Sahand Communications in Mathematical Analysis (SCMA) Vol. 3 No. 2 (2016), 1-11
http://scma.maragheh.ac.ir

THE ANALYSIS OF A DISEASE-FREE EQUILIBRIUM OF HEPATITIS B MODEL

REZA AKBARI[1*], ALI VAHIDIAN KAMYAD[2], ALI AKBAR HEYDARI[3], AND AGHILEH HEYDARI[4]

Abstract. In this paper we study the dynamics of Hepatitis B virus (HBV) infection under administration of a vaccine and treatment, where the disease is transmitted directly from the parents to the offspring and also through contact with infective individuals. Stability of the disease-free steady state is investigated. The basic reproductive rate, R_0, is derived. The results show that the dynamics of the model is completely determined by the basic reproductive number R_0. If $R_0 < 1$, the disease-free equilibrium is globally stable and the disease always dies out and if $R_0 > 1$, the disease-free equilibrium is unstable and the disease is uniformly persistent.

1. Introduction

Hepatitis B is an enormous challenge to global public health and it is caused by the hepatitis B virus (HBV). HBV can be transmitted by sexual contact, through the skin, by inoculation with contaminated blood or blood products, by transplantation of organs from infected donors, and perinatally from infected mothers. Chronic HBV infections is remained as a major public health problem worldwide. According to World Health Organization, an estimation of 2 billion people worldwide have been infected with the virus and about 350 million are carrying HBV, with HBV being responsible for approximately 600,000 deaths each year. Because of the high risk for HBV infection and large number of deaths associated with it, it is imperative to increase our understanding of HBV disease dynamics.

2010 *Mathematics Subject Classification.* 34D23, 37C75.
Key words and phrases. Hepatitis B virus (HBV), Basic reproduction number (R_0), Compound matrices, Disease-Free equilibrium state, Global stability.
Received: 21 September 2015, Accepted: 21 December 2015.
* Corresponding author.

One of the primary reasons for studying hepatitis B virus (HBV) infection is to improve control and finally to put down the infection from the population. Mathematical models can help us to gain insights into the disease transmission, assess the effectiveness of various preventive strategies, and then control of it eventually.

Anderson and May [1] used a simple mathematical model to illustrate the effects of carriers on the transmission of HBV. A hepatitis B mathematical model [13] was used to develop a strategy for eliminating HBV in New Zealand [12, 19]. Zou et al [24] also proposed a mathematical model to understand the transmission dynamics and prevalence of HBV in mainland of China. Pang et al [16] developed a model to explore the impact of vaccination and other controlling measures of HBV infection.

In this paper, we study the dynamics of hepatitis B virus (HBV) infection under administration of vaccination and treatment, where HBV infection is transmitted in two ways through vertical transmission and horizontal transmission. While the horizontal transmission is reduced through the administration of vaccination to those susceptible, the vertical transmission is reduced through the administration of treatment to infected individuals; therefore, the vaccine and the treatment play different roles in controlling the HBV [2]. In this study, we present a complete mathematical analysis for the global stability problem at the disease-free equilibrium of a mathematical model for hepatitis B virus infection with two controls: vaccination and treatment, and we assume that the control parameters $u_1(t)$ and $u_2(t)$ are constant functions. In order to study the global stability of the disease-free equilibrium, we apply the approach in Kamgang and Sallet [7, 16]. We obtain simple sufficient conditions that the disease free equilibrium is globally asymptotically stable.

The rest of the paper is organized as follows: In Section 2, we proposed an HBV infection model with vaccination and treatment. In Section 3, the basic reproductive rate, R_0, is derived. In Section 4, we analyze the local stability and global stability of the disease-free equilibrium. Finally, the conclusions are summarized in Section 5.

