

ANALYSIS AND MODELLING OF PREVALENCE OF HEPATITIS B USING DIFFERENTIAL EQUATIONS: A CASE STUDY OF THE TANO NORTH DISTRICT

ABSTRACT

We use the SIR model Kermack and Mckendrick (Kermack and Mckendrick, 1927) and modify it for hepatitis B with vaccination. The main goal is to use existing clinical hepatitis B data from the biostatistics department of the Tano North district health directorate to formulate a mathematical model to understand the dynamics in the Tano North district and assist decision makers to formulate the best ideas to prevent, control and eradicate the disease. Analyses is made of the existence and stability of the disease free and endemic equilibria. It is proven that the disease free equilibrium is locally asymptotically stable if the basic reproductive ratio, $R_0 < 1$ and when $R_0 > 1$ we have the endemic equilibrium. MATLAB was used for the programming and simulations.

Keywords: control of disease spread, differential equations, hepatitis B, prevention, eradication of disease

INTRODUCTION

Hepatitis, inflammation of the liver caused by viruses, bacterial infections, or continuous exposure to alcohol, drugs, or toxic chemicals, such as those found in aerosol sprays and paint thinners (Ganem & Prince, 2004). Inflammation is the painful, red swelling that result when tissues of the body become injured or infected (Williams, 2006). Inflammation can cause organs

to not work properly. Hepatitis can also result from an autoimmune disorder, in which the body mistakenly sends disease-fighting cells to attack its own healthy tissue, in this case the liver(Barker *et al.*, 1996). The liver is located in the upper right hand side of the abdomen, mostly behind the rib cage. The liver of an adult normally weighs close to three pounds. No matter what its cause, hepatitis reduces the liver's ability to perform life-preserving functions, including filtering harmful infectious agents from the blood, storing blood sugar and converting it to usable energy forms, and producing many proteins necessary for life (Edmunds *et al.*, 1993).

When doctors speak of viral hepatitis, they usually are referring to hepatitis caused by a few specific viruses that primarily attack the liver. There are several hepatitis viruses; they have been named types A, B, C, D, E, F (not confirmed), and G (Anderson *et al.*, 1992). As our knowledge of hepatitis viruses grows, it is likely that this alphabetical list will become longer (Hahnea *et al.*, 2004). The most common hepatitis viruses are types A, B, and C (Anderson *et al.*, 1991).

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV) (Edmunds *et al.*, 1993). It is a major global health problem and the most serious type of viral hepatitis (Cui *et al.*, 2006). Originally known as "serum hepatitis", the disease has caused epidemics in parts of Asia and Africa, and it is endemic in China (Williams, 2006). About a third of the world population has been infected at one point in their lives, including 350 million who are chronic carriers which causes 620,000 deaths worldwide each year (WHO, 2010; Shepard *et al.*, 2006).

45 Hepatitis B virus is transmitted between people by direct blood-to-blood contact or semen and
 46 vaginal fluid of an infected person (Chang, June 2007). Modes of transmission are the same as
 47 those for the human immunodeficiency virus (HIV), but the hepatitis B virus is 50 to 100 times
 48 more infectious (Thornley *et al.* 2008). Unlike HIV, the hepatitis B virus can survive outside the
 49 body for at least seven days. During this time, the virus can still cause infection if it enters the
 50 body of a person who is not protected by the vaccine (Liu, G.-T., *et al.*, 2002).

51 The hepatitis B vaccine contains a protein (antigen) that stimulates the body to make protective
 52 antibodies. Examples of hepatitis B vaccines available include hepatitis B vaccine-injection
 53 (Engerix-B, Recombivax-HB). Three doses (given at 0, 1, and 6 months of age) are necessary to
 54 assure protection (Edmunds *etal.*, 1993). There are also combination vaccines on the market that
 55 provide protection against hepatitis B and other diseases (Kretzschma *et al.* 2002). Hepatitis B
 56 vaccines are effective and safe. Up to 95% of vaccinated individuals form effective antibodies
 57 when they get the vaccine and are protected from hepatitis B (Shepard *et al.*, 2006; Maynard *e*
 58 *tal.*, 1989).

59 We seek to model the transmission of a disease through a population. Such modeling is very
 60 important to the study of epidemiology and the practice of medicine, since examining the relative
 61 effect of factors that govern the spread of a disease can help communities and health workers
 62 better prepare for and combat an outbreak.

63 A detailed understanding of the transmission of the hepatitis B virus and other emerging
 64 pathogens is crucial in its containment. Mathematical models can give insight into potential
 65 impact interventions. The complex interaction of different infection control strategies and their
 66 likely impact on transmission can be predicted using mathematical models.

The hepatitis B infection is an increasing burden on our health care systems. Hepatitis B is not only one of the leading causes of morbidity and mortality, but it is also a serious health problem in Ghana and the hepatitis B virus is on the rise worldwide. Mr Stephen Corquaye, a Clinical Pharmacist, Korle Bu Teaching Hospital, who was speaking at the launch of the World Hepatitis Day organized by the Pharmaceutical Society of Ghana last year on the 28th of July, 2011 said ‘it is estimated that about four million people in the country are infected with the Hepatitis B virus’. This figure is quite alarming looking at the rate of transmission of the hepatitis B virus. Mr Yusuf Inua, a pharmacist at the MOH (ministry of health), who is also the Head of Logistics at the MOH, pledged Government’s commitment towards the fight against the disease and urged corporate entities to also come on board. He noted that the Ministry will soon carry out a program for hepatitis B as it has done for malaria and HIV and AIDS to minimize its prevalence. This thesis may assist in that direction.

