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Analysis of an Epidemic Model of Multiple Disease Transmission with Vaccination and Therapeutic Drug Regimen

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Authors' contributions

This work was carried out in collaboration between both authors ANM and SMF. The idea of this work was given by author ANM. Both authors read and approved the final manuscript.

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Abstract

In this paper we discuss a new epidemic model for the dynamics of infectious disease in the presence of vaccine and therapeutic treatment is proposed and analyzed theoretically as well as numerically. The disease is transmitted from infected individuals and contaminated water to susceptible and vaccinated individuals, the proposed model includes a linear functional response.

Keywords: Disease transmission; epidemiological model; on-trivial equilibrium; disease-free equilibrium; stability analysis.

1 Introduction

In the last three decades, epidemic models have been widely studied (see, [1,2,3,4,5,6]). Two of the main aspects of modelling on infectious disease are:

1. The functional form of the force of infection, namely the function describing the mechanism of disease transmission.
2. The description of intervention policy to contrast the disease spread (vaccination, treatment, health campaign, etc.).

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Many authors have proposed more realistic models that assume a non-linear incidence rate [7,8,9,10]. Diseases are caused in many ways, it is transmitted by contact with infected person, by drinking contaminated water or by eating food that has been contaminated by the faeces of an infected person. Recently there have been many mathematical modelling focused on modelling and simulating the nature of the cholera dynamics [11,12,13,14]. Once such an effective vaccine has been developed, epidemiological question such as what proportion of the susceptible population must be immunized in order to eradicate the disease must be addressed. Recently the vaccination model has proposed by many authors [14,15]. The aim of this paper is to design a new model for multiple transmission ways of infectious disease that incorporates a preventive vaccine (Given to susceptible individuals) and a therapeutic drug regimen (administered to infected individuals). The dynamical behavior of the proposed model has been investigated analytically as well as numerically.

2 The Mathematical Model

Consider an epidemiological model consists of susceptible individuals(t), vaccinated individuals V(t), infected individuals I(t) and contaminated water W(t), where S(t) represents the numbers of susceptible individuals, V(t) represents the number of vaccinated individuals, I(t) represents number of infected individuals and W(t) pathogen concentration in the contaminated water, under the following assumptions:

1. The disease is transmitted from infected individuals to susceptible individuals by contact rate $\frac{k_1 I}{1+aS+bI}$ and it is transmitted from infected individuals to vaccinated individuals by contact rate $\frac{k_2 I}{1+aV+bI}$. These transmission functions display saturation effect accounting for the fact that the number of contacts an individual reaches some maximal value due to the spatial or social distribution of the population and it is considered by Diekmann and Kretzschmar [16]. It is transmitted from contaminated water to susceptible individuals according to the non-linear incidence rate of the form $\frac{\beta_1 W(t)}{1+W(t)}$ and vaccinated individuals by $\frac{\beta_1 W(t)}{1+W(t)}$, however, the infected individuals do not grow.
2. A preventive vaccine is given the susceptible individuals with vaccination coverageσ.
3. A therapeutic drug regimen administered to infected individuals with therapeutic coverage α
4. The concentration of pathogens in the contrasted water is increased by contacting the infected individuals with contact rate γ. Furthermore, assume μ is the natural death of the populations, d is the death rate of pathogens in water and π is the recruitment of susceptible individuals. Thus, the dynamical of such a model can be represented in the following set of equations.

$$\begin{aligned}
\frac{dS}{dt} &= \pi + \alpha I - \frac{k_1 IS}{1+aS+bI} - \frac{\beta_1 WS}{1+W} - (\sigma+\mu)S \\
\frac{dV}{dt} &= \sigma S - \frac{k_2 IV}{1+aV+bI} - \frac{\beta_2 WV}{1+W} - \mu V \\
\frac{dI}{dt} &= \frac{k_1 IS}{1+aS+bI} + \frac{\beta_1 WS}{1+W} + \frac{k_2 IV}{1+aV+bI} + \frac{\beta_2 WV}{1+W} - (\alpha+\mu)I \\
\frac{dW}{dt} &= \gamma I - dW
\end{aligned} \tag{1}$$

