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SENSITIVITY ANALYSIS OF TREATMENT AND COUNSELING IN A CO INFECTION MODEL OF HIV/AIDS, TUBERCULOSIS AND MALARIA

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ABSTRACT

This study presents a co infection deterministic model defined by a system of ordinary differential equations for HIV/AIDS, malaria and tuberculosis. The model is analyzed to investigate the potential impact of counseling and treatment on disease progression by carrying out sensitivity analysis of the reproduction number with respect to counseling and treatment. The sensitivity indices of the reproduction numbers R_H, R_{HM}, R_{HT} and R_{HMT} with respect to treatment and counseling for the HIV/AIDS individuals showed that counseling is the most sensitive parameter in controlling the co infections.

Keywords: *: HIV/AIDS - TB and Malaria, equilibria, stability, bifurcation, sensitivity, counseling, treatment.*

1. INTRODUCTION

Sensitivity analysis on mathematical disease modeling investigates the potential impact of the model parameters on disease progression by computing the partial derivatives of the reproduction number $R0$ with respect to the parameters. The basic reproduction number $R0$ is defined as the average number of secondary infections an infectious individual would cause over his infectious period in an entirely susceptible population. When $R_o < 1$; then an infectious individual is causing, on average, less than one new infection and thus the disease does not invade the population. On the other hand, when $R_o > 1$ then an infectious individual is causing, on average, more than one new infection and thus the disease invades and persist in the population. HIV/AIDS remains one of the leading causes of death in the world with its effects most devastating in sub Saharan Africa. One of the key factors that fuels the high incidence of HIV/AIDS in Sub Saharan Africa is its dual infection with malaria and tuberculosis [16].

Audu *et al*. [4] investigated the possible impact of co infections of tuberculosis and malaria on the $CD4^+$ cell counts of HIV/AIDS patients and established the following: The healthy control group recorded a median $CD4^+$ cell counts of 789 cells/ µl (789 cells per mm^3 of blood); subjects infected with HIV/AIDS only recorded a median $CD4^+$ cell counts of 386 cell/ µl; subjects co infected with HIV/AIDS and TB recorded a median $CD4^+$ cell counts of 268 cell/ µl; subjects co infected with HIV/AIDS and malaria recorded a median $CD4^+$ cell counts of 211 cell/µl and those co infected with HIV/AIDS, malaria and TB recorded the lowest median $CD4^+$ cell counts of 182 cell/µl.

This study explores the joint dynamics of the simultaneous co infections of HIV/AIDS, TB and malaria to nvestigate the potential impact of counseling and treatment on disease progression.

2. MODEL FORMULATION AND DESCRIPTION

To study the dynamics of HIV/AIDS, malaria and TB co infection, a deterministic model is formulated described by a system of ordinary differential equations. The model sub-divide the human population into the following epidemiological classes: $S_H(t)$ - Susceptible population at time t, $I_M(t)$ - Malaria infectives at time t, $I_H(t)$ - HIV cases at time t, $I_A(t)$ - AIDS cases at time t, $I_T(t)$ - TB cases at time t. $I_{HM}(t)$ - Those co infected with malaria and HIV at time t, $I_{AM}(t)$ - Those co infected with malaria and AIDS at time t, $I_{MT}(t)$ - Those co infected with malaria and TB at time t, $I_{HT}(t)$ - Those co infected with HIV and TB at time t, $I_{AT}(t)$ - Those co infected with AIDS and TB at time t, $I_{HMT}(t)$ - Those co infected with HIV, Malaria and TB at time t, $I_{AMT}(t)$ - Those co infected with AIDS, Malaria and TB at time t. The total human population ($N_H(t)$) is therefore denoted by: $N_H(t) = S_H(t) + I_M(t) + I_H(t) + I_A(t) + I_T(t) + I_{HM}(t) + I_{AM}(t) + I_{MT}(t) + I_{HT}(t) + I_{AT}(t) + I_{HMT}(t) + I_{AMT}(t)$.

The vector (mosquito) population at time t denoted by $N_V(t)$ is sub-divided into the following classes: $S_V(t)$ - Vector susceptibles at time t, $I_V(t)$ – Vector infectives at time t. The total vector population $N_V(t)$ is given by $N_V(t) = S_V(t) + I_V(t)$.