In the natural history of HBV infection it is estimated that 10% to 33% of those who develop persistent infection end up with chronic hepatitis of which 20% to 50% may develop liver cirrhosis (world health organization, 2000). Hepatitis B is considered an important public health problem necessitating high priority strategies for prevention and control (Maynard *et al.*, 1989). An estimated worldwide carrier of hepatitis B virus is 350 million, with an estimated 50 million chronic carriers of HBV in Africa (Lavanchy., 2004). In sub-Saharan Africa, carrier rates range from 9% to 20% (world health organization, 2004). HBV is endemic in Ghana with sero-prevalence rates ranging from 6.7% to 10% in blood donors, 6.4% in pregnant women and 15.6% in children among the general population. In jaundiced patients the rate is 54.1% (Acheampong, 1991).

90

91 The purpose of this study is to investigate the sero-prevalence of HBV infections among patients
 92 in the Tano north district. In a report by the district health directorate this year it was noted that
 93 there has been a considerable increase in the number of cases since 2009 to date. For instance the
 94 incidence has increased by 22% from 2010 to 2011. Therefore measures must be put in place to
 95 reduce the incidence of the disease. The district has put in place policies to eradicate hepatitis B,
 96 we seek to know how effective those policies are. There is also a vaccination program initiated
 97 by the district, we investigate if the program is helping and the number of people they have to
 98 vaccinate to put the disease under control.

99

100 The purpose of this thesis is to predict the spread of the hepatitis B disease in the Tano North
 101 district using differential equations, to do mathematical analysis of the model and to interpret the
 102 results of the model and by carrying out sensitivity analysis of the basic reproduction number on
 103 various parameters, we shall suggest some optimal strategies to control HBV infection in the
 104 Tano North District.

105

106 MATHEMATICAL MODELING

107 In the last two decades, mathematical models have been used frequently to study the
 108 transmission dynamics of HBV in various regions. Anderson and May (1991) used a simple
 109 deterministic, compartmental mathematical model to illustrate the effects of carriers on the
 110 transmission of HBV. Anderson *et al.* (1992) and Williams *et al.* (1996) described models of the
 111 sexual transmission of HBV, which include heterogeneous mixing with respect to age and sexual
 112 activity. Edmunds *et al.* (1993) illustrated the relation between the age at infection with HBV and

the development of the carrier state. Medley *et al.* (2001) gave 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.* (2008) applied the model of Medley *et al.* (2001) 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 (Edmunds *et al.*, 1996c), and little is known on the rates and patterns of sexual contact in developing countries. McLean and Blumberg (1994) and Edmunds *et al.* (1996a) studied models of HBV transmission on developing countries and Williams *et al.* (1996) described a model of HBV in the UK.

We propose a mathematical model to understand the trans-mission dynamics and prevalence of HBV in the Tano North district. The model is constructed based on the characteristics of HBV transmission in the Tano North district and the model of Kermack and Mckendrick, (1927). The immunity after vaccination is lifetime (Sun *et al.*, 2002). Therefore, we divide the host population into three epidemiological groups: the proportion susceptible to infection S ; those infected I ; removed and with protective immunity R . Fig. 1 illustrates the three compartments and model variables.

MATERIALS AND METHOD

Data was collected from all the nine health facilities in the district and complied by the district statistician. The data was then taken to the district health director for endorsement. Again, we went to the Regional Statistical Service, Brong Ahafo Region to take data on the population and the population growth rate. The following were our values and parameter estimations;

- TOTAL POPULATION (N)= 74775
- INITIAL NUMBER OF INFECTED INDIVIDUALS (I_0)= 25
- INITIAL NUMBER OF SUSCEPTIBLE INDIVIDUALS (S_0)= 73475
- FINAL NUMBER OF SUSCEPTIBLE INDIVIDUALS (S_∞)=71246
- RECOVERY RATE (β)=0.984155
- INFECTIOUS RATE (α)=1.0058
- RELATIVE REMOVAL RATE (ρ)=0.97848
- DEATH RATE (μ)=0.0094
- VACCINATED SUSCEPTIBLE (P)=0.017051



Figure 1. Flow chat of HBV transmission of a population

Where α is the transmission rate coefficient and β is the removed rate coefficient.

The model is given by three ordinary differential equations:

$$\frac{dS}{dt} = -\alpha SI(1)$$

$$\frac{dI}{dt} = \alpha SI - \beta I \quad (2)$$

$$\frac{dR}{dt} = \beta I \quad (3)$$

With initial conditions $S(0) = S_0 > 0, I(0) = I_0 > 0, R(0) \geq 0$.

