



Stability and Numerical Analysis of Malaria- mTB- HIV/AIDS Co-infection

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ABSTRACT

In this paper, we develop a mathematical model to examine the transmission dynamics of curable malaria, curable mTB and non-curable HIV/AIDS and their co-infection. The size of population has been taken as varying due to the emigration of susceptible population. The total population is divided into five subclasses as susceptible, malaria infected, mTB infected, HIV infection and AIDS by assuming co-infection among them. The model has two basic parts, qualitative and numerical. In qualitative part, we analyze the transmission dynamics of this co-infection by using equilibrium and stability analysis. In numerical part, the computational simulation is used to transmission flow of disease among various classes. The sensitive analysis is also performed.

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1. INTRODUCTION

Despite the development of antibiotics and vaccine, infectious diseases are still one of the major causes of human mortality, particularly in developing countries. The death toll in India from malaria and mTB, mycobacterium tuberculosis, is still very significant and the number of HIV infected people is quite high in India. The HIV, human immunodeficiency virus, leads to acquired immunodeficiency syndrome (AIDS). According to global report at Geneva (2004), 40 million people, worldwide, are infected with HIV, and due to this disease about 20 million people have died in last two decades. About 14000 people are newly infected each day. The disease HIV is untreatable, and only with the help of the antiretroviral therapy (ART) life span of an infected person can be increased and can remain healthy before acquired full-blown AIDS. The risk of being HIV infected can be reduced by using less risky behavior like using safety measures in sexual activities or avoiding sharing of needle for injection drug users. A good number of adults have adopted safer sexual behavior in response to the AIDS epidemic [1, 2].

Mathematical models are playing a vital role in analyzing the spread of infectious diseases among the people [3, 4] and predicting the timing and extent of infection [5].

It is observed that in developing countries mTB and malaria are very common infections occurring among HIV-positive persons. Co-infection of TB and HIV are playing leading role in deaths from infectious diseases [6]. The spread of HIV infection plays vital role in increasing the mTB infection due to break down of the immune system. A person infected with mTB may have latent or active infection. If the infection is latent then this infection will not take off the form of active disease due to the strong immune system. It may happen that a person will remain infected with latent TB for years or forever. For infectiveness of HIV - related TB, DOTS strategy has been recommended by WHO to control the TB (Tuberculosis) [7]. There are other ways to control the TB cases like reducing HIV infection by some intervention programmes, providing understanding of spreading HIV, treating the patients by HAART etc. [8]. When the susceptible individuals who are not infected with TB, get infection first, they enter into latent infection class of TB. The latent TB becomes active TB or TB disease at the rate of 0.001 per year in case of HIV negative [9-11] and in case of HIV positive latent

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TB progresses TB disease at the rate of 0.1 per year [12-15]. Persons who are re-infected with TB, only 4.9% cases of TB leads to active disease for HIV-negatives and 50% cases of Latent TB progresses to TB disease in case of HIV- positive infection [16]. The HIV cases in the population increase more rapidly in the presence of other diseases particularly mTB; to control the spread of HIV, the mTB must be treated effectively [17, 18].

The HIV infection also increases risk of developing severity of malaria [19]. In the area of high malaria transmission, the HIV infection enhances the mortality rate among severe malaria cases by 1.6 to 2.5 fold. To control the impact of HIV on malaria, HAART technique has been recommended [20]. In area of high intensity transmission, HIV-1 increases the incidence of clinical among adults [21]. The effect of HIV-1 on malaria incidence is more apparent in adults as compared to children [22]. The impact of HIV-1 on malaria in sub-Saharan African population was studied and distribution of CD4 count among HIV infected persons was modeled [23] studied an age-structured homogeneous epidemic model. The education campaigns on HIV/AIDS are much more effective to slow down the HIV epidemic [24, 25]. There is a recent literature that addresses the development of various mathematical models of infectious disease; to slow down the infection rate the different techniques viz global stability, explicit series solution, study of vaccination, bifurcation analysis etc. are used to solve the different mathematical models [26-34].

Both mTB and malaria enhances the risk of progression of HIV and decrease the survival period of patients with HIV infection. In view of this it is very relevant to study the co-infection of malaria-mTB-HIV/AIDS in the population.

Our model is extended version of ref. no. 18 (co-infection of mTB-HIV/AIDS), the addition of one compartment of malaria in the form of co-infection of malaria-mTB-HIV/AIDS make the set of equations complex.

The organization of paper is as follows. In section 2, description of the model and notations used for mathematical formulation are given. Section 3 contains governing equations and their solution in micro-vessel and tissue region. Section 4 provides equilibrium analysis. In section 5, the stability analysis is given. The numerical results are provided in section 6. Finally, in section 7, conclusions are drawn.

2. THE MATHEMATICAL FORMULATION AND NOTATIONS

The total population is divided into five classes as susceptible class of persons, treatable malaria infected population, mTB infected population, HIV infected class of persons and class of people with AIDS. Let S

(t), I_1 (t), I_2 (t), I_3 (t), and A (t) be susceptible population, malaria infected population, mTB infected population, HIV infected population and population with AIDS at time t, respectively.

We assume that susceptible individuals enter into the population from outside the system with constant immigration rate Q. The susceptible individuals become malaria infected at the rate of β_1 . The susceptible individuals contact the mTB infected individuals at the rate of β_2 and the contacted persons become mTB infected. The transmission rate per unit time between a HIV infected individual and susceptible individual is β_3 . Some malaria infected individuals get HIV infection following the contact with HIV infective at the rate β_4 and mTB infected population gets infection following the contact with HIV infective at the rate β_5 . Let ϵ be the rate at which the HIV infected individuals' progress to AIDS and α be the death rate due to AIDS. Also let d is the natural death rate from each class. λ_1 and λ_2 denote the rates at which individual leave the malaria infected class and mTB infected class respectively, due to temporary immunity and again become susceptible. We also consider that there is no co-infection of malaria and mTB but getting HIV infection, there is a co-infection of malaria-mTB-HIV/AIDS. The rate of transition diagram of infectious diseases is shown in Figure 1.

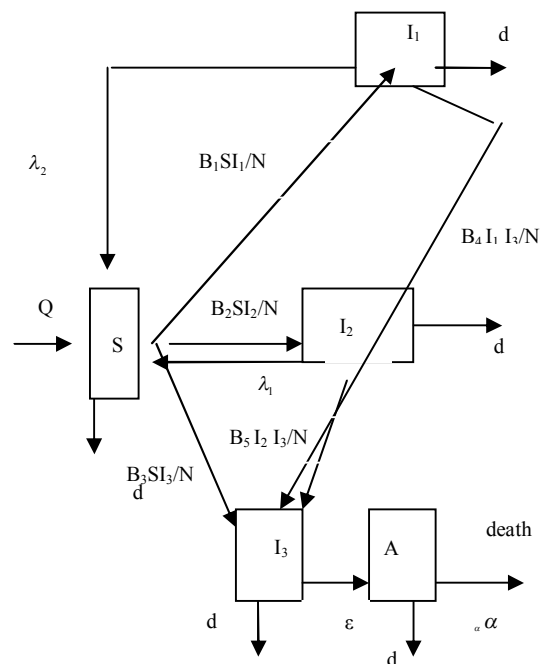


Figure 1. Graphical depiction of the transmission dynamics of the disease.

