Australian Journal of Basic and Applied Sciences, 3(3): 1607-1615, 2009
ISSN 1991-8178

Stochastic and Monte Carlo Simulation for the Spread of Thehepatitis B

[1]I.A. Moneim, [2]M. Al-Ahmed and [3]G.A. Mosa

[1.3]Department of Mathematics, Faculty of Science, Benha University, Benha 13518 - Egypt.
[2]Department of Quantitative Methods, Faculty of Administrative Science, King Saud University, Riyadh, Saudi Arabia.

Abstract: Modelling and simulation of human biology is one of the most recent and interesting techniques. Infectious and cell diseases are very serious major public health problems. These diseases are still an open fields of study. Some of these diseases are never understood yet others need more and more effort to be modelled and solved completely. The hepatitis B virus (HBV) is considered to be among the most dangerous infectious diseases in the world (Martcheva, 2003) and (El-Zayadi *et al.,* 2001). Constructing mathematical and simulation models for HBV , is the main aim of this paper. Understanding, possibly control and predicting the nature of the dynamics of these diseases are also important tasks of our study. It has been shown that, there is a threshold level of the basic reproduction rate $R0$ which depends on the disease parameters, under which the disease dies out from the population and above this value the disease fires up. This parameter value is used in both stochastic and Mont Carlo simulations. In this paper we study first, a stochastic model for the spread of the HBV. We use the method of the stochastic partial differential equations given in (Kapur, 1992; Jacoby, 1981) and (Report No. 193), to drive our stochastic model and then try to solve this model. Finally Monte Carlo simulations have been conduct for this disease using a random infection rate.

Key words: Stochastic Modelling, Monte carlo, Simulation, HBV, Threshold value.

INTRODUCTION

A few number of qualitative studies of hepatitis have been carried out, most of them studied hepatitis C (Kapur, 1988; Das *et al.,* 2005) studied a similar stochastic model for the spread of hepatitis C. Moneim *et al.,* (Murthy *et al.,* 1990) studied hepatitis C with different types of virus genome. One of the few works studying HBV was due to Moneim (Moneim, 2006) he studied a deterministic model for the spread of HBV in Egypt. Threshold levels were derived from this model to prevent epidemics from the population. It has been found that the disease is stable under certain conditions to control the spread of the disease. However around 300 million persons world wide suffer from chronic (HBV) infection 25-30 % of whom eventually will die from chronic sequel. The prevalence of HBV infection varies from country to country and depends upon a complex mix of behavioral, environmental and host factors. However about 10 % go onto chronic hepatitis B then after twenty years develop hepato-cellular carcinoma, this depend on the virus persistence. Blood, Blood products and Shared syringes act as medical transmissions of HBV. Also the disease can transmitted through the use of shared razors and teeth brushes. There another way for the transmission of HBV infection, the blood sucking insects as mosquitoes and bed-bugs. HBV can transmitted by Sexual intercourse but in a rare manner this is been reported as a result of the obtained increase of the cases among sexual partners of infected individuals. HBV can be transmitted vertically from mother to heir newborns Moneim, (2006). The incubation period of HBV varies from six weeks to six months. Here in this paper we study a stochastic model for the spread of the Hepatitis B Virus. We use the method of the stochastic partial differential equations which described in Isham Jacoby, (1981) and Kapur (Report No. 193) to drive our stochastic model and try to solve this model numerically. Mont Carlo Simulation is been used to study a more realistic model than considering the assumption that the population can not be mixed in a homogenous manner. Thus this assumption is replaced by the one that each person has its own chance to catch the disease from another infected person.

Corresponding Author: I.A. Moneim, Department of Mathematics, Faculty of Science, Benha University, Benha 13518 - Egypt.
E-mail: moneim97@yahoo.com

That is, the infection rate is taken as a random value of specific uniform distribution. The mean value of this uniform distribution is equal to the suggested value which is used in both the deterministic and stochastic version of this model in section two.

The Model:

The epidemiological features of the HBV lead to the following assumption about the trans-mission of the disease:

1. The population has a constant size, N and divided into four groups: Susceptible, latent, infective and recovered. The birth and death occur at a constant and equal rate b.
2. All newborns are susceptible.
3. The population moves from latent class to join the infected one at a constant rate σ.
4. The population is mixing in a homogenous manner i.e. every person has the same chance to becoming in contact with an infected person.
5. The transmission of the HBV infection occurs at a constant rate β, proportional to the number of contacts between the susceptible and infective individuals.
6. Recovery occurs at a constant rate α proportional to the number of infective individuals. Recovery conferees permanent immunity.

