#### DECLARATION

I hereby declare that this thesis titled: A mathematical model for the transmission dynamics and control of hepatitis B virus, is a collection of my original research work and it has not been presented for any other qualification anywhere. Information from other sources (published or unpublished) has been duly acknowledged.

-----

ABDULRAHMAN, Sirajo PhD/SSSE/2008/246 FEDERAL UNIVERSITY OF TECHNOLOGY MINNA, NIGERIA SIGNATURE & DATE

#### CERTIFICATION

The thesis titled: A mathematical model for the transmission dynamics and control of hepatitis B virus, by ABDULRAHMAN, Sirajo (PhD/SSSE/2008/246) meets the regulations governing the award of the degree of Doctor of Philosophy (PhD) of Federal University of Technology, Minna and it is approved for its contribution to scientific knowledge and literary presentation.

PROF. N. I. AKINWANDE	
MAJOR SUPERVISOR	Signature & Date
PROF. O. B. AWOJOYOGBE	
CO-SUPERVISOR	Signature & Date
DR. U. Y. ABUBAKAR	
CO-SUPERVISOR	Signature & Date
PROF. Y. M. AIYESIMI	
HEAD OF DEPARTMENT	Signature & Date
PROF. G. N. NSOFOR	
DEAN OF SCHOOL OF NATURAL AND APPLIED SCIENCES	Signature & Date
PROF. (Mrs.) S. N. ZUBAIRU	
DEAN OF POSTGRADUATE SCHOOL	Signature & Date

#### **DEDICATION**

This thesis is dedicated to the memory of my Guardians: Late Bima of Enagi Alhaji Abdulrahman Hassan Enagi and Hajiya Fatima Kakajummai. May the Almighty Allah forgive and reward them with eternal bliss.

#### ACKNOWLEDGEMENTS

I wish to express my sincere and profound gratitude to my teacher, mentor, advisor and major supervisor Prof. Ninuola Ifeoluwa Akinwande and other members of my supervisory team; Prof. O. B. Awojoyogbe and Dr. U. Y. Abubakar. Their patience, kindness, tolerance, advice, guidance, encouragement, constant and constructive criticisms, corrections and suggestions led to the final form of this work.

I am indeed grateful to the Head of department Prof. Y. M. Aiyesimi and Prof. K. R. Adeboye. Their kindness and tolerance towards me since 1994 during my PGD Computer Science program to date really gives me full momentum in undertaking this research work. My special gratitude goes to the Postgraduate coordinator Dr. A. Ndanusa, Dr. M. Jiya, Dr. R. Olayiwola, Dr. A. I. Enagi, Mr. O. R. Jimoh, Mr. S. Abubakar, Mr. A. Yusuf and Mr. U. M. Sanda for their constant encouragement throughout the period of this research. The supports of all the academic and non-academic staff of the department are well appreciated.

I wish to acknowledge the knowledge acquired from late Professor C. O. A. Sowunmi, late Professor R. O. Ayeni, Professor A. R. Kimbir, Professor G. C. E. Mbah, Professor M. O. Ibrahim, Professor A. B. Gumel, Professor F. Benyah, Professor C. Castillo-Chavez and Professor H. W. Hethcote. Their writings have indeed helped not only me but every mathematical epidemiologist.

I am grateful to my family, parents, friends, brothers and sisters for their prayers, encouragement and support throughout the period of this study.

Above all, I thank Almighty Allah, the Most Gracious and the Most Merciful.

#### ABSTRACT

In the work, we developed and analyzed a deterministic model for the transmission dynamics and control of hepatitis B virus (HBV) in a population with vital dynamics (birth and death removal rates are not equal), incorporating vertical transmission, sexual maturity and the effects of condom usage and vaccination coverage which are influenced by public enlightenment campaign. We obtained the effective basic reproduction number  $R_c$  which can be used to control the transmission of the disease and hence, established the conditions for local and global stability of the disease-free equilibrium. Bifurcation analysis was carried out using centre manifold theory which revealed a forward bifurcation for the model. Furthermore, sensitivity analysis carried out shows that birth and death removal rates, HBV sexual transmission probability per contact rate and average total sexual contacts rate are highly sensitive parameters that affect the transmission dynamics of HBV in any population. This means that vaccination, condom usage, reduced-average total sexual contacts and birth rates are good strategies that can lead to controlling HBV. Numerical simulations validated the analytical results and further revealed that HBV vaccination of new births only at any coverage rate cannot bring about disease control. But vaccination of sexually active susceptible individuals at about 30% coverage rate can put the disease under control. Two feasible solutions to HBV infection problem in Nigeria were obtained as the present control strategy is not effective enough to even reduce the disease morbidity.

