) + P^*\mu + E^*(\vartheta + \mu)$$

$$+ \theta I + I^*(\mu + \gamma + \varepsilon) + R^*(\mu + \rho)$$

$$Y = \mu S + \frac{S^*}{S}(\pi + \rho R + \omega V) + \mu V + \frac{V^*\alpha S}{V} + \mu P$$

$$+ \frac{P^*\delta V}{P} + \mu E + \frac{E^*\beta I S}{E} + (\mu + \varepsilon)I + I^*\theta + \frac{I^*}{I}\vartheta E + \mu R + \frac{R^*\gamma I}{R}.$$

Then, equation (35) is written as

$$\frac{dL}{dt} = X - Y. \tag{36}$$

This implies that the endemic equilibrium point is the largest set of compact invariant singletons in $\{S = S^*, V = V^*, P = P^*, E = E^*, I = I^*, R = R^*\} \in \Omega : \frac{dL}{dt} = 0$. Therefore, the endemic equilibrium point is globally asymptotically stable in Ω, if $X \leq Y$.

3.10. Sensitivity analysis and it's interpretation

A sensitivity analysis of the basic parameters is performed to determine their impact on the basic reproductive number. It also helps to measure the relative change of the variable as the basic parameter changes. Therefore, to perform the sensitivity analysis of the basic parameter on basic reproductive number, we used the formula given by $P_{x_i} R_0 = \frac{\partial R_0}{\partial x_i} * \frac{x_i}{R_0}$, where the parameter P is sensitivity indicators and x_i is the parameter in the basic reproductive number.

1. For $x_i = \pi$, $P_\pi R_0 = \frac{\partial R_0}{\partial \pi} * \frac{\pi}{R_0} = \frac{\vartheta\beta\pi(\delta+\omega+\mu)}{\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)} > 0$

2. For $x_i = \beta$, $P_\beta R_0 = \frac{\partial R_0}{\partial \beta} * \frac{\beta}{R_0} = 1 > 0$

3. For $x_i = \alpha$, $P_\alpha R_0 = \frac{\partial R_0}{\partial \alpha} * \frac{\alpha}{R_0} = -\frac{\pi\beta\vartheta\alpha(\delta+\mu+\omega)(\delta+\mu)}{(\alpha+\mu)(\delta+\mu)+\omega\mu)[\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)]} < 0$

4. For $x_i = \omega$, $P_\omega R_0 = \frac{\partial R_0}{\partial \omega} * \frac{\omega}{R_0} = \frac{\pi\beta\vartheta\alpha\omega(\delta+\mu)}{((\alpha+\mu)(\delta+\mu)+\omega\mu)[\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)]} > 0$

5. For $x_i = \delta$, $P_\delta R_0 = \frac{\partial R_0}{\partial \delta} * \frac{\delta}{R_0} = -\frac{\omega\alpha\pi\beta\vartheta\delta}{((\alpha+\mu)(\delta+\mu)+\omega\mu)[\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)]} < 0$

6. For $x_i = \theta$, $P_\theta R_0 = \frac{\partial R_0}{\partial \theta} * \frac{\theta}{R_0} = \frac{\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)}{\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)} > 0.$

7. For $x_i = \gamma$,

$$P_\gamma R_0 = \frac{\partial R_0}{\partial \gamma} * \frac{\gamma}{R_0}$$

$$= -(\frac{\pi\beta\vartheta(\delta+\mu+\omega)}{((\alpha+\mu)(\delta+\mu)+\omega\mu)(\vartheta+\mu)(\mu+\gamma+\varepsilon)} + \frac{1}{\mu+\gamma+\varepsilon}) *$$

$$(\frac{\gamma(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)}{\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)}) < 0.$$

8. For $x_i = \vartheta$,

$$P_\vartheta R_0 = \frac{\partial R_0}{\partial \vartheta} * \frac{\vartheta}{R_0} = \frac{\beta(\delta+\mu+\omega)\vartheta\pi\mu}{[\vartheta\beta\pi(\delta+\omega+\mu)+\theta(\mu+\vartheta)((\alpha+\mu)(\delta+\mu)+\omega\mu)](\vartheta+\mu)(\mu+\gamma+\varepsilon)} > 0.$$

The basic parameter with a positive sensitivity indicator such as β, θ, ϑ and ω has a great impact on the spread of rubella in the community if its value is increased by keeping the other parameters unchanged. However, rates with negative sensitivity indicators, such as α, γ and δ have the function of controlling (minimizing) rubella when their value increases (Table 2).