Let, S, L, I and R represent the number of susceptible, latent, infective and recovered individuals respectively. As σ is the rate in which the persons move from the latent to the infective group the latent period is $1/\sigma$, and the recovery period is $1/\sigma$ Bailey, (1975).

These assumptions lead to the following deterministic model which describing the spread of the infectious hepatitis B virus Moneim, (2006).

$$\frac{dS}{dt} = bN - bS - \beta SI \tag{1}$$

$$\frac{dL}{dt} = \beta SI - (b+\sigma)L \tag{2}$$

$$\frac{dI}{dt} = \sigma L - (b+\alpha)I \tag{3}$$

$$\frac{dR}{dt} = \alpha I - bR \tag{4}$$

with $S + L + I + R = N$. The basic reproductive number of this model which is the average value of the expected number of secondary cases produced by a single infected person entering the population at the disease free equilibrium is:

$$R_0 = \frac{\sigma\beta N}{(b+\sigma)(b+\alpha)} \tag{5}$$

This model has been solved and analyzed in Moneim, (2006). It has been shown that when $R_0 < 1$ in value the disease dies out and the disease free equilibrium point (N,0,0) is stable. But if $R_0 > 1$there is another endemic equilibrium point which is stable in this case and the disease takes off.

Now, we focus on the stochastic version of this pervious model. Let $P_{nmhk}(t)$ be the probability that there are n susceptible persons, m latent persons, h infective persons by HBV and k recovered persons respectively in our system, and let $f_{ijuq}\Delta t + o(\Delta t)$ gives the probability that the numbers (n, m, h, k) change to $(n+I, m+j, h+u, k+q)$ in the time interval $(t, t+\Delta t)$. So moving a person from a class to another or adding a person to any class by birth or removing a one by death, changing the system state from {n, m, h, k} to another and this depends on the disease parameters as follows:

$$f_{1,0,0,0}(n,m,h,k) = b(n+m+h+k), \quad f_{-1,0,0,0}(n,m,h,k) = bn,$$
$$f_{-1,1,0,0}(n,m,h,k) = \beta nh, \quad f_{0,-1,0,0}(n,m,h,k) = bm,$$
$$f_{0,-1,1,0}(n,m,h,k) = \sigma m, \quad f_{0,0,-1,0}(n,m,h,k) = bh,$$
$$f_{0,0,-1,1}(n,m,h,k) = \alpha h, \quad f_{0,0,0,-1}(n,m,h,k) = bk,$$

and

The general form of the stochastic partial differential equation describing our model is given as follows (Murthy *et al.,* 1990) and (Herbert and Isham, 1998):

$$\frac{\partial \phi(t;x,y,z,w)}{\partial t} = \sum_{i\neq 0}\sum_{j\neq 0}\sum_{u\neq 0}\sum_{q\neq 0}(x^i y^j z^u w^q - 1) f_{ijuq}\left(x\frac{\partial}{\partial x}, y\frac{\partial}{\partial y}, z\frac{\partial}{\partial z}, w\frac{\partial}{\partial w}\right)\phi \tag{6}$$

where φ(t; x; y; z, w) is a probability generating function which defined as,

$$\phi(t;x,y,z,w) = E(x^n y^m z^k w^k) = \sum_n \sum_m \sum_k \sum_k p_{nmkk}(t)\, x^n y^m z^k w^k \tag{7}$$

Equation (6) is the four dimensions version of the stochastic partial differential equation given in (Kapur, 1992)and (Isham, 1995). Then, the basic stochastic partial differential equation for the generating function φ(t; x, y, z, w) becomes,

$$\begin{aligned}\frac{\partial \phi(t;x,y,z,w)}{\partial t} &= (x^1 y^0 z^0 w^0 - 1) b\left(x\frac{\partial}{\partial x} + y\frac{\partial}{\partial y} + z\frac{\partial}{\partial z} + w\frac{\partial}{\partial w}\right)\phi \\ &+ (x^{-1} y^0 z^0 w^0 - 1) b\left(x\frac{\partial}{\partial x}\right)\phi + (x^{-1} y^1 z^0 w^0 - 1)\beta\left(\left(x\frac{\partial}{\partial x}\right)\left(z\frac{\partial}{\partial z}\right)\right)\phi \\ &+ (x^{-1} y^0 z^0 w^0 - 1) b\left(x\frac{\partial}{\partial x}\right)\phi + (x^{-1} y^1 z^0 w^0 - 1)\sigma\left(y\frac{\partial}{\partial y}\right)\phi \\ &+ (x^0 y^0 z^{-1} w^0 - 1) b\left(z\frac{\partial}{\partial z}\right)\phi + (x^0 y^0 z^{-1} w^1 - 1)\sigma\left(y\frac{\partial}{\partial y}\right)\phi \\ &+ (x^0 y^0 z^0 w^{-0} - 1) b\left(w\frac{\partial}{\partial w}\right)\phi\end{aligned} \tag{8}$$