3. THE GOVERNING EQUATIONS

The transition flow of diseases among various classes is governed by the system of equations as given below:

$$\frac{dS}{dt} = Q - \frac{\beta_1 S I_1 + \beta_2 S I_2 + \beta_3 S I_3}{N} - dS + \lambda_1 I_1 + \lambda_2 I_2 \tag{1}$$

$$\frac{dI_1}{dt} = \frac{\beta_1 S I_1}{N} - \frac{\beta_4}{N} I_1 I_3 - dI_1 - \lambda_1 I_1 \tag{2}$$

$$\frac{dI_2}{dt} = \frac{\beta_2 S I_2}{N} - \frac{\beta_5}{N} I_2 I_3 - dI_2 - \lambda_2 I_2 \tag{3}$$

$$\frac{dI_3}{dt} = \frac{\beta_3 S I_3}{N} + \frac{\beta_4}{N} I_1 I_3 + \frac{\beta_5}{N} I_2 I_3 - dI_3 - \epsilon I_3 \tag{4}$$

$$\frac{dA}{dt} = \epsilon I_3 - dA - \alpha A \tag{5}$$

The total population at time t is denoted by $N(t) = S(t) + I_1(t) + I_2(t) + I_3(t) + A(t)$ and Equations (1)-(5) can be written as:

$$\frac{dN}{dt} = Q - dN - \alpha A \tag{6}$$

$$\frac{dI_1}{dt} = \frac{\beta_1(N - I_1 - I_2 - I_3 - A)}{N} I_1 - \frac{\beta_4}{N} I_1 I_3 - dI_1 - \lambda_1 I_1 \tag{7}$$

$$\frac{dI_2}{dt} = \frac{\beta_2(N - I_1 - I_2 - I_3 - A)}{N} I_2 - \frac{\beta_5}{N} I_2 I_3 - dI_2 - \lambda_2 I_2 \tag{8}$$

$$\frac{dI_3}{dt} = \frac{\beta_3(N - I_1 - I_2 - I_3 - A)}{N} I_3 + \frac{\beta_4}{N} I_1 I_3 + \frac{\beta_5}{N} I_2 I_3 - dI_3 - \epsilon I_3 \tag{9}$$

$$\frac{dA}{dt} = \epsilon I_3 - dA - \alpha A \tag{10}$$

4. EQUILIBRIUM ANALYSIS

$$Q - dN - \alpha A = 0 \tag{11}$$

$$\frac{\beta_1(N - I_1 - I_2 - I_3 - A)}{N} I_1 - \frac{\beta_4}{N} I_1 I_3 - dI_1 - \lambda_1 I_1 = 0 \tag{12}$$

$$\frac{\beta_2(N - I_1 - I_2 - I_3 - A)}{N} I_2 - \frac{\beta_5}{N} I_2 I_3 - dI_2 - \lambda_2 I_2 = 0 \tag{13}$$

$$\frac{\beta_3(N - I_1 - I_2 - I_3 - A)}{N} I_3 + \frac{\beta_4}{N} I_1 I_3 + \frac{\beta_5}{N} I_2 I_3 - dI_3 - \epsilon I_3 = 0 \tag{14}$$

$$\epsilon I_3 - dA - \alpha A = 0 \tag{15}$$

4. 1. Theorem 1. There are seven equilibrium values or points:

(I) Equilibrium when population is free from the disease.

$$P_0\left(\frac{Q}{d}, 0, 0, 0, 0\right)$$

The equilibrium point is obtained.

(II) When the population is malaria infected only. In this case $I_2 = I_3 = A = 0$, as such the equilibrium point is given by

$$P_1\left(\frac{Q}{d}, \frac{Q}{d\beta_1}(\beta_1 - (d + \lambda_1)), 0, 0, 0\right)$$

It is possible only when $\beta_1 > (d + \lambda_1)$

(III) When the population is mTB infected only. For this case $I_1 = I_3 = A = 0$, thus equilibrium point is:

$$P_2\left(\frac{Q}{d}, 0, \frac{Q}{d\beta_2}(\beta_2 - (d + \lambda_2)), 0, 0\right)$$

This case exists only if $\beta_2 > (d + \lambda_2)$

(IV) When the population is HIV infected but free from malaria and mTB, the equilibrium point is-

$$P_3(N, 0, 0, I_3, A)$$

where

$$N = \frac{1}{d}\left(Q - \frac{\alpha\epsilon}{\alpha + d} I_3\right), A = \frac{\epsilon}{d + \alpha} I_3$$

$$I_3 = \frac{\frac{Q}{\beta_3}(d + \alpha)(\beta_3 - (d + \epsilon))}{d(d + \alpha + \epsilon) + \alpha\epsilon(\beta_3 - (d + \epsilon))}$$

This case exists only if $\beta_3 > (d + \epsilon)$.

(V) When the population is free from mTB but co-infection of malaria-HIV prevails. The equilibrium point for this case is:

$$P_4(N, I_1, 0, I_3, A)$$

where

$$N = \frac{1}{d}\left(Q - \frac{\alpha\epsilon}{\alpha + d} I_3\right), A = \frac{\epsilon}{d + \alpha} I_3,$$

$$I_1 = \frac{\frac{Q}{d}(\beta_1 - (d + \lambda_1)) - \left(\frac{\alpha\epsilon}{d(d + \alpha)}(\beta_1 - (d + \lambda_1)) + \beta_4 + \frac{\alpha + d + \epsilon}{\alpha + d} \beta_1\right) I_3}{\beta_1}$$

The equilibrium point P_4 exists if:

$$\beta_1 > (d + \lambda_1), \beta_2 > (d + \lambda_2), \beta_3 > (d + \epsilon),$$

$$(\beta_3 - (d + \epsilon)) - \frac{\beta_3 - \beta_4}{\beta_1}(\beta_1 - (d + \lambda_1)) > 0$$

$$\frac{\beta_3 - \beta_4}{\beta_1} \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_1 - (d+\lambda_1)) + \beta_4 + \frac{\alpha+d+\varepsilon}{\alpha+d} \beta_1 \right) + \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_3 - (d+\varepsilon)) + \beta_3 \frac{d+\alpha+\varepsilon}{d+\alpha} \right) > 0$$

(VI) When the population is malaria infection free but co-infection of mTB-HIV exists. Then the equilibrium point is:

$$P_5(N, 0, I_2, I_3, A)$$

$$N = \frac{1}{d} \left(Q - \frac{\alpha \varepsilon}{\alpha+d} I_3 \right), \quad A = \frac{\varepsilon}{d+\alpha} I_3,$$

$$I_2 = \frac{\frac{Q}{d} (\beta_2 - (d+\lambda_2)) - \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_2 - (d+\lambda_2)) + \beta_5 + \frac{\alpha+d+\varepsilon}{\alpha+d} \beta_2 \right) I_3}{\beta_2}$$

$$I_3 = \frac{Q \left[(\beta_3 - (d+\varepsilon)) - \frac{\beta_3 - \beta_4}{\beta_1} (\beta_1 - (d+\lambda_1)) \right]}{d \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_1 - (d+\lambda_1)) + \beta_4 + \frac{\alpha+d+\varepsilon}{\alpha+d} \beta_1 \right) + \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_3 - (d+\varepsilon)) + \beta_3 \frac{d+\alpha+\varepsilon}{d+\alpha} \right)}$$

In this case P_5 is positive only when,

$$\beta_1 > (d+\lambda_1), \quad \beta_2 > (d+\lambda_2), \quad \beta_3 > (d+\varepsilon),$$

$$(\beta_3 - (d+\varepsilon)) - \frac{\beta_3 - \beta_4}{\beta_1} (\beta_1 - (d+\lambda_1)) > 0$$

$$\frac{\beta_3 - \beta_4}{\beta_1} \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_2 - (d+\lambda_2)) + \beta_5 + \frac{\alpha+d+\varepsilon}{\alpha+d} \beta_2 \right) + \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_3 - (d+\varepsilon)) + \beta_3 \frac{d+\alpha+\varepsilon}{d+\alpha} \right) > 0$$

and

$$\frac{Q}{d} (\beta_2 - (d+\lambda_2)) - \left(\frac{\alpha \varepsilon}{d(d+\alpha)} (\beta_2 - (d+\lambda_2)) + \beta_5 + \frac{\alpha+d+\varepsilon}{\alpha+d} \beta_2 \right) I_3 > 0$$

(VII) When co-infection of malaria-mTB-HIV exists In this case also, we consider that malaria infected population is not immigrated, so that the equilibrium point is:

$$P_6(N^*, I_m^*, I_t^*, I_h^*, A^*)$$

where

$$N^* = \frac{1}{d} \left(Q - \frac{\alpha \varepsilon}{\alpha+d} I_3^* \right), \quad A^* = \frac{\varepsilon}{d+\alpha} I_3^*,$$

$$I_1^* = \frac{\frac{Q}{d} R_1 - \beta_1 I_2^* - (DR_1 + \beta_1 D_1 + \beta_4) I_3^*}{\beta_1}$$

$$I_2^* = \frac{\frac{Q}{d} \left(R_3 + \frac{\beta_4 - \beta_3}{\beta_1} R_1 \right) - \left[D \left(R_1 + \frac{\beta_4 - \beta_3}{\beta_1} R_3 \right) + D_1 \beta_5 + \beta_4 \frac{\beta_3 - \beta_4}{\beta_1} \right] I_3^*}{\beta_4 - \beta_3}$$

$$I_3^* = \frac{\frac{Q}{d} \left(R_2 - \frac{\beta_2}{\beta_1} R_1 \right)}{(DR_2 + \beta_2 D_1 + \beta_5) - \frac{\beta_2}{\beta_1} (DR_1 + \beta_1 D_1 + \beta_4)}$$

