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An Avian-Human Influenza Epidemic Model with Vaccination

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Abstract: A deterministic mathematical model to explore the impact of vaccination on the transmission dynamics of avian influenza both in birds and humans is studied. Vaccinations are important prevention and control measures for the spread of avian influenza. A reproductive number R for the model is defined and it is found that the DFE (Disease Free Equilibrium) is stable provided R<1 and it is unstable if R≥1 Also, if R>1 endemic equilibrium point exists and it is locally asymptotically stable. By stability analysis of ordinary differential equation, the criteria for global stability of DFE and endemic equilibrium are also obtained. By computer simulation it is found that if the growth rate at which vaccine based immunity wane increases, the infective human population decreases. Also, sensitivity analysis of the endemic equilibrium point is carried out.

Key words: Avian influenza, bird population, human population, mumerical simulation, stability analysis, sensitivity analysis

INTRODUCTION

Millions of people are affected each year by seasonal out breaks of influenza (also known as flu) which kills about 500000 individuals every year (WHO, 2007). Human's influenza viruses appear as 3 distinct serotypes: A, B and C. Among these types, the virus A is epidemiologically the most important for humans since, it can recombine its genes with those of strains circulating in animal populations (birds, swine and horses). The influenza A viruses have been responsible for the vast majority of epidemics and all recorded pandemics (Ferguson *et al*., 2003) which usually results from uncontrolled replication and spread of a single virus strain (Alexander *et al*., 2004, 2008). Influenza virus which infects usually only non human's animals some time infects humans. The spread of avian influenza in Asia of late years is one of the examples. In Hong Kong (1997) the news that a human was infected with avian influenza from birds was reported. After that, infection to human of avian influenza occurred successively. It is known that already 133 human's have been infected in Asia since late 2003 and killed 68.

It was formerly believed that the avian influenza virus cannot infect humans but recent reports showed that the avian influenza has now caused 385 human infections (as of June 19, 2008) with an approximate 50% mortality rate. In human's, avian influenza virus causes the similar symptoms as the other types of influenza. These include fever, cough, sore throat, muscle aches, conjunctivitis and in severe cases, severe breathing problems and pneumonia that may be fatal. The severity of the infection will depend to a large part on the state of the infected human's immune system and if the victims have been exposed to the same kind of virus before and they have partial immunity. Since, human-cells have receptor for human virus and avian-cells have receptor for avian virus, it was formerly believed that avian influenza virus cannot infect humans. Now, it is true that avian influenza virus can infect humans. These cases warn that a pandemic of avian influenza may occur in the human world. Moreover, the (highly pathogenic) avian influenza has a high death rate which is about 100% for birds and >70% for humans. This rate is extremely high since, the death rate of influenza virus in 1918 was several percent. Therefore, a pandemic of avian influenza may cause the greater influence to the human world than the pandemic of influenza occurred in 1918. Fortunately, avian influenza cannot be transmitted among humans yet. But if avian influenza virus has the affinity for human cells, it denotes the possibility that avian influenza can be transmitted among humans. It is possible that avian influenza virus may become to have the affinity for human cells.

When avian influenza mutates to be able to be transmitted among humans, it is not clear whether mutant avian influenza will have still high death rate or not. However, it is predicted among experts that mutant avian influenza which has the ability to be transmitted among

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human will occur. Several recent studies on influenza modeling have focused on the influence of prevention and control measures including vaccination, antiviral use (Ferguson *et al*., 2003; Alexander *et al*., 2004, 2008). Annually, the virus affects 25-50 million people with an estimated 20-40 thousand influenza-related deaths in the United States (Regan and Fowler, 2002). Because of the illness and high number of deaths associated with influenza, particularly among the elderly (Cox and Subbarao, 1999; Deguchi and Tagasugi, 2000) much attention has been focused on preventive strategies (Earn *et al*., 2002; Hak *et al*., 2002; Levin *et al*., 2004). Although, vaccination has been an effective strategy against influenza infection (Blumberg *et al*., 1996; Monto *et al*., 2001; Wood, 2001), current preventive vaccines consisting of inactivated virions do not protect all vaccine recipients equally. The vaccine based protection is dependent on the immune status of the recipient (Hethcote, 2000; Scherer and McLean, 2002) for general references). Vaccination is an important control measure to reduce spreading of such diseases. Various modeling studies have been made to study the role of vaccination on the spread of infectious diseases (Farrington, 2003; Naresh *et al*., 2008; Gumel and Moghadas, 2003).

MATERIALS AND METHODS

The mathematical model: The model consists of 6 ordinary differential equation which specify the rate of change of four categories of individuals in the human population and 2 categories of the bird population over time. The human population consists of a class susceptible individual (S_1) a class of individuals under Vaccinated (V_1) a class Infected Individuals (I_1) and a class of individuals who recover with temporary immunity (R_1) while the bird population consists of a class of susceptible population (S_0) and a class of infected population. Suppose the human population N_1 where:

$$N_1 = S_1+V_1+I_1+R_1$$

and the bird population N_0 where:

$$N_0 = S_0 + I_0$$

have constant mortality rates μ and μ_0, respectively. A proportion ε of the population is under chemotherapy (i.e., given influenza prevention drugs) while (1-ε) are not. We let β_1-β_3 be the effective contacts between susceptible individuals and infected birds population, individuals under vaccinated and infected bird population and susceptible bird population and infected bird population, respectively.

