

UNDER PEER REVIEW₁

Research paper

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3 ANALYSIS AND MODELLING OF PREVALENCE OF HEPATITIS B USING 4

DIFFERENTIAL EQUATIONS: A CASE STUDY OF THE TANO NORTH DISTRICT

5ABSTRACT 6We use the SIR modelKermack and Mckendrick (Kermack and Mckendrick, 1927)

and modify it 7for hepatitis B with vaccination. The main goal is to use existing clinical hepatitis B

data from 8the biostatistics department of the Tano North district health directorate to formulate a

9mathematical model to understand the dynamics in the Tano North district and assist decision

10makers to formulate the best ideas to prevent, control and eradicate the disease. Analyses is made

11of the existence and stability of the disease free and endemic equilibria. It is proven that the

12disease free equilibrium is locally asymptotically stable if the basic reproductive ratio, $R_0 < 1$ and

13when $R_0 > 1$ we have the endemic equilibrium. MATLAB was used for the programming and

14simulations.

15Keywords: control of disease spread, differential equations, hepatitis B, prevention, eradication 16of
disease

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18INTRODUCTION 19Hepatitis, inflammation of the liver caused by viruses, bacterial infections, or

continuous 20exposure to alcohol, drugs, or toxic chemicals, such as those found in aerosol sprays and paint

21thinners (Ganem & Prince, 2004). Inflammation is the painful, red swelling that result when 22tissues of

the body become injured or infected(Williams, 2006). Inflammation can cause organs

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Comment [n1]: In clinical sciences, hepatitis divided to 3 category, acute Hepatitis, chronic Hepatitis and fulminant Hepatitis. It is better to explain about that.

23to not work properly. Hepatitis can also result from an autoimmune disorder, in which the body
24mistakenly sends disease-fighting cells to attack its own healthy tissue, in this case the 25liver(Barkeret
al., 1996). The liver is located in the upper right hand side of the abdomen, mostly 26behind the rib cage.
The liver of an adult normally weighs close to three pounds. No matter what 27its cause, hepatitis reduces
the liver's ability to perform life-preserving functions, including 28filtering harmful infectious agents from
the blood, storing blood sugar and converting it to usable 29energy forms, and producing many proteins
necessary for life (Edmunds *et al.*, 1993). 3031When doctors speak of viral hepatitis, they usually are
referring to hepatitis caused by a few 32specific viruses that primarily attack the liver. There are several
hepatitis viruses; they have been 33named types A, B, C, D, E, F (not confirmed), and G (Anderson *et al.*,
1992). As our knowledge 34of hepatitis viruses grows, it is likely that this alphabetical list will become
longer (Hahnea *et al.*, 352004). The most common hepatitis viruses are types A, B, and C (Anderson *et al.*,
1991). 3637Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV)
38(Edmunds *et al.*, 1993). It is a major global health problem and the most serious type of viral 39hepatitis
(Cui *et al.*, 2006). Originally known as "serum hepatitis", the disease has caused 40epidemics in parts of Asia
and Africa, and it is endemic in China (Williams, 2006). About a third 41of the world population has been
infected at one point in their lives, including 350 million who 42are chronic carriers which causes 620,000
deaths worldwide each year (WHO, 2010; Shepard *et al.*, 2006). 4445Hepatitis B virus is transmitted
between people by direct blood-to-blood contact or semen and 46vaginal fluid of an infected person (Chang,
June 2007). Modes of transmission are the same as 47those for the human immunodeficiency virus (HIV),
but the hepatitis B virus is 50 to 100 times 48more infectious (Thornley *et al.* 2008). Unlike HIV, the
hepatitis B virus can survive outside the 49body for at least seven days. During this time, the virus can still
cause infection if it enters the 50body of a person who is not protected by the vaccine (Liu, G.-T., *et al.*,
2002). 51The hepatitis B vaccine contains a protein (antigen) that stimulates the body to make protective
52antibodies. Examples of hepatitis B vaccines available include hepatitis B vaccine-injection 53(Engerix-B,

Comment [n2]: The most common result of all of Hepatitis is Cirrhosis. In this section should be explained about cirrhosis and causes.

Comment [n3]: The other important function of liver is producing critical hormones

Comment [n4]: Hepatitis D virus can not be alived without HBV. patients must be coinfectd with both of Viruses.

