MODELLING AND SIMULATION OF THE SPREAD OF HBV DISEASE

BY

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A RESEARCH REPORT SUBMITED TO THE DEPARTMENT OF MATHEMATICS, FACULTY OF EDUCATION IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF BACHELORS DEGREE IN SCIENCE WITH EDUCATION OF KABALE UNIVERSITY

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DECLARATION

I **NlYlRORA IGNATIUS,** declare that this is my original work and it has never been submitted in University for any award.

saran. …… Date: 19/01/2021

Nl\'IRORA IGNATIUS

(RESEARCHER)

APPROVAL

This is to certify that this report has been done under my supervision and is now ready for submission for examination

Signature .. ~

Date: 19/01/2021

Katende Ronald

(Research supervisor)

DEDICATION

I dedicate this research report to my parents, brothers and sisters for the support **and** words of encouragement without forgetting my friend and my supervisor for his guidance. May the almighty God reward you abundantly and I promise never to forget you for the unending love and care you have always shown to me.

ACKNOWLEDGEMENT

Before going into thick of things, I would like to add a few heartfelt words for the people who were part of this research project in numerous ways. A large number of lecturers and students have made valuable suggestions which have been incorporated in this work. lt is not possible to acknowledge all of them individually. I take this opportunity to express my profound gratitude and ineptness to them.

Foremost I owe great thanks to my God for his blessing and guidance in my study, especially throughout this year. I would like to express thanks and appreciation to my Supervisor for supporting me during the entire research project period and providing me with valuable advice and experience. Without his help and guidance this research proposal would not have been possible.

Lastly I am exceedingly grateful to my family support, I owe them a lot for their guidance and encouragement because they have always been there for me. This would not have been achieved and succeeded without their supports.

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ABSTRACT

The study was to modeling and simulation of the spread of HBV disease. It was guided by specific objectives that were to find out the disease free equilibrium of the spread of Hepatitis B Virus, to determine sensitivity analysis on Ro to ascertain which parameter that is most sensitive and that should be targeted by way of intervention and to examine the local stability of the model equation using the modified implicit function theorem. The first result of our simulations confirms that the disease free equilibrium is globally asymptotically stable when *Ro*< 1. On the other hand if R> 1 there is a stable endemic solution. I presented a sample of the results obtained in these simulations. a sample of the effect of considering the transition rate between latent and susceptibles. Also we give a bifurcation diagram of the infected population against the vaccination rate which shows that when *Ro* :S I the values of the infected population I@) tends to its disease free equilibrium values. This model shows that when the vaccination fails to force the basic reproduction number to be less than one in value the disease fires up and approaches an endemic level. This result is obtained for the case that the vaccination rate p = 0.5.

CHAPTER ONE
INTRODUCTION

1.0 Introduction

This chapter comprise of the Background of the study, Statement of the problem, Objectives of the study, Scope of the study and significance of the study

1. 1 Background of Study

The spread of the HBV in Uganda has posed a lot of threat to health and well being citizens in Uganda. It is evident that about a third of the world's population, approximately 2 billion people gets infected with hepatitis B virus in their life time. About 360 million people remain chronically infected carriers of the disease, most of whom are unaware of their HBV status and about 20%-- 30% of whom will eventually die from chronic sequel. The prevalence of HBV infection varies from country to country, depending upon a complex behavioral, environmental and host factors. Chronic HBV can lead to hepatocellular carcinoma after 20 years among persons with chronic HBV infection; the risk for premature death from cirrhosis or hepatocellular carcinoma is 15%25%.

Hepatitis Bis a disease that is characterized by inflammation of the liver and is caused by infection by the hepatitis B virus. According to (WHO, 2002) stated that hepatitis may be caused by drugs or viral agents; these viral agents include the hepatitis A, B, C, D, E,F, G and H viruses. Hepatitis Bis one of the world's most serious health problems. More than a billion people around the world have serological indicators of past or present infection with hepatitis B virus (HBV).

Over 300 million people are chronic carriers of the virus. The fast spread of HBV shows that is very communicable. Zou, (20 I 0).

It is evident according to WHO, (2002) that HBV infection can be transmitted from mother to child (vertical), contact with an infected person (horizontal transmission), sexual contact (homosexual and heterosexual transmission) with infected partners, exposure to blood or other infected fluids and contact with HBV contaminated instruments.

HBV control measures include vaccination, education, screening of blood and blood products; and treatment CDC, (2005).

Anderson, (I 991) stated that epidemiological models help to capture infection or disease transmission mechanisms in a population in a mathematical frame-work in order to predict the behavior of the disease spread through the population.

1.2 Statement of Problem

What really instigated the study was the massive spread ofHBV in Uganda and most of the African countries. Several efforts have been put in place by the federal government of Uganda and world health organization (WHO) through the ministry of health in Uganda to combat HBV.

Secondly mathematicians all over the world have come with up with several model to help solve the model and simulate the spread of HBV; there have been a lot of failed model.

t .3 Aims and Objectives of study

The main aim of the research work is evaluate the modeling and simulation of the spread of HBV

1.4. Specific objectives

1. To find out the disease free equilibrium of the spread of Hepatitis B Virus
ii. To determine sensitivity analysis on R to ascertain which parameter that is most sensitive and that should be targeted by way of intervention.