The effective contact rate between human and bird populations may be defined as the average number of contacts per given time that will lead to the infection of one population if the other population is infectious. θ is the rate at which vaccine based immunity wanes; γ is the recovery rate from infection and σ is the rate of loss of immunity acquired by infection. The dynamics of the disease is modeled by the following system of differential equations:

$$\begin{aligned}
\dot{S}_1(t) &= \mu(1-\varepsilon)N_1 - \mu S_1(t) - \beta_1 S_1(t)\frac{I_0(t)}{N_0} + \theta V_1(t) + \sigma R_1(t)\\
\dot{V}_1(t) &= \mu\varepsilon N_1 - \beta_2 V_1(t)\frac{I_0(t)}{N_0} - (\mu+\theta)V_1(t)\\
\dot{I}_1(t) &= \beta_1 S_1(t)\frac{I_0(t)}{N_0} + \beta_2 V_1(t)\frac{I_0(t)}{N_0} - (\gamma+\mu)I_1(t)\\
\dot{R}_1(t) &= \gamma I_1(t) - (\mu+\sigma)R_1(t)\\
\dot{S}_0(t) &= \mu_0 N_0 - \mu_0 S_0(t) - \beta_3 S_0(t)\frac{I_0(t)}{N_0}\\
\dot{I}_0(t) &= \beta_3 S_0(t)\frac{I_0(t)}{N_0} - \mu_0 I_0(t)
\end{aligned} \tag{1}$$

All the parameters in the model are positive. Introducing the following fractions:

$$s_1 = \frac{S_1(t)}{N_1}, v_1 = \frac{V_1(t)}{N_1}, i_1 = \frac{I_1(t)}{N_1}, r_1 = \frac{R_1(t)}{N_1}, s_0 = \frac{S_0(t)}{N_0} \text{ and } i_1 = \frac{I_0(t)}{N_0}$$

Also using the relations $r_1 = 1\text{-}v_1\text{-}i_1\text{-}s_1$ and $s_0 = 1\text{-}i_0$ and system Eq. 1 reduces to:

$$\begin{aligned}
\dot{s}_1 &= \pi - (\mu+\sigma)s_1 - \beta_1 s_1 i_0 + (\theta-\sigma)v_1 - \sigma i_1\\
\dot{v}_1 &= \mu\varepsilon - \beta_2 v_1 i_0 - (\mu+\theta)v_1\\
\dot{i}_1 &= \beta_1 s_1 i_0 + \beta_2 v_1 i_0 - (\gamma+\mu)i_1\\
\dot{i}_0 &= \beta_3 i_0(1-i_0) - \mu_0 i_1
\end{aligned} \tag{2}$$

where, $\pi = \mu(1\text{-}\varepsilon) + \sigma$ in the region, $\Omega = \{(s_1, v_1, i_1, i_0)/0 \le s_1+v_1+i_1 \le 1, 0 \le i_0 \le 1\}$. The vector field of system on the boundary of Ω does not point to the exterior of Ω, the solution of the system remains in Ω for all $t>0$ and thus, the problem is well posed and biologically meaningful.

RESULTS AND DISCUSSION

The system has 2 non negative equilibria:

$$E_1(\bar{s}_1, \bar{v}_1, 0, 0) \text{ and } E_2(\bar{\bar{s}}_1, \bar{\bar{v}}_1, \bar{\bar{i}}_1, \bar{\bar{i}}_0)$$

Existence of disease free equilibria $E_1(\bar{s}_1,\bar{v}_1,0,0)$: Here $\bar{s}_1$ and $\bar{v}_1$ are the solution of the following equations:

$$\pi-(\mu+\sigma)\bar{s}_1+(\theta-\sigma)\bar{v}_1=0 \quad (3)$$

$$\mu\varepsilon-(\mu+\sigma)\bar{v}_1=0 \quad (4)$$

clearly from Eq. 4, we get:

$$\bar{v}_1=\frac{\mu\varepsilon}{(\mu+\theta)}>0 \text{ or } \bar{v}_1=\phi>0$$

Where:

$$\phi=\frac{\mu\varepsilon}{(\mu+\theta)}$$

also from Eq. 3, we get:

$$\bar{s}_1=\left[\frac{\pi+(\theta-\sigma)\phi}{(\mu+\sigma)}\right]>0$$

Since $\pi=\mu(1-\varepsilon)+\sigma$, so it can write $\bar{s}_1=1-\phi>0$, so the equilibrium point $E_1(\bar{s}_1,\bar{v}_1,0,0)$ exists.

