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Research Article

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On Horizontal Transmission of Hepatitis B Virus Infection on Graphs

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Abstract Hepatitis B is one of the leading infectious diseases of human. Approximately one third of the world's population has serological markers of past or present infection with hepatitis B virus (HBV) and 350–400 million people are chronic HBV surface antigen (HBs Ag) carriers. The objective of this study is to simulate the effects of household contacts on horizontal transmission dynamics of HBV. A graph was constructed, where a population is divided into household cliques and each member of the household is connected to some members of the global community by the mechanism of the random graph. The playing out of HBV transmission was simulated for various sizes of household cliques. The results show that the level of prevalence increases with the size of the household clique. Thus, the effect of the size of household clique on horizontal transmission of HBV is significant.

Keywords Hepatitis B, horizontal transmission, clique, graph

1. Introduction

Hepatitis means swelling of the liver. Hepatitis B is an infectious liver disease caused by infection with the hepatitis B virus. The infection can be acute (short-term), with an illness which may be mild with few or no symptoms or serious requiring management in a medical facility. Other people, especially infants and young children, do not recover from the acute stage. Instead, the infection remains and becomes a "chronic" or lifelong infection. Chronic hepatitis B refers to infection when the hepatitis B virus continues to be active in the person's body for more than 6 months [1]. Hepatitis B is one of the world's most serious health problems. Approximately one third of the world's population has serological evidence of past or present infection with hepatitis B virus (HBV) and 350–400 million people are chronic HBV surface antigen (HBsAg) carriers [2-7].

The routes of HBV transmission include sexual, percutaneous (intravenous drug use), perinatal, horizontal, transfusion, nosocomial and organ transplantation [8-9].

Horizontal transmission includes household, intrafamiliar and child-to-child transmission via minor breaks in the skin or mucous membranes [10].

HBV control measures include vaccination, education, screening of blood and blood products; and treatment [11]. However, hepatitis B viral mutants can emerge in patients as a result of selection pressure from either immune response or treatment options. The concern is that carriers with HBV mutants can still infect vaccinated individuals and mount resistance to antiviral drugs [12-13].

Epidemiological models help to capture infection or disease transmission mechanisms in a population in a mathematical frame-work to predict the behavior of the disease spread through the population. Mathematical models have become important tools in analyzing the spread and control of infectious diseases. Understanding the transmission characteristics of infectious diseases in communities, regions and countries across the world in model frame works can lead to better approaches to decreasing the transmission of these diseases [14].

Recently, mathematical models have been used to study the transmission dynamics of HBV in various communities, regions and countries across the world. Anderson and May [14] proposed a simple deterministic, compartmental mathematical model to investigate the effects of carriers on the transmission of HBV. Anderson

and May [15] and Williams *et al* [16] presented models of sexual transmission of HBV, which include heterogeneous mixing with respect to age and sexual activity. Edmunds *et al* [17] explored the relation between the age at infection with HBV and the development of the carrier state. Medley *et al* [18] proposed a model to show that the prevalence of infection is largely determined by a feedback mechanism that relates the rate of transmission, average age at infection and age-related probability of developing carriage following infection. Thornley *et al* [19] applied the model of Medley *et al* [18] to predict chronic hepatitis B infection in New Zealand. The prevalence of HBV in developing countries is different from that in developed countries, since it appears that the rate of transmission in childhood is the major determinant of the level of HBV endemicity and little is known on the rates and patterns of sexual contact in developing countries [20]. Mclean and Blumberg [21] and Edmunds *et al* [22] studied models of HBV transmission in developing countries and Williams *et al* [16] described a model of HBV in UK. O'Leary *et al* [23] proposed a mathematical model to investigate the effect of Hepatitis B vaccine and anti-viral treatment among the Canadian Inuit population. An optimal control model of Hepatitis B transmission dynamics was proposed by Mehmood [24]. Zou *et al* [25] proposed a mathematical model to investigate the transmission dynamics and prevalence of HBV in mainland China. Zou *et al* 26] used a mathematical model to study the sexual transmission dynamics of hepatitis B virus in China. Zhang *et al* [27] proposed a model to explore the transmission dynamics of hepatitis B virus in China.

