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Advances in Applied Science Research, 2012, 3 (5):3200-3205

ISSN: 0976-8610
CODEN (USA): AASRFC

A Model for Hepatitis C with Saturated Chronic infection rate

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ABSTRACT

Dynamics of an SEI model with acute and chronic stages were studied with mass action incidence by Yuan and Yang [11]. They formulated and analyzed it especially for the case of Hepatitis C virus. A reinvestigation of this model is presented in this paper to study the stability with a general nonlinear incidence rate in chronic stage. Basic Reproduction number R_0 has been obtained. When $R_0 < 1$, the disease free equilibrium point is globally stable. In case $R_0 > 1$, there exist endemic equilibrium, for which stability is also discussed.

Key Words: Hepatitis C, Epidemiology, Reproduction number, Stability,

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INTRODUCTION

Hepatitis C has been characterized as a disease by a long chronic stage. It is a viral infection of the liver which was first recognized as a separate disease in 1975 and was previously referred to as 'non A - non B' hepatitis. The most common symptom of acute hepatitis is fatigue and jaundice. However, the diagnosis of hepatitis C is difficult due to the fact that vast majority of cases are asymptomatic. That's why this is called 'the silent epidemic' [17]. R Colina and C. Aazmbuja [13] analyzed the evidence of the increasing diversification of Hepatitis C. As there is no evidence for partial or temporary immunity, the models prepared are with consideration that the treated or recovered individuals come back to the susceptible class. Several studies are there for the treatment of epidemics with different kind of incidence rates which measures the transfer rate of susceptible to get infected [3,8,16,19,20]. Bilinear and standard incidence rates have been frequently used in classical epidemic models [7]. Simple dynamics of these models seem related to such functions. Several different incidence rates have been proposed by researchers in epidemic models. Different models for mutually intersecting species are also studied [12,14]. A model of prey-predator with a generalized transmission function for unsaturated zone has been analyzed by Mehta et al. [6]. Capasso and Serio [18] introduced saturated incidence rate g (I)S into epidemic models. This is important because the number of effective contacts between infective individuals and susceptible individuals may saturate at high infective levels due to crowding of infective individuals or due to protection measures by the susceptible individuals. Non linear incidence rates of the form $\beta I^p S^q$ were investigated by Liu et. al. [20,21] A very general form of non linear incidence rate was considered by Derrick and Driessche [23]. For acute and chronic states, very few investigations have been appeared. Yuan and Yang [11] studied it with mass action incidence. Global analysis of an epidemic model with acute and chronic stages is proposed and analyzed by Luo and Xiang [5]. In another recent contribution the dynamical behavior of an SEI model is investigated by Luo and Xiao [4]. They have assumed that acutely infected mass has the inhibition effect of the susceptible individuals. Since the chronic stage lasts for a longer period, it must be responsible for this change. In the present paper we have reinvestigated the Model of Yuan and Yang [11] with saturated incidence rate in the chronic stage.

2. The Mathematical Model:

Using the symbols, notations and basic assumptions of [10], the model we consider for reinvestigation can be expressed as:

$$\frac{dS}{dt} = bN - \beta I\frac{S}{N} - \frac{\gamma V}{(1+\alpha_1 V)}\frac{S}{N} - dS + \alpha V$$

$$\frac{dE}{dt} = \beta I\frac{S}{N} + \frac{\gamma V}{(1+\alpha_1 V)}\frac{S}{N} - dE - \varepsilon E$$

$$\frac{dI}{dt} = \varepsilon E - (d+k)I$$

$$\frac{dV}{dt} = kI - (d+\alpha)V \qquad (2.1)$$

and for the total population

$$\frac{dN}{dt} = (b-d)N$$

We consider the case b=d which implies that the population is stationary.

