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Avian Influenza with Drug Resistance

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Abstract – In this paper, avian influenza epidemic model with drug resistance effect is investigated. The basic reproduction number R_0 find out using next generation method. The local and global stability of a disease free and endemic equilibrium of the system is studied and discussed. Numerical simulations are carried out to investigate the influence of the key parameters on the spread of the disease, to support the analytical conclusion and illustrate possible behavioral scenarios of the model.

Keywords – *Avian influenza, drug resistance, stability, basic reproduction.*

1. Introduction

The year ended cost of affliction illness and the developing threat of evolution of a comprehensive strain make it all important to revisit of present accessible treatment options. Adamantane and neuraminidase inhibitors (NAIS), two divisions of drugs, are at present accessible treatment of influenza, although to treat influenza adequately combat to both divisions at drugs intimidate our ability. Underlying the appearance of day combat helps in letter consider at the mechanism. It will approve health authorization to make more adequate else of antiviral, over the cause of an influenza infection on a periodic basis, or in the content of a pandemic, preceding production on the appearance at drug combat in afflictions. A has been centralize largely an epidemiological model which represent the spreading of drug combat infection across a population. For developing approach to interrupt the diffusion of drug combat once it emerges,

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such studies are important, they do not provide insight into how the drug combat break affair during the continuity at a single infection, and on what timescale the appearance of drug combat to NAIS has been examined by an early modeling study, during a single infection. In which, it is found that NAI combat could arrive in the absence at drug treatment, admitting at low level, even if the break is slightly less fit than the wild-type virus. To appraise the fitness difference which is caused by drug combat mutation has been studies and used several models. Alternative studies have used models to optimize treatment regimens to reduce the emergence of drug resistant mutants. However, some of the biological processes that might self or hinder the appearance of drug combat are yet not tried to examined by any study [2].

2. Mathematical Model

Basic Model. Shuqinche [1] has proposed the model for the avian influenza

$$\begin{aligned}
\frac{dX}{dt} &= c - \frac{wXY}{1+\delta Y} - dX \\
\frac{dY}{dt} &= \frac{wXY}{1+\delta Y} - (d+m)Y \\
\frac{dS}{dt} &= b - \frac{\beta SY}{1+\delta Y} - \alpha S \\
\frac{dI}{dt} &= \frac{\beta SY}{1+\delta Y} - (\varepsilon+\alpha+\gamma)I \\
\frac{dR}{dt} &= \gamma I - \alpha R
\end{aligned} \tag{2.1}$$

Modified Model.

$$\begin{aligned}
\frac{dX}{dt} &= c - \frac{wXY}{1+\delta Y} - dX \\
\frac{dY}{dt} &= \frac{wXY}{1+\delta Y} - (d+m)Y \\
\frac{dS}{dt} &= b - \frac{\beta SY}{1+\delta Y} - \alpha S \\
\frac{dI}{dt} &= \frac{\beta SY}{1+\delta Y} - (\varepsilon+\alpha+\gamma+\eta)I \\
\frac{dR_{ES}}{dt} &= \eta I - (\alpha+\sigma)R_{ES} \\
\frac{dR}{dt} &= \gamma I - \alpha R + \sigma R_{ES}
\end{aligned} \tag{2.2}$$

Parameter description. The human is divided into three compartments S, I, R the number of susceptible, infected and recovered respectively, the birds are divided into susceptible poultry (X) and infected poultry (Y).

Parameter	description
C	natural birth rate of avian
b	natural birth rate of human
d	the natural mortality of poultry
α	the natural mortality of human
m	due to the mortality illness of poultry
ε	due to the mortality illness of human
w	stands for infectious rate of susceptible poultry to infected poultry
β	stands for infected poultry of the infection
	rate of susceptible human individuals
γ	the recovery rate that infects individuals through treatment
η	resistance rate to treatment
σ	recovery rate after second line of resistance treatment