1.5 Research Question

1. How to find out the disease free equilibrium of the spread of HBV disease.
11. How to find out sensitivity analysis on Ro to ascertain which parameter that is most sensitive and that should be targeted by way of intervention.

1.6 Scope of Study

The study was carried out on modeling and simulation of the spread of HBV disease. It covered the areas oflocal stability of the model equation and it was carried out for a period from 2019 to 2020

1. 7 Significance of study

The study on modeling and simulating of the spread of HBV disease wi 11 be of immense benefit to the ministry of health of Uganda, the World health organization (WHO) and other researchers that wishes to carryout similar research on the above topic as it will discuss the local stability of

the model equation using the modified implicit function theorem and also sensitivity analysis on Ro to ascertain which parameter that is most sensitive and that should be targeted by way of intervention.

1.8 Definition of Key Terms

Asymptotic stability says that a system starting is some 8-ball around the equilibrium will converge to the equilibrium. **Stability** means that the solution of the differential equation will not leave the -ball. But **asymptotic stability** means that the solution does not leave the c-ball and goes to the origin.

The equilibrium of (2) is said to be globally asymptotically stable in probability if, for any, there exists such that and for any initial condition.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

A survey of literature on the research topic makes the researcher familiar and more knowledgeable with the existing studies and provides further information, which helps to focus on a particular problem and lay the foundation for and greater knowledge. lt creates an accurate picture on the information presently available on the subject.

A review of literature for the present study is to gather knowledge about:

a) A major silent killer disease such as hepatitis B

b) A mucosa! immune system, which plays a major role in oral immunization.

c)A suitable and effective delivery system with different biodegradable polymers and adjuvants for oral administration of vaccines.

2.2 Hepatitis B- The disease

Hepatitis Bis a serious liver disease, caused by hepatitis B virus. The disease is transmitted through human body fluids such as blood and serum. It is an alarming public health problem worldwide. Its methods of transmission include through mother to baby (perinatal), sexual contact and the use of improper injection techniques. More than two billion amongest the population alive today, would have been infected at some time or other in their lives by the hepatitis B virus (HBV) and approximately 350 million of them are the carriers of the chronically infected disease Kane, (1995). Out of these 25-30% would die as a consequence of the infection WHO, (2003). These carriers are at high risk of this serious illness and death from cirrhosis of liver and/or primary liver cancer would kill more than one million of them, per year. They also constitute a reservoir of infected individuals, who perpetuate the infection from generation to generation.

2.3 Mode of Transmission

The hepatitis B virus is carried in the blood and other body fluids. The virus is present in the blood, saliva, semen, vaginal secretions, menstrual blood, and to a lesser extent, perspiration, breast milk, tears and urine of infected individuals.

The highly resilient virus, is easily transmitted through contact with infected body fluids. It is usually spread by contact with blood in the following ways.

i) Perinatal (mother to child) transmission is one of the most common and serious mode of HB V transmission. Perinatal transmission occurs from mothers, who are positive for both the hepatitis B surface antigen (HBsAg). More than 90% of these women are chronic HBV carriers, although those acutely infected with the virus, during pregnancy, may also transmit to their children.. Infected newborns rarely develop acute hepatitis, although reports of fatal fulminant hepatitis have been reported .. These carriers form a pool of infectious individuals, who will infect others in the community and eventually, their own offspring.

ii) Child to child transmission, also called horizontal transmission, is responsible for majority of HBV infections and their carriers. Transmission between children occurs during social contact through cuts, scrapes, bites and scratches. The skin lesions, such as, impetigo, scabies, abrasions and infected insect-bites, play an important role. These lesions provide a route for the virus to leave the body of the infected children, as well as, one to enter into the body of susceptible children.

iii) Transmission through an unsafe injection, needle-prick or reuse of unsterile needles, and use of contaminated needles Onah et al, (2014), and other medical and dental equipment's. Survey in developed countries have revealed, that up to 30% of injections used for immunization, are not found sterile. Disposable syringes are reused and reusable syringes are improperly sterilized, resulting in a significant risk of transmission of blood-borne pathogens. Auto-destruct syringes and single use pre-filled devices, can reduce the transmission by averting inappropriate use .In some western countries, needle-sharing by drug abusers is also causative. If sterile needles are not used, it is possible to transmit hepatitis B, through body-piercing, tattooing, drug injection and acupuncture. The hepatitis B virus can also be transmitted by sharing razors, tooth brushes, nail-clippers and ear-rings.

iv) Transmission during sexual intercourse through contact with blood or other body fluids. Hepatitis B is the major infective occupational hazard to the following: Healthcare workers. Emergency personnel Staff of jails, prisons and group homes.

Hepatitis-Bis not transmitted casually. It cannot be spread through sneezing, coughing, hugging or eating food prepared by someone, who is infected.

2.4 Diagnosis

The doctor examines a patient and look for signs of liver damage, such as yellowing skin or belly pain. Tests that can help diagnose hepatitis B or its complications are:

- **Blood tests.** Blood tests can detect signs of the hepatitis B virus in your body and tell your doctor whether it's acute or chronic. A simple blood test can also determine if you're immune to the condition.

- **Liver ultrasound.** A special ultrasound called transient elastography can show the amount of liver damage.
- **Liver biopsy.** Your doctor might remove a small sample of your liver for testing (liver biopsy) to check for liver damage. During this test, your doctor inserts a thin needle through your skin and into your liver and removes a tissue sample for laboratory analysis.

