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THE STABILITY ANALYSIS OF A MATHEMATICAL MODEL IN THE PRESENCE OF A PREVENTIVE VACCINE

Kazi Aminur Rahman
Department of Mathematics, University of Dhaka, Bangladesh.
Jannatun Nayeem
Department of Arts and Sciences, Ahsanullah University of Science and Technology Dhaka, Bangladesh.
and
Mr. Md. Abu Salek [1]
Institute of Natural Sciences, United International University, Dhaka-1209, Bangladesh.
email: salekphd@gmail.com

ABSTRACT

Various kinds of deterministic models for the spread of infectious disease in populations have been analyzed mathematically and applied to specific diseases. In this paper a deterministic model for the dynamics of an infectious disease in the presence of a preventive vaccine is formulated. The model is a special case of a more general model, which is also applicable to other models of infectious diseases. The three-dimensional model which assumes a non-linear incidence rate is analyzed qualitatively to determine the stability of its equilibria. This model is used to investigate the potential impact of the optimal vaccine coverage threshold needed for disease control and eradication.

Key words: Non-linear incidence, Vaccine coverage threshold, infectious diseases, Stability analysis, Basic reproduction number, Endemic equilibrium.

I. INTRODUCTION

The epidemiology of infectious diseases has moved beyond identifying agents and risk factors to a more detailed understanding of the mechanisms controlling the distribution of infections and disease in populations. The basic types of deterministic models for infectious diseases which are spread by direct person to person contract in a population with various parameters have been widely studied [1]. One of the most important concerns about any infectious disease is its ability to invade a population. Many epidemiological models have a disease free equilibrium (DFE) at which the population remains in the absence of disease [2]. The classical SIR models are very important as conceptual models (similar to predator-prey and competing species models in ecology). The SIR epidemic modeling yields the useful concept of the threshold quantity which determines when an epidemic occurs, and formulas for the peak infective fraction and the final susceptible fraction [3]. The conventional SIR model for disease transmission has been broadly studied (see the reference, [4-6]). The majority of these discussions assume the rate of a bilinear mass action. In this paper, we try to present a model for the transmission dynamics of an infectious disease that incorporates a non-linear incidence rate, a preventive vaccine that is given to susceptible individuals. In order to control or eradicate the communicable disease, it is essential to have a preventive vaccine that provides lasting protection. According to reference [4], effective vaccines have been used successfully to control smallpox, polio and measles. Once such a potent vaccine (with high enough efficacy) has been developed, important epidemiological questions, such as what proportion of the susceptible population must be immunized in order to eradicate the disease, must be addressed. The model we propose will be analyzed qualitatively to determine the optimal vaccine coverage level needed to effectively control or eradicate the disease. The model we propose will be analyzed qualitatively in Section 3 and Section 4 to determine the stability of its associated equilibria and the optimal vaccine coverage level needed to effectively control or eradicate the disease.

[1] For all correspondence

II. MODEL FORMULATION

In our model, we have divided the population into three classes: Susceptible individuals, vaccinated individuals and infected individuals. We denote the population of those who are susceptible as X, who are vaccinated as Y and those who subsequently infected as Z respectively. Populations enter the susceptible class at constant rate δ. The transmission probabilities of susceptible and vaccinated individuals are λ_1 and λ_2 respectively, here the average number of contact rate is γ. It is realistically assumed that $\lambda_2 \le \lambda_1$, because of reducing or eliminating the incidence of infection due to vaccination. Natural death rate are assumed to be η and the vaccination coverage of susceptible represented by the parameter σ. The structure of the model is summarized in Figure 1. (See Appendix)

The differential equations of the model are given by:

$$\frac{dX}{dt} = \delta - \frac{\gamma\lambda_1 Z}{1+Z}X - \sigma X - \eta X \qquad (1a)$$

$$\frac{dY}{dt} = \sigma X - \frac{\gamma\lambda_2 Z}{1+Z}Y - \eta Y \qquad (1b)$$

$$\frac{dZ}{dt} = \frac{\gamma\lambda_1 Z}{1+Z}X + \frac{\gamma\lambda_2 Z}{1+Z}Y - \eta Z \qquad (1c)$$

