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Mathematical modelling and analysis of viral disease outbreak with partial immunity and incubation period

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ABSTRACT

In this paper, a mathematical model is proposed with three classes of population namely, susceptible, incubated and infected. The incubation period is defined as the time from exposure to onset of viral disease, and when limited to infectious viral disease, corresponds to the time from infection with a microorganism to symptom development. Immunity(natural or caused by vaccination) plays an important role in recovery of a disease, due to strong immunity a portion of incubated class rejoins susceptible class without being infected. The stability behavior of the trivial, disease free and endemic steady states are studied, it is found that the instability of disease free state leads to the existence of the endemic state. The possibility of Hopf-bifurcation of the endemic equilibrium is studied, considering the transfer rate from susceptible to incubated population as bifurcation parameter. Finally, a threshold value of bifurcation parameter is determined numerically for a particular set of parameters.

Introduction

Mathematical methods are widely used for understanding mechanisms in the spread of infectious diseases. Modelling the disease infections has been gaining great interest in the study of epidemiology. The mathematical study of epidemics has come up with an astonishing number of models with explanations for the spread and cause of epidemic outbreaks [1-9,12].

While modelling an epidemic process we need to make the following assumptions: (1) the population affected, (2) the way the disease is spread and (3) the mechanism of recovery from the population. In population dynamics either we can consider the population is *closed*, so that immigration, emigration, birth and disease-unrelated death can be neglected, or *open*. Again, in epidemiology, the population can be classified into three broad classes: (a) *Susceptible* - population which can be infected. (b) *Incubated* or latent or exposed - population infected by the disease, but not infectious and (c) *Diseased* or infective or infectious - an individual may become infectious after disease outbreaks. The period before the symptoms appear is the *incubation period*. A portion of diseased population rejoins to susceptible population due to medication or hospitalization.

As the simple *SIS* model suggests, the population from the susceptible class joins or transfer to the infected class continuously. But in practice this process is not regular, in fact, it is in the case of any viral disease and many other disease. The susceptible individual stays for a definite period after leaving the susceptible class and joining the infected class, this intermediate period may be termed as incubation period.

The incubation period is defined as the time from exposure to onset of disease and when limited to infectious disease, corresponds to the time from infection with a microorganism to symptom development [9].

During the incubation period of acute infections disease, which is subsequently followed by a symptomatic period, it should be noted that infected host can be infections. The incubation period of infectious disease offers various insights into clinical and public health practices, as well as it is important for epidemiological and ecological studies [9]. The incubation period is useful not only for making rough guesses as to the causes and sources of infection of individual cases [1, 2, 7], but also for developing treatment strategies to extend the incubation period, for performing early projection of disease prognosis and when the incubation period is clearly associated with clinical severity due to dose response mechanism [2, 5, 6, 9].

Recently [4], studied the dynamics of susceptible, incubated, and diseased class, but they have not considered that a portion of the incubated population may rejoin to the susceptible class due to immunization(natural immunity and immunity caused by vaccination etc).

Keeping in view of the above, in this paper we will study the role of the incubation period in a disease model by assuming an intermediate class, namely the incubated population class between the susceptible and infected population classes. Further assume that a portion of the incubated population rejoin to the susceptible population due to immunization.

The Mathematical Model

Let $S(t)$ and $D(t)$ be the population densities at any time t of susceptible and diseased class, respectively. Suppose that there is no vertical transmission of the disease and susceptible population is logistically growing with intrinsic growth rate r and carrying capacity K. Let α be the disease contact rate and p be the rate of removal population from disease class and out of which γ fraction of infected population will rejoin i

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susceptible class. Then the dynamics of the "susceptible-infected" population is governed by following:

$$\frac{dS}{dt} = rS\left(1-\frac{S}{K}\right) - \alpha SD + \gamma D \quad (1)$$

$$\frac{dD}{dt} = \alpha SD - pD \quad (2)$$

In our present study, we have considered that susceptible population instead of joining infected class directly, will now go through an intermediate class termed as incubated class. The incubation period is defined as the time from exposure to onset of disease.