Where $S, I, W, V \in \boldsymbol{R}^+$ and $S(0) \geq 0, I(0) \geq 0,$ and $W(0) \geq 0$

Here, all the parameters are positive. In addition, since the right side of each equation in the system(1) is a continuous function and has continuous partial derivatives on the state spaceR_+^4. Therefor, they can be

considered as Lipischizian function on R_+^4, so that the solution of the system (1) with initiate in the non-negative octant are existed and unique, and from the system (1) we obtain

$$\frac{d(S+V+I)}{dt} = \pi - \mu(S+V+I)\ ,$$

$$\Longrightarrow \lim_{t\to\infty} Sup(S+V+I) = \frac{\pi}{\mu}$$

$$\Longrightarrow \frac{dW}{dt} \leq \frac{\gamma\pi}{\mu} - dW$$

$$\Longrightarrow \lim_{t\to\infty} Sup\ W \leq \frac{\gamma\pi}{d\mu}$$

Therefore, all the solutions of the system (1) which initiate in R_+^4 are bounded uniformly.

3 The Existence of Equilibrium Points

The system (1) has at most two non-negative equilibrium point[R]

i. The disease-free equilibrium is $E_1 = \left(\frac{\pi}{\sigma+\mu} + \frac{\sigma\pi}{\mu(\sigma+\mu)}, 0, 0\right)$
ii. The non-trivial equilibrium is $E_2 = (\bar{S}, \bar{V}, \bar{I}, \bar{W})$, where

$$\bar{W} = \frac{\gamma}{\mu}\bar{I}, \bar{S} = f_1(\bar{I})\ \bar{V} = f_2(\bar{I}) \quad \text{with}$$
$$f_1(\bar{I}) = \frac{1}{2A_1}\left(-B_1 + \sqrt{B_1^2 + 4A_1C_1}\right),$$
$$f_2(\bar{I}) = \frac{1}{2A_2}\left(-B_2 + \sqrt{B_2^2 + 4A_2C_2}\right),$$
$$A_1 = \frac{\beta_1\gamma\bar{I}}{\mu+\gamma\bar{I}} + \sigma + \mu,$$
$$A_2 = \frac{\beta_2\gamma\bar{I}}{\mu+\gamma\bar{I}} + \mu,$$
$$B_1 = \frac{1}{a}(A_1(1+b\bar{I}) + K_1\bar{I}) - \pi - \alpha\bar{I},$$
$$B_2 = \frac{1}{a}(A_2(1+b\bar{I}) + K_2\bar{I}) - \alpha f_1(\bar{I}),$$
$$C_1 = \frac{1}{a}(\pi + \alpha\bar{I})(1+b\bar{I}),$$
$$C_2 = \frac{\sigma}{a}f_1(\bar{I})(1+b\bar{I})$$

And $\bar{I}$ is a root of the following function

$$F(I) = \frac{\gamma}{\mu+\gamma I}\left(\beta_1 f_1(I) + \beta_2 f_2(I)\right) + \frac{K_1 f_1(I)}{1+af_1(I)+bI} + \frac{K_2 f_2(I)}{1+af_2(I)+bI} - \alpha - \mu$$

Now, $F(I)$: $\left[0, \frac{\pi}{\mu}\right] \to R$ is a continuous function, and consider the following condition

$$F(0) > 0 \text{ (or } F(0) < 0) \text{ and } F(\pi) < 0 \text{ (or } F(\pi) > 0) \tag{2}$$

$$\frac{dF(I)}{dI} < 0 \quad \text{for all } I \in \left[0, \frac{\pi}{\mu}\right] \tag{3}$$

Then by using intermediate value theorem $F(I)$ has a unique positive root namely, $\bar{I} \in [0, \rho]$ and hence the non triavl equilibrium $E_2 = (\bar{S}, \bar{V}, \bar{I}, \bar{W})$ exists uniquely in the $IntR_+^4$ if and only if the conditions $(2,3)$ are holds.

4 Disease Free Equilibrium

In this section, the local stability conditions for both free equilibrium and non-trivial disease are determined.