CHAPTER THREE

METHODOLOGY

3.1 introduction

This chapter contains model description and area of the study

3.2 Model Description

This Chapter covered the model specification and description; state the assumption of the model. **3.3 Model**

Consider a more complicated and realistic SEIR model with vaccination. This type of model which takes account of the spread of disease in the latency state. Here we investigate the effect of the infectivity of the latent population in addition to the transmission between the susceptibles and infective populations. The model makes the following assumptions:

a) The total population size is a constant *N.* and the population is divided into four groups:

i) The susceptible class, *S,* comprising those people who are capable of catching the disease; ii) The exposed class. E. comprising those individuals who are infected but not yet infectious;

iii) The invectives,/, comprising those who are infected and capable of transmitting the disease;

iv) The recovered class. *R,* comprising those individuals who are immune.

b) The per capita birth rate is a constant μ.

c) The population is uniform and mixes homogeneously.

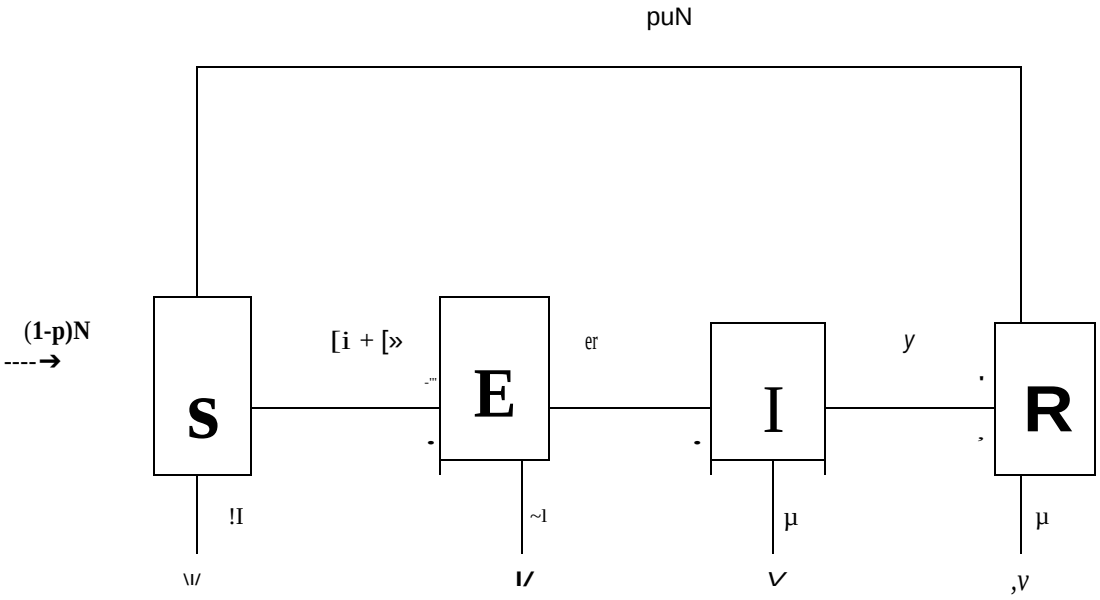
d)The infection rates Bi and B are defined as the total rates at which potentially infectious contacts occur between two individuals (in other words contacts which will result in the transmission of infection if one of the individuals is susceptible and the other is infectious for Bi and B .

e) The exposed individuals move from the latent class to the infective class at a constant rate *a* and conditional on survival to the end of it, is *a.*

f) The infective move from the infective class to the recovered class at a constant rate y, where y is the average infectious period. conditional on survival to the end of it.

The SEIR model for the spread of infectious diseases can be written as a set of four coupled nonlinear ordinary differential equations as follows:

3.3 **Model compartments**



3.3.1 Model System

$$\frac{dS}{dt} = \mu(1-p)N-\mu S-P1SI$$

$$\frac{dE}{dt} = BISE+ [SI- (o+)E$$

$$\frac{di}{dt} = oE- (+y)I$$

$$\frac{dR}{dt} = p\mu N+yl -\mu R$$

The basic reproduction number is defined as the average value of the expected number of secondary cases produced by a single newly infected person entering the population at the disease Free State. In this model the average value of the expected number of secondary cases produced by a single infected person is in the positively invariant subset of

R+4:r2={ (S,E,LC)IS,E,l,C~O,S+E+l+C~m}.

For convenience, leta 1 =µ+0,a2=µ+yl ,a3==µ+y2-µmv,a4==µ+y2. System may has two equilibria in 2: the disease-free equilibrium

P= (So. *Eo, lo,* Co)== *(w,* 0, 0, 0) and the endemic equilibrium P^* = (S*,

E, j*,* C*),whereSFala2a3~0(a3+aylq)==mp0,IFl-

Ip0oa3ovoqylala2a3.E+=+ylol+,C=qla3I».

The positive endemic equilibrium state P exists for all p_0 > I, where the parameterp0=Bo@(+o)(+yl)Bouqyl(+o)(+y)(+y2-ov)is the basic reproductive number got by the next generation matrix when the fraction of vertical transmission ovC is not considered to be new infections. Conversely, if ovC is taken as new infections, we have another basic reproductive number

RO=I2Boot+0)+y)+BoaqI+0)(+yl)(+y2)ov+y2+\2,where A=l(ala2a4)2(Boca 4+[0cuqlvala2)2-4ala2a4B000v>0.

