A MATHEMATICAL MODEL FOR HAV

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In this paper we present an SEITR epidemic model for HAV. We consider asymptotical stability in disease free equilibrium point. We prove that the other equilibrium point is not sign stable. We also prove that SEITR model has not any periodic orbit.

Keywords: Epidemic model, Hepatit, Disease free equilibrium point
MSC2010: 37C75, 37C35.

1. Introduction

In this paper we are going to present a model to describe the method of infection for the virus of hepatit of type A.
In this model we have five boxes, which are called susceptible, latent or exposed, infectious, treatment or vaccination and recover.
We know that in many infectious diseases there is an exposed period after transmission of infection from susceptible to potentially infective members. Moreover potential infected persons can transmit infection. If the exposed period is short, then we ignore potential infection in the model. In the infections with long exposed period this parameter can not be ignored.
In the case of vaccination before the beginning of an epidemic, we must consider both exposed period and the period of treatment. In HAV we accept with such situation. We know that forty percent of hepatitis viruses are of type A. Infectious hepatitis, which produce by one spices of entrovirus, with RNA jenom, from picornaviridae family. That's exposed period is approximately one month, and then jaundice significant will be appearance.
Ninety percent of children and fifteen to twenty five percent adults are infected without clinical significant. We often used murdered HAV vaccination for children and adults in the exposed period.
Also in dangerous thunder like hepatitits that may occur 1-3 per 1000 in infected persons by HAV, and it's mortality rate is about eighty percent.

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In this paper we consider an epidemiological model. We divide the population into five classes: susceptible, latent or exposed, infectious, treatment or vaccination and recovered. We denote their sizes by S, E, I, T and R respectively. We used of the abridgment $SEITR$. This model is an extension of the models presented in [2,3,4,5,6]. In SEITR model a susceptible individual first goes through exposed period after infection before becoming infectious. We also assume that a fraction δ of individuals in the infection period will use of treatment or vaccination.
In section 2, the $SEITR$ model and R_0 are formulated.
In section 3, we present a condition for asymptotical stability of the disease-free equilibrium Q_0 and a bifurcation point of the system.
The sign unstability of the endemic equilibrium Q_* is considered in section 4.
In section 5, we prove that there are only two equilibrium points for HAV.
The periodic orbit is considered in section 6.

2. **Model Formulation**

With the notation of the previous section the size $N(t)$ of the total population in time t for HAV consideration is: $S(t) + E(t) + I(t) + T(t) + R(t)$. We denote the transmission rate (per capita) by β. μ and λ are the natural mortality rate and the birth rate respectively. We denote the recovery rate in class I by α. Also we denote the rate of leaving exposed class by k.
In SEITR the fraction γ denotes per unit time of infected persons who are selected for treatment. Moreover we assume that the treatment reduces infections with the fraction δ. The treatment reduces the incidence of Hepatitis A by 90 percent We denote the rate of removal from the treated class by η.
f denotes the fraction of αI members who leaving the infected class at time t to the recovery class and the remaining fraction $(1 - f)$ die because of disease. Moreover we suppose that the fraction f_T of ηT members leaving the treatment class at time t. One must pay attention to this point that all the parameters are between zero and one. How could we write the differential system? We supposed that an average member of the population who makes contact to transmit infection at time t to the others is $\beta N(t)$ per unit time, where $N(t)$ represents the total population size. Since the probability of a random contact by an infective with a susceptible is $\frac{S(t)}{N(t)}$, then the number of new infections in unit time is $\beta N(t)\frac{S(t)}{N(t)}$, giving a rate of new infections who they are in the exposed class, i.e. $\beta N(t)\frac{S(t)}{N(t)}(I(t)+\delta T(t)) = \beta S(t)(I(t)+\delta T(t))$. So $\beta S(t)(I(t)+\delta T(t))$ is a rate of the people who leaving the class $S(t)$ at time t. Also we assume that all newborns are susceptible so a rate of new susceptible is $\lambda N(t)$ at time t. And $\mu S(t)$ is a rate of the individuals who leaving the population by death. So
$\dot{S} = -\beta S(I + \delta T) + \lambda N - \mu S.$
The rate $kE(t)$ of exposed individuals who infected will be entranced to the

