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Impact of Antiviral Treatment of Avian Influenza in Poultry Farm

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Abstract. In the present paper, we have focused on the antiviral treatment of avian influenza to predict the situation of the disease and analyzed the stability of the model at the equilibrium points (disease-free and endemic). In this concern, we have applied the SITR model based on the well-known SIR model to calculate the basic reproduction number and final size relation. Important parameters, such as susceptible, infective, treatment, and removal (SITR) rate under the compartmental method have been studied theoretically. The analytical results highlight that the model results are locally and globally stable at disease-free equilibrium if the basic reproduction number is less than one and it is locally and globally stable at endemic equilibrium if the basic reproduction number is greater than one. The numerical simulations of the developed model (SITR) are performed graphically with the help of the Range-Kutta method and we have also observed that each compartment has much affected by the infection and death rate, whereas re-susceptive has no significant effect on compartments.

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Keywords: Avian influenza; Treatment; Drug resistance; Stability; Jacobi Matrix; Lyapunov.

Index to information contained in this paper

1. Introduction

Avian influenza (H5N1) was first reported and diagnosed at ICCDRB in Bangladesh in 2008 and every year it is infrequently spread out in the Asia subcontinent as well as Bangladesh. The transmission of this influenza occurs in Bangladesh because of its geographical and tropical conditions. The migration of birds to Bangladesh from other countries (such as Russia, East Europe and Asia) is one of the major factors to spread out this disease. Avian influenza may be highly pathogenic or low pathogenic based on the virus's molecular characteristics. For low pathogenic poultry show no major signs of disease and exhibit several symptoms of illness such as loose feathers and a drop in decrease of production. For highly pathogenic they show several disease symptoms with high mortality up to 100% [23].

The control strategy of avian influenza targets to minimize the risk factors and transmission from birds to birds or birds to humans or humans to humans. Vaccination of avian influenza is the first stage to prevent and if the diseases are spread out then antiviral treatment is the alternative option for protecting the poultry from influenza. Treatment may be gives to diagnose infective of seasonal influenza and it is short supplied [5].

There are no specific treatments for avian influenza, but treatment with broad-spectrum antibiotics control secondary pathogens, and increasing house temperature may reduce morbidity and mortality, although treatment with antiviral compounds is not recommended. Treatment with the combination of immune-modulators and antiviral agent significantly reduce mortality rate and it is relatively high over 10%-50% [26]. The mortality rate due to

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avian influenza is very high up to 90-100% within 48 hours [21]. Parvin et al. [20] studied the Mortality rate of commercial chicken in Bangladesh and showed that it was higher in Mymensingh (70-75%) compared to lower in Tangail (35%).

Several antiviral treatments were applied for avian influenza (AIV), such as Amantadine, Rimantadine, oseltamivir, Zanamivir, etc. and usually, these were used with water or food to the birds. Amantadine is the cheapest antiviral drugs for controlling of AIV, which can be used to the infected poultry only with water or foods. The morbidity, mortality, and transmissibility were decreased after using amantadine; resulting egg production was increased [24]. But avian influenza in both humans and birds were mostly resistant to amantadine [6,8,15] and Govorkova et al. [14] found that AIV amantadine-resistant was double (62.2%) compared with the number at resistant strains of avian origin (31.6%). All recovered birds were susceptible again due to antiviral treatment for avian influenza [17,24].

The stability analysis of an epidemic model is very important but very complicated. When a model is formulated, it is very momentous to analyze the stability. Mainly, researchers use two methods: (i) the first method represented by Lyapunov is called direct method, and (ii) the second is indirect method and the system may be stable or unstable at the equilibrium points [12]. The SIR model is derived for transmitted disease considering several assumptions, and mathematical analysis becomes more significant by relaxing some assumptions, remembering this, the SIR model is deterministic but there are no probabilities [2]. To the model of annual influenza, treatment population can affect the susceptive and infect the new population and treatment can reduce the infection rate. If expose period is very short of the outbreak and we can avoid that for this seasonal influenza.

Some researchers [3,7,19] studied the frictional order SIR model, and found the stability of the model. Casagrandi et al. [7] developed the SIRC model of influenza A type virus with cross-immune population and showed that prevalence of a virus was maximum for an intermediate value of basic reproduction number $(\mathfrak{R}_0)$ and increasing of cross-immune complicate the system. Shahed et al. [22] discussed asymptotic stability at disease-free equilibrium for fractional-order SIRC model of influenza A and found that at disease-free equilibrium it will be locally stable if $\mathfrak{R}_0 < 1$ and unstable if $\mathfrak{R}_0 > 1$ [22]. Yang et al. [25] developed the SIR model of influenza for self-management and vaccination scenario of the outbreak of the disease and shown that early intervention of self-management and vaccination is more effective than the later intervention [25]. The effective of drug treatment can be very important factor to control the outbreak of the disease and treatment effects adversely in the pandemic influenza [13]. Das et al. [9] studied the SIR model with treatment effect on the removal rate of the transmitted disease and found the stability of the model at two equilibrium points, which were the similar to Shahed et al. [22]. However, separate treatment compartment is not considered, since the population of treatment can infect the susceptive.

From the above studies, it is clear that there is a scope to investigate the avian influenza by compartment method. Therefore, we intend to investigate the effect of treatment of the population of SITR model with the antiviral treatment using compartment method. We will also describe the stability of the model at two equilibrium points. Finally, we will analyze the dynamical variable of the model numerically and graphical.

2. Mathematical formulation

2.1 *Model description*

For seasonal influenza epidemic come and go in a short time. In compartmental model, the

population is divided into several compartments, and diseases are transmitted into these dynamical compartments [16]. According to the compartmental model, we divided the total population into four compartments: Susceptible (S), Infective (I), Treatment (T), and Removal (R). Infected individuals can transmit disease to susceptible. Let β is the transmitted rate to the susceptible. A is the input of uninfected population which is including in susceptible compartment. α and η are the removal rate of the population that is removed for self-immune system and treatment, respectively. γ is the rate to take dug treatment for infected individual and death rate is μ. We take that, the resistance of the drugs of the virus is a rate of δ.

These assumptions lead to the mathematical model as

$$\frac{dS}{dt} = A - \mu S - \beta S(I + \delta T) + \lambda R, \tag{1}$$

$$\frac{dI}{dt} = \beta S(I + \delta T) - (\mu + \alpha + \gamma)I, \tag{2}$$

$$\frac{dR}{dt} = \alpha I + \eta T - \mu R - \lambda R, \tag{3}$$

$$\frac{dT}{dt} = \gamma I - \eta T - \mu T, \tag{4}$$

where $S(0) \geq 0,\ I(0) \geq 0,\ R(0) \geq 0,\ T(0) \geq 0$ and $S_\infty = \lim_{t\to\infty} S(t) > 0,\ \lim_{t\to\infty} I(t) = \lim_{t\to\infty} T(t) = 0$ represent the initial and boundary conditions, respectively. The physical description of this problem is given in Figure (1).