2. Description of the model

In this section, we present the mathematical formulation of the compartmental model of hepatitis B, which consists of a system of differential equations [8]. The model is based on the characteristics of HBV transmission. We divide the total population into five compartments, that are the susceptible individuals S(t); infected but not yet infectious individuals (exposed) E(t); acute infection individuals I(t); chronic HBV carriers C(t); and recovered R(t) for Hepatitis B virus (HBV) infection

that propagates through contact between the infected and the susceptible individuals and also through of infected parents. The flow diagram (Figure1) and the system are given in the following [8]:

$$
\begin{aligned}
\dot{S}(t) &= \nu - \nu p_1 C - \nu p_2 R - \rho(I+\theta C)S - \nu S - u_1 S + \lambda_4 R,\\
\dot{E}(t) &= \rho(I+\theta C)S - (\nu+\lambda_1)E,\\
\dot{I}(t) &= \lambda_1 E - (\nu+\lambda_2)I,\\
\dot{C}(t) &= \nu p_1 C + p_3\lambda_2 I - (\nu+\lambda_3)C - u_2 C,\\
\dot{R}(t) &= \nu p_2 R + (1-p_3)\lambda_2 I + \lambda_3 C - \nu R - \lambda_4 R + u_1 S + u_2 C.
\end{aligned} \tag{2.1}
$$

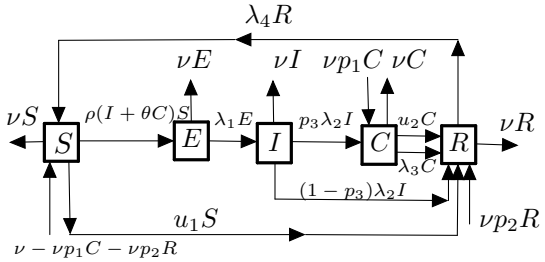

FIGURE 1. Diagram for the HBV dynamics with two controls

In these equations, all the parameters are nonnegative. The main parameters are listed in Table 1.

TABLE 1. Definition of parameters used in system (2.1)

Parameter	Description
ν	Birth (and death) rate
ρ	Transmission rate
θ	Infectiousness of carriers relative to acute infections
λ_1	Rate moving from exposed to acute
λ_2	Rate at which individuals leave the acute infection class
λ_3	Rate moving from carrier to recovery
λ_4	Loss of recovery rate
p_1	Probability of infected newborns
p_2	Probability of immune newborns
p_3	Proportion of acute infection individuals become carriers
u_1	Proportion of the susceptible that is vaccinated per unit time
u_2	Proportion of the chronic HBV carriers that is treated per unit time

For simplicity, we normalize the population size to 1; i.e. now S, E, I, C and R are, respectively, the fraction of the susceptible, the exposed, the acute infective, the carriers and the recovered individuals in the population and $S+E+I+C+R=1$ holds [8, 16]. Hence, the fifth

equation may be omitted, and the Eq. (2.1) becomes:

$$\begin{aligned}
\dot{S}(t) &= \nu - \nu p_1 C - \rho(I + \theta C)S - \nu S - u_1 S, \\
&\quad + (\lambda_4 - \nu p_2)(1 - S - E - I - C), \\
\dot{E}(t) &= \rho(I + \theta C)S - (\nu + \lambda_1)E, \\
\dot{I}(t) &= \lambda_1 E - (\nu + \lambda_2)I, \\
\dot{C}(t) &= \nu p_1 C + p_3 \lambda_2 I - (\nu + \lambda_3)C - u_2 C.
\end{aligned} \tag{2.2}$$

Let

$$X(t) = S(t) + C(t) + I(t) + C(t),$$

then,

$$S + E + I + C \leq \frac{\nu + \lambda_4}{\nu + \lambda_4 - \nu p_2},$$

and

$$S \leq \frac{\nu + \lambda_4}{\nu + \lambda_4 + u_1 - \nu p_2},$$

So,

$$\Pi = \left\{ (S, E, I, C) \in \mathbb{R}^4_+ \mid S \leq \frac{\nu + \lambda_4}{\nu + u_1 + \lambda_4 - \nu p_2}, \quad S + E + I + C \leq \frac{\nu + \lambda_4}{\nu + \lambda_4 - \nu p_2} \right\},$$

is positively invariant [8]. Hence, the system is mathematically well-posed. There, for initial starting point $x \in \mathbb{R}^4_+$, the trajectory lies in Π. Therefore, we shall focus our attention only in the region Π.