Existence of endemic equilibria $E_2(\bar{\bar{s}}_1,\bar{\bar{v}}_1,\bar{\bar{i}}_1,\bar{\bar{i}}_0)$: The non trivial endemic equilibrium point $E_2(\bar{\bar{s}}_1,\bar{\bar{v}}_1,\bar{\bar{i}}_1,\bar{\bar{i}}_0)$ is the positive solution of the following algebraic equations:

$$\pi-(\mu+\sigma)\bar{\bar{s}}_1-\beta_1\bar{\bar{s}}_1\bar{\bar{i}}_0+(\theta-\sigma)\bar{\bar{v}}_1-\sigma\bar{\bar{i}}_1=0 \quad (5)$$

$$\mu\varepsilon-\beta_2\bar{\bar{v}}_1\bar{\bar{i}}_0-(\mu+\theta)\bar{\bar{v}}_1=0 \quad (6)$$

$$\beta_1\bar{\bar{s}}_1\bar{\bar{i}}_0+\beta_2\bar{\bar{v}}_1\bar{\bar{i}}_0-(\gamma+\mu)\bar{\bar{i}}_1=0 \quad (7)$$

$$\beta_3\bar{\bar{i}}_0.(1-\bar{\bar{i}}_0)-\mu_2\bar{\bar{i}}_0=0 \quad (8)$$

now from the Eq. 8, we have:

$$\beta_3\bar{\bar{i}}_0.(1-\bar{\bar{i}}_0)-\mu_0\bar{\bar{i}}_0=0$$
$$\Rightarrow\bar{\bar{i}}_0=0 \text{ or } \beta_3\bar{\bar{i}}_0=\beta_3-\mu_0$$
$$\Rightarrow\bar{\bar{i}}_0=0 \text{ or } \bar{\bar{i}}_0=\frac{\mu_0}{\beta_3}(R-1)$$

Where:

$$R=\frac{\beta_3}{\mu_0}$$

also from the Eq. 6, we get:

$$\mu\varepsilon-\beta_2\bar{\bar{v}}_1\bar{\bar{i}}_0-(\mu+\theta)\bar{\bar{v}}_1=0$$
$$\Rightarrow\bar{\bar{v}}_1=\frac{\mu\varepsilon}{\left[\beta_2\frac{\mu_0}{\beta_3}(R-1)+(\mu+\theta)\right]}=b^* \text{ (say)}$$

now from 5 and 7, we get:

$$\bar{\bar{s}}_1=\frac{\pi+(\theta-\sigma)\bar{\bar{v}}_1-\sigma\bar{\bar{i}}_1}{(\mu+\sigma+\beta_1\bar{\bar{i}}_0)} \quad \text{and} \quad \bar{\bar{s}}_1=\frac{(\gamma+\mu)\bar{\bar{i}}_1-\beta_2\bar{\bar{v}}_1\bar{\bar{i}}_0}{\beta_1\bar{\bar{i}}_0}$$

So, it can write:

$$\frac{\pi+(\theta-\sigma)\bar{\bar{v}}_1-\sigma\bar{\bar{i}}_0}{(\mu+\sigma+\beta_1\bar{\bar{i}}_0}=\frac{(\gamma+\mu)\bar{\bar{i}}_1-\beta_2\bar{\bar{v}}_1\bar{\bar{i}}_0}{\beta_1\bar{\bar{i}}_0}$$
$$\Rightarrow\bar{\bar{i}}_1=\frac{\beta_1\bar{\bar{i}}_0\{\pi+(\theta-\sigma)\bar{\bar{v}}_1+\beta_2\bar{\bar{v}}_1\bar{\bar{i}}_0(\mu+\sigma+\beta_1\bar{\bar{i}}_0\}}{\{(\mu+\sigma+\beta_1\bar{\bar{i}}_0)(\gamma+\mu)+\sigma\}}$$
$$\Rightarrow\bar{\bar{i}}_1=\frac{\beta_1\frac{\mu_0}{\beta_3}(R-1)\left\{\pi+b^*\left[(\theta-\sigma)+\beta_2\frac{\mu_0}{\beta_3}(R-1)\left(\mu+\sigma+\beta_1\frac{\mu_0}{\beta_3}(R-1)\right)\right]\right\}}{\left\{\left(\mu+\sigma+\beta_1\frac{\mu_0}{\beta_3}(R-1)\right)(\gamma+\mu)+\sigma\right\}}=c^* \text{ (say)}$$

Since:

$$\bar{\bar{s}}_1=\frac{\pi+(\theta-\sigma)\bar{\bar{v}}_1-\sigma\bar{\bar{i}}_1}{(\mu+\sigma+\beta_1\bar{\bar{i}}_0)}$$

Now put value of $\bar{\bar{v}}_1,\bar{\bar{i}}_1$ and $\bar{\bar{i}}_0$ we get:

$$\Rightarrow\bar{\bar{s}}_1=\frac{\pi+(\theta-\sigma)b^*-\sigma c^*}{\left\{\mu+\sigma+\beta_1\frac{\mu_0}{\beta_3}(R-1)\right\}}$$

Hence, non trivial endemic equilibrium point E_2 exists if R>1.

