KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI

DETERMINISTIC SIR MODEL OF HEPATITIS B VIRUS INFECTION AND THE IMPACT OF VACCINATION

(THE CASE OF SUNYANI MUNICIPALITY)

BY

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A THESIS SUBMITTED TO THE DEPARTMENT OF MATHEMATICS, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY IN PARTIAL FUFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MSC. INDUSTRIAL MATHEMATICS

JUNE 2015

DECLARATION

I hereby declare that this submission is my own work towards the award of the MSc. degree and that, to the best of my knowledge, it contains no material previously published by another person nor material which had been accepted for the award of any other degree of the university, except where due acknowledgment had been made in the text.

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DEDICATION

To my lovely wife Mrs. Margaret Asiedua Botwe-Boafo, my lovely sons; Kojo Okorie Botwe-Boafo and Kofi Kodie Botwe-Boafo. Also to my parents Mr & Mrs Ofori-Botwe.

ABSTRACT

Deterministic SIR Models with essential factors such as Susceptible, Infective and Removal was formulated. This is to understand the Mechanisms of Hepatitis B Virus Infections in the Sunyani Municipality. Deterministic SIR Model without and with Demographic turn-over were respectively used to understand HBV Epidemic and Endemic situation of the population. An SIR Vaccination Model was included to assess the impart of Vaccination. In the first Model, the Reproductive Number was estimated as $R_0 = 1.957 > 1$ which shows epidemic population. The Model indicated that, modeling with 10 susceptible with an infective, about 90% of the population would be infected during the period of epidemic. The Reproductive Number for the second Model was estimated as $R_0 = 1.022$ which shows an endemic population. This Model has two equilibrium states; the disease-free equilibrium state and the endemic equilibrium state. The two equilibrium states were found to be Asymptotically Stable. The Vaccination Model shows a decrease in the Infective whiles the group to which Vaccination was given increased. The Reproductive Number (R_v) was estimated as $R_v = 0.511<1$.The study shows that Infectious Rate and Reproductive Number play important roles in prevalence of disease in the population. Our findings show that an increase in Infectious rate produces

$R_0 > 1$ whiles a decrease in Infectious rate produces $R_0 < 1$. Per the data from Sunyani Municipal Hospital, an Infectious rate of at most 1% and Vaccination rate of at least 60% can curb the situation and eventually eradicate HBV Infection in the Municipality.

This thesis was written using LaTex Platform whiles MATLAB Code was used for the programming.

ACKNOWLEDGMENT

Unto the Lord we give glory. I am grateful to the Almighty God for His mercies, protection, guidance and most importantly for how far He has brought me.

My profound gratitude goes to my Supervisor, Rev. Dr. William Obeng Denteh for guiding and directing the success of this thesis work. Rev. I am grateful. My appreciation also goes to entire staff of Department of Mathematics , Kwame Nkrumah University of Science and Technology (KNUST) for the opportunity. I must also appreciate the contribution of Mr. Alex Perprah of Catholic University College.

My deepest appreciation goes to my family for their supports. Also to Nana Kyere-Sacrifice, Mr. Richard Mensah, Ghana Statistical Service, Sunyani, Mrs. Evenly Gyamah, Sunyani Municipal Hospital for their assistance.

Finally, I am grateful to my fellow postgraduate students at the Mathematics Department, KNUST for their contribution and encouragement during the period of study on campus.

CONTENTS

LIST OF ABBREVIATION

AIDS ..... Acquired Immune Deficiency Syndrome CDC .....Center for Disease Control

DE .....Differential Equation HA, HB, HC ..... Hepatitis A, Hepatitis B, Hepatitis C HAV, HBV, HBC .. Hepatitis A Virus, Hepatitis B Virus, Hepatitis C Virus

HBIG .....Hepatitis B Immune Globulin HBsAb ..... Hepatitis B Surface Antibody

HIV ..... Human Immunodeficiency Virus NGO ..... Non Governmental Agency

IDU .....Injecting Drug user KBTH .....Korle Bu Teaching Hospital KNUST .....Kwame Nkrumah University of Scienc and Technology MPC .....Model Predictive Control ODE .....Ordinary Differential Equation

SIR ..... Susceptible, Infective and Removal

SEIVR .....Susceptible, Expose, Infective, Vaccination and Removal

WHO .....World Health Organisation

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CHAPTER 1

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

"Hepatitis" is a general term used to mean inflammation of the liver and can be caused by a variety of viruses such as hepatitis A, B, C, D and E according to Hollinger and Ling (2001). It also refers to a group of viral infections that affect the liver. The condition can be self - limiting or can progress to fibrosis (scarring), cirrhosis or liver cancer as described by Ganem and Prince (2004).

According to WHO (2014), hepatitis viruses are the most common cause of hepatitis in the world. However, other causes of infections are toxic substances (e.g. alcohol, some drugs) and autoimmune disease (a disease occurring when the body makes antibodies against the liver tissue) can also cause hepatitis.

The five (5) types viruses (A, B, C, D and E) causing the Hepatitis diseases are of greatest concern because of the burden of illness and death they cause, and the potential for outbreaks and epidemic spread (Hollinger and Ling, 2001). In particular, types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer by WHO (2014). Among the five (5) viruses causing the Hepatitis, the most common types are the A, B, and C. Based on the viruses, we have Hepatitis A, Hepatitis B and Hepatitis C Virus infections. For the purpose of this study, we concentrated on the type known as Hepatitis B Virus infection.

Hepatitis A Virus (HAV) infection is a form of viral Hepatitis transmitted in food, causing fever and jaundice. This give rise to Hepatitis A (HA) disease. Whereas,

Hepatitis C Virus (HCV) infection causes Hepatitis C (HC) disease and is another form of viral Hepatitis transmitted in infected blood, causing chronic liver disease, according to Owusu-Ansah (2013)

Hepatitis B Virus (HBV) infection is the most common serious infection of the liver that can lead to premature death, liver cancer or liver failure known as Hepatitis B (HB) disease. Hepatitis B is a severe form of viral hepatitis transmitted in infected blood, causing fever, debility, and jaundice. The disease is also referred to as type B hepatitis, serum hepatitis and homologous serum jaundice according to Mahoney and Kane (1999).

In 1965, Dr. Baruch Blumberg discovered Hepatitis B virus. Originally, the virus was called the 'Australia Antigen' because it was named as a result of an Australian aborigine's blood sample that reacted with an antibody in the serum of an American haemophilia patient by Wikipedia (2014).

Dr. Blumberg developed a blood test for the Hepatitis B virus. In 1971, the blood banks began using the test to screen blood donations and the risk of Hepatitis B infections from blood transfusion decreased by 25% according to Wikipedia (2014).

HB is a potentially life-threatening liver infection and it is a major global health problem. It causes chronic liver disease and chronic infection and puts people at high risk of death from cirrhosis of the liver and liver cancer according to WHO (2014).

The danger of HB is that it is asymptomatic. This means that those living with the condition do not show any symptom until their liver is partially or wholly damaged (Ganem and Prince, 2004). This not withstanding causes the disease to spread freely like wild fire since those affected are not aware of their condition. Besides, the condition is about (50-100)% infectious than HIV/AIDS. This implies that the organism

which causes Hepatitis-B can be isolated in all body fluids like saliva, sweat, blood etc. This makes it possible for the organism to spread through mere sharing of spoons, tooth brush, barbering machines, pedicure and manicure procedures, sharing of syringes and needles (especially Drug Addicts), kissing and casual sex (Owusu-Ansah et al, 2013)

Any person with a Hepatitis B Virus is a potential source of infection for others that are susceptible. The investigation of infected persons can prevent further transmission by identifying contacts who require vaccination or other preventive interventions and by detecting outbreaks, determining the cause, implementing appropriate control measures; CDC (2013).

1.1.1 Stages of Hepatitis B Virus Infection

There are two stages of Hepatitis B Virus infections namely Acute Hepatitis B Virus infection and Chronic Hepatitis B Virus infection. A new infection is called Acute HBV. This may go away on its own in the first six months of infection. Most people do not need any therapy at the early stage of the disease. Thus, if an adult gets infected with the HBV, there is about 90% chance that the person's immune system (the body's defense system) will fight the disease off in the first six months (the acute stage) and no treatment might be necessary; this according to Shepard and Simard (2006).

Acute Hepatitis B does not need treatment but with a strong humane immune system, the body can clear the virus within six months. The patient needs to follow up with blood test to confirm recovery from an acute infection.

According to Wilson and Carman (1998), people who tested positive for the hepatitis B virus for more than six months are diagnosed as having a Chronic Hepatitis B. They were not able to get rid of the virus and it still remains in their blood. People with

Chronic Hepatitis B live long and healthy life if managed well with the required medications.

1.1.2 Hepatitis B, the Cause and the Transmission

Lavanchy (2004) said; HBV is a non Cytopathic virus. This means that the virus itself does not cause direct damage to liver cells. Instead, it is the immune system's aggressive response to the virus that usually leads to inflammation and damage to the liver (hepatitis). However, HBV can cause damage to the genetic material inside the liver cells. This can lead to liver cancer which, like hepatitis, can also be fatal.

HBV is very similar to HIV in the ways it is transmitted; that is through direct blood-to-blood contact and through sexual activity. However, blood levels of HBV are much higher than for HIV or the HCV, making this virus much easier to transmit in certain situations (e.g., from mother to child during delivery).

HBV is present in blood, semen, and vaginal fluids and is transmitted primarily through sexual activity. Another major transmission route is sharing injection drug equipment (including needles, cookers, tourniquets) and, to a lesser extent, non-injection drugs (cocaine straws and crack pipes) due to the possibility of exposure to blood. Pregnant women who have hepatitis B can also transmit the virus to their babies, most likely during birth.

1.1.3 Symptoms of Hepatitis B

Most people do not experience any symptoms; especially children in the case of Acute Hepatitis B. However, some people have acute illness with symptoms that last several weeks, including yellowing of the skin and eyes (jaundice), fever, Grey-colored stools, dark urine, extreme fatigue, nausea, loss of appetite, joint pains, vomiting and abdominal pains; according to Diekmann and Heesterbeek (2000).

Many people with chronic Hepatitis B do not have symptoms and do not know they are infected. Even though a person has no symptoms, the virus can still be detected in the blood. Symptoms of Chronic Hepatitis B can take up to 30 years to develop. Damage to the liver can silently occur during this time. When symptoms do appear, they are similar to acute infection and can be a sign of advanced liver disease (Diekmann and Heesterbeek, 2000).

1.1.4 Hepatitis B Treatments

Hepatitis B can be treated with medication. It involves taking tablets everyday or having an injection under the skin once a week. Treatment may be for 12 months or lifelong. The aim of treatment is to make the Hepatitis B virus inactive so that it no longer causing damage to the liver.

One can also maintain a healthy diet (drink plenty of water); reduce or stop alcohol intake; avoid medications that may cause further damage to your liver and getting plenty of rest most of the time (Diekmann and Heesterbeek, 2000).

There are treatments for those who have developed Chronic Hepatitis B. Chronic Hepatitis B virus may be treated with anti-viral medication such as Adefovir, Entecavir, Interferon, Lamivudine, Telbivudine and Tenofovir. Most of these drugs are not available or accessible in Ghana. However, lamivudine which is cheaper and accessible in Ghana, the body develops resistance to it after two year (Owusu-Ansah et al, 2013).

Treatment of the Chronic Hepatitis B does not cure the disease but suppress it. Chronic Hepatitis B is manageable like Diabetes. The goal of the treatment is to improve the quality of life and survival rate of the patients by preventing progression of the disease to cirrhosis and end stage of liver disease.

1.1.5 Hepatitis B Vaccination

Vaccination is the administration of antigenic material (a vaccine) to stimulate an individual's immune system to develop adaptive immunity to a pathogen. Vaccines can prevent or ameliorate morbidity from infections. (en.wikipedia.org/wiki/Vaccination).

There is a safe and effective vaccine for hepatitis B. More than one million doses have been given around the world. The vaccine is a series of three shots given over a six-month period that will provide a lifetime of protection. You cannot get hepatitis B from the vaccine – there is no human blood or live virus in the vaccine.

The hepatitis B vaccine is recommended for all new born and children up to 18 years of age, and all high-risk adults. All infants should receive the first dose of the vaccine at birth, or before leaving the hospital. In most states, children need the hepatitis B vaccine for school entry. The vaccine is recommended for anyone who lives in close contact with, or is a sexual partner of an infected individual. In addition, the vaccine is recommended to anyone who is at risk of infection through their job, lifestyle choices, or other life circumstances.

If someone has received the hepatitis B vaccine, then a simple blood test can tell whether they are protected. If they have responded to the vaccine series, the blood test will show a positive result for the hepatitis B surface antibody (HBsAb+). After the first dose of HBV vaccine, there can be up to 50% protection. After the second dose, there can be up to 80% protection. It is very important to receive the third shot to ensure 100%, long-term protection; CDC (2013).

1.1.6 Geographical Distributions

Hepatitis B prevalence is highest in sub-Saharan Africa and East Asia. Most people in these regions become infected with the hepatitis B virus during childhood. The adult population ranging between 5–10% is chronically infected; by WHO (2014).

High rates of chronic infections are also found in the Amazon and the Southern parts of Eastern and Central Europe. In the Middle East and the Indian subcontinent, an estimated 2–5% of the general population is chronically infected. Less than 1% of the population in Western Europe and North America is chronically infected, by WHO (2014).

More than 240 million people have chronic (long-term) liver infections. More than 780,000 people die every year due to the acute or chronic consequences of hepatitis B. A vaccine against hepatitis B has been available since 1982. Hepatitis B vaccine is 95% effective in preventing infection and its chronic consequences, and was the first vaccine against a major human cancer; by WHO (2014). In the year 2014, research revealed that viral hepatitis is the eighth (8^{th}) leading cause of death worldwide according to WHO (2014).