Hence

$$\begin{aligned}\frac{\partial \phi(t;x,y,z,w)}{\partial t} &= \beta_2 (y-x)\frac{\partial^2 \phi}{\partial x \partial z} + b(x-1)^2 \frac{\partial \phi}{\partial x} + (b(yx - 2y + 1) + (z-y)\sigma)\frac{\partial \phi}{\partial y} \\ &+ (b(zx - 2x + 1) + (w-z)\alpha)\frac{\partial \phi}{\partial x} + b(wx - 2w + 1)\frac{\partial \phi}{\partial w}\end{aligned} \tag{9}$$

Equation (9) represents our basic stochastic partial differential equation of the spread of the Hepatitis B Virus. Equation (9) is transformed into a system of ordinary differential equations for the 4 means, variances and co-variances of the original variables *n, m, h* and *k* by differentiating equation (9) with respect to x, y, z and w respectively, and setting these variables to the value of one Then we obtain, the differential equations governing the means μ_n, μ_m, μ_h and μ_k, of the original variables *n, m, h* and *k* respectively as follows:

$$\frac{d\mu_n}{dt} = -b\mu_n + b(\mu_k + \mu_m + \mu_n) - \beta(\mu_k \mu_n + \sigma_{nk}), \tag{10}$$

$$\frac{d\mu_m}{dt} = (-b-\sigma)\mu_m + \beta(\mu_k \mu_n + \sigma_{nk}), \tag{11}$$

$$\frac{d\mu_h}{dt} = (-b-\alpha)\mu_h + \sigma\mu_m, \tag{12}$$

$$\frac{d\mu_k}{dt} = \alpha\mu_h - b\mu_k. \tag{13}$$

Where σ_{nh} is the co-variance of the variables *m, h*.

Similarly the following differential equations give the variances $\sigma_n^2, \sigma_m^2, \sigma_h^2, \sigma_k^2$ and co-variances $\sigma_{nm}, \sigma_{nh}, \sigma_{nk}, \sigma_{mh}, \sigma_{mk}$, and σ_{hk}, of the variables n; m; h and k respectively:

$$\frac{d\sigma_n^2}{dt} = b\mu_k + b\mu_m + 2b\mu_n + \mu_h(b + \beta\mu_n(2\mu_n - 1)) + 2b\sigma_{nk} - \beta\sigma_{nh} + 2\beta\mu_n\sigma_{nk} + 2b\sigma_{nk} + 2b\sigma_{nm} - 2\beta(\frac{\partial^3 P_{nmkk}}{\partial x^2 \partial z})_{1,1,1,1} \tag{14}$$

$$\frac{d\sigma_m^2}{dt} = -2(b+\sigma)\sigma_m^2 + \mu_m(b+\sigma - 2\beta(\mu_h\mu_n + \sigma_{nh})) + \beta(\mu_h\mu_n + \sigma_{nh} + 2(\frac{\partial^3 P_{nmkk}}{\partial x \partial y \partial z})_{1,1,1,1}) \tag{15}$$

$$\frac{d\sigma_h^2}{dt} = (b+\alpha)(\mu_h - 2\sigma_h^2) + \sigma(\mu_m + 2\sigma_{mh}) \tag{16}$$

$$\frac{d\sigma_k^2}{dt} = \alpha\mu_h + b\mu_k + 2\alpha\sigma_{nk} - 2b\sigma_k^2 \tag{17}$$

$$\frac{d\sigma_{nm}}{dt} = b(\sigma_m^2 + \sigma_{mh} + \sigma_{mk}) - (b+\sigma)\sigma_{nm} + \beta((\mu_m - \mu_n)(\mu_h\mu_n + \sigma_{nh}) - (\frac{\partial^3 P_{nmhk}}{\partial x \partial y \partial z})_{1,1,1,1} + (\frac{\partial^3 P_{nmhk}}{\partial x^2 \partial z})_{1,1,1,1}) \tag{18}$$

$$\frac{d\sigma_{nh}}{dt} = b(\sigma_h^2 + \sigma_{hh} + \sigma_{mh}) - (b+\alpha)\sigma_{nh} + \beta(-1+\mu_h)(\mu_h\mu_n + \sigma_{nh}) + \sigma\sigma_{nm} - \beta(\frac{\partial^3 P_{nmhk}}{\partial x \partial z^2})_{1,1,1,1} \tag{19}$$