Where

$$R_1 = \beta_1 - (d+\lambda_1), \quad R_2 = \beta_2 - (d+\lambda_2), \quad R_3 = \beta_3 - (d+\varepsilon),$$

$$D = \frac{\alpha \varepsilon}{d(\alpha+d)} \quad \text{and} \quad D_1 = \frac{d+\alpha+\varepsilon}{\alpha+d}$$

The equilibrium point P_6 positive only when

$$\beta_1 > (d+\lambda_1), \quad \beta_2 > (d+\lambda_2), \quad \beta_3 > (d+\varepsilon),$$

$$\frac{Q}{d} R_1 - \beta_1 I_2^* - (DR_1 + \beta_1 D_1 + \beta_4) I_3^* > 0,$$

$$\frac{Q}{d} \left(R_3 + \frac{\beta_4 - \beta_3}{\beta_1} R_1 \right) - \left[D \left(R_1 + \frac{\beta_4 - \beta_3}{\beta_1} R_3 \right) + D_1 \beta_5 + \beta_4 \frac{\beta_3 - \beta_4}{\beta_1} \right] I_3^* > 0$$

$$R_2 - \frac{\beta_2}{\beta_1} R_1 > 0$$

And

$$(DR_2 + \beta_2 D_1 + \beta_5) - \frac{\beta_2}{\beta_1} (DR_1 + \beta_1 D_1 + \beta_4) > 0$$

4. 2. Interpretation

(a) When the population maintains itself at a fixed level and the equilibrium conditions are satisfied, then that particular point is called equilibrium point. When the population is free from disease then the equilibrium size of population is Q/d . For other cases of infections, the equilibrium size of population is reduced. From the equilibrium analysis, it is found that there are three basal reproduction numbers viz $R_1 = \frac{\beta_1}{d+\lambda_1}$, $R_2 = \frac{\beta_2}{d+\lambda_2}$ and

$$R_3 = \frac{\beta_3}{d+\varepsilon}. \quad \text{If } \beta_1 \leq (d+\lambda_1), \quad \beta_2 \leq (d+\lambda_2) \quad \text{and} \quad \beta_3 \leq (d+\varepsilon),$$

then the infection of malaria, mTB and HIV respectively will die out and disease will not become endemic.

(b) Now we draw some other inferences from equilibrium values for co-infection of mTB-HIV. In this case also the population size is reduced from

Q/d to $\frac{1}{d}\left(Q - \frac{\alpha\varepsilon}{\alpha+d}I_3^*\right)$. The higher contact rate

β_2 (β_3) enhances the infection rate of mTB (HIV). The effect of mTB recovery rate (λ_2) is also clear from the equilibrium values that the higher values of λ_2 reduces the mTB infection but susceptible population increases; the effect of conversion rate (ε) from HIV to AIDS is that the higher values of ε for time being increases the number of AIDS patients and they will die out by disease-induced deaths. But ultimately the AIDS cases are reduced due to reduced cases of HIV.

- (c) Co-infection of malaria-HIV. In this case also, the equilibrium population size is reduced from Q/d to $\frac{1}{d}\left(Q - \frac{\alpha\varepsilon}{\alpha+d}I_3^*\right)$. The infection rate of malaria (HIV)

increases as contact rate β_1 (β_3) increases. From the equilibrium point, it is noted that higher values of temporary recovery rate (λ_1) decreases the malaria infection and enhances the population of susceptible individuals. On increasing the susceptible population, the HIV cases increase what we expect from experience. Thus, we can say that the temporary recovery rate enhances the HIV cases. The conversion rate (ε) from HIV to AIDS has significant effect on AIDS. Death rate increases as ε increases but HIV cases decreases.

- (d) Now we examine the co-infection of malaria-mTB-HIV. For this case the population size reduces and all type infection increases as immigration rate increases. The higher values of d decrease the infection cases in each. The higher contact rates β_1 , β_2 and β_3 enhances the infection of malaria, mTB and HIV, respectively. The increase in contact rates β_1 and β_2 also enhances the susceptible population. It is straightforward that on increasing λ_1 (λ_2), the infection reduces and susceptible population increases. AIDS and HIV cases increase as λ_1 (λ_2) decreases. The effect of conversion parameter (ε) is very significant. On increasing ε , the death rate (α) due to AIDS increases but AIDS and HIV cases reduce. Thus we conclude that the malaria and mTB infections have significant effect in fueling HIV and AIDS.

5. STABILITY ANALYSIS

We discuss the stability analysis of equilibrium points by taking small perturbations in consideration.

Case I-IV. Equilibrium points when population is either free from infection or infected only by one

disease. For the case when population is free from disease, the equilibrium point P_0 is locally stable when $\beta_1 < (d + \lambda_1)$ (i.e. $R_1 < 1$), $\beta_2 < (d + \lambda_2)$ (i.e. $R_2 < 1$) and $\beta_3 < (d + \varepsilon)$ (i.e. $R_3 < 1$) otherwise unstable. But in case when population is infected by any single disease, the equilibrium points P_1 , P_2 , and P_3 are unstable. R_1 , R_2 and R_3 are the basal reproduction numbers for the malaria, mTB and HIV infection respectively.

Case V. The coefficients of a biquadratic equation give all roots with negative real part. Routh-Hurwitz conditions are: $a_i (i=1,2,4) > 0$ and $a_3(a_1a_2 - a_3) > a_1^2a_4$. For these conditions the equilibrium P_4 is locally stable.

$$\omega^4 + a_1\omega^3 + a_2\omega^2 + a_3\omega + a_4 = 0$$

Where

$$a_1 = 2d + \alpha - \delta_1 - \delta_2$$

$$a_2 = d(d + \alpha) + \delta_1\delta_2 - (2d + \alpha)(\delta_1 + \delta_2) + \varepsilon\beta_3 \frac{I_3'}{N'} + (\beta_4 - \beta_3)(\beta_1 + \beta_4) \frac{I_1'}{N'} \frac{I_3'}{N'}$$

$$a_3 = \delta_1\delta_2(2d + \alpha) - d(d + \alpha)(\delta_1 + \delta_2) + \varepsilon\beta_3(2d - \alpha - \delta_1) \frac{I_3'}{N'}$$

$$+ (\beta_4 - \beta_3)((2d + \alpha)(\beta_1 + \beta_4) + \varepsilon\beta_1) \frac{I_1'}{N'} \frac{I_3'}{N'}$$

$$a_4 = d(d + \alpha) \left(\delta_1\delta_2 + (\beta_1 + \beta_4)(\beta_4 - \beta_3) \frac{I_1'}{N'} \frac{I_3'}{N'} \right)$$

$$+ \varepsilon(\alpha - d) \left(\delta_1\beta_3 + \beta_1(\beta_3 - \beta_4) \frac{I_1'}{N'} \right) \frac{I_3'}{N'}$$

Where

$$\delta_1 = \beta_1 - (d + \lambda_1) - \beta_1 \frac{2I_1' + I_3' + A'}{N'} - \beta_4 \frac{I_3'}{N'}$$

$$\delta_2 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I_3' + I_1' + A'}{N'} + \beta_4 \frac{I_1'}{N'}$$

otherwise unstable.