III. STABILITY ANALYSIS OF DFE

3.1. Disease-free equilibrium

We investigate the local stability of the steady state by finding the eigenvalues of the associated Jacobian matrices. The model has a disease-free equilibrium (DFE), obtained by setting the right hand sides of (1) to zero, given by

$$\delta - \frac{\gamma\lambda_1 Z}{1+Z}X - \sigma X - \eta X = 0 \qquad (2)$$

$$\sigma X - \frac{\gamma\lambda_2 Z}{1+Z}Y - \eta Y = 0 \qquad (3)$$

$$\frac{\gamma\lambda_1 Z}{1+Z}X + \frac{\gamma\lambda_2 Z}{1+Z}Y - \eta Z = 0 \qquad (4)$$

giving the disease-free equilibrium:

$$\varepsilon_0 = \left(\frac{\delta}{\eta+\sigma}, \frac{\delta\sigma}{\eta(\eta+\sigma)}, 0\right)$$

where 0 indicates that there is no infected people (i.e. no disease) in the population.

3.2. Jacobian matrix at DFE and local stability:

The Jacobian of the linearized model (1) at ε_0 is

$$J_a = \begin{pmatrix} -\sigma-\eta & 0 & \dfrac{\gamma\lambda_1\delta}{\eta+\sigma} \\ \sigma & -\eta & \dfrac{\gamma\lambda_2\delta\sigma}{\eta(\eta+\sigma)} \\ 0 & 0 & \dfrac{\gamma\lambda_1\delta}{\eta+\sigma} + \dfrac{\gamma\lambda_2\delta\sigma}{\eta(\eta+\sigma)} - \eta \end{pmatrix}$$

with eigenvalues $l = -(\eta+\sigma),\ m = -\eta$ and $n = \dfrac{\gamma\lambda_1\delta}{\eta+\sigma} + \dfrac{\gamma\lambda_2\delta\sigma}{\eta(\eta+\sigma)} - \eta$. Since all the model parameters are positive, it follows that $l, m < 0$. Thus, the equilibrium ε_0 is locally asymptotically stable provided $n < 0$.

3.3. The basic reproduction number

The basic reproduction number $\Re_b$, is "the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual" [8]. Here, we have found the basic reproduction number using the reference [4], as

$$\Re_b = \frac{\gamma\lambda_1\delta}{\eta(\eta+\sigma)} + \frac{\gamma\lambda_2\delta\sigma}{\eta^2(\eta+\sigma)}$$

Lemma 1:

The DFE ε_0 is locally asymptotically stable if $\Re_b < 1$ and unstable if $\Re_b > 1$.

By considering $\Re_b$ as a function of σ $\left(i.e.\ \Re_b = \Re_b(\sigma)\right)$, it follows that

$$\Re_b' = \frac{\gamma\delta(\lambda_2 - \lambda_1)}{\eta(\eta+\sigma)^2}$$

Since $\lambda_2 \le \lambda_1$ it is clear that $\Re_b'(\sigma) \le 0$ for $0 \le \sigma \le 1$. Thus $\Re_b$ is a decreasing function. This indicates the impact of vaccination in reducing the basic reproduction number $\Re_b$.

Furthermore, there is unique σ_c such that $\Re_b(\sigma_c) = 1$ given by

$$\sigma_c = \left(\frac{1-\Re_{b1}}{\Re_{b2}-1}\right)\eta$$

where, $\Re_{b1}=\frac{\gamma\lambda_1\delta}{\eta^2}$, $\Re_{b2}=\frac{\gamma\lambda_2\delta}{\eta^2}$

Notice that at $\sigma=0$, $\Re_b$ reduces to $\Re_{b1}$. Since $\Re_{b1}\geq\Re_{b2}$ (because $\lambda_1\geq\lambda_2$), we consider the case $\Re_{b2}<1<\Re_{b1}$. In this range, σ_c is positive, here also note that $\sigma<0$ is biologically unrealistic.