$$\frac{d\sigma_{nk}}{dt} = \alpha\sigma_{nh} + \beta\mu_k(\mu_h\mu_n + \sigma_{nh}) + b(\sigma_{hk} + \sigma_k^2 + \sigma_{nm} - \sigma_{nk}) - \beta(\frac{\partial^3 P_{nmhk}}{\partial x \partial z \partial w})_{1,1,1,1} \tag{20}$$

$$\frac{d\sigma_{mh}}{dt} = -\sigma\mu_m + \sigma\sigma_m^2 - (2b+\alpha+\sigma)\sigma_{mh} + \beta(-(-1+\mu_h)(\mu_h\mu_n + \sigma_{nh}) + (\frac{\partial^3 P_{nmhk}}{\partial x \partial^2 z})_{1,1,1,1}) \tag{21}$$

$$\mu_n + \sigma_{nh}) + (\frac{\partial^3 P_{nmhk}}{\partial x \partial z \partial w})_{1,1,1,1} \tag{22}$$

$$\frac{d\sigma_{hk}}{dt} = -\alpha\mu_h + \alpha\sigma_h^2 - (2b+\alpha)\sigma_{hk} + \sigma\sigma_{mk} \tag{23}$$

Some of the above equations involve third moments of our variables, alternatively we use an approximation to the third moments in terms of the mean, variances and co-variances by assuming our variables obey a specific distribution. Here we use a multivariate Normal distribution where, the third center moments of this distribution are zero, so tri-variate Normal variables W_1, W_2 and W_3 satisfy the following equation (using the notation $mi = E(W_i)$, $m_{ij} = E(W_i\ W_j)$).

$$E(W_1W_2W_3) = m_1m_{23} + m_2m_{13} + m_3m_{12} - 2m_1m_2m_3 \quad (24)$$

Now, the differential equations for variances and co-variances of our *n, m, h* and *k* becomes as follows,

$$\frac{d\sigma_n^2}{dt} = b\mu_k + b\mu_m + 2b\mu_n + \mu_h(b + \beta\mu_n - 2\beta\sigma_n^2) + 2b\sigma_{nb} + \beta\sigma_{nk}2\beta\mu_n\sigma_{nk} + 2b\sigma_{nk} + 2b\sigma_{nm} \quad (25)$$

$$\frac{d\sigma_m^2}{dt} = (b+\sigma)(\mu_m - 2\sigma_m^2) + \beta(2\mu_n\sigma_{mh} + \sigma_{nh} + \mu_h(\mu_n + 2\sigma_{nm})) \quad (26)$$

$$\frac{d\sigma_h^2}{dt} = (b+\sigma)(\mu_h - 2\sigma_h^2) + \sigma(\mu_m + 2\sigma_{mh}) \quad (27)$$

$$\frac{d\sigma_k^2}{dt} = \alpha\mu_h + b\mu_k + 2\alpha\sigma_{hk} - 2b\sigma_k^2 \quad (28)$$

$$\frac{d\sigma_{nm}}{dt} = b(\sigma_m^2 + \sigma_{mh} + \sigma_{mk}) - (b+\sigma)\sigma_{nm} - \beta(\mu_n(\sigma_{mh} - \sigma_{nh}) + \sigma_{nh} + \mu_h(\mu_n - \sigma_h^2 + \sigma_{nm})) \quad (29)$$

$$\frac{d\sigma_{nh}}{dt} = (b - \beta\mu_n)\sigma_h^2 + b(\sigma_{hk} + \sigma_{mh}) - (b + \alpha + \beta\mu_h)\sigma_{nh} + \sigma\sigma_{nm} \quad (30)$$

$$\frac{d\sigma_{nk}}{dt} = (b - \beta\mu_n)\sigma_{hk} + b(\sigma_h^2 + \sigma_{mk}) + \alpha\sigma_{nh} - (b + \beta\mu_h)\sigma_{nk} \quad (31)$$

$$\frac{d\sigma_{mh}}{dt} = -\sigma\mu_m + \sigma\sigma_m^2 - (2b + \alpha + \sigma)\sigma_{mh} + \beta(\mu_n\sigma_h^2 + \mu_h\sigma_{nh}) \quad (32)$$

$$\frac{d\sigma_{mk}}{dt} = \beta\mu_n\sigma_{hk} + \alpha\sigma_{mh} - (2b + \sigma)\sigma_{mk} + \beta\mu_h\sigma_{nk} \quad (33)$$

$$\frac{d\sigma_{hk}}{dt} = -\alpha\mu_h + \alpha\sigma_b^2 - (2b + \alpha)\sigma_{hk} + \sigma\sigma_{mk} \quad (34)$$

Then, we can easily solve the system of differential equations (10) - (13) and (25) - (34) numerically.