It is easy to see that p0=R0 only when v = 0. p_0= I is equivalent to RO= I, and p_0 < I if and only if RO< I. In this paper, we take p_0 as our basic reproductive number.

Table *2.1.* Definitions or parameters used in model.

Symbol	Definition
ft	Birth and death rate
cv	Proportion of birth that is unsuccessfully immunized
v	Proportion of children developing to HBV carriers born to carrier mothers
$f]$	Transmission coefficient
a	Infectiousness of carriers relative to acute infections
a	Rate of transfer from exposed to acute infection
$'1$	Rate moving from acute class to chronic or immunized class
q	Rate leaving acute infection and progressing to carrier
$y2$	Rate moving from carrier to immunized

lt has been shown that with constant transmission rates [y and [2 our model has one and only one disease free equilibrium (DFE) and another endemic equilibrium state of our SEIR model. In this paper, simulation results have been conducted for parameter values which insure that if the vaccination parameter p is not large enough, to force the basic reproductive number Ro to be less than one in value, the disease remains endemic in the population. In the other hand simulations of our model are conducted to show up the effect of introducing the disease transmission between latent and susceptible populations.

3.4 Area of Study

The study was carried out in Kabale district because it is where cases of HB are so high in the past 4 years. According to district health officer of Kaba le district Dr Besigensi, out of I 000 people that have been tested in 2020, five of them have been found to be having HBV

CHAPTER FOUR

RESULTS

4.1 Introduction

In this section we study numerically the behaviour of the system. The system of linear ordinary differential I:::quations have been solved numerically by using the software package XPPAUTO and using the following parameter set from the literature, *(b*= 0.015, B = 0.000025.0 = 6,y= 4) Musa, (2009).

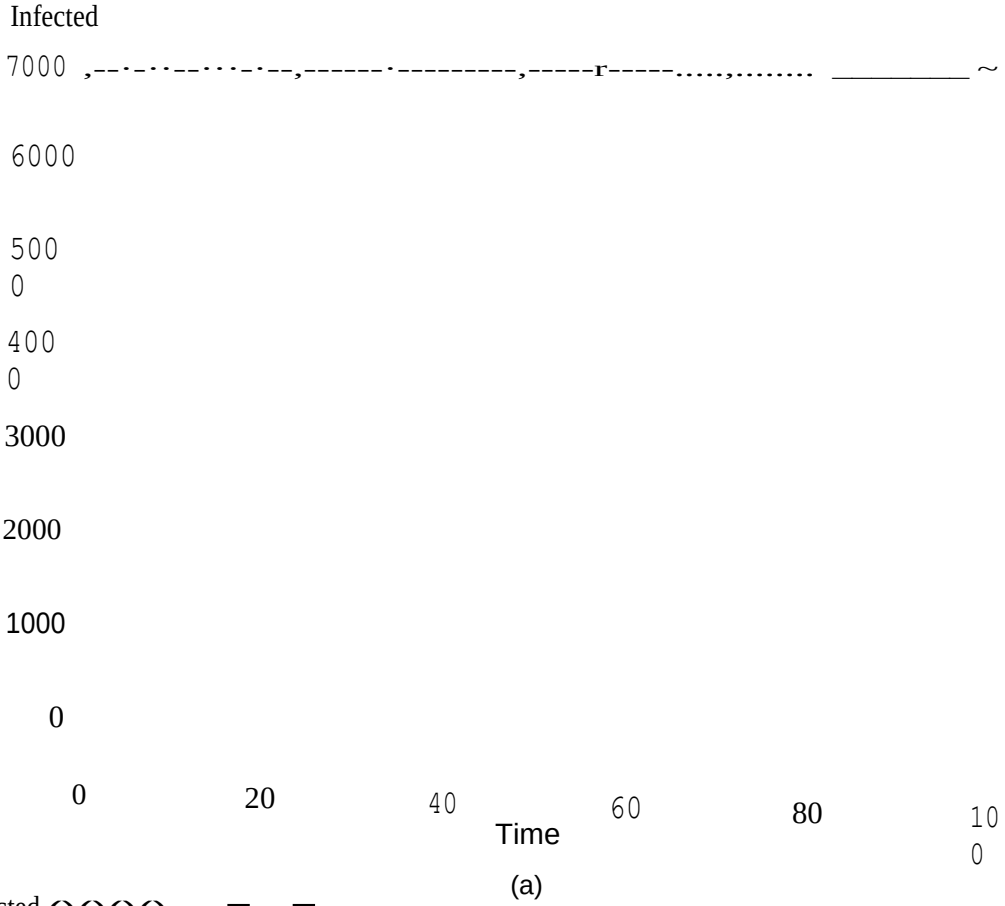
Also we simulate our system for two different states one if *Ro*< I and the other one when *Ro*> I we found that. disease has a threshold level *P* for the reproductive number *Rato* be under one in value which the disease to die out. If the vaccination value *pis* not sufficient then *Ro* stays above one in value and the disease becomes endemic.