Lemma 2:

The DFE ε_0 is locally asymptotically stable if $\sigma>\sigma_c$ and unstable if $\sigma\leq\sigma_c$.

This lemma clearly implies that if the vaccine coverage level exceeds the threshold (σ_c), then the DFE is the only equilibrium and it is locally asymptotically stable and consequently, the disease can be eradicated.

IV. EXISTANCE AND STABILITY OF ENDEMIC EQUILIBRIUM

4.1. Condition for existence of endemic equilibrium

Although the endemic equilibria (EE) are difficult (or impossible) to express in closed form, we offer a technique for determining the conditions for disease prevalence $(Z\neq0)$ based on a "vaccination function" as follows. Equation (4) can be rewritten as:

$$\frac{\gamma\lambda_1 Z}{1+Z}X+\frac{\gamma\lambda_2 Z}{1+Z}Y=\eta Z$$

$$\Rightarrow\frac{\gamma\lambda_1}{1+Z}X+\frac{\gamma\lambda_2}{1+Z}Y=\eta \quad (7)$$

also from (2) and (3) can respectively be expressed as,

$$X=\frac{\delta(1+Z)}{\gamma\lambda_1 Z+(\sigma+\eta)(1+Z)} \quad (8)$$

and

$$Y=\frac{\delta\sigma(1+Z)^2}{[\gamma\lambda_1 Z+(\sigma+\eta)(1+Z)][\gamma\lambda_2 Z+\eta(1+Z)]} \quad (9)$$

Substituting (8) and (9) into (7) leads to the "vaccination function" $(on[0,\infty])$

$$\sigma=\sigma(Z)=\frac{[\gamma\lambda_2 Z+\eta(1+Z)][\eta\{\gamma\lambda_1 Z+\eta(1+Z)\}-\gamma\lambda_1\delta]}{[\gamma\lambda_2\delta-\eta\{\gamma\lambda_2 Z+\eta(1+Z)\}](1+Z)}$$

It is easy to show that

$$\sigma(0)=\left(\frac{1-\Re_{b1}}{\Re_{b2}-1}\right)\eta=\sigma_c$$

and

$$\lim_{Z\to+\infty}\sigma(Z)=-\frac{\gamma^2\lambda_1\lambda_2+\gamma\lambda_1\eta+\gamma\lambda_2\eta+\eta^2}{\gamma\lambda_2+\eta}<0$$

Since $\Re_{b2}<1$, then

$$\gamma\lambda_2\delta-\eta[\gamma\lambda_2 Z+\eta(1+Z)]<0 \quad \text{for} \quad Z\geq0$$

Thus the sign of $\sigma(Z)$ depends on the sign of the function, where

$$g(Z)=\eta^2-\gamma\lambda_1\delta+\eta(\gamma\lambda_1+\eta)Z$$

Owing to the assumption that $\Re_{b1}>1$, the function $g(Z)$ has a unique root.

Thus, $g(Z)=0$

implies $Z_c=\frac{\gamma\lambda_1\delta-\eta^2}{\eta(\gamma\lambda_1+\eta)}=\frac{\eta(\Re_{b1}-1)}{\gamma\lambda_1+\eta}$

Therefore, $g(Z)\leq0$ for $0\leq Z\leq Z_c$ and $g(Z)>0$ for $Z>Z_c$. Thus

$$\sigma(Z)>0 \text{ for } 0\leq Z\leq Z_c$$
$$\sigma(Z_c)=0$$
$$\sigma(Z)<0 \text{ for } Z>Z_c.$$

It is easy to verify that the function $\sigma'(Z)$ has at most two roots for $Z\geq0$, and the equation $\sigma(Z)=\sigma_c$ has at most one root for $Z>0$. It is significant, therefore to study the qualitative behavior of $\sigma(Z)$ based on the sign of $\sigma'(0)$ as follows:

Case 1: $\sigma'(0)>0$

In this case, there exists $\tilde{Z}>0$ such that $\sigma(Z)$ is increasing for $Z\in(0,\tilde{Z})$ and decreasing for $Z>\tilde{Z}$. Thus, there is a unique Z_0 with $\tilde{Z}<Z_0<Z_c$ such that

$(i)\ \sigma(Z)>\sigma_c$ for $Z\in(0,Z_0)$

$(ii)\ \sigma(Z)<\sigma_c$ for $Z>Z_0$ and

$(iii)\ \sigma(0)=\sigma(Z_0)=\sigma_c\ (\Re_b=1)$ (See Fig. 2)

Case 2: $\sigma'(0)<0$

Here, $\sigma(Z)$ is a decreasing function and $\sigma(Z)<\sigma_c$ for $Z>0$ (see Fig. 3)

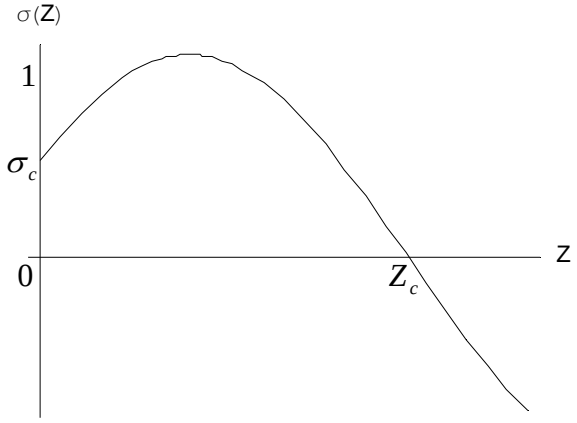

Fig. 2 Graph of the function $\sigma(Z)$ vs $(Z \geq 0)$, when $\sigma'(0) > 0$.

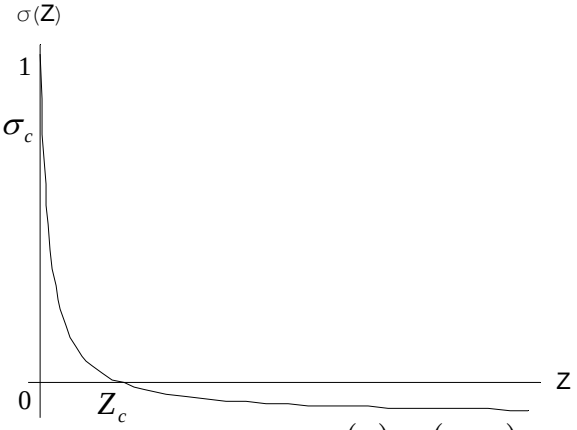

Fig. 3 Graph of the function $\sigma(Z)$ vs $(Z \geq 0)$ when $\sigma'(0) < 0$.

It should be noted that in both cases 1 and 2 endemic equilibria, Z_c exists in the absence of vaccination $(\sigma = 0)$. When σ is increasing in the interval $\sigma \in (0, \sigma_c]$, the infected state remains stable. In fact expectedly higher values of σ lead to corresponding decrease in the steady–state values of the number of infected individuals. The uninfected state is stable for $\sigma \in (\sigma_c, 1]$ (in this case, $\Re_b < 1$). Furthermore, the model undergoes a backward bifurcation at Z_0 from a prevalence state to the disease free state ε_0 (where, $\sigma(Z_0) = \sigma_c$; see Fig. 2). If $\sigma(Z)$ is decreasing from values $\sigma(Z) > \sigma_c$ to values below σ_c ($\sigma'(0) < 0$; see Fig. 3), the model undergoes a forward bifurcation at $Z = 0$ from ε_0 to a prevalence state $(Z \neq 0)$. We note that a typical infective individual will undergo a random walk through the infective classes, possibly moving both forward and backward several times before being removed from the population [8]. It is mentioning that the number of non-trivial equilibria of the model (1) depends on the sign of $\sigma'(0)$. From cases 1 and 2, it can be seen that, in addition to the DFE, there is one (see Fig. 2 and 3 when $\sigma(Z) \leq \sigma_c$) or even two equilibria (see Fig. 2 when $\sigma(Z) > \sigma_c$) of the model (1).

