Stochastic analysis of AIDS Epidemiology

by

Moremi Morire OreOluwapo Labeodan

Submitted in partial fulfilment of the requirements for the degree

Doctor of Philosophy

in the Faculty of Natural and Agricultural Sciences

University of Pretoria

Pretoria

May 2009

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

DECLARATION

I declare that the thesis that I hereby submit for the degree Doctor of Philosophy at the University of Pretoria is my own work and has not previously been submitted by me for degree purposes at any other university or institution.

---------- ----------

Date

ACKNOWLEDGEMENT

God Almighty, the author of all wisdom and the source of all creations: Thank you. To you be all honour and obeisance.

Professor V. S. S. Yadavalli: A big thank you for your unflinching patient support, invaluable advice and continual supervision throughout the course of this work. You indeed made me have a continual thirst for research into HIV and AIDS.

Department of Statistics Staff: Thank you for your support especially the H.O.D in person of Professor N. A. S. Crowther, Mrs P Britz, Dr. R. A. Kasonga, Mrs E. M. Basson and Mrs A. D. Corbett.

Oluseun: My loving husband, you have been a strong pillar and support. Thank you. At last the victory is ours.

Dad: Thank you for believing in me and thus investing in my future always.

Siblings and their spouses: Thank you for all the support, care, words of encouragement and prayers.

Parents-In-law: Thank you.

Ubogus: What can I say? … Thank you.

Family and Friends: Thank you.

DEDICATION

This thesis is dedicated to the loving memories of my:

Mother

Dr. (Mrs.) Oluwatosin Aduke Akin – Ojo

Paternal Grandmother

Mrs. Rachel Omolu Ojo

Maternal Grandfather

Chief Isaac Adeniyi Oni

Maternal Grandmother

Mrs. Comfort Taiwo Kolapo

SUMMARY

In this thesis, some issues about the human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) have been addressed by concentrating on the stochastic modelling of the dynamics of the viruses. The aim of this thesis is to determine parameters such as the mean number of free HIV, infectious free HIV and non-infectious free HIV which are essential in determining incubation period of the virus, the disease progression of an infected individual and the efficacy of the treatment used. This thesis comprises of six chapters.

The first two chapters are introductory to the viruses and reasons why HIV-1 is given priority over HIV-2 are given. The pathogenesis of the virus is addressed. This is because knowledge of the pathogenesis and strains of the virus has become essential in the study of HIV in vivo dynamics which is still paving ways into extensive research of the ways to contain the disease better.

In chapter three the distribution functions of the HIV incubation period and seroconversion time are determined via stochastic models by building on previous work of Lui et al. (1988) and Medley et al. (1988). Also AIDS incidence projection was done using the Back-calculation method.

Chapter four deals with the formulation of stochastic model of the dynamics of HIV in an infected individual. Two stochastic models are proposed and analysed for the dynamics of the viral load in a HIV infected person and the multiplication process of the virions inside an infected T4 cell. Also a numerical illustration of the stochastic models derived is given.

In chapter five, the T4 cell count which is considered one of the markers of disease progression in HIV infected individual is examined. WHO has recently advocated that countries encourage HIV infected individuals to commence antiretroviral treatments once their T4 cell count is 350 cells per ml of blood. This is because when the T4 cell count is low, the T4 cells are unable to mount an effective immune response against antigens (and any such foreign matters in the body) and consequently, the individual becomes susceptible to opportunistic infections and lymphomas. We developed a stochastic catastrophe model to obtain the mean, variance and covariance of the uninfected, infected and lysed T4 cells; also the amount of toxin produced in a HIV infected person from the time of infection to the present time is derived. A numerical illustration of the correlation structure between uninfected and infected T4 cells, and infected and lysed T4 cells is portrayed.

Antiretrioviral treatments were introduced while we await a cure. Treatment with single drug failed due to the fact that HIV evolved rapidly because of its high replication rate. Thus drug resistance to single therapeutic treatment in HIV infected individuals has promoted research into combined treatments. In chapter six a stochastic model under combined therapeutic treatment is derived. Mean numbers of free HIV, infectious free HIV and non-infectious free HIV are obtained. Variance and co-variance structures of our parameters were obtained unlike in previous work of Perelson et al. (1996), Tan and Xiang (1999).

TABLE OF CONTENT

CHAPTER THREE: A STOCHASTIC POINT PROCESS MODEL OF THE INCUBATION PERIOD OF A HIV INFECTED INDIVIDUAL

CHAPTER FOUR: STOCHASTIC MODEL OF THE GROWTH OF HIV IN AN INFECTED INDIVIDUAL

CHAPTER FIVE: THE T4 CELL COUNT AS A MARKER OF HIV PROGRESSION IN THE ABSENCE OF ANY MECHANISM

CHAPTER SIX: A STOCHASTIC MODEL OF THE DYNAMICS OF HIV UNDER A COMBINATION THERAPEUTIC INTERVENTION

TABLES

FIGURES