3. Disease-free equilibrium point and Basic reproduction number

In this section, we assume that the control parameters $u_1(t)$ and $u_2(t)$ are constant functions. Model given by system (2.2) has a unique disease-free equilibrium, obtained by setting the right-hand sides of system (2.2) to zero. Disease-free equilibrium point $E_0 = (S_0, 0, 0, 0)$, where

$$S_0 = \frac{\nu - \nu p_2 + \lambda_4}{u_1 + \nu + \lambda_4 - \nu p_2},$$

is always feasible. In the absence of vaccination, this is reduced to the equilibrium $(1, 0, 0, 0)$.

Definition 3.1 ([20])**.** The basic reproduction number, denoted R_0, is the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual.

Using the notation in Van den Driessche and Watmough [20], we have

$$\mathbf{F} = \begin{bmatrix} 0 & \rho S_0 & \rho\theta S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

$$\mathbf{V} = \begin{bmatrix} \nu + \lambda_1 & 0 & 0 \\ -\lambda_1 & \nu + \lambda 2 & 0 \\ 0 & -p_3\lambda_2 & \nu + \lambda_3 + u_2 - \nu p_1 \end{bmatrix}.$$

The reproduction number is given by $\rho(FV^{-1})$, and

$$R_0 = \rho(FV^{-1}) \tag{3.1}$$

$$= \frac{\rho\lambda_1(\nu + \lambda_3 + u_2 - p_1\nu + \theta p_3\lambda_2)}{(\nu + \lambda_1)(\nu + \lambda_2)(\nu + \lambda_3 + u_2 - p_1\nu)} S_0. \tag{3.2}$$

Remark 3.2. We should note from (3.1) that the use of both vaccine and treatment controls to reduce the value of R_0, and at the same time effects of both intervention strategies on R_0 are not simply the addition of two independent effects, rather they multiply together in order to improve overall effects of population level independently.

4. Stability analysis

Firstly, we analyze the local stability of the disease-free equilibrium.

Theorem 4.1. *If $R_0 < 1$, then the disease-free equilibrium is locally asymptotically stable.*

Proof. The Jacobian matrix of system (2.2) at the disease-free equilibrium is

$$\mathbf{J_0} = \begin{bmatrix} -(\nu + \lambda_4 - \nu p_2 + u_1) & -(\lambda_4 - \nu p_2) & -(\rho S_0 + \lambda_4 - \nu p_2) & -(\nu p_1 + \lambda_4 - \nu p_2 + \theta\rho S_0) \\ 0 & -(\nu + \lambda_1) & \rho S_0 & \theta\rho S_0 \\ 0 & \lambda_1 & -(\nu + \lambda_2) & 0 \\ 0 & 0 & p_3\lambda_2 & \nu p_1 - \nu - \lambda_3 - u_2 \end{bmatrix}.$$

The characteristic polynomial of J_0 given by

$$P(\lambda) = [\lambda + l_0][\lambda^3 + l_1\lambda^2 + l_2\lambda + l_3].$$

where

$$\begin{aligned} l_0 &= \nu + u_1 + \lambda_4 - \nu p_2, \\ l_1 &= 3\nu + \lambda_1 + \lambda_2 + \lambda_3 + u_2 - \nu p_1, \\ l_2 &= (\nu + \lambda_2)(\nu + \lambda_3 + u_2 - \nu p_1) + (\nu + \lambda_1)(2\nu + \lambda_2 + \lambda_3 + u_2 - \nu p_1) - \lambda_1\rho S_0, \\ l_3 &= (\nu + \lambda_1)(\nu + \lambda_2)(\nu + \lambda_3 + u_2 - \nu p_1) - \lambda_1\rho S_0(\nu + \lambda_3 + u_2 + \theta p_3\lambda_2 - \nu p_1). \end{aligned}$$

We need to verify the following two conditions:

a. $l_0,\ l_1,\ l_2,\ l_3 > 0$,
b. $l_1 l_2 - l_3 > 0$.