2.1 DEFINITION OF PARAMETERS

It is assumed that susceptible humans are recruited into the population at a constant rate either by birth or recovery from malaria and TB. They acquire infection with either HIV/AIDS, malaria or TB and move to the infectious classes. Susceptible mosquitoes are recruited into the mosquito population at a constant rate. They acquire malaria infection following a blood meal feeding on infected malaria humans, becomes infectious and move to the infectious class.

The recruitment rate of humans into the susceptible population is denoted by Λ_H while that of vectors (mosquitoes) is denoted by Λ_V and are both assumed to be constant. The natural death rate of humans is given by d_n while that of vectors is given by d_v. The death rates due to AIDS, malaria and TB in humans are da, d_m and d_t respectively. The parameters d_{am}, d_{mt}, d_{at} and d_{amt} account for the combined death rates in the I_{AM}, I_{MT}, I_{AT} and I_{AMT} classes respectively. The parameters r_m and r_t are the recovery rates from malaria and TB respectively due to effective treatment. It is assumed that the recovered individuals do not acquire temporary immunity to either or both diseases thus become susceptible again. The model assumes that susceptible humans cannot simultaneously get infected with malaria, HIV/AIDS and TB since the transmission mechanics are completely different for the three diseases. The model further assumes that humans acquire HIV/AIDS through sexual contacts between an infective and a susceptible.

The average force of infection for HIV/AIDS denoted λ_{ah} is given by

$$\lambda_{ah} = \frac{\beta_a(1-\delta)c_1(I_H + I_{HM} + I_{HT})}{N_H} \qquad (2.1.1)$$

where βa is the average transmission probability of HIV/AIDS between an infective and a susceptible per sexual contact and c_1 is the per capita number of sexual contacts of susceptible humans with HIV/AIDS infected individuals per unit time. The parameter δ measures the effectiveness of counseling through condom use and a reduction in the number of sexual partners, where $0 \leq \delta \leq 1$. Effective counseling reduces the value of the parameter c_1.

The model assumes that the classes I_{HMT}, I_A, I_{AM}, I_{AT} and I_{AMT} do not transmit the virus due to acute ill health and noticeable AIDS symptoms. Define α_1 as the number of bites per human per mosquito (biting rate of mosquitoes), β_m as the transmission probability of malaria in humans per bite thus the force of infection with malaria for humans, denoted λ_{mh} is given by

$$\lambda_{mh} = \frac{\alpha_1\beta_m I_V}{N_H} \qquad (2.1.2)$$

whereas the average force of infection with malaria for vectors, denoted λ_{mv} is given by

$$\lambda_{mv} = \frac{\alpha_1\beta_v(I_M + I_{HM} + I_{MT} + I_{AM} + I_{HMT} + I_{AMT})}{N_H} \qquad (2.1.3)$$

where β_v is the transmission probability of malaria in vectors from any infected human. Finally the average force of infection for TB denoted λ_{th} is given by

$$\lambda_{th} = \frac{\beta_t c_2(I_T + I_{HT} + I_{MT} + I_{HMT} + I_{AMT} + I_{AT})}{N_H} \qquad (2.1.4)$$

where β_t is the transmission probability of TB in humans and c_2 is the average per capita contact rate of susceptible humans with TB infected individuals. The rate of progression from HIV to AIDS for the untreated HIV cases is p. The parameters $\theta_1 p$, $\theta_2 p$ and $\theta_3 p$ account for increased rates of progression to AIDS for individuals co infected with HIV - TB, HIV - malaria and HIV malaria - TB respectively where $\theta_1 < \theta_2 < \theta_3$.

Define α as the proportion of the HIV/AIDS infectives receiving effective treatment. This involves the administration of ARV'S that keeps the HIV patients from progressing to AIDS while transferring the AIDS patients back to the HIV classes. The modification parameters e^h_m, e^h_t and e^h_{mt} account for the reduced susceptibility to infection with HIV for individuals in the I_M, I_T and the I_{MT} classes respectively due to reduced sexual activity as a