3. Equilibria of the System

$$\begin{aligned}
\frac{dX}{dt} &= c - \frac{wXY}{1+\delta Y} - dX \\
\frac{dY}{dt} &= \frac{wXY}{1+\delta Y} - (d+m)Y \\
\frac{dS}{dt} &= b - \frac{\beta SY}{1+\delta Y} - \alpha S \\
\frac{dI}{dt} &= \frac{\beta SY}{1+\delta Y} - (\varepsilon + \alpha + \gamma + \eta) I \\
\frac{dR_{ES}}{dt} &= \eta I - (\alpha + \sigma) R_{ES} \\
\frac{dR}{dt} &= \gamma I - \alpha R + \sigma R_{ES}
\end{aligned} \tag{3.1}$$

disease free equilibrium point

$$E_0\left(X^0, Y^0, S^0, I^0, R^0{}_{ES}\right) = \left(\frac{c}{d}, 0, \frac{b}{\alpha}, 0\right)$$

We can find the basic reproductive numbers using the next generation method

$$\frac{dX}{dt} = F - V$$

where

$$F = \begin{bmatrix} \frac{wXY}{1+\delta Y} \\ 0 \end{bmatrix}, \quad V = \begin{bmatrix} -d & 0 \\ 0 & -(d+m) \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & \frac{cw}{d(d+m)} \\ 0 & 0 \end{bmatrix}$$

The largest Eigen value of FV^{-1}, the basic reproduction number is expressed as

$$R_0 = \frac{cw}{d(d+m)}$$

Endemic equilibrium point

$$c - \frac{wXY}{1+\delta Y} - dX = 0$$
$$\frac{wXY}{1+\delta Y} - (d+m)Y = 0$$
$$b - \frac{\beta SY}{1+\delta Y} - \alpha S = 0$$
$$\frac{\beta SY}{1+\delta Y} - (\varepsilon + \alpha + \gamma + \eta)I = 0$$
$$\eta I - (\alpha + \sigma)R_{ES} = 0$$
$$\gamma I - \alpha R + \sigma R_{ES} = 0$$

$$E_*\left(X^*, Y^*, S^*, I^*, R^*{}_{ES}\right)$$

Where

$$X^* = \frac{d+m-c\delta}{d\delta + w},$$

$$Y^* = \frac{cw - d(d+m)}{(d+m)(d\delta + w)},$$

$$S^* = \frac{b\left(1+\delta Y^*\right)}{\beta Y^* + \alpha\left(1+\delta Y^*\right)}$$

$$I^* = \frac{b\beta Y^*}{\left(\varepsilon+\alpha+\gamma+\eta\right)\left(\beta Y^* + \alpha\left(1+\delta Y^*\right)\right)},$$

$$R^*_{ES} = \frac{\eta I^*}{\left(\alpha+\sigma\right)}$$

Theorem 3.1. if $R_0 < 1$, the system (3.1) only exists the disease-free equilibrium $E_0\left(\frac{c}{d},0,\frac{b}{\alpha},0,0\right)$ when $R_0 > 1$, there exists only one endemic equilibrium

$$E_*\left(\frac{d+m-c\delta}{d\delta+w}, \frac{cw-d\left(d+m\right)}{\left(d+m\right)\left(d\delta+w\right)}, \frac{b\left(1+\delta Y^*\right)}{\beta Y^* + \alpha\left(1+\delta Y^*\right)}, \frac{b\beta Y^*}{\left(\varepsilon+\alpha+\gamma+\eta\right)\left(\beta Y^* + \alpha\left(1+\delta Y^*\right)\right)}, \frac{\eta I^*}{\left(\alpha+\sigma\right)}, \right)$$

4. Local Stability of the Disease Free Equilibrium

In this section we find the local stability of the disease free and endemic equilibrium.

Theorem 4.1. The disease free equilibrium E_0 is locally asymptotically stable, if $R_0 < 1$.

