



Mathematics Model of COVID-19 with Two-Stage Vaccination, Symptomatic, Asymptomatic, and Quarantine Individuals

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ABSTRACT

The COVID-19 mathematical model began to develop since the disease appeared at the end of 2019. This model is used to investigate the characteristics of the spread of a disease. This research developed a model of COVID-19 based on the SEIR model which was further developed by dividing the infected subpopulation into symptomatic and asymptomatic, adding quarantine of infected individuals and vaccination in two steps. Making this model begins with making a compartment diagram of the disease and then forming a system of differential equations. After the model is formed, the disease-free equilibrium point, endemic equilibrium point, and basic reproduction number (R_0) are obtained. Analysis of the stability of the disease-free equilibrium point was locally asymptotically stable if $R_0 < 1$ and an endemic equilibrium point existed if $R_0 > 1$. Numerical simulation for the model that has been made is in line with the analysis. Furthermore, the sensitivity analysis of the basic reproduction number obtained that the parameters that have a significant effect on the spread of COVID-19 are the rate of the first dose vaccination, the rate of contact with symptomatic or asymptomatic individuals, and the rate of quarantine of symptomatic infected individuals.

Keywords: COVID-19; equilibrium point; basic reproduction number; sensitivity analysis

INTRODUCTION

SARS-CoV-2 is the virus that causes Coronavirus Disease 2019 (COVID-19) and first discovered at Wuhan, Hubei Province, China [1]. The current level of COVID-19 has become a pandemic because the virus has infected almost the entire world, not just in one area [2]. It is recorded that until July 1, 2021, or more than one year since this infection was first discovered, COVID-19 has infected up to 222 countries in the world with 182,989,419 infected cases, 11,452,155 active cases, and 3,962,991 deaths [3]. The first case of COVID-19 in Indonesia was discovered on March 2, 2020, the two positive patients are domiciled in Depok, West Java. After the discovery of the first two positive patients, the positive number of COVID-19 in Indonesia continued to increase [4]. Until July 1, 2021, or more than a year after the first case in Indonesia, it was recorded that this virus had infected 2,203,108 individuals, with 258,826 active cases and 58,995 deaths [5]. In addition to symptomatic infected individuals, some asymptomatic infected individuals have a very large potential to transmit COVID-19 [6]. Research [7] analyzing susceptible individuals who came into contact with infected individuals found that infected

individuals without symptoms were less likely to transmit infection than symptomatic infected individuals.

One of the hopes that the COVID-19 pandemic will quickly subside and return all the things like before is with a vaccine. On January 11, 2020, the genetic sequence of SARS-CoV-2, the virus that caused this pandemic was published. This has triggered various research institutions in the world to carry out developments related to the COVID-19 vaccine. The vaccine for COVID-19 is not a cure. Vaccines create immunity against COVID-19, prevent the emergence or possibility of serious illness, or reduce serious symptoms that appear. The use of this rapidly researched vaccine is based on an emergency clearance from the World Health Organization (WHO) [8]. Several types of vaccines in the world have received Emergency Use Listing (EUL) and Emergency Use Authorization (EUA) from WHO including AstraZeneca, Pfizer, Janssen, Sinovac, Moderna, Sinopharm and, Sinovac [9].

One way to find out and anticipate bigger things in the spread of COVID-19 is to make a modeling of the disease. A number of studies on the mathematical model of COVID-19 was carried out, including Gabriel O. Fosu et al. [10], who made various types of models ranging from SIR to SEIR with quarantine and vaccination, but they only analyzed the SIR model. Furthermore, Idris Ahmed et al. [11] developed the SEIQR model by dividing the infected compartment into 2 parts, namely symptomatic infection (I_S), and asymptomatic infection (I_A). Enahoro A. Iboi et al. [12] made another development on his SEIR model by adding vaccinated individuals, dividing compartment E into two parts and dividing symptomatic infected individuals (I_S) asymptomatic infected individuals (I_A) and hospitalized individuals (I_H).

In this research, an SEIR COVID-19 spread model will be developed with quarantine and vaccination. In addition, it also divides people with COVID-19 with symptoms and without symptoms. Based on this model, the disease-free equilibrium point and the endemic equilibrium point will be searched, then the basic reproduction number (R_0) will be searched. Furthermore, from the disease-free equilibrium point, stability will be searched using the Jacobi matrix eigenvalue analysis using the Routh-Hurwitz Criteria. After that, a model simulation will be carried out to provide a geometric picture of the solution and to support the theorem. Then an analytical sensitivity of the model parameters to the basic reproduction number was carried out to find out which parameters dominantly affect the spread of COVID-19.

METHODS

This research begins with a literature study. We created a mathematical model of covid-19 from the study [12] then added a 2-dose vaccination and quarantine compartment. Next, we will find the disease-free equilibrium point and the endemic equilibrium point. Then we find the basic reproduction number using the next generation matrices. The local stability of the disease-free equilibrium point was analyzed with the help of the Routh-Hurwitz Criteria. Afterwards, the model simulation is performed using the 4th-order Runge-Kutta method that has been made to strengthen the analysis in the previous stage.

RESULTS AND DISCUSSION

Model Formulation

Assumptions for the mathematical model of COVID-19 with 2-dose vaccination, symptomatic, asymptomatic and quarantine are as follows: (1) The population is

assumed to be closed, there is no movement of people out or into the area. (2) Birth and death rates are assumed to be the same with rate μ , which mean the population is constant. (3) Every individual born is assumed to be in good health but has a risk of infection because it is not immune to disease. (4) Disease transmission occurs through direct contact between susceptible individuals and symptomatic or asymptomatic individuals. (5) Infected individuals are divided into symptomatic and asymptomatic. (6) Symptomatic and asymptomatic individuals who are detected must be quarantined. (7) Asymptomatic infected individuals who are not detected can recover on their own. (8) Vaccination is used to reduce the risk of susceptible individuals being infected. (9) Vaccination is carried out in 2 steps. (10) Death from disease is negligible. Based on the assumption, the model can be made a scheme for the spread of COVID-19 disease with 2 doses of vaccination, symptomatic infection, asymptomatic infection, and quarantine as shown in Figure 1.