Across the country Ghana, millions of Ghanaians are living with Hepatitis B Virus. Most people in Ghana are living with the disease. They are neither aware of their status nor receiving care and treatment. In every hundred (100) people in Ghana, there is the chance of having thirteen (13) people infected with the disease (Owusu-Ansah et al, 2013). Raising awareness about Hepatitis B is crucial since this would effectively stem the tide of new infections, ensuring that those affected receive proper treatment, and fighting any societal stigma.

Ghana Medical Journal Report, Chronic Hepatitis B is considered an important public health problem necessitating high priority strategies for prevention and control. HBV infections is endemic in Ghana with sero - prevalence rate ranging from 6.7% to 10% in blood donors, 6.4% in pregnant women and 15.6% in children among the general population; according to Blankson and Tettey (2005).

Edington in his study of Hepatitis in Ghana, observed that the commonest disease leading to death at autopsy was cirrhosis of the liver. Unpublished data on the cause of death over 20 years period from 1980 to the year 2000 from the Department of Pathology, Korle Bu Teaching Hospital (KBTH) confirmed this observation (Blankson and Tettey, 2005).

Cirrhosis is characterised by degeneration of the liver cells, inflammation, and thickening of tissue (Oxford Dictionary). It is the end stage of Chronic liver disease which is generally irreversible. Among other causes of liver diseases like alcoholisms in Ghanaian population, Hepatitis B and its Chronic infections if not manage well would result to Cirrhosis.

The Continent Africa is highly susceptible to HBV infection, yet research works to understand and control the disease is limited in the region. The use of Mathematical Methods in finding solutions to the disease epidemiology, especially Ghana and other countries in sub-Sahara Africa where the situation is escalating is also limited. It is against this background that this work, formulates a Deterministic SIR Model with the use of differential equations to study and understand the mechanisms of HBV infection in the Sunyani Municipality.

Ghana is located in West Africa bordering on the Gulf of Guinea. Ghana is bounded by Ivory Coast to the west, Burkina Faso to the north, Togo to the east and the Atlantic Ocean to the south.

Ghana was formally called the Gold Coast and was first seen by the Portuguese traders in 1470. This was followed by the English in 1553, the Dutch in 1595 and Swedes in the 1640s. The British was the Country that actually ruled Ghana (Gold Coast) starting from 1820. However, their rule was quelled by the resistance of the Ashanti in 1901, one of the dominant tribes in Ghana. Ghana finally became an independent country in March 6, 1957 and as result of a plebiscite, a republic status was achieved in July 1, 1960; by Infoplease (2015).

Ghana has a land area of 88,811 square meters (230,020 sq km); a total area of 92,456 square meters (239,460 sq km) and a total Population of 25,758,108 (2014 est.). It has a growth rate of 2.19%; birth rate of 31.4/1000; infant mortality rate of 38.52/1000 and life expectancy of 65.75%; according to Infoplease (2015). The country Ghana is divided into ten (10) administrative regions which includes Brong Ahafo Region with capital Sunyani.

Brong Ahafo Region shares borders with the Western, Ashanti and Northern Regions. It also shares international boundary with the Republic of Ivory Coast.
It has a large forest area in the places bordering the Western and Ashanti Regions whiles areas near the Northern Region have a transitional Savannah vegetative cover. Such areas like Atebubu, Yeji, Sene, Tain, Kintampo (some districts and municipal assemblies) and others have been captured under the Savannah Accelerated Development Authority because they fall in the transition zone of the northern ecology; by Wikipedia (2014).

Sunyani is a city; the capital of Sunyani Municipal and Brong-Ahafo Region of Ghana. Sunyani has a population of 248,496 people as of 2012 census. Sunyani is surrounded by the forested Southern Ashanti uplands, the city of Sunyani arose as an outpost camp for elephant hunters during the 19th century. The name Sunyani was derived from the Akan word for elephant "Osono". Although considerably smaller than nearby

Kumasi, Sunyani is growing rapidly and has effectually engulfed the suburbs of Fiapre and Abesim, amongst others. Sunyani is a clean and well maintained city with a thriving economy; according to Wikipedia (2014)

Sunyani is home to several higher educational institutions in the country, including the Sunyani Polytechnic, the University of Energy and Natural Resources, the Catholic University College at Fiapre. Other institutions with satellite centres in the city include University of Ghana, University of Cape Coast, and the Kwame Nkrumah University of Science and Technology- KNUST that holds part-time and long distance programs in Sunyani, by Wikipedia (2014).

The economy of Sunyani is predominantly agrarian with approximately 48% of the population engaged in agriculture production. About 24% of the population is employed in the service sector, followed by commerce and industry which employed 15% and 13% of the populace, respectively; by Wikipedia (2014). The city of Sunyani has three hospitals, one of which is the Sunyani Municipal Hospital. Eight clinics and three maternity homes also operate in Sunyani.

1.2 PROBLEM STATEMENT OF THE STUDY

The progress in understanding the natural history of hepatitis B virus made it possible the use of Mathematical Models to understand the Mechanisms of HBV infections. Transmission from one person to another has increased over the years. This has resulted in many deaths worldwide since it is difficult to cure viral diseases. Many people in Ghana today have less or no knowledge of HBV infection, the effects, the challenges and the burdens it possess to individuals, communities and the nation as a whole. HB is potentially life threatening liver disease and is a major global health problem. It is a disease which researchers described as next to HIV infection. It is however, preventable thanks to the availability of vaccines.

In Ghana today, one in every twelve Ghanaians is living with a chronic (life-long) HB, and one in four of those living with Chronic HB will die from liver cancer or liver failure. The good news is that the effects can be avoided or prevented with appropriate education, monitoring and treatments. Therefore, Hepatitis B can be eradicated by understanding the mechanisms of infections through research works, thus the Model formulation.

1.3 OBJECTIVES OF THE STUDY

This thesis work seeks to achieve the following objectives:

1. To develop a Deterministic SIR Models to study the Mechanism of the Hepatitis B Virus (HBV) infections.
2. To use the Models to analyse the dynamics of HBV infections and to evaluate the long-term effectiveness of the vaccination programme.
3. To understand the implications of these Models in relations to HBV infections in Sunyani Municipality.

1.4 METHODOLOGY

This thesis work formulated a Deterministic Models through the use of ordinary differential equations. The study involves construction of three Models. The first Model involves a Deterministic Model for a population without the Demographic turn over with analysis of threshold conditions that allowed the epidemics to occur. The second Model dealt with Deterministic Model with Demographic turn over. This couple with determination of various equilibrium points and stability analysis in each case of equilibrium point. A Vaccination Model was included to assess the impart of Vaccination in the population coupled with its equilibrium point analysis. The use of

Reproduction Number (R_0) was crucial to determine epidemic and endemic situation of the population. SIR Model with its phase portrait diagrams were also considered.

Bio Statistic Data on Hepatitis B Virus infection from 2000 to 2014 was obtained from Sunyani Municipal Hospital to test the Models with various analyses. Information was solicited from printed and electronic form. Search engines like Google and Yahoo were used. Simulations of the models were done using Matlab codes to determine the behaviour patterns of the Models.

1.5 JUSTIFICATION

The use of Mathematical Methods to study disease epidemiology date back since 1960. Daniel Bernoulli used Mathematical method to study techniques of protections against smallpox. In 1927, W.O. Kermack and A.G. McKendrick used differential equations to understand cholera epidemic. Since then, many scientists have used Mathematical Models to understand dynamisms and mechanisms of diseases; by Alfonseca and Torrea (2000). In our part of the world only few researchers study diseases with the use of Mathematical Models.

This study serves as an aid to understand the mechanisms of HBV infections in the case study area. The study would afford health practitioners the opportunities in learning new ideas in controlling the mechanisms of Hepatitis B virus infections.

It also serves as awareness creation for the people in the Sunyani Municipalities and its environs. Like HIV/AIDS, it is difficult to tell who is the carrier of Hepatitis B disease.

The study area would benefit immensely from some critical analysis involved in the study of HBV infections. It would help decision makers to evaluate the effectiveness of interventions put in place to combat the HB disease.

The Municipal Directorate monitoring system for HBV infection if put in place would be provided with a crucial tool for revealing changes in the pattern of the disease in the community through this work.

Finally, this piece of academic work is an addition to the few available one's and it is a source of reference for Mathematicians and other Research Scientists for further studies.

1.6 THESIS ORGANISATION

The thesis was organised into five (5) chapters. The Chapter One introduces the Background to the study. It also talked about the Problem Statement,the Objective of the study, Methodology, Justification and as well as the Organization of the thesis presented. Chapter Two presented the review of relevant works that have been done previously in HBV infections and its related issues. The use of differential equations to model epidemiology of HBV infections by other writers and academic researchers were dealt with in this chapter. This comes with various supported relevant references. Chapter Three deals with Methodology. It explained the Mathematical Models selected, and reasons for selection. It also discussed Mathematical methods used in analyzing various data. The Chapter Four dealt with the analysis of results of model estimations using data obtained and the various theories. The use of Matlab code to stimulate models for better understanding of the thesis work was captured. Chapter Five put together the major findings from the entire thesis work. It summarised and highlighted the most salient points discovered followed by conclusions, recommendations and a topic suggested for further studies.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

This section concentrated primarily on the review of empirical related literatures on Hepatitis B infection. It also includes various types of models and the methods used. The focus is on models with particularly intervention analysis. We also emphasised on data, findings and conclusions of the related subject matter.

2.2 EMPIRICAL REVIEW OF RELATED LITERATURE

To start with, Momoh and Ibrahim (2011) developed a Mathematical Model that was described as MSIR Model, to understand the effect of combining passive immunisation with treatment of infectious Hepatitis B in controlling the spread of Hepatitis B disease. The MSIR Model was partitioned into four compartments of passively immune infants (M), susceptible individuals (S), infected individuals (I) and removed individuals (R).

The immunised compartment changes due to the fact that the proportion of immunised individual child reduces due to the expiration of duration vaccine efficacy. Another assumption of the changes in the immunised compartment is that of the natural death rate. The susceptible population increases due to the coming of the individual from the immunised compartment due to the expiration of duration of vaccines efficacy. The susceptible again reduces due to natural death rate and infection within. In the same way the population dynamic of the infectious class grows with the incidence rate and also reduces by natural death rate and successful cure of infectious hepatitis B patients. Lastly, the dynamics of the removed with immunity class increases with successful cure of infectious hepatitis B patients at a rate and decrease by natural death as well.

The administration of the HBIG (Hepatitis B Immune Globulin) vaccines at birth protect children from early infections of Hepatitis B but the efficacy of the vaccines expires with time. After establishing the existence of equilibrium state and also analysing the epidemic equilibrium state, they discovered from their models that, the epidemic equilibrium state is stable when the contact rate is less than 0.8 and becomes unstable at a contact rate of 0.8 and above.

They concluded that effort must be made to bring down the contact rate and increasing the duration of efficacy of vaccines used in passive immunisation programmes. This is the responsibility of Governments and immunisation partners.

Sutton and Edmuds (2006) explained that it is the individuals that make up the injecting drug user (IDU) population in England and Wales. These people are at risk from blood - borne viruses due to the sharing of injecting paraphernalia. A vaccination programme was introduced offering HBV vaccine at reception into prison at some selected prisons in England and Wales.

They considered the impart of prison vaccination on the incidence and prevalence of HBV in the injecting drug user population of England and Wales. A dynamic Mathematical Model of the transmission of HBV in IDUs was developed with key model assumptions and parameters being subject to sensitivity analyses.

The Model was developed with the assumptions that the vaccination coverage on prison reception is 5% in 2002, 10% in 2003 and then increases linearly up to 50% of prison receptions being vaccinated by 2006.

In a typical epidemiological model of HBV natural history and transmission dynamics, the IDU population is stratified into six groups as the basis of the model development.

There were those susceptible to infection (S), those infected but were not yet infectious (L), acute infection (A), that is, are in the initial highly infectious stage. The carriers (C); vaccinated (V), that is, those that have been vaccinated and immune from infection; and those with protective immunity (R), this is due to recovery from either carrier or acute stages of infection. The model includes an injecting carrier length dependent force (FOI) defined as per the capita rate at which susceptible become infected.

The IDUs enters the model at the start of the year into the first injecting carrier length cohort. The individuals change cohort at the beginning of each new year. The rates of parameters were with respect to both injecting carrier length and time at which individual flow from one epidemiological state to another. These were explained by a system of differential equations.

The analyses of their Model showed that the incidents of HBV in IDUs might be reduced by almost 80% in 12 years. The Model further estimated that the HBV prevalence may be reduced from approximately 18% in 2002 to 7% in 2015. They empasised that the Model developed demonstrated that HBV vaccination on prison reception can have a significant impart on the prevalence and incidence of HBV in the IDU population over time.

In discussion of findings as estimated by the Deterministic Model, it was realised that HBV vaccination programme in prisons on the incidence and prevalence of HBV in the IDU has much impart on the population of England and Wales.

Molaei and Waezizzdeh (2012) developed an epidemic Model for hepatitis of type B where the essential factors for the epidemic appeared. They described the factors of the epidemic as susceptibility, expose factor, vaccination, infection and recovery. Their

investigation covered the following; • Asymptotic stability in disease free equilibrium points.

- Asymptotic stability in endemic equilibrium point.
- Equilibrium point that is not asymptotic.

They described the model by regarding the five factors as five boxes, that is, susceptible, latent or exposed, infections, vaccination and recovery box. By these factors they described their epidemic Model abbreviated as SEIVR Model which is a typical modification of standard SIR Model.