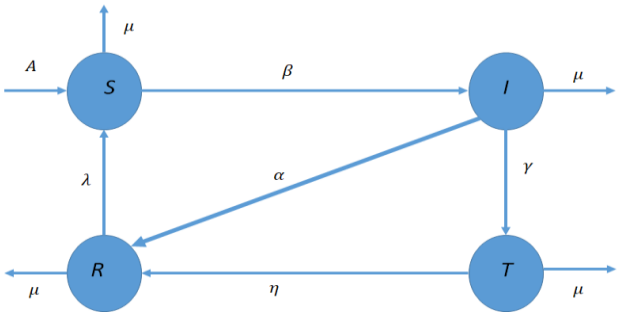

Figure 1. Sketch of the model described by the Eqs. (1)-(4).

2.2 *Disease-free equilibrium*

For diseases-free equilibrium, an equilibrium solution of the systems of Eqs. (1)-(4), that is,

$$\frac{dS}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = \frac{dR}{dt} = 0,$$

can be found with aid of $I = 0$. After solving the above system and using the initial conditions, we have $T = R = 0$ and $S = \frac{A}{\mu}$. Thus, diseases-free equilibrium becomes

$$(S_0, I_0, T_0, R_0) = (\frac{A}{\mu}, 0, 0, 0)$$

Proposition 2.1 Prove that the basic reproduction number of the proposed model can be written as

$$\Re_0 = \frac{A\beta(\eta + \mu + \delta\gamma)}{\mu(\eta + \mu)(\alpha + \mu + \gamma)}.$$

Proof We can separate the proposed model into two categories as disease and non-disease compartments.

(i) Disease compartments

$$\frac{dI}{dt} = \beta S(I + \delta T) - (\mu + \alpha + \gamma)I\,,$$

$$\frac{dT}{dt} = \gamma I - \eta T - \mu T\,,$$

(ii) Non-disease compartments

$$\frac{dS}{dt} = A - \mu S - \beta S(I + \delta T) + \lambda R,$$

$$\frac{dR}{dt} = \alpha I + \eta T - \mu R - \lambda R,$$

In general, the above disease and non-disease compartments can be written as

$$\frac{\partial x_i}{\partial t} = f_i(x_i, y_i) - v_i(x_i, y_i) \tag{5}$$

$$\frac{\partial y_i}{\partial t} = g(x_i, y_i) \tag{6}$$

where x_i and y_i be the subpopulations in disease and non-disease compartments, respectively. f_i and v_i are the rate of secondary infections increased in i th disease compartment and the rate of disease other cases such as progression, death, recovery decreased in the i th disease compartment, respectively. Then, we get $f_i = \begin{pmatrix} \beta S(I + \delta T \\ 0 \end{pmatrix}$ and $v_i = \begin{pmatrix} (\mu + \alpha + \gamma)I \\ -\gamma I + (\eta + \mu)I \end{pmatrix}$.

We assume that all new infections are secondary infections and infected by infected population, and linearizing the above system (Eqs. (5)-(7)) for diseases compartment we get $x' = (F - V_1)x$, where

$$F = \frac{\partial f_i}{\partial x_i}(0, y_0) \text{ and } V_1 = \frac{\partial v_i}{\partial x_i}(0, y_0)$$

which gives

$$F = \begin{pmatrix} \beta S_0 & \beta\delta S_0 \\ 0 & 0 \end{pmatrix} \text{ and } V_1 = \begin{pmatrix} \mu + \alpha + \gamma & 0 \\ -\gamma & \eta + \mu \end{pmatrix}.$$

According to Diekmann and Heesterbeek [10], the next-generation matrix is $k = FV_1^{-1}$ at diseases free-equilibrium and the basic reproduction number is the positive eigenvalue of the matrix *k*, Driessche et al. [11] and given by

$$\Re_0 = \frac{A\beta(\eta+\mu+\delta\gamma)}{\mu(\eta+\mu)(\alpha+\mu+\gamma)}. \tag{7}$$

■

Proposition 2.2 Show that the disease-free equilibrium of the model is locally asymptotically stable if $\Re_0 < 1$, and unstable $\Re_0 > 1$.

Proof The Jacobian matrix *J* is given by

$$J = \begin{bmatrix} \beta S - (\mu+\alpha+\gamma) & \beta\delta S & \beta(I+\delta T) & 0 \\ \gamma & -(\eta+\mu) & 0 & 0 \\ -\beta S & -\beta\delta S & -\mu-\beta(I+\delta T) & \lambda \\ \alpha & \eta & 0 & -(\mu+\lambda) \end{bmatrix}. \tag{8}$$

At disease free-equilibrium, Eq. (8) becomes

$$J = \begin{bmatrix} F-V_1 & 0 \\ U_1 & U_2 \end{bmatrix}$$

where $U_1 = \begin{bmatrix} -\beta S_0 & -\beta\delta S_0 \\ \alpha & \eta \end{bmatrix}$ and $U_2 = \begin{bmatrix} -\mu & \lambda \\ 0 & -(\mu+\lambda) \end{bmatrix}$.

The disease-free equilibrium is locally asymptotically stable, if the eigenvalues of Jacobian matrix at disease-free equilibrium have a negative real part. Since the eigenvalues of *J* are that of $F-V_1$ and U_2. It is clear that the eigenvalues of U_2 are negative (Driessche et al. [11]).

Thus, the stability of *J* is depended on the eigenvalues of $F-V_1$. That is, the disease-free equilibrium is stable if all the eigenvalues of $F-V_1$ have the negative real part. Here F is non-negative and V_1 is non-singular.