result of ill health where $e_m^h < 1$, $e_t^h < 1$, $e_{mt}^h << 1$. The parameters e_a^m, e_h^m, e_{ht}^m, e_{at}^m, account for the increased susceptibility to infection with malaria for individuals already infected with AIDS, HIV, HIV - TB and AIDS - TB respectively due to suppressed immune system where $e_a^m > 1$, $e_h^m > 1$, $e_{ht}^m > 1$, $e_{at}^m > 1$. It is also clear that $e_a^m < e_{at}^m$ and $e_h^m < e_{ht}^m$. The parameters e_h^t, e_a^t, e_{mh}^t and e_{am}^t account for the increased susceptibility to infection with TB for individuals already infected with HIV, AIDS, HIV - malaria and AIDS - malaria respectively due to suppressed immune system where $e_h^t > 1$, $e_a^t > 1$, $e_{hm}^t > 1$, $e_{am}^t > 1$. Again $e_h^t < e_{hm}^t$ and $e_a^t < e_{am}^t$. Malaria and TB does not lead to the depletion of the $CD4^+$ cell counts, however their association with HIV/AIDS leads to a significant reduction in the $CD4^+$ cell counts within an individual leading to faster progression to AIDS. Combining all the aforementioned assumptions and definitions, the model for the transmission dynamics of HIV/AIDS, TB and malaria is given by the following system of differential equations.

2.2 THE MODEL EQUATIONS

$$\begin{aligned}
\frac{dS_H(t)}{dt} &= \Lambda_H + r_m I_M(t) + r_t I_T(t) - \lambda_{ah} S_H(t) \qquad (2.2.1)\\
&\quad -\lambda_{mh} S_H(t) - \lambda_{th} S_H(t) - d_n S_H(t)\\
\frac{dI_M(t)}{dt} &= \lambda_{mh} S_H(t) + r_t I_{MT}(t) - r_m I_M(t) - e_m^h \lambda_{ah} I_M(t)\\
&\quad -\lambda_{th} I_M(t) - d_n I_M(t) - d_m I_M(t).\\
\frac{dI_H(t)}{dt} &= \lambda_{ah} S_H(t) + r_m I_{HM}(t) + r_t I_{HT}(t) - (1-\alpha) p I_H(t)\\
&\quad -e_h^m \lambda_{mh} I_H(t) - e_h^t \lambda_{th} I_H(t) - d_n I_H(t) + \alpha I_A(t).\\
\frac{dI_A(t)}{dt} &= (1-\alpha) p I_H(t) + r_m I_{AM}(t) + r_t I_{AT}(t) - e_a^m \lambda_{mh} I_A(t)\\
&\quad -e_a^t \lambda_{th} I_A(t) - d_a I_A(t) - d_n I_A(t) - \alpha I_A(t)\\
\frac{dI_T(t)}{dt} &= \lambda_{th} S_H(t) + r_m I_{MT}(t) - e_t^a \lambda_{ah} I_T(t) - \lambda_{mh} I_T(t)\\
&\quad -d_n I_T(t) - d_t I_T(t) - r_t I_T(t)\\
\frac{dI_{MH}(t)}{dt} &= e_h^m \lambda_{mh} I_H(t) + e_m^a \lambda_{ah} I_M(t) + r_t I_{HMT}(t) - r_m I_{HM}(t) - e_{hm}^t \lambda_{th} I_{HM}(t) +\\
&\quad \alpha I_{AM}(t) - d_m I_{HM}(t) - (1-\alpha)\theta_2 p I_{HM}(t) - d_n I_{HM}(t)\\
\frac{dI_{AM}(t)}{dt} &= (1-\alpha)\theta_2 p I_{HM}(t) + e_a^m \lambda_{mh} I_A(t) - r_m I_{AM}(t) - d_m I_{AM}(t) - \alpha I_{AM}(t)\\
&\quad +r_t I_{AMT}(t) - e_{am}^t \lambda_t I_{AM}(t) - d_n I_{AM}(t) - d_a I_{AM}(t) - d_{am} I_{AM}(t).\\
\frac{dI_{MT}(t)}{dt} &= \lambda_{th} I_M(t) + \lambda_{mh} I_T(t) - r_m I_{MT}(t) - e_{mt}^a \lambda_{ah} I_{MT}(t) - r_t I_{MT}(t)\\
&\quad -d_m I_{MT}(t) - d_n I_{MT}(t) - d_t I_{MT}(t) - d_{mt} I_{MT}.
\end{aligned}$$