Public health policy on the design of various HBV control programs has benefitted a lot from the recommendations of the previous mathematical modelers and much success has been recorded. However, available data in various regions on the prevalence of HBV infection show a slow pace of control [28]. Much still needs to be done until HBV infection is eradicated from the global community.

Our focus in this article is modeling of horizontal transmission of HBV. Since horizontal transmission includes household contact, we partition our population into households and connect members of the households to the global community with the aid of a random graph. A similar network for S-I-R model has been proposed by Ball *et al* (2009). For a general knowledge of graphs and their theory, we refer the reader to [29-39].

For a review of graph or network-based models, we refer the reader to Quax [40] and Tolentino [41]. Bai *et al* [42] propose a network spreading model for HIV, wherein each individual is represented by a node of the transmission network and the edges are the connections between individuals along which infection may spread. The sexual activity of each individual, measured by its degree, is not homogeneous but obeys power law distribution. Sloot *et al* [43] did stochastic simulation of HIV population through complex networks. The node-degrees obey power law distribution while the time evolution of the network is determined by a Markov process. Kretzchmar *et al* [44] did modeling prevention strategies for gonorrhea and chlamydia using stochastic network simulations. Their simulation model is discrete time Markov model describing pair formation and separation and disease transmission as stochastic processes. Morris and Kretzchmar [45] used stochastic simulations to investigate the effect of concurrent partnerships on transmission dynamics in networks. Quax [40] did modeling and simulation of propagation of infectious diseases in a homosexual population. The author constructed Kronecker graphs, with the node degrees obeying the power law distribution.

The plan of this work is as follows. Section 2 is devoted to model formulation. Simulation experiments are performed in section 3. Results are presented and discussed in sections 4 and 5 respectively. Finally conclusion is passed in section 6.

2. Model Formulation

A finite population is partitioned into k households of size n, wherein each household forms a clique and each member of the household connects to some members of the global community by the mechanism of the random graph. Each member of the population may be in one of the states: susceptible, acute infection state, carrier state and carriers in state of treatment. Susceptible individuals may become infected after contact with infected individuals. We adopt the recipe by Jaquet and Pechal [46] and represent each of the infected states by some arbitrary number L of states I_n $(n = 1, \ldots, L)$, each corresponding to one "stage" of the disease. Each of these stages is characterized by a real parameter α_n which we call infectiousness and which determines the probability that an individual in that stage infects another susceptible individual.

The underlying assumptions of our model are as follows.

(1) We set the number of susceptible individuals and select an of infected node randomly.
(2) At each time step for each susceptible node i, denote m_1, m_2 and m_3 for the numbers of its neighbouring infected nodes in the acute state, in the carrier state, and in the carrier state receiving treatment respectively. The probability that i will become infected in the next time step is
$p_1 = 1 - (1 - \beta_1)^{m_1}(1 - \beta_2)^{m_2}(1 - \beta_3)^{m_3}$
β is the transmission probability per contact.
(3) At each time step, each infected node may die with probability ε_1 (for the infected in the acute phase), ε_2 (for the infected in the carrier state) and ε_3 (for the infected carrier on treatment).
(4) At each time step, each susceptible node die with probability ε_4 .
(5) At each time step, the dead nodes are replaced each with probability ξ.
(6) At each time step, infected nodes in the acute phase proceed to the carrier state with probability λ_1.