Numerical Simulation:

The system of coupled non-linear ordinary differential equations (10) - (13) along with (25) - (34) describe the means, variances and co-variances of the S, E, I and R, is been solved numerically with the help of the software Mathematica 5.1 and using estimated parameter values as follows: *b* = 002= 001= 002), which used by Moneim (Moneim, 2006) and (El-Zayadi *et al.,* 2001). Using different parameter values of the reproduction number R_0so that R_0 can be less than one in value and for another parameter set that makes $R_0 > 1$ we obtain different types of numerical solution of the stochastic model of the hepatitis B virus. If $R_0 < 1$ the solution goes to an asymptotic value which is the disease free solution, as the mean value of E, I and R figure 1(b), (c) and (d) tend to zero as the time becomes large, while the mean value of the susceptible population S tends to the total population number N figure 1(a). In this case $R_0 < 1$, when *t* becomes very large,the model becomes a stochastic model of population growth of pure birth and death process. These results confirm the stability of the equilibrium point (N, 0, 0, 0) from the analytical study.

In the other hand if we take parameter values large enough so that $R_0 > 1$, The disease raises up and becomes endemic. Figures 2(a) show that, the Mean of susceptibles*n* decreases to approach its equilibrium value *(S)* as *t* becomes very large. this means that the equilibrium value of mean of susceptibles independent on increasing of the total population size. While Figures 2(b), (c) and (e) represent the means of latents *m,* infectives*h* and recovers *k* respectively and show that all solutions are increasing to approach an asymptotic endemic level for each compartment. These endemic levels are stable when $R_0 > 1$. These simulation results agree with the analytical asymptotic stability results of the endemic equilibrium point *(SL I R)* when $R_0 > 1$ for the deterministic model from the analytical study.