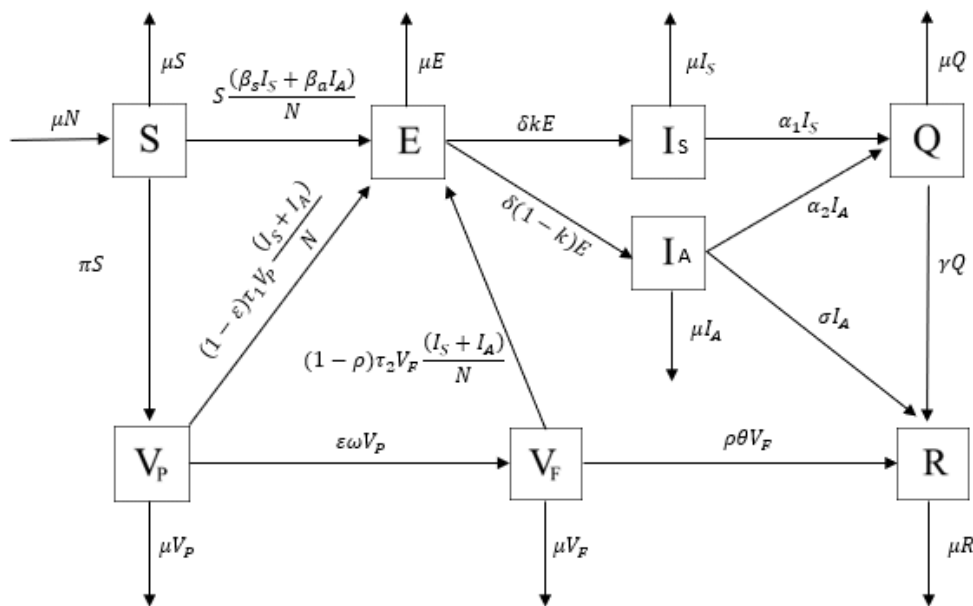


Figure 1. Compartment diagram of COVID-19 spread

In Figure 1 the individual population is divided into 8 compartments. Compartment of susceptible individuals (S), compartment of individuals who have received vaccine dose 1 (V_P), compartment of individuals who have received dose 2 of vaccine (V_F), compartment of latent individuals (E), compartment of symptomatic infected individuals (I_S), compartment of asymptomatic infected individuals (I_A), compartment of quarantined individuals (Q), and compartment of individuals who have recovered from disease or are immune to disease (R). Every birth (μ) will be a susceptible individual (S) with the potential to be infected with COVID-19. To reduce the potential for infection, 2 doses of vaccination are carried out, susceptible individuals will receive 1 dose of vaccine (V_P) at a rate of π . Individuals who have received vaccine dose 1 still have the potential to be infected by τ_1 and affected by the proportion of vaccine efficacy by $1 - \epsilon$. Individuals who have received vaccine dose 1 will receive vaccine dose 2 (V_F) at a rate of ω and the proportion of vaccine efficacy is ϵ . Individuals who have received dose 2 of the vaccine still have the potential to be infected at a rate of τ_2 and are affected by the proportion of vaccine efficacy by $1 - \rho$. Each susceptible individual, who has received dose 1 of the vaccine and has received dose 2 of the vaccine, who is infected will become a latent individual (E).

The rate of susceptible individuals to become latent individuals is β_s when contact with symptomatic infected individuals and β_a when contact with asymptomatic infected individuals. Latent individuals will become symptomatic infected individuals (I_S) with a rate of δ and a proportion of k . Latent individuals will become asymptomatic infected individuals (I_A) with a rate of δ and a proportion of $1 - k$. Symptomatic infected individuals will quarantine (Q) at a rate of α_1 . Asymptomatic infected individuals who are detected will also be quarantined at a rate of α_2 . Asymptomatic infected individuals who are not detected can recover naturally due to the body's immune factor at a rate of σ . Individuals who have received 2 doses of the vaccine will get immunity (R) at a rate of θ and efficacy of ρ . Individuals who do quarantine will recover (R) at a rate of γ . Each compartment has a natural death of μ .

The mathematical model of COVID-19 with 2 doses of vaccination, symptomatic infected, asymptomatic infected and quarantine is obtained as follows:

$$\begin{aligned}
 \frac{dS}{dt} &= \mu N - S \frac{(\beta_s I_S + \beta_a I_A)}{N} - \pi S - \mu S \\
 \frac{dV_P}{dt} &= \pi S - (1 - \varepsilon) \tau_1 V_P \frac{(I_S + I_A)}{N} - \varepsilon \omega V_P - \mu V_P \\
 \frac{dV_F}{dt} &= \varepsilon \omega V_P - (1 - \rho) \tau_2 V_F \frac{(I_S + I_A)}{N} - \rho \theta V_F - \mu V_F \\
 \frac{dE}{dt} &= S \frac{(\beta_s I_S + \beta_a I_A)}{N} + (1 - \varepsilon) \tau_1 V_P \frac{(I_S + I_A)}{N} + (1 - \rho) \tau_2 V_F \frac{(I_S + I_A)}{N} - \delta E - \mu E \\
 \frac{dI_S}{dt} &= \delta k E - \alpha_1 I_S - \mu I_S \\
 \frac{dI_A}{dt} &= \delta (1 - k) E - \alpha_2 I_A - \sigma I_A - \mu I_A \\
 \frac{dQ}{dt} &= \alpha_1 I_S + \alpha_2 I_A - \gamma Q - \mu Q \\
 \frac{dR}{dt} &= \gamma Q + \sigma I_A + \rho \theta V_F - \mu R
 \end{aligned} \tag{1}$$