Stability analysis: Now, we analyze the stability of equilibria E_1 and E_2. The local stability results of these equilibria are stated in the following theorem.

Theorem 1: The equilibrium E_1 is stable provided R<1 and it is unstable if R≥1 and the equilibrium E_2 is locally asymptotically stable if R>1.

Proof: The varational matrix M_1 at $E_1(\bar{s}_1, \bar{v}_1, 0, 0)$ at corresponding to the system is given by:

$$M_1 = \begin{pmatrix} -(\mu+\sigma) & (\theta-\sigma) & -\sigma & -\beta_1\bar{s}_1 \\ 0 & -(\mu+\theta) & 0 & -\beta_2\bar{v}_1 \\ 0 & 0 & -(\gamma+\mu) & \beta_1\bar{s}_1+\beta_2\bar{v}_1 \\ 0 & 0 & 0 & (\beta_3-\mu_0) \end{pmatrix}$$

Then the characteristic polynomial of M_1 is given by:

$$P(\lambda)=(\beta_3-\mu_0-\lambda)(-\gamma-\mu-\lambda)$$
$$(-\mu-\theta-\lambda)(-\mu-\sigma-\lambda)=\mu_0(R-1-\lambda)$$
$$(-\gamma-\mu-\lambda)(-\mu-\theta-\lambda)(-\mu-\sigma-\lambda)$$

Thus the eigenvalue of matrix M_1 are:

$$\lambda_1=R-1,\ \lambda_2=-(\gamma+\mu),\ \lambda_3=-(\mu+\theta),\ \lambda_4=-(\mu+\sigma)$$

So, E_1 is stable if and only if the eigenvalues of the varational matrix have negative real part i.e. if and only if $R<1$ then E_1 is stable if and only if $R<1$ and $R\geq 1$ then E_1 is unstable because one eigenvalue of varational matrix must be positive or zero. Now the varational matrix M_2 at $E_2(\bar{\bar{s}}_1, \bar{\bar{v}}_1, \bar{\bar{i}}_1, \bar{\bar{i}}_0)$ corresponding to the system of Eq. 2 is given by:

$$M_2 = \begin{pmatrix} -(\mu+\sigma)-\beta_1\bar{\bar{i}}_0 & (\theta-\sigma) & -\sigma & -\beta_1\bar{\bar{s}}_1 \\ 0 & -\beta_2\bar{\bar{i}}_0-(\mu+\theta) & 0 & -\beta_2\bar{\bar{v}}_1 \\ \beta_1\bar{\bar{i}}_0 & \beta_2\bar{\bar{i}}_0 & -(\gamma+\mu) & \beta_1\bar{\bar{s}}_1+\beta_2\bar{\bar{v}}_1 \\ 0 & 0 & 0 & -\mu_0(R-1) \end{pmatrix}$$

The characteristic polynomial of M_2 is given by:

$$P(\lambda)=(-\mu_0(R-1)-\lambda)\begin{pmatrix} -G-\lambda & (\theta-\sigma) & -\sigma \\ 0 & -H-\lambda & 0 \\ \beta_1\bar{\bar{i}}_0 & \beta_2\bar{\bar{i}}_0 & -(\gamma+\mu)-\lambda \end{pmatrix}$$

Where:

$$G=(\mu+\sigma)+\beta_1\bar{\bar{i}}_0,\ H=(\mu+\theta)+\beta_2\bar{\bar{i}}_0$$
$$P(\lambda)=(\mu_0(R-1)+\lambda)\left\{(G+\lambda)(H+\lambda)(\gamma+\mu+\lambda)-\sigma\beta_1\bar{\bar{i}}_0(H+\lambda)\right\}$$
$$=(\mu_0(R-1)+\lambda)(\lambda^3+A\lambda^2+B\lambda+C)$$

Therefore, the eigenvalues of the matrix M_2 are $-\mu_0(R-1)$ and the roots of the polynomial:

$$q(\lambda)=\lambda^3+A\lambda^2+B\lambda+C$$

Where:

$$A=\left((\mu+\sigma+\beta_1\bar{\bar{i}}_0)+(\beta_2\bar{\bar{i}}_0+\mu+\theta)+(\gamma+\mu)\right)$$
$$B=\begin{pmatrix}(\gamma+\mu)(\mu+\sigma+\beta_1\bar{\bar{i}}_0+\mu+\theta+\beta_2\bar{\bar{i}}_0)+(\mu+\sigma+\beta_1\bar{\bar{i}}_0)\\(\mu+\theta+\beta_1\bar{\bar{i}}_0)-\sigma\beta_1\bar{\bar{i}}_0\end{pmatrix}$$
$$C=(\mu+\sigma+\beta_1\bar{\bar{i}}_0)(\beta_2\bar{\bar{i}}_0+\mu+\theta)(\gamma+\mu)-\sigma\beta_1\bar{\bar{i}}_0)(\beta_2\bar{\bar{i}}_0+\mu+\theta)$$