class $I(t)$ at time t. So
$\dot{E} = \beta S(I + \delta T) - \mu E - kE$.
$\alpha I(t)$ denotes the rate of recovered infective people who entrance to the class $R(t)$ at time t and the rate $\mu I(t)$ of the population are going out of the population because of death. Also a rate $\gamma I(t)$ of infective people are going to the treatment class at time t. So
$\dot{I} = kE - (\alpha + \mu + \gamma)I$.
$\eta T(t)$ is the rate of the people, who they are received the treatment, and they will be recovered at time t. So
$\dot{T} = \gamma I - (\eta + \mu)T$.
A rate $\alpha f I(t)$ of infective people and a rate $\eta f_T T(t)$ of treatment individuals are recovered at time t. So
$\dot{R} = \alpha I f + \eta T f_T - \mu R$.
The rates $(1-f)\alpha I(t)$ and $(1-f_T)\eta T(t)$ of the population left the population by death. Hence $\dot{N} = -(1-f)\alpha I - (1-f_T)\eta T + \lambda N - \mu N$.
So we have the following mathematical model.

$$\begin{cases} \dot{S} = -\beta S(I + \delta T) + \lambda N - \mu S \\ \dot{E} = \beta S(I + \delta T) - \mu E - kE \\ \dot{I} = kE - (\alpha + \mu + \gamma)I \\ \dot{T} = \gamma I - (\eta + \mu)T \\ \dot{N} = -(1-f)\alpha I - (1-f_T)\eta T + \lambda N - \mu N \\ \dot{R} = \alpha I f + \eta T f_T - \mu R \end{cases} \tag{1.1}$$

The flow chart of SEITR model is:

$$\begin{array}{rcl} S \to E \to I & \to & R \\ & \downarrow & \\ & T & \to R \end{array}.$$

In order to calculate the basic reproduction number R_0, we assume that $S(0) = K = N(0)$. We know that an infected person in a totally susceptible population causes βK new infected people in unite time, and the mean time spent in the exposed compartment is $\frac{1}{k}$. Also the mean time spent in the infections compartment is $\frac{1}{\alpha+\gamma}$.
In addition, a fraction $\frac{\gamma}{\alpha+\gamma}$of infected persons are treated. While in the treatment stage the number of new infected person caused in unit time is $\delta\beta K$, and the mean time in the treatment class is $\frac{1}{\eta}$. So

$$R_0 = \frac{K\beta}{k} + \frac{K\beta}{\alpha+\gamma} + \frac{\gamma}{\alpha+\gamma}\frac{\delta\beta K}{\eta}.$$

3. Asymptotical Stability Analysis

From the biological consideration, the phase space of the model is:

$$T_0 = \{(S, E, I, T, N) : 0 \leq S + E + I + T \leq N\}.$$

Before an epidemic outbreak the point $Q_0 = (K, 0, 0, 0, K)$ is the disease free equilibrium point of the model, and it exists for all non negative values of the parameters.

Theorem 3.1. In the model (1.1) if $R_0 < 1$ then:
(a) If $\lambda < \mu$ and then disease free equilibrium Q_0 is locally asymptotically stable.
(b) If $\lambda = \mu$ then the disease free equilibrium Q_0 is unstable.
(c) If $\lambda > \mu$ then the disease free equilibrium Q_0 is locally stable but Q_0 is not locally asymptotically stable.
Proof.
(a) The linearization matrix of the system (1.1) at the equilibrium Q_0 is

$$\begin{pmatrix} -\mu & 0 & -\beta K & -\delta\beta K & \lambda \\ 0 & -(\mu+k) & \beta K & \delta\beta K & 0 \\ 0 & k & -(\alpha+\mu+\gamma) & 0 & 0 \\ 0 & 0 & \gamma & -(\mu+\eta) & 0 \\ 0 & 0 & -(1-f)\alpha & -(1-f_T)\eta & \lambda-\mu \end{pmatrix}$$