Where $N = S + V_P + V_F + E + I_S + I_A + Q + R$ then obtained $\frac{dN}{dt} = 0$, thus $N(t) = c$ where c is positive integer. Since $N(t)$ is constant, then system (1) can be formed into a non-dimensional model in order to simplify the model. The proportion of many individuals in each compartment can be expressed as:

$$s = \frac{S}{N}, v_p = \frac{V_P}{N}, v_f = \frac{V_F}{N}, e = \frac{E}{N}, i_s = \frac{I_S}{N}, i_a = \frac{I_A}{N}, q = \frac{Q}{N}, r = \frac{R}{N} \tag{2}$$

Divide equation (1) by $N(t)$ and express them as in (2) to obtain a non-dimensional mathematical model (3). In equation (3), variable r is ignored since it does not affect the other compartments.

$$\begin{aligned}
 \frac{ds}{dt} &= \mu - s(\beta_s i_s + \beta_a i_a) - \pi s - \mu s \\
 \frac{dv_p}{dt} &= \pi s - (1 - \varepsilon)\tau_1 v_p (i_s + i_a) - \varepsilon \omega v_p - \mu v_p \\
 \frac{dv_f}{dt} &= \varepsilon \omega v_p - (1 - \rho)\tau_2 v_f (i_s + i_a) - \rho \theta v_f - \mu v_f \\
 \frac{de}{dt} &= s(\beta_s i_s + \beta_a i_a) + (1 - \varepsilon)\tau_1 v_p (i_s + i_a) + (1 - \rho)\tau_2 v_f (i_s + i_a) - \delta e - \mu e \quad (3) \\
 \frac{di_s}{dt} &= \delta k e - \alpha_1 i_s - \mu i_s \\
 \frac{di_a}{dt} &= \delta(1 - k)e - \alpha_2 i_a - \sigma i_a - \mu i_a \\
 \frac{dq}{dt} &= \alpha_1 i_s + \alpha_2 i_a - \gamma q - \mu q
 \end{aligned}$$

Disease Free Equilibrium Point

A disease-free equilibrium point can be obtained when there are no infected individuals in the population. To fulfill this, it must be $i_s = 0$ and $i_a = 0$. The disease-free equilibrium point is obtained as follows:

$$E_0(s, v_p, v_f, e, i_s, i_a, q) = \left(\frac{\mu}{\pi + \mu}, \frac{\pi \mu}{(\pi + \mu)(\varepsilon \omega + \mu)}, \frac{\varepsilon \omega \pi \mu}{(\pi + \mu)(\omega + \mu)(\rho \theta + \mu)}, 0, 0, 0, 0 \right) \quad (4)$$

Basic Reproduction Number (R_0)

The basic reproduction number can be obtained by finding the maximum eigenvalue of the next generation matrix [13]. The next-generation matrix is obtained from the infected subsystem equation. Take the equation which is the new infection case and also the change in the infected case in the system. Infected subsystem in (3) is e, i_s, i_a, q . Linearization of the infected subsystem at the disease-free equilibrium point. Can be represented by the following Jacobian matrix (J):

$$J_{E_0} = \begin{bmatrix} \frac{de}{de} & \frac{de}{di_s} & \frac{de}{di_a} & \frac{de}{dq} \\ \frac{di_s}{de} & \frac{di_s}{di_s} & \frac{di_s}{di_a} & \frac{di_s}{dq} \\ \frac{di_a}{de} & \frac{di_a}{di_s} & \frac{di_a}{di_a} & \frac{di_a}{dq} \\ \frac{dq}{de} & \frac{dq}{di_s} & \frac{dq}{di_a} & \frac{dq}{dq} \end{bmatrix}$$

Decomposition of the Jacobian matrix (J) into a matrix $J = F - V$, where F is the transmission matrix and V is the transition matrix.

$$F = \begin{bmatrix} 0 & \frac{\beta_s \mu (\varepsilon \omega + \mu) (\rho \theta + \mu) + \tau_1 \pi \mu (\rho \theta + \mu) + \tau_2 \varepsilon \omega \pi \mu}{(\pi + \mu) (\varepsilon \omega + \mu) (\rho \theta + \mu)} & \frac{\beta_a \mu (\varepsilon \omega + \mu) (\rho \theta + \mu) + \tau_1 \pi \mu (\rho \theta + \mu) + \tau_2 \varepsilon \omega \pi \mu}{(\pi + \mu) (\varepsilon \omega + \mu) (\rho \theta + \mu)} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} (\delta + \mu) & 0 & 0 & 0 \\ -\delta k & (\alpha_1 + \mu) & 0 & 0 \\ -\delta(1-k) & 0 & (\alpha_2 + \sigma + \mu) & 0 \\ 0 & -\alpha_1 & -\alpha_2 & (\gamma + \mu) \end{bmatrix}, FV^{-1} = \begin{bmatrix} M_1 & M_2 & M_3 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$M_1 = \left(\frac{\beta_s \mu BC + \tau_1 \pi \mu C + \tau_2 \varepsilon \omega \pi \mu}{ABC} \right) \left(\frac{\delta k}{DE} \right) + \left(\frac{\beta_a \mu BC + \tau_1 \pi \mu C + \tau_2 \varepsilon \omega \pi \mu}{ABC} \right) \left(\frac{\delta(1-k)}{DF} \right),$$

$$M_2 = \left(\frac{\beta_s \mu BC + \tau_1 \pi \mu C + \tau_2 \varepsilon \omega \pi \mu}{ABCE} \right), M_3 = \left(\frac{\beta_a \mu BC + (1-\varepsilon)\tau_1 \pi \mu C + (1-\rho)\tau_2 \varepsilon \omega \pi \mu}{ABCF} \right)$$

where $A = (\pi + \mu)$, $B = (\varepsilon\omega + \mu)$, $C = (\rho\theta + \mu)$, $D = (\delta + \mu)$, $E = (\alpha_1 + \mu)$ dan $F = (\alpha_2 + \sigma + \mu)$. Next, R_0 can be obtained by computing the spectral radius (ρ) or the largest absolute value of the eigenvalues of FV^{-1} , which can be expressed as:

$$R_0 = \rho(FV^{-1}) = M_1$$

$$R_0 = \left(\frac{\beta_s \mu BC + \tau_1 \pi \mu C + \tau_2 \varepsilon \omega \pi \mu}{ABC} \right) \left(\frac{\delta k}{DE} \right) + \left(\frac{\beta_a \mu BC + \tau_1 \pi \mu C + \tau_2 \varepsilon \omega \pi \mu}{ABC} \right) \left(\frac{\delta(1-k)}{DF} \right). \quad (5)$$

