Mathematical model SI-SIRT of avian influenza epidemic with treatment on human

M Kharis¹, T A Prasetyo² and S B Waluya¹

¹Department of Mathematics, Universitas Negeri Semarang, Indonesia
²Information Technology, Faculty of Informatics and Electrical Engineering, Institut Teknologi Del, Indonesia

*Corresponding author: kharis.mat@mail.unnes.ac.id

Abstract. Avian influenza is a terrible respiratory infectious disease caused by the avian influenza virus. The great concern of the world's health experts is the possibility of spreading avian influenza and becoming an uncontrollable pandemic. The study's purpose was to derive, analyze, and interpret the mathematical model's simulation of the avian influenza epidemic with treatment on humans. This paper constructed a mathematical model formed by SI-SIRT (Susceptible poultry, Infectious poultry, Susceptible human, Infected human, Treated human, Recovered human). We obtained a reproduction number ($R_0$) from analyzing the model. $R_0$ is a formula to determine whether the disease will disappear or spread over in the future. The free disease equilibrium point was local asymptotically stable if $R_0 < 1$, and the endemic equilibrium point was local asymptotically stable if $R_0 > 1$.

1. Introduction
Influenza is a virus infection that affects mainly the nose, throat, bronchi, and lungs [1]. The illness usually occurs about a week and is characterized by fever, muscle aches, headache, septic throat, and cough. Influenza is a disease caused by the myxovirus virus. Influenza viruses are divided into three types, i.e., A, B, and C type [2]. Influenza usually is called the flu that infects poultry and mammals [3]. Typically, the Influenza virus is transmitted through the air by coughing or sneezing, which will spread to some aerosols containing the virus [4]. One of the most dangerous influenza types is avian influenza. Avian influenza is a terrible respiratory infectious disease caused by influenza virus type A with subtype H5N1 [5]. The avian influenza virus belongs to the genus influenza and family Orthomyxoviridae. The virus is classified into two categories: low pathogenic avian influenza (LPAI) virus and highly pathogenic avian influenza (HPAI) virus [6]. Highly pathogenic avian influenza (HPAI) first emerged in 1996 in Eastern Asia and circulated amongst avian populations [7].

A wide range of A-type Influenza viruses from pigs and birds have infected humans in the last decade, sometimes with severe clinical consequences [8]. The viruses then adapted to chickens and other land-based birds, such as pheasants, chukars, and other minor domestic poultry [9]. Humans, birds, pigs, horses, and other animals can be infected with the avian influenza virus [10]. This virus can be transmitted between poultry and transmitted from poultry to humans [11]. Not all avian influenza viruses cause the same clinical manifestations [12]. On the other hand, infection control ferrets showed mild clinical signs and no mortality to the same virus [13]. Avian influenza is transmitted from birds to poultry and birds to humans through saliva, mucus from the nose, and dirt [14].
A deep understanding of the disease dynamics would provide essential guidelines for effective prevention and control strategies [15]. Numerous efforts are made to eradicate such diseases, such as improved sanitation and modern treatment [16]. Therefore, a renewable treatment of avian influenza is needed. Strategically deployed medical treatments can significantly reduce the number of exposed and infected persons [17] optimal medication and hospitalization strategies that will enable us to eliminate influenza while minimizing our cost and resources [18]. Research Pourghanbari [19] was yielding those different oseltamivir concentrations that may inhibit the avian influenza virus. Comparison MOEO (Melissa Officinalis Essential Oil) with oseltamivir showing that the lemon balm oil component can act as an antiviral agent to treat humans infected with avian influenza [19]. Sambiloto and Temu Ireng extract potentially candidates for antiviral ingredients that may be needed to combat avian influenza virus infection [20].

Mathematical modeling is a handy and essential tool for studying infectious diseases' transmission dynamics [21]. Avian influenza epidemics can be presented in mathematical modeling. Mathematical modeling of the avian influenza epidemic can help understand and predict future bird flu epidemic control so that pandemic does not occur [22]. Khari and Amidi [23], Chong et al. [24], Derouch & Boutayeb [25], Kimbir et al. [26], Tuncer & Martcheva [27], and Martcheva [28] had developed and analyzed mathematical models of avian influenza epidemics.