Here it is noted that A are always positive and B>0, C>0 if:

$$\begin{pmatrix}(\gamma+\mu)\ (\mu+\sigma+\beta_1\bar{\bar{i}}_0+\mu+\theta+\beta_2\bar{\bar{i}}_0)+\\(\mu+\sigma+\beta_1\bar{\bar{i}}_0)\ (\mu+\theta+\beta_2\bar{\bar{i}}_0)\end{pmatrix}>\sigma\beta_1\bar{\bar{i}}_0$$

And:

$$(\mu+\sigma+\beta_1\bar{\bar{i}}_0)(\gamma+\mu)>\sigma\beta_1\bar{\bar{i}}_0, \text{respectively}$$

So for R>1 we have AB>C, A>0, B>0) and C>0 then the following Routh-Hurwitz conditions for the polynomial P, the state E_2 is locally asymptotically stable for R>1.

Global stability

Theorem: For $R\leq 1$ the state $E_1(\bar{s}_1, \bar{v}_1, 0, 0)$ is globally asymptotically stable. Also, the state $E_2(\bar{\bar{s}}_1, \bar{\bar{v}}_1, \bar{\bar{i}}_1, \bar{\bar{i}}_0)$ is globally asymptotically stable with respect to the all solution initiating in the positive orthant if the following inequalities are satisfied:

$$(\theta-\sigma)^2<\frac{4}{9}(\mu+\sigma+\beta_1\bar{\bar{i}}_0)(\mu+\theta)$$
$$(\beta_1\bar{\bar{i}}_0-\sigma)^2<\frac{4}{9}(\mu+\sigma+\beta_1\bar{\bar{i}}_0)(\gamma+\mu)$$
$$(\beta_1 s_1)^2<\frac{4}{9}(\mu+\sigma+\beta_1\bar{\bar{i}}_0)\beta_3$$
$$(\beta_1\bar{\bar{i}}_0)^2<\frac{4}{9}(\mu+\theta)(\gamma+\mu)$$
$$(\beta_2 v_1)^2<\frac{4}{9}(\mu+\theta)\beta_3$$
$$(\beta_1 s_1+\beta_2 v_1)^2<\frac{4}{9}(\gamma+\mu)\beta_3$$

Proof: Now, it is considered the following Liapunov function $K = i_0$ thus: $K = i$.

$$\Rightarrow\dot{K}=\beta_3 i_0(1-i_0)-\mu_0 i_0=-\mu_0 i_0\left(1-\frac{\beta_3}{\mu_0}(1-i_0)\right)=-\mu_0 i_0[1-R(1-i_0)]$$
$$\Rightarrow\dot{K}=-\mu_0 i_0[Ri_0+(1-R)]$$

So, in Ω and for R≤1 we have K≤0:

$$\dot{K} = 0 \Rightarrow -\mu_0 i_0 [Ri_0 + (1-R)] = 0$$

$$\Rightarrow \text{If } R<1 \text{ then } i_0 = 0 \text{ and if } R = 1 \text{ then } i_0 = 0$$

Therefore, from the LaSalle invariance principle (Ma *et al*., 2004) it follows that all trajectories satisfying in Ω approach E_1 for R≤1.

It remained to show that global stability of E_2 so, it is considered the following positive definite function about $E_2 = (\bar{s}_1, \bar{v}_1, \bar{i}_1, \bar{i}_0)$:

$$U(s_1, v_1, i_1, i_0) = \frac{1}{2}(s_1 - \bar{s}_1)^2 + \frac{1}{2}(v_1 - \bar{v}_1)^2 + \frac{1}{2}(i_1 - \bar{i}_1)^2 + \left(i_0 - \bar{i}_0 - \bar{i}_0 \log \frac{i_0}{\bar{i}_0}\right)$$

Now differentiating above equation with respect to t, we get:

$$\frac{dU}{dt} = (s_1 - \bar{s}_1)\frac{d\bar{s}_1}{dt} + (v_1 - \bar{v}_1)\frac{d\bar{v}_1}{dt} + (i_1 - \bar{i}_1)\frac{d\bar{i}_1}{dt} + \frac{(i_0 - \bar{i}_0)}{i_0}\frac{d\bar{i}_0}{dt}$$