Table 3. Parameter, Description, Value and Source.

Parameter	Description	Value	Source
π	The recruitment rate	0.015	Prawoto et al. (2020)
β	Contact rate	0.4	Al Qurashi (2020)
ϑ	Exposure rate	0.85	Prawoto et al. (2020)
ε	Death rate due to rubella disease	0.08	Assumed
δ	Rate of second vaccination dose	1	Assumed
μ	Natural death rate	0.4	Koca (2018)
γ	Recovery rate	0.15	Prawoto et al. (2020)
θ	Rate of infected infants	0.55	Assumed
α	Rate of first vaccinated dose	0.3	Baleanu et al. (2020)
ω	waning rate of first vaccination dose	0.6	Assumed
ρ	Rate of temporary immunity	0.01	Assumed
μ	Natural death rate	0.4	Koca (2018)
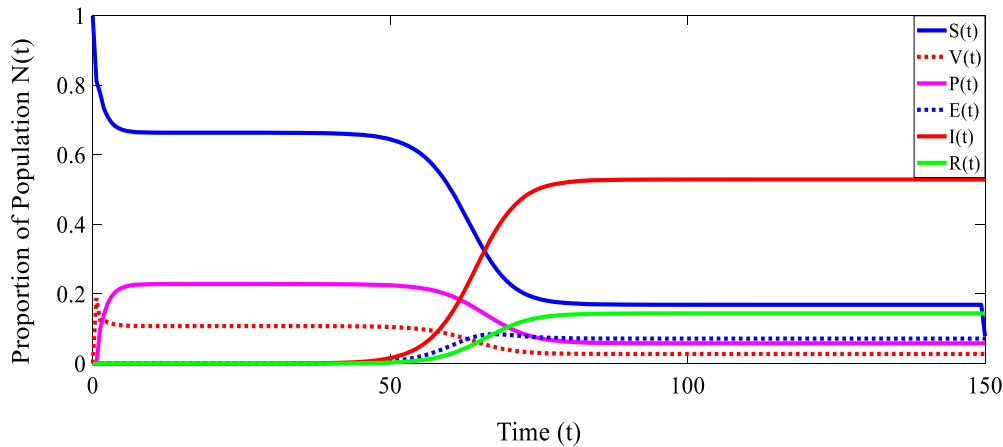
Fig. 2. Graph of a system of ordinary differential equations (1) applying all parameters.

4. Numerical simulations

Investigating the qualitative behavior of the developed model is performed using numerical simulation. The simulation mainly focuses on the exposed and infected classes and observes their behavior over time as their associated parameters change. The numerical analysis of the model is shown by displaying the graphs using the MATLAB R2020a computer software and for loop method of the Matlab program. To perform the numerical simulation, the values of parameters were taken from related published articles and made assumptions for some of the other parameters of the model, whose values and sources are provided in the Table.

Fig. 2 is drawn using the parameter values provided in Table 3 that represent the graph of susceptible $S(t)$, vaccinated $V(t)$, protected $P(t)$, exposed $E(t)$, infected , $I(t)$ and recovered $R(t)$. The figure shows that the susceptible, vaccinated and protected populations are close to zero and as time increases, the population in the infected class will increase.