In notations, N represent the total population in time t for the model. The factors of the HBV epidemic according to their study, expressed the factors as $S(t)+E(t)+I(t)+V(t)+R(t) = N(t)$. They used various parameters to denote the following; transmission rate, the natural mortality rate and the birth rate. Also the recovery rate in the I class and the leaving rate of the exposed class were denoted by some other parameters. In the research, all the various parameters were determined. The combinations of the values of these parameters gave the various equilibrium points and stabilities. A system of Ordinary Differential Equations were used to deduce the Mathematical Model.

In the analyses, Asymptotic Stability means there was no vaccination in the population before an endemic outbreak and it is the disease free equilibrium point of the Model. At this state, the reproductive number R_0 is less than one (1). That is, $R_0 < 1$, the SEIVR Model is asymptotically stable. At the endemic equilibrium point, the Model SEIVR has no equilibrium point and is also said to be asymptotically stable.

Molaei and Waezizzdeh (2012) tried identifying another equilibrium point for HBV Model which never was. For this, it was described as been the situation where there

were no disease death. That is, the birth rate and natural mortality rate are equal. In this they said the model is not asymptotically stable.

Zhao and Lu (2000) in a research work explained that in 1986, China was a region endemic with HBV infection. It was before the universal infant immunisation was introduced. There was about 60% prevalence rate of infection in the population and 10% chronic HBV carriers.

Zhao and Lu (2000) developed a Mathematical Model to predict the dynamics of HBV transmission and evaluate the long – term effectiveness of vaccination programme in China. A compartmental model expressed by a set of partial differential equations based on the characteristic of HBV infection was used. Parameters in the model were expressed as a non – linear function of age and time since vaccination. Data from sero – survey was used to estimate these parameters used in the model.

The entire population was divided into five compartments. These are susceptible $S(a,t)$, latent period $L(a,t)$, temporary HBV carriers $T(a,t)$ chronic HBV carriers $C(a,t)$ and the immune $I(a,t)$. The ${}^{0}a^{0}$ represents the age whiles ${}^{0}t^{0}$ represents the length time of follow – up.

According to the natural history of HBV, a susceptible individual acquires an acute HBV infection through effective contact with a temporary or a chronic HBV carrier, and shifts to the next compartment called the latent period. The individual becomes temporary (acute) HBV carriers after persistent latent period. The acute infection either get cleared or progressed to the chronic state of HBV. If the acute infection get cleared the individual recovers and becomes immune which is also lifelong state.

The Model had it that, if all new-borns are vaccinated according to schedule, the rate of HBV carriage will decline sharply over time to 0.2% in 70 years. At that point, the

ratio of acute hepatitis B will be less than 0.5% and the chronic hepatitis B will be around 5%.

Zhao and Lu (2000) concluded that China can control HBV infections in just one generation, and eventually eliminate it. According to them, the Model shows that vaccination coverage was the most important indicator for the elimination of HVB transmission. There should be higher coverage, that is the key controlling factor to eliminating HBV infection. Also another possible means is to find ways to immunise all infants throughout the country, especially in poor rural areas.

Hepatitis B is the most common serious viral infection and a leading cause of death in mainland China according to Zou and Ruan (2009). A total of 130 million people in China are carriers of HBV, this is almost a third of the people infected with HBV worldwide. This could also be said to represent 10% of the general population of China. Among them 30 million are chronically infected and 300,000 people die from HBV – related disease in China every year. Statistically, this accounted for 40% to 50% of HBV related deaths worldwide. China HBV prevalence rate was still high despite an effective vaccination programme for new - born babies since 1990s even though there was an improvement (Zou and Ruan, 2009).

They developed a Mathematical Model to understand the transmission dynamics and prevalence of HBV infection in China. The Model was constructed based on the characteristics of HBV transmission in China. They considered six epidemiological groups: the proportion susceptible to infection S; those latently infected L; acute infections A; carriers C; recovered with protective immunity R; and immune following vaccination V. They assumed that population of new - born carriers born to carriers are less than the sum of the death of carriers and the population moving from carrier to immune state. Based on the six epidemiological groupings, six ordinary differential equations were developed.

In the analysis, they estimated the basic reproductive number R_0 to be $R_0 = 2.406$. The implication is that hepatitis B was endemic in China and was approaching its equilibrium with the current immunisation and control measures. They suggested that the optimal control strategies are a combination of immunisation of new - born babies, retroactive immunisation of susceptible adults, and reduction of contacts by individuals. These must be done with a wide coverage area in order to succeed the fight against hepatitis B.

A continuous simulation of Mathematical Models were proposed for two different epidemic situations; HB in a cohort of new-borns followed for life, and one of the danger groups in the current AIDS epidemic by Alfonseca and Torrea (2000).

Alfonseca and Torrea (2000) in their paper, used differential equations to model Hepatitis B among a cohort of the total population, and AIDS restricted to a homosexual population where the parameters used can be viewed as a mathematical expectations of random variables subject to a Poisson distribution. The systems of differential equations generated were solved numerically by an object oriented computer language OOCSMP. The OOCSMP compiler automatically generates C++ or Java codes that include a graphic simulation environment that makes it very easy to test different alternatives of the values of the parameters used. This enabled the developed Model to obtain the most appropriate approximation for the behaviour of the affected populations compatible with the existent data.

Alfonseca and Torrea (2000) concluded that the set of differential equations used has proved useful to model the development of different epidemics and to test the effect of different policies for prevention and treatment. It was also found that the model is very powerful tool that can be used to compare alternatives and estimate costs and effectiveness.

Min and Kuang (2002), Based on the anti – HBV infection therapy clinical data of the Peginterferon Alfa – 2a plus placebo for HBeAg – Positive chronic Hepatitis B patients, a Mathematical Model was developed. The Model consists of three systems of differential equations which were used to describe and understand the dynamics host cells, viruses, the immune system, as well as predict the long term curative effects.

A system of equations comprising three differential equations were proposed for the first 56 days of the Peginterfero Alfa – 2a treatment. During the next 286 days of the Peginterferon Alfa – 2a treatment, another set of differential equations was developed to describe the scenario. Again another set of equations was developed after 24 weeks of treatment for follow – up. All the parameters of the systems of equations were determined. This was followed by determining two equilibrium points. The two equilibrium points represent patient's recovery and patient's persistent HBV infection.

Min and Kuang (2002) Mathematical Model shows that numerical simulations indicates that patients whose plasma HBV DVA levels equal the mean HBV DVA levels of all patients will need to prolong their treatment time for 19 years in order to completely eliminate the HBV virus in infected hepatocytes. They proposed that their research supports the use of Peginterferon Alfa – 2a as a first – line therapy for patients with HBeAg – positive chronic Hepatitis B.

The HBV infects the liver cells (hepatocytes) and usually cause both acute and chronic disease. It is however believed that host factors, in particular immune responses, are responsible for determining whether the infection is cleared or becomes Chronic HBV infection; this is according to Stanca and Perelson (2007).

They developed dynamic models to analyse the changes in Hepatitis virus level during drug therapy. Their models typically considered uninfected (T), Infected (I) and hepatocytes and free virus (V). They assumed target cells susceptible to infection are produced at a constant rate λ, die at per capita rate d, and become infected at a rate kTV . This is proportional to both the target cell concentration and the virus concentration. Infected hepatocytes are thus produced at rate kTV and are assumed to die at constant rate δ per cell. Upon infection, hepatocytes produce virus at rate p per infected cell, and virus is cleared at rate c per virion. They also used differential equations to establish the dynamics of the system in which the models were developed.

They validate the model against experimental data to determine how well it represents the biological system and, consequently, how useful are its predictions. They found that a cell – mediated immune response plays an important role in controlling the virus after the peak in viral load.

According to Elaiw and Aly (2013), Modeling, analysis, and control of HBV infection have attracted the interests of Mathematicians during the recent years. The several existed Mathematical Models, have adequately explained the dynamics of HBV infections as well as the effect of antiviral drug therapies. Upon the achievement of these various Mathematical Models, none completely exhibit all that is observed clinically and account for the full course of infection. In addition to the inaccuracies that HBV dynamics suffer from, some disturbances / uncertainties may arise in the modeling process.

In their paper, they used a system of nonlinear ordinary differential equations to describe the dynamics of HBV. The disturbances or uncertainties were modeled in the dynamic model of HBV as additive bonded disturbances. They try to inhibit viral

production and prevent new infections by incorporating two types of drug therapies in the model.

The Model was described as nonlinear control system with control input; defined to be dependent on the drug dose and drug efficiency. They also described a treatment schedules for infected patients by using multi - rate model predictive control (MPC). The MPC method help in determining the optimal treatment schedules and help stabilising the HBV infection system around the uninfected steady state.

2.3 CONCLUSIONS & REMARKS ON LITERATURE REVIEW

The review was about the use of Mathematical Models to explain the dynamics and mechanisms of HBV infections. The Models were based on the characteristics of HBV infections. Whiles some based the process of infections on the standard SIR model, others based theirs on variations of the standard SIR model.

The Reproductive Number R_0 was used in the analyses and to determine basis of having endemic HB population or otherwise.

This work looked at the mechanisms of Hepatitis B Virus infections by using a deterministic models based on standard SIR model developed by Kermack and Mckendrick; Kermack and MacKendrick (1927).

CHAPTER 3

METHODOLOGY

3.1 INTRODUCTION

In this Chapter, the focus is on Deterministic SIR Models. The models, represented by ordinary differential equations (ODE) captured the characteristics of Hepatitis B virus infection. The characteristics include Susceptible (S), Infectious (I) and Removal (R), which were assumed to be groups formed out of the population (N). Dynamics of ordinary differential equations were reviewed and applied to the formation of the Deterministic SIR Model. Equilibrium points were determined coupled with its stability.

In disease epidemiology, Basic Reproductive Number (R_0) is very important in investigating the qualitative dynamics of a deterministic model with solution paths and phase portraits. Thus, we involved in our study; the Basic Reproductive Number and how it is applied. Finally, the study incorporated Vaccination Model to understand the impact of Vaccination in the population.

3.2 DIFFERENTIAL EQUATION (DE)

In order to apply mathematical methods to physical or real life problems, the dynamics/mechanisms of HBV infections were formulated in mathematics terms as being the Mathematical Model for this problem. Since rates of change are represented mathematically by derivatives, the models consist of system of equations relating an unknown function and one or more of its derivatives. Such equations are called differential equations. In oder words, an equation containing the derivatives of one or more unknown function (dependent variables), with respect to one or more independent variables, is said to be a differential equation (DE) according to Zill and Cullen (2009).

3.2.1 Ordinary Differential Equation

An Ordinary Differential Equation (ODE) is a differential equation for a single variable. An ODE contains ordinary derivative (Zill and Cullen, 2009). ODE have been used in various forms of studies. It is used for; Population Dynamics, Newton's Law of Cooling / Warming, Chemical Reactions, Mixtures Draining in a tank, Falling bodies, Spread of diseases and many others.

An equation of the form;

$$\frac{dy}{dt} = f(t,y) \quad \text{or} \quad y' = f(t,y) \tag{3.1}$$

Where $f : R^2 \longrightarrow R$ is a function of two or more variables. The mathematical notation $\frac{dy}{dt}$ or y' represents the derivative of the variable y (dependent variable) with respect to t (independent variable). The expression in Eqn.3.1 is called ordinary differential equation (ODE).

Differential equations can be classified as first order, second order etc. depending on the highest derivatives that appeared in the equation. Thus, the Eqn.(3.1) is a first order derivative. A notation $\frac{d^2y}{dt^2}$ contains in a differential equation makes the equation a second order derivative. The equation is n^{th} order derivative if it contains $\frac{d^n y}{dt^n}$.

The Degree of Differential Equation is the power of the highest ordered derivatives of the equation. Thus, $(\frac{dy}{dt})^2 - 3y = 0$ is an ODE of second degree whiles Eqn.(3.1) is of first degree.

3.2.2 Solution of Ordinary Differential Equation

A solution to a differential equation is a function y that satisfies a given differential equation. Given a differential equation below:

$\frac{d^n y}{dt^n} = f(t, y, y', ..., y^{(n-1)})$ (3.2)

on the interval $\alpha < t < \beta$ is a function of ϕ such that $\phi^0, \phi^{00}, ..., \phi^n$ exist and satisfies the equation $\phi^{(n)}(t) = f[t, \phi(t), \phi^0(t), ..., \phi^{(n-1)}]$ (3.3) for every t in $\alpha < t < \beta$.

If Eqn.(3.1) is a real – valued function, then $y = \phi(t)$ is a real – valued solution.

For example; $\frac{dR}{dt} = kR$ has the solution to be $R = \phi(t) = ce^{kt}$, $-\infty < t < \infty$,

where c is a constant and can be determined. If $\phi(t) = ce^{kt}$, then $\phi^0(t) = cke^{kt}$. The expression $\frac{dR}{dt} - kR = 0$ holds. This implies that $\phi(t) = ce^{kt}$ is a solution of $\frac{dR}{dt} = kR$.

Also, if $y^{00} - y = 0$, assuming $\phi(t) = e^t$, then $\phi^0(t) = e^t$ and $\phi^{00}(t) = e^t$, it implies that $y^{00} = y$ holds. Hence $\phi(t) = e^t$ is a solution of $y^{00} - y = 0$.

3.2.3 Initial Condition(s)

It is sometime the case that one is interested in only one solution among all solutions to a differential equation. One way to select one particular solution of a differential equation is to require that $y(t_0) = y_0$, that is, the solution at a given point t_0 takes the given value y_0. The point t_0 is usually called the initial point, and the condition $y(t_0) = y_0$ is called the initial condition.

An initial value problem for the equation $\frac{dy}{dt} = -2y$ with constants t_0, y_0.

The function y^0s solution is that; $\frac{dy}{dt} = -2y \Longrightarrow y(t_0) = y_0$.

3.2.4 General Solution

This is the general form that the solution to a differential equation can take and does not take any initial conditions for the given differential equation.