Case VI. The coefficients of a biquadratic equation give all roots with negative real part. Routh-Hurwitz conditions are: $b_i (i=1,2,4) > 0$ and $b_3(b_1b_2 - b_3) > b_1^2b_4$. For these conditions the equilibrium is locally stable.

$$\omega^4 + b_1\omega^3 + b_2\omega^2 + b_3\omega + b_4 = 0$$

Where

$$b_1 = 2d + \alpha - \delta_3 - \delta_4$$

$$b_2 = d(d + \alpha) + \delta_3\delta_4 - (2d + \alpha)(\delta_3 + \delta_4) + \varepsilon\beta_3 \frac{I_3'}{N'}$$

$$+ (\beta_2 + \beta_5)(\beta_3 - \beta_3) \frac{I_2'}{N'} \frac{I_3'}{N'}$$

$$b_3 = \delta_3\delta_4(2d + \alpha) - d(d + \alpha)(\delta_3 + \delta_4) + \varepsilon\beta_3(d - \alpha - \delta_3) \frac{I_3'}{N'}$$

$$+ (\beta_5 - \beta_3)((2d + \alpha)(\beta_2 + \beta_5) + \varepsilon\beta_2) \frac{I_2'}{N'} \frac{I_3'}{N'}$$

$$b_4 = d(d + \alpha) \left(\delta_3 \delta_4 + (\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2'}{N'} \frac{I_3'}{N'} \right) + \varepsilon(\alpha - d) \left(\delta_3 \beta_3 + \beta_2(\beta_3 - \beta_5) \frac{I_2'}{N'} \right) \frac{I_3'}{N'}$$

Where

$$\delta_3 = \beta_2 - (d + \lambda_2) - \beta_2 \frac{2I_2' + I_3' + A'}{N'} - \beta_5 \frac{I_3'}{N'}$$

$$\delta_4 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I_3' + I_2' + A'}{N'} + \beta_5 \frac{I_2'}{N'}$$

otherwise unstable.

Case VII. Routh-Hurwitch conditions are:

$$c_i (i = 1, 3, 4, 5) > 0$$

$$\text{and } (c_1 c_4 - c_5)(c_1 c_2 c_3 - c_2^2 - c_1^2 c_4) > c_5 (c_1 c_2 - c_3)^2 + c_1 c_5^2$$

For these conditions the equilibrium point P₆ is locally stable.

$$\omega^5 + c_1 \omega^4 + c_2 \omega^3 + c_3 \omega^2 + c_4 \omega + c_5 = 0$$

The coefficients of above equation give all roots with negative real part, where

$$c_1 = 2d + \alpha - \gamma_1 - \gamma_2 - \gamma_3$$

$$c_2 = d(d + \alpha) + \gamma_1(\gamma_2 + \gamma_3) - (2d + \alpha)(\gamma_1 + \gamma_2 + \gamma_3) - \gamma_2 \gamma_3 + \varepsilon \beta_3 \frac{I_3'}{N'} + (\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2'}{N'} \frac{I_3'}{N'}$$

$$c_3 = \psi_1 - \varepsilon \psi_2 - \psi_3$$

$$c_4 = \chi_1 - \chi_2 - \varepsilon(\chi_3 - \chi_4 - \chi_5) \frac{I_3^*}{N^*} + (\beta_1 + \beta_4)(\beta_4 - \beta_3) \frac{I_1^*}{N^*} \frac{I_3^*}{N^*} - \beta_1 \beta_2 \frac{I_1^*}{N^*} \frac{I_2^*}{N^*}$$

$$c_5 = \phi_1 + \phi_2 - \varepsilon d \phi_3 - \alpha \varepsilon \phi_4 + \beta_1 \beta_2 \gamma_3 \frac{I_1^*}{N^*} \frac{I_2^*}{N^*}$$

where

$$\psi_1 = (2d + \alpha)(\gamma_1(\gamma_2 + \gamma_3)) - d(d + \alpha)(\gamma_1 + \gamma_2 + \gamma_3) + \gamma_1 \gamma_2 \gamma_3$$

$$\psi_2 = \beta_3(\gamma_1 + \gamma_2) + \beta_1(\beta_3 - \beta_4) \frac{I_1^*}{N^*} - \beta_3 d + \beta_3 \alpha \frac{I_3^*}{N^*}$$

$$\psi_3 = (2d + \alpha)(\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*}$$

$$\chi_1 = d(d + \alpha) \left(\gamma_1(\gamma_2 + \gamma_3) - \gamma_2 \gamma_3 + (\beta_2 + \beta_5)(\beta_3 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \right)$$

$$\chi_2 = \gamma_1 \left(\gamma_2 \gamma_3 - (\beta_2 + \beta_5)(\beta_3 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \right)$$

$$\chi_3 = d \beta_3(\gamma_1 + \gamma_2) + d \beta_1 + d \beta_1(\beta_3 - \beta_4) \frac{I_1^*}{N^*}$$

$$\chi_4 = \gamma_1 \gamma_2 \beta_3 - \beta_1 \beta_2 \beta_4 \frac{I_1^*}{N^*} \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} + \beta_1 \beta_2(\beta_3 + \beta_5) \frac{I_1^*}{N^*} \frac{I_2^*}{N^*} + \beta_1(\beta_3 - \beta_4) \gamma_2 \frac{I_1^*}{N^*}$$

$$\chi_5 = \beta_3 \gamma_2 + \beta_1(\beta_3 - \beta_4) \frac{I_1^*}{N^*} + 2 \beta_2(\beta_3 + \beta_5) \frac{I_2^*}{N^*}$$

$$\phi_1 = d \gamma_1 (d + \alpha) \left((\beta_2 + \beta_5)(\beta_3 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} - \gamma_2 \gamma_3 \right)$$

$$\phi_2 = (\beta_3 - \beta_4)(\beta_1 \beta_5 - \beta_2 \beta_4) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \frac{I_1^*}{N^*}$$

$$\phi_3 = (\beta_1 \beta_2(\beta_4 - \beta_3 - \beta_5)) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \frac{I_1^*}{N^*} - \gamma_1 \gamma_2 \beta_3 - \beta_2(\beta_3 + \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} - \gamma_2 \beta_1(\beta_3 - \beta_4) \frac{I_3^*}{N^*} \frac{I_1^*}{N^*}$$

$$\phi_4 = (\beta_3 + \beta_4 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \frac{I_1^*}{N^*} - \gamma_1 \gamma_2 \beta_3 \frac{I_3^*}{N^*} + \gamma_1 \beta_2(\beta_3 - \beta_4) \frac{I_3^*}{N^*} \frac{I_2^*}{N^*} + \gamma_2 \beta_1(\beta_3 - \beta_4) \frac{I_3^*}{N^*} \frac{I_1^*}{N^*}$$

$$\gamma_1 = \beta_1 - (d + \lambda_1) - \beta_1 \frac{2I_1^* + I_2^* + I_3^* + A^*}{N^*} - \beta_4 \frac{I_3^*}{N^*}$$

$$\gamma_2 = \beta_2 - (d + \lambda_2) - \beta_2 \frac{2I_2^* + I_1^* + I_3^* + A^*}{N^*} - \beta_5 \frac{I_3^*}{N^*}$$

$$\gamma_3 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I_3^* + I_1^* + I_2^* + A^*}{N^*} + \beta_4 \frac{I_1^*}{N^*} + \beta_5 \frac{I_2^*}{N^*}$$

6. NUMERICAL ANALYSIS

In previous section, we have presented results of the existence of equilibrium solutions and local stability of the equilibrium solutions by linearising the set of equations analytically, but in this section we shall explore the behavior of the system and stability of the endemic equilibrium; to analyze this the analytic tools are not much convenient. Therefore, Range-Kutta fourth order method is the convenient one to find numerical solution of the set of equations with suitable parameters of the model in MATLAB software. The default parameter values are:

$$Q = 2000, \beta_1 = 0.925, \beta_2 = 0.925, \beta_3 = 0.285, \beta_4 = 1.10, \beta_5 = 1.15, \text{ and } d = 0.021, \lambda_1 = 0.3, \lambda_2 = 0.29, \varepsilon = 0.2 \text{ and } \alpha = 1.0$$

the initial values are:

$$N(0) = 20000, I_1(0) = 3000, I_2(0) = 4000, I_3(0) = 4000, A(0) = 600$$

The co-infection equilibrium values are computed as follows:

$$N^* = 33235.00, I_1^* = 3742.90, I_2^* = 2105.00, I_3^* = 6647.00, A^* = 1302.00$$

λ_1	0.0	0.1	0.2	0.3	0.4	0.5
R ₁	44.04	7.64	4.18	2.88	2.17	1.77
I ₁	50102	41072	33207	3742.4	1432.8	368.34
λ_2	0.0	0.1	0.2	0.3	0.4	0.5
R ₂	45.04	8.64	5.38	2.89	1.99	1.42
I ₂	46102	38243	29563	3554.9	1342.7	234.56