So its characteristic equation is:

$$(-\mu - \lambda')(\lambda - \mu - \lambda')(\lambda'^3 + a_1\lambda'^2 + a_2\lambda' + a_3) = 0,$$

where

$$a_1 = 3\mu + k + \alpha + \gamma + \eta.$$

$$a_2 = (\mu + \alpha + \gamma)(2\mu + \eta + k) + (\mu + k)(\mu + \eta) - k\beta K.$$

and

$$a_3 = (\mu + k)(\mu + \alpha + \gamma)(\mu + \eta) - k\beta K(\mu + \eta + \delta\gamma).$$

then by (i)
$a_3 > (\mu+k)(\mu+\alpha+\gamma)(\mu+\eta) + \beta K\eta(\alpha+\gamma) - k((\alpha+\gamma)\eta+\mu) \geq (\mu+k)(\mu+\alpha+\gamma)(\mu+\eta) + \beta K\eta(\alpha+\gamma) - k((\alpha+\gamma)+\mu) = (\mu+\alpha+\gamma)((\mu+k)(\mu+\eta) - k) + \beta K\eta(\alpha+\gamma)$.
So we only need to prove $(\mu+k)(\mu+\eta) - k \geq 0 \qquad (*)$.
If we consider the equation

$$\mu^2 + \mu(\eta + k) - k = 0.$$

then $\Delta = (k+\eta)^2 - 4k$. If $\Delta \leq 0$ then we have the relation (*). If $\Delta > 0$ then the two roots

$$\mu_1 = \frac{-(\eta+k) + \sqrt{(\eta+k)^2 - 4k}}{2},\ \mu_2 = \frac{-(\eta+k) - \sqrt{(\eta+k)^2 - 4k}}{2}$$

are negative. So we have the relation (*).
$R_0 < 1$ implies

$$(i)(\eta + \delta\gamma + \mu) < \frac{(\alpha+\gamma)\eta + \mu}{K\beta} - \frac{\eta(\alpha+\gamma)}{k}.$$

and

$$(ii)\beta K < k.$$

(i) and (ii) implies $a_1 a_2 > a_3 > 0$. by Hurwitz criterion, the disease free equilibrium Q_0 is locally asymptotically stable [4,5,6].
(b) Since in the matrix there is a zero eigenvalue. Then Q_0 is unstable.
(c) In the matrix all eigenvalues are nonzero. So Q_0 is locally stable. Since $\lambda - \mu > 0$, then the matrix has a positive eigenvalue. So Q_0 is not locally asymptotically stable. □
The other equilibrium point is $Q_* = (S_*, E_*, I_*, T_*, N_*)$ where

$$S_* = \frac{\lambda N_*}{\beta(I_* + \delta T_*) + \mu}.$$

$$E_* = \frac{\alpha+\mu+\gamma}{k}(\frac{\mu+\eta}{\gamma})T_*.$$

$$I_* = \frac{\mu+\eta}{\gamma}T_*.$$

$$N_* = \frac{(1-f)\alpha(\alpha+\mu+\gamma)(\mu+\eta) + (1-f_T)\eta\gamma k}{k\gamma(\lambda-\mu)}T_*.$$

$T_* = (\mu(\mu+k)(\alpha+\mu+\gamma)(\mu+\eta)(\lambda-\mu)/(k\frac{\beta(\eta+\mu+\delta\gamma)}{\gamma}[\lambda((1-f)\alpha(\frac{\mu+\eta}{\gamma}) + (1-f_T)\eta) - \frac{(\mu+k)(\alpha+\gamma+\mu)(\mu+\eta)(\lambda-\mu)}{k\gamma}])$.
This point is in the interior of the positive space if

$$\lambda > \mu$$

and

$$\lambda((1-f)\alpha(\frac{\mu+\eta}{\gamma}) + (1-f_T)\eta > \frac{(\mu+k)(\alpha+\mu+\gamma)(\eta+\mu)(\lambda-\mu)}{k\gamma}.$$

4. Sign Stability

When biological phenomena are modelled by differential equations the values of the parameters involved can often be determined only crudely with significant errors. If we have a square matrix at hand then it is important to know how much its stability depends on the actual values of the entries and how sensitive is it for variation of the entries.