Now characteristic equation of $F-V_1$ can be written as

$$\lambda_1^2 - \lambda_1 \times \text{ trace of } (F-V_1) + \text{determinent of } (F-V_1) = 0$$

$$\lambda_1^2 + \lambda_1[2\mu+\alpha+\gamma+\eta) - \beta\frac{A}{\mu}] + (\mu+\alpha+\gamma)(\eta+\mu) - \beta\frac{A}{\mu}(\eta+\mu+\delta\gamma) = 0$$

According to Routh-Hurwitz's condition the system will be stabile if

$$[2\mu+\alpha+\gamma+\eta) - \beta\frac{A}{\mu}] > 0 \text{ and } (\mu+\alpha+\gamma)(\eta+\mu) - \beta\frac{A}{\mu}(\eta+\mu+\delta\gamma) > 0,$$

which give that $\Re_0 = \frac{A\beta(\eta+\mu+\delta\gamma)}{\mu(\eta+\mu)(\alpha+\mu+\gamma)} < 1$. Consequently, we can prove that it will be unstable if $\Re_0 > 1$. This completes the proof. ■

Proposition 2.3 Show that the disease-free equilibrium of the model is globally

asymptotically stable if $\Re_0 < 1$, and unstable $\Re_0 > 1$.

Proof we introduce the linear Lyapunov function in the following way:

$$L_1 = CI + DT$$

where *C* and *D* are constants and the derivative of Lyapunov function can be written as

$$\dot{L}_1 = C\dot{I} + D\dot{T}$$

Using the value of $\dot{I}$ and $\dot{T}$ from Eqs. (2) and (3).

$$\begin{aligned}
&\dot{L}_1 \\
&= C(\beta S(I + \delta T) - (\mu + \alpha + \gamma)I) + D(\gamma I - \eta T - \mu T) \\
&= C\beta SI - C(\mu + \alpha + \gamma)I + D\gamma I + C\beta S\delta T - D(\eta + \mu)T \\
&= (\mu + \alpha + \gamma)\left[C(\frac{\beta S}{\mu + \alpha + \gamma} - 1)I + D\frac{\gamma}{\mu + \alpha + \gamma} I + C\frac{\beta S\delta}{\mu + \alpha + \gamma} T - D\frac{(\eta + \mu)}{\mu + \alpha + \gamma} T \right]
\end{aligned} \tag{9}$$

where 'dot' represents differentiation with respect to time. A perturbation method can be applied to Eq. (9), while the reproduction number takes the form as $D = \frac{\beta S\delta}{(\eta + \mu)} C$ and since $S = S_0 = A/\mu$ at disease free-equilibrium. And after simplifying Eq. (9) becomes $(\mu + \alpha + \gamma)(\Re_0 - 1)I = \dot{L}_1$.

The disease free-equilibrium is globally asymptotically stable if $\dot{L}_1 \le 0$ and above Eq. (9) provides that $\Re_0 < 1$. ■

2.3 *Endemic equilibrium*

For endemic equilibrium, an equilibrium solution of the systems of Eqs. (1)-(4) can be found

$$\frac{dS}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = \frac{dR}{dt} = 0$$

with $I \neq 0$. After solving the above system in the case of endemic equilibrium, we have the following relations

$$S_e = \frac{S_0}{\Re_0},\ I_e = \frac{(\mu + \lambda)(\mu + \eta)}{\mu(\eta + \mu)(\mu + \alpha + \gamma + \lambda) + \lambda\mu\gamma}(1 - \frac{1}{\Re_0}),\ T_e = \frac{\gamma}{\eta + \mu} I_e,\ R = \frac{\alpha(\eta + \mu) + \eta\gamma}{(\mu + \lambda)(\eta + \mu)} I_e.$$

Thus, endemic equilibrium is (S_e, I_e, T_e, R_e).

Proposition 2.4 Prove that the endemic equilibrium of the model is locally asymptotically stable if $\Re_0 > 1$, and unstable $\Re_0 < 1$.

Proof The Jacobian matrix *J* is given by the Eq. (8) and at endemic equilibrium (S_e, I_e, T_e, R_e) the Jacobian matrix becomes as

$$\begin{bmatrix} \beta S_e - (\mu+\alpha+\gamma) & \beta\delta S_e & \beta(I_e+\delta T_e) & 0 \\ \gamma & -(\eta+\mu) & 0 & 0 \\ -\beta S_e & -\beta\delta S_e & -\mu-\beta(I_e+\delta T_e) & \lambda \\ \alpha & \eta & 0 & -(\mu+\lambda) \end{bmatrix}$$

and this can be written briefly as $J = \begin{bmatrix} P_1 & P_2 \\ P_3 & P_4 \end{bmatrix}$ where

$P_1 = \begin{bmatrix} \beta S_e - (\mu+\alpha+\gamma) & \beta\delta S_e \\ \gamma & -(\mu+\lambda) \end{bmatrix}$, $P_2 = \begin{bmatrix} \beta(I_e+\delta T_e) & 0 \\ 0 & 0 \end{bmatrix}$, $P_3 = \begin{bmatrix} -\beta S_e & -\beta\delta S_e \\ \alpha & \eta \end{bmatrix}$,

and $P_4 = \begin{bmatrix} -\mu-\beta(I_e+\delta T_e) & \lambda \\ 0 & -(\mu+\lambda) \end{bmatrix}$.

The endemic equilibrium is locally asymptotically stable, if the eigenvalues of Jacobian matrix at endemic equilibrium have a negative real part. Since the eigenvalues of J are those of P_1 and P_4. Moreover, the eigenvalues of P_4 will be negative, if $\mu+\beta(I_e+\delta T_e)$ or $\beta(I_e+\delta T_e)$ is negative.

Let $A_1 = \dfrac{(\mu+\lambda)(\mu+\eta)}{\mu(\eta+\mu)(\mu+\alpha+\gamma+\lambda)+\lambda\mu\gamma}$ and $A_2 = \dfrac{\gamma}{\eta+\mu}$ then $\beta(I_e+\delta T_e)$ becomes $\beta A_1(1+\delta A_2)\left(1-\dfrac{1}{\Re_0}\right)$ which will be negative iff $\Re_0 > 1$. ■

Proposition 2.5 If $\Re_0 > 1$, then show that at the endemic equilibrium, the proposed model is globally asymptotically stable.

