SIR Mathematical Model of Convalescent Plasma Transfusion Applied to the COVID-19 Pandemic Data in Indonesia to Control the Spread of the Disease

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Abstract. In this paper we develop a mathematical model of disease transmission dynamics. Although some vaccines for some infectious diseases are available, there are some cases where handling new emerging infectious diseases, such as COVID-19 pandemic, is still a difficult problem to handle. Preventive actions, such as wearing masks, distance guarding, frequent hand washing, and others are still the most important interventions in handling the transmission of this disease. Recently, several countries have allowed the use of convalescent plasma transfusion (CPT) in the management of moderate and severe COVID-19 patients. Several early studies of this use have yielded prospective results with reduced mortality rates. A recent work also shows that using a simple discrete mathematical model of CPT could reduce the outbreak of disease transmission, in the sense of reducing the peak number of active cases and the length of the outbreak itself. In this paper, we use a continuous SIR model applied to COVID-19 pandemic data in Indonesia to address an important question whether convalescent plasma transfusion may reduce the transmission of the disease.

Keywords: Convalescent Plasma Transfusion (CPT), COVID-19 pandemic, SIR mathematical model.

1. Introduction
Literature on mathematical models of epidemics are abundant. They are developed and explored by many researchers in different fields, covering both epidemiology in humans [1], animals[2] and plants [3]. In general, mathematical epidemiological models are expected to provide understanding of the dynamics of epidemics which then be used as a basis for reducing the possibility of spreading outbreak of disease infections. Recently, mathematical modeling has been regaining its popularity with the occurrence of COVID-19 pandemic. It is used mainly in understanding the COVID-19 transmission, predicting short-term and long-term number of infections and exploring some possible intervention to stop or control the pandemic.
Since the pandemic's announcement, almost every country has made a concerted effort to combat the disease, albeit with a wide range of responses. Efforts are generally focused on handling cases of infection, preventing transmission, and developing early detection methods for monitoring disease transmission. Convalescent plasma transfusion (CPT) is currently being used. Several governments have already advocated for the use of this method to combat COVID-19. CPT is not a new concept. For more than a century, the CPT has been used as a passive immunization strategy in the prevention and treatment of epidemic infections [4]. The first documented use dates back to 1918-1920, when it was used during the Spanish influenza A (H1) pandemic. The first documented use dates back at least to 1918-1920, when it was used to treat Spanish influenza A (H1N1) pneumonia, but it could be even older [5]. This method is being considered as a potential therapy for patients infected with COVID-19 [6]. Some studies showed that the convalescent plasma could reduce the mortality risk of a patient with the CPT treatment [7]. Details study can be found in [8] and [9]. Currently in Europe there are at least 20 countries participating in the program to support the use of COVID-19 convalescent plasma (CCP) therapy in curing the COVID-19 patients (https://europeanbloodalliance.eu/activities/convalescent-plasma-cpp/). Other countries outside Europe also begin to utilize the CPT, such as USA, Kuwait, and Indonesia [10].

The effect of CPT is generally accepted to be a clinical effect on the individual of the patient who receives CPT treatment. Many references show that the effect is a reduction in the patient's mortality risk. So far, the impact of CPT application on the population is unclear. Only a few mathematical model papers (e.g. [11]) use a mathematical modeling approach to address this issue. We present a simple mathematical model for assessing the impact of CPT on disease transmission in this paper. The model is not specific to COVID-19, but rather a more general transmission model in the form of a simple SIR model. In this paper, a mathematical modeling approach is used to answer an important question whether convalescent plasma transfusion can reduce the COVID-19 transmission when it is applied to the real data. Here we will apply the model to COVID-19 data from Indonesia.

2. Model Formulation

2.1. SIR model in a Closed Population

Let us assume that in a closed population, the population is divided into three different compartments depending on the health status, i.e. the susceptibles ($S$), the infectious ($I$) and the recovered ($R$) compartments with $N(t) = S(t) + I(t) + R(t) = N$, where $N$ is a constant. Without loss of generality we may set $N = 1$ when we consider the population as a fraction of each compartment. The most simplest continuous SIR model is given by

$$\frac{dS}{dt} = -\beta S(t)I(t); \quad \frac{dI}{dt} = \beta S(t)I(t) - \alpha I(t); \quad \frac{dR}{dt} = \alpha I(t).$$

(1)

Where $\beta$ is the effective contact rate or the force of infection and $\alpha$ is the the removal rate. All rates are assumed to be constant.