These are modified by introducing the vaccinated susceptible individuals in the population. Those who receive the vaccine gain a life time immunity (Edmunds et al., 1996b). Figure 2 illustrates the variations;

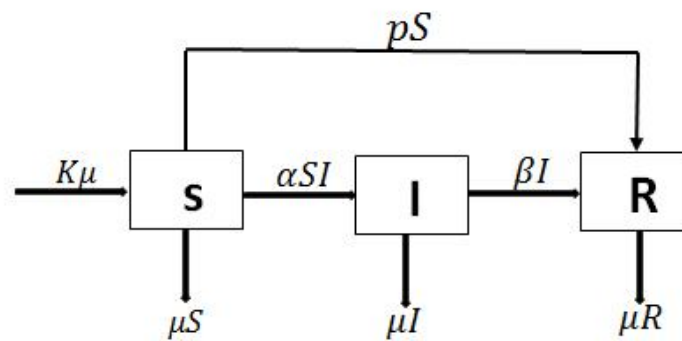


Figure 2. Flow chat of HBV transmission with vaccination in a population

Where;

$K\mu$ = birth rate of the population

pS = vaccinated susceptible

μ = natural death rate

α = infection rate

β =recovery rate

163

$$\frac{dS}{dt} = \mu K - \alpha SI - \mu S - pS \quad (4)$$

$$\frac{dI}{dt} = \alpha SI - (\beta + \mu)I \quad (5)$$

$$\frac{dR}{dt} = \beta I - \mu R + pS \quad (6)$$

164 The reproductive ratio R_0 of hepatitis B with vaccination can be calculated from equations (4),
165 (5) and (6) as follows;

166 The Jacobian matrix for the equations will be written as;

$$J(S, I, R) = \begin{bmatrix} -\alpha I - \mu - p & -\alpha S & 0 \\ \alpha I & \alpha S - \beta - \mu & 0 \\ p & \beta & -\mu \end{bmatrix}$$

167 The first two equations (4) and (5) do not depend on R. Thus, we need to consider the system of
168 equations

$$\mu K - \alpha SI - \mu S - pS = 0$$

$$\alpha SI - \beta I - \mu I = 0$$

169 Therefore the Jacobian matrix becomes

$$J(S, I) = \begin{bmatrix} -\alpha I - \mu - p & -\alpha S \\ \alpha I & \alpha S - \beta - \mu \end{bmatrix}$$

170

171 In order to determine the stability of the systems (4) and (5), we substitute $I = 0$ into the
172 linearized Jacobian matrix to find the eigenvalues as follows

$$J(S, 0) = \begin{bmatrix} -\mu - p & -\alpha S \\ 0 & \alpha S - \beta - \mu \end{bmatrix}$$

$$\text{Det}(J - \lambda) = \begin{vmatrix} -\mu - p - \lambda & -\alpha S \\ 0 & \alpha S - \beta - \mu - \lambda \end{vmatrix}$$

$$\text{Det}(J - \lambda) = 0$$

$$(-\mu - p - \lambda)(\alpha S - \beta - \mu - \lambda) = 0$$

$$-\mu - p - \lambda = 0$$

$$\lambda_1 = -\mu - p$$

173 Also

$$[(\alpha S - \beta - \mu) - \lambda] = 0$$

$$-\lambda = -(\alpha S - \beta - \mu)$$

$$\lambda_2 = \alpha S - \beta - \mu$$

174 The parameter ranges are as follows, $0 < \mu < 1, 0 < p < 1, 0 < \beta < 1$ and $0 < \alpha < 1$. λ_2
 175 depends on α, β, S and μ . Although, the first term αS is positive, the second and third terms are
 176 negative. This implies that the sign of λ_2 depends on αS , but $0 < \alpha < 1$. If S becomes large, λ_2
 177 will be positive and if S becomes small, α will make the value of the first term small, thereby
 178 making the value of λ_2 negative. Therefore $\alpha S \ll \beta$ and λ_2 is negative. Also $p \square \beta$ and that
 179 makes λ_2 the most negative.

180 Therefore λ_2 is the dominant eigenvalue, since it is the most negative eigenvalue.

$$R_0 = \lambda^* \times (\text{infectious period}) + 1$$

181 We now consider the initial condition $S = S_0$

$$R_0 = \left(\frac{\alpha S_0 - \beta - \mu}{1} \right) \times \frac{1}{(\mu + \beta)} + 1$$

$$R_0 = \frac{\alpha S_0 - \beta - \mu}{(\mu + \beta)} + 1$$

$$R_0 = \frac{\alpha S_0 - \beta - \mu + \mu + \beta}{(\mu + \beta)}$$

$$R_0 = \frac{\alpha S_0}{(\mu + \beta)} \quad (7)$$

182 This is the average number of secondary infections caused by one infected individual during the
 183 mean course of infection in the case where the number of susceptible is counted from the disease
 184 free equilibrium; that is the total susceptible of the population when disease is free (Wang *et al.*,
 185 2004). When $R_0 > 1$ there is an endemic and the solution is unstable but when $R_0 < 1$ a positive
 186 equilibrium occurs and the solution is stable (Shepard *et al.*, 2006).