Proof Letting the Lyapunov function following as

$$L_2 = (S - S_e - S_e \ln\frac{S}{S_e}) + (I - I_e - I_e \ln\frac{I}{I_e}) + A(T - T_e - T_e \ln\frac{T}{T_e}) + B(R - R_e - R_e \ln\frac{R}{R_e}).$$

After differentiating the Lyapunov function which gives

$$\dot{L}_2 = (1-\frac{S_e}{S})\dot{S} + (1-\frac{I_e}{I})\dot{I} + A(1-\frac{T_e}{T})\dot{T} + B(1-\frac{R_e}{R})\dot{R} \tag{10}$$

Since (S_e, I_e, T_e, R_e) is the equilibrium point of the model then, we can write Eqs. (1)-(4) as

$$A - \mu S_e - \beta S_e(I_e+\delta T_e) + \lambda R_e = 0, \tag{11}$$

$$\beta S_e(I_e+\delta T_e) - (\mu+\alpha+\gamma)I_e = 0, \tag{12}$$

$$\gamma I_e - (\eta+\mu)T_e = 0, \tag{13}$$

$$\alpha I_e + \eta T_e - (\mu+\lambda)R_e = 0. \tag{14}$$

The first term of Eqs. (10) can be written with the help of Eq. (1) as

$$(1-\frac{S_e}{S})\dot{S} = (1-\frac{S_e}{S})[A-\mu S-\beta S(I+\delta T)+\lambda R]$$

Using the value of A form Eq. (11), the above term becomes

$$(1-\frac{S_e}{S})\dot{S} = (1-\frac{S_e}{S})\left[\mu S_e(1-\frac{S}{S_e})+\beta S_e\left(I_e+\delta T_e\right)\left(1-\frac{S\left(I+\delta T\right)}{S_e\left(I_e+\delta T_e\right)}\right)+\lambda R\left(1-\frac{R_e}{R}\right)\right]$$

$$= \mu S_e(2-\frac{S_e}{S}-\frac{S}{S_e})+\beta S_e\left(I_e+\delta T_e\right)\left(1-\frac{S_e}{S}+\frac{I+\delta T}{I_e+\delta T_e}-\frac{S\left(I+\delta T\right)}{S_e\left(I_e+\delta T_e\right)}\right)$$

$$+\lambda R\left(1-\frac{R_e}{R}-\frac{S_e}{S}+\frac{R_eS_e}{RS}\right)$$

Similarly, we have found the second, third and fourth terms.
Second term:

$$(1-\frac{I_e}{I})\dot{I} = (1-\frac{I_e}{I})\left[\beta S(I+\delta T)-(\mu+\alpha+\gamma)I\right]$$

$$(1-\frac{I_e}{I})\dot{I} = (1-\frac{I_e}{I})\beta S_e\left(I_e+\delta T_e\right)\left[\frac{S\left(I+\delta T\right)}{S_e\left(I_e+\delta T_e\right)}-\frac{I}{I_e}\right]$$

$$= \beta S_e\left(I_e+\delta T_e\right)\left[\frac{S\left(I+\delta T\right)}{S_e\left(I_e+\delta T_e\right)}-\frac{I}{I_e}-\frac{SI_e\left(I+\delta T\right)}{S_eI\left(I_e+\delta T_e\right)}+1\right]$$

Third term:

$$(1-\frac{T_e}{T})\dot{T} = (1-\frac{T_e}{T})\left[\gamma I-\eta T-\mu T\right] = (1-\frac{T_e}{T})\gamma I_e\left(\frac{I}{I_e}-\frac{T}{T_e}\right) = \gamma I_e\left(\frac{I}{I_e}-\frac{T}{T_e}-\frac{T_eI}{TI_e}+1\right)$$

Fourth term:

$$(1-\frac{R_e}{R})\dot{R} = (1-\frac{R_e}{R})\left[\alpha I+\eta T-(\mu+\lambda)R\right]$$

$$= (1-\frac{R_e}{R})(\alpha I_e+\eta T_e)\left(\frac{\alpha I+\eta T}{\alpha I_e+\eta T_e}-\frac{R}{R_e}\right)$$

$$= (\alpha I_e+\eta T_e)\left(\frac{\alpha I+\eta T}{\alpha I_e+\eta T_e}-\frac{R}{R_e}-\frac{R_e(\alpha I+\eta T)}{R(\alpha I_e+\eta T_e)}+1\right)$$

Therefore, the Lyapunov function can be written in differential form as

$$\dot{L}_2 = \mu S_e(2-\frac{S_e}{S}-\frac{S}{S_e})+\beta S_e\left(I_e+\delta T_e\right)\left(4-\frac{S_e}{S}-\frac{I}{I_e}-\frac{SI_e\left(I+\delta T\right)}{S_eI\left(I_e+\delta T_e\right)}-\frac{I_e+\delta T_e}{I+\delta T}\right)$$

$$+\lambda R\left(3-\frac{R_e}{R}-\frac{S_e}{S}-\frac{RS}{R_eS_e}\right)+A\gamma I_e\left(3-\frac{I_e}{I}-\frac{T}{T_e}-\frac{T_eI}{TI_e}\right) \qquad (15)$$

$$+B(\alpha I_e+\eta T_e)\left(3-\frac{R}{R_e}-\frac{R_e(\alpha I+\eta T)}{R(\alpha I_e+\eta T_e)}-\frac{\alpha I_e+\eta T_e}{\alpha I+\eta T}\right)$$

$$-\beta S_e\left(I_e+\delta T_e\right)\left(\frac{I_e+\delta T_e}{I+\delta T}+\frac{I+\delta T}{I_e+\delta T_e}-2\right)-\lambda R\left(\frac{RS}{R_eS_e}+\frac{R_eS_e}{RS}-2\right)$$
$$-A\gamma I_e\left(\frac{I}{I_e}+\frac{I_e}{I}-2\right)-B(\alpha I_e+\eta T_e)\left(\frac{\alpha I+\eta T}{\alpha I_e+\eta T_e}+\frac{\alpha I_e+\eta T_e}{\alpha I+\eta T}-2\right)$$

Since the arithmetic mean exceeds the geometric mean, then we can express the following inequalities:

$$2-\frac{S_e}{S}-\frac{S}{S_e}\le 0,$$

$$4-\frac{S_e}{S}-\frac{I}{I_e}-\frac{SI_e\left(I+\delta T\right)}{S_eI\left(I_e+\delta T_e\right)}-\frac{I_e+\delta T_e}{I+\delta T}\le 0,$$

$$3-\frac{I_e}{I}-\frac{T}{T_e}-\frac{T_eI}{TI_e}\le 0,$$

$$3-\frac{R_e}{R}-\frac{S_e}{S}-\frac{RS}{R_eS_e}\le 0,$$

$$3-\frac{R}{R_e}-\frac{R_e(\alpha I+\eta T)}{R(\alpha I_e+\eta T_e)}-\frac{\alpha I_e+\eta T_e}{\alpha I+\eta T}\le 0.$$

Inside the bracket of sixth, seventh, eighth and ninth terms of Eq. (15) can be expressed as $a+\frac{1}{a}-2=\frac{(a-1)^2}{a}\ge 0,\ a\ne 0$. Thus $\dot{L}_2(S,I,T,R)\le 0$. If $S=S_e,\ I=I_e,\ T=T_e$ and $R=R_e$ then $\dot{L}_2(S,I,T,R)=0$. Therefore, the largest invariant set $\left(S_e,I_e,T_e,R_e\right)\in\Gamma$ is $\left\{\in^*\right\}$, where $\in^*$ is the endemic equilibrium. According to LaSalle's invariant principle $\in^*$ is globally asymptotically stable every solution approach to the endemic equilibrium $\left(S_e,I_e,T_e,R_e\right)$ of the model as $t\to\infty$ for $\Re_0>1$.

