Mathematical Model of Seasonal Influenza with Treatment in Constant Population

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Abstract. Seasonal Influenza is one of disease that outbreaks periodically at least once every year. This disease caused many people hospitalized. Many hospitalized people as employers would infect production quantities, distribution time, and some economic aspects. It will infect economic growth. Infected people need treatments to reduce infection period and cure the infection. In this paper, we discussed about a mathematical model of seasonal influenza with treatment. Factually, the disease was held in short period, less than one year. Hence, we can assume that the population is constant at the disease outbreak time. In this paper, we analyzed the existence of the equilibrium points of the model and their stability. We also give some simulation to give a geometric image about the results of the analysis process.

1. Introduction

In 2009 avian influenza was become epidemic and followed by swine flu epidemic [1]. Those epidemics made some death cases and many people hospitalization. The strain of H5N1 virus was identified as a cause of avian influenza epidemic, and Strain of H1N1 virus was identified as a cause of swine influenza while the cause of seasonal influenza is H3N2 virus. The symptoms of all influenza disease is similar. Influenza viruses were responsible for many death cases and many people hospitalization. Seasonal influenza usually doesn't cause death, and it has some effects economically i.e. productivity of employee will decrease, some production process needs longer time, some distribution of goods was suspended [2].

Factually, the infected persons need some treatments to cure infection like drugs assimilation and hospitalization. In [3], it was stated extending oseltamivir to infected children (1 – 3 years old) which don't exceed 24 hours after the symptoms give the significant result. Oseltamivir is known as the only one exact drug for the children under 15 years old. Committee on Infectious Diseases ([4]) also stated treatment should be offered as early as possible. In [5], it was stated that early treatment with antiviral medications may reduce the severity and duration of symptoms, hospitalizations, and complications (otitis media, bronchitis, pneumonia), and may reduce the use of outpatient services and antibiotics, extent, and quantity of viral shedding, and possibly mortality in certain populations. In [6], it was stated that giving the drug in earlier time will be reduced the infection period. In [6], it was also stated diagnosis and treatment would be faster the result of oseltamivir therapy. Urashima [7] suggested that one of the actions to reduce the incidence of influenza A, especially in specific subgroups of schoolchildren was vitamin D3 supplementation. In [8], it was stated that using oseltamivir prophylaxis can shorten the duration of influenza outbreaks. In [9,10], there were mutated viruses that have immunities of oseltamivir.

2. Methods

The first step to do this research was literacy study. In this step, we study the fact and some assumptions from various scientific literacy. The facts were also got from our previously research (see
After that, we complete the facts with some assumptions to build the model. The second step was building and analyzing mathematics model. In this step, we build the mathematics model and then analyze it to determine the equilibrium points and their stability. The third step was making a simulation with parameters value got from our previously research in 2015.

3. Mathematics Model

[11] stated that was no difference periods date between age group except average infection period with treatment between child and elderly and also treatments were effective to all of the human age criteria. Almost all of period date had no significant difference so that we can neglect the human age criteria. We also got the fact that seasonal influenza doesn't cause death (almost any). In this paper, we assume that the population is constant. Transfer diagram of a seasonal epidemic is given in Figure 1.

![Figure 1](image)

**Figure 1.** Transfer diagram of seasonal epidemic with treatment

Where $N$ is the total population, $S$ is a total number of the susceptible person, $I$ is a total number of an infected person, $T$ is a total number of treated person, and $R$ is the total number of recovered person. The meaning of parameters in the model was given in Table 1. From Figure 1 we construct the system of an ordinary differential equation as System 1.

\[
\begin{align*}
\frac{dS}{dt} &= \mu N + \theta R - \left( \frac{\beta S}{N} \frac{I}{N} + \mu S \right) \\
\frac{dI}{dt} &= \beta S \frac{I}{N} - \left[ \alpha(1-p)I + p + \mu \right]I \\
\frac{dT}{dt} &= pI - (\mu + \gamma)T \\
\frac{dR}{dt} &= \alpha(1-p)I + \gamma T - (\mu + \theta)R \\
S + I + T + R &= N
\end{align*}
\]

Because the population is constant so we can define new variables, i.e. $s = \frac{S}{N}$, $i = \frac{I}{N}$, $\tau = \frac{T}{N}$, and $r = \frac{R}{N}$. Hence, System 1 changes to System 2.
\[
\begin{align*}
\frac{ds}{dt} &= \mu + \theta r - (\beta s i + \mu s) \\
\frac{di}{dt} &= \beta s i - [\alpha(1-p) + p + \mu] i \\
\frac{d\tau}{dt} &= p i - (\mu + \gamma) \tau \\
\frac{dr}{dt} &= \alpha(1-p) i + \gamma \tau - (\mu + \theta) r \\
s + i + \tau + r &= 1
\end{align*}
\]

(2)

### Table 1. The meaning of parameters

| Parameter | The Meaning |
|-----------|-------------|
| \( \mu \) | Birth rate is assumed same with death rate |
| \( \beta \) | The probability of infectious contact was happen |
| \( \alpha \) | Recovery rate without treatments |
| \( \gamma \) | Recovery rate with treatments |
| \( p \) | the proportion of infected person get treatments |
| \( \theta \) | Immunity loss rate |

The existence of equilibrium points of System (2) is given in Theorem 1.

