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Dynamical Behavior of HBV in a Population

Tayebe Waezizadeh, Maryam Mohammad Rezaei

Department of Pure Mathematics, Faculty of Mathematics and Computer, Shahid Bahonar University of Kerman, Kerman, Iran,
e-mail: waezizadeh@uk.ac.ir, maryammath.mania@yahoo.com

Abstract: The present study investigates a mathematical model for HBV carried out in a district of Kerman. The statistical sample comprises all men and women living in that district. Two different mathematical models are introduced for HBV related to this population. Data analysis was carried out with MATLAB programming. The results indicate that there is a meaningful relationship between the vaccination and epidemic disease.

Keywords: Mathematical models, epidemiology, Runge-Kutta method, differential equation systems.

1. Introduction

Spreading infection is a cause of a great anxiety for the human population. In the past centuries, when an epidemic disease appeared in a society, a large number of people would die consequently. For instance, small-pox appeared in Mexico in the 16th century, leading to a population decrease from 30 million to 2 million within 50 years [2]. To prevent and control an infectious disease, it is important to know the mechanism of spread and the dynamic of transmission [7, 15].

Albeit the mathematical modeling of infectious diseases dates back to 1760, when Bernoulli used mathematical modeling to describe the small-pox for the first time [26]. The comprehensive study of infectious diseases by mathematical models was inaugurated at the beginning of the 20th century [1, 2, 18]. Notably, Hamer introduced a model for the Measles in 1906. In 1911, the physicist Ross applied differential mathematical modeling techniques in order to model the transmission of Malaria from Mosquito to human. Then, in 1926, Kermak and Makendrick introduced the famous SIR model so as to describe the epidemic plague that happened in London in 1666 [7, 26, 34].

To prevent and control an infectious disease more effectively, it is of high importance to entirely understand the mechanism of the spread and dynamics of the transmission of the disease, and then provide applicable predictions and guidance so as to establish strategies that can be applied in practice. It is remarkable that during 20th century, a variety of mathematical models for infectious disease have been formulated and described based on population dynamics, behavior of disease

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transmissions, features of the infectious agents and other social and physiological factors [4, 5, 6, 17, 29, 30, 35].

2. Literature Review

Hepatitis B, HBV for short, is one of the prevalent diseases in developing countries. It is caused by the Hepanda virus, which attacks the liver. It can cause both acute and chronic disease [3, 16, 19, 21].

The transmission of HBV to a healthy individual is by contact with the blood or body fluid of an infected person in the same way as HIV. However, HBV is 50 to 100 times more infectious than HIV [27, 28].

The major factors in getting infected with HBV are

- from mother to baby at birth,
- unsafe injections and transfusions,
- unprotected sexual contact.

In general, viral diseases do not respond to any specific treatment [23, 24]. In this case, either patients would regard for their health conditions or patients' bodies naturally produce proper antibodies to act against the virus. Vaccination is the most preferable strategy to protect a society against epidemic disease [23, 28, 30].

The virus starts to replicate increasing just 3 days after entering the liver cells. Nonetheless, the illness manifests itself after approximately 45 days [31]. It is detectable that HBV has an infectious period of 3 months [24, 25, 29].

About 2 billion people have been infected with the virus around the world and about 350 million suffer from chronic infection [9, 21, 22, 27]. It is estimated that around 600000 people die every year due to acute and chronic consequences of hepatitis B, and 50 million new cases are diagnosed annually. Furthermore, about 25 percent of adults who become chronically infected during childhood die from liver cancer or cirrhosis [9, 25, 28].

Recent collected data demonstrates that the overall prevalence of HBV in Iran is less than 3 percent [10]. Making attempt to raise general public awareness about HBV transmission along with performing the vaccination program for all newborns, health care workers and those at risk of HBV infection, initiated from 1993, have influenced the health outcome [10]. The reported prevalence of HBV infection in Iran have been on the fall from about 3.5 percent in 1990s to 2.14 percent in 2000s [11].

Researches show that the prevalence of HBV in Iran has a geographical variation. Several researches have been conducted into the rate of infectious transmission in different provinces of

Iran. In 2006, Behbahani et al. worked on 2000 samples and 131$(6.55\ percent)$ blood samples were found to be positive for anti-HBC. The study was undertaken to assess the prevalence of HBV in Fars [12].