The first result of our simulations confirms that the disease free equilibrium is globally asymptotically stable when *Ro* I. On the other hand if *Ro*> I there is a stable endemic solution. Here we present a sample of the results obtained in these simulations. We give a sample of the effect of considering the transition rate between latent and susceptibles. Also we give a bifurcation

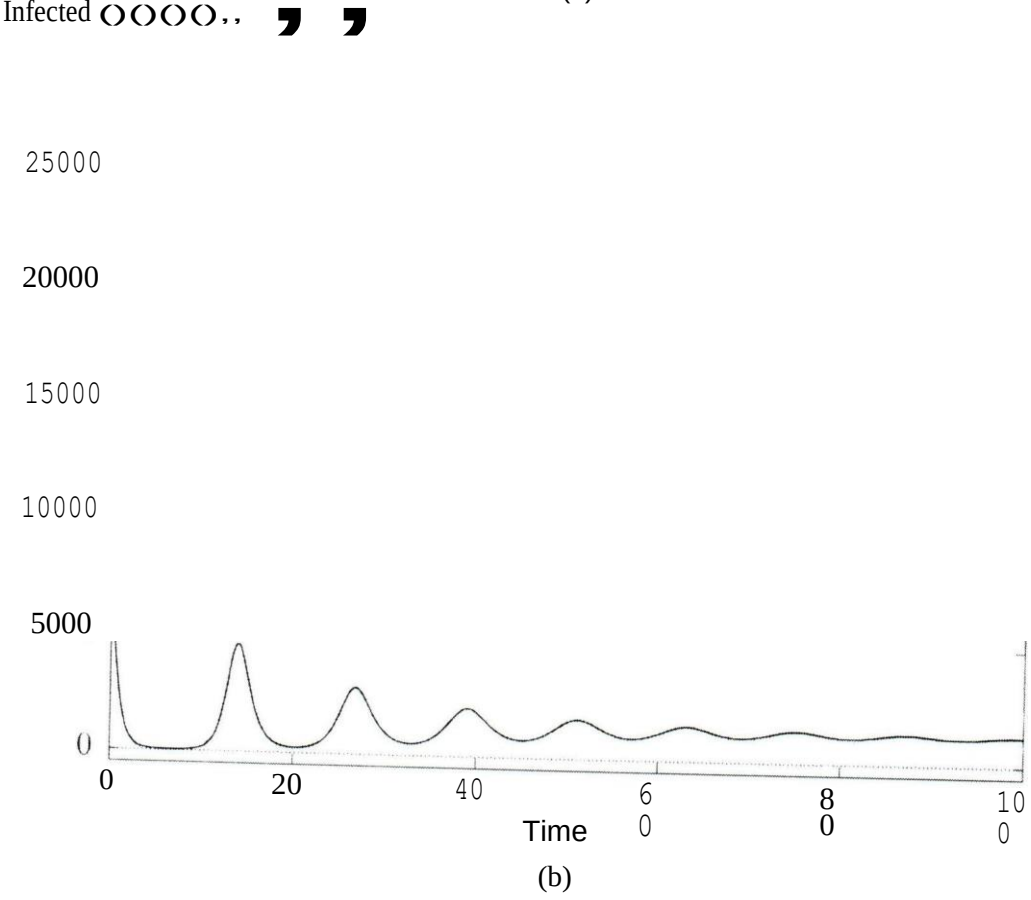
diagram of the infected population against the vaccination rate which shows that when *R0*<*S* I the values of the infected population/(/) tends to its disease free equilibrium values. This model shows that when the vaccination fails to force the basic reproduction number to be less than one in value the disease fires up and approaches an endemic level. This result is obtained for the case that the vaccination rate *p* = 0.5.

Lia, (2009) studies numerically the behaviour of the system 111 response to changes in *p,* the vaccination rate. We use the basic idea that, sectioning the endemic stable equilibrium solutions by looking at Poineare sections and plotting the sections of the endemic equilibrium solutions against the vaccination value *p* to obtain the number.

12.


Infected
7000
6000
5000
4000
3000
2000
1000
0
0
20
40
60
80
100
Time

(a)


Infected
25000
20000
15000
10000
5000
0
0
20
40
60
80
100
Time

(b)

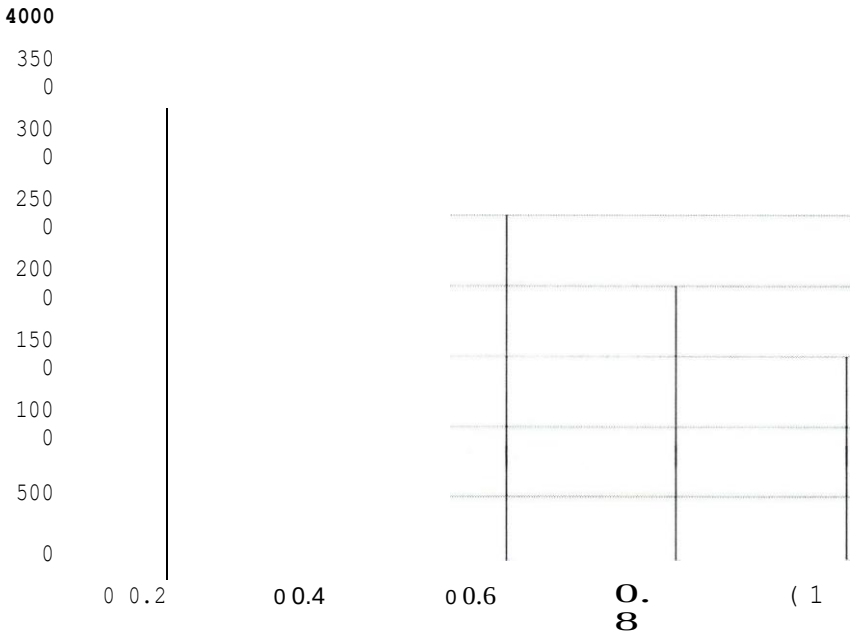
The number of infected population against time corresponding to parameter values of HBV (a) when the vaccination rate (p = 0.96) which is large enough so that, Ro< l and (b) when the vaccination rate, p = 0.5, is not sufficient enough to keep Ro<! .of points in each section (Monien.1.A., 2003). These points represent the period of the stable long term periodic solution of our model. We have taken the simulation parameters for all of the bifurcation diagrams presented here as stated above and the total population size N was 1,000,000.