Let $I(t)$ be the population density of incubated class at any instant of time t. Further we have considered that due to strong immune system (natural immunity or immunity caused by vaccination etc.) a fraction of incubated population will again rejoin to the susceptible class. Let α be viral disease contact rate and due to immunization the β fraction of incubated population is recovered and it joins to the susceptible class again. Let γ is the fraction of the disease population joining to susceptible class after recovery from viral disease and θ is fraction of incubated class population that will go to the disease class. Again, let p and σ are total removable population from disease class and incubated class, which includes death due to viral disease and natural death of diseased population and incubated population respectively. Thus with this assumptions, our population dynamics, i.e., "susceptible-incubated-infected-susceptible (with partial immunity)" is governed by the following set of differential equations:

$$\frac{dS}{dt} = rS\left(1-\frac{S}{K}\right) - \alpha SD + \gamma D + \beta I \quad (3)$$

$$\frac{dI}{dt} = \alpha SD - \sigma I \quad (4)$$

$$\frac{dD}{dt} = \theta I - pD \quad (5)$$

where initial populations are $S(0) > 0$, $I(0) > 0$ and $D(0) > 0$ and total population at any instant t is $N(t) = S(t) + I(t) + D(t)$. Again due to natural death of incubated and diseased class, we can consider,

$$\sigma > \beta + \theta \quad \text{and} \quad p > \gamma. \quad (6)$$

Now, on removing the dimensions of the parameters of the above system (3)-(5) using following:

$$x = \frac{S}{K}; y = \frac{I}{K}; z = \frac{D}{K}; \tau = rt,$$

we get the following re-scaled system:

$$\frac{dx}{d\tau} = x(1-x) - axz + bz + cy \quad (7)$$

$$\frac{dy}{d\tau} = axz - dy \quad (8)$$

$$\frac{dz}{d\tau} = ey - hz \quad (9)$$

where

$$a = \frac{\alpha K}{r}; b = \frac{\gamma}{r}; c = \frac{\beta}{r}; d = \frac{\sigma}{r}; e = \frac{\theta}{r}; h = \frac{p}{r}$$

and $x(0) > 0$, $y(0) > 0$ and $z(0) > 0$. Then (6) reduces to $d > c + e$ and $h > b$.

In the next section, we will study the existence of all possible steady states of the system and the boundedness of the solutions.

Existence Of Equilibrium Points And Boundedness

There are three biologically feasible equilibria for the system (7)-(9), (i) $E_0 = (0,0,0)$ is the trivial steady state; (ii) $E_1 = (1,0,0)$ is the disease free steady state and (iii) $E^* = (x^*, y^*, z^*)$ is endemic equilibrium state, where

$$x^* = \frac{dh}{ae}; y^* = \frac{dh}{ae}\frac{(1-\frac{dh}{ae})}{(d-\frac{be}{h}-c)} \text{ and } z^* = \frac{d}{a}\frac{(1-\frac{dh}{ae})}{(d-\frac{be}{h}-c)}.$$

Further, it is clear form the above expression that $E^* \in R_+^3$, if $\frac{ae}{dh} > 1$.

The basic reproduction number (R0) of an infection is defined by Diekmann & Heesterbeek [14] as the "expected number of secondary cases per primary case in a completely susceptible population".

The basic reproduction number for the system (7)-(9) is given by $R_0 = \frac{ae}{dh}$. Thus endemic equilibrium E* exists if $R_0 > 1$.