3.2.5 Particular Solution

This is a specific solution to a given differential equation; it does not satisfies the differential equation only, but also satisfies a given initial condition(s).

3.3 ANALYSIS OF NON-LINEAR SYSTEM

A continuous differential equation of non – linear system of n^{th} - order is represented in the form;

$y'_1(t) = f_1(x_1(t),x_2(t),\ldots,x_n(t))$ $y'_2(t) =$

$f_2(x_1(t),x_2(t),\ldots,x_n(t))$

$y'_3(t) = f_3(x_1(t),x_2(t),\ldots,x_n(t))$ (3.4)

……

……

$y'_n(t) = f_n(x_1(t),x_2(t),\ldots,x_n(t))$

which can be expressed in matrix form as shown below

$Y(t) = f(Y(t),t)$ (3.5) where $Y = [y_1, y_2, \ldots, y_n]^T$ and $f = [y_1, y_2, \ldots, y_n]^T$. In this, T means transpose;

according to Lungu and Kgosomore (2007)

In analyzing non - linear systems, the nature of the system is given by the non - linear equations. This thesis involves non – linear equations; since real life problems may only be modeled by non – linear systems. Therefore, in analyzing, we considered equilibrium points, linearisation and stability as tools for analyzing non – linear systems (Lungu and Kgosomore, 2007).

3.3.1 Equilibrium Points

Suppose the $F(x,y) = f(x,y) \in R^2$ has an equilibrium point (μ,ν), then $f(\mu,\nu) = 0$. This means that $(x,y) = (\mu,\nu)$ is a solution at all time t. We determine the equilibrium point by solving the equation $f(x,y) = 0$.

Consider modeling of a dynamic system by the differential equations below:

$$F(x,y) = -4y + 2xy - 8 \quad (1)$$
$$G(x,y) = 4y^2 - x^2 \quad (2) \qquad (3.6)$$

In determining the equilibrium point(s), we assumed

$$F(x,y) = 0 \text{ and } G(x,y) = 0 \qquad (3.7)$$

In solving Eqn.(3.7) simultaneously, we obtained its solutions. The solutions are the equilibrium point(s) and also known as the critical point(s). These points are $(-2,-1)$ and $(4,2)$.

3.3.2 Linearizing Non – Linear Systems

Non – linear systems are linearised by employing the techniques of Jacobian Matirix.

For example, consider the system in Eqn.(3.6); The Jacobian Matrix J is given as;

$$J(F,G) = \begin{pmatrix} \frac{\partial F}{\partial x} & \frac{\partial F}{\partial y} \\ \frac{\partial G}{\partial x} & \frac{\partial G}{\partial y} \end{pmatrix}, \text{ that is,}$$

$$\frac{\partial F}{\partial x} = 2y \qquad \frac{\partial F}{\partial y} = -4 + 2x$$
$$\frac{\partial G}{\partial x} = -2x \qquad \frac{\partial G}{\partial y} = 8y$$

So that the linearized form of the system in Eqn.(3.6) is given as

$$J(F,G) = \begin{pmatrix} 2y & 2x - 4 \\ & \end{pmatrix} \qquad (3.8)$$

$$\begin{matrix} & \\ -2x & 8y \end{matrix}$$

Substituting the equilibrium points (-2,-1) and (4,2) into Eqn.(3.8) gives the coefficient matrix which is still the linearized form of Eqn.(3.6) and more analysis can be performed.

Thus, the coefficient matrices for the equilibrium points (-2,-1) and (4,2); we have

$$J(-2,-1) = A = \begin{matrix} -2 & -8 \\ -4 & -8 \end{matrix} \quad (1)$$

$$J(4,2) = B = \begin{matrix} 4 & 4 \\ -8 & 16 \end{matrix} \quad (2) \qquad (3.9)$$

3.3.3 Stability of a System

Stability properties describe how a system behaves if its state is initiated close to, but precisely at a given equilibrium point.

Consider the system; $\frac{\partial x}{\partial t} = f(x, y)$

and $\frac{\partial y}{\partial t} = g(x, y)$

Where *f,g* are differentiable with continuous partial derivatives and they both vanish at the point (x_0,y_0). Considering the Jacobian Matrix as described above at the point (x_0,y_0);

$$J(f,g) = \begin{pmatrix} \frac{\partial f}{\partial x}(x_0,y_0) & \frac{\partial f}{\partial y}(x_0,y_0) \\ \frac{\partial g}{\partial x}(x_0,y_0) & \frac{\partial g}{\partial y}(x_0,y_0) \end{pmatrix}$$

Every Jacobian Matrix has coefficient matrix at a given equilibrium point say (x_0,y_0). The characteristic equation is determined follow by eigenvalues.

3.3.4 Eigenvalues and Critical Points

A scalar λ is called an eigenvalue of the $n \times n$ matrix 'A' if there is a nontrivial solution x of $Ax = \lambda x$. Such an x is called an eigenvector corresponding to the eigenvalue λ. The scalar λ(a real or complex number) can be determined as well as x which is a vector. For a scalar λ, there exist a vector x such that ($Ax = \lambda x$) holds for some $x \neq 0$. The vector is called an eigenvector of 'A' corresponding to the eigenvalue λ. Therefore, $Ax = \lambda x$.

The eigenvalue λ can be determined using the relation:

$$|A - \lambda I| = 0 \qquad (3.10)$$

Where I is $n \times n$ identity matrix.

Conditions for Eigenvalue and Stability

- If all eigenvalues (λ) of J (evaluated at the point (x_0, y_0)) have negative real part, then (x_0, y_0) is stable.
- If all eigenvalues (λ) have positive real part, the point (x_0, y_0) is considered to be unstable point.
- If eigenvalues have opposite signs, then the point (x_0, y_0) is considered to be unstable saddle.

Critical points are related to eigenvalues. That is, they are the solutions to the characteristic equations called the eigenvalue. The solutions to the characteristic equation $\lambda = \lambda_1$ and $\lambda = \lambda_2$ are derived by using the relation in Eqn.(3.10).

Consider the matrix $A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix}$ with $I = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$

Using the relation $|A - \lambda I| = 0$, we have;

$$det(A - \lambda I) = \begin{vmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{vmatrix} = \lambda^2 - (a_{11} + a_{22})\lambda + a_{11}a_{22} - a_{12}a_{21} = 0$$

We let $u = (a_{11} + a_{22})$ called the Trace of Matrix A. $v = a_{11}a_{22} - a_{12}a_{21}$ known as the determinant of A.

This gives the characteristic (quadratic) equation $\lambda^2 - u\lambda + v = 0$, whiles u, v are the coefficients.

We defined 4 as the discriminant and it is expressed as $4 = u^2 - 4v$.

The solution of the characteristic equation is given by $\lambda_1 = \frac{1}{2}(u + \sqrt{\triangle})$ and $\lambda_2 = \frac{1}{2}(u - \sqrt{\triangle})$

The product and addition representation of the quadratic equation is given by

$\lambda^2 - u\lambda + v = \lambda^2 - (\lambda_1 + \lambda_2)\lambda + \lambda_1\lambda_2 = 0$

The u and v are the sum and product of the eigenvalues.

$u = \lambda_1 + \lambda_2$ $v = \lambda_1\lambda_2$ and $4 = (\lambda_1 - \lambda_2)^2$

We summarized this into the table below;

Table 3.1: Eigenvalue criteria for Critical Points

Name	Trace of A	Determinant of A	Discriminant	Comments on $\lambda_1\lambda_2$
	$u = \lambda_1 + \lambda_2$	$v = \lambda_1\lambda_2$	$4 = (\lambda_1 - \lambda_2)^2$	

Node		v>0	$4 \geq 0$	Real, Same Sign
Saddle Point		$v < 0$		Real, Opposite Sign
Center	$u = 0$	$v > 0$		Pure Imaginary
Spiral Point	u 6= 0		$4 < 0$	Complex, Imaginary

Example:

Consider the coefficient matrix (1) of Eqn.(3.9); using $|A - \lambda I| = 0$, the characteristic equation is $\lambda^2 - (traceA)\lambda + det(A) = 0 \Longrightarrow \lambda^2 + 10\lambda - 16 = 0$, where $traceA = (-2 + -8) = -10$ and $detA = -16$. Hence $\lambda_1 = -11.4$ and

$\lambda_2 = 1.^4$.

Therefore, the equilibrium point (-2,-1) is unstable (saddle) due to the opposite signs of the eigenvalues. The point (4,2) is also unstable. The eigenvalues (λ) are positive.

Critical points may also be classified in terms of their stability. Stability means, that a small disturbance of a system changes the behaviour of the system only slightly at all future time t. A critical point (x_0,y_0) of the system is called stable if all trajectories of the system that are close to (x_0,y_0) remain close to (x_0,y_0) at all future time.

Table 3.2: Stability criteria for Critical Points

Types of Stability	$u = \lambda_1 + \lambda_2$(Trace)	det$v = \lambda_1\lambda_2$
Stable & Attractive	$u < 0$	$v > 0$
Stable	$u \leq 0$	$v > 0$
Unstable	$u > 0$	$v < 0$

- If $v = \lambda_1\lambda_2 > 0$, then both eigenvalues are positive, negative or complex conjugates.

- If $u = \lambda_1 + \lambda_2 < 0$, then both eigenvalues are negative or have a negative real part. Hence the given point is stable and attractive.

- If $4 < 0$, then the eigenvalues are complex conjugates, thus $\lambda_1 = b + i\beta$ and $\lambda_2 = b - i\beta$, and

- If $u = \lambda_1 + \lambda_2 < 0$, then this gives a spiral point that is stable and attractive.

The Phase Plane (Phase Portrait)

It is a graphical representation of the nature of the solution of a given system of differential equation. The Cartesian plane where the phase portrait resides is called the phase plane. The parametric curves traced by the solutions are called trajectories. It is the stability of the equilibrium or critical point that determines the kind of phase plane to have.

Consider the following examples that are useful in this work.

1. Consider the system of equations below:

$$\dot{x} = -4x + y \qquad (1)$$

$$\dot{y} = 2x - 3y \qquad (2) \qquad (3.11)$$

The Jacobian Matrix is

$$J(\dot{x}, \dot{y}) = \begin{pmatrix} \frac{\partial \dot{x}}{\partial x} & \frac{\partial \dot{x}}{\partial y} \\ \frac{\partial \dot{y}}{\partial x} & \frac{\partial \dot{y}}{\partial y} \end{pmatrix}$$

The coefficient matrix of Eqn.3.11 is given as;

$$J(\dot{x}, \dot{y}) = \begin{matrix} \\ -4 & 1 \\ \\ 2 & -3 \end{matrix}$$

Using the relation $|A - \lambda I| = 0$; we derived the characteristic equation as;

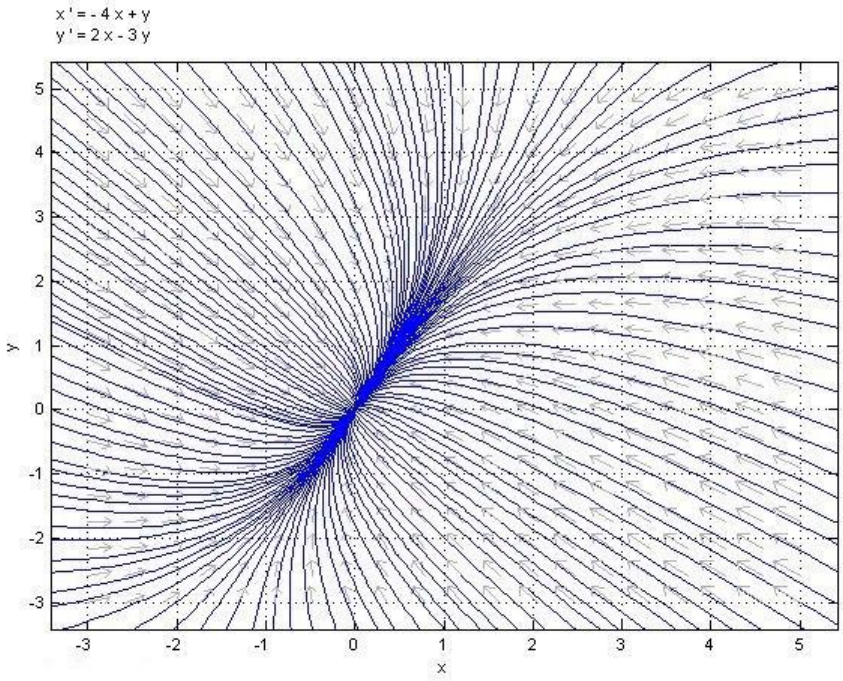
$\lambda^2 + 7\lambda + 10 = 0$.

The eigenvalues are: $\lambda_1 = -2$ and $\lambda_2 = -5$.

The eigenvalues of Eqn.(3.11) are negative, thus Eqn.3.11 is a Stable System known as the Improper Node.

The Phase Portrait diagram of the system in Eqn.(3.11) is shown below.

Figure 3.1: Stable (Improper Node) Phase Portraits



Generated using dfield8 and pplane8 of Matlab with axes; x-axis: $-3 \leq x \leq 5$ and the y-axis: $-3 \leq y \leq 5$.

Where $x^0 = x$ and $y^0 = y$.