In this article, the issue to be discussed is the mathematical model giving a treatment on epidemic avian Influenza with humans and poultry population is inconsistent. The discussion includes an analysis of the model established to determine the equilibrium point and stability of the mathematical model's equilibrium point. Furthermore, the model simulation with specific parameter values is given.

2. Methods
The methods and techniques used in the mathematical analysis of epidemics are outlined [29]. The technique used in this research is problem determination, problem formulation, literature study, and conclusion. The steps to be taken in this research include: (a) collecting facts related to the avian flu epidemic from relevant writings, (b) preparation of assumptions as a supporter and complementary in the practice of the mathematical model, (c) the formation of mathematical models, (d) analysis processes of the model include determining the equilibrium points of the model and their stability (e) numerical simulation of the analytical results to provide a geometric representation of the results of the analysis, and (f) conclusion.

3. Result and Discussion
The facts collected from various sources include (1) Every avian Influenza active poultry cannot be cured. The process of vaccination and biosecurity in avian influenza available poultry is only a measure to reduce infection rates but not eliminate viruses [30]. (2) Any active avian influenza can spread viruses to other birds and mammals, including humans [10, 11, 28]. The development of new subtypes of avian influenza virus formed by mutations can infect cells in the human body resulting in the spread of bird Influenza from poultry to humans [24, 31]. (3) Every individual human being active in avian influenza can only recover if treatment is done [32]. It happens because the avian flu virus can increase serum angiotensin II levels so that humans may develop acute respiratory distress syndrome (ARDS) [32]. (4) Comparison MOEO (Melissa Officinalis Essential Oil) with oseltamivir showing that the lemon balm oil component can act as an antiviral agent to treat humans infected with avian influenza [19]. (5) Sambiloto and Temu Ireng extract potentially candidates for antiviral ingredients that may be needed to combat avian influenza virus infection [20].

Assumptions were added in the preparation of mathematical models, i.e. (1) The birth rate of poultry and humans is not constant. (2) Birth and death occur. (3) Every poultry has the same chance of getting infected. (4) Every individual human being has the same opportunity to be infected. (5) Pure death (not due to the avian influenza virus) occurs in all classes. (6) Deaths in avian influenza active poultry caused by a virus of avian flu and mass burning. (7) Deaths from avian influenza viruses in human individuals occur only in the class of infected individuals. (8) Individuals who have isolated avian influenza enter
the class of infected human individuals. (9) Individuals who have been given the avian influenza virus treatment will experience death if taking drugs regularly. (10) Individuals who have recovered can be re-infected. The poultry population is divided into two classes, namely $S_b, I_b$ (Susceptible bird, Infectious bird) and the human population is divided into four classes, namely $S_h, I_h, T_h, R_h$ (Susceptible human, Infectious human, Treatment human, Recovery human). A mathematical model was established with the variables and parameters present in the mathematical model based on these classes.

Based on the above facts and assumptions, a mathematical model of the mathematical model giving treatment on epidemic avian Influenza with human and poultry populations is inconstant available. The transfer chart is shown in Figure 1.

![Figure 1. Diagram of individual transfer in Avian Influenza Epidemic with Humans Treatment](image)

where $N_b$ is the poultry population size, $N_h$ is the size of the human population, $S_b$ is the number of susceptible poultry, $I_b$ is the number of infectious poultry, $S_h$ is the number of susceptible humans, $I_h$ is the number of contagious humans, $T_h$ is the number of treated human, and $R_h$ is the number of recovered humans. The mean parameters were given next. $\mu_b$ is the rate of natural death of poultry, $\alpha_b$ is the rate of death of poultry due to avian influenza infection, $\eta$ is the rate of death of poultry caused by burning, $\beta_1$ is the probability of infectious contact between healthy poultry and infected poultry, $\beta_2$ is the probability of contagious contact between susceptible human and infected poultry, $\mu_h$ is the human natural mortality rate, $\delta_h$ is the human death rate due to avian influenza-infected, $\gamma$ is the proportion of humans who get treatment, $\kappa$ is the rate of healing after treatment, and $\sigma$ is the rate of immune degradation.