Define the basic reproduction number as follows

$$R_0 = \frac{1}{\alpha}\left(\frac{\gamma\beta_1\pi}{d(\sigma+\mu)} + \frac{\gamma\sigma\beta_2\pi}{d\mu(\sigma+\mu)} + \frac{K_1\pi}{\sigma+\mu+a\pi} + \frac{\sigma K_2\pi}{\mu(\sigma+\mu)+a\sigma\pi} - \mu\right)$$

Theorem (1). If $R_0 < 1$, then the disease free equilibrium is locally asymptotically stable.

Proof

The Jacobean of linearized system (1) at $E_1 = \left(\frac{\pi}{\sigma+\mu} + \frac{\sigma\pi}{\mu(\sigma+\mu)}, 0, 0\right)$ is

$$J_1 = \begin{pmatrix} -\sigma-\mu & 0 & \alpha - \dfrac{K_1\pi}{\sigma+\mu+a\pi} & -\dfrac{\beta_1\pi}{\sigma+\mu} \\ \sigma & -\mu & -\dfrac{K_2\sigma\pi}{\mu(\sigma+\mu)+a\sigma\pi} & \dfrac{\beta_2\sigma\pi}{\mu(\sigma+\mu)} \\ 0 & 0 & \dfrac{K_1\pi}{\sigma+\mu+a\pi} + \dfrac{K_2\sigma\pi}{\mu(\sigma+\mu)+a\sigma\pi} - \alpha - \mu & \dfrac{\beta_1\pi}{\sigma+\mu} + \dfrac{\beta_2\sigma\pi}{\mu(\sigma+\mu)} \\ 0 & 0 & \gamma & -d \end{pmatrix}$$

Then the characteristic equation of J_1 can be written as:
either

$$(-\sigma-\mu-\lambda)(-\mu-\lambda)(\lambda^2 + D_1\lambda + D_2) = 0$$

or

$$\lambda_s = -\sigma-\mu \ \ and \ \ \lambda_v = -\mu \ \text{ or } \ (\lambda^2 + D_1\lambda + D_2) = 0$$

Where λ_s and λ_v represent the eigenvalues of J_1 in the S-direction and V-direction respectively. So

$$D_1 = d + \alpha + \mu - \frac{K_1\pi}{\sigma+\mu+a\pi} - \frac{K_2\sigma\pi}{\mu(\sigma+\mu)+a\sigma\pi}$$

$$D_2 = d\alpha + d\mu - \frac{\gamma\beta_1\pi}{\sigma+\mu} - \frac{\gamma\beta_2\sigma\pi}{\mu(\sigma+\mu)} - \frac{dK_1\pi}{\sigma+\mu+a\pi} - \frac{dK_2\sigma\pi}{\mu(\sigma+\mu)+a\sigma\pi}$$

Clearly, $\lambda_s < 0 \ \ and \ \lambda_v < 0$. If the basic reproduction number $R_0 < 1$, then
$D_1 > 0$ and $D_2 > 0$.

Thus the eigenvalues of J_1 in the I-direction, and W-direction have negative real parts. Therefore, the disease free equilibrium is locally asymptotically stable.

Theorem (2).

Suppose that the non-trivial equilibrium point exists. Then it is locally asymptotical stable if the following conditions hold.

$$\sigma + \mu + \frac{\beta_1 \bar{W}}{1+\bar{W}} + \frac{K_1 \bar{I}(1+b\bar{I})}{(1+a\bar{S}+b\bar{I})^2} < \left|\alpha - \frac{K_1 \bar{S}(1+a\bar{S})}{(1+a\bar{S}+b\bar{I})^2}\right| + \frac{\beta_1 \bar{S}}{(1+\bar{W})^2}$$

$$\mu + \beta_2 < \sigma + \frac{\beta_2 \bar{V}}{(1+\bar{W})^2}$$

$$\frac{\bar{I}}{\bar{V}} < \frac{1+a\bar{V}}{1+b\bar{I}}$$

$$b < min\left\{\frac{1+b\bar{I}}{\bar{S}}, \frac{1+b\bar{I}}{\bar{V}}\right\}$$

$$\gamma(\beta_1 \bar{S} + \beta_2 \bar{V}) < d\bar{W}(\beta_1 + \beta_2) + \frac{d(\beta_1 \bar{S} + \beta_2 \bar{V})}{(1+\bar{W})^2}$$

$$d < \gamma$$

Proof: The Jacobean of linearized system (1) at $E_2 = (\bar{S}, \bar{V}, \bar{I}, \bar{W})$