2. Below is our next system;

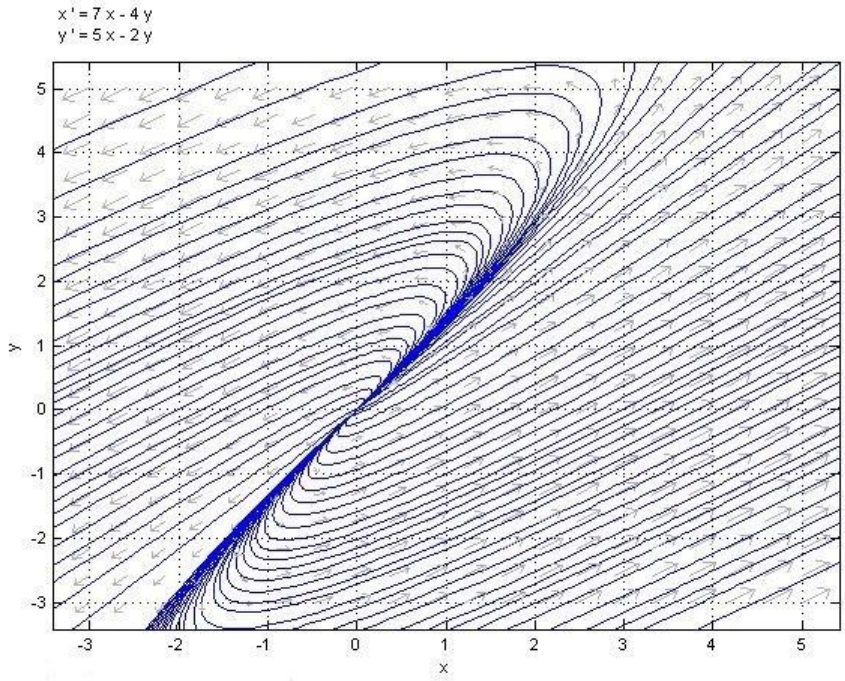
$$\dot{x} = 7x - 4y \quad (1)$$

$$\dot{y} = 5x - 2y \quad (2) \qquad (3.12)$$

Following the same procedure in example 1 above, the eigenvalues are given $\lambda_1 = 2$ and $\lambda_2 = 3$. This is Unstable System since the λ values are positive.

Below is the Phase Portrait diagram.

Figure 3.2: Unstable (Proper Node) Phase Portraits



Generated using dfield8 and pplane8 of Matlab with axes; x-axis: $-3 \leq x \leq 5$ and the y-axis: $-3 \leq y \leq 5$. Where $x^0 = x$ and $y^0 = y$.

3. Finally, we consider another form of stability where eigenvalues (λ) have opposite sign. This is called Unstable Saddle. Consider system of differential equations in Eqn.(3.13) below.

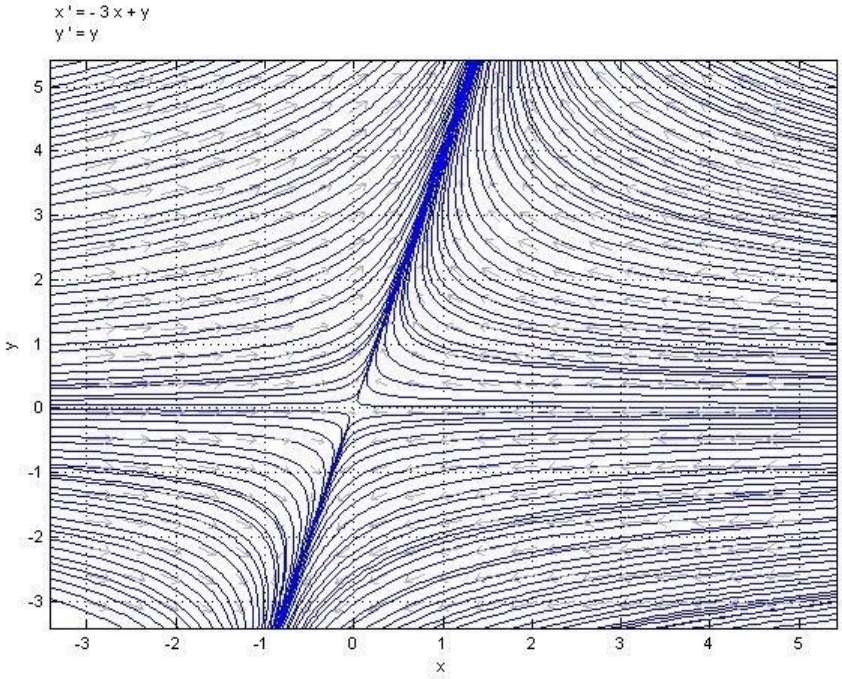
$$\dot{x} = 3x + y \qquad (1)$$

$$\dot{y} = -y \qquad (2) \qquad (3.13)$$

This system also gives eigenvalues of $\lambda_1 = -3$ and $\lambda_2 = 1$.

The Phase Portraits diagram is shown below;

Figure 3.3: Unstable Saddle Phase Portrait



Generated using dfield8 and pplane8 of Matlab with axes; x-axis: $-3 \leq x \leq 5$ and the y-axis: $-3 \leq y \leq 5$. Where $x^0 = x$ and $y^0 = y$.

4. Spiral is a form of stability where the eigenvalues (λ) derived from the characteristic equation are complex numbers.

5. Center is another form of stability, and it is the case where the eigenvalues (λ) are zero.

3.4 DETERMINISTIC MODELS

A Deterministic Model is specified by a set of equations that describe exactly how the system will evolve over time. This is a Mathematical Model in which outcomes are

precisely determined through known relationships among states and events, without any room for random variation. In such models, a given input will always produce the same output, such as in a known chemical reaction.

Mathematically, a Deterministic Model for a system dynamics is represented as:

$$\frac{dy}{dt} = y^{\cdot} = f(t,y) \tag{3.14}$$

Where $f(t,y)$ is a function depending on parameters that are random variables on its own. So that Eqn.(3.14) allows you to make predictions of $y^{\cdot}$ based on the random variable (t,y). The "prediction" does not necessarily occur in the past, future, or even the present. It is simply a hypothetical, "what-if" statement.

A Deterministic Model identifies what would be the outcome if we were to use a particular value of (t,y). For example, what would be the maximum stress $y^{\cdot}$ that a bridge could bear, if we were to use (t,y) – thickness of concrete. Answers to these types of "what-if" questions help to make plans accordingly. This type of model is "deterministic" because $y^{\cdot}$ is completely determined if we know the value(s) of the random variables (t,y).

3.4.1 Basic Reproductive Number

Basic Reproductive Number is defined as the expected number of new infections from a single infected individual placed into a population of fully susceptible individuals. An important part of disease modeling is to determine the Basic Reproductive Number, denoted as R_0. The Basic Reproductive Number is important since it tells us if a population is at risk from a disease or not. The parameter provides significant insight into the transmission dynamics of a disease and can be a guide to develop strategies to control the spread of disease.

The R_0 is affected by the infectious rate and removal rate. In this research, we denote infectious rate by β and removal rate by γ. Therefore; $R_0 = \frac{\beta}{\gamma}$.

In a typical epidemiology analysis, $R_0 > 1$ shows increase occurrence of disease in the chosen population of study. In simple term, there will be epidemic.

According to Earn (2008), the situation where $R_0 < 1$ shows a decrease occurrence of disease, and will eventually be eliminated. A single infected individual introduced into the population will die, without being not able to replicate itself by new infection. However, $R_0 = 1$ is the case of constant occurrence of disease or endemic.

Basic Reproductive Number also helps us to predict who will not become infected at all. This is done by looking at how the SIR model behaves as time $t \to \infty$. According to Keeling (2001), Mathematicians Kermack and McKendrick came up with the equation $S_\infty = \exp(S_\infty - 1)R_0$, where S_∞ is the number of people who will always remain in the susceptible group in the population.

3.4.2 Deterministic SIR Model (Without Demography)

In a total population N individuals, we model HBV infections using compartmental SIR Model. The compartments are susceptible (S), HBV infected (I) and removed (R). So that at any point in time , the population N is made up with this three compartments as in Eqn.(3.16) below:

$$S_t + I_t + R_t = N \tag{3.16}$$

where $S,I,R \geq 0$; represent the compartmentalized of individual in the population.

Model Formulation

Classical SIR Model assumes that individuals that leave one compartment must enter another. It is assumed that the population is that of epidemic. We considered the following assumptions:

- The individuals in susceptible compartment is infected by contact with an infected individuals from the HBV infected compartment. This explains how the infective(I) compartment was recruited.

- The individuals, once infected either die, isolated or recover with immunity. This formed the removal compartment.

- Age, sex, social status, race do not affect the probability of infection.

- There is no inherited immunity.

- The members of the population mix homogeneously (have the same interactions with one another to the same degree).

The following notations represent proportion of the total population N.

$s_t = \frac{S_t}{N}$; fraction of the population Susceptible.

$i_t = \frac{I_t}{N}$; fraction of the population Infective.

$r_t = \frac{R_t}{N}$; fraction of the population Removed. Thus;

$s_t + i_t + r_t = 1$ (3.17)

The model does not consider demographic turnovers (birth and death) and remains constant, however, all infections are assumed to end with recovery.

Further, we assume that;

- The rate of contact between susceptible and infective is proportional to the product of number of Susceptible (S) and Infective (I). The generation of new infection is βSI, where $\beta > 0$ is a parameter for infectious rate.
- The infective are removed to the removed class at a rate proportional to the number of infective, thus γI where $\gamma > 0$ denotes removal/recovery rate.
- This research did not consider incubation period, that is, a susceptible who contracts the disease is infective right away.

Figure 3.4 below is the flowchart of SIR Model of the dynamics of HBV infections.

Figure 3.4: Flowchart of SIR Model without Demography

Flowchart of SIR Model of a Population without Demographic turn-over.

The differential equations governing the models are;

$$\frac{ds}{dt} = -\beta si \qquad s(0) = s_0 \geq 0 \qquad (1)$$

$$\frac{di}{dt} = \beta si - \gamma i \qquad i(0) = i_0 \geq 0 \qquad (2) \qquad (3.18)$$

$$\frac{dr}{dt} = \gamma i \qquad r(0) = r_0 \geq 0 \qquad (3)$$

Where $s_0 = \frac{S_0}{N}$, $i_0 = \frac{I_0}{N}$ and $r_0 = \frac{R_0}{N}$ are the initial fraction of susceptible, infective and removal respectively.

The removal (r) does not appear in the first two equations of Eqn.(3.18), thus, the model is reduced to two equations below by neglecting the third equation.

$$\frac{ds}{dt} = -\beta si \qquad s(0) = s_0 \geq 0 \qquad (1)$$

$$\frac{di}{dt} = \beta si - \gamma i \qquad i(0) = i_0 \geq 0 \qquad (2) \qquad (3.19)$$

We derived the term $\frac{di}{ds}$(product differential) by combining (1) and (2) of Eqn.(3.19), this gives:

$$\frac{di}{ds} = \frac{di}{dt} \times \frac{dt}{ds} = (\beta si - \gamma i) \times \frac{1}{-\beta si}$$

$$\frac{di}{ds} = \frac{\beta si - \gamma i}{-\beta si} \qquad (3.20)$$

Simplifying Eqn.(3.20) gives the equivalent equation; $\frac{di}{ds} = -1 + \frac{\gamma}{\beta s}$. But the Reproduction Number by definition and according to our model is given as $R_0 = \frac{\beta}{\gamma}$ where $\rho = \frac{1}{\gamma}$ the average infectious period. Therefore, we have;

$$\frac{di}{ds} = -1 + \frac{1}{R_0 s} \qquad (3.21)$$

Integrating Eqn.(3.21) and simplifying gives; $log(S_\infty) = R_0(S_\infty - 1)$.

Thus, R_0 can be expressed as;

$$R_0 = \frac{log(S_\infty)}{(S_\infty - 1)} \qquad (3.22)$$

Threshold Phenomenon and R_0

Initial stages after $I(0) = 0$ infectives introduced into the population of $S(0) = 0$ susceptibles, epidemic can occur or invasion of disease can fade off. From (2) of Eqn.(3.19), we have; $\frac{di}{dt} = -\beta si - \gamma i = i(\beta s - \gamma)$.

If $S(0) < \frac{\gamma}{\beta} = \frac{1}{R_0}$, then we should expect $\frac{di}{dt} < 0$. The disease dies or fade off from the population. This is because susceptible must exceed a critical threshold condition for an epidemic to occur in the population by Kermack and McKendrick, 1927. That is, everyone in the population is initially assumed to be susceptible so that $S(0) = 1$ and $R_0 > 1$ for an epidemic.

Condition for Epidemic

Epidemic occurs if the number of infected individuals in the population increases.

Thus, $\frac{di}{dt} > 0$ $\Longrightarrow$ $\beta si - \gamma i > 0$, so that, $\frac{\beta si}{\gamma} > i$

At the outset of an epidemic, nearly everyone is susceptible. So we can say $s \approx 1$, hence we take $s = 1$, so that $\frac{\beta}{\gamma} = R_0 > 1$.

This gives the condition of epidemic situation, where the Basic Reproductive Number; $R_0 > 1$. Conversely if $R_0 < 1$, then there is no epidemic.

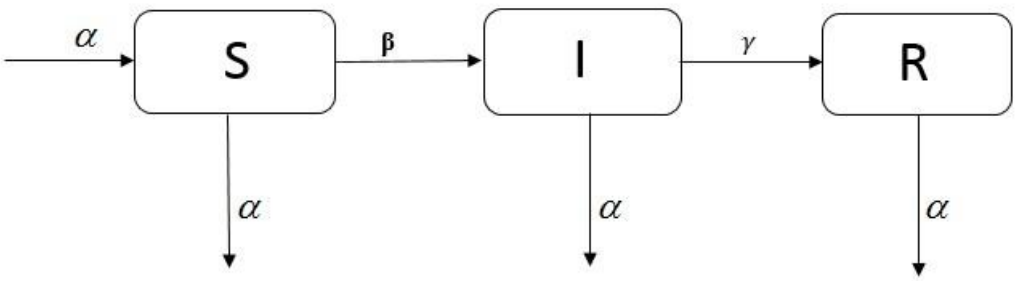
3.4.3 Deterministic SIR Model (With Demography)

In this case, we consider demographic turnover of the population. The three compartments remain the same in the formulation of this model. The assumption is that the individuals in any of the compartments suffer natural mortality in a given rate α. Historically, α is also crude birth rate which is an addition to the susceptible compartment to keep total population constant. Thus;

$$\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0 \tag{3.23}$$

The schematic diagram for the model in this instance is equivalent to an endemic model. Thus, our SIR model assumed the form below:

Figure 3.5: Flowchart of SIR Model with Demography



Flowchart of SIR Model of a Population with Demographic turn-over.