Now, we will show that all the solutions of the system (7)-(9) are bounded in a region $B \subset R_+^3$. We consider the following function:

$$w(\tau) = x(\tau) + y(\tau) + z(\tau) \quad (10)$$

Then differentiating (7) with respect to τ and substituting the values from (7)-(9), we get

$$\frac{dw}{d\tau} = x(1-x) - (d-c-e)y - (h-b)z.$$

If we choose a positive real number $\eta = min\{d-c-e, h-b\}$, then

$$\frac{dw(\tau)}{d\tau} + \eta w(\tau) \le x(1+\eta) - x^2 = f(x).$$

Again $f(x)$ is maximum at $x = (1+\eta)/2$ and hence $f(x) \le (1+\eta)^2/4 = M$ (say). Hence

$$\dot{w}(\tau) + \eta w(\tau) \le M.$$

Now, using comparison theorem, as $\tau \to \infty$, then

$$sup\ w(\tau) \le \frac{M}{\eta}.$$

Therefore,

$$0 \le x(\tau) + y(\tau) + z(\tau) \le \frac{M}{\eta},$$

and let us consider the set $B = \{(x, y, z) \in R_+^3 : 0 \le x(\tau) + y(\tau) + z(\tau) \le \frac{M}{\eta}\}$, hence we can state the following lemma:

LEMMA 1. The system (7)-(9) is uniformly bounded in the region $B \subset R_+^3$.

Dynamics of the System

We have already established that the system (7)-(9) has three equilibrium points, namely, $E_0 = (0,0,0)$, $E_1 = (1,0,0)$ and $E^* = (x^*, y^*, z^*)$ in the previous section. Again, the general variational matrix corresponding to the system is given by

$$J = \begin{bmatrix} 1-2x^*-az^* & c & -ax^*+b \\ az^* & -d & ax^* \\ 0 & e & -h \end{bmatrix}$$

Now, corresponding to the trivial steady state $E_0 = (0,0,0)$ the Jacobian J has the following eigen values $\lambda_i = 1, -d, -h$; hence E_0 is repulsive in x-direction and attracting in $y-z$ plane. Clinically it means when there is no susceptible population then there will be no mass in incubated and in infected class. Hence, E_0 is a saddle point.

Again, corresponding to the disease free equilibrium point $E_1 = (1,0,0)$, we have following eigen values $\lambda_1 = -1$ and $\lambda_{2,3}$ are the roots of the following quadratic equation:

$$\lambda^2 + (d+h)\lambda + (dh - ae) = 0,$$

when $dh > ae$, i.e., $R_0 < 1$, then the both the roots have negative real part and thus $E_1(1,0,0)$ is a locally stable in this case.

Further, from the existence of E^* and the stability condition of E_1, it is clear that the instability of the disease free equilibrium will lead to the existence of the endemic equilibrium. Now, we will examine the local behavior of the flow of the system around the endemic equilibria E^*. The characteristic equation corresponding to the equilibrium is

$$P(\lambda) = \lambda^3 + A_1\lambda^2 + A_2\lambda + A_3 = 0 \qquad (11)$$

where

$$\begin{aligned} A_1 &= 2x^* + az^* + d + h - 1 \\ A_2 &= (d+h)(2x^* + az^* - 1) - acz^* \\ A_3 &= ahz^*(d - \frac{be}{h} - c) = hd(1 - x^*). \end{aligned}$$

Since $(2x^* + az^* - 1) > x^* > 0$, on substitution the values of x^* and z^*, it can be easily verified that $A_i > 0$, for $i = 1,3$ and $A_2 > 0$ if $dh(h+d+c) \geq ace$. Now, from Routh-Hurwitz criterion a set of necessary and sufficient conditions for all the roots of the equation (11) having negative real part are $A_i > 0, i = 1,2,3$ and $A_1A_2 > A_3$.