# TABLE OF CONTENTS

Content	Page
Cover Page	
Title Page	i
Declaration	ii
Certification	iii
Dedication	iv
Acknowledgements	v
Abstract	vi
Table of Contents	vii
List of Tables	x
List of Figures	xi
Glossary of Abbreviations	xiii
Glossary of Symbols	xiv

## **CHAPTER ONE**

1.0	INTRODUCTION	1
1.1	Background of Study	1
1.2	Statement of the Problem	4
1.3	Motivation for Study	5
1.4	Justification of Study	5
1.5	Scope and Limitations of Study	6
1.6	Definition of Terms	6
1.7	Aim and Objectives	7

## **CHAPTER TWO**

2.0	LITERATURE REVIEW	8
2.1	Mathematical Models of Hepatitis B Virus Transmission and Control	8
СНА	PTER THREE	
3.0	MATERIALS AND METHODS	16
3.1	Model Development	16
3.2	Solution of the Model Equations	25
3.3	Existence of Equilibria	29
3.4	Linearization	35
3.5	Disease-free Equilibrium State	37
3.6	Endemic Equilibrium State	47
СНА	PTER FOUR	
4.0	<b>RESULTS AND DISCUSSION</b>	61
4.1	Variables and Population-dependent Parameters Values Estimation	61
4.2	Population-independent Parameters Value Estimation	71
4.3	Relative Importance of Each Parameter in the Transmission and Prevalence of the Disease through Sensitivity Analysis	77
4.4	Validation and Extension of Analytical Results by Numerical Method	83
4.5	Effects of Condom Usage and Vaccination Coverage on the Control of Hepatitis B Virus Transmission	86
4.6	Mathematical Solutions to Hepatitis B Virus Transmission in Nigeria	88

## **CHAPTER FIVE**

5.0	CONCL	USION AND RECOMMENDATIONS	94
5.1	Conclusi	on	94
5.2	Recommendations		96
REFE	CRENCES	5	97
APPE	NDIX A	Castillo-Chavez <i>et al.</i> (2002) Theorem for Global Stability of Disease-free Equilibrium	103
APPE	NDIX B	Castillo-Chavez and Song (2004) Bifurcation Theorem	104
APPE	CNDIX C	Computation of Basic Reproduction Number, $R_0$ Using Maple Software	106
APPE	NDIX D	Computation of Sensitivity Analysis of $R_0$ with Respect to Some Parameter Values Using Maple Software	107

# LIST OF TABLES

Table		Page
4.1	Total Number of Vaccinated (Nigerians) New Births from 2004 to	
	2010	62
4.2	Okoye et al. (2006) Sero-epidemic Survey of Hepatitis B in Nigeria	63
4.3	Re-evaluation of Okoye et al. (2006) Survey to Present Time (2010)	65
4.4	Hypothetical and Nigerian (year 2010) Model Variables and Population-dependent Parameters Values	71
4.5	Values for Population-independent Parameters of the Model	77
4.6	Sensitivity Indices of $R_0$ to Model Parameters. The Parameters are Ordered from the Most Sensitivity to the Least	79

# LIST OF FIGURES

Figure		Page
3.1	Schematic Diagram of HBV Transmission and Control Model	16
4.1	Effect of Average Number of Sexual Partner(s), <i>y</i> on Basic Reproduction Number, $R_0$ . Parameter Values used are as in Table 4.4 and Table 4.5 with $b = 0.027$ , $\mu = 0.021$ and $p = 0.06$	80
4.2	Effect of Per Capital Birth Rate, <i>b</i> and Natural Death Rate $\mu$ on Basic Reproduction Number. Parameter Values used are as in Table 4.5 with $c = 20, p = 0.06, b = 0.027$ (for $\mu$ ) and $\mu = 0.016$ (for <i>b</i> )	81
4.3	Total Number of Infected Individuals with Different Initial Variables Conditions: $I(0) = 100$ and $I(0) = 1000$ . Control Parameters used are as in Table 4.4 and Table 4.5 with $\tau_b = \tau_U = \tau_F = \tau_C = 0.01$ , $b = 0.048$ , $\mu = 0.021$ , $\rho = 0.06$ and $c = 40$ which gives $R_c = 8.979$	84
4.4	Total Number of Infected Individuals with Different Initial Variables Conditions: $I(0) = 100$ and $I(0) = 1000$ . Control Parameters used are as in Table 4.4 and Table 4.5 with $\tau_b = \tau_U = \tau_F = \tau_C = 0.2$ , $b = 0.027$ , $\mu = 0.021$ , $\rho = 0.06$ and $c = 20$ which gives $R_c = 0.520$	85
4.5	Comparison of the Effective Basic Reproduction Number of 6 Different Control Strategy Levels. Parameter Values used are as in Table 4.5 with $b = 0.027$ , $\mu = 0.016$ , $c = 20$ and $\rho = 0.06$	87
4.6	Comparison between the Effects of Present Nigerian Control Strategy, Two Suggested Feasible Solutions and Absence of any Intervention on Total Number of Chronic Infections	89
4.7	Comparison between the Effects of Present Nigerian Control Strategy, Two Suggested Feasible Solutions and Absence of any Intervention on Total Mortality due to Acute (Fulminant) HBV Infection	90
4.8	Comparison between the Effects of Present Nigerian Control Strategy, Two Feasible Solutions and Absence of any Intervention on Mortality Due to Chronic HBV Infection	91
4.9	Comparison between the Effects of Low and High Immunizations of New Births only and Immunization of Sexually Active Susceptible Individuals,	