187 EQUILIBRIUM POINTS

188 In order to determine the stability of the model we first evaluate the equilibrium points or steady
 189 states of the system of the ordinary differential equations (4), (5), and (6). The points to be found
 190 are disease-free (where $I=0$), and endemic ($I \neq 0$). We set the right-hand side of the equations in
 191 the system (4), (5) and (6) to zero and then solve for the values of S, I, and R as follows:

192 At the steady state,

$$\frac{dS}{dt} = 0, \frac{dI}{dt} = 0 \text{ and } \frac{dR}{dt} = 0$$

$$\mu K - \alpha SI - \mu S - pS = 0 \quad (8)$$

$$\alpha SI - \beta I - \mu I = 0 \quad (9)$$

$$\beta I - \mu R + pS = 0 \quad (10)$$

193 From equation (9) above

$$(\alpha S - \beta - \mu)I = 0$$

$$I = 0 \text{ and } \alpha S - \beta - \mu = 0$$

$$\square S = \frac{\beta + \mu}{\alpha} \quad (11)$$

194 From equation (8)

$$\mu K = \alpha SI + \mu S + pS$$

$$\mu K = (\alpha I + \mu + p)S$$

$$\frac{\mu K}{S} = \alpha I + \mu + p$$

$$\frac{\mu K}{S} - \mu - p = \alpha I$$

$$\frac{\mu K}{S} - (\mu + p) = \alpha I$$

$$I = \frac{\mu K}{\alpha S} - \frac{(\mu + p)}{\alpha}$$

195 But from equation (11) $S = \frac{\beta + \mu}{\alpha}$

$$I = \frac{\mu K}{\alpha \left(\frac{\beta + \mu}{\alpha} \right)} - \frac{(\mu + p)}{\alpha}$$

$$I = \frac{\mu K}{\left(\frac{\alpha(\beta + \mu)}{\alpha} \right)} - \frac{(\mu + p)}{\alpha}$$

$$I = \frac{\alpha \mu K}{\alpha(\beta + \mu)} - \frac{(\mu + p)}{\alpha}$$

$$I = \frac{\alpha \mu K - (\beta + \mu)(\mu + p)}{\alpha(\beta + \mu)} \quad (12)$$

196 From equation (10)

$$\beta I - \mu R + pS = 0$$

$$\mu R = \beta I + pS$$

$$R = \frac{\beta I + pS}{\mu} \quad (13)$$

197 Substituting equations (11) and (12) into equation (13)

$$R = \frac{\beta \left[\frac{\alpha \mu K - (\beta + \mu)(\mu + p)}{\alpha(\beta + \mu)} \right] + p \left(\frac{\beta + \mu}{\alpha} \right)}{\mu}$$

$$R = \frac{\beta [\alpha \mu K - (\beta + \mu)(\mu + p)] + p(\beta + \mu)(\beta + \mu)}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\beta \alpha \mu K - \beta(\beta + \mu)(\mu + p) + p(\beta + \mu)(\beta + \mu)}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\beta \alpha \mu K + (\beta + \mu)[- \beta(\mu + p) + p(\beta + \mu)]}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\beta \alpha \mu K + (\beta + \mu)[- \beta \mu - \beta p + p\beta + P\mu]}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\beta \alpha \mu K + (\beta + \mu)[- \beta \mu + P\mu]}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\beta \alpha \mu K + (\beta + \mu)(\beta - P)(-\mu)}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\mu [\beta \alpha K - (\beta + \mu)(\beta - P)]}{\mu \alpha (\beta + \mu)}$$

$$R = \frac{\beta\alpha K - (\beta + \mu)(\beta - P)}{\alpha(\beta + \mu)} \quad (14)$$

$$(S^*, I^*, R^*) = \left[\frac{\beta + \mu}{\alpha}, \frac{\alpha\mu K - (\beta + \mu)(\mu + p)}{\alpha(\beta + \mu)}, \frac{\beta\alpha K - (\beta + \mu)(\beta - P)}{\alpha(\beta + \mu)} \right] \quad (15)$$

198 Now when $I = 0$, equation (8)

$$\mu K - \alpha SI - \mu S - pS = 0$$

$$\mu K - \alpha S(0) - \mu S - pS = 0$$

$$\mu K - \mu S - pS = 0$$

$$\mu K = \mu S + pS$$

$$\mu K = S(\mu + p)$$

$$S = \frac{\mu K}{\mu + p} \quad (16)$$

199 Putting $I = 0$, into equation (10)

$$\beta I - \mu R + pS = 0$$

$$\beta(0) - \mu R + pS = 0$$

$$-\mu R + pS = 0$$

$$\mu R = pS$$

$$R = \frac{pS}{\mu} \quad (17)$$

200 Substituting equation (11) into equation (17)

$$R = \frac{p \left(\frac{\mu K}{\mu + p} \right)}{\mu}$$

$$R = \frac{p\mu K}{\mu(\mu + p)}$$

$$R = \frac{pK}{(\mu + p)} \quad (18)$$

201

202 At the disease free equilibrium

$$(S^*, I^*, R^*) = \left(\frac{\mu K}{\mu + p}, 0, \frac{pK}{(\mu + p)} \right)$$

203

204

205

206

207 Stability Analysis of Disease-Free Equilibrium Point

208 To determine the stability of the system of the disease-free equilibrium (S,I)=(1,0), we will
 209 consider the linearized system of the equations (4) and (5) below about the equilibrium point by
 210 taking the Jacobian.

$$\frac{dS}{dt} = \mu K - \alpha SI - \mu S - pS$$

$$\frac{dI}{dt} = \alpha SI - (\beta + \mu)I$$

211 The Jacobian is therefore given by

$$J(S, I) = \begin{bmatrix} -\alpha I - \mu - p & -\alpha S \\ \alpha I & \alpha S - \beta - \mu \end{bmatrix}$$

212 The Jacobian matrix becomes

$$J(S, 0) = \begin{bmatrix} -\mu - p & -\alpha S \\ 0 & \alpha S - \beta - \mu \end{bmatrix}$$