3. Results and discussion

The control system, which is formed by the system of Eqs. (1)-(4) have solved numerically with the initial and boundary conditions. We have controlled numerical simulation using various choices of parameters (Table 1) and have observed the solution in each compartment.

Table 1. Various referenced value of parameters.

Parameters	Value	References
Infection rate (β)	0.006 per day	[4]
Mortality rate (μ)	50%-90%	[26]
Treatment rate (γ)	100%	…
Drug Resistance (δ)	31.6%-62.2%	[14]
Recovery rate without treatment (α)	0%-10%	[21]
Recovery rate with treatment (η)	10%-50%	[26]
Re-susceptive rate (λ)	100%	[24]

The results of the situation of each compartment are shown graphically in Figures (2) to (5) and antiviral treatment demonstrate the whole model.

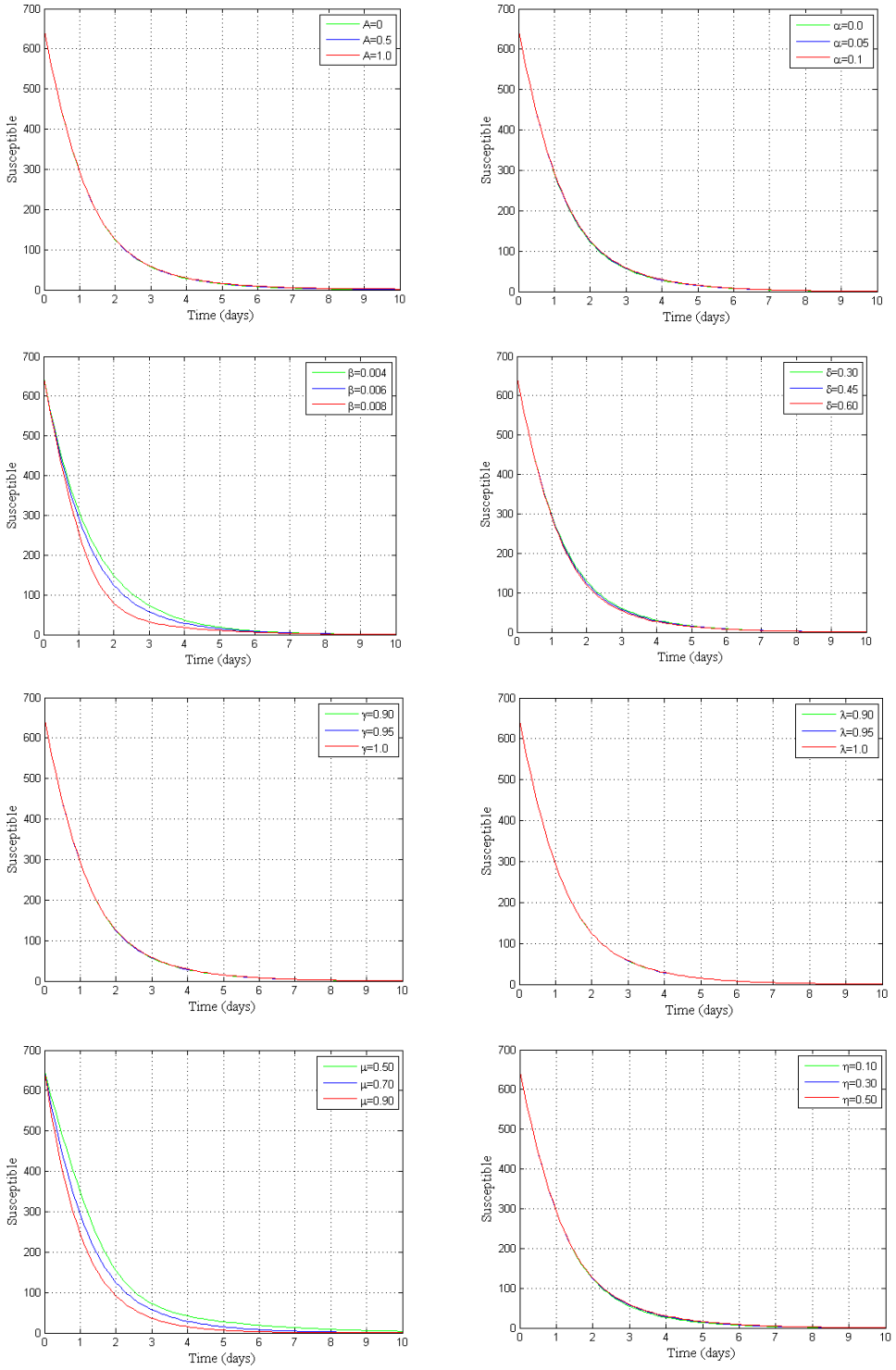

Figure 2. Variation of the susceptible with the variation of the parameters using tabulated values.