Parameters have the same meaning as in the SIR Model without Demographic turn-over above. The α denotes birth and death rate of the population. We assumed that birth rate is the same as death rate to keep the population fix.

The SIR Model is described by the system of differential equations below:

$$\frac{ds}{dt} = \alpha - \alpha s - \beta si \qquad s(0) = s_0 \geq 0 \qquad (1)$$
$$\frac{di}{dt} = \beta si - (\alpha+\gamma)i \qquad i(0) = i_0 \geq 0 \qquad (2) \qquad (3.24)$$
$$\frac{dr}{dt} = \gamma i - \alpha r \qquad r(0) = r_0 \geq 0 \qquad (3)$$

Consider (1) and (2) of Eqn.(3.24) since r does not affect s and i. This gives;

$$\frac{ds}{dt} = \alpha - \alpha s - \beta si \qquad s(0) = s_0 \geq 0 \qquad (1)$$
$$\frac{di}{dt} = \beta si - (\alpha+\gamma)i \qquad i(0) = i_0 \geq 0 \qquad (2) \qquad (3.25)$$

so that $r(t) = 1 - s(t) - i(t)$ according to Eqn.(3.17).

Assuming the entire population is susceptible, the Reproduction Number R_0 for the endemic model is given as; $R_0 = \frac{\beta}{\alpha+\gamma}$. This is so because now there are two possible reasons for leaving the infectious state; recovering and dying.

If $R_0 > 1$ and $\gamma < 1$, then $lim_{t\to\infty} I(t) = I_0 > 0$. There is an epidemic from the onset; $R_0 \times \frac{s(0)}{N} > 1$. If $R_0 \leq 1$, then $lim_{t\to\infty} I(t) = 0$, disease would eventually die off.

3.4.4 Equilibrium Points

In studying the Stability of the Model, we determined the equilibrium points of the differential equations governing the Model. These points are disease-free, where $i = 0$ and endemic, where $i \neq 0$.

In determining these points, Eqn.(3.25) was allowed to vanish, that is, $\frac{ds}{dt} = 0$ and $\frac{di}{dt} = 0$. This system of equations is solved simultaneously for s and i. Thus;

$$\alpha - \alpha s - \beta si = 0 \qquad (1)$$
$$\beta si - (\alpha+\gamma)i = 0 \qquad (2) \qquad (3.26)$$

From (2) of (3.26), we have $[\beta s - (\alpha + \gamma)]i = 0$.

Therefore, $i = 0$ and $\beta s - (\alpha + \gamma) = 0$ $\Longrightarrow i = 0$ and $s = \frac{\alpha+\gamma}{\beta}$. But $R_0 = \frac{\beta}{\alpha+\gamma}$.

Therefore, equation (2) of Eqn.(3.26) has solution $i = 0$ and $s = \frac{1}{R_0}$.

Substituting $i = 0$ and $s = \frac{1}{R_0}$ into (1) of Eqn.(3.26) produces the equilibrium points; $(s,i) = (1,0)$ and $(s,i) = [\frac{1}{R_0}, \frac{\alpha(R_0-1)}{\beta}]$ respectively. The equilibrium point $(s,i) = (1,0)$ is the disease-free equilibrium since $i = 0$, and the point $(s,i) = [\frac{1}{R_0}, \frac{\alpha(R_0-1)}{\beta}]$ is endemic equilibrium since $i \neq 0$.

3.4.5 Disease – Free Equilibrium

We determine the stability of the system at disease – free equilibrium by evaluating the Jacobian of the Eqn.(3.25) at the disease – free equilibrium point of $(s,i) = (1,0)$.

We re – write equation Eqn.(3.25) as shown below:

$X(s,i) = \alpha - \alpha s - \beta si$

$Y(s,i) = \beta si - (\alpha + \gamma)i$

Hence the Jacobian of X and Y is given as;

$$J(X,Y) = \begin{pmatrix} \frac{\partial X}{\partial s} & \frac{\partial X}{\partial i} \\ \frac{\partial Y}{\partial s} & \frac{\partial Y}{\partial i} \end{pmatrix} = \begin{pmatrix} -\alpha - \beta i & -\beta s \\ \beta i & \beta s - (\alpha + \gamma) \end{pmatrix}$$

Therefore, at equilibrium point $(s,i) = (1,0)$, we have;

$$J(s,i) = J(1,0) = \begin{pmatrix} -\alpha & -\beta \\ 0 & \beta - (\alpha + \gamma) \end{pmatrix}$$

If we let $A = \begin{pmatrix} -\alpha & -\beta \\ 0 & \beta - (\alpha + \gamma) \end{pmatrix}$, then using $|A - \lambda I|$ as in equation 3.10,

we have;

$$\begin{vmatrix} -\alpha - \lambda & -\beta \\ 0 & \beta - (\alpha + \gamma) - \lambda \end{vmatrix} = 0.$$

$$det(A - \lambda I) =$$

Since the Jacobian matrix is diagonal, the eigenvalues are given as:

$\lambda_1 = -\alpha$ and $\lambda_2 = \beta - (\alpha + \gamma)$.

Stability Analysis of Disease-free Equilibrium Point

- The equilibrium point is Asymptotically Stable means, both eigenvalues must be negative. $\lambda_1 = -\alpha < 0$, and $\lambda_2 = \beta - (\alpha + \gamma) < 0$, given that, $(\alpha + \gamma) > \beta$. The implication is that, a small population of infective introduced into the system would not cause a persistent infections, and that the population would return to disease-free state after some time.

  Consider $\lambda_2 = \beta - (\alpha + \gamma) < 0 \Longrightarrow \frac{\beta}{(\alpha+\gamma)} < 1$, that is, $R_0 < 1$ showing that the population is near disease - free equilibrium.

- Unstable disease free equilibrium point, also known as Unstable Saddle. In this situation, both eigenvalues must be of opposite signs. $\lambda_1 = -\alpha < 0$, a negative value; it means that $\lambda_2 = \beta - (\alpha+\gamma) > 0$, which is positive, given that $(\alpha + \gamma) < \beta$. The explanation is that an introduction of infective will result in a persistent infection. Hence, a disease-free population will result back to endemic population.

  We show the endemic situation by considering $\lambda_2 = \beta - (\alpha + \gamma) > 0 \Rightarrow$ $\frac{\beta}{(\alpha+\gamma)} > 1$, that is, $R_0 > 1$ which is endemic population as shown by the parameter R_0.

3.4.6 Endemic Equilibrium

We identified the equilibrium point $(s,i) = [\frac{1}{R_0}, \frac{\alpha(R_0-1)}{\beta}]$ to be the endemic equilibrium point. We evaluate the Jacobian Matrix given above at the endemic equilibrium point. This is given below:

$$J(s,i) = J[\tfrac{1}{R_0}, \tfrac{\alpha(R_0-1)}{\beta}] = \begin{pmatrix} -\alpha R_0 & \frac{-\beta}{R_0} \\ \alpha(R_0-1) & 0 \end{pmatrix} = B$$

Applying the characteristic equation according to Eqn.(3.10), we have;

$$det(B-\lambda I) = \begin{pmatrix} -\alpha R_0 - \lambda & \frac{-\beta}{R_0} \\ \alpha(R_0-1) & 0-\lambda \end{pmatrix} = \lambda^2 + (\alpha R_0)\lambda + \tfrac{\alpha\beta(R_0-1)}{R_0} = 0$$

Stability Analysis of Endemic Equilibrium

In the equation above, the eigenvalues values; λ_1 and λ_2 are negative, since the trace, $-\alpha R_0 < 0$, and the determinant, $\frac{\alpha\beta(R_0-1)}{R_0} > 0$, which means eigenvalues λ_1 and λ_2 are negative values. This satisfies that the endemic equilibrium is asymptotically stable (if $R_0 > 1$). The disease is always persistent in the population as long as $R_0 > 1$ without re – introduction of infective.

However, in the condition where $R_0 < 1$, it would become unstable endemic equilibrium. The implication is; the endemic situation is not feasible; and would result to disease – free equilibrium that is stable.

3.4.7 SIR Vaccination Model with R_v

Vaccination was introduced into the Susceptible(S) compartment to stimulate the group members' immune system; to develop adaptive permanent immunity against HBV infection. We used v to denote a portion of susceptible (μS) That goes to the removed(R) compartment directly. Parameter v is also the group to which vaccination

is given at the rate of μ. Parameters have the same meaning as in previous Models.

The SIR Vaccination Model is as below:

Flowchart of SIR Model of a Population with Vaccinated Segment.

The Vaccinated SIR Model is described by system of differential equations below:

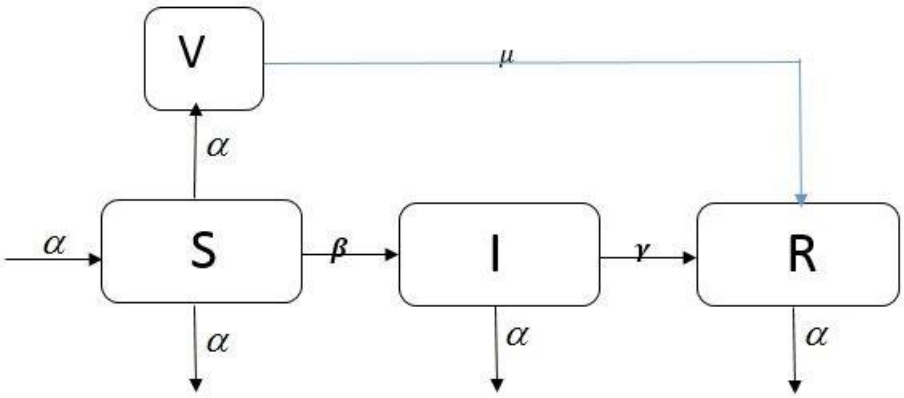
$$\frac{ds}{dt} = \alpha - \alpha\mu - \beta si - \alpha s \quad (1)$$

$$\frac{di}{dt} = \beta si - \gamma i - \alpha i \quad (2)$$

$$\frac{dv}{dt} = \alpha\mu - \alpha\nu \quad (3) \qquad (3.37)$$

$$\frac{dr}{dt} = \gamma i - \alpha r \quad (4)$$

Figure 3.6: Flowchart of SIR Vaccination Model



Equilibrium Points

We ignored (4) and consider (1), (2) and (3) of system of equations in Eqn.(3.37). The three equations are set to zero and solved simultaneously for s, i and v to determine the equilibrium points. Thus;

$$\alpha - \alpha\mu - \beta si - \alpha s = 0 \quad (1)$$

$$\beta si - \gamma i - \alpha i = 0 \quad (2) \qquad (3.38)$$

$$\alpha\mu - \alpha v = 0 \quad (3)$$

Two equilibrium points are identified:

1. The Disease-free Equilibrium Point; $(s,i,v) = (1-\mu, 0, \mu)$

2. The Endemic Equilibrium Point; $(s,i,\nu) = [\frac{\alpha+\gamma}{\beta}, \frac{\alpha[\beta(1-\mu)-\alpha-\gamma]}{\beta(\alpha+\gamma)}, \mu]$

Analysis of Equilibrium Point

- The point (s,i,ν) = $(1-\mu,0,\mu)$ is disease free for the fact that infection is non existence; i = 0 and $R_\nu < 1$.
- Conversely, the point $(s,i,\nu) = [\frac{\alpha+\gamma}{\beta}, \frac{\alpha[\beta(1-\mu)-\alpha-\gamma]}{\beta(\alpha+\gamma)}, \mu]$ is endemic because $i \neq 0$. We show that $R_\nu \geq 1$.

We solve for i in (1) and substitute into (2) of Eqn.(3.38) which produces;

$$s^2 - [(1-\mu) + \tfrac{\alpha+\gamma}{\beta}]s + (1-\mu)[\tfrac{\alpha+\gamma}{\beta}] = 0 \quad (3.39)$$

The discriminant of Eqn.(3.39) is given as;

$$\triangle = [(1-\mu) + \tfrac{\alpha+\gamma}{\beta}]^2 - 4[(1-\mu)(\tfrac{\alpha+\gamma}{\beta})]$$

However, for positive solution of Eqn.(3.39), $4 \geq 0$. Therefore, $[(1-\mu) + \frac{\alpha+\gamma}{\beta}]^2 \geq 0$, and $R_\nu \geq 1$, where $R_\nu = R_0(1-\mu)$; the Reproductive Number during vaccination.

Again, consider the fact $i > 0$ for endemic situation. This means that;

$i = \frac{\alpha[\beta(1-\mu)-\alpha-\gamma]}{\beta(\alpha+\gamma)} > 0$, that is, $\frac{\alpha\beta[(1-\mu)-\frac{\alpha+\gamma}{\beta}]}{\beta(\alpha+\gamma)} > 0$

$\implies \frac{\alpha\beta[(1-\mu)-\frac{1}{R_0}]}{\beta(\alpha+\gamma)} > 0 \implies R_0(1-\mu) > 1$, that is, $R_\nu > 1$ as required.

The vaccination has an impact on the existence of the two equilibrium points. This is because the susceptible (S) compartment is reduced by the vaccination rate μ. The Reproductive Number is given as $R_\nu = R_0(1-\mu)$ according to the SIR Vaccination Model, where R_0 is the Reproductive Number Endemic Model.