Also, derivative of U i.e., U can be written as the sum of the quadratics:

$$\frac{dU}{dt} = -\frac{1}{3}\alpha_{11}(s_1 - \bar{s}_1)^2 + \alpha_{12}(s_1 - \bar{s}_1)(v_1 - \bar{v}_1) - \frac{1}{3}(v - \bar{v}_1)^2 -$$
$$\frac{1}{3}\alpha_{11}(s_1 - \bar{s}_1)^2 + \alpha_{13}(s_1 - \bar{s}_1)(i - \bar{i}_1) - \frac{1}{3}(i - \bar{i}_1)^2 -$$
$$\frac{1}{3}\alpha_{11}(s_1 - \bar{s}_1)^2 + \alpha_{14}(s_1 - \bar{s}_1)(i_0 - \bar{i}_0) - \frac{1}{3}(i_0 - \bar{i}_0)^2 -$$
$$\frac{1}{3}\alpha_{22}(v_1 - \bar{v}_1)^2 + \alpha_{23}(v_1 - \bar{v}_1)(i_1 - \bar{i}_1) - \frac{1}{3}(i_1 - \bar{i}_1)^2 -$$
$$\frac{1}{3}\alpha_{22}(v_1 - \bar{v}_1)^2 + \alpha_{24}(v_1 - \bar{v}_1)(i_0 - \bar{i}_0) - \frac{1}{3}(i_0 - \bar{i}_0)^2 -$$
$$\frac{1}{3}\alpha_{33}(i_1 - \bar{i}_1)^2 + \alpha_{34}(i_1 - \bar{i}_1)(i_0 - \bar{i}_0) - \frac{1}{3}(i_0 - \bar{i}_0)^2$$

Where:

$$\alpha_{11} = (\mu + \sigma + \beta_1 \bar{i}_0), \alpha_{22} = (\mu + \theta), \alpha_{33} = (\gamma + \mu), \alpha_{44} = \beta_3,$$
$$\alpha_{12} = (\theta - \sigma), \alpha_{23} = \beta_2 \bar{i}_0, \alpha_{24} = \beta_2 v_1, \alpha_{34} = (\beta_1 s_1 + \beta_2 v_1),$$
$$\alpha_{13} = (\beta_1 \bar{i}_0 - \sigma), \alpha_{14} = \beta_1 s_1$$

Then the sufficient condition for dU/dt to be negative definite are:

$$(\alpha_{12})^2 < \frac{4}{9}\alpha_{11}\alpha_{22}, (\alpha_{13})^2 < \frac{4}{9}\alpha_{11}\alpha_{33}, (\alpha_{14})^2 < \frac{4}{9}\alpha_{11}\alpha_{44},$$
$$(\alpha_{23})^2 < \frac{4}{9}\alpha_{22}\alpha_{33}, (\alpha_{24})^2 < \frac{4}{9}\alpha_{22}\alpha_{44}, (\alpha_{34})^2 < \frac{4}{9}\alpha_{33}\alpha_{44}$$

Numerical simulation: In this study, there is presented numerically simulation to explain the applicability of the results discussed above. Researchers choose the following parameter in model (Eq. 2) are:

$$\mu = 0.2, \varepsilon = 0.2, \sigma = 0.04, \theta = 0.06, \beta_1 = 0.026,$$
$$\beta_2 = 0.035, \beta_3 = 0.045, \gamma = 0.09, \mu_0 = 0.02$$

With these values of parameters it can be checked that the endemic equilibrium E_2 exists and is given by:

$$\bar{s}_1 = 0.7896, \bar{v}_1 = 0.1431, \bar{i}_1 = 0.0489, \bar{i}_0 = 0.5556$$

Again with the set of parameters given, it can be verified that the conditions in theorem 1 and 2 is satisfied. This shows that E_2 is locally and globally asymptotically stable, respectively. The results of numerically simulation are displayed graphically in Fig. 1 and 2 the effect of various parameters i.e., γ_0 and β_1 on the infective human population have been shown. It is noted that these figures that as these parameters value increase, the infective human population decreases and increases, respectively. In Fig. 3 and 4 shows the effect of various parameters i.e., θ and β_3 on the infective human population. It is observed that these figures that as these parameters value increase, the infective human population decreases and increases, respectively.

For showing global stability simulation is performed for different initial positions in Fig. 5. From this figure it is clear that equilibrium state is globally asymptotically stable provided that we start away from the other equilibria.

Sensitivity analysis: Researchers now study sensitivity of the endemic equilibrium to changes in the value of the different parameters associated with the system. The results are shown in Table 1. The purpose of this analysis is to identify the parameters which are sensitive; estimation of these parameters in the field studies is to be done with sufficient care. Sensitivity of the endemic equilibrium point to changes in the parameter values is shown in Table 1. Regarding sensitivity of the endemic equilibrium level of susceptible population s_1 (t) the following features are observed:

- It is less sensitivity to changes in the value of parameters μ, β_1, θ, β_2, β_3, μ_0
- It is fairly sensitive to changes in σ, ε, γ