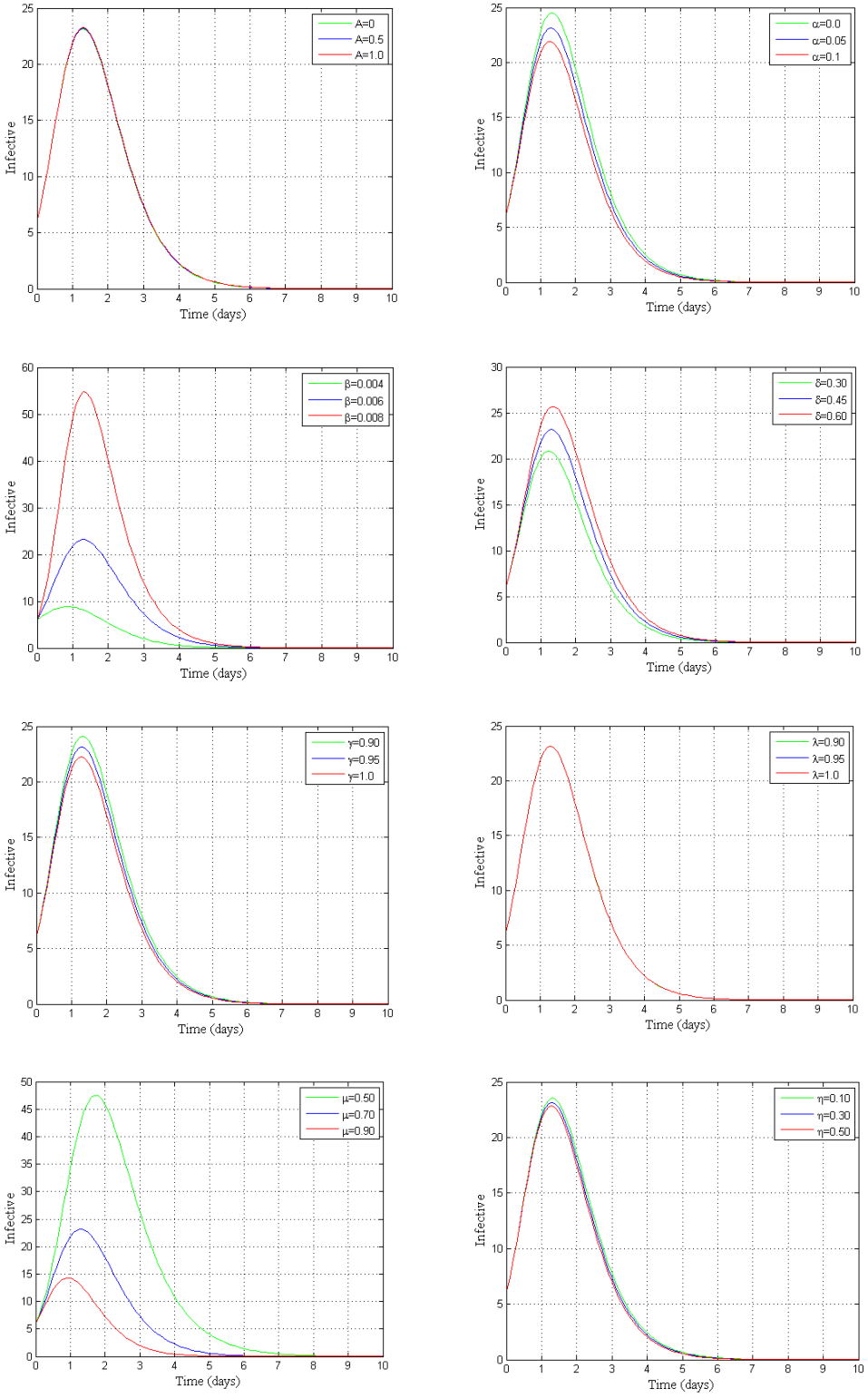

Figure 3. Variation of the infective with the variation of the parameters using tabulated values.

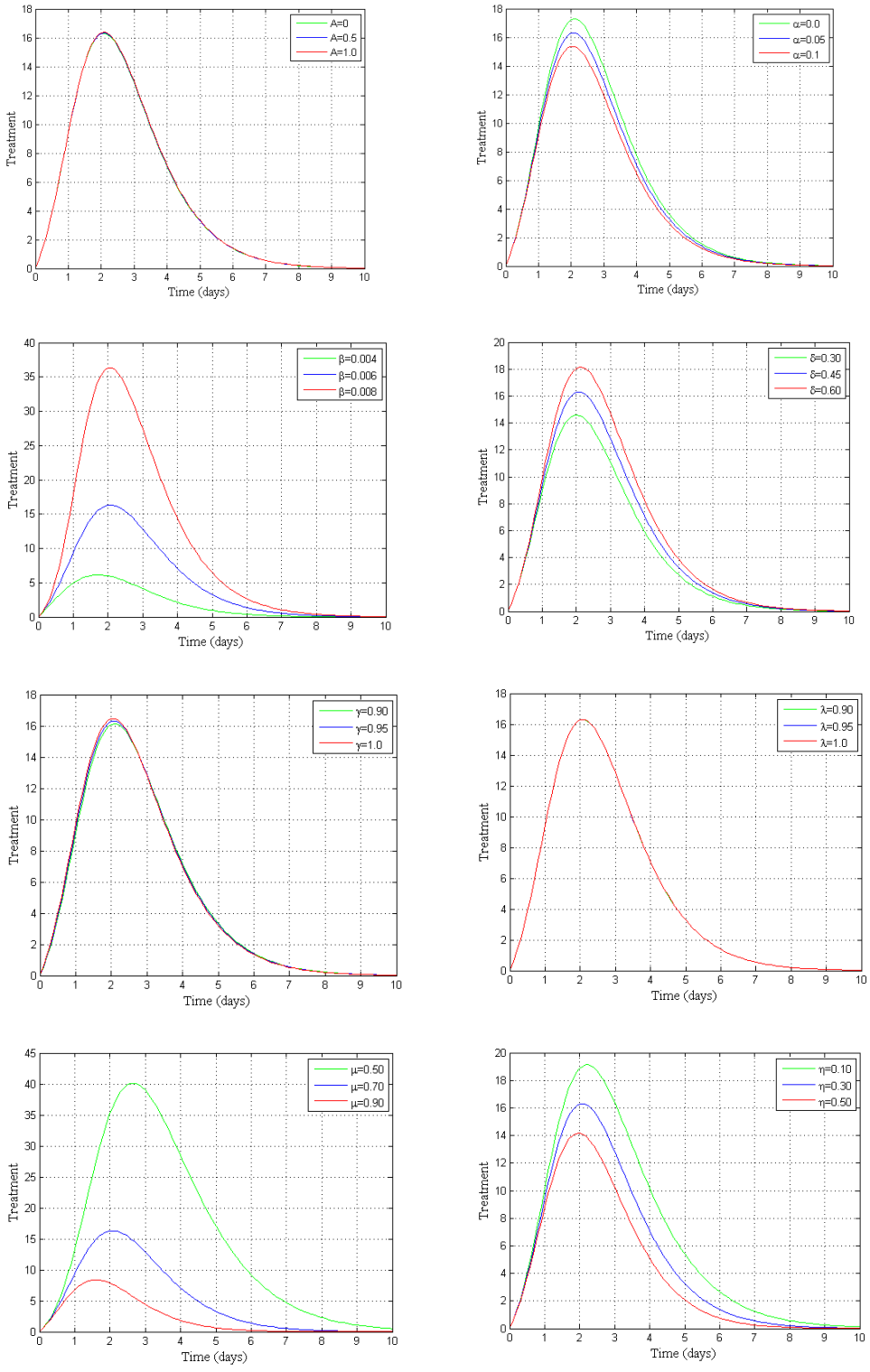

Figure 4. Variation of the treatment with the variation of the parameters using tabulated values.