Proof. The Jacobian matrix of system (3.1) is

$$J_0 = \begin{bmatrix} -d - \frac{wY}{1+\delta Y} & \frac{-wX\left(1+\delta Y\right) - \delta wXY}{\left(1+\delta Y\right)^2} & 0 & 0 & 0 \\ \frac{wY}{1+\delta Y} & \frac{wX\left(1+\delta Y\right) - \delta wXY}{\left(1+\delta Y\right)^2} - \left(d+m\right) & 0 & 0 & 0 \\ 0 & \frac{-\beta S\left(1+\delta Y\right) - \delta\beta SY}{\left(1+\delta Y\right)^2} & -\frac{\beta S}{\left(1+\delta Y\right)} - \alpha & 0 & 0 \\ 0 & \frac{\beta S\left(1+\delta Y\right) - \delta\beta SY}{\left(1+\delta Y\right)^2} & \frac{\beta S}{\left(1+\delta Y\right)} & \left(\varepsilon+\alpha+\gamma+\eta\right) & 0 \\ 0 & 0 & 0 & \eta & -\left(\alpha+\sigma\right) \end{bmatrix}$$

$$J_0 = \begin{bmatrix} -d & \frac{-wc}{d} & 0 & 0 & 0 \\ 0 & \frac{wc}{d} - (d+m) & 0 & 0 & 0 \\ 0 & -\frac{b\beta}{\alpha} & -\alpha & 0 & 0 \\ 0 & \frac{b\beta}{\alpha} & 0 & (\varepsilon+\alpha+\gamma+\eta) & 0 \\ 0 & 0 & 0 & \eta & -(\alpha+\sigma) \end{bmatrix}$$

$$|J_0 - \lambda I| = \begin{vmatrix} -d-\lambda & \frac{-wc}{d} & 0 & 0 & 0 \\ 0 & \frac{wc}{d} - (d+m) - \lambda & 0 & 0 & 0 \\ 0 & -\frac{b\beta}{\alpha} & -\alpha-\lambda & 0 & 0 \\ 0 & \frac{b\beta}{\alpha} & 0 & (\varepsilon+\alpha+\gamma+\eta)-\lambda & 0 \\ 0 & 0 & 0 & \eta & -(\alpha+\sigma)-\lambda \end{vmatrix}$$

$$-d\left[\frac{wc}{d} - (d+m) - \lambda\right]\alpha(\varepsilon+\alpha+\gamma+\eta)(\alpha+\sigma) \le 0$$

$$-(d+\lambda)\left[\frac{wc}{d} - (d+m) - \lambda\right](\alpha+\lambda)(\varepsilon+\alpha+\gamma+\eta-\lambda)(\alpha+\sigma-\lambda) = 0$$

for $R_0 < 1$, it is clear the matrix J_{E_0} has negative real parts. So, E_0 is locally asymptotically stable.

Theorem 4.2. The endemic equilibrium E_* is locally asymptotically stable if $R_0 > 1$.

Proof. The Jacobean matrix of system (3.1) is

$$J_{E_*} = \begin{bmatrix} -d - \frac{wY^*}{1+\delta Y^*} & \frac{-wX^*(1+\delta Y^*) - \delta wX^*Y^*}{(1+\delta Y^*)^2} & 0 & 0 & 0 \\ \frac{wY^*}{1+\delta Y^*} & \frac{wX^*(1+\delta Y^*) - \delta wX^*Y^*}{(1+\delta Y^*)^2} - (d+m) & 0 & 0 & 0 \\ 0 & \frac{-\beta S^*(1+\delta Y) - \delta\beta S^*Y}{(1+\delta Y)^2} & -\frac{\beta S^*}{(1+\delta Y)} - \alpha & 0 & 0 \\ 0 & \frac{\beta S^*(1+\delta Y) - \delta\beta S^*Y}{(1+\delta Y)^2} & \frac{\beta S}{(1+\delta Y)} & (\varepsilon+\alpha+\gamma+\eta) & 0 \\ 0 & 0 & 0 & \eta & -(\alpha+\sigma) \end{bmatrix}$$