Comment [n5]: Hepatitis C and Hepatitis B&D are more dangerous from other Hepatitis viruses(Rahimkhani et al, AJMR,2011)

Comment [n6]: The prevalence of Hepatitis B was modified on 2011 by WHO

Recombivax-HB). Three doses (given at 0, 1, and 6 months of age) are necessary to assure protection (Edmunds *et al.*, 1993). There are also combination vaccines on the market that provide protection against hepatitis B and other diseases (Kretzschma *et al.* 2002). Hepatitis B vaccines are effective and safe. Up to 95% of vaccinated individuals form effective antibodies when they get the vaccine and are protected from hepatitis B (Shepard *et al.*, 2006; Maynard *et al.*, 1989).

Comment [n7]: HBV vaccines have different types, the kind vaccine provided with recombinant protein antigens from HBV are safe.

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

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

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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).

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

Comment [n8]: 400 million in worldwide affected with chronic hepatitis B(rahimkhani et al ,AJMR,2011)

put the disease under control. 99100The purpose of this thesis is to predict the spread of the hepatitis B disease in the Tano North 101district using differential equations, to do mathematical analysis of the model and to interpret the 102results of the model and by carrying out sensitivity analysis of the basic reproduction number on 103various parameters, we shall suggest some optimal strategies to control HBV infection in the 104Tano North District.

105106MATHEMATICAL MODELING

107In the last two decades, mathematical models have been used frequently to study the 108transmission dynamics of HBV in various regions. Anderson and May (1991) used a simple 109deterministic, compartmental mathematical model to illustrate the effects of carriers on the 110transmission of HBV. Anderson *et al.* (1992) and Williams *et al.* (1996) described models of the 111sexual transmission of HBV, which include heterogeneous mixing with respect to age and sexual 112activity. Edmunds *et al.* (1993) illustrated the relation between the age at infection with HBV and 113the development of the carrier state. Medley *et al.* (2001) gave a model to show that the 114prevalence of infection is largely determined by a feedback mechanism that relates the rate of 115transmission, average age at infection and age-related probability of developing carriage 116following infection. Thornley *et al.* (2008) applied the model of Medley *et al.* (2001) to predict 117chronic hepatitis B infection in New Zealand. The prevalence of HBV in developing countries is 118different from that in developed countries, since it appears that the rate of transmission in 119childhood is the major determinant of the level of HBV endemicity (Edmunds *et al.*, 1996c), and 120little is known on the rates and patterns of sexual contact in developing countries. McLean and 121Blumberg (1994) and Edmunds *et al.* (1996a) studied models of HBV transmission on developing 122countries and Williams *et al.* (1996) described a model of HBV in the UK. 123124We propose a mathematical model to understand the trans-mission dynamics and prevalence of 125HBV in the Tano North district. The model is constructed based on the characteristics of HBV 126transmission 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 immunityR. Fig. 1 illustrates the three compartments and model variables.

MATERIALS AND METHOD

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$$I_0) = 25$$

$$(S_0) =$$

$$S_{\infty}) =$$

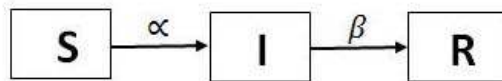
$$\beta) =$$

$$\alpha) = 3$$

$$10\% \quad \rho) =$$

$$\mu) =$$

$$\rho) =$$



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1. Flow chart of

pula

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α is the transi

β is

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

$$\frac{dI}{dt} = \alpha SI - \beta I$$

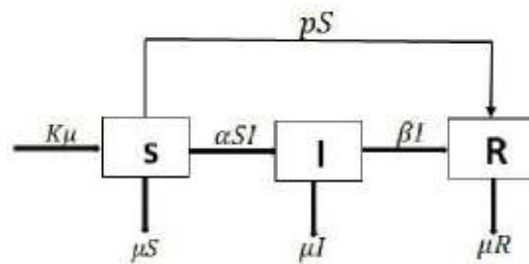
$$\frac{dR}{dt} = \beta I$$

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$$S(0) = S_0 > 0, I(0) = I_0 > 0, R(0)$$

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157 Where;

158 $K\mu$ = birth

159 pS = vac

160 μ =

161 α = i

162 β =r

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(4)

(5)

(6)

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

166The Jacobian matrix for t