3. Simulation

We perform the following simulation experiments. In all the experiments, we fix the population size at 5000. In the first experiment, we consider a scenario where the size of the household clique is 20. In the second episode, we fix the size of the household clique at 15. In the third experiment, we consider a situation where the size of the household clique is 10. In the fourth experiment, we simulate for the household clique of size 6. In the fifth episode, we consider a situation where the size of the household clique is 5. The household clique of size 4 is selected for the sixth experiment. In the seventh experiment, we consider a situation where the size of the household clique is 3. In the eighth experiment, we simulate for the household clique of size 2.
We use the following parameter values for the purpose of our simulations.
$\beta_1 = 0.05;\ \beta_2 = 0.0152;\ \beta_3 = 0.005;\ \varepsilon_1 = 0.018; \varepsilon_2 = 0.025;\ \varepsilon_3 = 0.02;\ \varepsilon_4 = 0.016;\ \xi = 0.03;\ \lambda_1 = 0.7.$
Remark: Due to scarcity of data some of these parameter values were assumed and others estimated. Research for the estimation of these parameter values is necessary. Our focus is household clique effect and that is what is investigated in this article.

4. Results Discussion

In this article, we investigate the effects of different clique sizes on the prevalence of hepatitis B virus infection. The main results are shown in Figures 1 through 8. Figure 8 demonstrates impact of household cliques of size 20. This result shows that size 20 cliques can precipitate a large epidemic size. As it is evidenced in our results, an epidemic can occur within cliques of size 4 and above, with the epidemic size proportional to the size of the clique. This can be observed in Figures 1 through 6. Our results in figures 7 and 8 show that an epidemic cannot occur within cliques of sizes 2 and 3. The findings in this study highlight the significance of the size of the household cliques on the horizontal transmission of hepatitis B.

The results of the simulation experiments are shown in the sequel.