Based on Figure 1, we got a mathematical model that was given in System (1).

\[
\begin{align*}
\frac{dS_b}{dt} &= A_b - \mu_b S_b - \beta_1 \frac{I_b}{N_b} S_b \\
\frac{dI_b}{dt} &= \beta_1 \frac{I_b}{N_b} S_b - (\mu_b + \alpha_b + \eta) I_b \\
N_b &= S_b + I_b \\
\frac{dS_h}{dt} &= A_h + \sigma R_h - \mu_h S_h - \beta_2 \frac{I_b}{N_b} S_h \\
\frac{dI_h}{dt} &= \beta_2 \frac{I_b}{N_b} S_h - (\mu_h + \delta_h + \gamma) I_h \\
\frac{dT_h}{dt} &= \gamma I_h - (\mu_h + \kappa) T_h \\
\frac{dR_h}{dt} &= \kappa T_h - (\mu_h + \sigma) R_h \\
N_h &= S_h + I_h + T_h + R_h
\end{align*}
\]

(1)

Let $S_b = N_b - I_b$ dan $S_h = N_h - I_h - T_h - R_h$. System (1) can be simplified to System (2).

\[
\frac{dN_b}{dt} = A_b - \mu_b N_b - (\alpha_b + \eta) I_b
\]
Theorem 1

After analyzing the existence of the equilibrium points of System (2), we got theorem 1

**Theorem 1**

Let \( R_0 = \frac{\beta_1}{(\mu_b + \alpha_b + \eta)} \).

1. If \( R_0 \leq 1 \) then System (2) has only one equilibrium point that is the disease-free equilibrium point \( (P_0) \) i.e.

\[
P_0 = (N_b, I_b, N_h, I_h, T_h, R_h) = \left( \frac{\lambda_b}{\mu_h}, 0, \frac{\lambda_h}{\mu_h}, 0, 0, 0 \right).
\]

2. If \( R_0 > 1 \) then System (2) has two equilibrium points i.e. \( P_0 \) and an endemic equilibrium point \( P_1 \) where

\[
N_b^* = \frac{\beta_1 \mu_b}{\beta_2 \mu_b + (\alpha_b + \eta)(\beta_1 - (\mu_b + \alpha_b + \eta))}, \quad I_b^* = \frac{A_{\lambda}(\beta_1 - (\mu_b + \alpha_b + \eta))}{\beta_1 \mu_b + (\alpha_b + \eta)(\beta_1 - (\mu_b + \alpha_b + \eta))},
\]

\[
N_h^* = \frac{\beta_3 \mu_b \lambda_h}{\beta_2 \mu_b + (\alpha_b + \eta)(\beta_1 - (\mu_b + \alpha_b + \eta))}, \quad I_h^* = \beta_3 \mu_b \lambda_h (\mu_b + \alpha_b + \eta),
\]

\[
T_h^* = \frac{\gamma I_h^*}{(\mu_h + k)}, \quad R_h^* = \frac{\kappa \gamma I_h^*}{(\mu_h + k)}.
\]

The analyzing processes of the equilibrium points stability gave the result in Theorem 2.

**Theorem 2**

Let \( R_0 = \frac{\beta_1}{(\mu_b + \alpha_b + \eta)} \). \( P_0 \) and \( P_1 \) were defined at Theorem 1.

1. The point \( P_0 = (N_b, I_b, N_h, I_h, T_h, R_h) \) locally asymptotically stable if \( R_0 < 1 \) and unstable if \( R_0 > 1 \).