The above graph represents the bifurcation diagram for HBV with two transmission rates for the infected and the susceptible. This shows that at small values of vaccination parameter the disease has a periodic solution of period one year. Increasing the value of p produces a two year periodic further increases generate a series of period doubling solutions until the behaviour of the system appears to become aperiodic and possibly chaotic.

However, increasing the vaccination rate more forces the infected number to drop down until approaching zero at p = 0.96.

fhis represents the number of infected population against time corresponding to parameter values of HBV when Ro> I. The black line plots the infected against time when, the latent are infectious. In this case. there is another contact rate [2 between susceptibles. The black line shows that, there is an endemic solution which is going up rapidly. This solution has some peaks which look to

periodic of long period.



The bifurcation diagrams of HBV parameter values of the number of infected against vaccination parameter *p*. red line plots the infected against time when infectivity of the latent is ignored By= 0. The red line shows that there are some peaks which have larger tops than the black one but; the line has small values all over the whole diagram. The green line represents the case that, there is a total isolation of the infected persons pi= 0. The green line shows the smallest peaks in the diagram. These peaks decay smoothly to be almost steady state.

4.1 Equilibrium Points

The system has two equilibrium points the first one is the disease free equilibrium (DFE) point

$$P* \equiv (S*, E*, I*, R*)$$

$$Pk_{-1} \quad (1- P)N) \quad 0 \quad 0 \quad 6$$

4.2 Stability of the Disease Equilibrium Point (DFE)

This section studies the stability of the disease free equilibrium (DFE) point $P = (S, 0, 0, R)$. In this case, there is no disease in the population as I=E =0. The Jacobian matrix of the system at the point 'P, (DFE) is given by

$$J_p = \begin{pmatrix} -\mu & -\beta_1 \hat{S} & -\beta_1 \hat{S} & 0 \\ 0 & -\beta_1(\mu - \sigma) & \beta_1 \hat{S} & 0 \\ 0 & \sigma & -(\mu+\gamma) & 0 \\ \alpha & 0 & \gamma & -\mu \end{pmatrix}$$

Theorem 1 *The disease free equilibrium point,* ***(S, 0, 0, R)*** *is locally asymptotically stable for the system.*

if **Ro< 1** , and unstable when **Ro> 1** .

Proof: From the characteristic equation of the matrix we have two negative eigenvalues, both of them equals to(-μ). The rest of the characteristic equation is given by,

$$Fa) = 1 + 1(2 + 6, S) \; (R\ 1)$$

From Equation above, if $Rn < I$. then~,$S < +o$ So. we found that all the eigenvalues of the matrix have negative real parts. Therefore, using the Routh-Hurwitz conditions for the stability of linear differential Equations, the disease free equiljbrin p9int *(S,* 0,0,R)is locally asymptotically **Theorem** *Th disde free eiifibrim oiiil. SRWild&Ifviviioti&ff fable fk*
stable if $R <$ I . If *Ro*> I this implies that Ro> 0. Thus the characteristic equation of the matrix must have a positive eigenvalue.

Therefore, the disease free equilibrium point, (S, 0,0, R)is unstable for the system. This completes the Proof of Theorem (1).

4.3 Global Stability of the Endemic Equilibrium Point

This section concerned with global stability of the endemic equilibrium point. The necessary and sufficient condition to the existence of the endemic point p.is that ***Ro>1.*** Similar technique to the proof to Theorem I in (korobeinikov, 2002) has been used in this section.

We start off by calculating the parameter values of the model at the equilibrium. From Equation at the equilibrium, we have that

$$0 = (1 - p)N\mu - \{3_1 S^*E^* - /3_1 S^* l^* - \mu S^*,$$ Therefore

$-\underline{!}\ S - Sr$ Similarly, From equation we get,

$$\mu + a = /31\, S^{\cdot} - 2£\cdot \quad /3\, S^{\cdot}\, r$$

Finally, from equation we can deduce that

$$\mu + 8 = -\frac{oE}{I^*}$$

Substuting we can deduce,

$$\frac{ds}{} = 5\ (\mu(1-p)n - \mu(1 \sim pn) - /3i(E - E^*) - /3_2(l - /^*))$$

at tne equmru we nlve tn s

$$\frac{dE}{dt} = E(S_s) + - \frac{ST}{E} - \frac{SI}{E}))$$

And

$$-,-E) \quad I \quad I$$

L et8,.. S . I , , E

and

$$k=(1-p)N$$

. Then substituting these values in Equilibrium we find that.