$J_1 = (b_{ij})$, i, j=1,2,3,4 where,

$b_{11} = -\sigma - \mu - \frac{\beta_1 \bar{W}}{1+\bar{W}} - \frac{K_1 \bar{I}(1+b\bar{I})}{(1+a\bar{S}+b\bar{I})^2}$, $b_{12} = 0$,

$b_{13} = \alpha - \frac{K_1 \bar{S}(1+a\bar{S})}{(1+a\bar{S}+b\bar{I})^2}$, $b_{14} = -\frac{\beta_1 \bar{S}}{(1+\bar{W})^2}$,

$b_{21} = \sigma$, $b_{22} = -\mu - \frac{\beta_2 \bar{W}}{1+\bar{W}} - \frac{K_2 \bar{I}(1+b\bar{I})}{(1+a\bar{V}+b\bar{I})^2}$,

$b_{23} = -\frac{K_2 \bar{V}(1+a\bar{V})}{(1+a\bar{V}+b\bar{I})^2}$ $b_{24} = -\frac{\beta_2 \bar{V}}{(1+\bar{W})^2}$,

$b_{31} = \frac{\beta_1 \bar{W}}{1+\bar{W}} + \frac{K_1 \bar{I}(1+b\bar{I})}{(1+a\bar{S}+b\bar{I})^2}$ $b_{32} = \frac{\beta_2 \bar{W}}{1+\bar{W}} + \frac{K_2 \bar{I}(1+b\bar{I})}{(1+a\bar{V}+b\bar{I})^2}$

$b_{33} = -\frac{bK_1 \bar{I}\bar{S}}{(1+a\bar{S}+b\bar{I})^2} - \frac{bK_2 \bar{I}\bar{V}}{(1+a\bar{V}+b\bar{I})^2} - \frac{\gamma\beta_1 \bar{S}}{d(1+\bar{W})} - \frac{\gamma\beta_2 \bar{V}}{d(1+\bar{W})}$ $b_{34} = \frac{\beta_1 \bar{S}+\beta_2 \bar{V}}{(1+\bar{W})^2}$

$b_{41} = b_{42} = 0$, $b_{43} = \gamma$ and $b_{44} = -d$

Now, from the theorem of Gerschgorin, the eigenvalues are in the following circles

$$|t - b_{11}| = |b_{13}| + |b_{14}|$$
$$|t - b_{22}| = |b_{21}| + |b_{23}| + |b_{24}|$$
$$|t - b_{33}| = |b_{31}| + |b_{32}| + |b_{34}|$$
$$|t - b_{44}| = |b_{41}| + |b_{42}| + |b_{43}|$$

If all the given conditions hold then

$$|b_{11}| < |b_{13}| + |b_{14}|$$
$$|b_{22}| < |b_{21}| + |b_{23}| + |b_{24}|$$
$$|b_{33}| < |b_{31}| + |b_{32}| + |b_{34}|$$
$$|b_{44}| < |b_{41}| + |b_{42}| + |b_{43}|$$

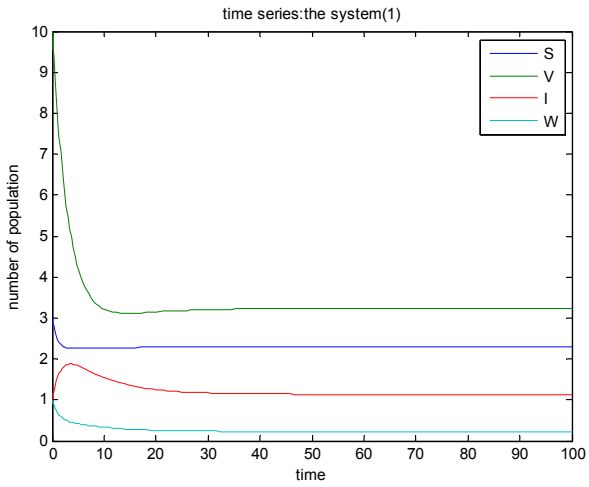
This means that all the eigenvalues are negative, and hence the non-trivial equilibrium is locally asymptotical stable.