The characteristic equation of jacobian matrix (4.2) at the endemic equilibrium point, $E_* = \left(X^*, Y^*, S^*, I^*, R_{ES}{}^*\right)$, is a fifth-degree polynomial given by

$$P(\lambda) = \lambda^5 + a_1\lambda^4 + a_2\lambda^3 + a_3\lambda^2 + a_4\lambda + a_5,$$

Where $a_i, i = 1, 2, 3, 4, 5$ are the coefficients. It can be shown that all the coefficients a_i are positive. The necessary and sufficient conditions for the local asymptotic stability of endemic equilibrium point E_1 are that the Hurwitz determinants H_i, are all positive for the Routh-Hurwitz criteria. For a fifth degree polynomial [3] these criteria are given by

$$H_1 = a_1 > 0,$$

$$H_2 = a_1a_2 - a_3 > 0,$$

$$H_3 = a_1a_2a_3 + a_1a_5 - a_1{}^2a_4 - a_3{}^2 > 0$$

$$H_4 = \left(a_3a_4 - a_2a_5\right)\left(a_1a_2 - a_3\right) - \left(a_1a_4 - a_5\right)^2 > 0$$

$$H_5 = a_5H_4 > 0$$

From which we can conclude whether the endemic equilibrium point is locally asymptotically stable or unstable.

5. Global stability of the disease free and endemic equilibrium.

Theorem 5.1. if $R_0 < 1$, the disease free equilibrium E_0 is globally asymptotically stable, if $R_0 > 1$, the disease free equilibrium E_0 is unstable.

Proof. Consider the lyapunov function

$$K_1 = X - X^0\, In\, X + Y$$

$$= X^1 - \frac{X^0}{X}X^1 + Y^{1.}$$

$$= X^1\left(1 - \frac{X^0}{X}\right) + Y^{1.}$$

$$= \left(1 - \frac{X^0}{X}\right)\left[c - \frac{wXY}{1+\delta Y} - dX\right] + \left[\frac{wXY}{1+\delta Y} - \left(d+m\right)Y\right]$$

$$= \left(1 - \frac{X^0}{X}\right)\left[dX^0 - dX - \frac{wXY}{1+\delta Y}\right] + \left[\frac{wXY}{1+\delta Y} - (d+m)Y\right]$$

$$= \frac{\left(X - X^0\right)}{X}\left[-d\left(X - X^0\right) - \frac{wXY}{1+\delta Y}\right] + \left[\frac{wXY}{1+\delta Y} - (d+m)Y\right]$$

$$= \frac{-d\left(X - X^0\right)^2}{X} - \frac{\left(X - X^0\right)}{X}.\frac{wXY}{1+\delta Y} + \frac{wXY}{1+\delta Y} - (d+m)Y$$

$$= \frac{-d\left(X - X^0\right)^2}{X} + \frac{wX^0Y}{1+\delta Y} - (d+m)Y$$

$$= \frac{-d\left(X - X^0\right)^2}{X} + (d+m)Y\left[\frac{wX^0}{(1+\delta Y)(d+m)} - 1\right]$$

$$\leq \frac{-d\left(X - X^0\right)^2}{X} + (d+m)Y$$

$$= \frac{-d\left(X - X^0\right)^2}{X} + (d+m)Y\left(R_0 - 1\right)$$

When $R_0 < 1,$ we can get $K_1^{\,1} \leq 0$ and $K_1^{\,1} = 0$ has no other closed trajectory in addition to E_0 is globally asymptotically stable iff $R_0 < 1.$

Theorem 5.2. The endemic equilibrium E_* is globally asymptotically stable if $R_0 > 1.$

Proof. Consider the Lyapunov function

$$K_2 = X^*\left(\frac{X}{X^*} - 1 - In\frac{X}{X^*}\right) + Y^*\left(\frac{Y}{Y^*} - 1 - In\frac{Y}{Y^*}\right)$$

Then

$$K_2^{\,1} = X^*\left(\frac{X^1}{X^*} - \frac{X^*}{X}.\frac{X^1}{X^*}\right) + Y^*\left(\frac{Y^1}{Y^*} - \frac{Y^*}{Y}.\frac{Y^1}{Y^*}\right)$$

$$K_2^{\,1} = \left(1 - \frac{X^*}{X}\right)X^1 + \left(1 - \frac{Y^*}{Y}\right)Y^1$$

$$= c\left(2 - \frac{X^*}{X} - \frac{X}{X^*}\right)$$

By the relationship of arithmetic mean and geometric mean.