4.1. Impact of contact rate on exposed and rubella-infected people

Here, we investigate the impact of contact rate on the exposed and infected people. As shown in Fig. 3 to the right, increasing the contact rate will significantly increase the number of infected people. This happens when susceptible individuals come into contact with rubella-infected individuals, contacting the urine of a rubella-infected person and sharing the same items, such as a cup. From the simulation results of Fig. 4 to the left, we can observe that increasing contact rate leads to an increase in the number of exposed individuals. Therefore, it is necessary to control the spread of rubella in the community.

4.2. Impact of vertical transmission and exposure rates on rubella-infected people

Fig. 4 from the right reveals the impact of infected newborns on the rubella disease dynamics. As it is seen from the figure, increasing the rate of infected newborns (passive infection of newborns caused by vertical transmission from mother to fetus) results in increasing the number of rubella-infected people in the community while keeping other parameters unchanged. The result is obtained by varying the value of θ from 0.45 to 0.65. Therefore, to eradicate rubella and reduce CRS, pregnant women must protect themselves from the interaction of rubella-contaminated materials. The impact of the exposure rate is shown in Fig. 4 on the left. It shows that if someone lives in the community for a long period of time without symptoms, the number of people infected with rubella will increase.

4.3. Impact of vaccination and treatment rates on rubella-infected people

As shown in Fig. 5 from the left, when the rate of first and second-dose vaccination increases, the number of rubella-infected individuals approaches zero. This reveals that if everyone is vaccinated before contacting this viral disease, especially new born babies who must receive the MMR vaccine twice, then rubella disease can be controlled. As shown in Fig. 5 from right, the impact of the treatment rate on the rubella-infected
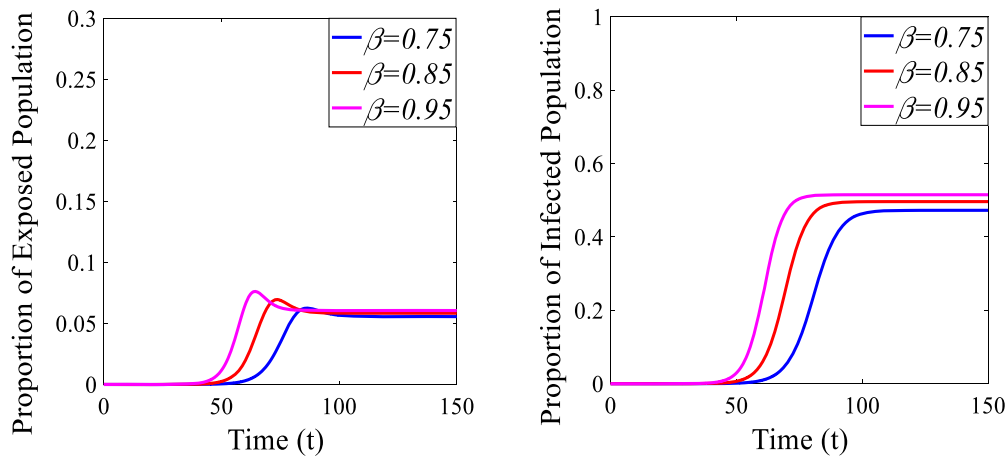
Fig. 3. Graph depicting the impact of contact rate on exposed and rubella-infected people.
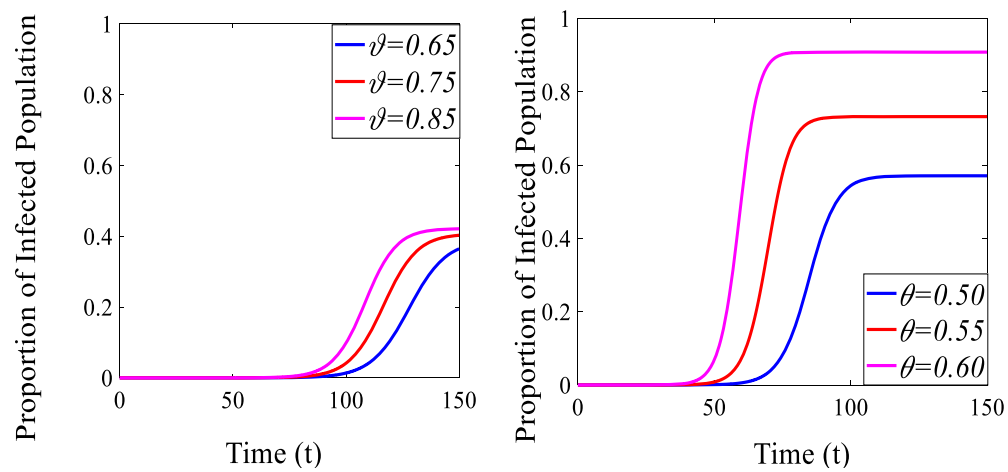