 $S_F$  only on Morbidity of Chronically Infected Individuals under Fifteen (15) Years of Age,  $C_U$ 

92

4.10 Comparison between the Effects of Low and High Immunizations of new Births only and Immunizations of Sexually Active Susceptible Individuals only on Morbidity of Chronically Infected Individuals at or above Fifteen (15) Years of Age,  $C_F$  93

# **GLOSSARY OF ABBREVIATIONS**

Anti-HBs	Hepatitis B surface antibody
CDC	Centre for Disease Control
СНВ	Chronic Hepatitis B
CIA	Central Intelligence Agency
EASL	European Association for the Study of the Liver
GAVI	Global Alliance for Vaccines and Immunization
HBcAg	Hepatitis B core Antigen
HBeAg	Hepatitis B e antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
НСС	Hepatocellular Carcinoma
IDU	Injecting Drug Users
SA	Sensitivity Analysis
SOGHIN	Society for Gastroenterology and Hepatology in Nigeria
UNICEF	United Nations Children's Fund
WHO	World Health Organization

## **GLOSSARY OF SYMBOLS**

$S_{U}(t)$	Susceptible individuals under fifteen (15) years of age at time $t$
$S_F(t)$	Susceptible individuals at or above fifteen (15) years of age at time $t$
V(t)	Vaccinated individuals at time t
$A_{U}(t)$	Acutely infected individuals under fifteen (15) years of age at time $t$
$A_F(t)$	Acutely infected individuals at or above fifteen (15) years of age at time $t$
$C_{U}(t)$	Chronically infected individuals under fifteen (15) years of age at time $t$
$C_F(t)$	Chronically infected individuals at or above fifteen (15) years of age at time $t$
R(t)	Removed individuals due to recovery from infection at time $t$
b	Natural birth rate of humans
μ	Death removal rate of humans
$\delta_{\scriptscriptstyle A}$	HBV-induced death rate of $A_U$ and $A_F$
$\delta_c$	HBV-induced death rate of $C_F$
x	Prevalence rate of HBV in the population
ξ	Average number of sexual contacts per year
у	Average number of sexual partners per year
С	Average total sexual contacts and thus, $c = \xi y$
р	HBV-Sexual transmission probability per contact rate and therefore $pc$ is the effective sexual contact rate in the absence of control measure (rate that leads
	to infection in the absence of any control measure)
η	Modification parameter associated with reduced sexual transmission rate by chronic individuals
ε	Condom efficacy

- $\varepsilon_c$  Condom efficacy
- $\tau_c$  Condom usage rate which is enhanced by public enlightenment campaign and

therefore  $\varepsilon_c \tau_c$  is the effective condom usage rate

- $\varepsilon_{\rho}$  Vaccine efficacy
- $\tau_b$  Vaccination coverage rate at birth which is enhanced by public enlightenment campaign and therefore  $\rho_b = \varepsilon_\rho \tau_b$  is the effective immunization rate at birth
- $\tau_U$  Vaccination coverage rate not at birth for  $S_U$  which is enhanced by public enlightenment campaign and therefore  $\rho_U = \varepsilon_{\rho} \tau_U$  is the effective immunization rate for  $S_U$  but not at birth
- $\tau_F$  Vaccination coverage rate for  $S_F$  which is enhanced by public enlightenment campaign and therefore  $\rho_F = \varepsilon_\rho \tau_F$  is the effective immunization rate for  $S_F$
- $\omega$  Loss (waning) rate of vaccination immunity
- $\theta$  Proportion of HBV-positive birth
- $\phi$  Modification parameter associated with reduced HBV-positive birth by  $C_F$
- $\sigma_s$  Rate of moving from  $S_U$  to  $S_F$
- $\sigma_A$  Rate of moving from acutely infected classes to chronically infected / removed classes
- $\sigma_{c}$  Rate of moving from  $C_{U}$  to  $C_{F}$
- $\varphi_U$  Proportion of  $A_U$  which progresses to  $C_U$ , while  $(1 \varphi_U)$  is the proportion removed and therefore  $\gamma_U = \sigma_A (1 \varphi_U)$  is the recovery rate from  $A_U$  to R
- $\varphi_F$  Proportion of  $A_F$  which progresses to  $C_F$ , while  $(1 \varphi_F)$  is the proportion removed and therefore  $\gamma_F = \sigma_A (1 \varphi_F)$  is the recovery rate from  $A_F$  to R
- $\gamma_c$  Rate of recovery from  $C_F$  to R

$$b_{A} = b\theta (1 - \varepsilon_{\rho}\tau_{b})$$

$$b_{C} = b\theta \phi (1 - \varepsilon_{\rho}\tau_{b})$$

$$\alpha_{A} = pc(1 - \varepsilon_{c}\tau_{c})$$

$$\alpha_{C} = pc\eta (1 - \varepsilon_{c}\tau_{c})$$

$$K_{1} = (\sigma_{S} + \rho_{U} + \mu)$$