213 Since S=1 and I=0 at the disease free equilibrium

$$\text{Det}(J - \lambda) = \begin{vmatrix} -\mu - p - \lambda & -\alpha S \\ 0 & \alpha S - \beta - \mu - \lambda \end{vmatrix} = 0$$

$$Det(J - \lambda) = 0$$

$$(-\mu - p - \lambda)(\alpha S - \beta - \mu - \lambda) = 0$$

$$\lambda_1 = -\mu - p \text{ and } \lambda_2 = \alpha S - \beta - \mu$$

214 For $Det(J - \lambda)$ to be asymptotically stable, both eigenvalues must be negative. From

215 $Det(J - \lambda) = 0$, it is clear that $\lambda_1 = -\mu - p$ is negative and therefore if $\lambda_2 = \alpha S - \beta - \mu < 0$
 216 then both eigenvalues are negative and $R_0 < 1$. Hence the disease free-equilibrium is
 217 asymptotically stable if $R_0 < 1$. On the other hand, if $\lambda_2 = \alpha S - \beta - \mu > 0$, then $Det(J - \lambda)$ is
 218 unstable.

219 RESULTS AND DISCUSSIONS

220 STABILITY ANALYSIS OF EQUILIBRIUM POINTS

$$(s^*, I^*) = \left(\frac{\beta + \mu}{\alpha}, 0 \right)$$

221 Substituting $\alpha = 1.00588, \mu = 0.0094, \beta = 0.984155$ into (s^*, I^*) gives

$$(s^*, I^*) = \left(\frac{0.984155 + 0.0094}{1.0058}, 0 \right)$$

$$(s^*, I^*) = (0.987826, 0)$$

222 Substituting this into the Jacobian matrix below gives

$$Det(J - \lambda) = \begin{vmatrix} -\mu - p - \lambda & -\alpha S \\ 0 & \alpha S - \beta - \mu - \lambda \end{vmatrix} = 0$$

$$\begin{aligned} \text{Det}(J - \lambda) &= \begin{vmatrix} -0.0094 - 0.017051 - \lambda & -1.0058(0.982615) \\ 0 & 1.0058(0.982615) - 0.984155 - 0.0094 - \lambda \end{vmatrix} \\ &= 0 \end{aligned}$$

223

$$\text{Det}(J - \lambda) = \begin{vmatrix} -0.026451 - \lambda & -0.988314 \\ 0 & 3.908 \times 10^{-7} - \lambda \end{vmatrix} = 0$$

$$(-0.026451 - \lambda)(3.908 \times 10^{-7} - \lambda) = 0$$

$$-1.03371 \times 10^{-8} + 0.026451\lambda - 3.908 \times 10^{-7}\lambda + \lambda^2 = 0$$

$$\lambda^2 + 0.026451\lambda - 1.03371 \times 10^{-8} = 0$$

$$\lambda_1 = -0.026451 \text{ and } \lambda_2 = 3.90796 \times 10^{-7}$$

224 This is a saddled point, since λ_1 and λ_2 have distinct eigenvalues. The equilibrium point
225 $(s^*, I^*) = (0.987826, 0)$ is therefore unstable. This is so because the transmission rate of HBV in
226 the Tano North District is greater than the recovery rate of the disease in the district.

227

228 Substituting $\alpha = 1.00588, \mu = 0.0294, \beta = 0.984155$ and $S_0 = 0.983283$ into R_0 gives

$$R_0 = \frac{1.0058 \times 0.982615}{(0.0094 + 0.984155)} = 0.994725$$

$$R_0 = 0.994725 < 1$$

229 Therefore with vaccination a positive equilibrium occurs and the solution is stable. When there is
230 an epidemic outbreak in a certain part of a country, a vaccination program is considered; this can
231 be expensive. Because of that, there is the need to decide how many people to be vaccinated in

order to control and contain the epidemic. In the same way, the required number of people that needs to be vaccinated in the Tano North District can be estimated as follows;

$$H_1 = \frac{R_0 - 1}{R_0} = \frac{1.00423 - 1}{1.00423} = 0.004212$$

Where H_1 is the herd immunity threshold. That is about 0.42% of the susceptible population should be immune in order to bring the spread of hepatitis B under total control in the Tano north district.

Research has shown that the vaccine for HBV has 95% effectiveness (Edmunds et al., 1993; McLean and Blumberg, 1994; Zhao et al., 2000). Knowing the efficacy of the vaccine we estimate the proportion of the population that need to be vaccinated.

This is given by

$$p > \frac{1 - \left(\frac{1}{1.00423}\right)}{0.95} = 0.004434$$

We can observe from calculation above that when the effectiveness is 95%, then about 0.44% of the population need to be vaccinated in order for $C_v < 1$. Where C_v is the Control Vaccination Number which is the average number of secondary cases generated by an infectious case during epidemic with control measure, in this case vaccination. The formula for estimating the control vaccination number is given by

$$C_v = R_0(1 - hp)$$

Where h is the vaccine efficacy (the effectiveness of the vaccine) and p is the vaccination coverage (the fraction of the population that has been vaccinated). The goal of researchers is to have $C_v < 1$ (Maynard *et al.*, 1989).