Again, solving the last inequality, we get a sufficient condition for stability given by $(h+d+c)(h+d) \geq ae.$ Hence, we can state the following theorem:

Theorem 1. The system (7)-(9) is locally stable around the endemic equilibrium point E^*, when $dh(h+d+c) \geq ace$ and $(h+d+c)(h+d) \geq ae.$

Further, we will study the Hopf-bifurcation of above system, taking "a" (i.e., the rate of transfer from susceptible to incubated population) as the bifurcation parameter. Now, the necessary and sufficient condition for the existence of the Hopf-bifurcation, if there exists $a = a_0$ such that (i) $A_i(a_0) > 0$, $i = 1,2,3$, (ii) $A_1(a_0)A_2(a_0) - A_3(a_0) = 0$ and (iii) if we consider the eigen values of the characteristic equation (11) of the form $\lambda_i = u_i + iv_i$, then $Re\frac{d}{da}(u_i) \neq 0$, $i = 1,2,3$. After substitution of the values, the condition $A_1A_2 - A_3 = 0$ becomes

$$\frac{1}{a^2}B_1 + \frac{1}{a}B_2 + B_3 = 0 \qquad (12)$$

where

$$\begin{aligned} B_1 &= \frac{d^2h^2}{e^2}\left[2 - \frac{dh}{(dh-be-ch)}\right]\left[2(d+h) + \frac{dh(c-d-h)}{(dh-be-ch)}\right], \\ B_2 &= \frac{dh}{e}\left[\frac{be+ch}{(dh-be-ch)} + d + h\right]\left[2(d+h) + \frac{dh(c-d-h)}{(dh-be-ch)}\right] \\ &\quad + \frac{dh}{e}\left[2 - \frac{dh}{(dh-be-ch)}\right]\left[\frac{bde+beh+ch^2}{dh-be-ch}\right] + \frac{d^2h^2}{e}, \\ B_3 &= \left[\frac{be+ch}{(dh-be-ch)} + d + h\right]\left[\frac{bde+beh+ch^2}{dh-be-ch}\right] - dh. \end{aligned}$$

For example, taking $b = 0.01$, $c = 0.01$, $d = 0.2$, $e = 0.01$ and $h = 0.08$, we get a positive root $a = 15.986$ of the quadratic equation (12). Therefore, the eigen values of the characteristic equation (11) at $a = 15.986$ are of the form $\lambda_{1,2} = \pm iv$ and $\lambda_3 = -w$, where v and w are positive real number.

Now, we will verify the condition (iii) of hopf-bifurcation. Put $\lambda = u + iv$ in (11), we get

$$(u+iv)^3 + A_1(u+iv)^2 + A_2(u+iv) + A_3 = 0. \qquad (13)$$

On separating the real and imaginary part and eliminating v between real and imaginary part, we get

$$8u^3 + 8A_1u^2 + 2(A_1^2 + A_2)u + A_1A_2 - A_3 = 0. \qquad (14)$$

It is clear from the above that $u(a_0) = 0$ iff $A_1(a_0)A_2(a_0) - A_3(a_0) = 0$. Further, at $a = a_0$, $u(a_0)$ is the only root, since the discriminant $8u^2 + 8A_1u + 2(A_1^2 + A_2) = 0$ is

$$64A_1^2 - 64(A_1^2 + A_2) < 0.$$

Again, differentiating (14) with respect to a, we have

$$\left(24u^2 + 16A_1u + 2(A_1^2 + A_2)\right)\frac{du}{da} + \left(8u^2 + 4A_1u\right)\frac{dA_1}{da} + 2u\frac{dA_2}{da} + \frac{d}{da}(A_1A_2 - A_3) = 0.$$

Now, since at $a = a_0$, $u(a_0) = 0$, we get

$$\left[\frac{du}{da}\right]_{a=a_0} = \frac{-\frac{d}{da}(A_1A_2 - A_3)}{2(A_1^2 + A_2)} \neq 0,$$

which will ensure that the above system has a hopf-bifurcation. Hence as the rate of transfer from susceptible to incubated population (or the rate of interaction between viral disease class and susceptible class), is a, when crosses its

threshold value, i.e., $a = a_0$, then susceptible, incubated and disease population starts oscillating around the endemic equilibrium point.