It is easy to see that $l_0,\ l_1 > 0$ and $l_2,\ l_3,\ l_1 l_2 - l_3 > 0$ if $R_0 < 1$. It follows from the Routh-Hurwitz criterion that the eigenvalues have negative real parts if $R_0 < 1$. Hence, the disease-free equilibrium of model (2.2) is local asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

□

Now, we study the global properties of the disease-free equilibrium. The following theorem provides the global property of the disease-free equilibrium. In order to study the global stability of the disease-free equilibrium, we apply the novel approach in Kamgang and Sallet [7, 16].

Definition 4.2 ([7])**.** We call any real square matrix with nonnegative off-diagonal entries a Metzler matrix.

Lemma 4.3. *Let M be a Metzler matrix, which is block decomposed:*

$$\mathbf{M} = \begin{bmatrix} A & B \\ C & D \end{bmatrix},$$

where A and D are square matrices. Then, M is Metzler stable if and only if A and $D - CA^{-1}B$ are Metzler stable.

Proof. see [7] p 3. □

Definition 4.4 (Regular splitting [7])**.** For a real Metzler matrix M, $M = K + N$ is a regular splitting if K is a Metzler stable matrix and $N \geq 0$ is a nonnegative matrix.

Lemma 4.5 ([7])**.** *Let $M = K+N$ be a regular splitting of a real Metzler matrix M, then, M is Metzler stable if and only if $\rho(-NA^{-1}) < 1$.*

Proof. see [7] p 4. □

Lemma 4.6. *If the following hypotheses $(i-v)$ are satisfied, the disease-free equilibrium (DFE) is globally asymptotically stable for system*

$$\begin{cases} \dot{X}_1 = A_1(X)(X_1 - X_1^*) + A_{12}(X)X_2, \\ \dot{X}_2 = A_2(X)X_2, \end{cases} \tag{4.1}$$

on the positively invariant set $\Omega \in R_+^{n_1+n_2}$ where $X_1 \in R_+^{n_1}$, $X_2 \in R_+^{n_2}$, $X = (X_1, X_2)$, and $X^* = (X_1^*, 0)$ denotes a disease-free equilibrium (DFE) of the system (4.1). The variable X_1 denotes the numbers (or densities) in the different compartments of susceptibles, immunes, recovered individuals etc., in other words all the individuals who are not infected and who are not transmitting the disease (e.g., quarantined). The variable X_2 denotes the numbers (or densities) of infected individuals; i.e., latent, infectious, carrying individuals and so on.

i. *The system is defined on a positively invariant set Ω of the nonnegative orthant. The system is dissipative on Ω.*

ii. *The sub-system:*

$$\dot{X}_1 = A_1(X_1, 0)(X_1 - X_1^*),$$

is globally asymptotically stable at the equilibrium X_1^* *on the canonical projection of* Ω *on* $R_+^{n_1}$.

iii. *The matrix* $A_2(X)$ *is Metzler and irreducible for any given* $X \in \Omega$.

iv. *There exists an upper-bound matrix* $\overline{A_2}$ *for*

$$\Lambda = \{A_2(X) : X \in \Omega\},$$

with the property that either $\overline{A_2} \notin \Lambda$ *or if* $\overline{A_2} \in \Lambda$ *(i.e.,* $\overline{A_2} = \max_\Omega \Lambda$*) then for any* $\overline{X} \in \Omega$*, such that* $\overline{A_2} = A_2(\overline{X})$*,* $\overline{X} \in R_+^{n_1} \times \{0\}$ *(i.e. the points where the maximum is realized are contained in the disease-free sub-manifold).*

v. $\alpha(\overline{A_2}) \leq 0$*, where* $\alpha(\overline{A_2})$ *is spectral bound of* $\overline{A_2}$.