In 2009, Merat et al considered 6583 randomly chosen subjects from three provinces in Iran, namely Tehran, Golestan and Hormozgan. The subjects aged between 18 and 65. The prevalence of hepatitis B surface antigen and anti-hepatitis B core antibody were 2.3 percent and 14.2 percent, respectively in Tehran. The corresponding items in Hormozgan were 13.3 percent and 2.7 percent, respectively, and in the case of Golestan, they were 5.1 percent and 36.9 percent, respectively [13]. Moreover, Fathimogaddam et al. perceived 1652 randomly chosen healthy individuals aged 1 to 90 from Mashhad, located in the Khorasan-e-Rasavi province, in 2011. The prevalence of HBV was found to be 1.39 percent [14].

According to the aforementioned researches, in spite of nationwide vaccination of newborns against HBV starting from 1992, hepatitis B virus infection had remained a key components of chronic liver disease in Iran.

In this paper, we introduce two mathematical models for HBV. We predict the number of infectious people in a city in the Kerman province by data information and number analysis. Although we can use these models for any population, we consider a statistical community of 77369 individuals living in the aforesaid vicinity. This statistical community has been observed during 2012. Moreover, should someone from this population consult a doctor in concern with HBV, then either all of their family will be vaccinated 3 times in 6 months or they will fall ill.

In the case of these models, we divide the population into five separate parts. Susceptible, exposed, vaccinated, infected and recovered individuals in which recovered ones are immune to the disease. The statistical population is divided regarding the genders of its members. The applied models are time dependent, because the population will change in different courses of time.

The paper is organized as follows. In the next section, we present the mathematical models and describe their structure. In section 3, we employ the numerical method, Runge-Kutta, to solve the differential equation system. In the end, we make projections and provide descriptions of the future of the disease by presenting diagrams that were drawn utilizing MATLAB programming.

3. Mathematical Models

In this section, we introduce two mathematical models for HBV considering two different cases. The first case concerns the situation in which there is enough vaccine available for everyone who needs it. Moreover, all newborns and those at risk receive vaccine. The second one arises when there is not enough vaccine and only newborns who are at risk receive vaccine.

We divide the population into five boxes as susceptible, exposed, vaccinated, infected and recovered class which are denoted by S, E, V, I and R respectively [20, 22, 32, 33]. Let $S(t)$, $E(t)$, $I(t)$ and $V(t)$ be the number of individuals who are in the class S, E, I and V at time t respectively, and suppose that $N(t)$ is the total population size at time t. Hence, $N(t) = S(t) + E(t) + I(t) + V(t) + R(t)$. We also put the total population and the population of each class into two major parts. Women who are denoted by $S_1, E_1, I_1, V_1, R_1, N_1$ and men who are indicated by S_2, E_2, I_2, V_2 and R_2 respectively. Thus

$$N_1(t) = S_1(t) + E_1(t) + I_1(t) + V_1(t) + R_1(t),$$
$$N_2(t) = S_2(t) + E_2(t) + I_2(t) + V_2(t) + R_2(t).$$

It is noticeable that newborns are delivered by individuals of group N_1 (women), ergo, only N_1 gives rise to the population increase.

In the first situation, there is enough vaccine for the population. Therefore, all the newborns are immune to receive vaccine, unless either mother is to be infected or to be exposed to the disease. In this model, an average member of the population makes contact with βN individuals per unit time, where N is total population size. The number of new infected individuals per unit time in concern with every infective contact is $(\beta N)\frac{S_1}{N}$, giving a new rate for infected class $\beta S_1 I$, where $I = I_1 + I_2$. A susceptible woman leaves the class S_1 at a rate of μS_1 or mS_1 per unit time, where the positive parameters μ and m are natural death and vaccination rates respectively. It is supposed that the rate at which the transfer from the exposed class to the infected class occurs is k. It is also supposed that αE_1 is the rate at which the individuals in the exposed period receive vaccine at time t.

λ is the birth rate. We assume that the birth rate of newborn boys and girls are equal. If the mother of a newborn is to be healthy, the baby will be included in R_1 or R_2. Otherwise, due to his or her health conditions, the baby will be included in one of the classes E_1, E_2, I_1 or I_2. $\frac{1}{\gamma}$ is the average length of the period of infection. Hence, infected individuals leave the class I at a rate of γI per unit of time. We assume that the fraction f of the γI members who leave the infected class at time t will recover and the remaining fraction, $(1-f)$, will die of the disease. Since the vaccination is not perfect, we suppose that a fraction of vaccinated individuals, say σ will get infected. Moreover, a fraction f_v of ηV_1 members will leave the infected class at time t and recover. Similarly, we can write equations for men.

