MATHEMATICAL MODEL FOR COINFECTION OF HIV/AIDS AND KAPOSI'S SARCOMA WITH TREATMENT

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I56/CE/25298/2013

A Research Project Submitted in Partial Fulfillment of the Requirements for the Award of the Degree of Master of Science in Applied Mathematics in the School of Pure and Applied Sciences of Kenyatta University

APRIL 2023

DECLARATION

I Joy Teng'an Juma declare that this project is my own work and has not been submitted to any University in part or whole for a degree award.

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Approval by Supervisors

This project has been submitted for examination to the School of Pure and Applied Sciences with my approval as the University Supervisor.

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DEDICATION

I dedicate this work to my husband Godfrey Ochieng and our two sons Max Odhiambo and Rene Ochieng.

ACKNOWLEDGMENT

Thanks be to God for strengthening me all through the period of research. His grace and mercy has been sufficient to me. I thank my supervisor Dr. Chepkwony for his encouragement, supervision and professional guidance on the project. Special thanks goes to the members of mathematics department Kenyatta University and all the lecturers who offered guidance on matters of research. Gratitude is extended to Dr. Kwach and Dr. Samuel Oke for their support towards project completion. Acknowledgement is extended to Mr. Godfrey Furechi and Mrs. Gentrix Khisa for their great support and inspiritment throughtout my study. I wish to thank my parents Mr. Wilfred Juma and Mrs. Grace Juma for their continuous prayers and encouragement not forgetting my siblings for their support and understanding.

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ABBREVIATIONS AND NOMENCLATURE

Abbreviations

HIV	Human immunodeficiency virus.
AIDS	Acquired immune deficiency syndrome.
KS	Kaposi's sarcoma
HHV-8	Human herpes virus 8
AIDS-KS	AIDS-related Kaposi's sarcoma
KSHV	Kaposi's sarcoma-associated herpes virus
ART	Antiretroviral therapy.
RT	Reverse transcriptase inhibitor.
PIs	Protease inhibitors
HAART	Highly active antiretroviral therapies.
NNRTIs	Non-nucleoside reverse transcriptase inhibitors
NRTIs	Nucleoside or nucleoside reverse transcriptase inhibitors
PrEP	Post-exposure prophylaxis
CD4+/T cell	White blood cell in charge of body immunity.
TB	Tuberculosis
DFE	Disease free equilibrium
NGM	Next generation matrix
$\mathcal{R}$	Basic reproduction number

Nomenclature

$S(t)$	Susceptible individuals to both HIV and Kaposi's sarcoma at time, t.
$H(t)$	HIV infected individuals at any time, t.
$K(t)$	KS individuals infected at time, t.
$I(t)$	HIV and KS co-infected Individuals at time, t.
$T(t)$	Total sum of HIV, KS and co-infection treatment at any time, t.
$A(t)$	Number of AIDS patients at time, t.
$N(t)$	Total human population at time, t.

Greek Symbols

λ	recruitment rate into the susceptible population
α_1	infection rate of S(t) compartment
α_2	rate of infection of susceptible individuals with Kaposi's sarcoma
ϕ	probability of coinfection of susceptible individuals with HIV and KS
b	natural recovery rate for KS infectives
μ	per capita natural death rate.
θ	proportion of KS infective who recovered after treatment.
δ	treatment rate,
α_3	contact infection rate of HIV infected individuals with KS
α_4	contact infection rate of KS infected individuals with HIV
γ	Kaposi sarcoma induced mortality rate
ρ	AIDS induced mortality rate
β_1	rate at which H(t) compartment go for treatment
β_2	rate at which K(t) compartment go for treatment
β_3	progression rate of coinfected HIV and KS for treatment
η	proportion of HIV infected individuals receiving treatment

ABSTRACT

HIV destroys T-cells in order to target the body's defence mechanism. Without treatment HIV infection advances in stages causing destruction and reduction in T-cells thus, rendering the body incapable of fighting other infections such as respiratory infections, sexually transmitted diseases and some cancers. Kaposi's sarcoma is the cancer that allows tumour to grow in an HIV-patient and its presence in a patient is an indication that HIV has fully developed to AIDS in the patient. AIDS-related Kaposi's sarcoma (AIDS-KS) is still one of the most common malignancies in Kenya and sub-Saharan Africa and is associated with high morbidity and mortality. Researches have indicated that AIDS-associated KS was on the rise in sub-Saharan Africa until the introduction of ART. It is of great significance to comprehend the impact of ART used on HIV/AIDS and the coinfection of HIV/AIDS and AIDS-related Kaposi's sarcoma. Mathematical models have been proven valuable to give a decisive quantitative information about the dynamics and pathogenesis of HIV, responses of the immunity to anti-retroviral treatment and to the study of the coinfection of HIV/AIDS and other opportunistic infections like Malaria, TB, Pneumonia and Hepatitis however the coinfection of HIV/AIDS and AIDS-related Kaposi's sarcoma has not been considered much incorporating the aspect of treatment. In this study, a mathematical model for the coinfection of HIV/AIDS and KS with treatment is developed and analysed to explore the effect of usage of ART on HIV/AIDS and the coinfection of HIV/AIDS and Kaposi's sarcoma. The model solution is explored for positivity and boundedness. The next generation matrix is used to derive the basic reproduction number of the model, while the disease free equilibrium point is determined for stability where it was verified that the infection-free equilibrium E_0 is locally asymptotically stable whenever $R_0^H < 1$ and $R_0^K < 1$. KS and HIV infection will go to extinction if the reproduction number is $<$ l and persist in the population if it is > 1. Numerical simulations is used to illustrate that by providing treatment to the HIV and the co-infected population immune system is strengthened and thus progression rate to AIDS is reduced.

Chapter 1

INTRODUCTION

1.1 BACKGROUND INFORMATION

The CD4 Lymphocyte cells, also called the T cells, are white cells that protect human against any external infection and are in abundance among the white blood cells. They are transported from the bone marrow to areas of the body under attack to fight the incoming disease, illness or infection. HIV is a virus that aims at destroying the T cells. HIV infection, as stated by Wang and Li (2006), gradually eradicate the T cells and eventually exposing the host to subsequent infections. These opportunistic infections include respiratory infections such as tuberculosis, pneumonia and STDs such as syphilis, gonorrhoea among others (Kimulu *et al.*, 2022a; Kimulu *et al.*, 2022b).

HIV infection advances in three stages. The stage 1 of HIV infection is the Acute HIV infection, which is experienced in less than four weeks of infection. During this time, the patient has symptoms like flu, fever and/or headache. HIV replicates speedily and transmits throughout the body destroying the soldier T cells. Introducing ART at this early stage usually prove very beneficial to the patient's health. The next stage is the chronic (or asymptomatic or clinical latency) HIV infection, where the virus rate of replication is very low. At this stage, the symptoms are subdued and the patient may seem very healthy while the virus continues to destroy the remaining T cells. Without treatment, the third stage is reached. This is the fully developed AIDS, a situation where the body immune system has been utterly destroyed beyond repairs. At this stage, the body immune system cannot fight incoming diseases or infections. It is at this stage that the cancer in the form of KS prevail.

People with AIDS easily transmit HIV to other human through the exchange of body fluid (Sierra *et al*., 2005).

In a clinical setting, the number of cells per cubic millimetre of blood is called the CD4 count measures. A normal human peripheral blood has a blood count between $500mm^{-3}$ and $1200mm^{-3}$. The CD4 count serves as a good indicator to track the progress of HIV infection from one stage to another. A CD4 count between $250mm^{-3}$ and $500mm^{-3}$ indicates a weakened immune system and might indicate HIV infection. An AIDS patient has a CD4 count less than $200mm^{-3}$ and it indicates that the immune system has been highly compromised. As of today, science has not provided any medicine to cure HIV, but the use of ART can enormously reduce the rate of replication of the virus. An HIV patient using ART drugs has a chance to have a healthier longer life because ART quashes the viral load (amount of the virus in a blood volume) to an unnoticeable extent. Based on the recent researches, it has been confirmed that the most reliable ART is the highly active antiretroviral therapies (HAART). PrEP is recommended for people who are without HIV but are often unavoidably exposed to HIV which consequently means that they are at the risk of getting infected. PrEP prevents such people from getting infected (AIDS, 2016; HIV/AIDS, 2016).

HIV is commonly transmitted from infected individuals to uninfected ones through unprotected sex, and an exchange of body fluids, mother-to-child transmission at birth or during breastfeeding, and sharing tattooing or piercing needles and needles used for injecting drugs. Transmission can greatly be controlled by: Practicing abstinence or being faithful to one sexual partner, using new needles always during injection (WHO,2019).

A common illness among HIV patients who have good CD4 count is the KS. It is a cancer in form of tumour in HIV patients. KS, caused by human herpes virus 8 (HHV-8), is listed among diseases associated with HIV/AIDS (Fang *et al.,* 2017) with spread commonly among African gay men (Betsem *et al*., 2014). According to Warpe (2014), KS builds up when cancer cells, septic blood cells and infected blood vessels begin to grow, without stoppage, under the skin, in lymph nodes, in mouth lining. They show up as red or purple patches or lesions starting from one or many body-parts simultaneously. The presence of the HHV-8 in the mouth makes its transmission possible via kissing with an infected individual, or lubricating the genitals with saliva during sex, or during oral sex (common among gays). The immune system of a healthy individual is able to keep the HHV-8 under control and to also ensure it does not develop into KS. Meanwhile, the presence of HHV-8 in an HIV patient, not using ART, is prone to quickly metamorphose into KS. Classic KS lesions are more often treated with chemotherapy.

1.2 STATEMENT OF THE PROBLEM

The co-existence of several pathogens in a single host leading to concurrent infections is called coinfection. KS is listed among diseases associated with HIV/AIDS. Kaposi's sarcoma sprouting from AIDS (AIDS-KS) is a major manace in Kenya and sub-Saharan Africa. Mathematical models provides insights into the spread and pathogenesis of HIV, responses of the immunity to anti-retroviral treatment and to the study of the coinfection of HIV/AIDS and other opportunistic infections such as Tuberculosis, Pneumonia and Hepatitis. However, there are very limited studies on the coinfection of HIV/AIDS and AIDS-related Kaposi's sarcoma incorporating the aspect of treatment. In this project a mathematical model for the coinfection of HIV/AIDS and KS with treatment is developed

and analysed to comprehend the impact of ART used on HIV/AIDS and the coinfection of HIV/AIDS and AIDS-related Kaposi's sarcoma.