We know that

$$\left(2-\frac{X^*}{X}-\frac{X}{X^*}\right)\leq 0$$

$K_1^{\,1}\leq 0$ iff $(X,Y)=(X^*,Y^*)$, $K_2^{\,1}=0$. Thus by LaSalle invariance principal $E_*(X^*,Y^*,S^*,I^*,R^*_{ES})$ is globally asymptotically stable.

6. Numerical Simulation

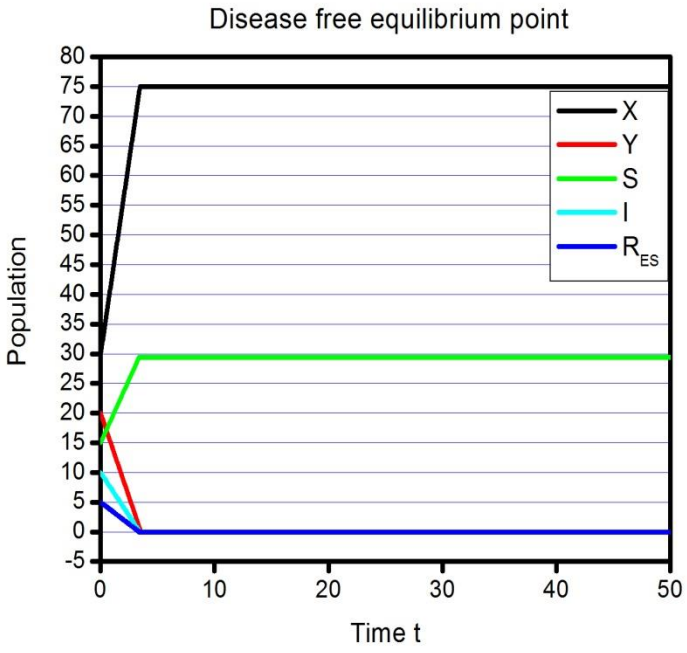

Figure 1.

Suppose the parameters are $C=3, \beta=0.02,\ d=0.04,\ w=0.012,\ m=0.96, b=1,\ \alpha=0.068,$ $\varepsilon=0.62, \gamma=0.39,\ \delta=0.05, \eta=0.15,\ \sigma=0.0411,$ Let the initial value of the system as X,Y,S,I,R_{ES} are 30,20,15,10,5 respectively. Then we obtain $R_0=0.9<1,$ $E_0\left(X^0,Y^0,S^0,I^0R^0_{ES}\right)=(75,0,29.41,0,0)$ Therefore by theorem 5.1, E_0 is globally asymptotically stable (see in figure 1)

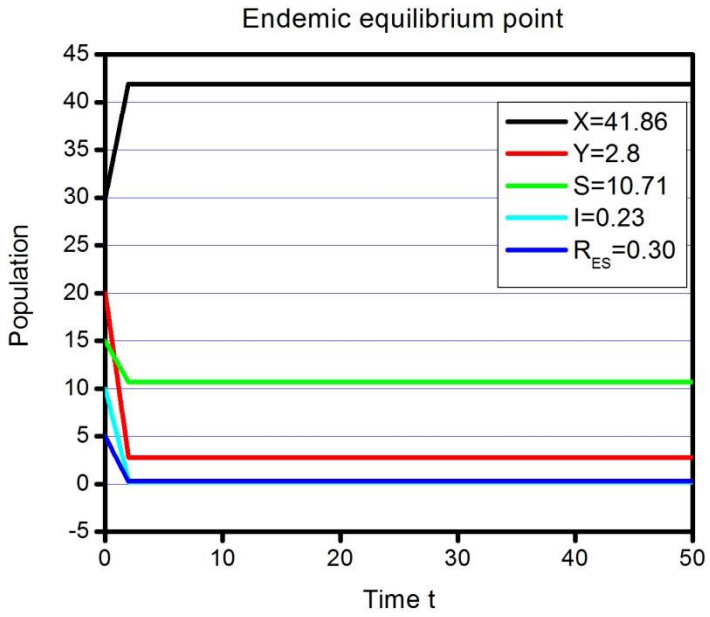

Figure 2.