The basic reproduction number is defined as the average number of the second infection that occurred when the first infection started to infect all susceptible population [13]. In general, if $R_0 < 1$ then the disease will disappear and if $R_0 > 1$ then the disease will become epidemic. Further interpretation of R_0 on (5) is discussed in the following.

Endemic Equilibrium Point

The endemic equilibrium point occurs when the infected class is not zero or the disease has become epidemic in a population. Must be $i_s^* > 0$ and $i_a^* > 0$.

$$i_s^* = \frac{\delta k e^*}{\alpha_1 + \mu} \quad (6)$$

$$i_a^* = \frac{\delta(1-k)e^*}{\alpha_2 + \sigma + \mu} \quad (7)$$

$$s^* = \frac{\mu}{(\beta_s i_s^* + \beta_a i_a^*) + \pi + \mu} \quad (8)$$

$$v_p^* = \frac{\pi s^*}{(1-\varepsilon)\tau_1(i_s^* + i_a^*) + \varepsilon\omega + \mu} \quad (9)$$

$$v_f^* = \frac{\varepsilon\omega v_p^*}{(1-\rho)\tau_2(i_s^* + i_a^*) + \rho\theta + \mu} \quad (10)$$

$$q^* = \frac{\alpha_1 \left(\frac{\delta k e^*}{\alpha_1 + \mu} \right) + \alpha_2 \left(\frac{\delta(1-k)e^*}{\alpha_2 + \sigma + \mu} \right)}{\gamma + \mu} \quad (11)$$

$$a_0 e^{*3} + a_1 e^{*2} + a_2 e^* + a_3 = 0 \quad (12)$$

Where

$$a_0 = (\beta_s \delta k DF + \beta_a \delta(1-k)DE)(M\tau_1 \delta x)(N\tau_2 \delta x)$$

$$a_1 = (\beta_s \delta k DF + \beta_a \delta(1-k)DE)(M\tau_1 \delta x C + N\tau_2 \delta x B) + ADEF(M\tau_1 \delta x)(N\tau_2 \delta x) - (\beta_s \mu \delta k F + \beta_a \mu \delta(1-k)E)(M\tau_1 \delta x)(N\tau_2 \delta x)$$

$$a_2 = (\beta_s \delta k D F + \beta_a \delta (1 - k) D E) B C + A D E F [(M \tau_1 \delta x) C + (N \tau_2 \delta x) B] - (\beta_s \mu \delta k F + \beta_a \mu \delta (1 - k) E) (M \tau_1 \delta x C + N \tau_2 \delta x B) - N \tau_1 \tau_2 \pi \mu (\delta x)^2 E F$$

$$a_3 = A B C D E F (1 - R_0), M = (1 - \varepsilon), N = (1 - \rho) \text{ and } x = \left(\frac{k}{E} + \frac{(1-k)}{F} \right).$$

Theorem 1. Assumed $E_1 = (s^*, v_p^*, v_f^*, e^*, i_s^*, i_a^*, q^*)$ is endemic equilibrium point. E_1 exists if $R_0 > 1$.

Proof. The existence of an equilibrium point is indicated with each positive element according to the conditions for the formation of this model. We will prove that equation (12) has at least one positive root. According to Descartes' Rules of Sign [14], a polynomial will have as many positive roots as the change in a sign that occurs in the coefficients of the equation. Then it will be proven that there is at least one sign change in the equation. It is clear that $a_0 > 0$. Take the coefficient a_3 and it will be proved that its value is negative. With $R_0 > 1$, the value of $a_3 < 0$ is obtained, then there is at least one positive root in the equation according to [14]. So, Theorem 1 is proven to be true. ■

Stability Analysis of Disease-Free Equilibrium Point

Theorem 2. Disease equilibrium point E_0 asymptotically stable if $R_0 < 1$.

Proof. Analysis of the stability of the disease-free equilibrium point can be determined by finding the eigenvalues of the Jacobian matrix around the disease-free equilibrium point E_0 [15].

$$J_{(E_0)} = \begin{bmatrix} -A & 0 & 0 & 0 & -\frac{\beta_s \mu}{A} & -\frac{\beta_a \mu}{A} & 0 \\ \pi & -B & 0 & 0 & -\left(\frac{\tau_1 \pi \mu}{AB}\right) & -\left(\frac{\tau_1 \pi \mu}{AB}\right) & 0 \\ 0 & \omega & -C & 0 & -\left(\frac{\tau_2 \omega \pi \mu}{ABC}\right) & -\left(\frac{\tau_2 \omega \pi \mu}{ABC}\right) & 0 \\ 0 & 0 & 0 & -D & Y & Z & 0 \\ 0 & 0 & 0 & \delta k & -E & 0 & 0 \\ 0 & 0 & 0 & \delta(1 - k) & 0 & -F & 0 \\ 0 & 0 & 0 & 0 & \alpha_1 & \alpha_2 & -G \end{bmatrix} \quad (13)$$

$$A = (\pi + \mu), B = (\varepsilon \omega + \mu), C = (\rho \theta + \mu), D = (\delta + \mu), E = (\alpha_1 + \mu), F = (\alpha_2 + \sigma + \mu), G = (\gamma + \mu), Y = \left(\frac{\beta_s \mu}{A} + \frac{\tau_1 \pi \mu}{AB} + \frac{\tau_2 \omega \pi \mu}{ABC} \right) \text{ and } Z = \left(\frac{\beta_a \mu}{A} + \frac{\tau_1 \pi \mu}{AB} + \frac{\tau_2 \omega \pi \mu}{ABC} \right).$$