1.3 JUSTIFICATION

It is recorded that 84% of the world case of KS is found in sub-Saharan Africa, making KS a common cancer in Sub-Saharan Africa occurring in the context of immunodeficiency. According to the available statistics, the same region is heavily impacted by HIV/AIDS than any other. Currently, 38 million people have HIV and 690,000 died in 2019 from HIV and/or its complications according to world health organization. Without treatment HIV and KS coinfection can reduce lifespan. Therefore, massively expanded prevention and treatment is fundamental in disease monitoring. Modelling the coinfection of HIV and KS is uncommon in literature yet they redound to the understanding of HIV and KS synergy. The model proposed in the current study incorporates prevention and treatment for both HIV/AIDS and KS.

1.4 OBJECTIVES

1.4.1 General Objective

To study a mathematical model for coinfection of HIV/AIDS and Kaposi's Sarcoma with treatment.

1.4.2 Specific Objectives

The specific objectives of this study are to;

i. Model coinfection of HIV/AIDS and Kaposi's sarcoma with treatment.
ii. Establish the solution to the model remain positive (or zero) and bounded.
iii. Determine the disease free equilibrium point of the model and the local stability.

iv. Obtain the basic reproduction number.

1.5 SIGNIFICANCE OF THE STUDY

Mathematical models have been proven valuable to give a decisive quantitative information about the dynamics and pathogenesis of HIV, responses of the immunity to anti-retroviral treatment and to the study of the coinfection of HIV/AIDS and other opportunistic infections like Malaria, Tuberculosis, Pneumonia and Hepatitis. Results from here provides important insights into coinfection and prompt treatment of HIV and KS to boost the immune system and reduce the progression rate to AIDS class. Morever, this study is useful in policy and guideline formulation, planning and making appropriate decisions in monitoring and evaluation of the HIV response. This study is also beneficial to the public health sector, community and NGOs in coming up with intervention strategies to prevent HIV and KS infections. Other researchers in the related field can extend the model to consider other transmission modes of HHV-8 with an aim of determining the most effective combination of antiretroviral treatment for HIV patients with KS.

Chapter 2

LITERATURE REVIEW

HIV prevention and treatment with an aim of ending AIDS is a key national health strategic objective**.** This is achieved by improving on the medicine, promoting diagnosis and enhancing a patient-centered mode of service delivery. Despite the measures in place, 1.5 million people are projected to live with HIV in Kenya, out of which 1,136,000 are on ART, according to National AIDS & STI Control Program 2018. AIDS-related Kaposi's sarcoma (AIDS-KS) caused by HIV co-infection with HHV-8 remains endemic in Kenya and sub-Saharan Africa (Onyango & Njiru, 2004; Lupia *et al*., 2017).

To understand the mechanisms and the dynamics of HIV and KS coinfection as well as establishing the disease transmission, prevention and control strategies, mathematical model has been used. Through quantitative, qualitative analysis and numerical simulations, definite treatment regimens to boost anti-viral immunity and enhance a long-term control of the virus have been designed. A survey of some studies on mathematical models of HIV dynamics as well as HIV and KS coinfection is presented.

Tarfulea (2018) unravelled the influence how mitosis influence HIV transmission using a mathematical model. Four dynamic variables were considered in the model. It was shown that the DFE is locally asymptotically stable if $\mathcal{R} \ll 1$. The author further recommended that the stability and other properties of the infected equilibrium be determined in future. In their work, Zhang and Wang (2018) studied the model for the variability of HIV infection of T cells, with response of the immune and rate of cure. They developed a mathematical model that catered for the concentration of cells that are not infected, concentration of cells that are infected and are able to produce a virus and the concentration

of *CTLs*. They analysed the local stability of the DFE, immune absence and immune present equilibriums using the characteristic equation and Hurwitz criterion and obtained $\mathcal{R}$. Their model suggested that the T-cells concentration is a good criterion to measure the progression of HIV infection. Thus, the cure rate increases as the concentration of T cells increase. Their work extends the model constructed by Zhou *et al.* (2008) that considered the pathology of HIV with cure rate. Wang and Li (2006) proposed a model with a simplified logistic growth of the susceptible CD4+T cells. Their main interest was to thoroughly investigate global dynamics of the model and the qualitative changes resulting from changes in logistic terms. The results indicated that if $\mathcal{R} < 1$, the T cells will get rid of the HIV infection but otherwise, the infection remains. The global stability region for chronic-infection was also obtained.

Ogunlaran and Noutchie (2016) used minimum drug therapy to minimize viral load. They made an assumption that the logistic growth function incorporated constant recruitment and death of new uninfected cells. TheT-cells infection rate by free virions was assumed to be saturated by overcrowding of free virions and choice of the patient on protection measures. Numerical simulation results were used to confirm the effectiveness of the treatment strategy. Vaidya and Rong (2017) integrated several drug-related parameters into the model. The results show that once a patient reaches the latent stage, it impossible to remove the virus completely by any treatment; rather the treatment suppresses the viral load. Srivastava *et al.* (2009) developed and analysed a stochastic model for HIV on the viremia level.

Modelling within host viral infections with drug therapy give rise to dynamical systems whose local and global analysis is very essential. Ferrari and Marcus (2018) adopted and

analysed a fractional order model invented by Arafa *et al.* (2013) that shows how HIV acts in a human body when there is treatment with RT inhibitor. They estimated the amount of healthy cells, infected cells and viral load over time. Their findings led to a conclusion that undetectable level of virus density will be achieved if the efficacy of the drug is not less than 88.375%. The authors further recommended that a new model with other drugs different from the RT inhibitor, or combinations of them be considered in future and the stability corresponding to the infectious state be analysed.

Cai *et al*. (2009) included treatment in the model. The authors established the model has two infective stages; the asymptomatic and symptomatic phases and proved that $\mathcal{R}$ is enough to unravel the dynamics of HIV. In 2016, Hikal and Zahra investigated a fractional order time delay model with treatment. The population in their model was divided into a susceptible class, asymptomatic infection phase, symptomatic infection phase and the group of AIDS patients. The obtained results concurred with those of Cai *et al*. (2009). Prevention of HIV and providing test and ART treatment as a fight against HIV infection was quantified by Omondi *et al*. (2018); who constructed a model for epidemiological HIV trends. Through sensitivity analysis, the authors concluded that effective contact rates intensify HIV transmission while effectiveness of ART inhibit incidence rate.

KS exists as Classical, endemic, AIDS-associated epidemic and Transplant KS. In 2020, Chimbola constructed a model that depicted the progenitor/B-cells interaction in under the action of HHV-8 virus to show how it ends in KS. The author investigated the global properties of classical KS by direct Lyapunov method.

Motlhale *et al.* (2022) studied the incidence of KS in sub-Saharan Africa to ascertain how use of ART affects KS incidence. Their findings showed that ART rollout corresponds to

a reduction in KS incidence in sub-Saharan Africa, though reductions in HIV incidence could not be established. Meanwhile, inadequate information to confirm a reduction in KS incidence despite the infusion of ART within some areas in sub-Saharan Africa remains a challenge to public health, contrasts to its decline in developed countries due to ART treatment.

By considering 16,431 adults (over 18 years old), Akanbi *et al*. (2022) examined KS prevalence trend between 2006-2017 in Nigeria to determine the increasing effects of HIV program on KS. Their findings indicated that there was a spike in KS prevalence in 2009–2011 but remained stable for other periods. Even with the expansion in ART, delay to enrol for HIV care has ensured that there is no significant impact on KS, resulting in low CD4 cell count and thus increasing KS risk. They recommended intervention implimentation targeting early HIV diagnosis and ART administeration to reduce KS risk. It is crucial to assess how these interventions affect the KS risk among patients starting HIV treatment.

Common opportunistic infections associated with HIV/AIDS include TB, Pneumonia, Malaria and KS. Co-infection refers to the state in which a host is infected by multiple species of pathogens at the same time (Roeger *et al*. (2009); Nthiiri *et al.* (2015); Mukandavire *et al*. (2009); Barley *et al*. (2012)). Nani and Jin (2011) and Lungu *et al*. (2013) are some works that have been conducted on the coinfection of KS and HIV.

Focusing on the models which incorporate treatment intervention and are relevant to our study, Szomolay and Lungu (2014) formulated a mathematical model for AIDS-KS incorporating pharmacodynamics of HAART to find out how the strategy of treatment stops the disease growth. They found out that giving HAART for HIV-1 and HHV-8 coinfection can eliminate HIV only or both HIV and KS; but adoptive immunotherapy

alone can obliterate KS only. Numerical Simulations indicated that the adherence level strongly depends on the choice of HAART and how long the HAART is administered.

In 2011, Nani and Jin introduced a mathematical model that employed a system of non-linear deterministic differential equations to analyze the patho-physio-dynamics of Kaposi sarcoma (KS) in AIDS patients undergoing Highly Active Antiretroviral Therapy (HAART). The model accounted for clinically relevant immunological parameters and interactions that could be biologically measured. Using investigative computer simulations, the researchers explored the impact of CD8+ T cell adoptive transfer on the dynamics of KS during HAART.

Lungu *et al*. (2013) developed a system of ODEs to quantitatively determine optimal levels of HAART treatment for patients co-infected with HIV and KS in regions with high HIV prevalence. They conducted a qualitative stability analysis of equilibrium states and discovered that the disease-free equilibrium is universally attractive when the reproductive number is below 1. Hence, to eliminate the disease, the reproductive number should be decreased to less than one. According to their findings, if 10 percent of the HIV population receives HAART treatment, approximately 87% of the AIDS population would be protected from co-infection with HIV and Kaposi's Sarcoma. Provision of HAART helps to reduce the transmission of HIV and the risk of acquiring another fatal disease for HIV/AIDS patients. The researchers suggested that HIV screening should be expanded to encompass testing for HHV-8 and KS counseling in sub-Saharan countries.

KS is still responsible for morbidity and mortality in sub-Saharan Africa after nearly two decades of ART. HIV infected individuals with KS have a higher mortality risk and profound immunosuppression compared to those without KS (Bray *et al*.,2018). The impact of ART used on HIV/AIDS and the coinfection of HIV/AIDS and AIDS-related Kaposi's sarcoma among patients under HIV care in sub Saharan Africa remains unclear. This study endeavors to provide important insights into HIV/AIDS and KS coinfection. A mathematical model for coinfection of HIV/AIDS and Kaposi's sarcoma is developed and analysed. Incorporation of HAART as a treatment strategy to boost the immune system and reduce the progression rate to AIDS class will be investigated.