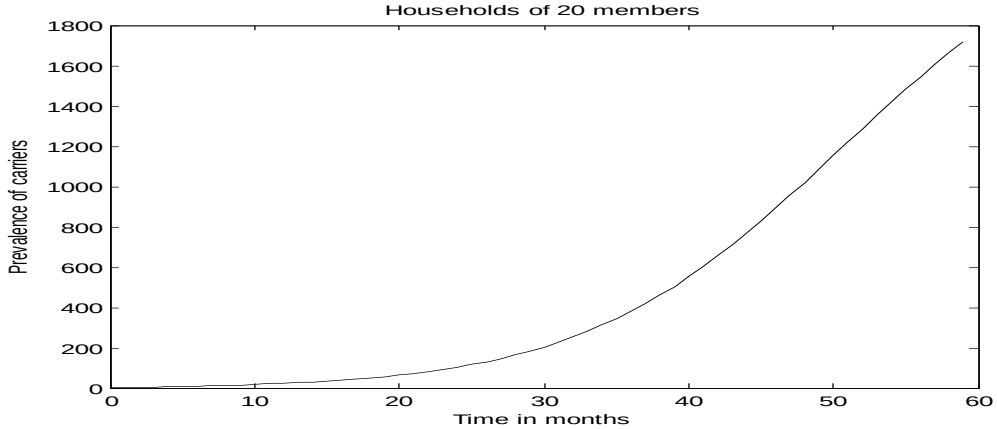

Figure 1: Graph showing the prevalence of HBV, S(0)=5000,C(0)=1,clique size=20

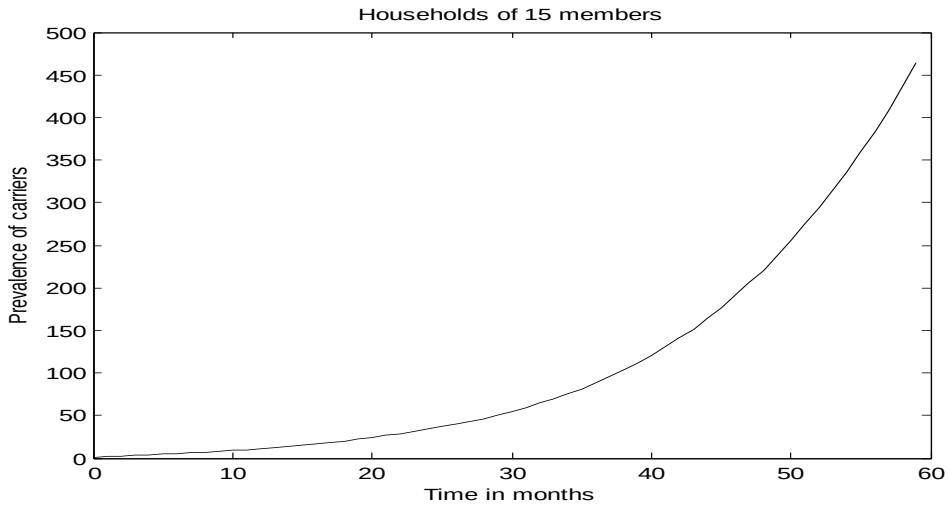

Figure 2: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=15

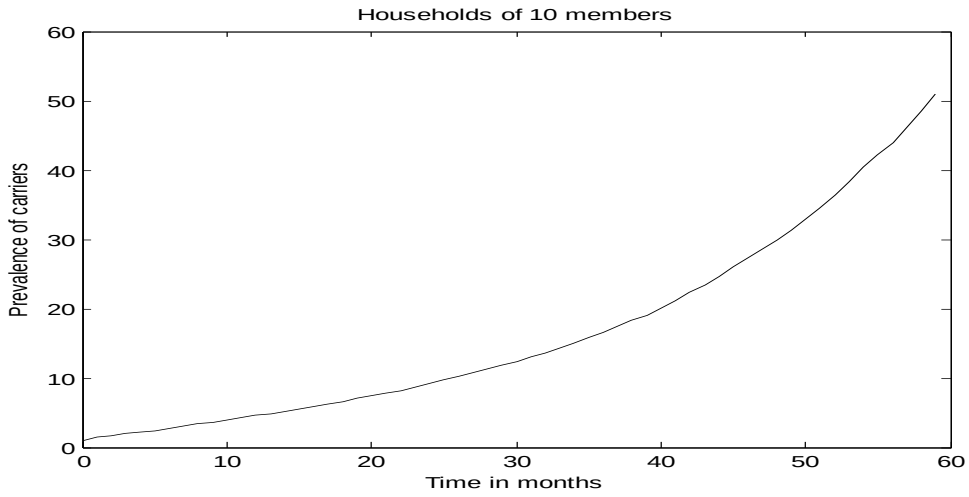

Figure 3: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=10

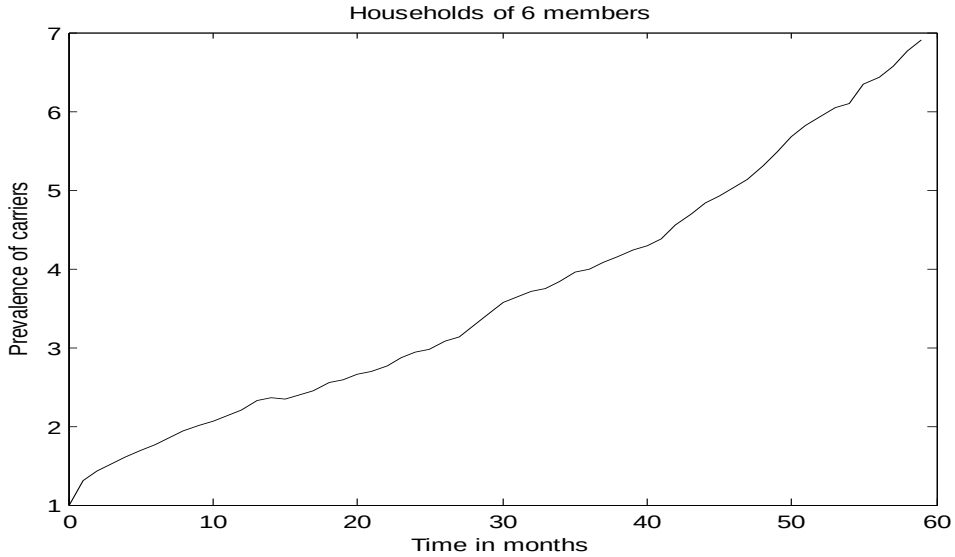