Therefore, the model is

$$\begin{aligned}
\dot{S_1} &= -\beta(1-m)S_1 I - \mu S_1 - mS_1,\\
\dot{E_1} &= \beta(1-m)S_1 I - (\alpha+(1-\alpha)k+\mu)E_1 + \lambda E_1,\\
\dot{I_1} &= (1-\alpha)kE_1 - (\mu+\gamma)I_1 + \beta\sigma IV_1 + \lambda I_1,\\
\dot{V_1} &= \alpha E_1 + mS_1 - \beta\sigma IV_1 - \eta V_1,\\
\dot{R_1} &= \gamma f I_1 + \eta f_v V_1 + \lambda(S_1+R_1) - \mu R_1,\\
\dot{N_1} &= -(1-f)\gamma I_1 - (1-f_v)\eta V_1 + \lambda N_1 - \mu N_1,\\
\dot{S_2} &= -\beta S_2(1-m)I - \mu S_2 - mS_2,\\
\dot{E_2} &= \beta S_2(1-m)I - (\alpha+(1-\alpha)k+\mu)E_2 + \lambda E_1,\\
\dot{I_2} &= (1-\alpha)kE_2 - (\mu+\gamma)I_2 + \beta\sigma IV_2 + \lambda I_1,\\
\dot{V_2} &= \alpha E_2 + mS_2 - \beta\sigma IV_2 - \eta V_2,\\
\dot{R_2} &= \gamma f I_2 + \eta f_v V_2 + \lambda(S_1+R_1) - \mu R_2,\\
\dot{N_2} &= -(1-f)\gamma I_2 - (1-f_v)\eta V_2 + \lambda N_1 - \mu N_2.
\end{aligned}$$

The flow chart for this model is given in the following figure.

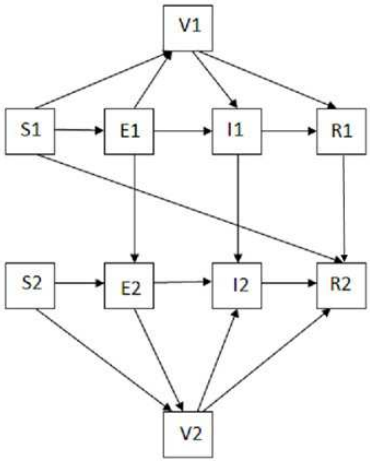

FIGURE 1. Flow chart for the model with enough vaccine for the population

In the second case, it is presumed that there is not enough vaccine, and as a result, only newborns who are at risk will receive it. Therefore, $\lambda = \lambda_1 + \lambda_2$, in which λ_1 is the rate of newborns that are

at risk and λ_2 is the rate of the others. Considering these assumptions, the mathematical model is

$$\begin{aligned}
\dot{S_1} &= -\beta(1-m)S_1 I - \mu S_1 - mS_1 + \lambda_2 S_1,\\
\dot{E_1} &= \beta(1-m)S_1 I - (\alpha + (1-\alpha)k + \mu)E_1 + \lambda E_1,\\
\dot{I_1} &= (1-\alpha)kE_1 - (\mu+\gamma)I_1 + \beta\sigma IV_1 + \lambda I_1,\\
\dot{V_1} &= \alpha E_1 + mS_1 - \beta\sigma IV_1 - \eta V_1,\\
\dot{R_1} &= \gamma f I_1 + \eta f_v V_1 + \lambda_1(S_1+R_1) - \mu R_1,\\
\dot{N_1} &= -(1-f)\gamma I_1 - (1-f_v)\eta V_1 + \lambda N_1 - \mu N_1,\\
\dot{S_2} &= -\beta S_2(1-m)I - \mu S_2 - mS_2 + \lambda_2 S_1,\\
\dot{E_2} &= \beta S_2(1-m)I - (\alpha + (1-\alpha)k + \mu)E_2 + \lambda E_1,\\
\dot{I_2} &= (1-\alpha)kE_2 - (\mu+\gamma)I_2 + \beta\sigma IV_2 + \lambda I_1,\\
\dot{V_2} &= \alpha E_2 + mS_2 - \beta\sigma IV_2 - \eta V_2,\\
\dot{R_2} &= \gamma f I_2 + \eta f_v V_2 + \lambda_1(S_1+R_1) - \mu R_2,\\
\dot{N_2} &= -(1-f)\gamma I_2 - (1-f_v)\eta V_2 + \lambda N_1 - \mu N_2.
\end{aligned}$$