Chapter 3

METHODOLOGY

3.1 INTRODUCTION

This chapter describes and formulates HIV/AIDS- Kaposi's sarcoma co-infection model.

3.2 MODEL FORMULATION

We now formulate and describe the spread trend of HIV/AIDS – KS co-infection with treatment model.

Assumptions taken into account in formulating the model:

i. The population that is susceptible to acquiring an HIV or KS infection is referred to as the general population. Their risk of getting infected is directly proportional to the density of people infected with HIV and KS, respectively.
ii. The transmission of HIV from an infective to susceptive is through horizontal transmission.
iii. All parameters are positive.
iv. The treatment is for both HIV and KS patients

The population at any time is categorized into six different compartments depending on their disease status as shown in the flowchart for the HIV/AIDS and KS spread, with their coinfection in a single host, in Figure (3.1).

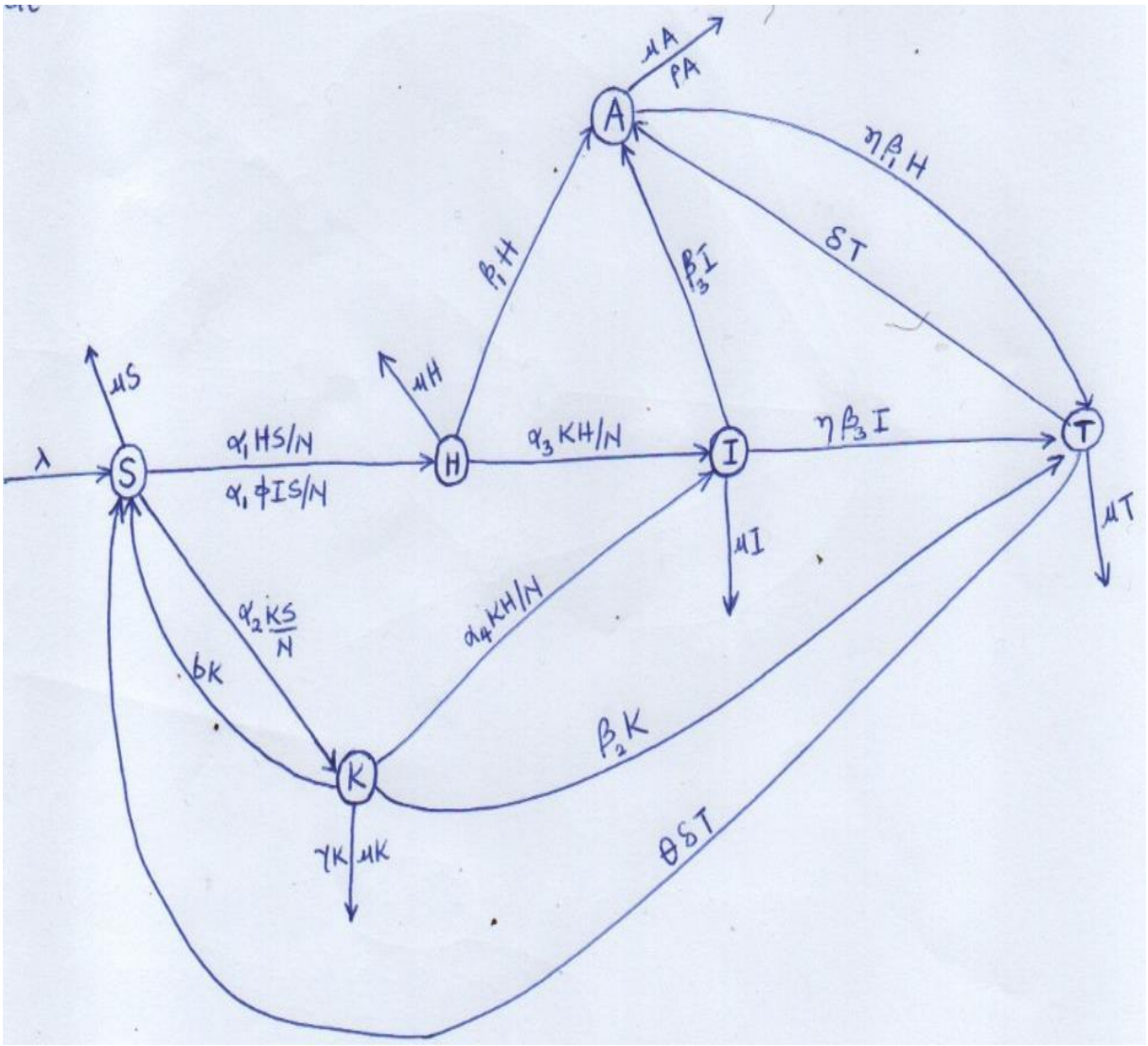

Figure 3.1: *Flow chart of the co-infection of HIV and KS*

The resulting system of equations modeling the description stated takes the form:

$$\frac{dS}{dt} = \lambda - \left(\frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N}\right)S - \frac{\alpha_2 \mathrm{K}}{N}S - \mu S + bK + \theta\delta T$$

$$\frac{dH}{dt} = \frac{\alpha_1(H+\phi I)}{N}S - \frac{\alpha_3 K}{N}H - (\beta_1 + \mu)H$$

$$\frac{dK}{dt} = \frac{\alpha_2 K}{N}S - \frac{\alpha_4 H}{N}K - (\beta_2 + b + \gamma + \mu)K \qquad (3.1)$$

$$\frac{dI}{dt} = \frac{\alpha_3 K}{N}H + \frac{\alpha_4 H}{N}K - (\beta_3 + \mu)I$$

$$\frac{dT}{dt} = \eta\beta_1 H + \eta\beta_3 I + \beta_2 K - \mu T - \theta\delta T - (1-\theta)\delta T$$

$$\frac{dA}{dt} = (1-\eta)\beta_1 H + (1-\eta)\beta_3 I + (1-\theta)\delta T - (\rho + \mu)A$$

The force of infection in the above model is taken as the probability of exposure to HIV, KS or both HIV and KS co-infected individual. Susceptible individuals have the tendency to contract HIV when they interact with either the HIV-infected class or the coinfected class. The rate of interaction with HIV infected individuals is α_1, therefore $\frac{\alpha_1 \mathrm{HS}}{N}$ individuals will migrate from the the susceptible class due to interaction with the HIV class and $\frac{\alpha_1 \phi \mathrm{IS}}{N}$ will migrate from the susceptible class into the HIV-infected class due to interaction of the susceptible class and the coinfected individuals.Susceptible individuals increases due to (i) newly recruited individuals, (ii) those who recover naturally from KS infection and (iii) through fully recovery after treatment while the infected individuals join the HIV, KS or the co-infected classes H(t), K(t) and I(t) respectively and progress for treatment at the rates β_1, β_2 and β_3 respectively. We assume that the recovered individuals can still be infected by KS or HIV. Thus a fraction of the HIV and co-infected individuals join the treatment class

T (t) while the rest progress to AIDS class A (t). The KS infected individuals join the treatment compartment and the fraction that fully recover after treatment move back to the susceptible class while the remaining join the AID class where they die a natural death or death due to the suppressed immunity.

Chapter 4

QUALITATIVE ANALYSIS

4.1 INTRODUCTION

In this chapter, we analyze the HIV/AIDS- Kaposi's sarcoma co-infection model. The nonlinear system (3.1) is linearized at its critical points and equilibrium solution found. Characteristic equation and Hurwitz criterion are adopted to find the model's local stability. The basic reproduction number $\mathcal{R}$ for this model is determined using the next generation matrix.

4.2 THE MODEL ANALYSIS

4.2.1 Positivity and Boundedness of Solutions

Theorem 1: *Solutions equations* (3.1) *whose initial conditions are from* R_+^6 *tend to and remains in* Ω *at all time.*

Proof: Summing the equations in (3.1);

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dH}{dt} + \frac{dK}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dA}{dt} \tag{4.1}$$

By putting each equation of system (3.1),

$$\frac{dS}{dt}+\frac{dH}{dt}+\frac{dK}{dt}+\frac{dI}{dt}+\frac{dT}{dt}+\frac{dA}{dt}$$

$$=\left[\lambda-\left(\frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N}\right)S-\frac{\alpha_2\mathrm{K}}{N}S-\mu S\ +bK+\ \theta\delta T\right]$$

$$+\left[\frac{\alpha_1(H+\phi I)}{N}S-\frac{\alpha_3 K}{N}H-(\beta_1+\mu)H\right]$$

$$+\left[\frac{\alpha_2 K}{N}S-\frac{\alpha_4 H}{N}K-(\beta_2+b+\gamma+\mu)K\right]$$

$$+\left[\frac{\alpha_3 K}{N}H+\frac{\alpha_4 H}{N}K-(\beta_3+\mu)I\right]+\ [\eta\beta_1 H+\eta\beta_3 I+\beta_2 K-(\delta+\mu)T]$$

$$+[(1-\eta)\beta_1 H+(1-\eta)\beta_3 I+(1-\theta)\delta T-(\rho+\mu)A] \qquad (4.2)$$

$$\frac{dN}{dt}=\lambda-\left(\frac{\alpha_1\ (\mathrm{H}+\Phi\mathrm{I})}{N}\right)S-\frac{\alpha_2\ \mathrm{K}}{N}S-\mu S\ +bK+\ \theta\delta T+\frac{\alpha_1(H+\phi I)}{N}S-\frac{\alpha_3 K}{N}H$$

$$-\beta_1 H-\mu H+\frac{\alpha_2\ K}{N}S-\frac{\alpha_4 H}{N}K-\beta_2 K-\ bK-\gamma K-\mu K+\ \frac{\alpha_3 K}{N}H$$

$$+\ \frac{\alpha_4 H}{N}K-\beta_3 I-\mu I+\eta\beta_1 H+\eta\beta_3 I+\beta_2 K-\ \delta T-\ \mu T+\ \beta_1 H-\eta\beta_1 H$$

$$+\ \beta_3 I-\eta\beta_3 I+\delta T-\theta\delta T-\ \rho A-\ \mu A \qquad (4.3)$$

$$\frac{dN}{dt}=\lambda-(S\ +\ H\ +\ K\ +\ I\ +\ T\ +\ A)\mu-\ \gamma K-\ \ \rho A \qquad (4.4)$$