Figure 4: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=6

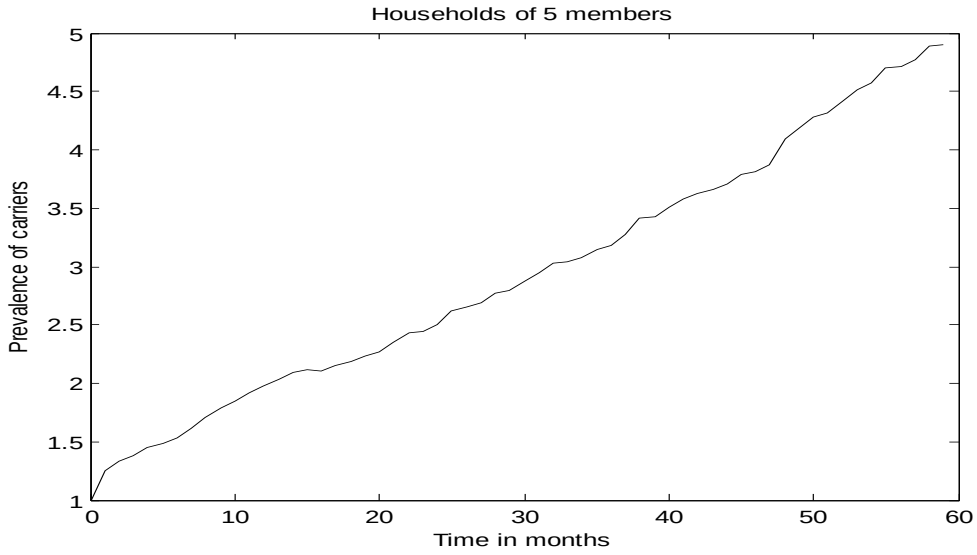

Figure 5: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=5

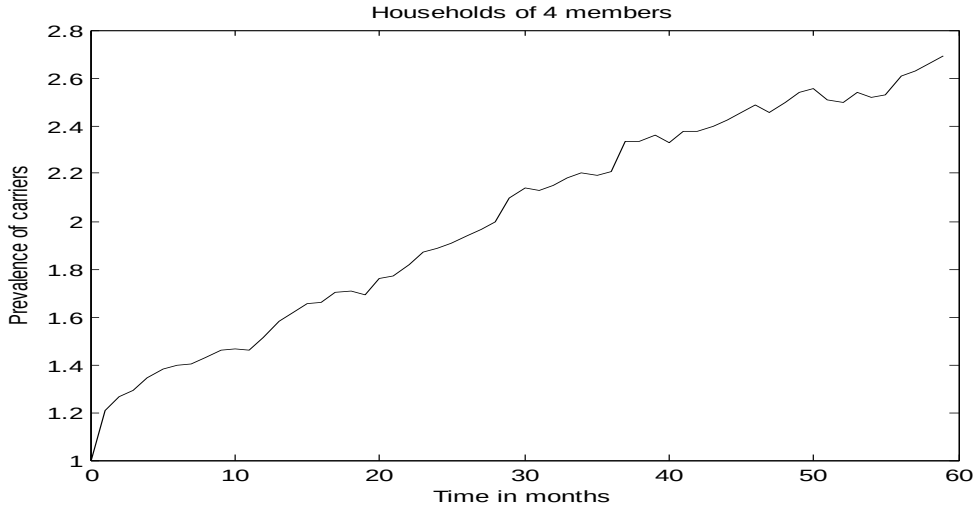

Figure 6: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=4

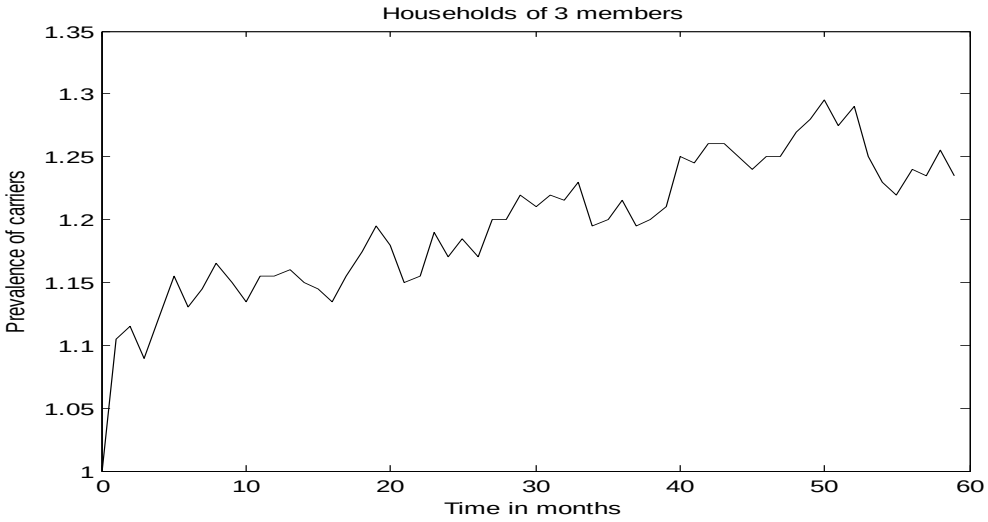

Figure 7: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=3

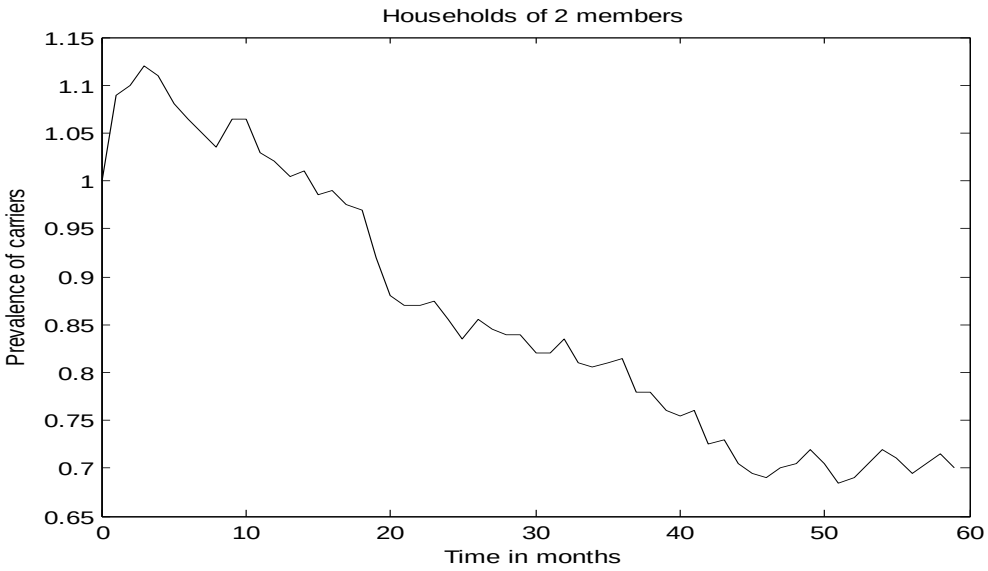

Figure 8: Graph showing the prevalence of HBV,S(0)=5000,C(0)=1,clique size=2

5. Conclusion

In this article, we have developed and investigated the effects of horizontal transmission dynamics of HBV on a graph. The results emphasize the significance of the size of the household cliques on the horizontal transmission of HBV.

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