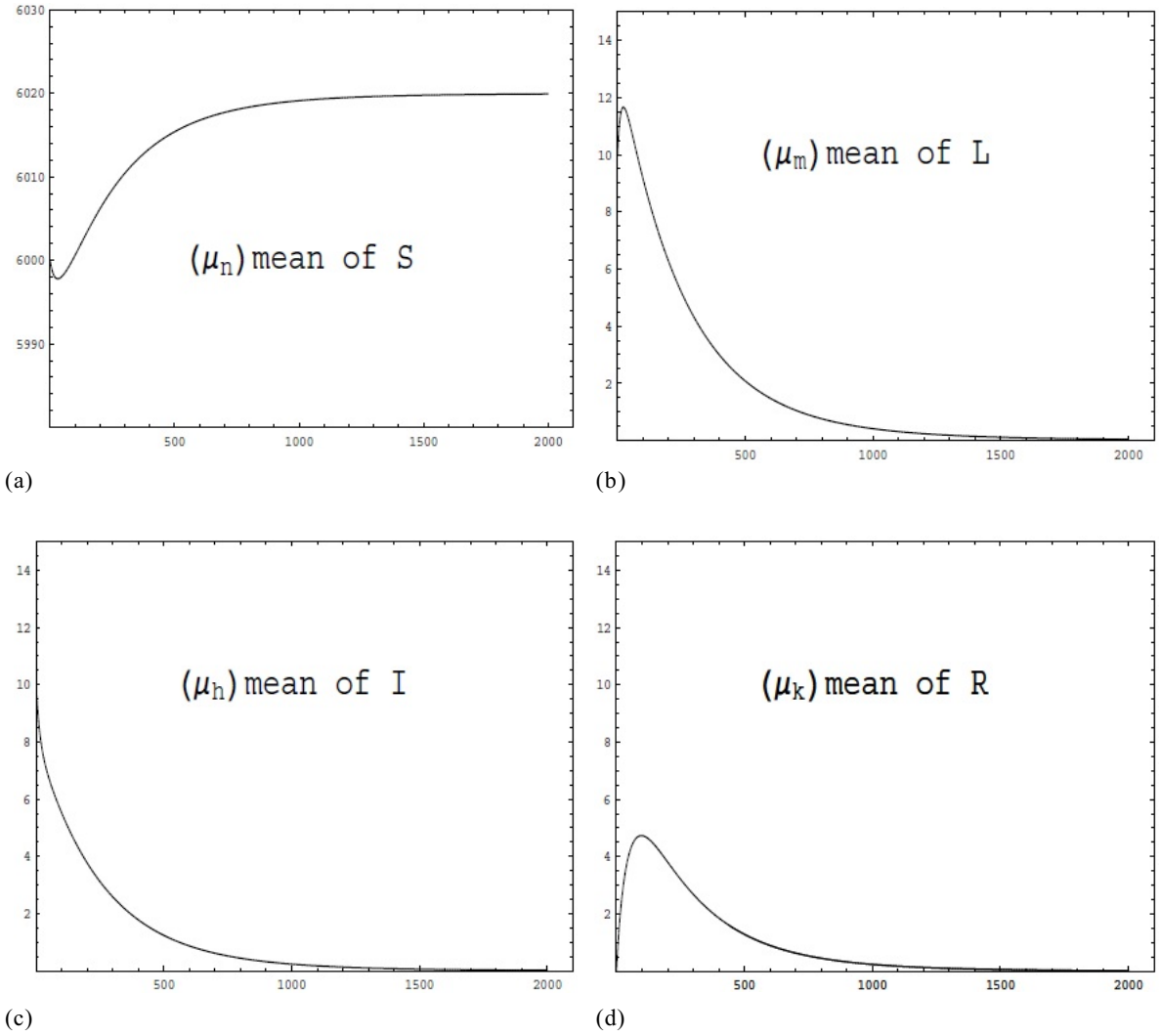
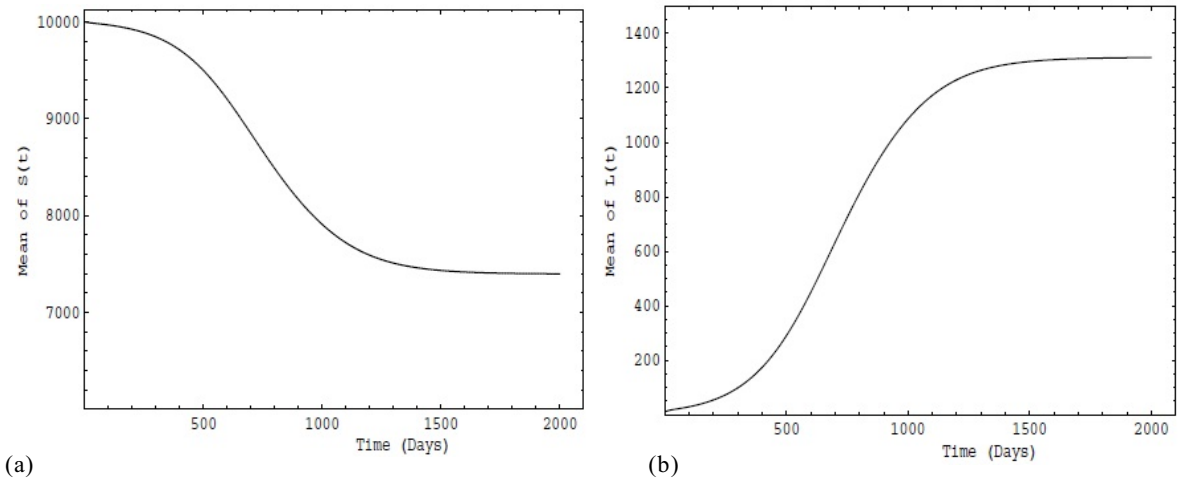
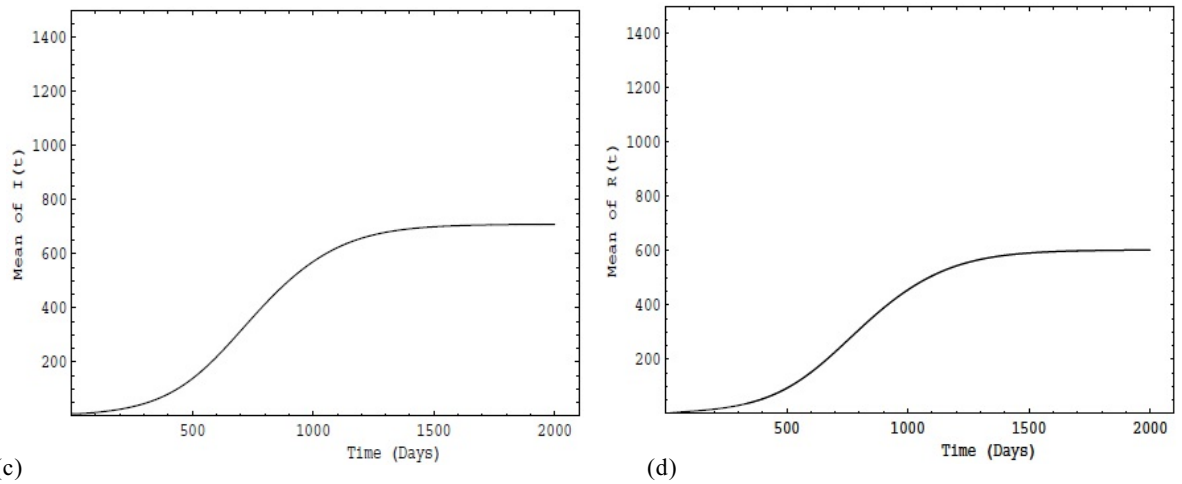


Fig. 1: Mean of (a) Susceptibles, (b) Latents, (c) Infectives and (d)Recovers against time for HBV at $R_0 < 1$.