The characteristic equation is obtained as follows:

$$(\lambda + G)(\lambda + C)(\lambda + B)(\lambda + A)P = 0 \quad (13)$$

where

$$P = \lambda^3 + (D + E + F)\lambda^2 + (DE + EF + DF - Y\delta k - Z\delta(1 - k))\lambda + (DEF - Y\delta k F - Z\delta(1 - k)E) \quad (14)$$

Based on equation (13) from matrix $J_{(E_0)}$ we get $\lambda_1 = -G, \lambda_2 = -C, \lambda_3 = -B$, and $\lambda_4 = -A$. Since the values of A, B, C , and G are positive, the real part of the four eigenvalues is negative. The other three eigenvalues were obtained as follows. In equation (14) we get $a_0 = 1, a_1 = (D + E + F), a_2 = (DE + EF + DF - Y\delta k - Z\delta(1 - k))$ and $a_3 = (DEF - Y\delta k F - Z\delta(1 - k)E)$. To find out the sign of the real part of the other eigenvalues, the Routh-Hurwitz criterion is used [13], with the condition $\frac{a_1}{a_0} > 0, \frac{a_2}{a_0} > 0$, and $\frac{a_3}{a_0} > 0$. For $\frac{a_1}{a_0} > 0$, we get: $\frac{a_1}{a_0} = D + E + F = \delta + \alpha_1 + \alpha_2 + \sigma + 3\mu > 0$. Then it's proved that $\frac{a_1}{a_0} > 0$.

From (5), we have

$$R_0 = \frac{Y\delta kF + Z\delta(1-k)E}{DEF}$$

For $\frac{a_2}{a_0} > 0$, we get:

$$\begin{aligned} \frac{a_2}{a_0} &= DE + DF + EF - Y\delta k - Z\delta(1-k) \\ &= \frac{Z(1-k)DE^2 + YkDF^2 + YkEF^2 + Z(1-k)E^2F}{YkF + Z(1-k)E} + \frac{DEF(Yk + Z(1-k))}{YkF + Z(1-k)E}(1 - R_0) \end{aligned}$$

Because D, E, F, Y , and Z are positive, then it's proved that $\frac{a_2}{a_0} > 0$ if only if $R_0 < 1$.

For $\frac{a_3}{a_0} > 0$, we get:

$$\frac{a_3}{a_0} = DEF - Y\delta kF - Z\delta(1-k)E = (\delta + \mu)(\alpha_1 + \mu)(\alpha_2 + \sigma + \mu)(1 - R_0)$$

Then it's proved that $\frac{a_3}{a_0} > 0$ if only if $R_0 < 1$. Thus, the first condition of the Routh-Hurwitz criteria $\frac{a_1}{a_0} > 0, \frac{a_2}{a_0} > 0, \frac{a_3}{a_0} > 0$ proved.

According to the Routh-Hurwitz criteria, all eigenvalues will be negative if $\Delta_1, \Delta_2, \Delta_3 > 0$. Define the Routh-Hurwitz matrix:

$$H = \begin{bmatrix} a_1 & a_0 & 0 \\ a_3 & a_2 & a_1 \\ 0 & 0 & a_3 \end{bmatrix}$$

The value of Δ_1 from matrix H obtained:

$$\Delta_1 = |a_1| = D + E + F = \delta + \alpha_1 + \alpha_2 + \sigma + 3\mu > 0$$

Then it's proved that $\Delta_1 > 0$. The value of Δ_2 from matrix H obtained:

$$\begin{aligned} \Delta_2 = \begin{vmatrix} a_1 & a_0 \\ a_3 & a_2 \end{vmatrix} &= (D + E + F) \left(\frac{Z(1-k)DE^2 + YkDF^2 + YkEF^2 + Z(1-k)E^2F}{YkF + Z(1-k)E} \right) \\ &+ \left(\frac{(YkD + Z(1-k)D + YkE + Z(1-k)F)}{YkF + Z(1-k)E} \right) DEF(1 - R_0) \end{aligned}$$

Because D, E, F, Y and Z are positive, then it's proved that $\Delta_2 > 0$ if only if $R_0 < 1$.

The value of Δ_3 from matrix H obtained:

$$\Delta_3 = \begin{vmatrix} a_1 & a_0 & 0 \\ a_3 & a_2 & a_1 \\ 0 & 0 & a_3 \end{vmatrix} = a_3(\Delta_2)$$

In the previous equation, it has been proven that $a_3 > 0$ and $\Delta_2 > 0$. Then it's proved that $\Delta_3 > 0$.

The determinant of the Routh-Hurwitz matrix $\Delta_1, \Delta_2, \Delta_3$ has a positive value if and only if $R_0 < 1$. So, the characteristic equation (13) has a negative real root part. Based on the results obtained, it can be concluded that the disease-free equilibrium point E_0 is locally asymptotically stable. ■

Model Simulation

The mathematical model of COVID-19 with 2 doses of vaccination, symptomatic, asymptomatic, and quarantine has been formed and analyzed and then carried out

numerical simulations. In this simulation, values are given for each parameter that has been determined. This simulation was carried out using the 4th-order Runge-Kutta method. Below are given the parameter values obtained from various reference sources.