We proceed by doing the Sensitivity Analysis of R_0 of Hepatitis B without Vaccination

- a. If α and β values are increased and S_0 remains the same, that is 2.0058 and 0.999155 respectively.

$$R_0 = \frac{\alpha S_0}{\beta} = \frac{2.0058(0.982615)}{0.999155} = 1.9726 > 1$$

That is to say, keeping the number of susceptible individuals in Tano North district constant any value of α and β greater than the values used in this thesis (thus $\alpha = 1.0058$ and $\beta = 0.984155$) will make R_0 greater than 1.

- b. If α and β values are reduced to $\alpha = 0.0058$ and $\beta = 0.884155$ but S_0 maintained at 0.982615.

$$R_0 = \frac{\alpha S_0}{\beta} = \frac{0.0058(0.982615)}{0.884155} = 0.006446 < 1$$

That is to say, reducing the values of α and β and maintaining the number of susceptible will make $R_0 < 1$.

Sensitivity Analysis of R_0 of Hepatitis B with Vaccination is also as follows;

- a. If α and β values are increased and S_0 remains the same, that is 2.0058 and 0.999155 respectively.

$$R_0 = \frac{\alpha S_0}{(\mu + \beta)} = \frac{2.0058(0.982615)}{(0.0094 + 0.999155)} = 1.95421 > 1$$

That is to say, when the values of α and β are increased above $\alpha = 1.0058$ and $\beta = 0.984155$, R_0 remains greater than 1 as required.

- b. If α and β values are reduced to $\alpha = 0.0058$ and $\beta = 0.884155$ but S_0 maintained at 0.982615.

$$R_0 = \frac{\alpha S_0}{(\mu + \beta)} = \frac{0.0058(0.982615)}{(0.0094 + 0.884155)} = 0.006378 < 1$$

266 That is to say, when the values of α and β are reduced below $\alpha = 1.0058$ and

267 $\beta = 0.984155$ the value of R_0 will be less than 1.

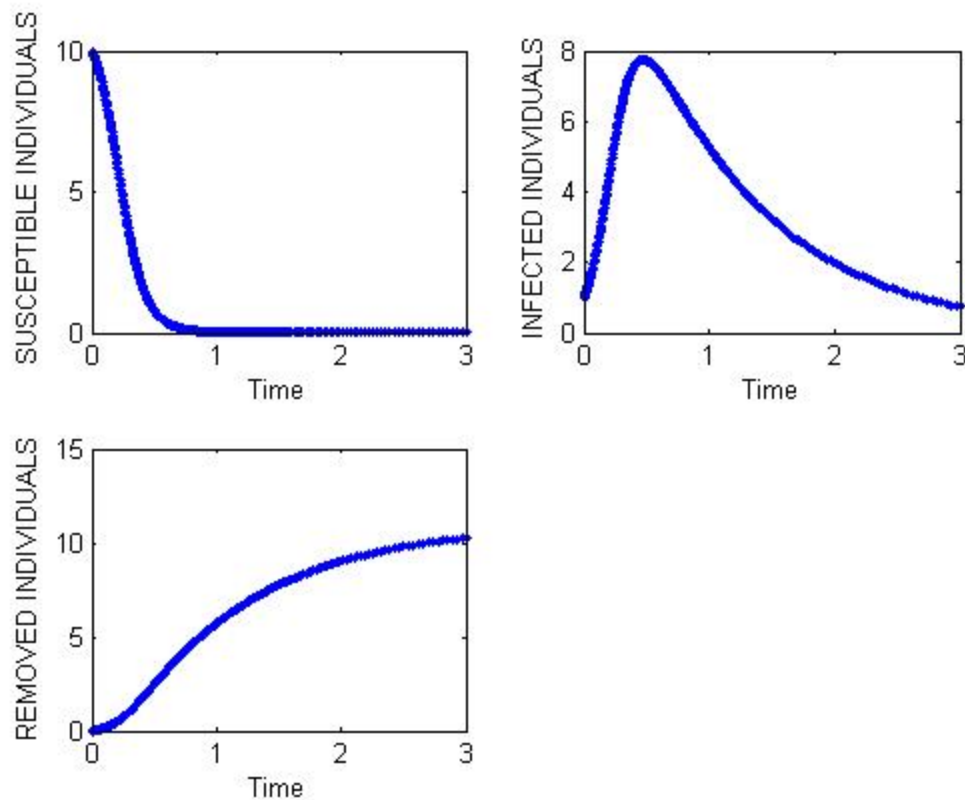
268
269 We proceed to simulate our model using Matlab R2012a (7.14.0.739). The values of S, I and R,
270 are altered and the changes that occur in model are observed.

271

272 **Sensitivity Analysis of Hepatitis B Transmission without Vaccination by Simulation.**

273 Assuming the number of susceptible in the population is 10 and there is no vaccinated individual
274 meaning no removed individuals, we introduce one infective into our system. The simulation
275 gives us these graphs.

276



277

278 **Figure 3. $S=10$, $I=1$ and $R=0$.**

279 You will observe that by a short period, the number susceptible would have decreased to zero.

280 This is because of the negative sign in the model. Since we assumed a constant population, the

281 number susceptible decrease to zero.

282

283 The number of infected individuals increases gradually till it reaches its peak value.

284

285 The removed individuals increase gradually that is due to deaths by infected individuals moving

286 from the infected compartment to the removed compartment.