The numerical results are shown graphically in Figures 2-8. In Figure 2, the distribution of population with time is shown for different classes without migration and without recovery rates i. e. $Q=0, \lambda_1 = \lambda_2 = 0$. It is seen that susceptible population decreases continuously and infected population increases initially because there is no migration and recovery. Therefore all infected ultimately develop AIDS and will ultimately meet the disease induced deaths. Thus the total population in this case will be eradicating after some time period. Figure 3 depicts the variation of population with migration and with recovery rates. It is noticed in the figure that due to recovery rates, mTB and malaria infected populations decrease and susceptible population initially decreases. After some time, due to migration it tends to be constant. However, infection is not eradicated and it persists in the population. Figure 4 shows the variation of mTB infected population with respect to time for different recovery rates. We notice that on increasing recovery rate λ_2 , the mTB infected population decreases, and in turn, the susceptible population increases. In Figures 5 and 6 we see that the increment in ε the HIV infected population decreases as they become part of the full blown AIDS population. In Figure 7 the variation of AIDS population for different values of disease- induced death rate is shown. It is seen that with the increase in disease-induced death rate the AIDS population decreases and ultimately dies away. The role of migration is shown in Figure 8. We observe that increasing migration increases the susceptible population and consequently increases AIDS population. From the above discussion, it is concluded that if mTB and malaria infections are treated significantly then acceleration to HIV infection can be kept under control.

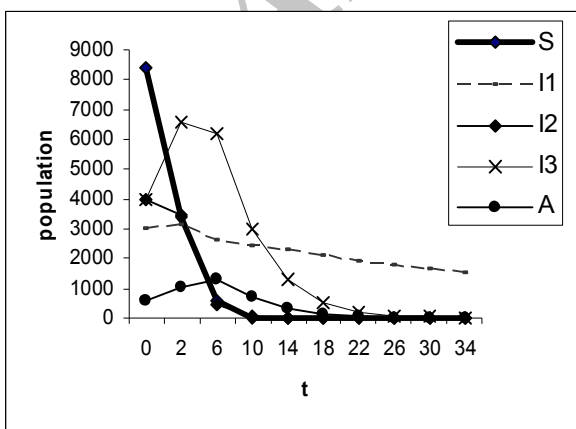


Figure 2. Variation of population in different classes for $Q=0, d=0.021, \lambda_1 = 0, \lambda_2 = 0, \alpha = 1$

$\beta_1 = 0.925, \beta_1 = 0.925, \beta_2 = 0.925, \beta_3 = 0.285, \beta_4 = 0.1.10, \beta_5 = 0.1.15,$

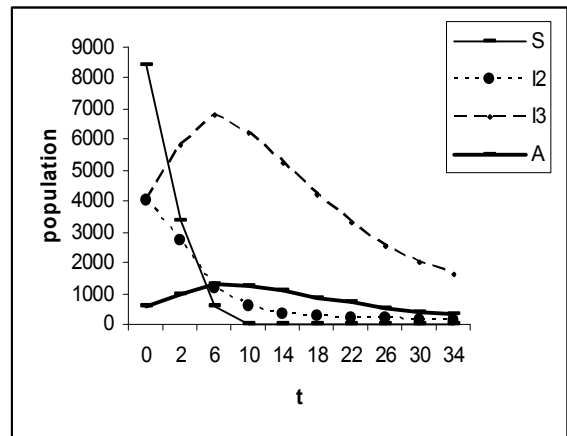


Figure 3. Variation of population in different classes for $Q=2000d=0.021, \lambda_1 = .925, \lambda_2 = .925, \alpha = 1,$

$\beta_1 = 0.925, \beta_1 = 0.925, \beta_2 = 0.925, \beta_3 = 0.285, \beta_4 = 0.1.10, \beta_5 = 0.1.15,$

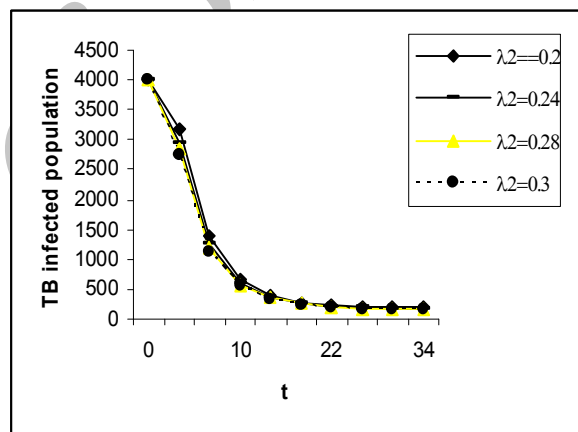


Figure 4. Variation of TB infected population for different values of λ_2

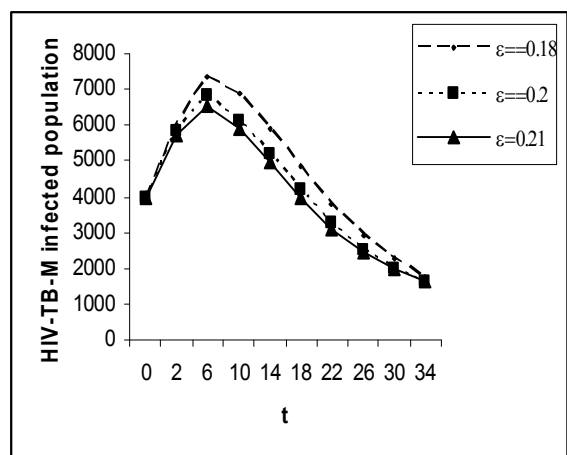


Figure 5. Variation of HIV-TB-Malaria infected population for different values of ε

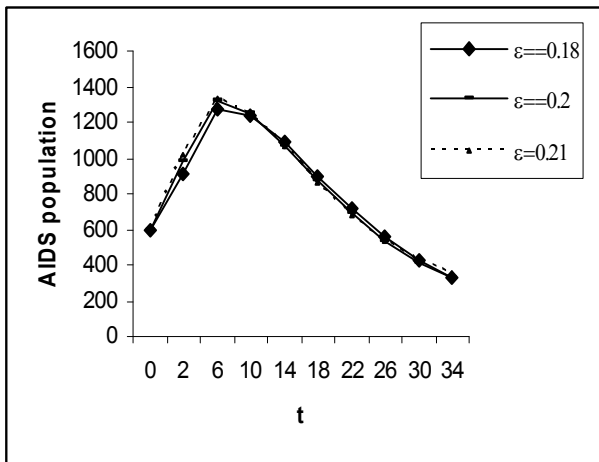


Figure 6. Variation of AIDS population for different values of ϵ

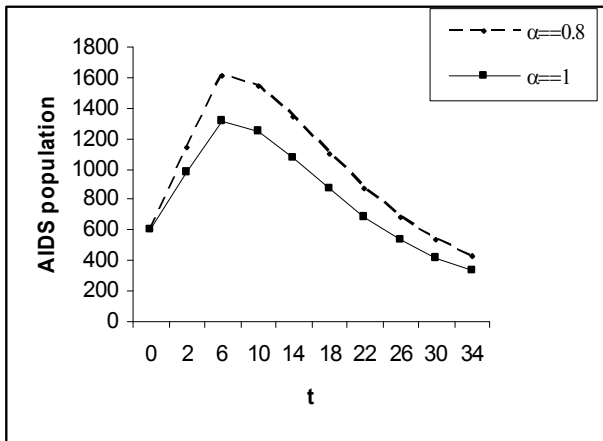


Figure 7. Variation of AIDS population for different values of α

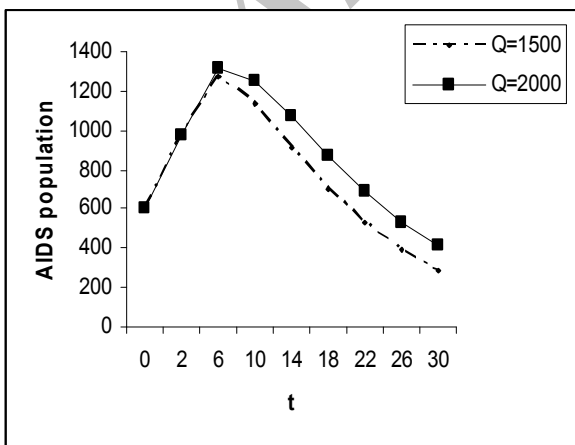


Figure 8. Variation of AIDS population for different values of Q

7. CONCLUSION

In this investigation, we have analyzed the transmission dynamics of malaria, mTB, HIV and AIDS. Our study has been devoted to examine the effect of malaria and mTB infection on transmission of HIV and AIDS by considering the three threshold parameters R_1 , R_2 and R_3 related to malaria infection, mTB infection and HIV infection, respectively. $R_1 < 1$, $R_2 < 1$ and $R_3 < 1$ then malaria, mTB and HIV infections die out, respectively and if $R_1 > 1$, $R_2 > 1$ and $R_3 > 1$ then all the infections exist. All the seven equilibrium points have been determined. The equilibrium point P_0 is locally asymptotically stable for the values of $R_1 < 1$, $R_2 < 1$ and $R_3 < 1$, whereas the equilibrium points P_1 , P_2 and P_3 are unstable. The point P_4 is locally stable, i. e., the population maintains itself at level of equilibrium whenever co-infection of malaria-mTB exists.