Table 1. Disease-free equilibrium point parameter values

No	Parameter	Values	Units	Reff	No	Parameter	Values	Units	Reff
1	μ	0.009	$\frac{1}{day}$	[16]	9	τ_1	$\frac{1}{28}$	$\frac{1}{day}$	[17]
2	β_s	0.3214	$\frac{1}{day}$	[12]	10	τ_2	$\frac{1}{119}$	$\frac{1}{day}$	[19]
3	β_a	0.7701	$\frac{1}{day}$	[12]	11	ω	$\frac{1}{28}$	$\frac{1}{day}$	[20]
4	δ	$\frac{1}{5.1}$	$\frac{1}{day}$	[12]	12	θ	$\frac{1}{28}$	$\frac{1}{day}$	[20]
5	k	0.65		[12]	13	α_1	0.0514	$\frac{1}{day}$	[12]
6	π	0.035	$\frac{1}{day}$	[17]	14	α_2	0.0514	$\frac{1}{day}$	[12]
7	ε	0.653		[18]	15	σ	$\frac{1}{7}$	$\frac{1}{day}$	[12]
8	ρ	0.653		[18]	16	γ	$\frac{1}{14}$	$\frac{1}{day}$	[12]

Based on the parameter values in table 1, the basic reproduction number is $R_0 = 0.9740939287$. Because the value of $R_0 < 1$ then the spread of the disease will slowly decrease and after a certain period time the population will be free from disease. The disease-free equilibrium point obtained $E_0 = (s, v_p, v_f, e, i_s, i_a, q) = (0.204546, 0.221497, 0.15982, 0, 0, 0, 0)$.

Simulation results using the 4th-order Runge-Kutta method at E_0 based on parameter values in table 1 with initial values $s(0) = 0.35$, $v_p(0) = 0.15$, $v_f(0) = 0.8$, $e(0) = 0.07$, $i_s(0) = 0.1$, $i_a(0) = 0.07$ and $q(0) = 0.08$ can be seen in Figure 2. Figure 2 shows the population of susceptible individuals decreased until day 30, then the individual population increased until day 1000 and was stable at 0.204546. The population of individuals who received dose 1 of the vaccine decreased until day 50, then the individual population increased until day 1000 and reached stability at the point of 0.221497. For the individual population who received dose 2 vaccination, it increased until day 1000 and was stable at 0.15982. The population of latent individuals increased in the first 5 days, then decreased until day 1000 approached the point 0 and was stable at that point. The population of asymptomatic individuals decreased, until day 500 the individual population approached the point 0 and was stable. The population of symptomatic individuals increased in the initial 20 days, then decreased until day 1000 approached the point 0 and was stable. The population of individuals who were quarantined increased until day 20, then decreased until day 1000, the individual population approached the point 0 and stable.

Simulation for the value of $R_0 > 1$. The parameter value of β_s increased to 0.7 and the parameter value of π decreased to 0.02. Based on these parameter values we found the basic reproduction number $R_0 = 2.661972975 > 1$. It is found that the endemic equilibrium point is $E_1 = (0.11662, 0.07033, 0.05044, 0.02773, 0.05852, 0.00936, 0.04338)$. The simulation results of the endemic equilibrium point with initial values $s(0) = 0.35$, $v_p(0) = 0.15$, $v_f(0) = 0.8$, $e(0) = 0.07$, $i_s(0) = 0.1$, $i_a(0) = 0.07$ and $q(0) = 0.08$ can be seen in Figure 3. Figure 3 shows the population of susceptible individuals decreased until day 20, then increased until day 200 and stable at 0.11662. The population of individuals who received doses of vaccines 1 and 2 decreased until day 200, then stable at 0.07033

for dose 1 and 0.05044 for dose 2. The population of latent individuals increased until day 10, then decreased until day 150, and was stable at 0.02773. The population of symptomatic infected individuals increased until day 20, then decreased until day 200, and was stable at 0.05852. The population of asymptomatic infected individuals decreased until 100 days and stable at 0.00936. The population of individuals who were quarantined increased until day 20, then decreased until day 200, and was stable at 0.04338.