Again we take the parameter $C=2, \beta=0.01, d=0.03, w=0.02, m=0.97, b=1, \alpha=0.069, \varepsilon=0.63, \gamma=0.301, \delta=0.05, \eta=0.15, \sigma=0.0411$ and X, Y, S, I, R_{ES} are 30,20,15,10,5 respectively. Then we obtain $R_0=1.33>1$, $E_*\left(X^*, Y^*, S^*, I^* R^*{}_{ES}\right)=(41.86, 2.8, 10.72, 0.23, 0.31)$ Therefore, by theorem 5.2, E_* is globally asymptotically stable (see in figure 2)

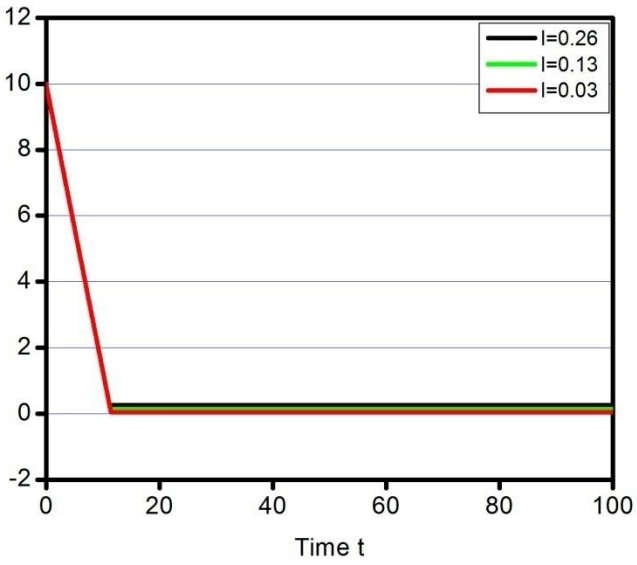

Figure 3. When η resistance rates to treatment increases then the steady state value I of the infective are decrease

If we change the value of η and keeping another parameter are fixed we can see that I^* decreases as η increases. Choose the value of $\eta = 0.01, \eta = 2, \eta = 7$ we get $I = 0.26, I = 0.13, I = 0.03$ respectively.

7. Conclusion

In this study, we formulate avian influenza epidemic model with saturated contact rate introduced by Shuqinche et al [1]. We have shown that if the basic reproduction number $R_0 < 1$ then E_0 globally asymptotically stable is disease out see Figure 2. If $R_0 > 1$ then E_+ exist i.e. disease persist. Numerical simulation indicates that when the disease is endemic, the steady state value I decrease as resistance rate to treatment η increases See Figure 3.

References

[1] C. Shuqinche, X. Yakui, Ma. Likang, The stability of highly pathogenic avian influenza epidemic model with saturated contact rate, Applied Mathematics, 5 (2014) 3365-3371.

[2] H. M. Dobrovolny, CAA. Beauchemin, Modelling the emergence of influenza drug resistance the roles of surface proteins, the immune response and antiviral mechanisms. PlosONE, 12 (7) (2017).

[3] P. Lancaster, Theory of Matrices, Academic press, New York, NY, USA (1969).

[4] S. Sharma, V. H. Badshah., V. Gupta, Global dynamics of highly pathogenic avian influenza epidemic model with vertical transmission function, International journal of advance research in Science and Engineering, 6 (9) (2017).

[5] S. Sharma, V. H. Badshah, V. Gupta, The highly avian influenza epidemic model with vertical transmission function in poultry, IOSR journal of Mathematics, 12 (3) (2016) 40-48,