4.2. Local stability analysis

To fully understand the local stability of a endemic equilibrium of (1), given by $\varepsilon^* = (X^*, Y^*, Z^*)$, we make the following change of coordinates:

$$p = X - X^* \quad , \quad q = Y - Y^* \quad , \quad r = Z - Z^*$$

We now discuss the stability of $\tilde{\varepsilon}^* = (0,0,0)$ of the transformed model:

$$\begin{aligned}
\frac{dp}{dt} &= \delta - \gamma\lambda_1 g(r+Z^*)(p+X^*) - \sigma(p+X^*) - \eta(p+X^*) \\
\frac{dq}{dt} &= \sigma(p+X^*) - \gamma\lambda_2 g(r+Z^*)(q+Y^*) - \eta(q+Y^*) \qquad (10) \\
\frac{dr}{dt} &= \gamma\lambda_1 g(r+Z^*)(p+X^*) + \gamma\lambda_2 g(r+Z^*)(q+Y^*) - \eta(r+Z^*)
\end{aligned}$$

where $g(r+Z^*) = \dfrac{r+Z^*}{1+(r+Z^*)}$. The fixed points of the equations (10) are given by

$$\frac{dp}{dt} = 0$$

$$\Rightarrow p := \psi_1 = \frac{\delta - \gamma\lambda_1 g(r+Z^*)X^* - \sigma X^* - \eta X^*}{\gamma\lambda_1 g(r+Z^*) + \sigma + \eta}$$

$$\frac{dq}{dt} = 0$$

$$\Rightarrow q := \psi_2 = \frac{\sigma(p+X^*) - \gamma\lambda_2 g(r+Z^*)Y^* - \eta Y^*}{\gamma\lambda_2 g(r+Z^*) + \eta}$$

$$\frac{dr}{dt} = 0$$

$$\Rightarrow r := \psi_3 = \frac{\gamma\lambda_1 g(r+Z^*)(p+X^*) + \gamma\lambda_2 g(r+Z^*)(q+Y^*)}{\eta} - Z^*$$

The Jacobian of $\psi = (\psi_1, \psi_2, \psi_3)$ at $(0,0,0)$ is

$$J_b=\begin{pmatrix} 0 & 0 & \dfrac{\gamma\lambda_1 g'(Z^*)X^*}{\gamma\lambda_1 g(Z^*)+\sigma+\eta} \\ \dfrac{\sigma}{\gamma\lambda_1 g(Z^*)+\eta} & 0 & \dfrac{\gamma\lambda_2 g'(Z^*)Y^*}{\gamma\lambda_2 g(Z^*)+\eta} \\ \dfrac{\gamma\lambda_1 g(Z^*)}{\eta} & \dfrac{\gamma\lambda_2 g(Z^*)}{\eta} & \dfrac{\gamma\lambda_1 g'(Z^*)X^*+\gamma\lambda_2 g'(Z^*)Y^*}{\eta} \end{pmatrix}$$

where

$$g'(Z^*)=\frac{df(r+Z^*)}{dr}(0)=\frac{1}{(1+Z^*)^2}$$

Let τ_1,τ_2 and τ_3 be the eigenvalues of J_b and $T=\max_{1\le i\le 3}|\tau_i|$. Then, the stability of the non-trivial equilibrium ε^* will depend on the threshold condition T [7].

Theorem 1:

The non-trivial equilibrium ε^* is locally asymptotically stable if $T<1$ and unstable if $T\ge 1$.

4.3. Numerical simulation and discussions

In order to illustrate the various theoretical results the threshold predicted in theorem, a number of numerical experiments (using Mathematica package) were carried out to compute the solutions of $\{(2),(3),(4)\}$ using the parameter values. The parameter values are estimated as follows: $\delta=700$, $\lambda_1=0.00001$, $\lambda_2=0.00000003$, $\eta=0.05$, $\gamma=4$. With this parameter values, the optimal vaccination coverage is $\sigma_c=0.527732$. We considered the cases $\sigma<\sigma_c$ and $\sigma>\sigma_c$. The results tabulated in Table 1 (see Appendix) are compared with those obtained theoretically from theorem (evaluating the eigenvalues of J_b at the considered parameter values and determining T).