Generally we are interested in looking at the steady state solution of the model. To find the steady state solution from (3) we need all the differential equations are zero hence we have $I^* = 0$, $S^* = \frac{\alpha}{\beta}$. 


Moreover, since 
\[ N(t) = S(t) + I(t) + R(t) = N \]
then we have
\[ R^* = N - S^* - I^* = \frac{\beta N - \alpha}{\beta} \].
Hence, the steady state solution is given by
\[ (S^*, I^*, R^*) = \left( \frac{\alpha}{\beta}, 0, \frac{\beta N - \alpha}{\beta} \right) \].

Here we can find the basic reproduction number as the following. The basic reproduction number is a threshold indicating the notion of the disease whether it could develop epidemic or not. The condition needed for a disease to develop an epidemic is that the number of the infective should be increased, i.e.
\[ \frac{dI}{dt} = \beta S(t) I(t) - \alpha I(t) > 0 \]
which implies
\[ \frac{\beta S(t)}{\alpha} > 1 \quad \text{or} \quad S(t) > \frac{\alpha}{\beta} \].
So if the current number of susceptibles is greater than \( \frac{\alpha}{\beta} \) then the number of infectives grows otherwise it declines. Let us write
\[ R_0 = \frac{\alpha}{\beta} \]
and define it as the basic reproduction number. At the outset of the epidemic, nearly everybody is susceptible, hence we may assume \( S(0) \approx 1 \) so we have the equality
\[ R_0 = \frac{\beta}{\alpha} > 1 \]
as the condition for the infectives to grow.

Note that there is a relation between the basic reproduction number with the susceptible equilibrium point, i.e. \( R_0 = \frac{1}{S^*} \). We have the following interpretation of the susceptible equilibrium point \( S^* \). A necessary condition for \( I(t) \) in equation (3) to be maximal is given by
\[ S^* = \frac{\alpha}{\beta} \].
We illustrate this necessary condition in figure 2 which shows the phase-port of the SIR system in the \((S, I)\)-plane. It is observed that all the solutions of \( I \) as a function of \( S \) with susceptible initial values greater than \( S^* \) (red dots in the figure) grow and reach their maximum value at \( S^* \). The eventual number of susceptible when the number of infectives reaches zero is called the final size indicating the fraction of the population escaped from getting infected. From the figure there is a clear relationship between different \( S^* \) (so that the basic reproduction number) with the position of the final size of susceptible for the same initial values of susceptible. In the next section we will explore how the CPT and the uncertainty of the initial values will affect the steady state (and hence the basic reproduction number) of the SIR model.

**2.2. SIR Continuous Model in a Closed Population**

In this section we assume that there is convalescent plasma transfusion (CPT) in the SIR model. We will consider two different rates of the CPT, i.e. 1). the rate is proportional to the number of infectious (I) and 2) the rate is proportional to both the number of infectious (I) and the number of recovered (R). Let us first consider the SIR model. In the former case we have
\[
\frac{dS}{dt} = -\beta S(t) I(t) ; \quad \frac{dI}{dt} = \beta S(t) I(t) - (\alpha + \varepsilon) I(t) ; \quad \frac{dR}{dt} = (\alpha + \varepsilon) I(t)
\]
while in the later case we have

\[
\frac{dS}{dt} = -\beta S(t)I(t) \quad \frac{dI}{dt} = \beta S(t)I(t) - (\alpha + \varepsilon R(t))I(t) \quad \frac{dR}{dt} = (\alpha + \varepsilon R(t))I(t)
\]

(3)

Here \( \varepsilon \) is the rate of the CPT. It is clear for the former case that the presence of the CPT is reducing the time of infection to stay in the infectious class and hence reducing the basic reproduction number. We will show for the more interesting case, in which the rate is proportional to both the number of infectious and recovered class (the later case), that the presence of the CPT increases the final size of susceptibles as shown in the following. The system has the steady state solution

\[
(S^*, I^*, R^*) = \left( \frac{\alpha + \varepsilon R^*}{\beta}, 0, \frac{\beta N - \alpha}{\beta + \varepsilon} \right) = \left( 0, \frac{\beta N - \alpha}{\beta + \varepsilon}, \frac{\alpha + \varepsilon N}{\beta + \varepsilon} \right).
\]