$$\frac{"0}{dt} - (( )-ore-D-Br@-) \quad S\ s$$

$$\frac{de}{dt} = (f31S^*(s-l) + f32 - (--l) \frac{S^* I^* si}{Ez \cdot e})$$

And

$$\frac{di}{dt} = \iota\alpha - \frac{E'}{I'}\left(e - 1\right)$$

Theorem 2 if Ro < 1, then the endemic equilibrium point, $P^* = (SET,R)$ asymptotically stable is globally for the system

Proof: Define a positive define function F such that

$$F = L_1(s - lns - 1) + 1_1(e - lne - 1) + 1_1(i - lni - 1)$$

where by

$$L_1 = S, L = E$$

and

$$— = | K_1 S^*(s - I) + K_2 ——(— - I)|$$

L. P2 R EI +- Zr

Now we prove that,

$\frac{dF}{dt}$ *is non opposite* definite function. Differentiating F and substituting by the values of **L,** =

:-,•,,>•,,;s.',/•.Y•·..- .. ,,,'··.c-•,••·._, .. >-.· ·,.-,.-L-i~.and .. L3,-, .. ,·.-- .. ·, •,···,,.. .... ; ......,' ,., ... ,,., , •, /'≤•.. ':,',c-:, ,, c>_.\, .. :-". ,, 'C =

we have,

"-L,"(a-!)+,(-{),(1-!)
dt dt s zdt i dt e

–ss–%(±-1)

=ss- 1%d 1,ee 1– BF@-1/Ee 1\,ss-1)+%'% · 1]+ i– 1)sr,&- 1)

l

$\frac{dF}{dt}$ = {1₂s* /* [i - 1) (:. - 1) + (e - 1) (~ - 1) - (s -l)(i - l)]+k(s - l)(! - 1)
1 e s

sT[1 - f- ~ + s] + k (2 - s - ~)

Rearranging Equation we *deduce that,*

dF e si 1 1
- = /1₂s*/* [3 - -:- - - - -] + (k - /1₂s*/*)(2 - S - -)
dt i e s S

As the arithmetic mean is greater than or equal to the geometric mean we find that **dF**
<0iffk ,SI > 0
dt

and all of s, I, and e are non-negative. Equation ensures that

k- R SI > 0
P2

$\frac{dF}{dt}$ = 0 *iff* s=I

and $i=e$ which can be presented by the following set,

!1 = {(S,£,/):S = S*,E/* = IE}.

The equilibrium point p' is the only invariant set of the system which contained entirely in the set 2.Hence by Liapunov's direct methods p* is globally asymptotically stable if Ro> I for the system .This completes the proof of theorem (2).

CHAPTER FIVE

SUMMARY AND DISCUSSION

This paper investigates the effect of using another way of producing new cases. This way is the fact that latent persons can pass the disease into susceptible. Also, vaccination of all newborns, at a constant rate, has been considered. It is documented that vaccination strategies are applied worldwide to vaccinate children in the early ages. For example, in China an effective vaccination program has been established for newborn babies since the 1990s, which has reduced chronic HBV infection in children. Unfortunately, the incidence of hepatitis Bis still increasing. This means that the vaccinated proportion is large enough to force the reproduction number to be less than one in value. Therefore, to control HBV infection vaccination, strategies need a treatment scheme as another leg to have a better control strategy for the disease.

The first result of this paper comes from the stability analysis of the DFE of our model. We find that the DFE is locally asymptotically stable when *Ro,* the basic reproduction number, is less than one. I(' *Ro* exceeds one, then the D FE point is unstable. WhenRo> I, there exists another equi I ibrium point which is the endemic point *Pk»* = *(S,E,IR*) . We deduced that if R>I, then $P = (S^*,b,1^*,R^*)$ is globally asymptotically stable for the system. We used Liapunov's direct methods to prove this result. Simulation results of our model have been conducted for HBV parameter set using different vaccination parameter values. From these results, we find that there is a critical ratio *c* 96% *P* = approximately, from which all the newborns must be vaccinated. This value is the sufficient condition to reduce susceptible number to be less than a critical value SC. This forces the basic reproduction number *Ro to* be less than one in value and the disease dies out. The threshold value *CS* can be driven as follows. From Equations, we have that

In the positively invariant subset of R+4:Q={(S,E,l,C)IS,E,l,C~0,S+E+1+C~w}. For convenience.