(c) (d)

Fig. 2: Mean of *(a)* Susceptibles, *(b)* Latents, *(c)* Infectives and (*d*)Recovers against time for HBV at $R_0 > 1$.

Monte-Carlo Simulation:

In the previous sections of this paper, the stochastic version of HBV model is been studied and its numerical simulation is conducted. The deterministic model shows that there is a thresh-old value for *R*0 above it the disease becomes endemic otherwise the disease dies out from the population. Stochastic results of the previous section shows a similar results for the deterministic model. Now we use the same parameter set which are used in both deterministic and stochastic models to conduct Mont Carlo simulation of our model. The parameters are as follows $b = 0.02$, $\beta = 0.017$, $\sigma = 0.01$, $\alpha = 0.02$. Here we use a more realistic assumption that the infection rate is a random variable. So, in this section the Monte-Carlo technique is used to simulate our model. The results obtained here by this method are compared with those of the deterministic and stochastic models.

The main point here is that, the assumption which says, the population is mixing in a homogenous manner, is replaced by the more realistic one which is each person has it is own chance to becoming in contact with an infected person and then to catch the disease from another infected person by a non-homogenous manner. Therefore, the parameter β is been taken as a random value of specific uniform distribution with a mean value equal the suggested value β =0.017 which is used in the previous sections. Then the deterministic model becomes

$$\frac{dS}{dt} = bN - bS - \beta^* SI \tag{35}$$

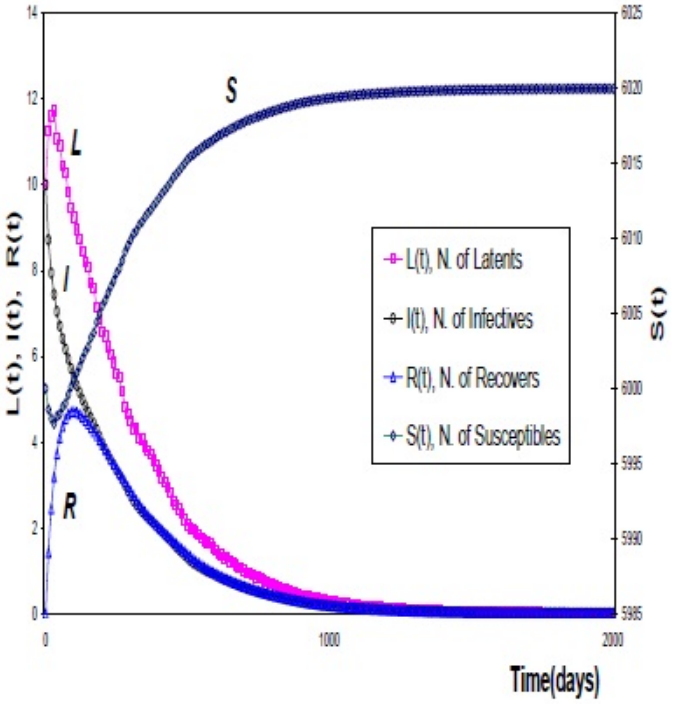
$$\frac{dL}{dt} = \beta^* SI - (b + \sigma)L \tag{36}$$

$$\frac{dI}{dt} = \sigma L - (b + \alpha)I \tag{37}$$

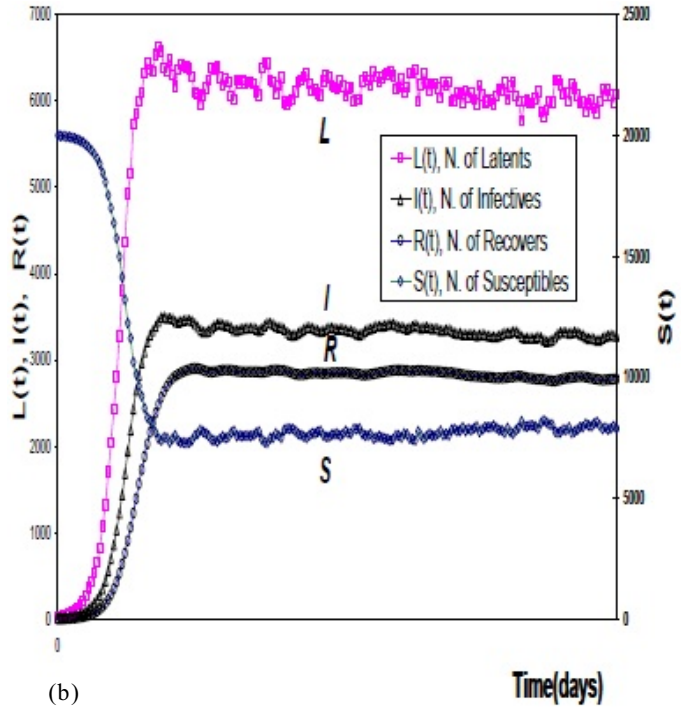
$$\frac{dR}{dt} = \alpha I - bR \tag{38}$$