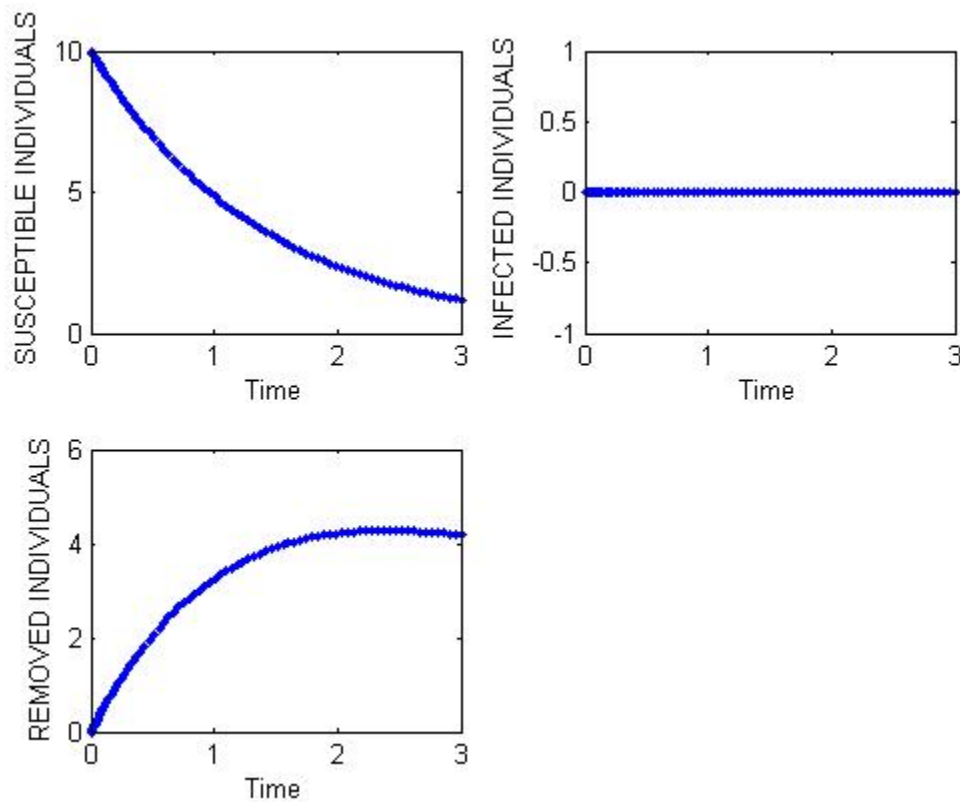


Figure 4. $S=10$, $I=0$ and $R=0$

It will observe that the number susceptible decrease in a short time and move to the removed compartment due to vaccination.

297 Since there is no infected individual in the population, the number remains a constant at zero.

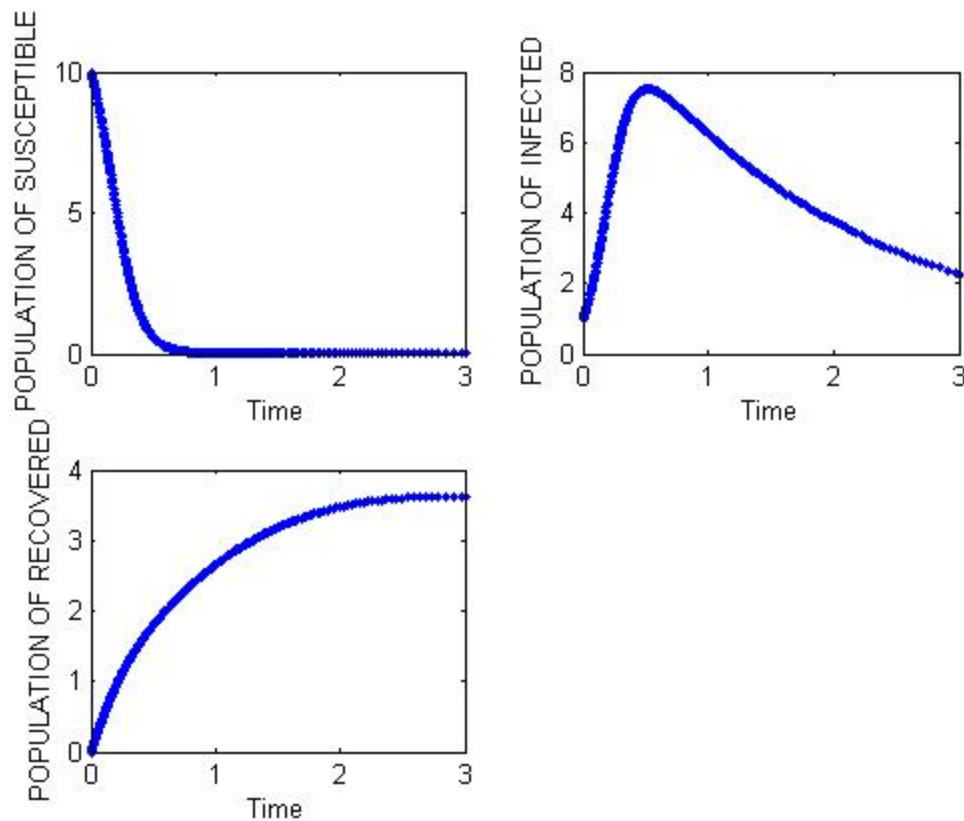
298 The number of removed individuals also gradually moves up as a result of vaccination of the
 299 susceptible. Those vaccinated move to the removed compartment straight. It will be observed
 300 that the graph begins to move down with time, which is due to natural death.