Setting N=1 and again using capital letters for the compartments, we get the system as follows:

$$\frac{dS}{dt} = b(1-S) - (\beta I + \frac{\gamma V}{1+\alpha_1 V})S + \alpha V$$

$$\frac{dE}{dt} = (\beta I + \frac{\gamma V}{(1+\alpha_1 V)})S - (b+\varepsilon)E$$

$$\frac{dI}{dt} = \varepsilon E - (b+k)I$$

$$\frac{dV}{dt} = kI - (b+\alpha)V$$

With initial conditions $S(0) = S_0, E(0) = E_0, I(0) = I_0, V(0) = V_0$

As S+E+I+V=1, replacing E=1-S-I-V and ignoring dE/dt ,we get the reduced system

$$\frac{dS}{dt} = b(1-S) - (\beta I + \frac{\gamma V}{1+\alpha_1 V})S + \alpha V$$

$$\frac{dI}{dt} = \varepsilon(1-S-I-V) - (b+k)I$$

$$\frac{dV}{dt} = kI - (b+\alpha)V \qquad (2.2)$$

Set Z={(S,I,V) € R^3 : S≥0, I≥0, V≥0 and S+I+V ≤ 1}. Clearly the set Z is an invariable set.

3. Equilibrium points and stability:

The system (2.2) has a disease free equilibrium point P_0 (1, 0, 0) and if the basic reproduction number R_0 is >1, an endemic equilibrium point P* (S*, I*, V*) exists where

$$S^* = 1 - \frac{[(b+k)(b+\alpha+\varepsilon)+\varepsilon\alpha]\,I^*}{\varepsilon(b+\alpha)}, \quad V^* = \frac{k}{b+\alpha}I^*$$

and I* is a positive root of the quadratic equation :

$$\beta\alpha_1 k\frac{[(b+k)(b+\alpha+\varepsilon)+\varepsilon\alpha]}{(b+\alpha)}I^2+[\frac{[(b+k)(b+\alpha+\varepsilon)+\varepsilon\alpha]}{(b+\alpha)}\{\beta(b+\alpha)+\gamma k\}+(b+k)(b+\varepsilon)\alpha_1 k-\beta\varepsilon\alpha_1 k]I$$
$$+(b+k)(b+\varepsilon)(b+\alpha)-\varepsilon(\beta(b+\alpha)+\gamma k)=0 \quad (3.1)$$

which has been obtained by setting the time derivatives of (2.2) equal to zero. Here the basic reproduction number R_0 is defined as

$$R_0=\frac{\varepsilon[\beta(b+\alpha)+k\gamma]}{(b+\alpha)(\varepsilon+b)(b+k)}=\frac{\beta\varepsilon}{(\varepsilon+b)(b+k)}+\frac{k\varepsilon\gamma}{(b+\alpha)(\varepsilon+b)(b+k)}$$

The first tem in the sum represents a contribution to the reproduction number due to secondary infections generated by an infective with acute hepatitis C.

4. Dynamical behavior:

The variation matrix of the system at the disease free equilibrium point is

$$J_0=\begin{pmatrix}-b & -\beta & -\gamma+\alpha\\ -\varepsilon & -(\varepsilon+b+k) & -\varepsilon\\ 0 & k & -(b+\alpha)\end{pmatrix}$$

The characteristic equation of it can be written as

$\lambda^3+A\lambda^2+B\lambda+C=0$ where

$A=(\alpha+3b+\varepsilon+k),$

$B=[(\alpha+b)(2b+\varepsilon+k)+(k+b)(\varepsilon+b)-\beta\varepsilon]$

$C=(\alpha+b)(k+b)(\varepsilon+b)-\varepsilon\{\beta(\alpha+b)+k\gamma\}$

Here A > 0 is obvious. When $R_0 < 1$, then C>0 which further implies

$(\alpha+b)(k+b)(\varepsilon+b)-\varepsilon\beta(\alpha+b)>0$ i.e. $(k+b)(\varepsilon+b)-\varepsilon\beta>0$

Hence B > 0. Now we calculate AB-C:

$$AB-C$$
$$=(\alpha+3b+\varepsilon+k)[(\alpha+b)(2b+\varepsilon+k)+(k+b)(\varepsilon+b)-\beta\varepsilon]-[(\alpha+b)(k+b)(\varepsilon+b)-\varepsilon\{\beta(\alpha+b)+k\gamma\}]$$

After simple algebraic calculations it reduces to

$$[(\alpha+3b+\varepsilon+k)(\alpha+b)(2b+\varepsilon+k)+\varepsilon k\gamma]+(2b+\varepsilon+k)[(k+b)(\varepsilon+b)-\beta\varepsilon]$$

which is > 0 as the last bracket is positive in case R_0 is < 1.