To see the effect of the CPT in the long-term transmission we could compare this steady state solution to the original SIR model in which the absence of the CPT. We found that the presence of the CPT increases the value at which the infection reaches its maximum value (peak). This affects the final size of susceptibles as shown in figure 1. The result is equivalent to the discrete model in [12].

![Phase portrait of the SIR model](image)

\( \gamma = 0.2; \, \beta = 0.8; \, S^* = 0.25; \, R_0 = 4 \)
\( \gamma = 0.6; \, \beta = 0.7; \, S^* = 0.86; \, R_0 = 1.17 \)

**Figure 1.** The phase-port of the SIR model (3) in the \((S, I)\)-plane showing the relationship between the susceptible equilibrium point \(S^*=1/R_0\) (red dot) as the point where the peak of \(I(S)\) occurs and the final size of susceptible for different values of \(R_0\) (higher \(R_0\) (left) and lower \(R_0\) (right)). All the solution with the initial values \(S(0)\) larger than \(S^*\) develop outbreak (have peaks at \(S^*\)) while those with the initial values \(S(0)\) lower than \(S^*\) do not develop outbreak.

**Result 1:**
a. The critical size of the susceptibles at which the infective reaches maximum in the presence of CPT is higher than the size in the absence of CPT.

b. The basic reproduction number of the SIR model in the presence of CPT is lower than the basic reproduction number of the SIR model in the absence of CPT.

**Proof:**

\[
\frac{S^*}{S^*_c} = \left( \frac{\alpha}{\beta} \right) \frac{\alpha + \varepsilon R_e}{\beta} = \frac{\alpha}{\alpha + \varepsilon R_e} < 1
\]

a. The ratio \( \frac{S^*}{S^*_c} \) is less than 1. 

b. It is clear from a) since the basic reproduction number are

\[
R_b = \frac{1}{S^*} \quad \text{and} \quad R_{0e} = \frac{1}{S^*_c}.
\]

In the following section we give an illustrative example using the COVID-19 data in Indonesia. Note that simulation on COVID-19 data for Indonesia in Section 3 shows that the final size (of susceptibles) is indeed positively correlated with the critical size of susceptibles \( S^* \). See also figure 4.

### 3. Parameter Estimation of SIR Model for COVID-19 Case in Indonesia

To illustrate the result we parameterize the SIR model with the COVID-19 data in Indonesia. The data are taken from Worldometer (total population of Indonesia, total confirmed case (Appendix 1), total death (Appendix 2), and total recovery (Appendix 3) data to generate susceptible data). Daily active case and daily recovery case are computed from the same data mentioned above. We then parameterize the SIR model with several data sets, i.e. with the number of data 62, 100, 200, 500, 510, and 528 for various reasons. The first three numbers (62, 100, 200) are chosen to see the effect of early exponential growth. The number 500 is used to cover complete data for the first wave with the inclusion of the first peak and few tails. The number 510 is used to cover the second wave just before the peak, and the number 528 is used to cover all the data (two significant peaks). The data for total cases and cumulative death cases are taken from [https://www.worldometers.info/coronavirus/country/indonesia/](https://www.worldometers.info/coronavirus/country/indonesia/) and the data for cumulative recovered case is taken from [https://covid19.go.id/peta-sebaran](https://covid19.go.id/peta-sebaran) used as the time series of \( R(t) \). The data of active cases is then computed resulting in the time series of \( I(t) \). The time series of \( S(t) \) is computed by assuming the total population of Indonesia in 2020. We do not consider vaccinated individuals in computing the number of susceptibles. The time series of \( S(t), I(t), \) and \( R(t) \) are then fitted using error sum square with the help of Maple 18. The results of the parameterization are presented in table 1. Figure 2 presents the graphical results for the predicted SIR model for the growth of infectious compartment in fraction with respect to the total of Indonesia population. The results may be inaccurate since we do not include the number of vaccinated persons to discount the number of susceptible. The results significantly depend on the number of data used in the parameterization process (table 1 and figure 3). In figure 5 we show the comparison of SIR model in the absence of CPT (equation 1) with the SIR model in the presence of CPT (equation 2).