**Theorem 1.**

Let \( R_0 = \frac{\beta}{\alpha(1-p) + p + \mu} \).

1. If \( R_0 \leq 1 \) then System (2) has only one equilibrium point i.e. nonendemic equilibrium point \( Q_0 = (s, i, \tau, r) = (1,0,0,0) \).

2. If \( R_0 > 1 \) then System (2) has two equilibrium points i.e. nonendemic equilibrium point \( Q_0 = (s, i, \tau, r) = (1,0,0,0) \) and endemic equilibrium point \( Q_1 = \left( s^*, i^*, \tau^*, r^* \right) \) where

\[
\begin{align*}
\frac{s^*}{R_0} &= 1, \quad i^* = \frac{R_0}{\mu + \gamma} \left( \frac{R_0 - 1}{\alpha(1-p) + p + \mu + \theta} \right) \\
\tau^* &= \frac{R_0}{\mu + \gamma} \left( \frac{R_0 - 1}{\alpha(1-p) + p + \mu + \theta} \right) \\
r^* &= \frac{\alpha(1-p) i + \gamma \tau - (\mu + \theta) r}{\mu + \gamma} \\
\end{align*}
\]

Proof.

The equilibrium points were a solution of System 3.

\[
\begin{align*}
\mu + \theta r^* - (\beta s^* i^* + \mu s^*) &= 0 \\
\beta s^* i^* - [\alpha(1-p) + p + \mu] i^* &= 0 \\
pi^* - (\mu + \gamma) \tau^* &= 0 \\
\alpha(1-p) i + \gamma \tau^* - (\mu + \theta) r^* &= 0 \\
s^* + i^* + \tau^* + r^* &= 1
\end{align*}
\]

From the second equation, we get \( i^* = 0 \) or \( s^* = \frac{\alpha(1-p) + p + \mu}{\beta} = \frac{1}{R_0} \).

The case of \( i^* = 0 \):

From the third and fourth equation, we get \( \tau^* = 0 \) and \( r^* = 0 \). From the fifth equation, we get \( s = 1 \).
Hence, we get a non-endemic equilibrium point \( i^* = (s^*, i^*, r^*, r^*) = (1, 0, 0, 0) \).

The case of \( i^* \neq 0 \):

Clear that \( s^* = \frac{a(1 - p) + p + \mu}{\beta} = \frac{1}{R_0} \). From the third equation, we get \( r^* = \frac{\beta i^*}{\mu + \gamma} \). From the fourth equation, we get \( r^* = \frac{a(1 - p)(\mu + \gamma)}{\mu + \theta} \). Substitute \( r \) and \( r \) to the first equation of System (3) and we obtain \( i^* = \frac{(\mu + \gamma)(1 - \frac{a(1 - p)}{\beta})}{(\mu + \gamma)(\mu + \gamma) + (\mu + \theta) + \psi} \). From the value of \( R_0 \), we get \( i^* = \frac{(\mu + \gamma)(1 - \frac{a(1 - p)}{\beta})}{(\mu + \gamma)(\mu + \gamma) + (\mu + \theta) + \psi} \). Clear that \( i^* > 0 \) if \( R_0 > 0 \). Because \( i^* > 0 \) if then \( r^* > 0 \) and \( r^* > 0 \). Hence we get an endemic equilibrium point \( Q_1 = (s^*, i^*, r^*, r^*) \) where all values were defined at Theorem 1. The stability of equilibrium points of System 2 is given in Theorem 2.

**Theorem 2.**

Let \( R_0 = \frac{\beta}{a(1 - p) + p + \mu} \).

1. If \( R_0 < 1 \) then the non-endemic equilibrium point \( Q_0 \) was locally asymptotically stable.
2. If \( R_0 > 1 \) then the non-endemic equilibrium point \( Q_0 \) was unstable and the endemic equilibrium point \( Q_1 \) was locally asymptotically stable.

**Proof.**

The Jacobian Matrix of System 2 was given below.

\[
J(Q) = \begin{bmatrix}
-\left(\frac{\beta k + \mu}{\beta} \right) & -\frac{\beta k}{\beta} & 0 & 0 \\
\beta k - \left[ a(1 - p) + p + \mu \right] & 0 & 0 & 0 \\
0 & 0 & -\left(\mu + \gamma \right) & 0 \\
0 & 0 & \left(\mu + \theta \right) & \gamma - \left(\mu + \theta \right)
\end{bmatrix}
\]  

where \( Q_1 = (s, t, r, r) \).