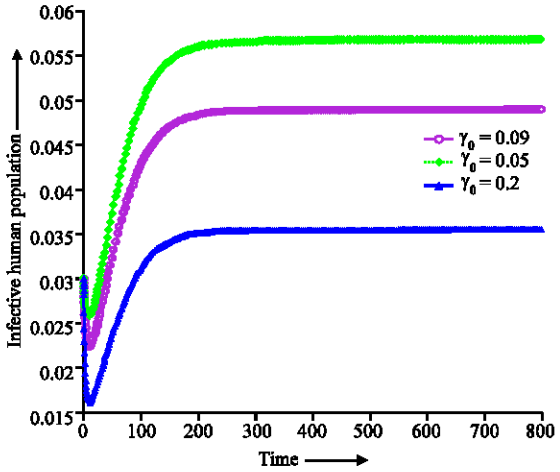

Fig. 1: Variation of infective human population for different growth rates of recovery

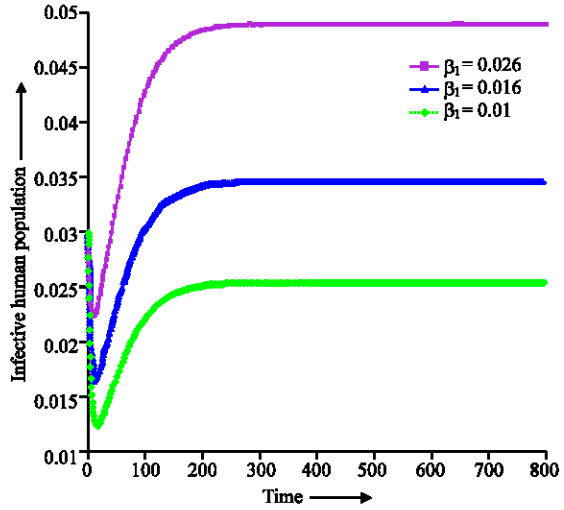

Fig. 2: Variation of infective human population for different effective contacts between susceptible individuals and infected birds population

The equilibrium level of vaccinated population v_1 (t) exhibits the following characteristics:

- It is less sensitivity to changes in the value of parameters β_2, β_3, μ_0
- It is fairly sensitivity to changes in μ, ε, θ
- It is insensitive to changes in the values of the parameter σ, β_1, γ

The equilibrium level of infective population i_1 (t) exhibits the following characteristics:

- It is less sensitivity to changes in the value of parameter ε, θ
- It is fairly sensitive to changes in μ, β_1, β_2, β_3, γ, σ, μ_0

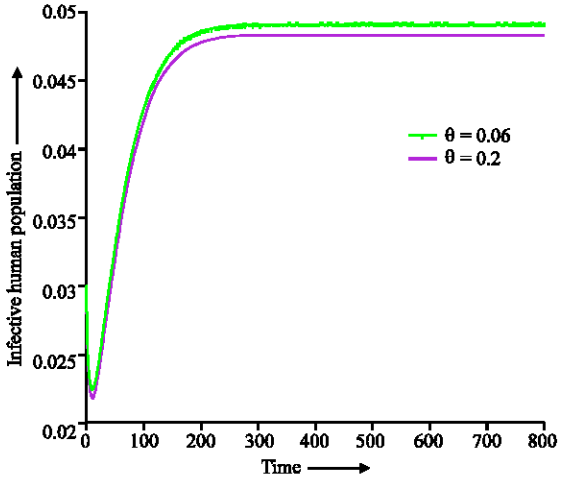

Fig. 3: Variation of infective human population for different rate at which vaccine based immunity wanes

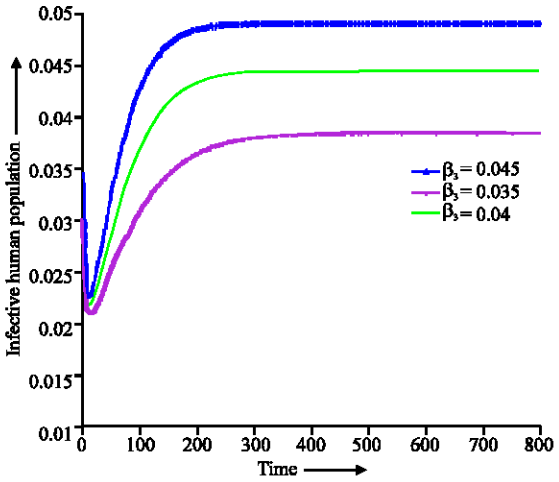

Fig. 4: Variation of infective human population for different effective contacts between susceptible bird population and infected bird population

The equilibrium level of infective bird population i_0 (t) exhibits the following characteristics:

- It is insensitivity to changes in the value of parameter μ, σ, β_1, θ, ε, β_2, γ
- It is fairly sensitive to changes in β_3, μ_0

Since, the spread of epidemic in the population is direct outcome of endemic infective population size, determination of the equilibrium level of the infective population size is the primary problem and more attention needs to be given to the estimation of those parameters to