**Table 1.** The SIR parameters found from COVID-19 data in Indonesia

| Number of data | \( \beta \): effective contact rate | \( \gamma \): removal rate |
|---------------|-----------------------------------|---------------------------|
| 62            | 0.161893139228068                 | 0.0175098181231386        |
| 100           | 0.125938510484078                 | 0.0279996218805884        |
| 200           | 0.0930368612464860                | 0.0359618052986100        |
| 500           | 0.0605773054031489                | 0.0304911343104908        |
| 510           | 0.0489516779169933                | 0.0218207538580899        |
3.1 Simulation of CPT with COVID-19 data for Indonesia

Currently only 17% of COVID-19 survivors are participating in the CPT donor program in Bandung (the capital of West Java Province, Indonesia). The Red Cross in this Province capital city is only able to serve between 25 to 30 donors who are willing to donate their CP due to the limited availability of the blood related machinery. If we assume all capital of the province in Indonesia have the same capacity, then there will be 850 to 1020 potential donors that could be facilitated (personal communication). Based on this figure we simulate the effect of CPT implementation using the parameterized SIR model with 528 data. The results are presented in figure 4, in which it shows that current practice of CPT resulting in relatively the same final size of susceptibles (individuals who escaped from getting the disease), the same final size of recovered individuals, and the same final size of infected individuals (figure 4b) as compared to the absence of CPT (Figure 4a). However, if there is an increase in the level of service from 1,030 to 1,030,000 individuals per day, then the final size of susceptible and recovered individuals slightly increase while the final size of infected individuals slightly decrease (figure 4c). The difference between the absence and presence of CPT becomes apparent when we increase the level of service to 3,090,000 individuals per day - almost the same level as the current target of the vaccination program in Indonesia (figure 4d). Figure 5 shows specifically the curve of the time series of the infected individuals. The figure reveals that the effect of CPT is both in reducing the peak and delaying the peak of the outbreak.

![Image](image_url)
Figure 2. The graphs of infective growth over time (blue lines) from the SIR model parameterized by COVID-19 data for Indonesia (red dots). Numbers indicates the number of data used in the estimation.

Figure 3. The graphs of effective contact rate and recovery rate as a function of data used in the parameterization process.
(c) With high capacity of CPT (1,020,000 services)

(d) With high capacity of CPT (3,060,000 services)

Figure 4. The graphs of the time series of the predicted susceptible individuals (blue line), infected individuals (red line), and recovered individuals (green line) from the SIR model in the absence (a) and presence of CPT (b, c, d) using SIR parameters from 528 data in the parameterization process. The results might be different if we use different number of data in the parameterization process.

Figure 5. The graphs of the time series of the predicted infected individuals from the SIR model in the absence ($\varepsilon = 0$) and presence of CPT ($\varepsilon = 1,020$, $\varepsilon = 1,020,000$, and $\varepsilon = 3,060,000$) using SIR parameters from 528 data in the parameterization process. The results might be different if we use different number of data in the parameterization process.
4. Conclusion

We have presented an SIR epidemic models with the effect of the convalescent plasma transfusion (CPT). The model was applied for the simulation of CCP transfusion using COVID-19 data in Indonesia. It revealed that the use of CPT was a prospective way in reducing the number of infections. In this case it could decrease the peak of the outbreak while also causes the delay of the outbreak occurrence.

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Appendices
Data used for SIR parameterization are:

1. Total Cases (https://www.worldometers.info/coronavirus/country/indonesia/)
2. Total Death (https://www.worldometers.info/coronavirus/country/indonesia/)
3. Total Recovery (https://covid19.go.id/peta-sebaran)
4. Total Population of Indonesia as 2020 (=273523615, https://www.worldometers.info/world-population/indonesia-population/)

The graphs of the data taken from various sources are shown in the following appendices:

Appendix 1 (Total Case)

Appendix 2 (Total Death)

Appendix 3 (Daily Recovery)