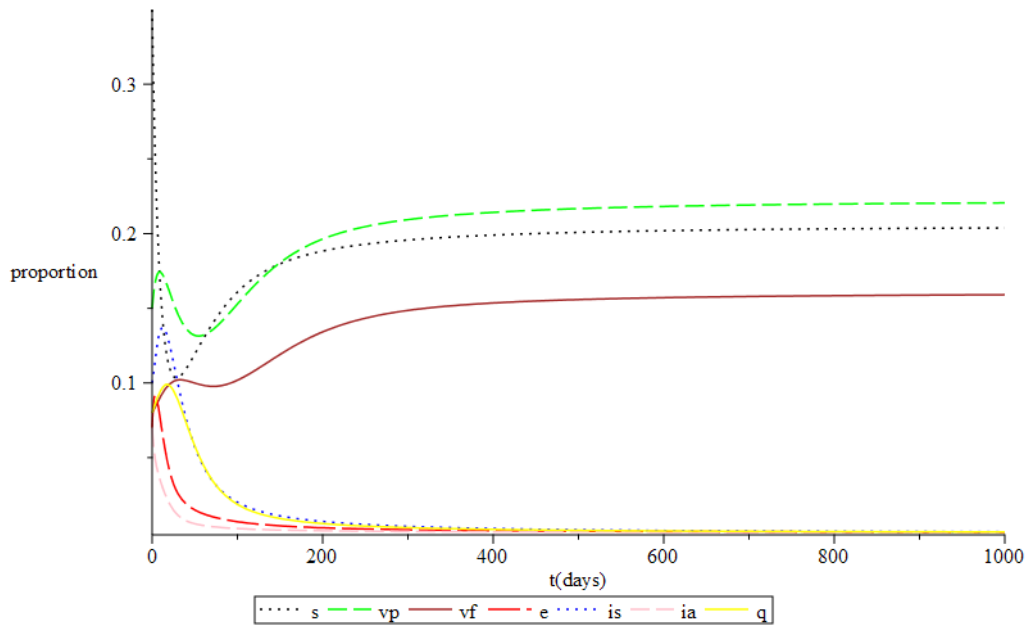


Figure 2. Simulation of disease-free equilibrium point

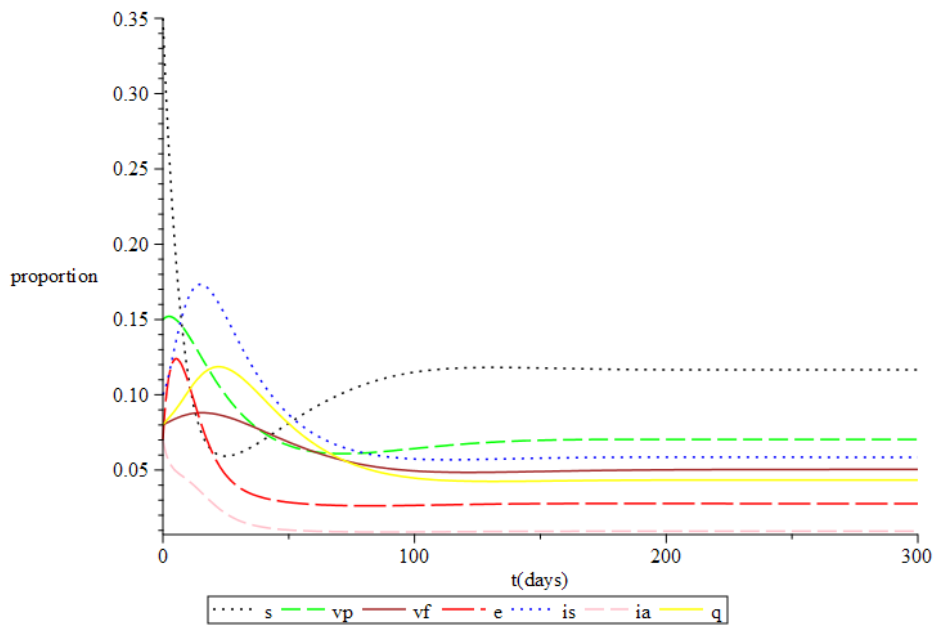


Figure 3. Simulation of the endemic equilibrium point

Next, a numerical simulation was performed by changing the value of the dose 1 vaccination rate (π). Simulations are carried out to determine how much influence the value of π .

Table 2. Numerical simulation of dose 1 vaccination

π	R_0	Condition of i_s and i_a
0.01	2.192400704	Become endemic, stable on day 300 and day 200
0.02	1.453014522	Become endemic, stable on day 350 and day 250
0.035	0.9780762026	The disease will disappear on day 1000 and day 500
0.06	0.6386181501	The disease will disappear on day 350 and day 200
0.09	0.4596977351	The disease will disappear on day 250 and day 150

In graphical it presented in figure 4.

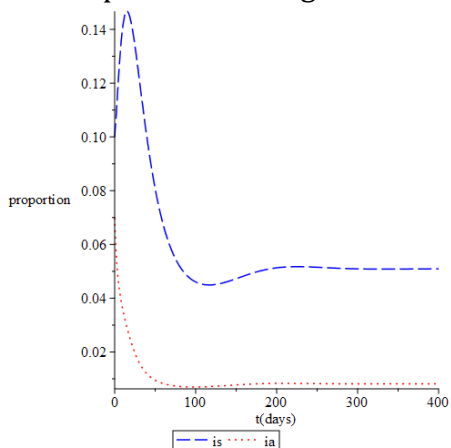


Figure 4. (a)

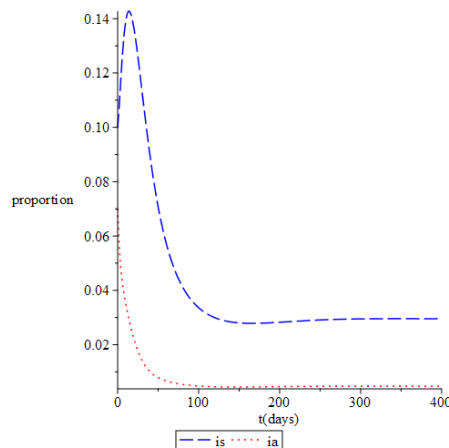


Figure 4. (b)

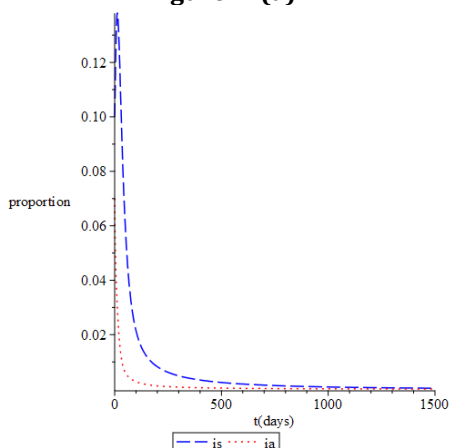


Figure 4. (c)

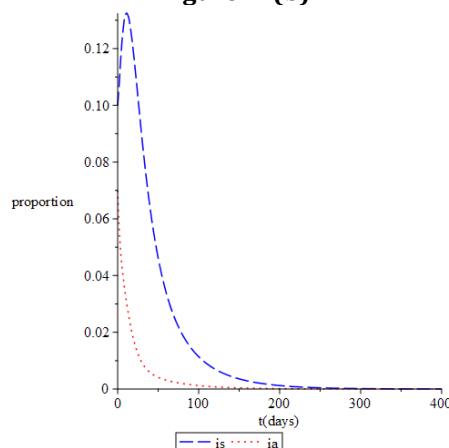


Figure 4. (d)