Proof. see [7] p 5. □

Now, we have the following theorem for the global stability of the disease-free equilibrium of system (2.2).

Theorem 4.7. *For the model* (2.2)*, the disease-free equilibrium is globally asymptotically stable if* $R_0 \leq 1$.

Proof. In order to prove the theorem and get the global asymptotic stability when $R_0 \leq 1$, we apply the lemma (4.6) and we have:

i. We put $X_1 = S$, $X_2 = (E, I, C)$ and $X = (S, E, I, C) = (X_1, X_2)$ according to [8]. The invariant domain Π is obviously a positively compact set.

ii. We put $P_0 = X^* = (X_1^*, 0)$, then

$$A_1(X) = -(\nu + u_1 + \lambda_4 - \nu p_2),$$

$$A_{12}(X) = \left[\; -\lambda_4 + \nu p_2, \quad -\rho S - \lambda_4 + \nu p_2, \quad -\rho\theta S - \lambda_4 - \nu p_1 + \nu p_2 \; \right],$$

then,

$$\dot{S}(t) = A_1(X)\left(S - \frac{\nu + \lambda_4 - \nu p_2}{\nu + u_1 + \lambda_4 - \nu p_2}\right),$$

hence

$$\dot{X}_1 = A_1(X)(X_1 - X_1^*).$$

This is a linear system which is globally asymptotically stable at

$$X_1^* = \frac{\nu + \lambda_4 - \nu p_2}{\nu + u_1 + \lambda_4 - \nu p_2}$$

iii. The matrix $A_2(X)$ is given by

$$A_2(X) = \begin{bmatrix} -(\nu+\lambda_1) & \rho S & \rho\theta S \\ \lambda_1 & -(\nu+\lambda_2) & 0 \\ 0 & p_3\lambda_2 & -(\nu+\lambda_3-u_2-\nu p_1) \end{bmatrix},$$

for any $X \in \Pi$, the matrix $A_2(X)$ is Metzler and irreducible.

iv. The maximum $A_2(\overline{X})$ is given by

$$A_2(\overline{X}) = \begin{bmatrix} -(\nu+\lambda_1) & \rho\frac{\nu+\lambda_4-\nu p_2}{\nu+u_1+\lambda_4-\nu p_2} & \rho\theta\frac{\nu+\lambda_4-\nu p_2}{\nu+u_1+\lambda_4-\nu p_2} \\ \lambda_1 & -(\nu+\lambda_2) & 0 \\ 0 & p_3\lambda_2 & -(\nu+\lambda_3-u_2-\nu p_1) \end{bmatrix}.$$

v. The hypothesis (v) requires that $\alpha(\overline{A_2}) \leq 0$. Writing $\overline{A_2}$ as a block matrix

$$\overline{\mathbf{A_2}} = \begin{bmatrix} A & B \\ C & D \end{bmatrix},$$

where

$$A = -(\nu+\lambda_1),$$
$$B = \begin{bmatrix} \rho\frac{\nu+\lambda_4-\nu p_2}{\nu+u_1+\lambda_4-\nu p_2} & \rho\theta\frac{\nu+\lambda_4-\nu p_2}{\nu+u_1+\lambda_4-\nu p_2} \end{bmatrix},$$
$$C = \begin{bmatrix} \lambda_1 \\ 0 \end{bmatrix},$$
$$D = \begin{bmatrix} -(\nu+\lambda_2) & 0 \\ p_3\lambda_2 & -(\nu+\lambda_3-u_2-\nu p_1) \end{bmatrix}.$$

According to Lemmas (4.3) and (4.5)

$$\overline{\mathbf{A_2}} = D - CA^{-1}B$$
$$= \begin{bmatrix} -(\nu+\lambda_2)+\frac{\rho\lambda_1 S_0}{\nu+\lambda_1} & \frac{\rho\theta\lambda_1 S_0}{\nu+\lambda_1} \\ p_3\lambda_2 & -(\nu+\lambda_3-u_2-\nu p_1) \end{bmatrix}.$$