2. The point \( P_1 = (N_b^*, I_b^*, N_h^*, I_h^*, T_h^*, R_h^*) \) locally asymptotically stable if \( R_0 > 1 \).

**Proof:**

The analyzing processes of the equilibrium points stability are done by determining the eigenvalues of the Jacobian matrix of System (2) for every equilibrium point.

For the point \( P_0 \), we got the eigenvalues i.e. \( \lambda_1 = -\mu_b, \lambda_2 = -\mu_b - \sigma, \lambda_3 = -\mu_b - \mu_h, \lambda_4 = -\mu_b - k, \lambda_5 = -\mu_h - \delta_h - \gamma, \) and \( \lambda_6 = (\mu_b + \alpha_b + \eta)(R_0 - 1) \). \( \lambda_6 \) is negative if \( R_0 < 1 \) and \( \lambda_6 \) is positive if \( R_0 > 1 \). Hence, the equilibrium point \( P_0 \) is locally asymptotically stable if \( R_0 < 1 \) and unstable if \( R_0 > 1 \).

The point \( P_1 \), we got the characteristics equation.

\[
\begin{pmatrix}
\beta_2 I_b^* \\
\beta_2 I_b^*
\end{pmatrix} \left( \frac{1}{\beta_2 I_b^*} \right) (\lambda^2 + a_1 \lambda + a_2) (b_0 \lambda^4 + b_1 \lambda^3 + b_2 \lambda^2 + b_3 \lambda + b_4) = 0
\]

where \( a_1 = (\mu_b + \alpha_b + \eta)(R_0 - 1) + \mu_b \)

\[
a_2 = \frac{R_0 (\mu_b + \alpha_b + \eta) \mu_b (R_0 - 1) + (\mu_b + \alpha_b + \eta) (\alpha_b + \eta)(R_0 - 1)^2}{R_0}
\]
3.1. Numerical Simulation

Simulations provide a geometric representation of the results of the analysis. The simulation is made using the Maple 18 program and is done by assigning values for each parameter according to the conditions of $R_0$. From [24], we got $A_p = 1000, A_h = 30, \mu_b = 0.01$, and $\beta_2 = 0.2$. From [26], we got $\eta = 0.6$. From [33], we got $\alpha_b = 0.02$. From [34], we got $\mu_h = 0.00128$. From [26], we got $\delta_h = 0.002$. From [35], we got $\sigma = 0.037$. We assumed $\gamma = 0.87$ and $\kappa = 0.9$.

\[
\frac{(\mu_b + \alpha_b + \eta)(R_0 - 1)[R_0\mu_b + (\alpha_b + \eta)(R_0 - 1)]}{R_0}
\]

\[
b_0 = N_b^*
\]

\[
b_1 = \beta_1^2 I_b + N_b^*(\mu_h + \delta_h + \gamma) + N_b^*[\mu_h + \sigma + (\mu_h + \kappa)] + N_b^*\mu_h
\]

\[
b_2 = \beta_1^2 I_b^2 + [\mu_h + \sigma + (\mu_h + \kappa)] + N_b^*[\mu_h + \delta_h + \gamma](\mu_h + \sigma + (\mu_h + \kappa)) + N_b^*[\mu_h + \delta_h + \gamma] + N_b^*\mu_h(\mu_h + \delta_h + \gamma)
\]

\[
b_3 = (\mu_h + \sigma)(\mu_h + \kappa)\beta_2^2 I_b^2 + (\mu_h + \sigma)(\mu_h + \kappa)N_h^*(\mu_h + \delta_h + \gamma) + \beta_2 I_b^2 \gamma
\]

\[
b_4 = \beta_2^2 I_b^2 \mu_h(\mu_h + \kappa) + N_b^*(\mu_h + \delta_h + \gamma)\mu_h(\mu_h + \kappa) + \beta_2 I_b^2 \gamma
\]

For $A^2 + a_1 A + a_2 = 0$:

Because $R_0 > 1$ then $a_1 > 0$ and $a_2 > 0$.