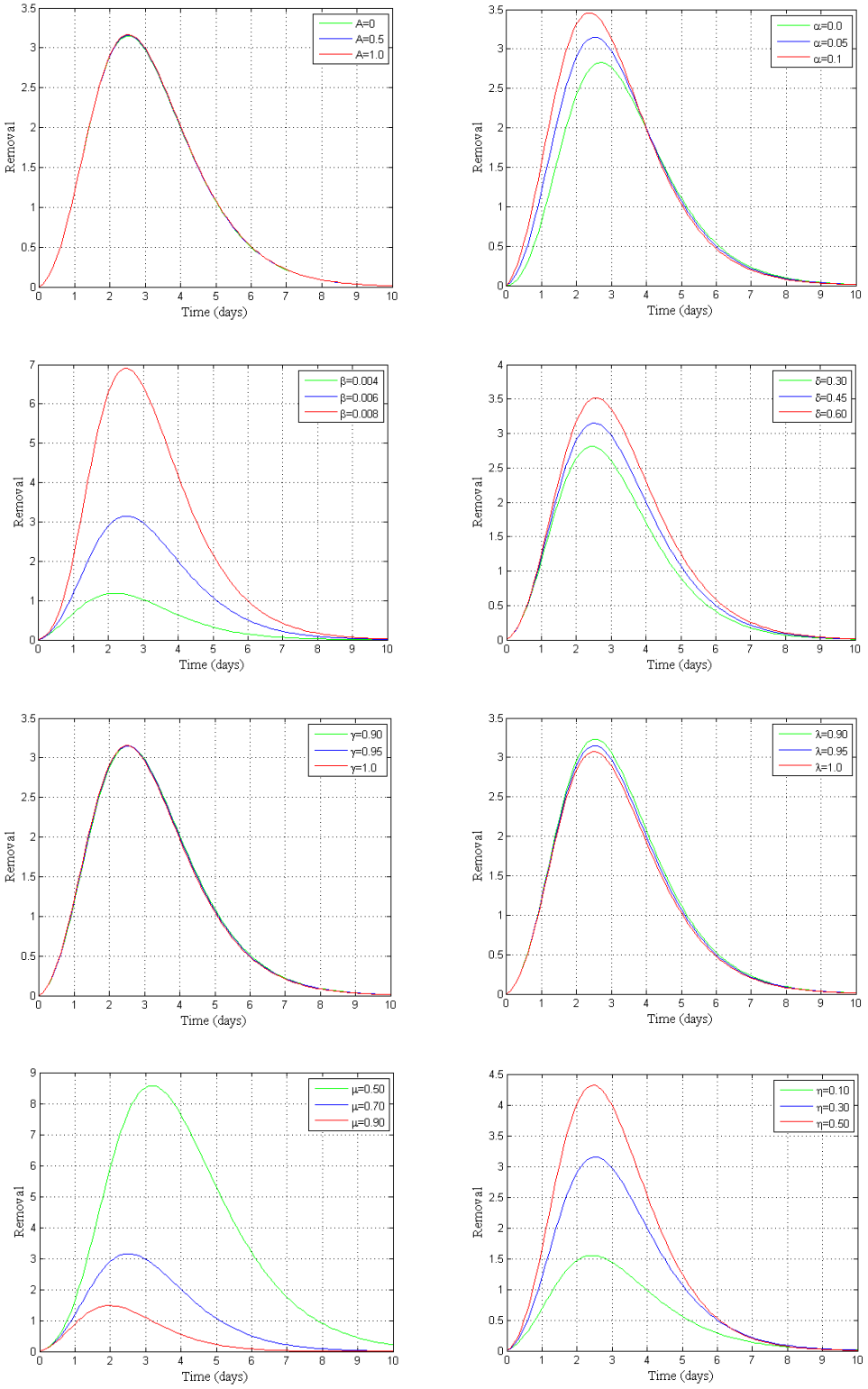

Figure 5. Variation of the removal with the variation of the parameters using tabulated values.

In Figure 1, variations of susceptive are represented against the variation of several parameters, such as migration rate, infraction rate, the resistance of drug rate, mortality rate, recovery rate, etc. The susceptive rate, other parameters have no significant depends on infection rate and it exponentially decreases with the increasing of time whereas effect (Figure 2).

In Figure 3, the infective rate increases from initial to a certain point and then decreases up to dismiss, and this compartment is much affected by infection rate, mortality rate, and recovery rate due to treatment. Moreover, it is also observed that the migration rate, drug resistance rate, and re-susceptive rate have no sensitive effect. In addition, the infective rate increases with the increase of infection and drug resistance rate and decreases with the increase of mortality rate. Similar results are found for the treatment compartment as infective compartment. In this compartment, individuals increase with the decreasing of removal rate due to treatment (Figure 4). Finally, we have observed in Figure 5 that the individual of removal compartment increases with the increase of infection, treatment, drug resistance, recovery rate, and decreases with the increase of mortality rate.

Finally, we have compared our present model's result with the Feng et al. [13] and Das et al. [9] and in Figure 6. In this figure, we have seen that the present model shows good agreement with the model of Das et al. [9], whereas, a slight difference observes with the model of Feng et al. [13]. The reason of difference occurs may be due to the value of the choice of the parameters.

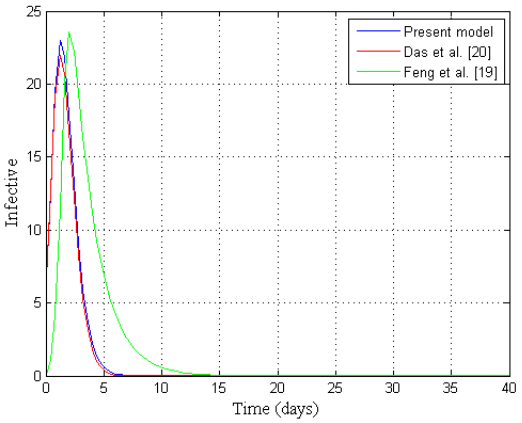

Figure 6. Comparison of the model results of infection with other's models.

4. Conclusion

In this study, a mathematical model (SITR) of influenza optimized by antiviral treatment was presented and discussed its stability at the equilibrium points in terms of basic reproduction number. Important parameters, such as susceptible, infective, treatment and removal rate under the compartment method were studied theoretically. The model result showed that it was locally and globally stable at disease-free equilibrium if the basic reproduction number is less than one ($\Re_0 < 1$) and locally and globally stable at endemic equilibrium if the basic reproduction number is greater than one ($\Re_0 > 1$). Moreover, the effects of several parameters on each compartment were presented graphically. In addition, we also compared the present model (SITR) with other's models and found good agreement.