$$
\begin{aligned}
\frac{dI_{HT}(t)}{dt} &= e_t^a\lambda_{ah}I_T(t) + r_mI_{HMT}(t) + e_h^t\lambda_{th}I_H(t) - e_{ht}^m\lambda_{mh}I_{HT}(t) - (1-\alpha)\theta_1pI_{HT}(t) \\
&\quad -d_nI_{HT}(t) - d_tI_{HT}(t) - r_tI_{HT}(t) + \alpha I_{AT}(t) \\
\frac{dI_{AT}(t)}{dt} &= e_a^t\lambda_tI_A(t) + r_mI_{AMT}(t) + (1-\alpha)\theta_1pI_{HT}(t) - \alpha I_{AT}(t) \\
&\quad -e_{at}^m\lambda_{mh}I_{AT}(t) - d_nI_A(t) - d_aI_{AT}(t) - d_tI_{AT}(t) - r_tI_{AT}(t) - d_{at}I_{AT} \\
\frac{dI_{HMT}(t)}{dt} &= e_{ht}^m\lambda_mI_{HT}(t) + e_{hm}^t\lambda_{th}I_{HM}(t) + e_{mt}^a\lambda_{ah}I_{MT}(t) + \alpha I_{AMT}(t) \\
&\quad -r_mI_{HMT}(t) - d_mI_{HMT}(t) - d_nI_{HMT}(t) \\
&\quad -(1-\alpha)\theta_3pI_{HMT}(t) - d_tI_{HMT}(t) - r_tI_{HMT}(t) - d_{mt}I_{HMT} \\
\frac{dI_{AMT}(t)}{dt} &= e_{at}^m\lambda_{mh}I_{AT}(t) + e_{am}^t\lambda_{th}I_{AM}(t) + (1-\alpha)\theta_3pI_{HMT}(t) \\
&\quad -r_mI_{AMT}(t) - d_mI_{AMT}(t) - d_aI_{AMT}(t) - \alpha I_{AMT}(t) \\
&\quad -d_nI_{AMT}(t) - d_tI_{AMT}(t) - r_tI_{AMT}(t) - d_{amt}I_{AMT} \\
\frac{dS_V(t)}{dt} &= \Lambda_V - \lambda_{mv}S_V(t) - d_vS_V(t) \\
\frac{dI_V(t)}{dt} &= \lambda_{mv}S_V(t) - d_vI_V(t).
\end{aligned}
$$

2.3 POSITIVITY AND BOUNDEDNESS OF SOLUTIONS

The model system 2.2.1 describes living populations therefore the associated state variables are non-negative for all time t > 0. The solutions of this model with positive initial data therefore remain positive for all time t > 0.

Lemma 2.1. *Let the initial data set be* $\{(S_H(0), S_V(0) > 0), (I_M(0), I_H(0), I_A(0), I_T(0), I_{HM}(0), I_{AM}(0), I_{MT}(0), I_{HT}(0), I_{AT}(0), I_{HMT}(0), I_{AMT}(0), I_V(0))\} \in \Psi$. *Then the solution set* $\{(S_H, S_V, I_M, I_H, I_A, I_T\ I_{HM}, I_{AM}, I_{MT}, I_{HT}, I_{AT}, I_{HMT}, I_{AMT}, I_V\}(t)$ *is positive for all time* $t > 0$.

Proof. Consider the first equation of 2.2.1 at time t

$$\frac{dS_H}{dt} = \Lambda_H + r_mI_M + r_tI_T - \lambda_{ah}S_H - \lambda_{mh}S_H - \lambda_{th}S_H - d_nS_H$$

then

$$\frac{dS_H}{dt} \geq -(\lambda_{ah} + \lambda_{mh} + \lambda_{th} + d_n)S_H$$

$$\int \frac{dS_H}{S_H} \geq -\int(\lambda_{ah} + \lambda_{mh} + \lambda_{th} + d_n)d(t)$$

$$S_H(t) \geq S_H(0)e^{-\int(\lambda_{ah}+\lambda_{mh}+\lambda_{th}+d_n)d(t)} \geq 0$$

From the second equation of 2.2.1 at time t

$$\frac{dI_M}{dt} = \lambda_{mh}S_H + r_tI_{TM} - r_mI_M - e_m^a\lambda_{ah}I_M - \lambda_{th}I_M - d_nI_M - d_mI_M.$$

then

$$\frac{dI_M}{dt} \geq -(r_m + e_m^a \lambda_{ah} + \lambda_{th} + d_n + d_m) I_M.$$

$$\frac{dI_M}{I_M} \geq -\int (r_m + e_m^a \lambda_{ah} + \lambda_{th} + d_n + d_m) dt.$$

$$I_M(t) \geq I_M(0) e^{-\int (r_m + e_m^a \lambda_{ah} + \lambda_{th} + d_n + d_m) dt} \geq 0.$$

We can proceed in a similar manner and show that all the state variables are positive for all time t.