Hence by the Routh – Herwitz theorem the disease free equilibrium point is locally stable for $R_0 < 1$.

Lemma 4.1 (see [10]). Assuming $f : [0,\infty) \to R$ is bounded, $k \in L^1(0,\infty)$, then

$$\limsup_{t\to\infty}\left|\int_0^t k(\theta)f(t-\theta)d\theta\right| \le |f|^{\infty}\|k\|_{L^1(0,\infty)}, \text{ where } |f|^{\infty}=\limsup_{t\to\infty}|f(t)|$$

Theorem 4.2. When $R_0 <1$, the disease-free equilibrium $P_0(1, 0, 0)$ is globally stable.

Proof. Since **,** When $R_0 < 1$ the point P_0 is locally stable, it is sufficient to show that P_0 is attractive globally for $R_0 <1$. We note that the global attractiveness of P_0 is equivalent to that of the disease-free equilibrium (1, 0, 0, 0) of system (2.2).

The second equation of (2.2) yields

$$\frac{dE}{dt} \le (\beta I + \frac{\gamma V}{(1+\alpha_1 V)}) - (b+\varepsilon)E$$

First, we solve the comparative equation

$\frac{dx}{dt} \le (\beta I + \frac{\gamma V}{(1+\alpha_1 V)}) - (b+\varepsilon)x$, which gives

$$x(t) = E_0\, x^{-(b+\varepsilon)t} + \int_0^t (\beta I + \frac{\gamma V}{(1+\alpha_1 V)}) x^{-(b+\varepsilon)(t-S)} dS$$

By the comparative principle, we have

$$\limsup_{t\to\infty} E(t) \le \limsup_{t\to\infty} \int_0^t [\beta I(t-S) + \frac{\gamma V(t-S)}{(1+\alpha_1 V(t-S))}] e^{-(b+\varepsilon)S} dS \tag{4.1}$$

From Lemma 4.1 we have

$$\limsup_{t\to\infty} E(t) \le [\beta \limsup_{t\to\infty} [I(t) + \gamma \limsup_{t\to\infty} V(t)] \int_0^\infty e^{-(b+\varepsilon)S} dS$$

$$\Rightarrow \limsup_{t\to\infty} E(t) \le \frac{\beta}{\varepsilon+b} \limsup_{t\to\infty} I(t) + \frac{\gamma}{\varepsilon+b} \limsup_{t\to\infty} V(t)] \tag{4.2}$$

By the last equation of (2.2), we have

$$v(t) = E^{-(b+\alpha)t} V_0 + k \int_0^t e^{-(b+\alpha)S} I(t-S) dS,$$

Therefore, $\limsup_{t\to\infty} V(t) \le k \limsup_{t\to\infty} I(t) \int_0^\infty E^{-(b+\alpha)S} dS$

$$= \frac{k}{b+\alpha} \limsup_{t\to\infty} I(t) \tag{4.3}$$

By Substituting lim sup $_{t\to\infty}$ E(t) of inequality (4.2) for the right side of the inequality (4.3), we get

$$\limsup_{t\to\infty} E(t) \le \frac{\beta}{\varepsilon+b} \limsup_{t\to\infty} I(t) + \frac{\gamma k}{(\varepsilon+b)(b+\alpha)} \limsup_{t\to\infty} I(t) \tag{4.4}$$

By the second equation of (2.2), we obtain

$I(t) = I_0 e^{-(k+b)S} + \varepsilon \int_0^t E(S) e^{-(k+b)(t-S)} dS$ Therefore,

$$\limsup_{t\to\infty} I(t) \le \frac{\beta}{k+b} \limsup_{t\to\infty} E(t) \tag{4.5}$$

By (4.4), we have

$$\limsup_{t\to\infty} E(t) \le [\frac{\beta\varepsilon}{(\varepsilon+b)(k+b)} \limsup_{t\to\infty} I(t) + \frac{\varepsilon\gamma k}{(\varepsilon+b)(b+\alpha)(b+k)}] \limsup_{t\to\infty} E(t) = R_0 \limsup_{t\to\infty} E(t)$$

(4.6)

By the inequality (4.6) and by $R_0 < 1$, we have

$\limsup_{t\to\infty} E(t) = 0$ and so $\lim_{t\to\infty} E(t) = 0$

By (4.3) and (4.5) we have

$$\lim_{t\to\infty} I(t) = 0 \text{ and so } \lim_{t\to\infty} V(t) = 0$$

Therefore, From S(t)+E(t)+I(t)+V(t) =1, it follows that lim $_{t\to\infty}$ S(t)=1.