The roots of the quadratics equation are $\lambda_1 = \frac{-a_1 - \sqrt{a_1^2 - 4a_2}}{2}$ and $\lambda_2 = \frac{-a_1 + \sqrt{a_1^2 - 4a_2}}{2}$ where $D = a_1^2 - 4a_2$

Because of $a_2 > 0$ caused $a_1^2 - 4a_2 < a_1^2$.

If $D > 0$ then $0 < D < a_1^2 \iff \sqrt{D} < a_1 \iff -a_1 + \sqrt{D} < 0$.

If $D < 0$ then $Re(-a_1 + \sqrt{D}) < 0$.

Hence, the quadratics equation has eigenvalues with a negative real part.

For $b_0 A^4 + b_1 A^3 + b_2 A^2 + b_3 A + b_4 = 0$:

We used the Routh-Hurwitz criterion to verify that the equation has roots with a negative real part.

We checked that (1) $b_0 > 0, b_1 > 0, b_2 > 0, b_3 > 0, b_4 > 0$, (2) $c_1 = b_1 b_2 - b_0 b_3 > 0$

(3) $c_2 = b_1 b_4 - c_1 b_2 > 0$, and (5) $d_1 c_2 > 0$.

Because all of $N_b^*, I_b^*, N_h^*, I_h^*, T_h^*$, and $R_h^*$ are positive then $b_0 > 0, b_1 > 0, b_2 > 0, b_3 > 0, b_4 > 0$

and $c_2 = b_1 b_4 > 0$.

We got that $c_1 = b_1 b_2 - b_0 b_3 = N_b^* F + \beta_1^2 I_b^2(2\mu_h + \sigma + \kappa) + \beta_2^2 I_b^2 \gamma + \beta_2 I_b^2 \mu_h + \beta_2 I_b^2 \delta_h$

where

\[
F = \beta_1^2 I_b^2(\mu_h + \delta_h + \gamma) + \beta_1^2 I_b^2(2\mu_h + \sigma + \kappa) + N_b^* \mu_h(2\mu_h + \sigma + \kappa), \quad \beta_1^2 I_b^2 \gamma + \beta_2 I_b^2 \mu_h + \beta_2 I_b^2 \delta_h
\]

Hence, $c_1 > 0$.

Let $d_1 = c_1 b_3 - c_1 b_2 = N_h^* G + I_b^2 H$

Where $G$ and $H$ positive value equations.

Because $d_1$ and $c_2$ are positive then $d_1 c_2 > 0$.

Hence the equation $b_0 A^4 + b_1 A^3 + b_2 A^2 + b_3 A + b_4 = 0$ have the roots with a negative real part.

Hence, the point $P_1 = (N_b^*, I_b^*, N_h^*, I_h^*, T_h^*, R_h^*)$ locally asymptotically stable if $R_0 > 1$. 
3.2. Simulation for $R_0 < 1$.

We used the value of $\beta_2 = 0.001, 0.1, 0.45,$ and $0.6$. The initial values are $N_b(0) = 4000$, $I_b(0) = 50$, $N_h(0) = 5000$, $I_h(0) = 12$, $T_h(0) = 10$, dan $R_h(0) = 9$. The simulation for this case was given in Fig. 2.
In Figure 2, we saw that every graph converges to the value represent the value of every variable in $P_0$ i.e $P_0 = (100000; 0; 23437.5; 0; 0; 0)$. This result agreed with theorem 2.

### 3.3. Simulation for $R_0 > 1$.  
We used the value of $\beta_1 = 0.67, 0.75, 0.88,$ and $0.94$. The initial values are the same as the simulation before. The simulation for this case was given in Fig. 3.
Figure 3. The simulation graphs of $R_0 > 1$.

In Figure 3, we saw that every graph converges to the value represent the value of every variable in $P_1$ respective for the value of $\beta_1$. This result agreed with theorem 2.

4. Conclusion

The mathematical model for this epidemic is the System of differential equations with six equations and six variables. The analysis result gave the value of $R_0$ that used to determine the condition of this epidemic for the future. The simulation agreed with the analysis results.
Acknowledgments
This research was funded by the DRPM Ministry of Research, Technology and Higher Education, Indonesia, especially in Penelitian Produk Terapan (PPT) scheme in 2017.