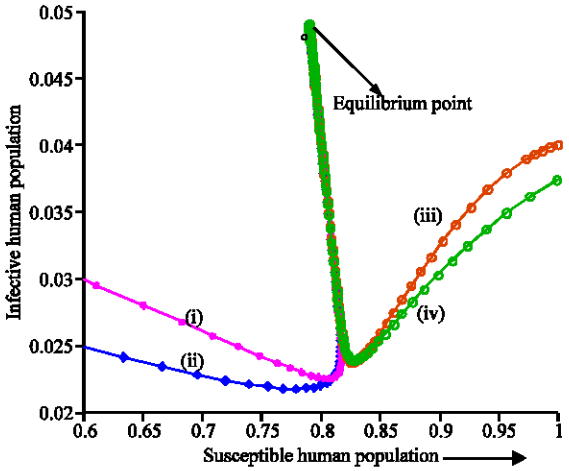

Fig. 5: Variation of infective human population with susceptible human population

Table 1: Percentage changes in the endemic equilibrium corresponding to different percentage changes in the parameters

	Change				
Parameters	(%)	in s_1 (%)	in v_1 (%)	in i_1 (%)	in i_0 (%)
$\mu = 0.2$	+50	0.6458	10.4822	-23.7219	0.0000
	+20	0.3292	5.0314	-11.0429	0.0000
	-20	-0.5192	-5.6387	14.1104	0.0000
	-50	-2.0770	-22.0825	43.5583	0.0000
$\sigma = 0.04$	+50	-8.9665	0.0000	-7.7092	0.0000
	+20	-3.7614	0.0000	-3.0674	0.0000
	-20	4.0020	0.0000	3.2719	0.0000
	-50	10.5623	0.0000	8.5889	0.0000
$\beta_1 = 0.026$	+50	-3.1028	0.0000	36.6053	0.0000
	+20	-1.2664	0.0000	14.9284	0.0000
	-20	1.2917	0.0000	-15.1329	0.0000
	-50	3.3054	0.0000	-38.8548	0.0000
$\theta = 0.06$	+50	1.7983	-1.3800	-0.4089	0.0000
	+20	0.7598	-4.1229	-0.2044	0.0000
	-20	-0.8358	4.5422	0.2044	0.0000
	-50	-2.2289	12.0894	0.6134	0.0000
$\varepsilon = 0.2$	+50	-9.2705	50.0349	2.4539	0.0000
	+20	-3.7107	20.0559	1.0224	0.0000
	-20	3.6980	-19.9860	-0.8179	0.0000
	-50	9.2578	-49.9651	-2.2494	0.0000
$\beta_2 = 0.035$	+50	-0.1266	-3.2145	8.5889	0.0000
	+20	-0.0506	-1.3277	3.6809	0.0000
	-20	0.0506	1.4675	-3.6809	0.0000
	-50	0.1393	3.7735	-9.6114	0.0000
$\beta_3 = 0.045$	+50	-1.7223	-1.7470	24.1309	26.2599
	+20	-0.8865	-0.9084	12.4744	13.3189
	-20	1.3551	1.4675	-18.8139	-20.0144
	-50	5.3951	5.6603	-75.2556	-76.5299
$\gamma = 0.09$	+50	0.1266	0.0000	-13.2924	0.0000
	+20	0.0506	0.0000	-5.7259	0.0000
	-20	-0.0630	0.0000	6.5439	0.0000
	-50	-0.1773	0.0000	18.2004	0.0000
$\mu_0 = 0.02$	+50	2.7482	2.8651	-38.2413	-40.0108
	+20	1.0764	1.1879	-15.1329	-16.0007
	-20	-1.0638	-1.0482	14.7239	15.9827
	-50	-2.6089	-2.6554	36.4000	39.9928

which infective class size is more sensitive. In this context, more care should be taken to estimate the parameters μ, β_1, β_2, β_3, γ, σ, μ_0.

CONCLUSION

Formerly, it was thought that human cannot be infected with avian influenza. But in Hong Kong in 1997, the news that a human was infected with avian influenza from a bird was reported. After this, infections to humans of avian influenza have been reported successively.

Fortunately, avian influenza cannot be transmitted directly from humans to humans yet. However, it is said among experts that mutant avian influenza which has the ability to be transmitted among humans will occur. In this study, researchers develop a mathematical model to explore the impact of vaccination on the transmission dynamics of influenza. Also, model deals with dynamics of human infection by avian influenza both in birds and in humans. There is proved the existence of an equilibrium point with no disease; define a reproductive number, R if $R<1$ then the DFE (Disease Free Equilibrium) is stable and it is unstable if $R\geq 1$. Also prove that an endemic equilibrium point exists for all $R>1$ and it is also locally asymptotically stable. By stability analysis of ordinary differential equation, the criteria for global stability of DFE and endemic equilibrium are also obtained.

It is concluded from the computer simulation if the growth rate at which vaccine based immunity wane increases, the infective human population decreases. Also, growth of recovery rate and effective contacts between susceptible individuals and infected birds population increases, the infective human population decreases. Sensitivity analysis of the endemic equilibrium to changes in the value of the different parameters associated with the system is done and it is found that parameters μ, β_1, β_2, β_3, γ, σ, μ_0 are the most sensitive parameters to the infective population.

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