The co-infection equilibrium points P_4 (malaria-HIV), P_5 (mTB-HIV) and P_6 (malaria-mTB-HIV) are always locally stable. Susceptible population enhances the infection rate. The disease becomes endemic due to immigration because immigration population is susceptible population. It is also found that higher temporary recovery rates increase the population of susceptible individuals. The infection may be controlled by reducing the susceptible population. Thus to reduce susceptible population, the permanent recovery is essential. The number of HIV infected cases increases due to the presence of other diseases, particularly malaria and mTB, separately and altogether. It is noticed that the HIV infection can be slowed down by treating malaria and mTB, effectively. For the sake of validity of our results, it is to be mentioned that on dropping malaria, our results of equilibrium and stability solutions are in agreement with the results of above ref. no. 18 and also ref. no. 22, 26.

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APPENDIX

Proof of theorem 2 is as follows:

A. I: The population is free from disease

Consider small perturbation about the equilibrium as $N = n + N', I_1 = i + I'_1, I_2 = i + I'_2, I_3 = i + I'_3, A = a + A'$. For equilibrium points $P_0, I'_1 = I'_2 = I'_3 = A' = 0$, so that for linearization and taking only first order quantities the set of Equations (6)-(10); yield:

$$\frac{dn}{dt} = -dn - \alpha a$$

$$\frac{di_1}{dt} = (\beta_1 - (d + \lambda_1))i_1$$

$$\frac{di_2}{dt} = (\beta_2 - (d + \lambda_2))i_2$$

$$\frac{di_3}{dt} = (\beta_3 - (d + \varepsilon))i_3$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha)a$$

The stability matrix X is formed from equations and is given by:

$$Y = \begin{bmatrix} -d & 0 & 0 & 0 & -\alpha \\ 0 & \beta_1 - (d + \lambda_1) & 0 & 0 & 0 \\ 0 & 0 & \beta_2 - (d + \lambda_2) & 0 & 0 \\ 0 & 0 & 0 & \beta_3 - (d + \varepsilon) & 0 \\ 0 & 0 & 0 & 0 & -(d + \alpha) \end{bmatrix}$$

The characteristic equation is $|Y - \omega I| = 0$ where ω is eigen value and I is identity matrix. The eigen values of Y are: $\omega_1 = -d, \omega_2 = \beta_1 - (d + \lambda_1), \omega_3 = \beta_2 - (d + \lambda_2), \omega_4 = \beta_3 - (d + \varepsilon), \omega_5 = -(d + \alpha)$. The first and last eigen values are always negative whereas second, third and fourth ones are negative only when $\beta_1 < (d + \lambda_1), \beta_2 < (d + \lambda_2), \beta_3 < (d + \varepsilon)$. Thus in this case, we conclude that the matrix is locally stable otherwise unstable.

A. II: When the population is malaria infected only.

Consider small perturbation about the equilibrium point P_1 by taking $N = n + N', I_1 = i_1 + I'_1, I_2 = i_2, I_3 = i_3, A = a$. Putting these values in the set of Equations (6)-(10), we have:

$$\frac{dn}{dt} = -dn - \alpha a \tag{AII.1}$$

$$\frac{di_m}{dt} = \left(\beta_1 - (d + \lambda_1) - \frac{2I'_1}{N'} \beta_1 \right) i_1 - \beta_1 \frac{I'_1}{N'} i_2 - (\beta_1 + \beta_4) \frac{I'_1}{N'} i_3 - \beta_1 \frac{I'_1}{N'} a - \beta_1 \frac{I'_1}{N'} n \tag{AII.2}$$

$$\frac{di_2}{dt} = (\beta_2 - (d + \lambda_2))i_2 - \beta_{st} \frac{I'_1}{N'} i_2 \tag{AII.3}$$

$$\frac{di_3}{dt} = (\beta_3 - (d + \varepsilon))i_3 - (\beta_3 - \beta_4) \frac{I'_1}{N'} i_3 \tag{AII.4}$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha)a \tag{AII.5}$$

All above equations (AII.1)-(AII.5) are linearly dependent; we may leave (AII.3)-(AII.5) equations.

The stability matrix Y is formed from equations by (AII.1)-(AII.2) and is given by:

$$Y = \begin{bmatrix} -d & 0 \\ 0 & \beta_1 - (d + \lambda_1) - \frac{2I'_1}{N'} \beta_1 \end{bmatrix}$$

The eigen values of matrix Y are: $\omega_1 = -d, \omega_2 = \beta_1 - (d + \lambda_1) - \frac{2I'_1}{N'} \beta_1$. Both the eigen values are negative, but the second value contradict the first case so that we conclude that the matrix is unstable for small perturbation.

A.III: When the population is mTB infected only.

Consider small perturbation about the equilibrium point P_2 by taking $N = n + N', I_1 = i_1, I_2 = i_2 + I'_2, I_3 = i_3, A = a$. Putting these values in the set of Equations (6)-(10), we have:

$$\frac{dn}{dt} = -dn - \alpha a \tag{AIII.1}$$

$$\frac{di_1}{dt} = \left(\beta_1 - (d + \lambda_1) - \beta_1 \frac{I'_2}{N'} \right) i_1 \tag{AIII.2}$$

$$\frac{di_2}{dt} = \left(\beta_2 - (d + \lambda_2) - \frac{2I'_2}{N'} \beta_2 \right) i_2 - \beta_1 \frac{I'_2}{N'} i_1 - (\beta_2 + \beta_5) \frac{I'_2}{N'} i_3 - \frac{I'_2}{N'} a \tag{AIII.3}$$

$$\frac{di_3}{dt} = \left(\beta_3 - (d + \varepsilon) - (\beta_3 - \beta_5) \frac{I'_2}{N'} \right) i_3 \tag{AIII.4}$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha)a \tag{AIII.5}$$

All Equations (AIII.1)-(AIII.5) are linearly dependent; we may leave (AIII.2), (AIII.4) and (AIII.5) equations. Then the stability matrix Y is given by:

$$Y = \begin{bmatrix} -d & 0 \\ 0 & \beta_2 - (d + \lambda_2) - \frac{2I'_2}{N'} \beta_2 \end{bmatrix}$$

The eigen values of matrix Y are: $\omega_1 = -d, \omega_2 = \beta_2 - (d + \lambda_2) - \frac{2I'_2}{N'} \beta_2$. In this case also the matrix is unstable for small perturbation.