The corresponding flow chart is as follows

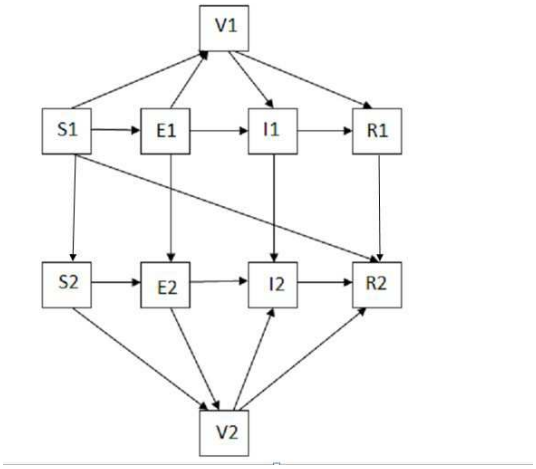

FIGURE 2. Flow chart for the model without enough vaccine for the population

Notations and values used in model are described in the following table.

In next sections, by using the Runge-Kutta method, we predict the future of the disease for the population under consideration with the two different cases.

Parameter	Description	Value
N	Total population size	77369
S	Number of susceptibles	76537
I	Number of infected individuals	48
E	Number of exposed individuals	118
V	Number of vaccinated individuals	1401
β	Infection rate	1.29×10^{-4}
μ	Natural death rate	0.005
γ	Recovery rate	0.005
m	Rate of vaccinated susceptible individuals	0.01
λ	Birth rate	0.014
1/k	Average time for exposed class	45

TABLE 1. Parameters and values for the model

4. The Numerical Method

First, we make a fruitful introduction to the Runge-Kutta method of order four [8]. Consider a differential equation system of order one.

$$\begin{aligned}
\frac{du_1}{dt} &= f_1(t,u_1,u_2,...,u_m),\\
\frac{du_2}{dt} &= f_2(t,u_1,u_2,...,u_m),\\
&\vdots\\
\frac{du_m}{dt} &= f_m(t,u_1,u_2,...,u_m).
\end{aligned}$$

with initial conditions $u_1(a) = \alpha_1, u_2(a) = \alpha_2, ..., u_m(a) = \alpha_m$, where $a \leq t \leq b$. We wish to find the functions $u_1, u_2, ..., u_m$. Let N be a natural number. Set $h = \frac{b-a}{N}$ and $t_j = a + jh$ for all $j = 0,1,2,...,N$. Additionally, for $i = 0,1,...,m$ and $j = 0,1,...,N$, assume that $w_{i,j}$ is an approximation of $u_i(t_j)$, where $w_{i,j}$ is the ith solution of u_i at the endpoint. Hence, the initial conditions are $w_{1,0} = \alpha_1, w_{2,0} = \alpha_2, ..., w_{m.0} = \alpha_m$.

Considering $w_{1,j}, w_{2,j}, ..., w_{m,j}$ to be computed, the values of $w_{1,j+1}, w_{2,j+1}, ..., w_{m,j+1}$ can be obtained by the following formula

$$w_{i,j+1} = w_{i,j} + \frac{1}{6}(k_{1,i} + 2k_{2,i} + 3k_{3,i} + k_{4,i}), \tag{1}$$

where for every i, we have

$$
\begin{aligned}
k_{1,i} &= h f_i(t_j, w_{1,j}, w_{2,j}, ..., w_{m,j}),\\
k_{2,j} &= h f_i(t_j + \frac{h}{2}, w_{1,j} + \frac{k_{1,1}}{2}, w_{2,j} + \frac{k_{1,2}}{2}, ..., w_{m,j} + \frac{k_{1,m}}{2}),\\
k_{3,j} &= h f_i(t_j + \frac{h}{2}, w_{1,j} + \frac{k_{2,1}}{2}, w_{2,j} + \frac{k_{2,2}}{2}, ..., w_{m,j} + \frac{k_{2,m}}{2}),\\
k_{4,j} &= h f_i(t_j + \frac{h}{2}, w_{1,j} + k_{3,1}, w_{2,j} + k_{3,2}, ..., w_{m,j} + k_{3,m}).
\end{aligned}
$$

Now, the initial conditions can be written as $w_{1,0} = S_1(0), w_{2,0} = E_1(0), w_{3,0} = I_1(0), w_{4,0} = V_1(0), w_{5,0} = N(0), w_{6,0} = S_2(0), w_{7,0} = E_2(0), w_{8,0} = I_2(0), w_{9,0} = V_2(0)$. By applying these conditions to Matlab programming, we solved the differential equation systems of our models, after that utilizing a couple of diagrams, we made a prediction about the future of disease.