with $S+L+I+R=N$

Where β^* is a random number generated by specific uniform distribution with mean value ($E(\beta^*)$ = 0017). We use the fourth order Rung-Kutta method, for solving systems of ordinary differential equations. The fourth order Rung-Kutta method produces accurate approximation (Isham, 1995) and (Murthy *et al.,* 1990). The present system (35) - (38) is solved by using this method with time step h = 10 and evaluate the mathematical mean of *S(t), L(t), I(t)* and *R(t)* of 1000 samples at each step to produce numerical solutions for means of *S(t), L(t), I(t)* and *R(t)* at any time. The results are shown in Figure (3).



(a)



(b)

Fig. 3: Mont Carlo simulation results for our HBV model (37)-(40) and plot the Susceptibles, Latents, Infectives and Recovers against time when *(a)* $R_0 < 1$ and *(b)* $R_0 > 1$

Conclusions:

In this paper we studied HBV models with susceptible, latent, infected and recovered populations. The stochastic model has been analyzed and solved numerically. We observed that the mean values of the four

compartment S, L, I and R tends to disease free state asymptotically when parameter values, which make $R_0 < 1$, are used. Otherwise the means go to endemic levels and the disease fires up in the population. Monte carlo simulations for a random infection parameter have been conducted. Moreover, the Monte Carlo simulations show similar results to those of the stochastic results, but with a little deference. In the Monte Carlo simulations there is a fluctuations around the asymptotic levels in both cases the disease free state when $R_0 < 1$ and the endemic level when $R_0 > 1$.

We may conclude that, the HBV disease free state is always possible and stable in all of our models, the deterministic, the stochastic and the Monte Carlo models. Control of blood to blood contamination and health eduction (drug users, surgeries, Dentists etc.,) is the only need to keep $R0$ below the threshold level and then to prevent the population from HBV epidemics.

REFERENCES

Bailey, N.T.J., 1975, The Mathematical Theory of Infectious Diseases and Its Applications: Griffin, London.

Das, P., D. Mukherjee and A.K. Sarkar, 2005. Analysis of a disease transmission model of hepatitis C. J. Biol. Syst., 13(4): 331-339.

El-Zayadi, A., H. Abaza, S. Shawky, M.K. Mohamed, O. Selim and H.M. Badran, 2001. Prevalence and epidemiological features of hepatocellular carcinoma in Egypt a single centre experience. Hepatology Research, 19: 170-179.

Herbert, J., V.S. Isham, 1998. On stochastic host-parasite interaction models, Departmentl Research Report No. 193 , Dept. Of Statistical Science, University College, London.

Isham, V.S. and M.S. Chan, 1998. A Stochastic Model of Schistosomiasis Immuno-Epidemiology. Mathematical Biosciences, 151: 179-198.

Isham, V.S., 1995. Stochastic models of host-macroparasite interaction, Ann. Appl. Probability, 5: 711-720.

Jacoby, L.S. and J. Skowalik, 1981. Mathematical Modelling with Computers: Prentice Hall, New Jersey.

Kapur, J.N., 1992. Mathematical Models in Biology and Medicine. Affiliated, East-Weast Press, New Delhi.

Kapur, J.N., 1988. Mathematical Modelling. Wiley Eastern Limited, New Delhi.

Martcheva, M. and C. Castillo-Chavez, 2003. Disease with choronic stage in a population with varying size. Math Biosci., 182: 1-25.

Maynard, J.E., 1990. Hepatitis B: Global Importance and Need for Control, Vaccine., 8: 18-20.

Moneim, I.A. and G.A. Mosa, 2006. Modelling the hepatitis C with different types of virus genome. Computational and Mathematical Methods in Medicine, 7(1): 3-13.

Moneim, I.A., 1995. Mathematical Modelling in Public Health with Special Emphasis on Infectious Hepatitis and ' or Schistosomiasis in Egypt. MSc. thesis, University of Benha, Egypt.

Murthy, D.N.P., N.W. Page and E.Y. Rodin, 1990. Mathematical Modelling. A Tool for Problem Solving in Engineering, Physical, Biological and Social Sciences. Oxford.

Nagle, K.R. and E.B. Saff, 1989. Fundamentals of Differential Equations: Banjamin Cummings, California.