A.IV: When the population is HIV infected but free from malaria and mTB,

Here also we consider small perturbation about the equilibrium point P_3 by taking $N = n + N'$, $I_1 = i_1$, $I_2 = i_2$, $I_3 = i_3 + I'_3$, $A = A + a$. Putting these values in the set of Equations (6)-(10), we have:

$$\frac{dn}{dt} = -dn - \alpha a \tag{AIV.1}$$

$$\frac{di_1}{dt} = \left(\beta_1 - (d + \lambda_1) - \beta_1 \frac{I'_3 + A}{N'} - \beta_4 \frac{I'_3}{N'} \right) i_1 \tag{AIV.2}$$

$$\frac{di_2}{dt} = \left(\beta_2 - (d + \lambda_2) - \beta_2 \frac{I'_3 + A}{N'} - \frac{I'_3}{N'} \beta_5 \right) i_2 \tag{AIV.3}$$

$$\frac{di_3}{dt} = \left(\beta_3 - (d + \varepsilon) - \beta_3 \frac{2I'_3 + A}{N'} \right) i_3 - (\beta_3 - \beta_4) \frac{I'_3}{N'} i_1 - (\beta_3 - \beta_5) \frac{I'_3}{N'} i_2 - \beta_3 \frac{I'_3}{N'} a \tag{AIV.4}$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha) a \tag{AIV.5}$$

Since Equations (AIV.1)-(AIV.5) are linearly dependent, we may leave (AIV.2) -(AIV.3) equations thus the stability matrix Y is given by:

$$Y = \begin{bmatrix} -d & 0 & 0 \\ 0 & \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I'_3 + A}{N'} & 0 \\ 0 & \varepsilon & -(d + \alpha) \end{bmatrix}$$

The latent roots of matrix Y are: $\omega_1 = -d$, $\omega_2 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I'_3 + A}{N'}$ and $\omega_3 = -(d + \alpha)$. The all latent roots are negative; this is the contradiction with the first case so that it is unstable.

A. VII: When the population is free from mTB but co-infection of malaria-HIV prevails.

Consider small perturbation about the equilibrium point P_6 by taking $N = n + N'$, $I_1 = i_1 + I'_1$, $I_2 = i_2$, $I_3 = i_3 + I'_3$, $A = A + a$. Putting these values in the set of Equations (6)-(10), we have:

$$\frac{dn}{dt} = -dn - \alpha a \tag{AVII.1}$$

$$\frac{di_1}{dt} = \left(\beta_1 - (d + \lambda_1) - \beta_1 \frac{2I'_1 + I'_3 + A}{N'} - \beta_4 \frac{I'_3}{N'} \right) i_1 - \beta_1 \frac{I'_1}{N'} i_2 - (\beta_1 + \beta_4) \frac{I'_1}{N'} i_3 - \beta_1 \frac{I'_1}{N'} a - \beta_1 \frac{I'_1}{N'} n \tag{AVII.2}$$

$$\frac{di_3}{dt} = \left(\beta_3 - (d + \varepsilon) - \frac{2I'_3 + I'_1 + A}{N'} \beta_3 + \frac{I'_1}{N'} \beta_4 \right) i_3 - (\beta_3 - \beta_4) \frac{I'_3}{N'} i_1 - \beta_3 \frac{I'_3}{N'} a - \beta_3 \frac{I'_3}{N'} i_2 - \beta_3 \frac{I'_3}{N'} n \tag{AVII.3}$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha) a \tag{AVII.4}$$

The stability matrix Y is formed from equations by (AVII.1)-(AVII.4) and is given by

$$Y = \begin{bmatrix} -d & 0 & 0 & -\alpha \\ -\beta_1 \frac{I'_1}{N'} & \beta_1 - (d + \lambda_1) - \beta_1 \frac{2I'_1 + I'_3 + A}{N'} & 0 & 0 \\ 0 & -\beta_4 \frac{I'_3}{N'} & -(\beta_1 + \beta_4) \frac{I'_1}{N'} & -\beta_1 \frac{I'_1}{N'} \\ -\beta_3 \frac{I'_3}{N'} & (\beta_4 - \beta_5) \frac{I'_3}{N'} & \beta_3 - (d + \varepsilon) - \frac{2I'_3 + I'_1 + A}{N'} \beta_3 & 0 \\ 0 & 0 & \frac{I'_1}{N'} \beta_4 & -\beta_3 \frac{I'_3}{N'} \\ 0 & 0 & \varepsilon & -(d + \alpha) \end{bmatrix}$$

The characteristic equation of given matrix Y is:

$$\omega^4 + a_1 \omega^3 + a_2 \omega^2 + a_3 \omega + a_4 = 0$$

where

$$a_1 = 2d + \alpha - \delta_1 - \delta_2$$

$$a_2 = d(d + \alpha) + \delta_1 \delta_2 - (2d + \alpha)(\delta_1 + \delta_2) + \varepsilon \beta_3 \frac{I'_3}{N'} + (\beta_4 - \beta_5)(\beta_1 + \beta_4) \frac{I'_1}{N'} \frac{I'_3}{N'}$$

$$a_3 = \delta_1 \delta_2 (2d + \alpha) - d(d + \alpha)(\delta_1 + \delta_2) + \varepsilon \beta_3 (2d - \alpha - \delta_1) \frac{I'_3}{N'} + (\beta_4 - \beta_5) \left((2d + \alpha)(\beta_1 + \beta_4) + \varepsilon \beta_1 \right) \frac{I'_1}{N'} \frac{I'_3}{N'}$$

$$a_4 = d(d + \alpha) \left(\delta_1 \delta_2 + (\beta_1 + \beta_4)(\beta_4 - \beta_5) \right) \frac{I'_1}{N'} \frac{I'_3}{N'} + \varepsilon (\alpha - d) \left(\delta_1 \beta_3 + \beta_1 (\beta_3 - \beta_4) \right) \frac{I'_1}{N'} \frac{I'_3}{N'}$$

where

$$\delta_1 = \beta_1 - (d + \lambda_1) - \beta_1 \frac{2I'_1 + I'_3 + A}{N'} - \beta_4 \frac{I'_3}{N'}$$

$$\delta_2 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I'_3 + I'_1 + A}{N'} + \beta_4 \frac{I'_1}{N'}$$

The coefficients of a biqadratic equation give all roots with negative real part. Routh-Hurwitch conditions are: $a_i (i = 1, 2, 4) > 0$ and $a_3 (a_1 a_2 - a_3) > a_1^2 a_4$. For these conditions the equilibrium P_6 is locally stable.

A. VI: When the population is malaria infection free but co-infection of mTB-HIV exists.

Here also we consider small perturbation about the equilibrium point P_5 . By substituting $N = n + N'$, $I_1 = i_1$, $I_2 = i_2 + I'_2$, $I_3 = i_3 + I'_3$, $A = A + a$, in Equations (6)-(10), we get:

$$\frac{dn}{dt} = -dn - \alpha a \tag{AVI.1}$$

$$\frac{di_2}{dt} = \left(\beta_2 - (d + \lambda_2) - \frac{2I_2' + I_3' + A'}{N'} \beta_2 - \frac{I_3'}{N'} \beta_5 \right) i_2 - (\beta_2 + \beta_5) \frac{I_2'}{N'} i_3 - \beta_2 \frac{I_2'}{N'} a - \beta_2 \frac{I_2'}{N'} n - \beta_2 \frac{I_2'}{N'} i_1 \tag{AVI.2}$$

$$\frac{di_3}{dt} = \left(\beta_3 - (d + \varepsilon) - \frac{2I_3' + I_2' + A'}{N'} \beta_3 + \frac{I_2'}{N'} \beta_5 \right) i_3 - \beta_3 \frac{I_3'}{N'} i_1 + (\beta_5 - \beta_3) \frac{I_3'}{N'} i_2 - \beta_3 \frac{I_3'}{N'} n - \beta_3 \frac{I_3'}{N'} a \tag{AVI.3}$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha) a \tag{AVI.4}$$

The stability matrix Y is formed from equations by (AVI.1)-(AVI.4) and is given by:

$$Y = \begin{bmatrix} -d & 0 & 0 & -\alpha \\ (\beta_2 - (d + \lambda_2)) \frac{I_2'}{N'} & \beta_2 - (d + \lambda_2) - \frac{2I_2' + I_3' + A'}{N'} \beta_2 & -\beta_2 \frac{I_3'}{N'} & -\beta_2 \frac{I_2'}{N'} \\ -\beta_2 \frac{I_3'}{N'} & -\frac{I_3'}{N'} \beta_5 & -(\beta_2 + \beta_5) \frac{I_2'}{N'} & -\beta_2 \frac{I_2'}{N'} \\ -\beta_3 \frac{I_3'}{N'} & (\beta_5 - \beta_3) \frac{I_3'}{N'} & \beta_3 - (d + \varepsilon) - \frac{2I_3' + I_2' + A'}{N'} \beta_3 & \beta_3 \frac{I_2'}{N'} \\ 0 & 0 & \varepsilon & -(d + \alpha) \end{bmatrix}$$