In the course of the study, the statistical population that is considered in this paper included 38684 women of which 21 were infected, 56 were in exposed period, 681 had received the vaccine and 18 had recovered. During the same period, there were also 38685 men of which 27 were infected, 62 were in the exposed class, 720 had received the vaccine and 23 people had recovered. There were 1143 newborns and 429 dead individuals.

In our models, the rate at which individuals leave the class E is $k = \frac{1}{45} = 0.02$ where 45 is the average time spent in the exposed class. The recovery rate is $\gamma = \eta = \frac{1}{180} = 0.005$ where 180 is the average time that was spent in infected class. The ways by which the disease is transmitted are varied. The most prevalent ones are: being in direct contact with an infected person's blood or body fluids, from mother to her baby and using an infected person's cosmetics. Thus, an infected person can effectively be in contact with his/her family and five to six people out of home. Furthermore, the average population of each family in the city was 4 in our study. Hence, an average number of the population who makes contact per unit of time sufficient to transmit the infection is βN. Ergo, $\beta = \frac{10}{77369} = 1.29 \times 10^{-4}$.

We know that the vaccination is not complete and around 90 percent of individuals who receive the vaccine will be immune. Therefore, the risk of infection for individuals who have received the vaccine is $\sigma = 0.1$. We can compute the other parameters in a similar way. In fact, we get $\lambda = 0.014$, $\mu = 0.005$, $m = 0.01$, $\alpha = 0.001$, and $f = f_v = 0.99$.

Now by utilizing this information in Matlab programming, we are capable of drawing diagrams for females and males. In these diagrams, $S_i(t), E_i(t), I_i(t), V_i(t)$ and $R_i(t)$ are considered a_i, b_i, c_i, d_i and e_i for $i = 1, 2$ respectively.

5. Implementation

In the first case, we assumed that there is enough vaccine for the population and all the newborns received it. The number of susceptible individuals was supposed to decrease, owing to the fact that nobody went to class S and the members of S were going to leave the class, partly due to receiving the vaccine and the others on account of being exposed to the infection and transferring to class E as a consequence. In fact, the susceptible individuals transferred to the exposed class at a fraction of $\beta(1-m)$. Consequently, the curve is on the fall.

On the other hand, due to the high rate of vaccination, a good many individuals in class E received the vaccine and recovered. Hence, after a while, the curve is steady at a constant level. Similarly, the number of individuals who are infected was expected to be on the rise. Nevertheless, the growth rate was in a lower slope. Therefore, the epidemic of HBV is not bound to happen for the considered population as can be seen in Figure 3 and 4.

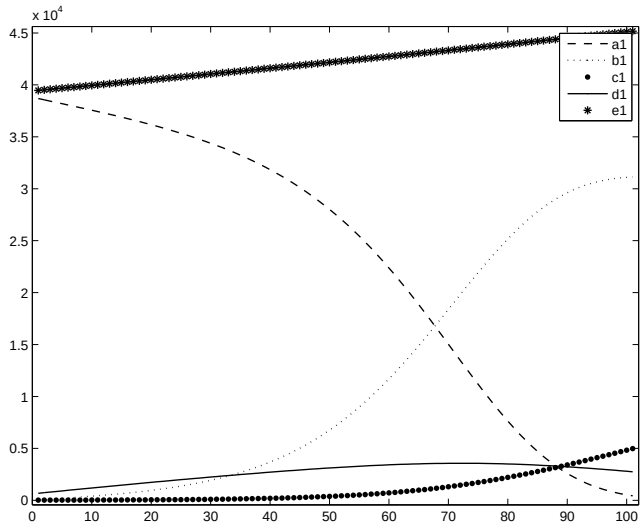

FIGURE 3. A solution of the system for women with initial conditions that are set as $(S_1(0), E_1(0), I_1(0), V_1(0), R_1(0)) = (37908, 56, 21, 681, 18)$. In this case, all the newborns and people who at risk will received the vaccine.

It is noticeable that the occurrence of the second model is contingent upon two key components. Consequently, the second model occurs, in case the birth rate is on the increase and the vaccination rate to be on the decline in a way that only the individuals who are at risk receive the vaccine. We considered $\lambda = 0.1$, notably 0.1 of newborns were at risk. Figures 5 and 6 illustrate the disease in the second model for women and men respectively. As the figures illustrate, the number of susceptible individuals was on the increase at the beginning. Nonetheless, as time went by, their number declined and eventually, remained steady at a constant level on account of the fact that loads of them get infected and transferred to class E.