The characteristic equation of $\overline{A_2}$ is given by

$$\det(\lambda I - (D - CA^{-1}B))$$
$$= \begin{vmatrix} \lambda+(\nu+\lambda_2-\frac{\rho\lambda_1 S_0}{\nu+\lambda_1}) & \frac{-\rho\theta\lambda_1 S_0}{\nu+\lambda_1} \\ -p_3\lambda_2 & \lambda+(\nu+\lambda_3-u_2-\nu p_1) \end{vmatrix}$$
$$= \lambda^2 + \Big(\nu+\lambda_2+\nu+\lambda_3+u_2-\nu p_1-\frac{\rho\lambda_1 S_0}{\nu+\lambda_1}\Big)\lambda$$
$$+ \Big((\nu+\lambda_2-\frac{\rho\lambda_1 S_0}{\nu+\lambda_1})(\nu+\lambda_3+u_2-\nu p_1)$$
$$- \frac{p_3\lambda_1\theta\rho\lambda_2 S_0}{\nu+\lambda_1}\Big) = 0.$$

It follows from the Routh Hurwitz criterion that the two eigenvalues have negative real parts if and only if $R_0 < 1$. When

$R_0 = 1$, one eigenvalues is zero and another is negative real root. Hence, $\overline{A_2}$ is a stable Metzler matrix if and only if $R_0 \leq 1$, that is $\alpha(\overline{A_2}) \leq 0$ if and only if $R_0 \leq 1$.

Then, hypotheses $(i - v)$ of lemma (4.6) are satisfied. Then, by Lemma (4.6), we have shown that the disease-free equilibrium is globally asymptotically stable if $R_0 \leq 1$. □

5. Conclusion

In the present paper, we examine the dynamic behavior of a S-E-I-C-R-S model of hepatitis B virus infection. To reduce the hazardous effect of the infection, we introduce two control variables $u_1(t)$ and $u_2(t)$ i.e. vaccination and treatment using optimal control strategy. We studied the existence and stability of the disease-free equilibria. It is rigorously established in Theorem (4.7) that the basic reproduction number R_0 is a sharp threshold parameter and completely determines the global dynamics of (2.2) in the feasible region Π. If $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable in Π, and the disease always dies out. If $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable by using the approach that given by Kamgang and Sallet.

References

[1] R.M. Anderson and R.M. May, *Infectious Disease of Humans: Dynamics and Control*, Oxford University Press, Oxford, 1991.

[2] S. Bhattacharyyaa and S. Ghosh, *Optimal control of vertically transmitted disease*, Computational and Mathematical Methods in Medicine. 11(4) (2010) 369-387.

[3] S. Bowong, J.J. Tewa, and J.C. Kamgang, *Stability analysis of the transmission dynamics of tuberculosis models*, World Journal of Modelling and Simulation. 7(2) (2011) 83-100.

[4] P.V.D. Driessche and J. Watmough, *Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission*, Math Biosci. 180 (2002) 29-48.

[5] Y. Enatsu, Y. Nakata, and Y. Muroya, *Global stability of SIRS epidemic models with a class of nonlinear incidence rates and distributed delays*, Published in Acta Mathematica Scientia, 32 (2012) 851-865.

[6] H. Hethcote, *The mathematics of infectious diseases*, SIAM Review, 42 (2000) 599-653.

[7] J.C. Kamgang and G. Sallet, *Computation of threshold conditions for epidemiological models and global stability of the disease-free equilibrium (DFE)*, Mathematical Biosciences, 213 (2008) 1-12.

[8] A.V. Kamyad, R. Akbari, A.A. Heydari, and A. Heydari, *Mathematical Modeling of Transmission Dynamics and Optimal Control of Vaccination and Treatment for Hepatitis B Virus*, Computational and Mathematical Methods in Medicine. Volume 2014, Article ID 475451, 15 pages.