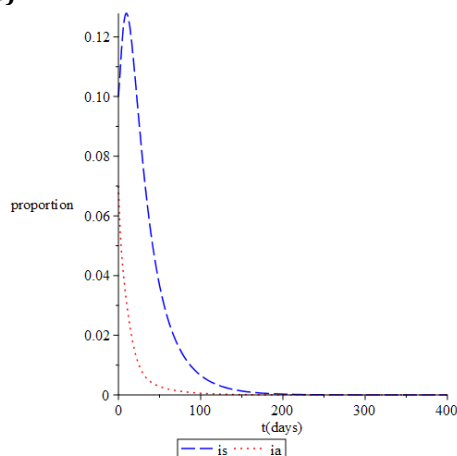


Figure 4. (e)

Figure 4. (a) simulation when $\pi = 0.01$, **(b)** simulation when $\pi = 0.02$, **(c)** simulation when $\pi = 0.035$, **(d)** simulation when $\pi = 0.06$, **(e)** simulation when $\pi = 0.09$

Sensitivity Analysis

The sensitivity index of a parameter is correlated with the basic reproduction number (R_0). This index provides information about the parameters with a significant impact on the value of R_0 . Parameters with a high impact on the value of R_0 indicate that these parameters have a big responsibility for the spread of COVID-19 [21]. The sensitivity index of a parameter can be calculated as follow:

$$C_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0} \tag{15}$$

Where p is the parameter for which the sensitivity index will be calculated. Using equation (15) and table 1, the sensitivity index from the parameter β_s will be calculated as follow:

$$C_{\beta_s}^{R_0} = \frac{\partial R_0}{\partial \beta_s} \times \frac{\beta_s}{R_0} = \frac{\mu \delta k}{(\pi + \mu)(\delta + \mu)(\alpha_1 + \mu)} \times \frac{\beta_s}{R_0} = 0.7026842660$$

The sensitivity index of all parameters is listed in table 3.

Tabel 3. Sensitivity index parameters

Parameter	Sensitivity Index	Parameter	Sensitivity Index
π	-0.7561096532	α_2	-0.06869884366
β_s	+0.6944182466	δ	+0.04388564886
α_1	-0.6198090944	τ_1	+0.03363455939
μ	+0.6184672689	ω	-0.02267885513
β_a	+0.2662368610	ρ	-0.01486623092
k	+0.2238170821	τ_2	+0.005710332735
σ	-0.1909361970	θ	-0.004120273967
ε	-0.08597386189		

Table 3 shows the sensitivity index of each parameter used in this model. In the table, the sensitivity index is ordered based on how much impact the parameter for the value of R_0 . The parameter index with a positive value indicates that if the parameter is increased while the other index remains, it will affect the value of R_0 which also increases, whereas if the parameter is decreased, the value of R_0 will also decrease. The parameter index with a negative value indicates that if the parameter is increased, the value of R_0 will decrease, whereas if the parameter is decreased, the value of R_0 will increase.

The sensitivity index shows that the parameter π (rate of individuals receiving dose 1 vaccine) is the parameter that has the most significant (negative) impact on the spread of COVID-19. It is known that the sensitivity index value of parameter $\pi = -0.7561096532$, by increasing (or decreasing) the value of parameter π by 10%, the value of R_0 will decrease (or increase) by 7.561096532%. The sensitivity index of parameter β_s (transmission rate if contact with symptomatic infected individuals) is the parameter that has the most significant (positive) impact on the spread of COVID-19. It is known that the sensitivity index value of the parameter $\beta_s = +0.6944182466$, by increasing (or decreasing) the value of the parameter β_s by 10%, the value of R_0 will increase (or decrease) by 6.944182466%.

The results of numerical simulations show that if the value of $R_0 < 1$ then the disease

will disappear from the population, but if the value of $R_0 > 1$ then the disease will remain in the population or become endemic. Based on the results of the sensitivity analysis, several actions can be taken to prevent the transmission of COVID-19 by making the value of $R_0 < 1$ based on table 3. (1) Accelerate the rate of dose 1 vaccination (π). The rate of dose 1 vaccination can be accelerated by facilitating public access to get vaccines. Adding health facilities for vaccination is one way to increase the rate of dose 1 vaccination. (2) Reducing the rate of contact with symptomatic infected (β_s) or asymptomatic infected (β_a). This can be done by following health protocols and reducing mobility, as has been recommended by the government. (3) Accelerate the quarantine rate for symptomatic infected individuals (α_1). The more individuals tested, the greater the probability of detecting infected individuals and this will make the rate at which individuals quarantine themselves will be greater.

CONCLUSIONS

The mathematical model of COVID-19 SVEIQR was obtained where compartment V was divided into dose 1 and dose 2, compartment I was divided into symptomatic and asymptomatic infected. The model obtained is a system of nonlinear differential equations. It has a disease-free equilibrium point and an endemic equilibrium point. Disease-free equilibrium point $E_0 = \left(\frac{\mu}{\pi + \mu}, \frac{\pi\mu}{(\pi + \mu)(\varepsilon\omega + \mu)}, \frac{\varepsilon\omega\pi\mu}{(\pi + \mu)(\omega + \mu)(\rho\theta + \mu)}, 0, 0, 0 \right)$ locally asymptotically stable when the value of $R_0 < 1$. The endemic equilibrium point $E_1(s, v_p, v_f, e, i_s, i_a, q)$ exists when the value of $R_0 > 1$.

Based on the model simulation, it is concluded that the disease will disappear if $R_0 < 1$, and the disease will persist in the population if $R_0 > 1$. This is consistent with the existing theorem. Based on the results of the sensitivity analysis, the parameter that has the most influence on the value of R_0 is obtained. Several things that can be done to make the disease disappear ($R_0 < 1$) are to increase the rate of vaccination dose 1 (π), reduce the rate of contact with symptomatic infected individuals (β_s) or asymptomatic infected individuals (β_a) and accelerate the quarantine rate for symptomatic infected individuals (α_1).

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