Definition 4.1. An n by n square matrix $A = [a_{ij}]$ is said to be sign stable if every n by n square matrix $B = [b_{ij}]$ of the same sign pattern (i.e. signb_{ij} =signa_{ij} for all $i, j = 1, 2, ..., n$), is a stable matrix.

for an n by n matrix $A = [a_{ij}]$ we can obtain an undirected graph G_A whose vertex set is $V = \{1, 2, ..., n\}$ and edges are$\{(i, j) : i \neq j, a_{ij} \neq 0 \neq a_{ji}, i, j = 1, 2, ..., n\}$.
Also a directed graph D_A can also attache to A with the same vertex set and edges $\{(i, j) : i \neq j, a_{ij} \neq 0, i, j = 1, 2, ..., n\}$.
A k-cycle of D_A is a set of distinct edges of D_A of the form :

$$\{(i_1, i_2), (i_2, i_3), ..., (i_{k-1}, i_k), (i_k, i_1)\}.$$

Let $R_A = \{i : a_{ii} \neq 0\} \subseteq V$, which are the numbers for them the corresponding element in the main diagonal of the matrix is not zero. An R_A-coloring of G_A is a partition of its vertices into two sets, black and white (one of which may be empty). Such that each vertex in R_A is black, no black vertex has precisely one white neighbor, and each white vertex has at least one white neighbor. A $V - R_A$ complete matching is a set M of pairwise disjoint edges of G_A such that the set of vertices of the edges in M contains every vertex in $V - R_A$.
By applying this concepts we are now able to state the following theorem.

Theorem 4.1.[2] An n by n real matrix $A = [a_{ij}]$ is sign stable if it satisfies the following conditions:
(i) $a_{ij} \leq 0$ for all i, j,
(ii) $a_{ij}a_{ji} \leq 0$ for all $i \neq j$,
(iii) The directed graph D_A has no k-cycle for $k \geq 3$,
(iv) In every R_A-coloring of the undirected graph G_A all vertices are black, and
(v) The undirected graph G_A admits a $V - R_A$ complete matching.
The matrix of the linearize system (1.1) at the equilibrium Q_* is given by

$$A = \begin{pmatrix} -\beta(I_* + \delta T_*) - \mu & 0 & -\beta S_* & -\beta\delta S_* & \lambda \\ \beta(I_* + \delta T_*) & -\mu - k & \beta S_* & \beta\delta S_* & 0 \\ 0 & k & -(\alpha + \mu + \gamma) & 0 & 0 \\ 0 & 0 & \gamma & -(\mu + \eta) & 0 \\ 0 & 0 & -(1 - f)\alpha & -(1 - f_T)\eta & \lambda - \mu \end{pmatrix}.$$

The next theorem implies that in HAV model the equilibrium point in the time of epidemic is not sign stable. This is a good news because in the case of sign stability we can not pass from epidemic in a long period of time.
Theorem 4.2. If $\lambda > \mu$ then above matrix is not sign stable.
Proof. We only need to consider the following matrix.

$$\begin{pmatrix} -1 & 0 & -1 & -1 & 1 \\ 1 & -1 & 1 & 1 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & -1 & -1 & 1 \end{pmatrix}$$

Since $a_{55} > 0$ then theorem 4.1 implies that the matrix A is not sign stable.□

Corollary 4.1. The previous theorem also implies if the natural mortality rate is grater than the birth rate then this model is not stable.

5. Only Two Equilibrium Points for HAV

In this section we show that although there is another equilibrium point for (1.1), but this new equilibrium point can not happen for HAV. For this purpose we consider the following cases.
Case 1. If there are no disease deaths i.e. $f = f_T = 1$, then $\lambda = \mu$. So the birth rate and natural mortality rate are equal. Thus we fined the equilibrium point $Q_* = (S_*, E_*, I_*, T_*, N_*)$ where

$$T_* = \frac{-\mu\gamma}{\beta(\mu + \eta + \delta\gamma)}.$$

So $T_* < 0$. Since T_* is a natural number then we find a contradiction. So Q_* can not happen for HAV.
Case 2. If $\lambda = \mu$ (the birth rate and natural mortality rate are equal) then we can not find the other equilibrium point because if we setting the right side of equations equal zero then we obtain

$$I_* = \frac{-(1 - f_T)\eta T_*}{(1 - f)\alpha}.$$

So $I_* < 0$. We know that I_* must be nonnegative everywhere. Thus Q_* can not happen for HAV.
Case 3. If all of patients die because of the disease, then $f = f_T = 0$ so we find the equilibrium point