Lemma 2.2. *The solutions of the model 2.2.1 are uniformly bounded in a proper subset* $\Psi = \Psi_H \times \Psi_V$

Proof. Let $\{(S_H, I_M, I_H, I_A, I_T\, I_{HM}, I_{AM}, I_{MT}, I_{HT}, I_{AT}, I_{HMT}, I_{AMT}\}(t) \in \mathbb{R}_+^{12}$,

be any solution with non-negative initial conditions. The rate of change of the total human population with time is given by:

$$\frac{dN_H}{dt} = \Lambda_H - d_n N_H - (I_M + I_{HM}(t) + I_{AM} + I_{MT} + I_{HMT} + I_{AMT}) d_m -$$

$$(I_T + I_{MT} + I_{HT} + I_{AT} + I_{HMT} + I_{AMT}) d_t - (I_A + I_{AM} + I_{AT} + I_{AMT}) d_a$$

$$-d_{am} I_{AM} - d_{mt}(I_{MT} + I_{HMT}) - d_{at} I_{AT} - d_{amt} I_{AMT}$$

The model system 2.2.1 has a varying human population size $\frac{dN_H}{dt} \neq 0$ and therefore a trivial equilibrium is not feasible. Whenever $N_H > \frac{\Lambda_H}{d_n}$, then $\frac{dN_H}{dt} < 0$. Since $\frac{dN_H}{dt}$ is bounded by $\Lambda_H - d_n N_H$, a standard comparison theorem by (Birkoff and Rota, 1989) shows that $0 \leq N_H(t) \leq N_H(0) e^{-d_n} + \frac{\Lambda_H}{d_n}(1 - e^{-d_n})$, where $N_H(0)$ represents the value of $N_H(t)$ evaluated at the initial values of the respective variables. Thus as $t \to \infty$, we have, $0 \leq N_H(t) \leq \frac{\Lambda_H}{d_n}$. In particular, $N_V(t) \leq \frac{\Lambda_H}{d_n}$, if $N_0 \leq \frac{\Lambda_H}{d_n}$. This shows that N_H is bounded and all the feasible solutions of the human only component of model 2.2.1 starting in the region Ψ_H approach, enter or stay in the region, where:

$$\Psi_H = \{(S_H, I_M, I_H, I_A, I_T, I_{MH}, I_{MA}, I_{MT}, I_{HT}, I_{TA}, I_{MHT}, I_{MAT}) : N(t) \leq \frac{\Lambda_H}{d_n}\}.$$

Similarly let $\{(S_V, I_V\}(t) \in \mathbb{R}_+^2$, be any solution with non-negative initial conditions. The rate of change of the total vector population with time is given by:

$\frac{dN_V}{dt} = \Lambda_V - (S_V(t) - I_V(t))d_v$. $\frac{dN_V}{dt} \neq 0$ and therefore a trivial equilibrium is not feasible. Whenever $N_V > \frac{\Lambda_V}{d_v}$, then $\frac{dN_V}{dt} < 0$. Since $\frac{dN_V}{dt}$ is bounded by $\Lambda_V - d_v N_V$, a standard comparison theorem by Birkoff and Rota (1989), shows that $0 \leq N_V(t) \leq N_V(0)e^{-d_v} + \frac{\Lambda_V}{d_v}(1 - e^{-d_v})$, where $N_V(0)$ represents the value of $N_V(t)$ evaluated at the initial values of the respective variables. Thus as $t \to \infty$, $0 \leq N_V(t) \leq \frac{\Lambda_V}{d_v}$. In particular, $N(t) \leq \frac{\Lambda_V}{d_v}$, if $N_0 \leq \frac{\Lambda_V}{d_v}$. This shows that N_V is bounded and all the feasible solutions of the vector only component of model 2.2.1 starting in the region Ψ_V approach, enter or stay in the region, where: $\Psi_V = \{(S_V, I_V) : N_V \leq \frac{\Lambda_V}{d_v}\}$. $\square$.