**The stability analysis of \( Q_0 \)**

The eigenvalues of matrix \( J(Q_0) \) were \( \lambda_1 = -\mu, \lambda_2 = -\left(\mu + \gamma \right), \lambda_3 = -\left(\mu + \theta \right), \) and 

\[
\lambda_4 = \left[a(1 - p) + p + \mu \right](R_0 - 1)
\]

Clear that \( \lambda_1, \lambda_2, \) and \( \lambda_3 \) are negative. Clear that \( \lambda_4 \) is negative when \( R_0 < 1, \lambda_4 \) is zero when \( R_0 = 1 \), and \( \lambda_4 \) is positive when \( R_0 > 1 \). If \( \lambda_4 \) is zero then the equilibrium point \( Q_0 \) is non-hyperbolic point. Hence we neglect the condition of \( R_0 = 1 \). Hence, if \( R_0 < 1 \) then the non-endemic equilibrium point \( Q_0 \) was locally asymptotically stable and if \( R_0 > 1 \) then the non-endemic equilibrium point \( Q_0 \) was unstable.

**The stability analysis of \( Q_1 \)**

The point \( Q_1 \) is exist only when \( R_0 > 1 \). The characteristic polynomial of the Jacobian matrix of \( Q_1 \) \( J(Q_1) \) is \( (\lambda + \mu)(\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3) = 0 \).
where \( a_0 = 1, \ a_1 = 2\mu + \gamma + \theta + \beta \theta^*, \ a_2 = \beta \theta^* [2\mu + \alpha (1-p) + p + \gamma] + \mu (\mu + \gamma + \theta) \)
\[
a_3 = \beta \theta^* [\mu + \gamma] (\alpha (1-p) + p + \mu) + \theta (\mu + p + \gamma) \]

From \( \lambda + \mu = 0 \) we get \( \lambda = -\mu \). Clear that \( a_1, \ a_2, \) and \( a_3 \) are positive.

Clear that \( a_1a_2 - a_3 = \beta \theta^* [\mu [2\mu + \alpha (1-p) + p] + \mu (2\mu + \gamma) + \theta (\mu + \alpha (1-p))] + \gamma (2\mu + \gamma + \theta + \beta \theta^*) \)

From the value above, it is true that \( a_1a_2 - a_3 > 0 \). Hence, the equation \( a_1x^3 + a_2x^2 + a_2x + a_3 = 0 \) satisfies Routh-Hurwitz criteria. It means all roots of the equation have negative real part. From the result of analysis, we get that all of roots of characteristic polynomial of \( J[q_1] \) have negative real part.

Hence, the endemic equilibrium point \( q_1 \) is locally asymptotically stable.

### 3.1. Minimum Value of \( p \)

The minimum value of \( p \) such that the influenza doesn’t spread widely can be determined from the value of \( R_0 \). We must bound the value of \( R_0 < 1 \) and we get \( p > \frac{\beta (\mu + \alpha)}{1 - \alpha} \). Clear that \( 0 \leq \alpha \leq 1 \), so if \( \beta \leq \mu + \alpha \) then every \( p > 0 \) will prevent the epidemic to spread widely.

### 4. Simulation

We will give the simulations for \( R_0 < 1 \) and \( R_0 > 1 \) using the parameters value which is got from our previously research. The parameters value is given in Table 2.

| Table 2. The parameters value of seasonal influenza in Central Java province |
|-------------------------------|------------------|
| Parameter                    | Average Value (day/days) |
| Incubation period            | 3.2               |
| Infection period without treatment | 10.2             |
| Infection period with treatment | 5.5               |
| Reinfection period           | 26.8              |

We also get the proportion of person taking treatments i.e. 96% or 0.96. From Table 2, we get the parameters value of mathematics model i.e. \( \mu = 0.00004 \) from the expectation of living period (65 years), \( \beta \) has range from 0 until 1, \( \alpha = 0.098 \) from Infection period without treatments, \( \gamma = 0.182 \) from Infection period with treatments, \( p = 0.96 \) from proportion of person taking treatments, and \( \theta = 0.037 \) from Reinfection period.

#### 4.1. Simulation for \( R_0 < 1 \)

We use the value of \( \beta = 0.5 \). The value of \( R_0 = 0.52 < 1 \). The simulations under this condition are given in Figure 2.
For $\beta = 0.5$ and $p = 0.96$ we can see that the value of $i(t)$ decreased faster. Because of that, the value of $\tau(t)$ and $r(t)$ also decrease but slower than $i(t)$. From the parameters value in this condition, we can determine that minimum value of $p$ is 45%.

4.2. Simulation for $R_0 > 1$

We use the value of $\beta = 1$ and $p = 0.5$. The value of $R_0 = 1.82 > 1$. The simulations under this condition are given in Figure 3. From the simulation in Figure 3, all of the graphics have to decrease sinusoidal graph. It was caused because the dynamic of every variable affects between one and other. It can also indicate that the eigen values of the Jacobian matrix for the endemic point have complex value.

Figure 2. Graphics of variables in model (a) $s(t)$ (b) $i(t)$ (c) $\tau(t)$, and (d) $r(t)$
5. Conclusion and Discussion
From analysis and simulation above, we get the dynamic of mathematics model of seasonal epidemic with treatment, especially for constant population. We also got the reproduction number which can be used to determine whether the epidemic spread widely or vanish. From that number, we get the minimum proportion of treated person. For the next research, we propose to make the mathematics model for non-constant population.

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