CHAPTER 4

ANALYSIS OF MODELS AND SIMULATIONS

4.1 INTRODUCTION

We focused on testing our models with data obtained. Parameter values were estimated from the data and fitted into the Models. The stability of the equilibrium points of these Models were then determined.

The Models were simulated to explore its behaviour pattern as we relate to the population of study.

Table 4.1: HBV Cases in the Sunyani Municipality(2010 - 2014)

Years	2000	2001	2002	2003	2004	2005	2006	2007
No. Cases	34	18	17	81	142	27	31	22
Years	2008	2009	2010	2011	2012	2013	2014	2015
No. Cases	171	204	191	145	211	351	355	-

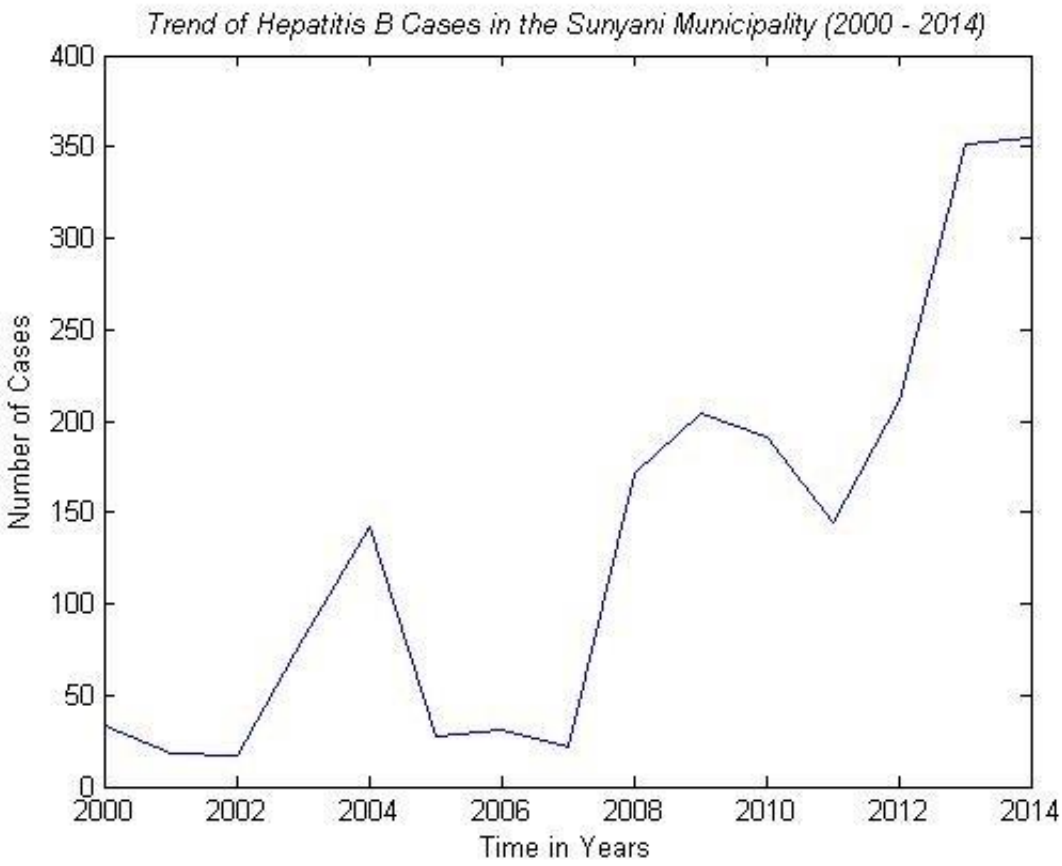
Source: Sunyani Municipal Hospital.

Table 4.2: Parameters and Values

Description	Parameters	Values
Birth Rate	α	0.085
Infectious Rate	β	0.182
Recovery Rate	γ	0.093
Vaccination Rate	μ	0.5

Source: Estimated from Data above.

Figure 4.1: Trend of HB Cases in Sunyani Municipality



4.2 POPULATION WITHOUT DEMOGRAPHY

The Reproductive Number of the population of Sunyani Municipality without demographic turn-over was given as; $R_0 = \frac{\beta}{\gamma}$. Hence, $R_0 = \frac{0.182}{0.093} = 1.957$.

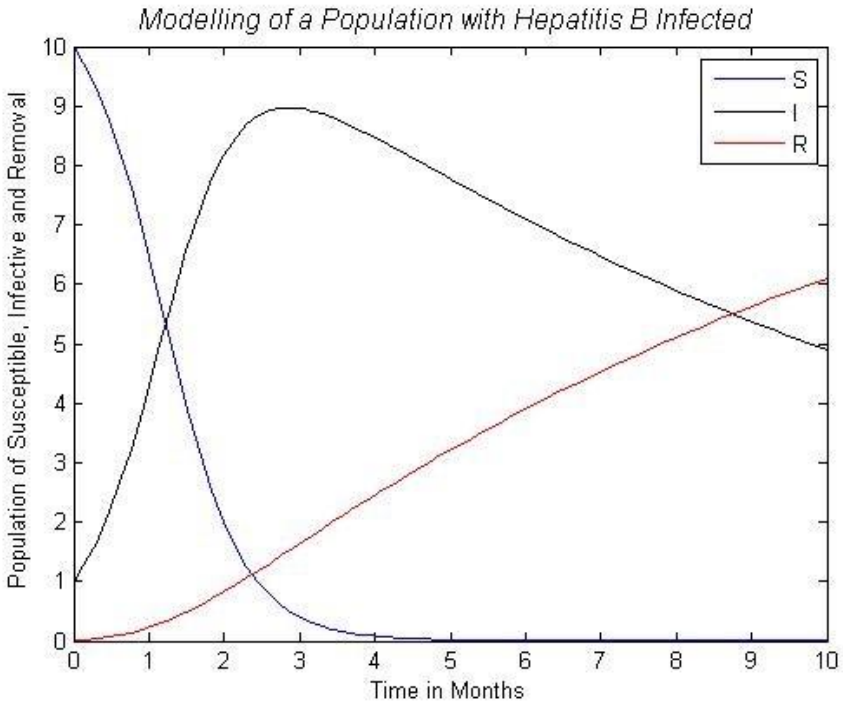
Sunyani Municipality of constant population without demography is Epidemic.

This is because Reproductive Number $R_0 = 1.957 > 1$. Averagely, one hepatitis B patient introduced into the population contacts/infects approximately 2 susceptible in the population of the Sunyani Municipality. That is, epidemic occurs when infectious rate (β) is greater than recovery rate (γ).

The equations of SIR Model without demography with parameter values are;

$\frac{ds}{dt} = -0.182si$ $\frac{di}{dt} = 0.182si - 0.093i$ $\frac{dr}{dt} = 0.093i.$

Figure 4.2: Epidemic Graph of Susceptible, Infective and Removal



In Figure 4.2, we model a population of 10 healthy people and one infective whiles we allowed time to run from 0 to 10 months. The graph depicts the behaviour of the population of Sunyani Municipality with parameter(β and γ) values. Notice how infective initially picks up steam and spreads quickly taking about 90% of the population. The susceptible population quickly drops to zero in the 5th week. Six out of a population of 11 people recovered. We modeled with $(s,i,r) = (10,1,0)$ given a situation of $(s,i,r) = (0,5,6)$ in the tenth month. The infectious/contact rate (β) contributed heavily to $R_0 = 1.957$; epidemic situation.

4.3 DETERMINISTIC MODEL FORMULATION

Model Equations were populated with parameter values to enable analyses.

4.3.1 Deterministic Model with Demography

Consider Eqn.3.25, we have;

$$\frac{ds}{dt} = \alpha - \alpha s - \beta si \quad (1)$$

$$\frac{di}{dt} = \beta si - (\alpha + \gamma) \quad (2) \qquad (4.1)$$

Substituting the parameter values from Table 4.1 above produces;

$$\frac{ds}{dt} = 0.085 - 0.085s - 0.182si \quad (1)$$

$$\frac{di}{dt} = 0.182si - (0.178)i \quad (2) \quad (4.2)$$

In endemic situation of the population, the Reproductive Number is given as; $R_0 = \frac{\beta}{\alpha+\gamma}$, that is, $R_0 = \frac{0.182}{(0.093+0.085)} = \frac{0.182}{0.178} = 1.022$

The result of $R_0 = 1.022$ shows the presence of the disease in the population. The value of R_0 is very close to one (1) indicating that the disease is not significantly fading out nor increasing. This is possible because infective compartment reduces through death (α) and recovery (γ) leaving the population to become endemic.

4.3.2 Equilibrium Points

Applying the equilibrium conditions, we allowed Eqn.4.2 to vanish while we solved simultaneously for the values of s and i. This produces;

$0.085 - 0.085s - 0.182si = 0$ (1)

$0.182si - (0.085 + 0.093)i = 0$ (2) (4.3)

From (2) of Eqn.(4.3), we have; $i = 0$ and $s = 0.978$.

Substitute $i = 0$ and $s = 0.978$ into (1) of Eqn.(4.3) produces the diseasefree equilibrium point $(s,i) = (1,0)$ and the endemic equilibrium point $(s,i) = (0.978,0.011)$.

4.3.3 Analysis of Equilibrium Points

We determine the stability of the two equilibrium points by evaluating the Jacobian of Eqn.4.2 at these two equilibrium points.

Re-write Eqn.(4.2) as shown below:

$X(s,i) = 0.085 - 0.085s - 0.182si$

$Y(s,i) = 0.182si - (0.178)i$

Hence the Jacobian matrix for X and Y is given by

$$J(X,Y) = \begin{bmatrix} -0.085 - 0.182i & -0.182s \\ 0.182s & 0.182s - 0.178 \end{bmatrix} \quad (4.4)$$

Disease-Free Equilibrium

We evaluate the Jacobian Matrix (4.4) at the disease - free equilibrium point of $(s,i) = (1,0)$.

$J(1,0) = \begin{bmatrix} -0.085 & -0.182 \\ 0 & 0.004 \end{bmatrix} = A$. The characteristic equation is;

$$det(A - \lambda I) = \begin{vmatrix} -0.085 - \lambda & -0.182 \\ 0 & 0.004 - \lambda \end{vmatrix} = \lambda^2 + 0.081 - 0.0034 = 0$$

Therefore, the eigenvalues are,

$\lambda_1 = -0.0405 + 0.00352i$ and $\lambda_2 = -0.0405 - 0.00352i$.

The complex conjugate eigenvalues indicated spiral disease - free equilibrium point. The stability is determined by the real parts.

Therefore, the equilibrium point $(s,i) = (1,0)$ is asymptotically stable. It is an indication that a small population of infective introduced into the population of Sunyani Municipality would not cause a persistent infections. The population would eventually return to disease-free state after some time.

Endemic Equilibrium

The equilibrium point $(s,i) = (0.978,0.011)$ is endemic because $i \, 6= 0$. We study its stability by using the Jacobian Matrix of Matrix(4.4) evaluated at the endemic equilibrium point. Therefore, we have;

$$J(0.978,0.011) = \begin{bmatrix} -0.0870 & -0.178 \\ 0.002 & 0.000004 \end{bmatrix} = B$$

The characteristic equation is given as;

$$det(B - \lambda I) = \begin{bmatrix} -0.0870 - \lambda & -0.178 \\ 0.002 & 0.000004 - \lambda \end{bmatrix}$$

$$\Longrightarrow \quad \lambda^2 + 8.7004 \times 10^{-2}\lambda - 3.563 \times 10^{-4} = 0$$

Therefore, eigenvalues are: $\lambda_1 = -4.309 \times 10^{-3}$ and $\lambda_2 = -8.2695 \times 10^{-2}$

The endemic equilibrium is also a stable equilibrium point due to the negative eigenvalues. The Hepatitis B disease is neither fading nor progressive, it is just present in the Municipality. The endemic situation of the population is also proven by the Reproductive Number $R_0 = 1.022 \, ' \, 1$.

4.4 SIR VACCINATION MODEL

The Reproductive Number of the Vaccination Model is $Rv = R_0(1-\mu)$. The R_0 is the Reproductive Number of the Endemic Model above. Thus $Rv = 0.511$.

The equations of the Vaccination Model with parameter values are given as;

$$\frac{ds}{dt} = 0.043 - 0.182si - 0.085s \quad (1)$$

$$\frac{di}{dt} = 0.182si - 0.178i \quad (2) \quad (4.11)$$

$$\frac{dv}{dt} = 0.043 - 0.085\nu \quad (3)$$

$$\frac{dr}{dt} = 0.093i - 0.085r \quad (4)$$

4.4.1 Equilibrium Points

We set the first three(3) equations to zero (0) whiles ignoring equation (4) and solve for s, i and ν.

Thus;

$0.043 - 0.182si - 0.085s = 0$ (1)

$0.182si - 0.178i = 0$ (2) (4.12)

$0.043 - 0.085\nu = 0$ (3)

There are two equilibrium points, these are:

1. The Disease-free Equilibrium Point $(s,i,\nu) = (0.506,0,0.50)$
2. The Endemic Equilibrium Point $(s,i,\nu) = (0.978,0.225,0.50)$

4.4.2 Analysis of Equilibrium Points

The effect of vaccination is easily seen on the existence of the two equilibrium points. Because in the SIR Vaccination Model, Susceptible was affected by the Vaccination parameter μ. That is, the susceptible compartment has been reduced by the vaccination rate (μ). The Infective has also reduced drastically leading to $R_\nu = 0.511 < 1$.