Since

$$N\ (t)=H(t)+S(t)+K(t)+T\ (t)+I(t)+A\ (t)$$

as from equation (3.1), we obtain

$$\frac{dN}{dt}=\lambda-\mu N-\ \gamma K-\ \ \rho A \qquad (4.5)$$

In the absence of KS and AIDS, equation (4.5) becomes;

$$\frac{dN}{dt} = \lambda - \mu N \tag{4.6}$$

According to the theorem by Birkhoff and Rota's (1982) on differential inequality, if

$$\frac{dN}{dt} \leq \lambda - \mu N \tag{4.7}$$

Which is solved by separation of variables as follows,

$$\frac{dN}{\lambda - \mu N} \leq dt \tag{4.8}$$

Integrating (4.8) on both sides we obtain

$$\int \frac{1}{\lambda - \mu N}\, dN \leq \int dt \tag{4.9}$$

Which implies that

$$-\frac{1}{\mu}\ln(\lambda - \mu N) \leq t + c \tag{4.10}$$

With *c* as the constant of integration. Thus

$$\ln(\lambda - \mu N) \geq -\mu(t + c) \tag{4.11}$$

Multiplying both sides of inequality (4.11) by exponential,

$$exp\,[\ln(\lambda - \mu N)] \geq exp[-\mu(t + c)] \tag{4.12}$$

$$(\lambda - \mu N) \geq e^{-\mu t}e^{-\mu C} \tag{4.13}$$

$$\lambda - \mu N \geq Be^{-\mu t} \tag{4.14}$$

The initial condition $N(0) = N_0$ in (4.14) gives

$$\lambda - \mu N_0 \geq Be^0 \Rightarrow B = \lambda - \mu N_0 \quad (4.15)$$

Substituting B in (4.14) yields,

$$\lambda - \mu N \geq (\lambda - \mu N_0)e^{-\mu t} \quad (4.16)$$

$$N \leq \frac{\lambda}{\mu} - \left[\frac{\lambda}{\mu} - \mathrm{N}_0\right] e^{-\mu t} \quad (4.17)$$

As $t \to \infty$, $N \leq \frac{\lambda}{\mu} - \left[\frac{\lambda}{\mu} - \mathrm{N}_0\right] e^{-\mu t} \to \frac{\lambda}{\mu}$ which implies that $0 \leq N \leq \frac{\lambda}{\mu}$. Thus, solutions set of system (3.1) tend to and remain in the region

$$\Omega = \left[(S, H, K, I, T, A) \in \Re+ : N \leq \frac{\lambda}{\mu}\right].$$

In conclusion, the model is well-posed. Hence, it suffices to consider its solutions in Ω.

■

Theorem 2: The solution space (S, H, K, I, T, A) remains positive whenever the initial conditions are such that $S(t_0) > 0$, $H(t_0) > 0$, $K(t_0) > 0$, $I(t_0) > 0$, $T(t_0) > 0$, $A(t_0) > 0$,

Proof: Starting with the first equation of system (3.1)

$$\frac{dS}{dt} = \lambda - \left(\frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N}\right) S - \frac{\alpha_2 \mathrm{K}}{N} S - \mu S + bK + \theta\delta T \geq -\mu S \quad \ldots\ldots\ldots\ldots\ldots\ldots (4.18)$$

$$\frac{dS}{dt} = -\mu S \Rightarrow \frac{dS}{S} = -\mu dt \Rightarrow \int_{t_0}^{t} \frac{dS}{S} = \int_{t_0}^{t} -\mu dt \Rightarrow [\ln S]_{t_0}^{t} = [-\mu t]_{t_0}^{t}$$

$$\Rightarrow \ln S(t) - \ln S(t_0) = -\mu(t - t_0) \Rightarrow \ln\left(\frac{S(t)}{\mathrm{S}(t_0)}\right) = -\mu(t - t_0)$$

$$\Rightarrow \frac{S(t)}{\mathrm{S}(t_0)} = \exp^{-\mu(\mathrm{t}-t_0)} \Rightarrow S(t) \geq S(t_0) \exp\left(-\mu(\mathrm{t} - t_0)\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4.19)$$

This clearly indicates that $S(t) \geq 0$ provided $S(t_0) > 0$. Next, from the second equation

$$\frac{dH}{dt} = \frac{\alpha_1(H+\phi I)}{N} S - \frac{\alpha_3 K}{N} H - (\beta_1 + \mu)H \geq -(\beta_1 + \mu)H \quad \text{(4.20)}$$

$$\Rightarrow \mathrm{H}(t) \geq H(t_0) \exp^{-(\beta_1+\mu)(\mathrm{t}-t_0)} \quad \text{(4.21)}$$

Thus, $\mathrm{H}(t) \geq 0$ provided $H(t_0) > 0$. From the third equation

$$\frac{dK}{dt} = \frac{\alpha_2 K}{N} S - \frac{\alpha_4 H}{N} K - (\beta_2 + b + \gamma + \mu)K \geq -(\beta_2 + b + \gamma + \mu)K \quad \text{(4.22)}$$

$$\Rightarrow \mathrm{K}(t) \geq K(t_0) \exp^{-(\beta_2+b+\gamma+\mu)(\mathrm{t}-t_0)} \quad \text{(4.23)}$$

Thus, $K(t) \geq 0$ provided $K(t_0) > 0$.

Considering the fourth equation

$$\frac{dI}{dt} = \frac{\alpha_3 K}{N} H + \frac{\alpha_4 H}{N} K - (\beta_3 + \mu)I \geq -(\beta_3 + \mu)I \quad \text{(4.24)}$$

$$\Rightarrow I(t) \geq I(t_0) \exp^{-(\beta_3+\mu)(\mathrm{t}-t_0)} \quad \text{(4.25)}$$

Which implies that $\mathrm{I}(t) \geq 0$ provided $I(t_0) > 0$. Considering the treatment class in the fifth equation

$$\frac{dT}{dt} = \eta\beta_1 H + \eta\beta_3 I + \beta_2 K - (\delta + \mu)T \geq -(\delta + \mu)T \quad \text{(4.26)}$$

$$\Rightarrow T(t) \geq T(t_0) \exp^{-(\delta+\mu)(\mathrm{t}-t_0)} \quad \text{(4.27)}$$

and so $T(t) \geq 0$, provided $T(t_0) > 0$. Finally, from the sixth equation

$$\frac{dA}{dt} = (1-\eta)\beta_1 H + (1-\eta)\beta_3 I + (1-\theta)\delta T - (\rho + \mu)A \geq -(\rho + \mu)A \quad \text{(4.28)}$$

$$\Rightarrow \mathrm{A}(t) \geq A(t_0) \exp^{-(\rho+\mu)(\mathrm{t}-t_0)} \quad \text{(4.29)}$$

and so $A(t) \geq 0$, provided $A(t_0) > 0$. Hence, any solution (S, H, K, I, T, A) of the system (3.1) is positive provided the initial conditions are positive. ■

4.2.2 Equilibrium Points

Given the problem

$$\dot{X} = f(x),\ x \in R^n \tag{4.30}$$

Definition 1. An equilibrium point of (4.30) is a point x ∈ R^n such that f(x) = 0.

The equilibrium points are obtained by setting each equation of the system (3.1) to 0

$$\lambda - \left(\frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N}\right)S - \frac{\alpha_2 \mathrm{K}}{N}S - \mu S + bK + \theta\delta T = 0 \quad \text{(4.31)}$$

$$\frac{\alpha_1(H+\phi I)}{N}S - \frac{\alpha_3 K}{N}H - (\beta_1 + \mu)H = 0 \quad \text{(4.32)}$$

$$\frac{\alpha_2 K}{N}S - \frac{\alpha_4 H}{N}K - (\beta_2 + b + \gamma + \mu)K = 0 \quad \text{(4.33)}$$

$$\frac{\alpha_3 K}{N}H + \frac{\alpha_4 H}{N}K - (\beta_3 + \mu)I = 0 \quad \text{(4.34)}$$

$$\eta\beta_1 H + \eta\beta_3 I + \beta_2 K - (\delta + \mu)T = 0 \quad \text{(4.35)}$$

$$(1-\eta)\beta_1 H + (1-\eta)\beta_3 I + (1-\theta)\delta T - (\rho + \mu)A = 0 \quad \text{(4.36)}$$

From equation (4.34)

$$(\beta_3 + \mu)I = \frac{(\alpha_3 + \alpha_4)HK}{N}$$

$$I = \frac{(\alpha_3 + \alpha_4)HK}{(\beta_3 + \mu)N} \quad \text{(4.37)}$$

From equation (4.35)

$$(\delta+\mu)T = \eta\beta_1 H + \eta\beta_3 I + \beta_2 K$$

$$T = \frac{\eta\beta_1 H}{(\delta+\mu)} + \frac{(\alpha_3+\alpha_4)\eta\beta_3 HK}{(\delta+\mu)(\beta_3+\mu)N} + \frac{\beta_2 K}{(\delta+\mu)}$$

$$T = \left[\frac{\eta\beta_1}{K} + \frac{\beta_2}{H} + \frac{(\alpha_3+\alpha_4)\eta\beta_3}{(\beta_3+\mu)N}\right]\frac{HK}{(\delta+\mu)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4.38)$$

From equation (4.36)

$$(\rho+\mu)A = (1-\eta)\beta_1 H + (1-\eta)\beta_3 I + (1-\theta)\delta T$$

$$(\rho+\mu)A = (1-\eta)\beta_1 H + \frac{(\alpha_3+\alpha_4)(1-\eta)\beta_3 HK}{(\beta_3+\mu)N} + \left[\frac{\eta\beta_1}{K} + \frac{\beta_2}{H} + \frac{(\alpha_3+\alpha_4)\eta\beta_3}{(\beta_3+\mu)N}\right]\frac{(1-\theta)\delta HK}{(\delta+\mu)}$$

$$A = \left[\frac{(1-\eta)\beta_1}{K} + \frac{(\alpha_3+\alpha_4)(1-\eta)\beta_3}{(\beta_3+\mu)N} + \left(\frac{\eta\beta_1}{K} + \frac{\beta_2}{H} + \frac{(\alpha_3+\alpha_4)\eta\beta_3}{(\beta_3+\mu)N}\right)\frac{(1-\theta)\delta}{(\delta+\mu)}\right]\frac{HK}{(\rho+\mu)}$$