Numerical Analysis

For example, taking values for the parameters $b = 0.01$, $c = 0.01$, $d = 0.2$, $e = 0.01$ and $h = 0.08$, we get a positive root $a = 15.986$ of the quadratic equation (12). which will ensure that the above system has a Hopf-bifurcation. Hence as the rate of transfer from susceptible to incubated population "a" (or the rate of interaction between viral disease class population and susceptible class) when crosses its threshold value $a = a_0$, then susceptible, incubated and disease population starts oscillating around the endemic equilibrium point. The above result is shown numerically in figure (1)-(3) when $b = 0.01$, $c = 0.01$, $d = 0.2$, $e = 0.01$ and $h = 0.08$ initial values $x(0) = 0.15$, $y(0) = 0.6$, $z(0) = 0.1$ with different values of a. In figure-1, we observed that the endemic equilibrium is stable, when $a < 15.986$, but when we cross the threshold value of $a = 15.986$, the above system starts oscillating around the endemic equilibrium, as shown in figure-2 and figure-3.

Conclusion

In this paper, a mathematical model of viral disease outbreak has been studied with three classes of population namely, susceptible, incubated and infected. The immune system plays an important role in recovery of a disease. It is further assumed that due to strong immunity a portion of incubated class rejoins susceptible class without being infected (diseased). It is observed that the system is bounded. The stability behavior of the trivial, disease free and endemic equilibrium state are studied. If $R_0 < 1$ disease free equilibrium point is locally stable and the disease dies out. The instability of disease free state leads to the existence of the endemic state, i.e., endemic equilibrium exists if $R_0 > 1$. If $dh(h+d+c) \geq ace$ and $(h+d+c)(h+d) \geq ae$, then the endemic equilibrium is locally stable.

We determine criteria for Hopf-bifurcation using disease transfer rate "a" as bifurcation parameter. It is shown that disease free equilibrium point is locally asymptotically stable when "a" is small, while a loss of stability by a Hopf bifurcation can occur as "a" increases. Hopf bifurcation has helped us in finding the existence of a region of instability in the neighborhood of a nonzero endemic equilibrium where the population will survive undergoing regular fluctuations. The above said results are shown numerically.We left some future extension of the proposed model including other type of interactions such as Holling type-2 or Holling type-3 sometimes they represent more realistic interactions in epidemiology.

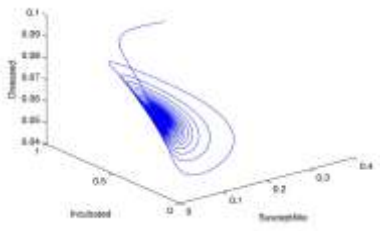

Figure 1. Stable endemic equilibrium E^*, for $a = 15.8$

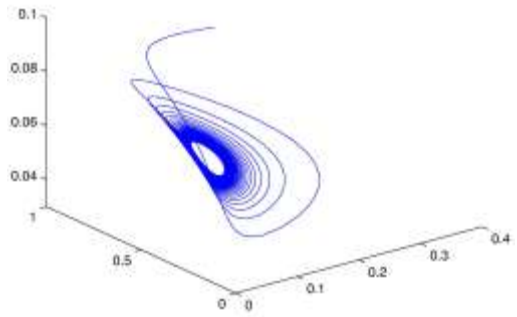

Figure 2. Oscillating endemic equilibrium E^*, for $a = 16.3$

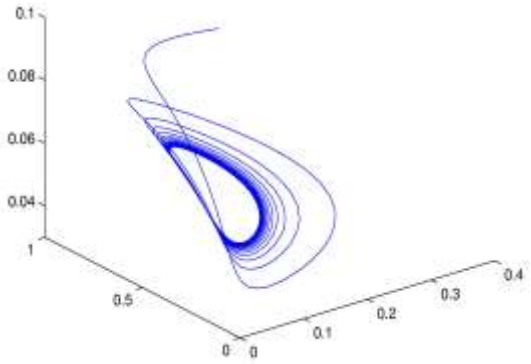

Figure 3. Oscillating endemic equilibrium E^*, for $a = 17.0$

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