2.4. LOCAL STABILITY OF THE DISEASE FREE EQUILIBRIUM

In the absence of infection by all the diseases, the model 2.2.1, has a steady-state solution called the disease-free equilibrium (DFE) given by

$$\mathcal{E}_0^{htm} = (S_H, I_M, I_H, I_A, I_T, I_{MH}, I_{MA}, I_{MT}, I_{HT}, I_{TA}, I_{MHT}, I_{MAT}, S_V, I_V) = (\frac{\Lambda_H}{d_n}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Lambda_V}{d_v}, 0).$$

Define F_i as the rate of appearance of new infections in the class or compartment i and $V_i = (V_i^- - V_i^+)$, where V_i^- is the rate of transfer of individuals out of compartment i, and V_i^+ is the rate of transfer of individuals into compartment i by all other means. Therefore: The Jacobian of F_i and V_i at the disease-free equilibrium denoted by F and V respectively is given by:

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_1\beta_m \\ 0 & a_1 & 0 & 0 & a_1 & 0 & 0 & a_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_t c_2 & 0 & 0 & \beta_t c_2 & \beta_t c_2 & \beta_t c_2 & \beta_t c_2 & \beta_t c_2 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \alpha_1\beta_v & 0 & 0 & 0 & \alpha_1\beta_v & \alpha_1\beta_v & \alpha_1\beta_v & 0 & 0 & \alpha_1\beta_v & \alpha_1\beta_v & 0 \end{pmatrix}$$

where: $a_1 = \beta_a(1 - \delta)c_1$

$$V = \begin{pmatrix} u_1 & 0 & 0 & 0 & 0 & 0 & -r_t & 0 & 0 & 0 & 0 & 0 \\ 0 & u_2 & -\alpha & 0 & -r_m & 0 & 0 & -r_t & 0 & 0 & 0 & 0 \\ 0 & z_1 & u_3 & 0 & 0 & -r_m & 0 & 0 & -r_t & 0 & 0 & 0 \\ 0 & 0 & 0 & u_4 & 0 & 0 & -r_m & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & u_5 & -\alpha & 0 & 0 & 0 & -r_t & 0 & 0 \\ 0 & 0 & 0 & 0 & z_2 & u_6 & 0 & 0 & 0 & 0 & -r_t & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & u7 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & u_8 & -\alpha & -r_m & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & z_3 & u_9 & 0 & -r_m & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & u_{10} & -\alpha & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & z_4 & u_{11} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & d_v \end{pmatrix}$$

where $z_1 = -(1-\alpha)p,\ z_2 = -(1-\alpha)\theta_2 p,\ z_3 = -(1-\alpha)\theta_1 p,\ z_4 = -(1-\alpha)\theta_3 p, , u_1 = r_m + d_n + d_m,\ u_2 = (1-\alpha)p + d_n,\ u_3 = \alpha + d_a + d_n,\ u_4 = d_n + d_t + r_t,\ u_5 = r_m + d_m + (1-\alpha)\theta_2 p + d_n,\ u_6 = r_m + d_m + \alpha + d_n + d_a + d_{am},\ u_7 = r_m + r_t + d_m + d_n + d_t + d_{mt},\ u_8 = (1-\alpha)\theta_1 p + d_n + d_t + r_t,\ u_9 = \alpha + d_n + d_{at} + d_t + r_t,\ u_{10} = r_m + d_m + d_n + (1-\alpha)\theta_3 p + d_t + r_t + d_{mt},\ u_{11} = r_m + d_m + d_a + \alpha + d_n + d_t + r_t + d_{amt}$

The basic reproduction number $R_0 = R_{HMT}$ is the maximum value of the spectral radius of the matrix FV^{-1} and is given by $R_{HMT} = \max\{R_M, R_H, R_T\}$. Where:

$$R_M = \frac{\alpha_1 \sqrt{\beta_m \beta_v}}{\sqrt{d_m d_v + d_n d_v + d_v r_m}} \tag{2.4.1}$$

$$R_T = \frac{\beta_t c_2}{d_n + d_t + r_t} \tag{2.4.2}$$

$$R_H = \frac{c_1(1-\delta)(\alpha + d_a + d_n)\beta_a}{(\alpha d_n + d_a d_n + d_n^2 + d_a p - \alpha d_a p + d_n p - \alpha d_n p)} \tag{2.4.3}$$