…. (4.39)

Summation of equation (4.31), (4.32) and (4.33) gives

$$\lambda - \left(\frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N}\right)S - \frac{\alpha_2 \mathrm{K}}{N}S - \mu S + bK + \theta\delta T + \frac{\alpha_1(H+\phi I)}{N}S - \frac{\alpha_3 K}{N}H - (\beta_1+\mu)H + \frac{\alpha_2 K}{N}S - \frac{\alpha_4 H}{N}K - (\beta_2+b+\gamma+\mu)K = 0$$

$$\lambda - \mu S + \theta\delta T - \frac{\alpha_3 K}{N}H - (\beta_1+\mu)H - \frac{\alpha_4 H}{N}K - (\beta_2+\gamma+\mu)K = 0$$

$$\mu S = \lambda + \theta\delta T - \frac{\alpha_3 K}{N}H - (\beta_1+\mu)H - \frac{\alpha_4 H}{N}K - (\beta_2+\gamma+\mu)K$$

$$S = \frac{\lambda}{\mu} + \left[\frac{\theta\delta T}{HK} - \frac{(\alpha_3 + \alpha_4)}{N} - \frac{(\beta_1 + \mu)}{K} - \frac{(\beta_2 + \gamma + \mu)}{H}\right]\frac{HK}{\mu} \ldots\ldots\ldots\ldots\ldots\ldots\ldots (4.40)$$

System (3.1) has the following steady states

i. **Disease free equilibrium point, E_0**

DFE is the absence of infection thus $K = H = 0$. Hence $I = 0,\ T = 0, A = 0$. Substituting $K = H = I = T = A = 0$ in equation (4.40), we obtain

$$S = \frac{\lambda}{\mu} \qquad (4.41)$$

So the DFE point with no infected individuals $(S_0 \neq 0, H_0 = 0, K_0 = 0, I_0 = 0, T_0 = 0, A_0 = 0)$ is given by

$$E_0 = \left(\frac{\lambda}{\mu}, 0, 0, 0, 0, 0\right)$$

ii. Endemic equilibrium point, E_1

E_1 is obtained by setting H =H_1 and K=K_1 So that;

$$I_1 = \frac{(\alpha_3 + \alpha_4)H_1\, K_1}{(\beta_3 + \mu)N} \qquad (4.42)$$

$$T_1 = \left[\frac{\eta\beta_1}{K_1} + \frac{\beta_2}{H_1} + \frac{(\alpha_3 + \alpha_4)\eta\beta_3}{(\beta_3 + \mu)N}\right]\frac{H_1\, K_1}{(\delta + \mu)} \qquad (4.43)$$

$$A_1 = \left[\frac{(1-\eta)\beta_1}{K_1} + \frac{(\alpha_3 + \alpha_4)(1-\eta)\beta_3}{(\beta_3 + \mu)N} + \left(\frac{\eta\beta_1}{K_1} + \frac{\beta_2}{H_1} + \frac{(\alpha_3 + \alpha_4)\eta\beta_3}{(\beta_3 + \mu)N}\right)\frac{(1-\theta)\delta}{(\delta + \mu)}\right]\frac{H_1\, K_1}{(\rho + \mu)} \qquad (4.44)$$

$$S_1 = \frac{\lambda}{\mu} + \left[\frac{\theta\delta T}{H_1\, K_1} - \frac{(\alpha_3 + \alpha_4)}{N} - \frac{(\beta_1 + \mu)}{K_1} - \frac{(\beta_2 + \gamma + \mu)}{H_1}\right]\frac{H_1\, K_1}{\mu} \tag{4.45}$$

Thus

$$E_1 = (S_1, H_1, K_1, I_1\, T_1, A_1)$$

4.2.3 Reproduction number

For the prevention and elimination of epidemics, the reproduction number, represented by R_0, is crucial. R_0 was defined by Driessche & Watmough (2002) and Oke *et al.* (2022) as the secondary infections counts that develop with the introduction of a single infected person into a population of totally susceptible people. If $R_0 < 1$, the epidemic ends since each affected person typically spreads the disease to no more than one other person. In contrast, if $R_0 > 1$, the epidemic spreads across the population because every infected individual creates an average of above one new infection. R_0 is calculated using the next generation matrix of the model denoted by, $\mathrm{F}V^{-1}$.

Thus, R_0 is;

$$R_0 = \rho(\mathrm{F}V^{-1})$$

where $\rho(\mathrm{F}V^{-1})$ is the spectral radius of the matrix $\mathrm{F}V^{-1}$.

$$F = \frac{1}{N}\begin{bmatrix} \alpha_1(\mathrm{H} + \phi\mathrm{I})S - \alpha_3 KH \\ \alpha_2 KS - \alpha_4 KH \\ (\alpha_3 + \alpha_4)KH \end{bmatrix}$$

$$V = \begin{bmatrix} (\beta_1 + \mu)H \\ (\beta_2 + b + \gamma + \mu)K \\ (\beta_3 + \mu)I \end{bmatrix}$$

and we find the Jacobian of F and V as follows

$$f = \nabla F = \frac{1}{N}\begin{bmatrix} \alpha_1 S - \alpha_3 K & -\alpha_3 H & \alpha_1 \phi S \\ -\alpha_4 K & \alpha_2 S - \alpha_4 H & 0 \\ (\alpha_3 + \alpha_4)K & (\alpha_3 + \alpha_4)H & 0 \end{bmatrix}$$

$$\mathcal{V} = \nabla V = \begin{bmatrix} \beta_1 + \mu & 0 & 0 \\ 0 & \beta_2 + b + \gamma + \mu & 0 \\ 0 & 0 & \beta_3 + \mu \end{bmatrix}$$

and thus,

$$\mathcal{V}^{-1} = \begin{bmatrix} \frac{1}{\beta_1 + \mu} & 0 & 0 \\ 0 & \frac{1}{\beta_2 + b + \gamma + \mu} & 0 \\ 0 & 0 & \frac{1}{\beta_3 + \mu} \end{bmatrix}$$

Now,

$$\mathrm{f}\,\mathcal{V}^{-1} = \frac{1}{N}\begin{bmatrix} \frac{\alpha_1 S - \alpha_3 K}{\beta_1 + \mu} & \frac{-\alpha_3 H}{\beta_2 + b + \gamma + \mu} & \frac{\alpha_1 \phi S}{\beta_3 + \mu} \\ \frac{-\alpha_4 K}{\beta_1 + \mu} & \frac{\alpha_2 S - \alpha_4 H}{\beta_2 + b + \gamma + \mu} & 0 \\ \frac{(\alpha_3 + \alpha_4)K}{\beta_1 + \mu} & \frac{(\alpha_3 + \alpha_4)H}{\beta_2 + b + \gamma + \mu} & 0 \end{bmatrix}$$

and at the DFE,

$$(\mathrm{f}\,\mathcal{V}^{-1})|E_0 = \frac{1}{N}\begin{bmatrix} \frac{\alpha_1 \lambda}{(\beta_1 + \mu)\mu} & 0 & \frac{\alpha_1 \phi \lambda}{(\beta_3 + \mu)\mu} \\ 0 & \frac{\alpha_2 \lambda}{(\beta_2 + b + \gamma + \mu)\mu} & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

The characteristics equation is

$$\begin{vmatrix} \frac{\alpha_1\lambda}{(\beta_1+\mu)\mu N} - m & 0 & \frac{\alpha_1\phi\lambda}{(\beta_3+\mu)\mu N} \\ 0 & \frac{\alpha_2\lambda}{(\beta_2+b+\gamma+\mu)\mu N} - m & 0 \\ 0 & 0 & -m \end{vmatrix} = 0$$

$$\left(\frac{\alpha_1\lambda}{(\beta_1+\mu)\mu N} - m\right)(-m)\left(\frac{\alpha_2\lambda}{(\beta_2+b+\gamma+\mu)\mu N} - m\right) = 0$$

$$\Longrightarrow m = 0, \frac{\alpha_2\lambda}{(\beta_2+b+\gamma+\mu)\mu N}, \frac{\alpha_1\lambda}{(\beta_1+\mu)\mu N}$$

$$\mathrm{R}_0 = \max\left\{0, \frac{\alpha_2\lambda}{(\beta_2+b+\gamma+\mu)\mu N}, \frac{\alpha_1\lambda}{(\beta_1+\mu)\mu N}\right\}$$

The reproduction numbers are;

$$R_0^H = \frac{\alpha_1\lambda}{(\beta_1+\mu)\mu N}, \qquad R_0^K = \frac{\alpha_2\lambda}{(\beta_2+b+\gamma+\mu)\mu N}$$

■

4.2.4 Local Stability

Theorem 1. If $R_0^H < 1$, $R_0^K < 1$ the DFE is locally asymptotically stable;

Proof:

We start by finding the Jacobian of the system (3.1) which gives

$$\begin{bmatrix} \frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N} - \frac{\alpha_2\mathrm{K}}{N} - \mu & -\frac{\alpha_1 S}{N} & -\frac{\alpha_2 S}{N} + b & -\frac{\alpha_1\phi S}{N} & \theta\delta & 0 \\ \frac{\alpha_1(\mathrm{H}+\phi\mathrm{I})}{N} & \frac{\alpha_1 S}{N} - \frac{\alpha_3 K}{N} - (\beta_1+\mu) & -\frac{\alpha_3 H}{N} & \frac{\alpha_1\phi S}{N} & 0 & 0 \\ \frac{\alpha_2 K}{N} & -\frac{\alpha_4 H}{N} & \frac{\alpha_2 S}{N} - \frac{\alpha_4 H}{N} - (\beta_2+b+\gamma+\mu) & 0 & 0 & 0 \\ 0 & \frac{\alpha_3 K}{N} + \frac{\alpha_4 K}{N} & \frac{\alpha_3 H}{N} + \frac{\alpha_4 H}{N} & -(\beta_3+\mu) & 0 & 0 \\ 0 & \eta\beta_1 & \beta_2 & \eta\beta_3 & -(\delta+\mu) & 0 \\ 0 & (1-\eta)\beta_1 & 0 & (1-\eta)\beta_3 & (1-\theta)\delta & -(\rho+\mu) \end{bmatrix}$$