Hence when R_0 <1, the disease-free equilibrium P_0 (1, 0, 0) is globally stable.

When $R_0 > 1$, $C = (\alpha+b)(k+b)(\varepsilon+b) - \varepsilon\{\beta(\alpha+b)+k\gamma\} < 0$, therefore the disease free equilibrium point is unstable. In case $R_0 > 1$, to see the stability of the endemic point, we find the variation matrix at the endemic point P*(S*, I*, V*)

$$J^* = \begin{pmatrix} -b-\beta I^* - \dfrac{\gamma V^*}{1+\alpha_1 V^*} & -\beta S & -\dfrac{\gamma S^*}{(1+\alpha_1 V^*)^2} + \alpha \\ -\varepsilon & -(\varepsilon+b+k) & -\varepsilon \\ 0 & k & -(b+\alpha) \end{pmatrix}$$

The characteristic equation of the matrix J* is

$$(-b-\beta I^* - \frac{\gamma V^*}{1+\alpha_1 V^*} - \lambda)[(b+\alpha+\lambda)(\varepsilon+b+k+\lambda)+\varepsilon k] + \varepsilon[(b+\alpha+\lambda)\beta S^* + \frac{\gamma k S^*}{(1+\alpha_1 V^*)^2} + -\alpha k] = 0$$

On simplifying we get this equation as

$\lambda^3 + E\lambda^2 + F\lambda + G = 0$ where

$$E = \beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*} + (\alpha+\varepsilon+3b+k) > 0$$

$$F = (\alpha+b)(\beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*} + \varepsilon + 2b + k) + (\beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*} + b)(b+\varepsilon+k) - \varepsilon\beta S^* + k\varepsilon$$

$$G = (\alpha+b)[(\beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*} + b)(b+\varepsilon+k) - \varepsilon\beta S^*] + \varepsilon k[(\alpha+b) + \beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*} - \frac{\gamma S^*}{(1+\alpha_1 V^*)^2}]$$

Note that the value of G can be rearranged as

$$G = (\alpha+b)\{b(b+\varepsilon+k)+\varepsilon k\} + (\beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*})\{(\alpha+b)(b+\varepsilon+k)+\varepsilon k\} - \varepsilon S^*\{\beta(\alpha+b) + \frac{k\gamma}{(1+\alpha_1 V^*)^2}\}$$

$$= (\alpha+b)(k+b)(b+\varepsilon) + (\beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*})\{(\alpha+b)(b+\varepsilon+k)+\varepsilon k\} - \varepsilon S^*\{\beta(\alpha+b) + \frac{k\gamma}{(1+\alpha_1 V^*)^2}\}$$

$$= (\beta I^* + \frac{\gamma V^*}{1+\alpha_1 V^*})\{(\alpha+b)(b+\varepsilon+k)+\varepsilon k\} + [(\alpha+b)(k+b)(b+\varepsilon) - \varepsilon S^*\{\beta(\alpha+b) + \frac{k\gamma}{(1+\alpha_1 V^*)^2}\}] \text{ In}$$

this sum, if S*< $1/R_0$, the factor $[(\alpha+b)(k+b)(b+\varepsilon) - \varepsilon S^*\{\beta(\alpha+b) + \dfrac{k\gamma}{(1+\alpha_1 V^*)^2}\}]$ is positive and so is G. Thus we conclude the above in the following theorem.

Theorem 4.3: When $R_0 > 1$, the endemic equilibrium point P*(S*, I*, V*) is a stable node or focus when G > 0 and EF-G > 0. P* is unstable node or focus when G < 0 or EF-G < 0. P* is center of the linear system if EF-G =0.

Acknowledgement

We are very grateful to Dr. B.K. Joshi, Retired professor, Govt. Engineering College, UJJAIN for useful guidance and help in the preparation of this paper.

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