5 Numerical Simulation

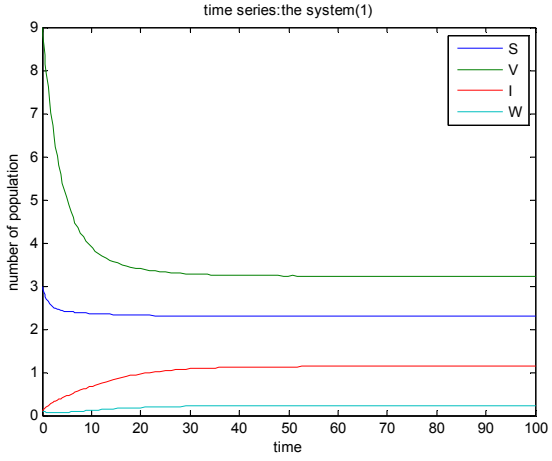
In this section, the dynamics of the system (1) is investigated numerically to confirm the analytical result and discuss the role of the vaccination coverage α and therapeutic coverage σ on the dynamical behavior of the system (1) for the following set of hypothetical, biologically feasible, set of parameters. The system (1) is solved numerically starting at different initial points as illustrated in (Fig. 1a, 1b).

$$\pi = 2, \mu = 0.3, a = 3, b = 4, k_1 = 0.9, k_2 = 0.5, \beta_1 = 0.2, \beta_2 = 0.1, d = 0.5, \gamma = 0.1$$

$$\alpha = 0.1, \sigma = 0.5$$



(a)



(b)

Fig. 1a, 1b. The solution of the system (1) approaches asymptotical the non-trivial equilibrium $(2.2995,\ 3.2315,\ 1.1357,\ 0.237\ 1)$ for the data given by eq (4) starting from two different initial points $(3, 10, 11)$ and $(3, 9, 0.1, 0.1)$

However, for the above set of data with $\alpha = 0.5, \sigma = 0.9$ then $R_0 < 1$ and system (1) approaches asymptotically to the disease free equilibrium $(1.6666,\ 4.999, 0, 0)$ as shown in Fig. 2.

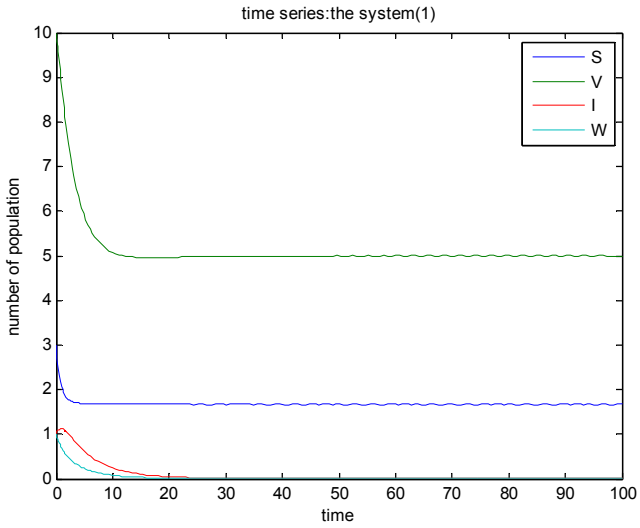


Fig. 2. System (1) approaches asymptotically to the disease free equilibrium (1.6666, 4.999, 0, 0) Starting from the initial point$(3, 10, 1, 1)$

6 Discussion and Conclusion

In this paper, a mathematical model for spreading disease through two ways of infectious disease that incorporates a preventive vaccine (Given to susceptible individuals) and a therapeutic drug regimen (administered to infected individuals). The uniqueness and bounded of solution of the model are discussed. The existence of all possible equilibrium is investigated. In addition the stability of the proposed model is performed. Moreover, in order to confirm our analyses results and specify which combination of parameters control the dynamical behavior of the system. Finally, numerical simulations are used for a biologically feasible set of hypothetical parameters. We have shown that if we increase the values of α *and* σ then the disease will be dying out.

Competing Interests

Authors have declared that no competing interests exist.

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