At the DFE (E_0), we have

$$J(E_0) = \begin{bmatrix} -\mu & -\frac{\alpha_1\lambda}{\mu N} & -\frac{\alpha_2\lambda}{\mu N} + b & -\frac{\alpha_1\phi\lambda}{\mu N} & \theta\delta & 0 \\ 0 & \frac{\alpha_1\lambda}{\mu N} - (\beta_1 + \mu) & 0 & \frac{\alpha_1\phi\lambda}{\mu N} & 0 & 0 \\ 0 & 0 & \frac{\alpha_2\lambda}{\mu N} - (\beta_2 + b + \gamma + \mu) & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\beta_3 + \mu) & 0 & 0 \\ 0 & \eta\beta_1 & \beta_2 & \eta\beta_3 & -(\delta + \mu) & 0 \\ 0 & (1-\eta)\beta_1 & 0 & (1-\eta)\beta_3 & (1-\theta)\delta & -(\rho + \mu) \end{bmatrix}$$

The characteristic equation is

$$\begin{vmatrix} -\mu - \mathrm{m} & -\frac{\alpha_1\lambda}{\mu N} & \frac{\alpha_2\lambda}{\mu N} + b & -\frac{\alpha_1\phi\lambda}{\mu N} & \theta\delta & 0 \\ 0 & \frac{\alpha_1\lambda}{\mu N} - (\beta_1 + \mu) - \mathrm{m} & 0 & \frac{\alpha_1\phi\lambda}{\mu N} & 0 & 0 \\ 0 & 0 & \frac{\alpha_2\lambda}{\mu N} - (\beta_2 + \mathrm{b} + \gamma + \mu) - \mathrm{m} & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\beta_3 + \mu) - \mathrm{m} & 0 & 0 \\ 0 & \eta\beta_1 & \beta_2 & \eta\beta_3 & -(\delta + \mu) - \mathrm{m} & 0 \\ 0 & (1-\eta)\beta_1 & 0 & (1-\eta)\beta_3 & (1-\theta)\delta & -(\rho + \mu) - \mathrm{m} \end{vmatrix} = 0$$

where m is the eigenvalue and by evaluating the sixth order determinant, we have;

$$(-\mu - m)(-(\rho + \mu) - m)(-(\delta + \mu) - m)\left(\frac{\alpha_1\lambda}{\mu N} - (\beta_1 + \mu) - m\right)$$

$$\left(\frac{\alpha_2\lambda}{\mu N} - (\beta_2 + b + \gamma + \mu) - m\right)(-(\beta_3 + \mu) - m) = 0 \ldots\ldots\ldots\ldots\ldots (4.46)$$

Equation has six roots:

$$m_1 = -\mu, m_2 = -(\rho + \mu), m_3 = -(\delta + \mu), m_4 = \frac{\alpha_1\lambda}{\mu N},$$

$$m_5 = \frac{\alpha_2\lambda}{\mu N} - (\beta_2 + b + \gamma + \mu), m_6 = -(\beta_3 + \mu).$$

m_1, m_2, m_3 and m_6 have have negative real part for all values of the parameters, but

$\mathrm{m}_4 < 0$ only if $\frac{\alpha_1\lambda}{\mu N} - (\beta_1 + \mu) < 0 \implies \frac{\alpha_1\lambda}{\mu N} < (\beta_1 + \mu)$

$\implies \frac{\alpha_1\lambda}{\mu N(\beta_1 + \mu)} < 1 \implies R_0^H < 1$

$\mathrm{m}_5 < 0$ only if $\frac{\alpha_2\lambda}{\mu N} - (\beta_2 + \mathrm{b} + \gamma + \mu) < 0 \implies \frac{\alpha_2\lambda}{\mu N} < (\beta_2 + \mathrm{b} + \gamma + \mu)$

$\implies \frac{\alpha_2\lambda}{\mu N(\beta_2 + \mathrm{b} + \gamma + \mu)} < 1 \implies R_0^K < 1$

Therefore, the DFE is locally asymptotically stable iff;

$$R_0^H < 1 \quad \text{and} \quad R_0^K < 1 \qquad \blacksquare$$

4.3 Numerical Procedure

The Runge-Kutta RK (4, 5) also called Dorman-Prince method is an adaptive numerical technique that computes the accurate solutions of IVP

$$X' = F(X), \quad X(t_0) = X_0 \tag{4.47}$$

where

$$X = (x_1, x_2, \cdots, x_n)^T, \quad F = (f_1, f_2, \cdots, f_n)^T, \quad X = \big(x_1(t_0), x_2(t_0), \cdots, x_n(t_0)\big)$$

using the Runge-Kutta of orders 4 and 5. The model equations are rewritten in the form of (4.47) by setting

$$X = (S, \quad H, \quad K, \quad I, \quad T, \quad A)^T; \quad \frac{d}{dt}X = \left(\frac{dS}{dt}, \quad \frac{dH}{dt}, \quad \frac{dK}{dt}, \quad \frac{dI}{dt}, \quad \frac{dT}{dt}, \quad \frac{dA}{dt}\right)^T$$

and

$$F(X) = \begin{pmatrix} \lambda - \left(\frac{\alpha_1(\mathrm{H} + \phi \mathrm{I})}{N}\right) S - \frac{\alpha_2 \mathrm{K}}{N} S - \mu S + bK + \theta\delta T \\ \frac{\alpha_1(H + \phi I)}{N} S - \frac{\alpha_3 K}{N} H - (\beta_1 + \mu) H \\ \frac{\alpha_2 K}{N} S - \frac{\alpha_4 H}{N} K - (\beta_2 + b + \gamma + \mu) K \\ \frac{\alpha_3 K}{N} H + \frac{\alpha_4 H}{N} K - (\beta_3 + \mu) I \\ \eta\beta_1 H + \eta\beta_3 I + \beta_2 K - \mu T - \theta\delta T - (1 - \theta)\delta T \\ (1 - \eta)\beta_1 H + (1 - \eta)\beta_3 I + (1 - \theta)\delta T - (\rho + \mu) A \end{pmatrix}$$

and thus

$$X' = F(X)$$

with the initial condition

$$X(t = 0) = (S_0,\ H_0,\ K_0,\ I_0,\ T_0,\ A_0).$$

The difference between the two solutions is considered as the error and the step size is adjusted based on the tolerance chosen. The modified Butcher table of the Dorman-Prince method (see Dorman and Prince, 1980; Oke, 2017) is

c	A
	b_{RK4}
	b_{RK5}

where,

$$A = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{1}{4} & \frac{3}{4} & 0 & 0 & 0 & 0 & 0 \\ \frac{11}{9} & -\frac{14}{3} & \frac{40}{9} & 0 & 0 & 0 & 0 \\ \frac{4843}{1458} & -\frac{3170}{243} & \frac{8056}{729} & -\frac{53}{162} & 0 & 0 & 0 \\ \frac{9017}{3168} & -\frac{355}{33} & \frac{46732}{5247} & \frac{49}{176} & -\frac{5103}{18656} & 0 & 0 \\ \frac{35}{384} & 0 & \frac{500}{1113} & \frac{125}{192} & -\frac{2187}{6784} & \frac{11}{84} & 0 \end{bmatrix}$$

$$b_{RK4} = \left[\frac{5179}{57600} \; 0 \; \frac{7571}{16695} \; \frac{393}{640} \; -\frac{92097}{339200} \; \frac{187}{2100} \; \frac{1}{40}\right]^T$$

$$b_{RK5} = \left[\frac{35}{384} \quad 0 \quad \frac{500}{1113} \quad \frac{125}{192} \quad -\frac{2187}{6784} \quad \frac{11}{84} \quad 0\right]^T$$

$$c = \left[0 \quad \frac{1}{5} \quad \frac{3}{10} \quad \frac{4}{5} \quad \frac{8}{9} \quad 1 \quad 1\right]^T.$$

The Dorman-Prince method is coded into ode45 MATLAB solver. The model (3.1) are solved using MATLAB ode45 solver with the tolerance set to 10^{-8}. The parameter values are chosen based on the study of (Lungu *et al*., 2013; Pandey & Galvani, 2019) as follows;

λ = 800; α_1 = 0.4801; α_2 = 0.002; α_3 = 0.001; α_4= 0.001; μ = 0.02; ρ = 0.333;

ϕ = 0.05; b = 0.2; θ = 0.3; δ = 0.01; γ = 0.1; η = 0.1; β_1 = 0.2, β_2 = 0.1, β_3 = 0.05

with initial condition

$$S(0) = 800, H(0) = 1, K(0) = 1, I(0) = 0, T(0) = 0 \text{ and } A(0) = 0.$$

Chapter 5

RESULTS AND DISCUSSION

5.1 INTRODUCTION

Effects of varying the parameters of the model on the different classes of the population will be discussed, we will draw the conclusion, recommendations and suggest future work of this study.

5.2 ANALYSIS OF RESULTS

Figure (5.1) – (5.5) illustrate the effects of varying the proportion of HIV infected individuals who have access to treatment. The effect of increasing the access of HIV-infected individuals to treatment is shown on the HIV-infected class as shown in figure (5.1). The population of the HIV-infected class decline as their access to treatment is increased. Due to increased access to treatment, a number of HIV-infected individuals are able to manage the disease and live normal life. This explains why figure (5.1) illustrates a decline in the population of the HIV-infected class. The effect of increasing the chance of treatment for HIV-infected individuals on the susceptible class is shown in figure 5.2. Since the population of the HIV-infected class decline with an increase in η, the susceptible class rises significantly due to the fact that the number of interactions between the susceptible class and the HIV-infected class reduces; leading to an increase in the susceptible subpopulation (see figure (5.2)). Figure (5.3) illustrate the decline in the coinfected class as the access of the HIV-infected individuals to treatment is increased and this is expected since the HIV-infected class aso declines with increase in access to treatment for the HIV-infected individuals. Figure (5.4) demonstrates that increasing the access of HIV-infected

individuals to treatment increases the population of the treated individuals which supports the outcome that susceptible class also increases (as shown in figure (5.2)). Clearly, a decrease in the HIV class will also lead to a decrease in the AIDS class as revealed in figure (5.5).

Figure (5.6) – (5.8) illustrate the response of the subpopulations to the willingness of the HIV-infected individuals to go for treatement. Increasing the willingness of the HIV-infected class to progress for treatment increases the susceptible class (see figure (5.6)) but a decline is found in both the HIV-infected class and HIV/KS coinfected class as illustrated by figures (5.7) and (5.8). Meanwhile, figure (5.9) indicates that if the willingness of the coinfected individuals are raised, then the coinfected subpopulation will decline.