In the first set of experiments, where $\sigma=0.3<\sigma_c$, a single positive endemic equilibrium exists. Here, $T<1$ and $\varepsilon_1^*=(2121,21211,1)$ is locally asymptotically stable using theorem 1. The other equilibrium $\varepsilon_2^*=(-721,21211,-0.9)$ is unstable because $T>1$ in this case again using theorem. Note that the equilibrium ε_2^* involves unrealistic negative values.

In the second set of experiments, where $\sigma=0.6>\sigma_c$, the non-trivial equilibria have negative components and are unstable ($T>1$ in both cases). In this case the DFE is locally asymptotically stable, so that the disease can be eradicated. This is consistent with Lemma 2. Overall; these simulation results verified the theoretical predictions in Lemma 2 and Theorem 1.

VI. CONCLUSION

A new deterministic model, which assumes non-linear incidence, is constructed and used to analyze the effect of a preventive vaccine on the transmission dynamics of an infectious disease. The model is rigorously analyzed to investigate the existence and stability of the associated equilibria. Numerical simulations were carried out using reasonable sets of parameter values to asses the impact of various vaccine features and characteristics on disease control. A threshold level of vaccine coverage (σ_c) needed for controlling or eradicating the disease has been qualitatively determined. Our study show that higher values of vaccine coverage (σ) that are lower than the threshold value significantly reduces the number of infected individuals, but never lead to disease eradication. Disease eradication is only feasible if the vaccination coverage level exceeds the threshold value when the vaccination function is decreasing. These theoretical findings have been verified numerically. Overall, this study shows that, the impact of vaccination with desirable characteristics can significantly help in halting the spread of infections diseases and controlling the diseases in future. As more prevention interventions become available, the tools of mathematical modeling will become increasingly important for helping us to understand and maximize the population level impacts these interventions can have.

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APPENDIX

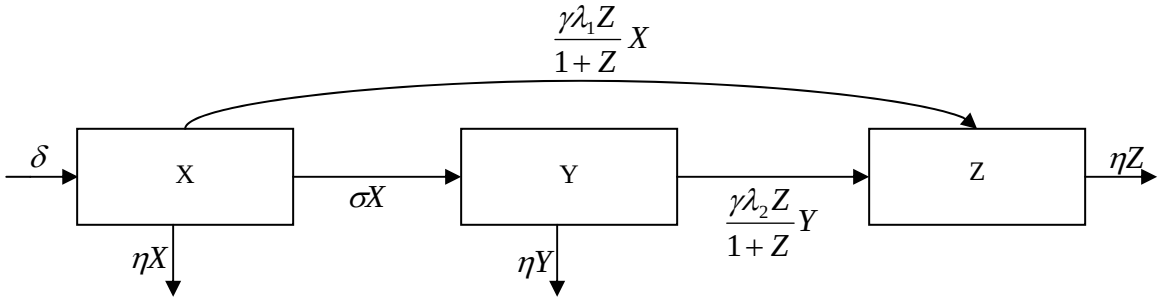

Fig 1: Model Structure.

Table 1: Simulation results for endemic equilibria using various values of σ.

σ	Non-trivial equilibria	τ_1	τ_2	τ_3	T
0.3	$\varepsilon_1^* = (2121, 21211, 1)$	0.436869	0.00102866	-0.000970859	<1
	$\varepsilon_2^* = (-721, 21211, -0.9)$	-52. 5882	-0.000563+0. 00447i	-0.000563-0.00447i	>1
0.6	$\varepsilon_1^* = (2121, 21211, -0.5)$	6.99089	-0.000030+0.00146i	-0.000030-0.00146i	>1
	$\varepsilon_2^* = (-721, 21211, -1.05)$	-210. 359	0.00787844	-0.006468	>1