References
[1] Nashrullah A, Supriyono and Kharis M 2013 Unnes J. Math. 2 46.
[2] Anggoro A D, Kharis M and Supriyono, Unnes J. Math. 2 55.
[3] Aulia N, Kharis M, and Supriyono 2016 Unnes J. Math. 5 192.
[4] Lanre G A and Olumide A O 2016 Idea J. Art Humanit. 2 71.
[5] Chaudhary S and Pahwa K 2013 J. Univers. Coll. Med. Sci. Teach. Hosp. 1 1.
[6] Pandig P S, Bunn D A, Pandem S A, and Aly S A 2013 Sci. Rep.
[7] Schrauwen E J and Fourc'hier R A 2014 Emerg. Microbes Infect
[8] Li C, Wang S, Bong G, Carter R A, Wang Z, Wang J, Wang C, Wang L, Wu G, Webster R G,
[9] Wang Y, Sun H, Sun Y, Liu J, and Pu J 2017 Emerg. Microbes Infect.
[10] Vemula S A, Zhao J, Liu J, Wang X, Biswas S and Hewlett I 2016 MDPI.
[11] Qin Y, Peter W, Horby T K and Tsang 2015 Major Artic. 61 563.
[12] Simon P F, Vega M A, Paradis E, Mendoza E, Combs K, Kobasa D and Beauchemin C 2016 Sci. Rep.
[13] Chang P, Kuchipudi S V, Mellits K H, Sebastian S, James J, Liu J, Shelton H, and Chang K 2015 Sci. Rep.
[14] Sya’banningtyas F S, Chotim M and Kharis M 2013 Unnes J. Math. 2 127
[15] Wang J and Liao S 2012 J. Biol. Dyn. 6 568.
[16] Jane S, Haldar P, and Kar K 2016 Int. J. Comput. Math.
[17] Modnak C 2017 Int. J. Biomath. 10 1.
[18] Khan A, Waileed M, and Imran C M 2015 Math. Comput. Model. Dyn. Syst.
[19] Pourghanbari G, Nili H, Moattari A and Ali M 2016 J. CrossMark 27 170.
[20] Setiyono A and Bermawie N 2016 J. Sain Vet. 31 27.
[21] Zhang X, Zou L, Chen J, Fang Y, Huang J, Zhang J, Liu S, Feng G, Yang C, and Ruan S 2017 J. Biol. Syst. 25 605.
[22] Kholisoh S, Waluya S B and Kharis M 2012 Unnes J. Math. 1 110.
[23] Kharis M and Amid M 2017 J. Phys.: Conf. Ser. 983 012116
[24] Chong N S, Tchuenche J M and Smith R J 2013 J. Theory Biosci.
[25] Derouich M and Boutayeb A 2008 J. Appl. Math. Sci. 2 1749.
[26] Kimbir A R, Aboiyar T, and Okolo P N 2014 J. IISTE Math. Theory Model. 4 15.
[27] Tuncer N and Martcheva M 2013 J. Biol. Syst. 21 1.
[28] Martcheva M 2013 Modeling and Implications for Control (USA: Department of Mathematics.
University of Florida).
[29] Gillis J 2016 Interdiscip. Sci. Rev. 4 306.
[30] Chong N S, Dionne B, and Smith R 2016 J. Math. Biol.
[31] Asmara W 2008 Peran Biologi Molekuler dalam Pengendalian Avian Influenza dan Flu Burung (Indonesia: Fakultas Kedokteran Hewan Universitas Gadjah Mada).
[32] Zou Z, Yan Y, Shu Y and Gao R 2014 J. Nat. Commun.
[33] Rahmalia D and Winarko M S Unisda J. Mat. Comput. Sci. 1 8.
[34] Tasmi and Nuraini N 2016 J. Math. ITB. 48 174.
[35] Kharis M and Arifudin R 2017 Phys.:Conf. Ser. 824 012034