301

302 Now, we decrease the number of susceptible to 9 and the number of removed individuals still at
 303 zero, we introduce one infective into our system. The simulation gives us these graphs.

304

305



306

307

308 Figure 5. $S=9$, $I=1$ and $R=0$

309 It will be observed that the number susceptible decrease in a short period. This is due to two
310 reasons:

- 311 1. People who have not been vaccinated acquiring the disease and moving to the infected
312 compartment.
- 313 2. The vaccinated one's moving to the removed compartment.

314

315 The infected graph moves up for some time and in a little while decreases, this is due to the
316 proportion of susceptible that were infected moving into the infective compartment. But they die
317 of the disease and hence the decrease in the graph.

318

319 The removed also increases due to vaccination of some portions of the number of susceptible. It
320 will be further observed that the disease is stabilized after some time.

321

322 CONCLUSION

323 The increasing use of the hepatitis B vaccine is having significant impact on the rate of HBV
324 transmission and related deaths in the Tano North district. An increase in the hepatitis B
325 vaccination coverage rate in the district will further decrease the prevalence of hepatitis B in the
326 district. Maintaining it will result in increase in the rate of transmission of hepatitis B in the Tano
327 North district which will affect the development of human resource in the district and country at
328 large.

329

The sensitivity analysis indicates that there exist a direct (linear) relationship between the transmission rate, and the reproductive ratio, R_0 . The higher the transmission rate relative to the recovery rate the higher the reproductive number whilst the lower the transmission rate relative to the recovery rate the lower the reproductive number since the natural death rate is relatively small.

The perturbation analysis of the disease free equilibrium revealed that when the reproductive number R_0 is less than unity the disease free equilibrium is stable, whilst when it is greater than unity the disease free equilibrium is unstable (Diekmann and Heesterbeek, 2000).

The herd immunity threshold shows that about 0.42% of the susceptible population of Tano North district should be immune in order for the disease not result in an epidemic. From further analysis with a control measure such as vaccination, and having a vaccine efficacy of 95% about 0.44% of the susceptible population should be vaccinated in order to have HBV under total control in the Tano North district.

Vaccinating these percentage of the entire population reduces the proportion of the susceptible population who risk infection upon outbreak.

The derivation and analysis of the modified SIR mathematical model (SIR), enabled a better understanding of the dynamics of the spread of HBV within the Tano North district population.

Numerical simulations and sensitivity analysis was extensively helpful in the determination of the effect of the various parameters especially the transmission rate and recovery rate on the spread of the disease.

The reproductive ratio estimated indicates that the disease outbreak will be epidemic in the district. About 0.42% of the susceptible population should be immune in order not to have an epidemic. The simulation results and the sensitivity analysis of the study confirmed the transmission rate and recovery rate as the dominant parameters in the spread of the disease in the district.

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APPENDIX

M-File for Hepatitis B Model without Vaccination

```
function dy=model(t,y,beta,alpha)
```

```
dy=zeros(3,1); % a column vector
```

```

446     dy(1)= -alpha*y(1)*y(2);
447     dy(2)= alpha*y(1)*y(2)-beta*y(2);
448     dy(3)= beta*y(2);
449
450     M-File for Hepatitis B Model with Vaccination
451     function dy=model(t,y,beta,alpha,k,p,mu)
452     dy=zeros(3,1); % a column vector
453     dy(1)= mu*k-alpha*y(1)*y(2)-mu*y(1)-p*y(1);
454     dy(2)= alpha*y(1)*y(2)-(beta+mu)*y(2);
455     dy(3)= beta*y(2)-mu*y(3)+p*y(1);
456
457
458     Scripts Used in Calling the M-File for Hepatitis B Model without Vaccination
459
460     alpha=1.0058;
461     beta= 0.984155;
462
463     options = odeset('RelTol',1e-9,'AbsTol',1e-9);
464     [T,Y] = ode15s(@sir,[0 12],[500 0 0],options, beta,alpha);
465     subplot(2,2,1)
466     plot(T,Y(:,1),'.')
467     xlabel('Time');ylabel('SUSCEPTIBLE INDIVIDUALS');
468     subplot(2,2,2)
469     plot(T,Y(:,2),'.')
470     xlabel('Time');ylabel('INFECTED INDIVIDUALS');

```

```

471 subplot(2,2,3)
472 plot(T,Y(:,3),'')
473 xlabel('Time');ylabel('REMOVED INDIVIDUALS');
474
475 Scripts Used in Calling the M-File for Hepatitis B Model with Vaccination
476 beta= 0.30417;
477 gamma= 0.2293;
478 mu= 0.21429;
479 k=0.5149;
480 p=0.1994;
481
482 options = odeset('RelTol',1e-9,'AbsTol',1e-9);
483 [T,Y] = ode15s(@sirV,[0 12],[500 0 0],options, beta,alpha,p,k,mu);
484 subplot(2,2,1), plot(T,Y(:,1),'')
485 xlabel('Time');ylabel('POPULATION OF SUSCEPTIBLE');
486 subplot(2,2,2), plot(T,Y(:,2),'')
487 xlabel('Time');ylabel('POPULATION OF INFECTED');
488 subplot(2,2,3), plot(T,Y(:,3),'')
489 xlabel('Time');ylabel('POPULATION OF RECOVERED');
490
491

```