4.5 NUMERICAL ANALYSIS AND SIMULATION

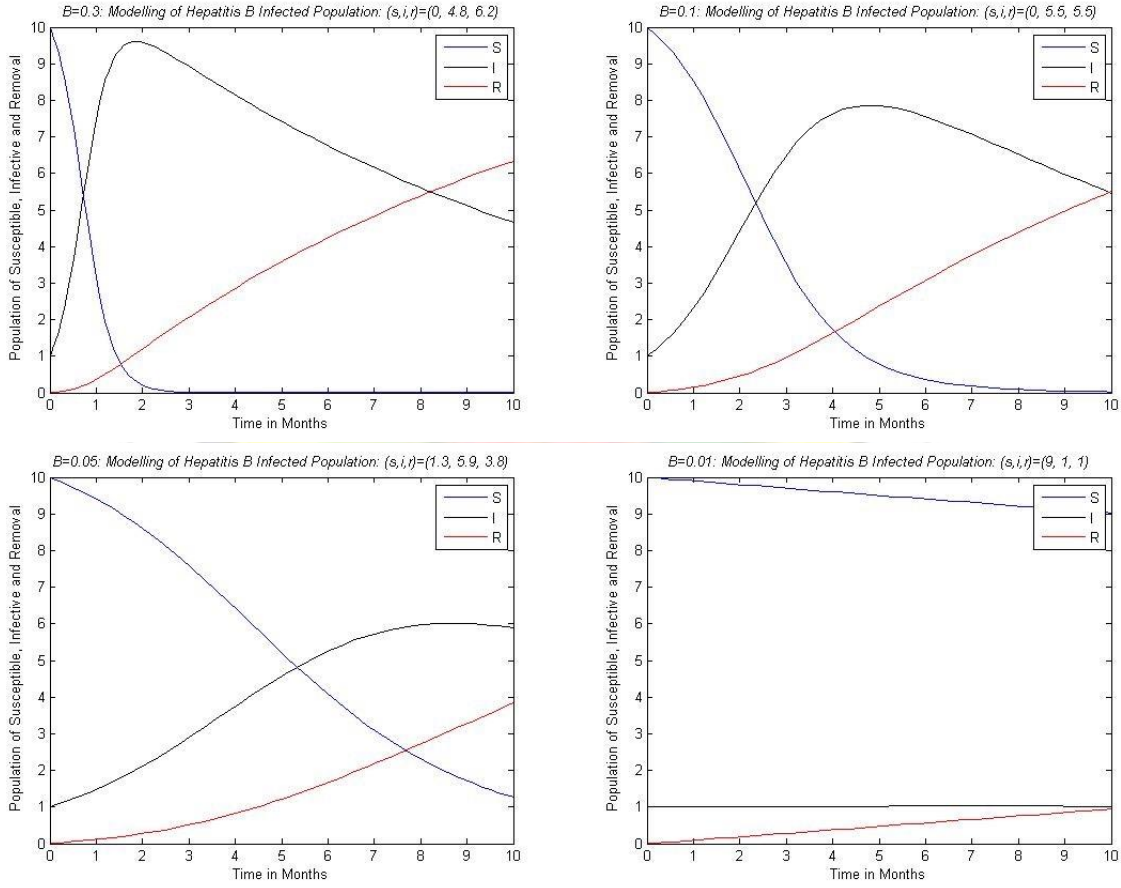
We simulate the three Models (Deterministic Model with and Without Demography, and the Vaccination Model) by considering numerical values of the parameters used

in this research work. We discuss the simulated equilibrium points in each case if necessary.

4.5.1 Simulation of Deterministic Model without Demography

In the Epidemic Model, a high infectious rate (β) reduces the Susceptible drastically whiles Infective goes high. We modeled with 10 Susceptible and an infective while time was allowed from 0 to 10 months. The correspondent Epidemic Equilibrium points are shown in each case on Figure 4.3 below. The conclusion is that the graphs provided a pictorial view of the population responses to changes in the infectious rate (β).

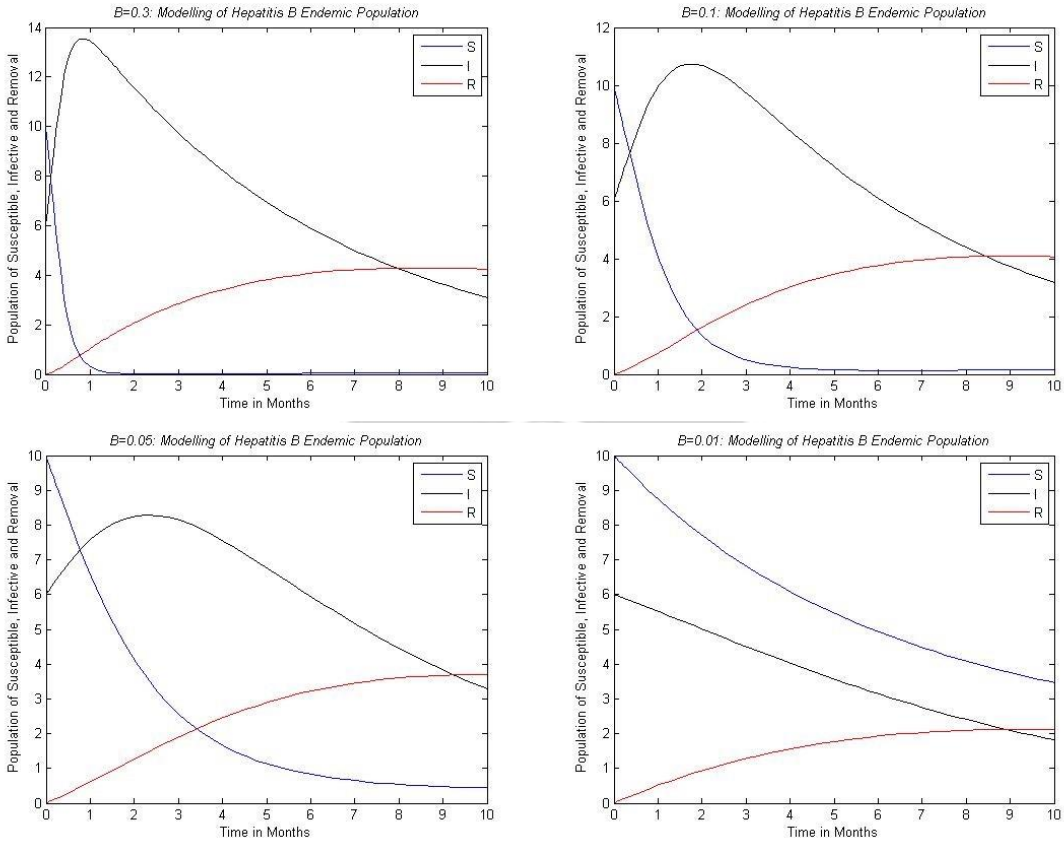
Figure 4.3: Simulation of Deterministic Model without Demography



4.5.2 Simulation of Deterministic Model with Demography

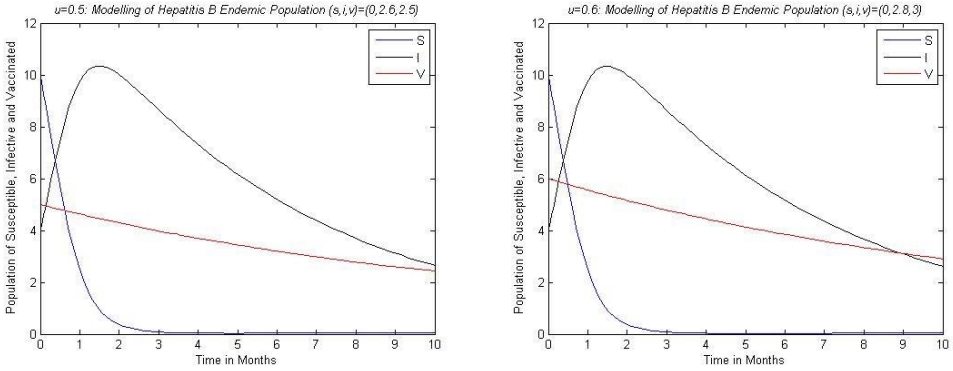
In the Endemic situation, more contacts within the population produces high infections. Notice how infective initially picks up steam and eventually reduces. This is shown in the two equilibrium points on the graphs in each case below.

Figure 4.4: Simulation of Deterministic Model with Demography



4.5.3 Simulation of Vaccination Model

Figure 4.5: Simulation of Vaccination Model



In the simulation of the Vaccination Model, we vary the value of μ (Vaccination rate). The higher value of μ decreases Infective and increases Vaccinated group.

CHAPTER 5

SUMMARY AND CONCLUSION

5.1 SUMMARY

The Deterministic Model without Demographic turn-over can be describe as Epidemic Model for the fact that the Reproductive Number $R_0 = 1.957 > 1$. The Epidemic graph in Figure 4.2 depicts the fact that 90% of the population was infected during epidemic. This was because of the high infectious rate (β). Whiles the rate of infection in the population was 0.182, the rate of recovery was as low as 0.093. The high infectious rate contributed to the value of the Reproductive Number (R_0). It is very important to implement control measures to reduce infection rate in the population whiles increasing the recovery rate.

In the Deterministic Model with Demography, the Reproductive Number is $R_0 = 1.022$. This was an indication of Endemic Population because R_0 ' 1. The Epidemic Population arises as a result of more infected people leaving the Infective group as compared to the Epidemic Model. The Reproductive Number in this case was contributed to by death rate (α) and recovery rate (γ).

Two equilibria were identified; Disease-free Equilibrium and Endemic Equilibrium. Both equilibria were stable based on Model analysis with data. Efforts should be made to maintain the equilibrium status of Disease-free whiles changing that of Endemic equilibrium. This is the work of Health Professional in the Municipality and other stakeholders in the sector.

The Vaccination Model's Reproductive Number is $R_v = 0.511 < 1$. The Reproductive Number in this case shows that the rate of infection is fading out. This is attributed to the impart of Vaccination in the Population. The simulated Vaccination Model indicates that a high Vaccination Rate (μ) turn to decrease Infective and increase the Vaccinated population. This must be encouraged to eradicate Hepatitis B disease in the Municipality.

5.2 CONCLUSION

The Deterministic Model with Demographic turn - over, Deterministic Model without Demographic turn-over and Vaccination Model were Models discussed. The effect of Hepatitis B infection on the population is largely influenced by the Reproductive Number (R_0). The Deterministic Model without Demographic turn-over is Epidemic Model since $R_0 \geq 1$ otherwise, there was no Epidemic situation. The $R_0 = 1$ indicates that the Deterministic Model with Demographic turn-over described an Endemic situation of the population.

A high infectious rate(β) leads to a high Reproductive Number. If the sum value of death(α) and recovery(γ) rates approaches the value of infectious rate(β), then Reproductive Number is likely to have the value one(1). This means that Epidemic and Endemic situation of the population can be avoided by keeping contact / infection rate (β) very low to avoid the HBV infections that leads to death sometimes.

The Reproductive Number(R_v) in the case Vaccination Model drastically changed ($R_v \leq 1$) implying the impart of Vaccination on the Population. The simulation of Vaccination Model confirmed Vaccination effect on the Infective population (I) which was reduced as a result of reduced infectious rate(β).

Thus, we conclude that infection rate(β) and the Reproductive Number(R_0) play a very important roles in occurrence of both Epidemic and Endemic situation of the population. This can be controlled by Vaccination.

Based on the data used during this research work, Hepatitis B Virus infections can be curbed and eradicated completely in the Sunyani Municipality. This is possible if the following suggestions are observed:

1. Infectious rate (β) must be kept below 1%.
2. The rate of Vaccination (μ) must be at least 60% of the Susceptible.
    - mass educating and sensitizing the populace is crucial in this fight against HBV infections.

<u>Further Studies</u>

We propose further studies particularly, a Mathematical Model that encompasses mechanisms of Acute-Chronic HBV infection.

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APPENDIX A

Matlab Codes for Modeling

Variables: s=x(1), i=x(2), r=x(3) and v=x(4)

Parameters: $\beta = 0.182$, $\gamma = 0.093$, $\alpha = 0.085$ and $\mu = 0.013$

1. Hepatitis B Model without Demographic turn over f =

$@(t,x)[-0.182 * x(1) * x(2);$

$0.182 * x(1) * x(2) - 0.093 * x(2);$

$0.093 * x(2)]$

$[t,xa] = ode45(f,[0\ 10],[10\ 1\ 0])$; plot(t,xa(:,1))

hold on

plot(t, xa(:,2), 'k')

plot(t, xa(:,3), 'r') hold

off

legend('S','I','R'); title('β = 0.182: (Modeling of Hepatitis B Infected Population)', 'FontSize',10) xlabel('Time in Months') ylabel('Population of Susceptible, Infective and Removal')

2. Hepatitis B Model with Demographic turn-over f =

$@(t,x)[0.085 - 0.085 * x(1) - 0.182 * x(1) * x(2);$

$0.182 * x(1) * x(2) - 0.178 * x(2);$

$0.093 * x(2) - 0.085 * x(3)]$

$[t,xa] = ode45(f,[0\ 10],[10\ 1\ 0]);$

plot(t,xa(:,1))

hold on

plot(t, xa(:,2), 'k')

plot(t, xa(:,3), 'r') hold

off

legend('S','I','R'); title('β = 0.182: (Modeling of Hepatitis B Infected Population)', 'FontSize',10) xlabel('Time in Months') ylabel('Population of Susceptible, Infective and Removal')

3. Hepatitis B Vaccination Model.

$f = @(t,x)[0.083 - 0.182 * x(1) * x(2) - 0.085 * x(2);$

$0.182 * x(1) * x(2) - 0.178 * x(2);$

$0.001 - 0.085 * x(4)]$

$[t,xa] = ode45(f,[0\ 10],[10\ 1\ 0]);$ plot(t,xa(:,1))

hold on

plot(t, xa(:,2), 'k')

plot(t, xa(:,3), 'r') hold

off

legend('S','I','R'); title('$\beta = 0.182$: (Modeling of Hepatitis B Infected Population)', 'FontSize',10) xlabel('Time in Months') ylabel('Population of Susceptible, Infective and Vaccinated')