$Q_* = (S_*, E_*, I_*, T_*, N_*)$ where

$$I_* = \frac{\mu+\eta}{\gamma}T_*$$
$$E_* = \frac{(\alpha+\mu+\gamma)(\mu+\eta)}{k\gamma}T_*$$
$$S_* = \frac{\lambda N_*}{\beta(I_*+\delta T_*)+\mu}$$
$$N_* = \frac{\alpha I_* + \eta T_*}{\lambda-\mu}$$
$$T_* = \frac{\mu(\mu+k)(\alpha+\mu+\gamma)(\mu+\eta)}{k\gamma[\lambda(\frac{\mu+\eta}{\gamma}+\eta)-\frac{(\mu+k)(\alpha+\mu+\gamma)(\mu+\eta)}{k\gamma}]\frac{\beta(\eta+\mu+\delta\gamma)}{\gamma}}$$

Since $N_* > 0$, then $\lambda > \mu$, moreover $T_* > 0$, implies

$$f(\mu) = k\lambda\alpha(\mu+\eta)+k\gamma\lambda\eta-(\mu+k)(\alpha+\mu+\gamma)(\mu+\eta) = -\mu^3-\mu^2(\alpha+\eta+k+\gamma)$$

$$-\mu(k\alpha\lambda+\alpha\eta+k\alpha+k\eta+k\gamma+\gamma\eta)-k\eta\alpha-k\eta\gamma+k\eta\alpha\lambda+k\gamma\eta\lambda.$$

Since

$$f^{'}(\mu) = -3\mu^2-2\mu(\alpha+\eta+k+\gamma)-k\alpha(1+\lambda)-\eta\alpha-k\eta-k\gamma-\gamma\eta < 0.$$

then f is a decreasing function so $f(\mu) < f(0) < 0$, for all $\mu \geq 0$. Thus Q_* can not happen for HAV.

6. **The Contagious Illness Is not Periodic**

In this section we are going to prove a good news on HAV. In fact we proved that HAV is not a periodic epidemic. Let us recall the Stokes's theorem.
Theorem 6.1.(Stokes's theorem)[1] Let M be a compact, oriented k-dimensional manifold with boundary and let ω be a smooth $(k-1)$-form on M. Then

$$\int_{\partial M}\omega = \int_M d\omega$$

(here ∂M is endowed with the boundary orientation, as described above.)
We can use of this theorem to prove that the system (1.1)has no closed orbit.
Theorem 6.2. SEITR has no any closed orbit.
Proof. If there is a periodic orbit such as C with the period T then we take M as region of $R^6$with the boundary C. Let ω be the 5-form on M defined by

$\omega = (-\beta S(I+\delta T) + \lambda N - \mu S)dE \wedge dI \wedge dT \wedge dN \wedge dR - (\beta S(I+\delta T) - (\mu+k)E)dS \wedge dI \wedge dT \wedge dN \wedge dR + (kE - (\alpha+\mu+\gamma)I)dS \wedge dE \wedge dT \wedge dN \wedge dR - (\gamma I - (\mu+\eta)T)dS \wedge dE \wedge dI \wedge dN \wedge dR + (-(1-f)\alpha I - (1-f_T)\eta T + \lambda N - \mu N)dS \wedge dE \wedge dI \wedge dT \wedge dR - (\alpha I f + \eta T f_T - \mu R)dS \wedge dE \wedge dI \wedge dT \wedge dN.$

Then

$$d\omega = (-\beta(I+\delta T) - 6\mu - \alpha - k - \gamma - \eta + \lambda)dS \wedge dE \wedge dI \wedge dT \wedge dN \wedge dR.$$

So

$$\int_M d\omega < 0$$

and

$$\int_{\partial M=C} \omega = 0$$

But Stokes's theorem[1] implies

$$\int_M d\omega = \int_{\partial M} \omega.$$

So $0 < 0$ which is a contradiction. Thus SEITR has no any periodic orbit..

7. **Conclusion**

In this paper, we discuss the $SEITR$ model for HAV. We derive a basic reproduction number R_0 and it determines the asymptotical stability of a stationary point (1.1); if $R_0 < 1$ then we show that a unique disease free equilibrium point Q_0 is asymptotically stable in the interior of the feasible region T_0, which we considered in section 3. We also find another stationary point Q_* which is not sign stable. The consideration of the stability of this point can be a topic for further research. Observational experience implies that this point should not be stable.

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