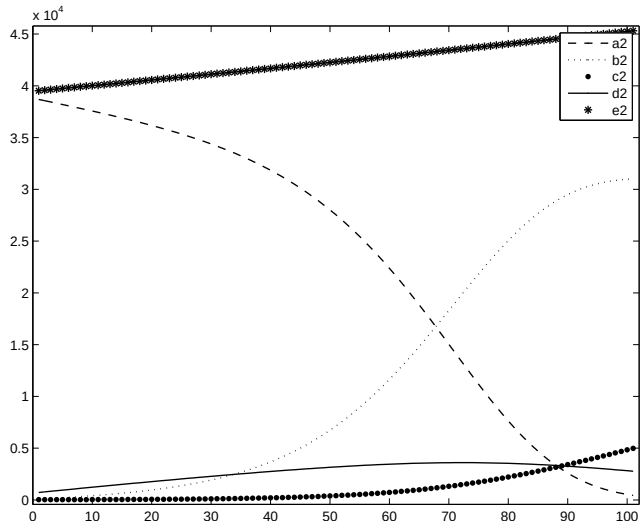

FIGURE 4. A solution of the system for men with initial conditions that are set as $(S_2(0), E_2(0), I_2(0), V_2(0), R_2(0)) = (37853, 62, 27, 720, 23)$. In this case, all the newborns and people who at risk will received the vaccine.

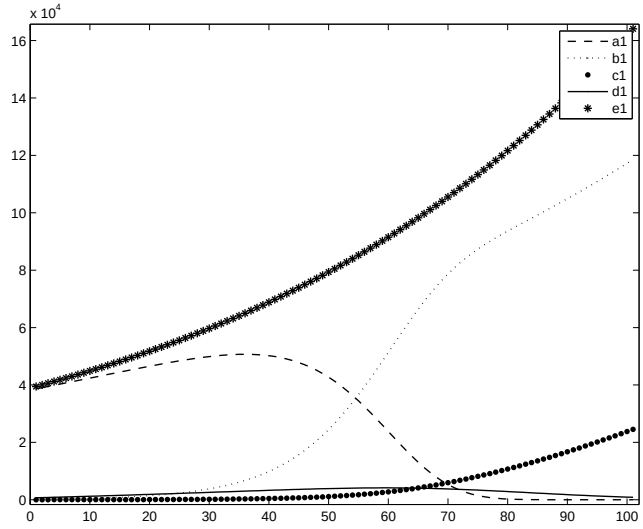

FIGURE 5. A solution of the system for women with initial conditions that are set as $(S_1(0), E_1(0), I_1(0), V_1(0), R_1(0)) = (37908, 56, 21, 681, 18)$. In this case, there is not enough vaccine for the population.

Thus, the curves for E and I have upward trends. As a result, the probability that the epidemic will happen in the future would be high.

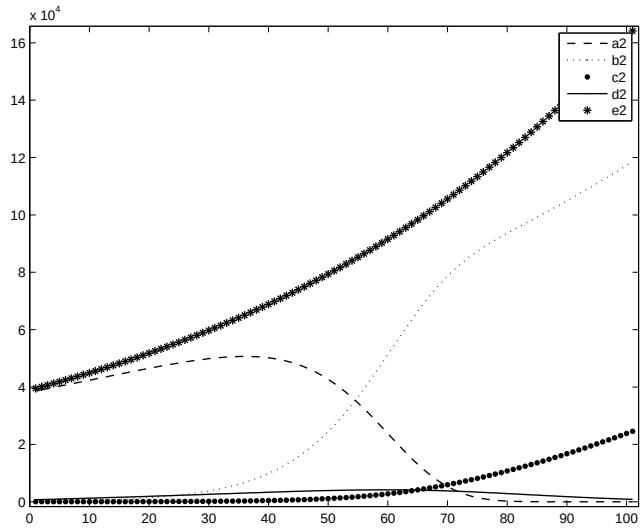

FIGURE 6. A solution of the system for men with initial conditions that are set as $(S_2(0), E_2(0), I_2(0), V_2(0), R_2(0)) = (37853, 62, 27, 720, 23)$. In this case, there is not enough vaccine for the population.

6. Conclusion

In this paper, two mathematical models for HBV related to a statistical sample were investigated. Specifically, the models are analyzed by applying a numerical method in MATLAB programming. In the end, the relationship between the vaccination and epidemic is investigated.

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