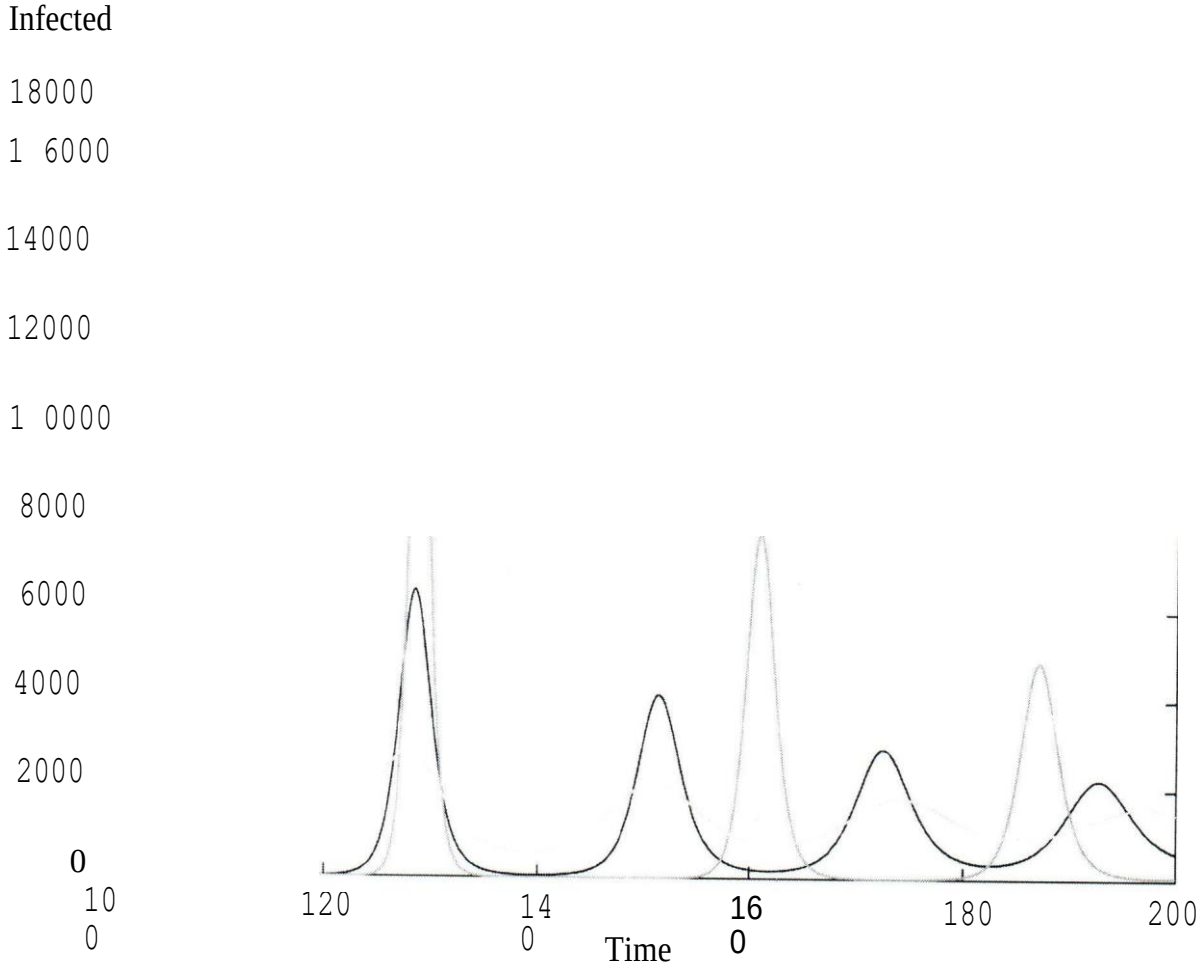
letal=u+o.a2=+yl.a3=+y2-ova4=u+y2. System may has two equilibria in 2: the disease-free equilibrium *Po*= (S. *Eo,* L. Co)= *(cv,* 0, 0, 0) and the endemic equilibrium *P*= *(S:,E,P*C'),whereS+=ala2a3~o(a3+aylq)=p0,Ir=I-Ip0coa3covoqyl+ala2a3.E+=+ylol+,C=qyla31+.

The positive endemic equilibrium state P exists for all $p_o > I$, where the parameterp0=Bo(+0)u+yl)+oaqyl@(+o)+yl)+y2-uov)is the basic reproductive number got by the next generation matrix when the fraction of vertical transmission *pcvvC* is not

considered to be new infections. Conversely, if *covC* is taken as new infections, we have another basic reproductive number

RO= 12~o(+o)+yl)+Bouqy lo(o)(+y)(+y2)+ov+y2+\2,where *A*=l(ala2a4)2(Boa 4+Booaql+@ova la2)2-4a la2a4[0ov>0.

It is easy to see that pO=RO only when *v* = 0. po= I is equivalent to RO=!, and *po* < I if and only ii' RO< I. In this paper, we take *po* as our basic reproductive number.



The number of infected population against time corresponding to parameter values of HBV when the vaccination rate is not sufficient enough to keep *Ro*<I, the black, red and green lines corresponding to/1=*0/:*= 0.000025), (pi= 0.000025, *[* = 0) and (pi= 0,[= 0.000025) Respectively.

If this condition fails, the susceptibles will be large enough to make the disease firs up and become endemic in the population. In this case, we got some high peaks. It is important to noteindicate that the black line which includes the infectivity of the latent is going up continuously and has a sustainable long term period solution.

The bifurcation diagram indicates that the vaccination parameter p can play as a key value of our model. This figure also shows that there are many endemic periodic solutions of our model. These solutions vary from biennial to large period or chaotic solutions. It is obvious to conclude that bifurcation gives a wide range of information about the dynamics of the HBV disease and indicates how the values of the vaccination rate affect the behaviour of the disease dynamics.

Finally, vaccinating all newborns by a rate greater than 96% is not reachable in practice. Therefore, from our results, it is important to declare that treatments or additional vaccination strategies are needed to control the spread of HBV in population. Controlling the disease means that reducing the susceptible by vaccination or reducing latent and infected by treatments scheme.

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