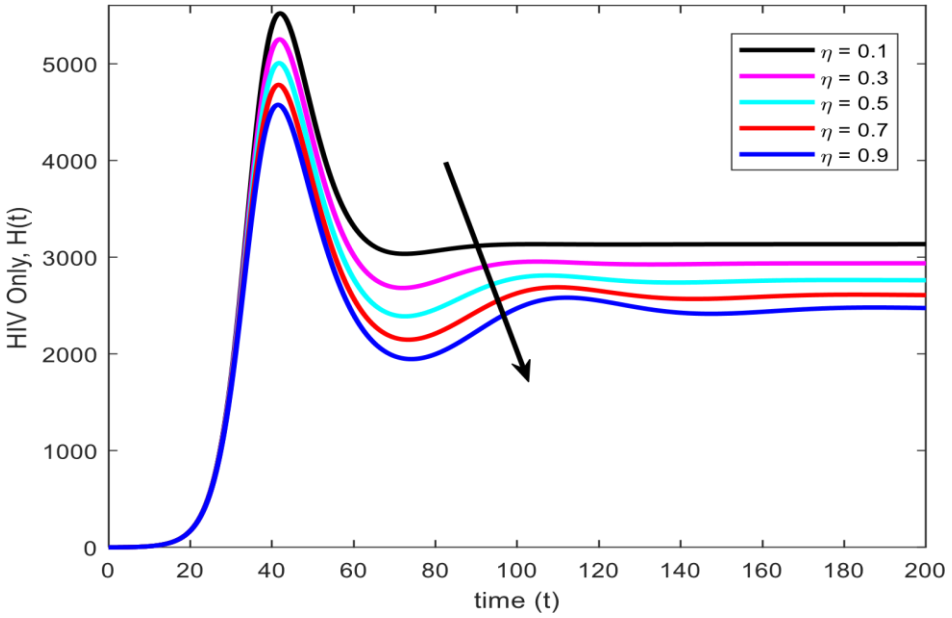

Figure 5.1: Effects of proportion of HIV infected individuals who get treated on HIV infected individuals

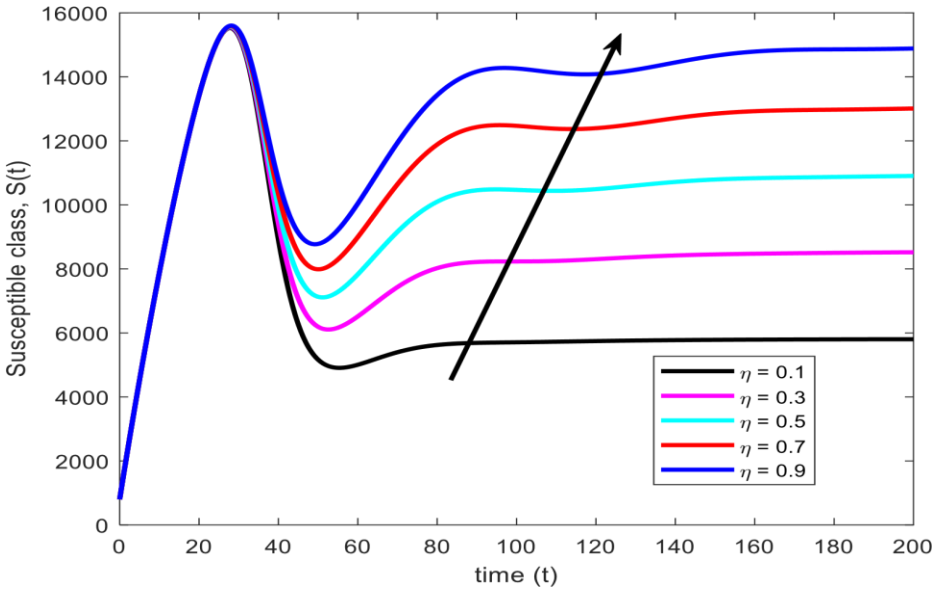

Figure 5.2: Effects of proportion of HIV infected individuals who get treated on the susceptible class

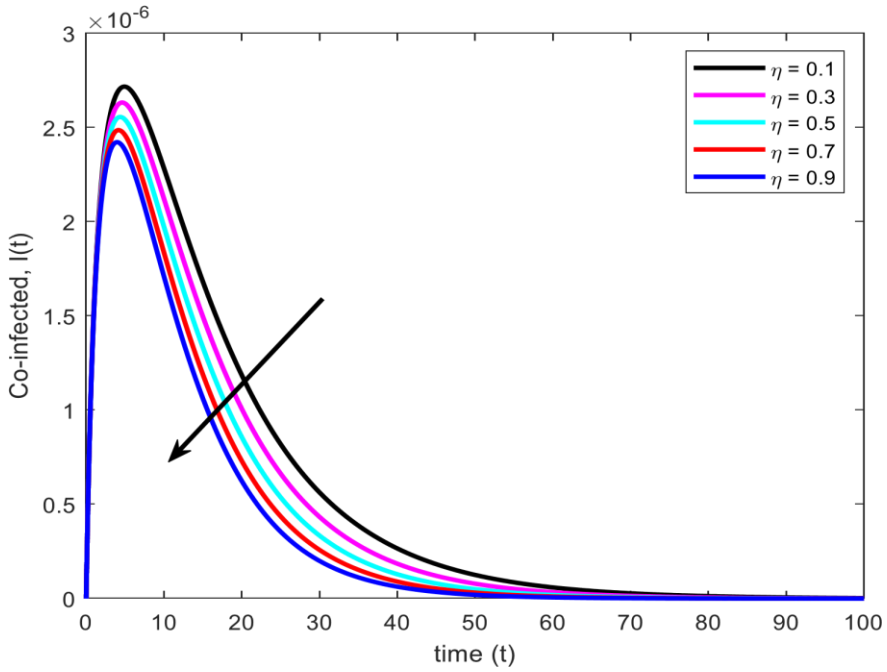

Figure 5. 3: Effects of proportion of HIV infected individuals who get treated on the individuals co-infected with HIV and Kaposi Sarcoma

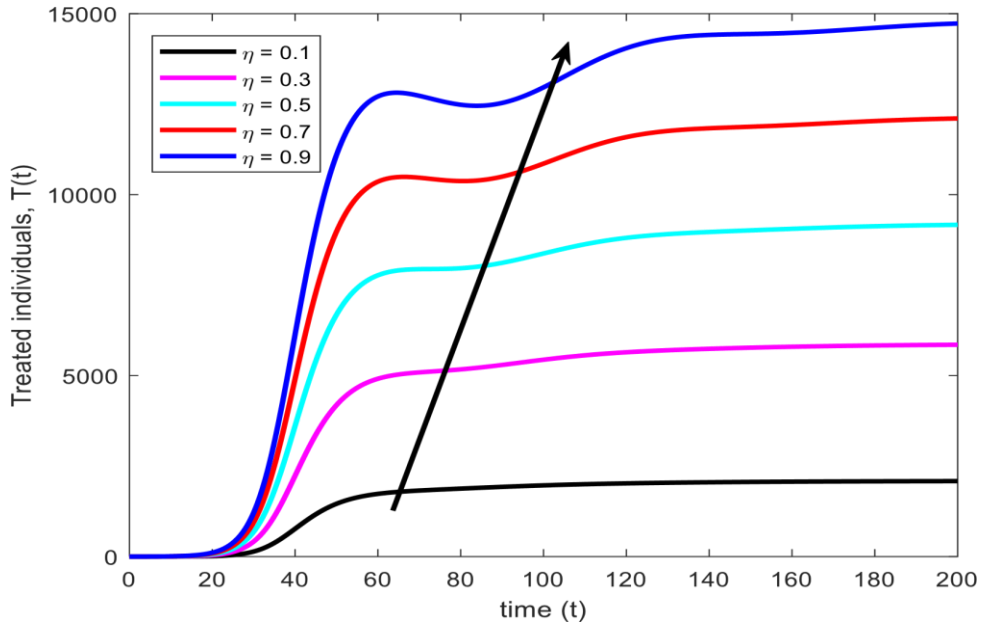

Figure 5.4: Effects of proportion of HIV infected individuals who get treated on the Treatment class

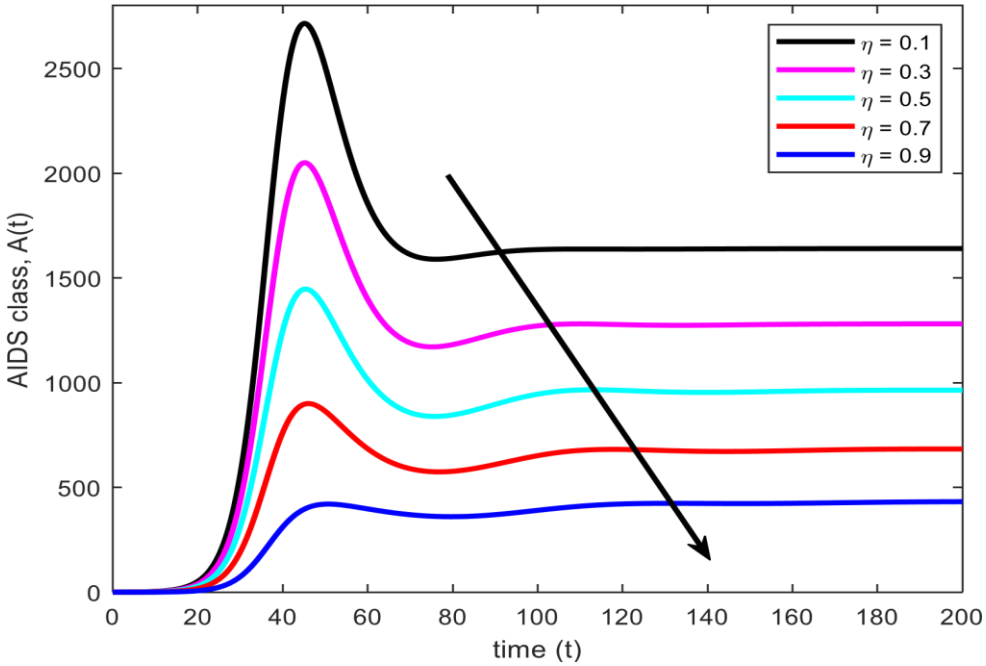

Figure 5.5: Effects of proportion of HIV infected individuals who get treated on the AIDS class