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References

[1] J. Alam, M. Giasuddin, M. A. Samad and M. J. F. A. Taimur, Recent evidence of avian influenza in Bangladesh: A review, World's Poultry Science Journal, **66 (3)** (2010) 455–464, doi:10.1017/S004393391000053X.
[2] L. J. S. Allen, An introduction to stochastic epidemic models, In Mathematical Epidemiology, Springer, (2008), 81–130.
[3] C. N. Angstmann, B. I. Henry and A. V. McGann, A fractional-order infectivity SIR model, Physica A: Statistical Mechanics and its Applications, **452** (2016) 86–93, doi:10.1016/j.physa.2016.02.029.
[4] P. K. Biswas et al., Avian influenza outbreaks in chickens, Bangladesh, Emerging Infectious Diseases, **14 (12)** (2008) 1909–1912, doi:10.3201/eid1412.071567.
[5] F. Brauer, Modeling influenza: Pandemics and seasonal epidemics, In Mathematical Epidemiology, Springer, (2008) 321–347.
[6] R. A. Bright, M. J. Medina, X. Xu, G. Perez-Oronoz, T. R. Wallis, X. M. Davis, L. Povinelli, N. J. Cox and A. I. Klimov, Incidence of adamantane resistance among influenza A (H3N2) viruses isolated worldwide from 1994 to 2005: a cause for concern, Lancet, **366 (9492)** (2005) 1175–1181, doi:10.1016/S0140-6736(05)67338-2.
[7] R. Casagrandi, L. Bolzoni, S. A. Levin and V. Andreasen, The SIRC model and influenza A, Mathematical Biosciences, **200 (2)** (2006) 152–169, doi:10.1016/j.mbs.2005.12.029.
[8] C. L. Cheung et al., Distribution of amantadine-resistant H5N1 avian influenza variants in Asia, The Journal of Infectious Diseases, **193 (12)** (2006) 1626–1629, doi:10.1086/504723.
[9] A. Das and M. Pal, A mathematical study of an imprecise SIR epidemic model with treatment control**.** Journal of Applied Mathematics and Computing, **56 (1-2)** (2018) 477–500.
[10] O. Diekmann and J. A. P. Heesterbeek, Mathematical epidemiology of infectious diseases, Wiley Series in Mathematical and Computational Biology, Wiley, West Sussex, England, (2000).
[11] P. Driessche J. Van Denand Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Mathematical Biosciences, **180 (1-2)** (2002) 29–48, doi:10.1016/S0025-5564(02)00108-6.
[12] H. Fathabadi, On stability analysis of nonlinear systems, Trends in Applied Sciences Research, **7** (2012) 651–662.
[13] Z. Feng, S. Towers and Y. Yang, Modeling the effects of vaccination and treatment on pandemic influenza**,** The AAPS Journal, **13 (3)** (2011) 427–437.
[14] E. A. Govorkova, T. Baranovich, P. Seiler, J. Armstrong, A. Burnham, Y. Guan, M. Peiris, R. J. Webby and R. G. Webster, Antiviral resistance among highly pathogenic influenza A (H5N1) viruses isolated worldwide in 2002-2012 shows need for continued monitoring, Antiviral Research, **98 (2)** (2013) 297–304, doi:10.1016/j.antiviral.2013.02.013.
[15] A. C. Hurt, P. Selleck, N. Komadina, R. Shaw, L. Brown and I. G. Barr, Susceptibility of highly pathogenic A(H5N1) avian influenza viruses to the neuraminidase inhibitors and adamantanes, Antiviral Research, **73 (3)** (2007) 228–231, doi:10.1016/j.antiviral.2006.10.004.
[16] W. O. Kermack and A. G. McKendrick, A contribution to the mathematical theory of epidemics, Proceedings of the Royal Society A., **115 (772)** (1927) 700–721, doi:10.1098/rspa.1927.0118.
[17] G. Lang, O. Narayan and B. T. Rouse, Prevention of malignant avian influenza by 1-adamantanamine hydrochloride, Arch Gesamte Virusforsch, **32 (2)** (1970) 171–184.
[18] Q. Lin, Z. Lin, P.Y. A. Chiu and D. He1, Seasonality of influenza A (H7N9) virus in China-Fitting simple epidemic models to human cases, PLoS ONE, **11 (3)** (2016), doi:10.1371/journal.pone.0151333.
[19] E. Okyere, F. Oduro, S. Amponsah, I. Dontwi and N. Frempong, Fractional order SIR model with constant population, Journal of Advances in Mathematics and Computer Science, **14 (2)** (2016) 1–12.
[20] R. Parvin, J. A. Begum, E. H. Chowdhury, M. R. Islam, M. Beer and T. Harder, Co-subsistence of avian influenza virus subtypes of low and high pathogenicity in Bangladesh: Challenges for diagnosis, risk assessment and control, Scientific Reports, **9** (2019), 8306, doi:10.1038/s41598-019-44220-4.
[21] S. Payungporn, S. Chutinimitkul, A. Chaisingh, S. Damrongwantanapokin, B. Nuansrichay and W. Pinyochon, Discrimination between highly pathogenic and low pathogenic H5 avian influenza A viruses, Emerging Infectious Diseases, **12 (4)** (2006) 700–701, doi:10.3201/eid1204.051427.
[22] M. E. Shahed and A. Alsaedi, The fractional SIRC model and influenza A, Mathematical Problems in Engineering, **2011** (2011), Article ID 480378, doi:10.1155/2011/480378.
[23] D. E. Swayne, Avian influenza vaccines and therapies for poultry, Comparative Immunology, Microbiology and Infectious Diseases, **32 (4)** (2009) 351–363, doi:10.1016/j.cimid.2008.01.006.
[24] R. G. Webster, Y. Kawaoka and W. J. Bean, Vaccination as a strategy to reduce the emergence of amantadine- and rimantadine-resistant strains of (H5N2) influenza virus, Journal of Antimicrobial Chemotherapy, **18** (1986) 157–164, doi:10.1093/jac/18.Supplement_B.157.

[25] K. H. Yang and J. Y. Hsu, A new SIR-based model for influenza epidemic, International Journal of Mathematical, Computational, Physical, Electrical and Computer Engineering, **6** (2012), 7, doi:10.5281/zenodo.1054948.

[26] S. Yuan, Drugs to cure avian influenza infection – multiple ways to prevent cell death, Cell Death Dis, **4 (10)** (2013), e835, doi:10.1038/cddis.2013.367.