[9] T.K. Kar and S. Jana, *A theoretical study on mathematical modelling of an infectious disease with application of optimal control*, Bio Systems, 111(1) (2013) 3750.

[10] T.K. Kar and A. Batabyal, *Stability analysis and optimal control of an SIR epidemic model with vaccination*, Biosystems. 104 (2011) 127-135.

[11] X. Liu and L. Yang, *Stability analysis of an SEIQV epidemic model with saturated incidence rate*, Nonlinear Analysis: Real World Applications, 13 (2012) 2671-2679.

[12] J. Mann and M. Roberts, *Modelling the epidemiology of hepatitis B in New Zealand*, Journal of Theoretical Biology. 269 (2011) 266-272.

[13] G.F. Medley and N.A. Lindop, *Hepatitis-B virus endemicity: heterogeneity, catastrophic dynamics and control*, Nature Medicine, 7(5) (2001) 619-624.

[14] A.A. Momoh, M.O. Ibrahim, and B.A. Madu, *Stability Analysis of an Infectious Disease Free Equilibrium of Hepatitis B Model*, Research Journal of Applied Sciences, Engineering and Technology, 3(9) (2011) 905-909.

[15] J.S. Muldowney, *Compound matrices and ordinary differential equations*, Rocky Mountain J. Math. 20 (1990) 857-872.

[16] J. Pang, J.A. Cui, and X. Zhou, *Dynamical behavior of a hepatitis B virus transmission model with vaccination*, Journal of Theoretical Biology. 265 (2010) 572-578.

[17] S. Sun, *Global Dynamics of a SEIR Model with a Varying Total Population Size and Vaccination*, Int. Journal of Math. Analysis, 6(40) (2012) 1985-1995.

[18] C. Sun, Y. Lin, and S. Tang, *Global stability for an special SEIR epidemic model with nonlinear incidence rates*, Chaos, Solitons and Fractals, 33 (2007) 290-297.

[19] S. Thornley, C. Bullen, and M. Roberts, *Hepatitis B in a high prevalence New Zealand population: A mathematical model applied to infection control policy*, Journal of Theoretical Biology. 254 (2008) 599-603.

[20] P. Van Den Driessche and J. Watmough, *Reproduction numbers and subthreshold endemic equilibrium for compartmental models of disease transmission*, Mathematical Biosciences, 180 (2002) 29-48.

[21] K. Wanga, A. Fan, and A. Torres, *Global properties of an improved hepatitis B virus model*, Nonlinear Analysis: Real World Applications, 11 (2010) 3131-3138.

[22] WHO, Hepatitis B Fact Sheet No. 204, *The World Health Organisation*, Geneva, Switzerland, 2013, http://www.who.int/mediacentre/factsheets/fs204/en/.

[23] S. Zhang and Y. Zhou, *The analysis and application of an HBV model*, Applied Mathematical Modelling, 36 (2012) 1302-1312.

[24] S.J. Zhao, Z.Y. Xu, and Y. Lu, *A mathematical model of hepatitis B virus transmission and its application for vaccination strategy in China*, Int.J.Epidemiol. 29 (2000) 744-752.

[25] L. Zou, W. Zhang, and S. Ruan, *Modeling the transmission dynamics and control of hepatitis B virus in China*, Journal of Theoretical Biology, 262 (2010) 330-338.

[1] Department of Mathematical Sciences, Payame Noor University, P.O.Box 19395-3697, Tehran, Iran.
E-mail address: r9reza@yahoo.com

[2] Department of Mathematics Sciences, University of Ferdowsi, Mashhad, Iran .
E-mail address: kamyad@math.um.ac.ir, avkamyad@yahoo.com

[3] Research Center for Infection Control and Hand Hygiene, Mashhad University Of Medical Sciences, Mashhad, Iran.
E-mail address: heydariaa@mums.ac.ir

[4] Department of Mathematical Sciences, Payame Noor University, P.O.Box 19395-3697, Tehran, Iran.
E-mail address: a_heidari@pnu.ac.ir, aghileheydari@yahoo.com