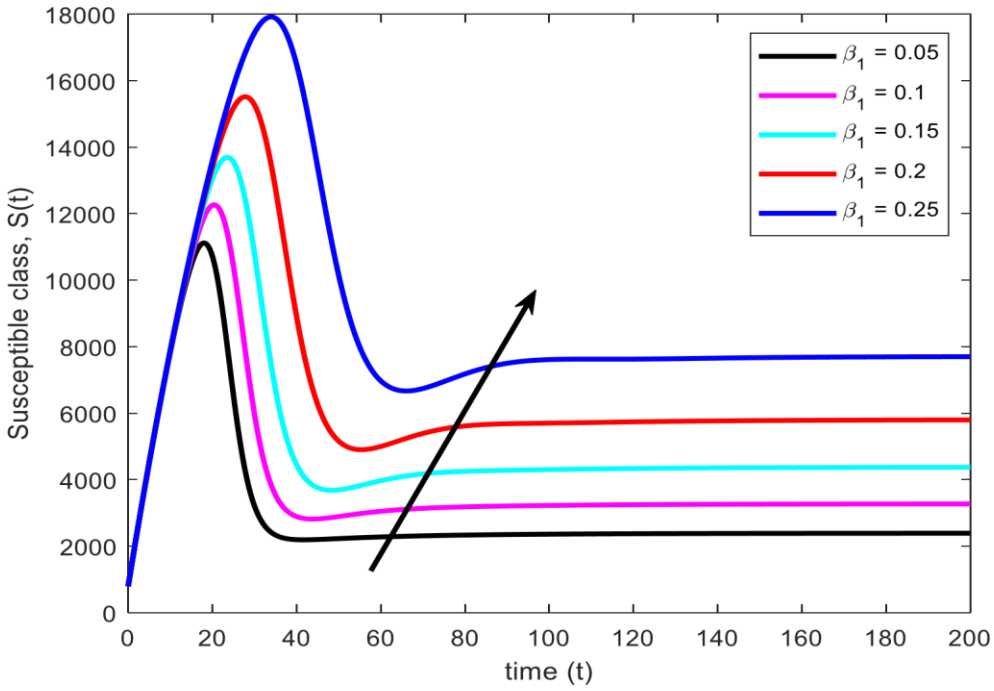

Figure 5.6: Effects of the rate at which HIV class get treated on the susceptible class

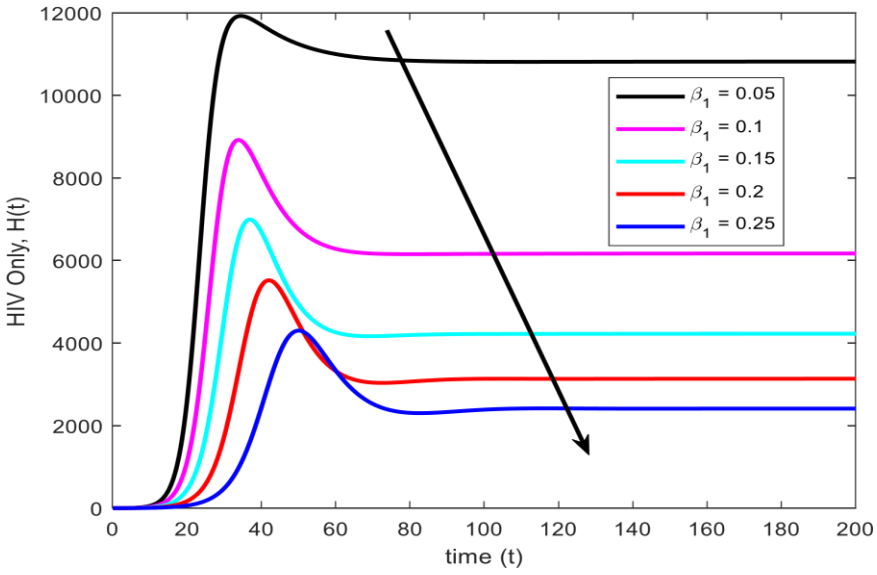

Figure 5.7: Effects of the rate at which HIV class get treated on HIV class.

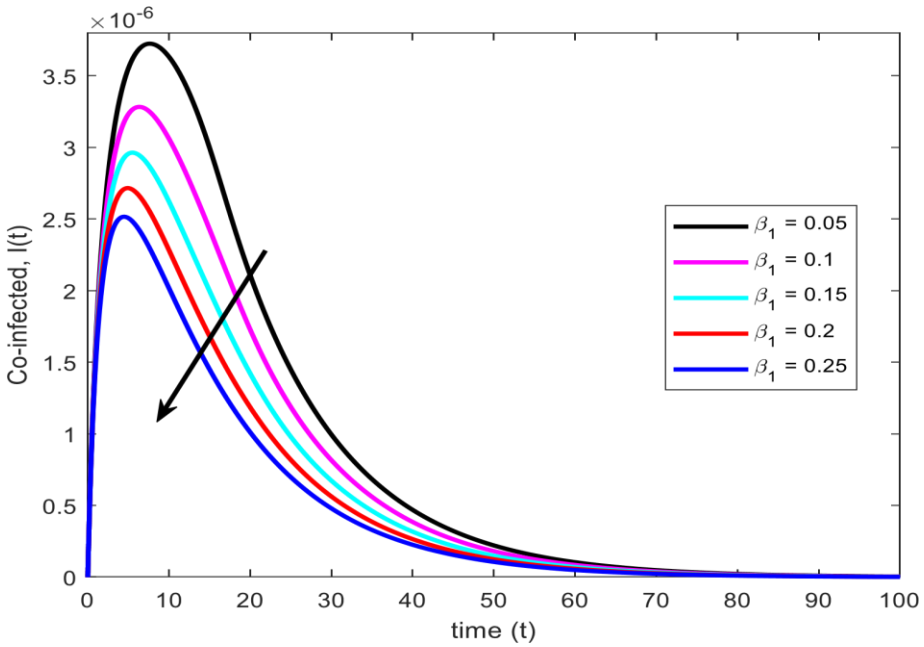

Figure 5.8: Effects of the rate at which HIV class get treated on co-infected individuals.

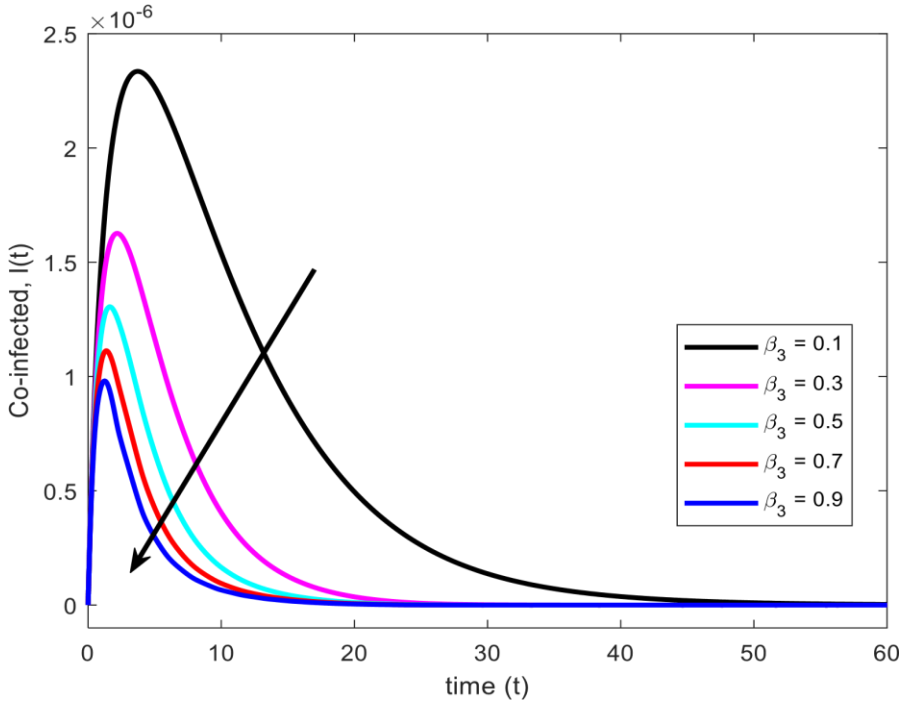

Figure 5.9: Effects of the coinfection treatment rate on the co-infected class

5.3 CONCLUSION

This work tried to investigate the response, of a population that individuals are coinfected with both HIV and Kaposi's Sarcoma diseases, to treatement by developing and analyzing a non linear mathematical model. HIV and KS affect millions of people across overlapping geo-graphic locations. The risk of transmission of both diseases can be increased because of co-infection if there no treatment and preventive measures in place. The model predicts that there is a potential increase in the HIV transmission if treatment of HIV and KS is not administered. Mathematical analysis of the model showed that the model is well posed and had a (DFE) with $E_0 = \left(\frac{\lambda}{\mu}, 0, 0, 0, 0, 0\right)$. Depending on the value of the infection rate and the death rate, the results proposed that there is existence of a unique endemic equilibrium $E_1 = (S_1, H_1, K_1, I_1 T_1, A_1)$. The infection-free equilibrium E_0 is locally asymptotically stable whenever $R_0^H < 1$ and $R_0^K < 1$. This means that KS and HIV diseases will persist in the population if the reproductive number is > 1 and it go to extinction if it is < 1.

5.4 RECOMMENDATION

HIV/AIDS and KS eradication are of concern in the developing countries. Thus, there exists a need to strengthen the control interventions and develop new ones that are more effective in combating the scourge. From the outcome of this study, it is seen that the populations of the HIV infected individuals and HIV/KS coinfected individuals decline due to an increases in the access and willingness to treatment, hence the following recommendation are proposed;

1. Co-infection of KS and HIV/AIDS program should strengthen the awareness and education campaigns with a lot of emphasis on the importance of prompt

recognition of symptoms, correct disease diagnosis, HIV screening and early commencement of ARV treatment to assist strengthen the immune response, which lowers the rate at which AIDS class progression occurs.

2. Researchers in the related field can extend the model to consider other transmission modes of HHV-8 with an aim of determining the most effective combination of antiretroviral treatment for HIV patients with KS.

5.5 FUTURE WORK

There is need to have comprehensive researches aimed at discovering effective methodological control strategies to curb the scourge of the two diseases thus analysis of the global properties and optimal control of the model should be incorporated. In future fractional differential equations instead of ordinary differential equations should be adopted.

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