2.5. PARAMETER VALUES FOR THE HIV/AIDS, TB AND MALARIA MODEL

Symbol	Parameter	Value (day^{-1})	Source
Λ_H	Recruitment rate of humans	4.38356×10^4	Kenya demographics profile (2014)
d_n	Natural death rate of humans	4.56630×10^{-5}	Kenya demographics profile (2014)
d_a	HIV/AIDS-induced death rate	1.09589×10^{-3}	WHO report (2014)
p	Progresion rate from HIV to AIDS (untreated)	2.73972×10^{-3}	Baryama, F. and Mugisha, T. (2007)
α	Proportion of the HIV/AIDS victims treated	1.64384×10^{-3}	Kenya NACC report (2014)
β_a	Transmission probability of HIV/AIDS	0.019	Baryama, F. and Mugisha, T. (2007)
c_1	Per capita number of sexual contacts	2.46575×10^{-2}	Kenya NACC report (2014)
δ	Effectiveness of counseling	Variable	
r_m	Proportion of malaria victims treated	1.86301×10^{-3}	WHO report (2013)
d_m	Death rate due to malaria	0.000345	Chitnis *et al* (2006)
α_1	Mosquito biting rate	0.125	Lawi *et al* (2011)
β_m	Transmission probability of malaria in humans	0.8333	Lawi *et al* (2011)
β_v	Transmission probability of malaria in vectors	(0 - 1)	Chiyaka and Dube (2007)
e_{at}^m	Increased susceptibility to malaria due to AIDS and TB co infections	10	Estimated
e_m^h	Reduced susceptibility to malaria due to reduced sexual activity	0.005	Estimated
Λ_V	Recruitment rate of vectors	6	Chiyaka and Dube (2007)
d_v	Death rate of mosquitoes	0.1429	Lawi *et al* (2011)
θ_1	Increased Progresion rate from HIV to AIDS due to TB	1.5	Estimated
θ_2	Increased Progresion rate from HIV to AIDS due to malaria	2	Estimated
θ_3	Progresion rate from HIV to AIDS due to TB and malaria	3	Estimated

Symbol	Parameter	Value (day^{-1})	Source
d_{am}	Death rate due to AIDS and malaria	0.0005175	Baryama, F. and Mugisha, T. (2007)
d_{at}	Death rate due to AIDS and tuberculosis	0.0016438356	WHO report (2013)
β_t	Transmission probability HIV of TB in humans	0.027	Juan and Castillo (2009)
c_2	contact rate of susceptible humans with TB infectives	15	Juan and Castillo (2009)
r_t	Proportion of TB victims treated	0.6	WHO report (2013)
d_{amt}	Death rate due to AIDS, malaria and TB	0.00069	Estimated
e_h^t	Increased susceptibility to TB due to AIDS infection	2.0	Estimated
e_a^t	Increased susceptibility to malaria due to HIV	6	Oluwaseun *et al* (2008)

Lemma 2.3. *The DFE of the HIV/AIDS,TB and malaria model is locally asymptotically stable (LAS) if $R_{HMT} < 1$, and unstable otherwise.*

Lemma 2.3 is illustrated numerically in figure 1 using $R_H = 0.51$, $R_T = 0.69$ and $R_M = 0.50$.

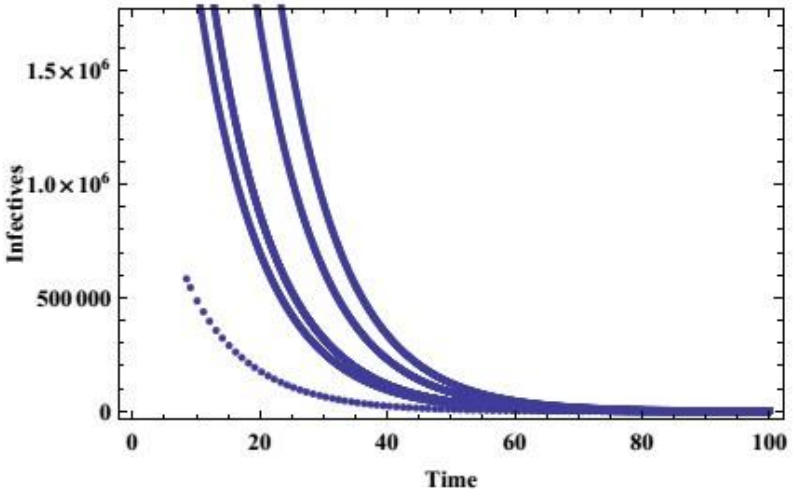

Figure 1

2.6 SENSITIVITY ANALYSIS OF TREATMENT AND COUNSELING

To investigate the potential impact of counseling and treatment on disease progression, sensitivity analysis of the repro duction numb ers with resp ect to counseling and treatment is carried out. The sensitivity index of R_H with respect to δ is given by:

$$R_H^{\delta} = -\frac{\delta}{1-\delta} \qquad (2.5.1)$$

The negative sign in equation 2.5.1 indicates that there is an expected decline in the rate of new HIV/AIDS infections when counseling is scaled up. Similarly, The sensitivity index of R_H with respect to α is given by:

$$R_H^{\alpha} = \frac{\alpha A_1\{-\frac{\beta_a c_1 A_2 A_3(1-\delta)}{A_1^2} + \frac{\beta_a c_1(1-\delta)}{A_1}\}}{\beta_a c_1 A_2(1-\delta)} \qquad (2.5.2)$$

$$A_1 = \alpha d_n + d_a d_n + d_n^2 + d_a p - \alpha d_a p + d_n p - \alpha d_n p$$
$$A_2 = \alpha + d_a + d_n$$
$$A_3 = d_n - d_a p - d_n p$$

Numerical simulations shows that the sensitivity index of R_H with respect to treatment is positive indicating that an increase in the proportions of those treated leads to an increase in new HIV cases as shown in figure 2.

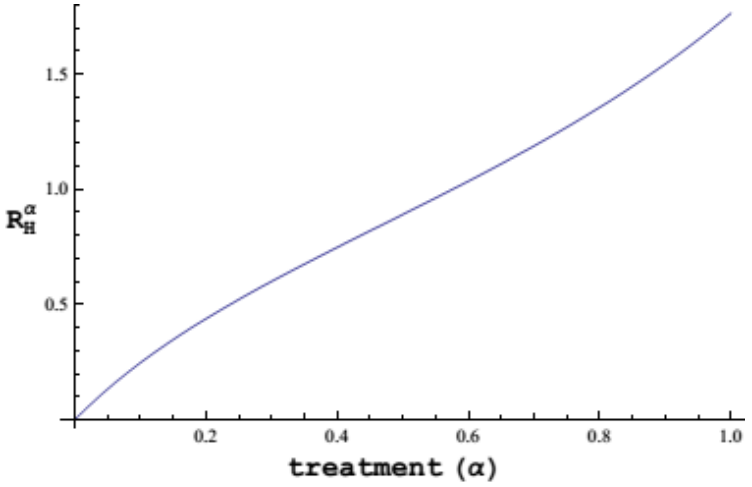

Figure 2

The sensitivity index of R_M with respect to r_m is given by

$$R_M^{r_m} = -\frac{d_v r_m}{2(d_m d_v + d_n d_v + d_v r_m)} \qquad (2.5.3)$$

.

Similarly, the sensitivity index of R_T with respect to r_t is given by

$$R_T^{r_t} = -\frac{r_t}{d_n + d_t + r_t} \qquad (2.5.4)$$

The negative sign in equations 2.5.3 and 2.5.4 indicates that there is an exp ected decline in the rate of new malaria and TB cases when treatment is scaled up. Numerical simulations using the parameter values in table 2.4.1 shows that the sensitivity index of R_H, R_M and R_T with respect to treatment and counseling yields $R_T^{rt} = -0.950226$, $R_H^{\alpha} = 0.420516$, $R_M^{r_m} = -0.413328$ and $R_H^{\delta} = -2.3333$ respectively. Assuming that $R_{HMT} = \max\{R_M, R_T, R_H\} = R_H$,

then counseling for the HIV/AIDS individuals is the most sensitive parameter for the control of HIV/AIDS, TB and malaria co infections.

3. CONCLUSION

In summery The local stability of the disease free equilibrium was investigated by Theorem 2 by Van, P. and Watmough, J. (2002). The theorem showed that the HIV/AIDS, TB and malaria co infection model have a disease free equilibrium point which is locally asymptotically stable whenever the reproduction number is less than unity. The sensitivity indices of the reproduction numbers R_H, R_{HM}, R_{HT} and R_{HMT} with respect to counseling for the HIV/AIDS individuals yields a negative sign indicating that there is an expected decline in the rate of new infections and co infections when counseling is scaled up. Similarly, the sensitivity indices of the malaria reproduction number (R_M) and the TB reproduction number R_T with respect to malaria and TB treatment yields a negative sign also indicating that there is an expected decline in the rate of new malaria and TB infections when treatment is scaled up. Numerical simulations of the sensitivity index of R_H with respect to ARV treatment yielded a positive gradient indicating that an increase in the proportions of those treated leads to an increase in new HIV cases

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