Fig. 4. Graph depicting the impact of exposed (left) and vertical transmission (right) rates on rubella-infected people.
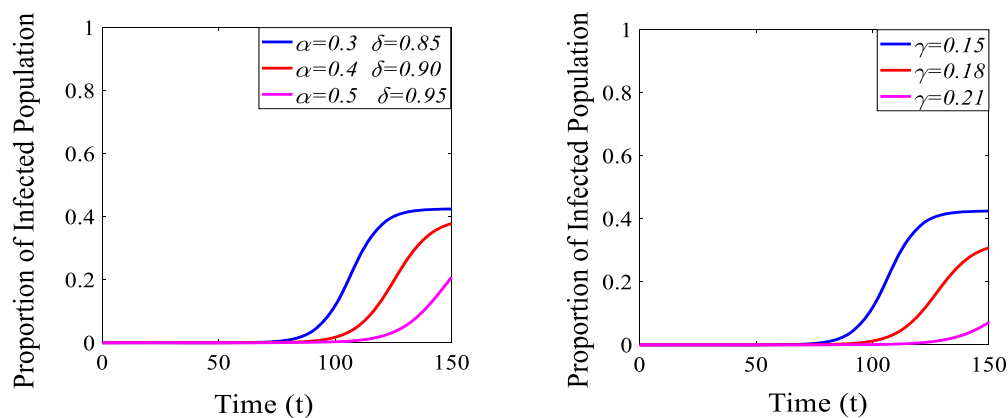

Fig. 5. A graph depicting the effect of vaccination doses (left) and treatment rate (right) on rubella-infected people.

people is studied, and the results of the numerical simulation are obtained by varying the value of the treatment rate while keeping the other parameters constant. Increasing the value of γ will result in a decrease in the number of rubella infections. This indicates that the increment in the value of this rate has a great contribution to reducing rubella disease in the community.

5. Discussion and conclusion

In this study, the SVPEIRS deterministic mathematical model of rubella disease dynamics is formulated and analyzed. The basic qualitative analysis of the model is discussed in Section 3. The result of the qualitative analysis shows that the solution of the constructed model is bounded and positive. The local stability of the disease-free equilibrium point in the developed model is determined using the Jacobian matrix and is locally

asymptotically stable if the number of secondary infected individuals caused by a single rubella infected individual is greater than one. The basic reproductive number is calculated using the next-generation matrix to determine the existence of the rubella disease in the community.

A sensitivity analysis that determines the contribution of each basic parameter to the dynamics of rubella disease is performed. The results of the analysis show that the recruitment rate (π), contact rate (β), vertical transmission (neonatal infection) rate (θ) and exposure rate (ϑ) all have positive sensitivity indicators. Increasing the value of these parameters has the greatest impact on the spread of the rubella disease. However, the treatment rate (γ), the first dose (α) and second dose rates (δ) have negative sensitivity indicator. Thus, they have a role in controlling rubella disease when their value increases.

Finally, using MATLAB R2020a computer software, the numerical simulation and the effect of the parameters that are used to investigate the effect of some basic parameters are performed and the result of the simulation is shown graphically. According to our simulation results, increasing values of some parameters like γ, α and δ as well as decreasing the values of β, θ and ϑ, have a significant role in controlling the spread of rubella in the community. Therefore, these findings suggest that healthcare professionals and policy-makers pay attention to these parameters.

Declarations

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