The characteristic equation of above given matrix Y is:

$$\omega^4 + b_1\omega^3 + b_2\omega^2 + b_3\omega + b_4 = 0$$

Where

$$b_1 = 2d + \alpha - \delta_3 - \delta_4$$

$$b_2 = d(d + \alpha) + \delta_3\delta_4 - (2d + \alpha)(\delta_3 + \delta_4) + \varepsilon\beta_3 \frac{I_3'}{N'} + (\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2'}{N'} \frac{I_3'}{N'}$$

$$b_3 = \delta_3\delta_4(2d + \alpha) - d(d + \alpha)(\delta_3 + \delta_4) + \varepsilon\beta_3(d - \alpha - \delta_3) \frac{I_3'}{N'} + (\beta_5 - \beta_3)((2d + \alpha)(\beta_2 + \beta_5) + \varepsilon\beta_2) \frac{I_2'}{N'} \frac{I_3'}{N'}$$

$$b_4 = d(d + \alpha) \left(\delta_3\delta_4 + (\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2'}{N'} \frac{I_3'}{N'} \right) + \varepsilon(\alpha - d) \left(\delta_3\beta_3 + \beta_2(\beta_5 - \beta_3) \frac{I_2'}{N'} \right) \frac{I_3'}{N'}$$

where

$$\delta_3 = \beta_2 - (d + \lambda_2) - \beta_2 \frac{2I_2' + I_3' + A'}{N'} - \beta_5 \frac{I_3'}{N'}$$

$$\delta_4 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I_3' + I_2' + A'}{N'} + \beta_5 \frac{I_2'}{N'}$$

The coefficients of a biquadratic equation give all roots with negative real part. Routh-Hurwitch conditions are: $b_i (i = 1, 2, 4) > 0$ and $b_3(b_1b_2 - b_3) > b_1^2b_4$. For these conditions the equilibrium is locally stable.

A. VIII: When co-infection of malaria-mTB-HIV exists.

Consider small perturbation about the equilibrium point P₇. Now substituting $N = n + N^*$, $I_1 = i_1 + I_1^*$,

$I_2 = i_2 + I_2^*$, $I_3 = i_3 + I_3^*$, $A = A^* + a$, in Equations (6)-(10), we have:

$$\frac{dn}{dt} = -dn - \alpha a \tag{AVIII.1}$$

$$\frac{di_1}{dt} = \left(\beta_1 - (d + \lambda_1) - \beta_1 \frac{2I_1^* + I_2^* + I_3^* + A^*}{N^*} - \beta_4 \frac{I_3^*}{N^*} \right) i_1 - \beta_1 \frac{I_1^*}{N^*} i_2 - (\beta_1 + \beta_4) \frac{I_1^*}{N^*} i_3 - \beta_1 \frac{I_1^*}{N^*} a - \beta_1 \frac{I_1^*}{N^*} n \tag{AVIII.2}$$

$$\frac{di_2}{dt} = \left(\beta_2 - (d + \lambda_2) - \frac{I_1^* + 2I_2^* + I_3^* + A^*}{N^*} \beta_2 - \frac{I_3^*}{N^*} \beta_5 \right) i_2 - \beta_2 \frac{I_2^*}{N^*} i_1 - (\beta_2 + \beta_5) \frac{I_2^*}{N^*} i_3 - \beta_2 \frac{I_2^*}{N^*} a - \beta_2 \frac{I_2^*}{N^*} n \tag{AVIII.3}$$

$$\frac{di_3}{dt} = \left(\beta_3 - (d + \varepsilon) - \frac{I_1^* + I_2^* + 2I_3^* + A^*}{N^*} \beta_3 + \frac{I_2^*}{N^*} \beta_4 + \frac{I_2^*}{N^*} \beta_5 \right) i_3 - (\beta_3 - \beta_4) \frac{I_3^*}{N^*} i_1 - \beta_3 \frac{I_3^*}{N^*} a - (\beta_3 - \beta_5) \frac{I_3^*}{N^*} i_2 - \beta_3 \frac{I_3^*}{N^*} n \tag{AVIII.4}$$

$$\frac{da}{dt} = \varepsilon i_3 - (d + \alpha) a \tag{AVIII.5}$$

The stability matrix Y is formed from equations by (AVIII.1)-(AVIII.5) and by equilibrium points as:

$$Y = \begin{bmatrix} -d & 0 & 0 & 0 & -\alpha \\ -\beta_1 \frac{I_1^*}{N^*} & \beta_1 - (d + \lambda_1) - \beta_1 \frac{2I_1^* + I_2^* + I_3^* + A^*}{N^*} & -\beta_1 \frac{I_3^*}{N^*} & -\beta_1 \frac{I_2^*}{N^*} i_2 & -(\beta_1 + \beta_4) \frac{I_1^*}{N^*} i_3 & -\beta_1 \frac{I_1^*}{N^*} a \\ -\beta_2 \frac{I_2^*}{N^*} & -\beta_2 \frac{I_2^*}{N^*} & \beta_2 - (d + \lambda_2) - \frac{I_1^* + 2I_2^* + I_3^* + A^*}{N^*} \beta_2 & -\frac{I_3^*}{N^*} \beta_5 & -(\beta_2 + \beta_5) \frac{I_2^*}{N^*} i_3 & -\beta_2 \frac{I_2^*}{N^*} a \\ -\beta_3 \frac{I_3^*}{N^*} & -(\beta_3 - \beta_4) \frac{I_3^*}{N^*} & -(\beta_3 - \beta_5) \frac{I_3^*}{N^*} & \beta_3 - (d + \varepsilon) - \frac{I_1^* + I_2^* + 2I_3^* + A^*}{N^*} \beta_3 & + \frac{I_2^*}{N^*} \beta_4 + \frac{I_2^*}{N^*} \beta_5 & -\beta_3 \frac{I_3^*}{N^*} \\ 0 & 0 & 0 & \varepsilon & 0 & -(d + \alpha) \end{bmatrix}$$

The characteristic equation of given matrix Y is:

$$\omega^5 + c_1\omega^4 + c_2\omega^3 + c_3\omega^2 + c_4\omega + c_5 = 0$$

where

$$c_1 = 2d + \alpha - \gamma_1 - \gamma_2 - \gamma_3$$

$$c_2 = d(d + \alpha) + \gamma_1(\gamma_2 + \gamma_3) - (2d + \alpha)(\gamma_1 + \gamma_2 + \gamma_3) - \gamma_2\gamma_3 + \varepsilon\beta_3 \frac{I_3^*}{N^*} + (\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*}$$

$$c_3 = \psi_1 - \varepsilon\psi_2 - \psi_3$$

$$c_4 = \chi_1 - \chi_2 - \varepsilon(\chi_3 - \chi_4 - \chi_5) \frac{I_3^*}{N^*} + (\beta_1 + \beta_4)(\beta_4 - \beta_3) \frac{I_1^*}{N^*} \frac{I_3^*}{N^*} - \beta_1\beta_2 \frac{I_1^*}{N^*} \frac{I_2^*}{N^*}$$

$$c_5 = \phi_1 + \phi_2 - \varepsilon d\phi_3 - \alpha\varepsilon\phi_4 + \beta_1\beta_2\gamma_3 \frac{I_1^*}{N^*} \frac{I_2^*}{N^*}$$

where

$$\psi_1 = (2d + \alpha)(\gamma_1(\gamma_2 + \gamma_3)) - d(d + \alpha)(\gamma_1 + \gamma_2 + \gamma_3) - \gamma_1\gamma_2\gamma_3$$

$$\psi_2 = \beta_3(\gamma_1 + \gamma_2) + \beta_1(\beta_3 - \beta_4) \frac{I_1^*}{N^*} - \beta_3 d + \beta_3 \alpha \frac{I_3^*}{N^*}$$

$$\psi_3 = (2d + \alpha)(\beta_2 + \beta_5)(\beta_5 - \beta_3) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*}$$

$$\chi_1 = d(d + \alpha) \left(\gamma_1(\gamma_2 + \gamma_3) - \gamma_2\gamma_3 + (\beta_2 + \beta_5)(\beta_3 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \right)$$

$$\chi_2 = \gamma_1 \left(\gamma_2\gamma_3 - (\beta_2 + \beta_5)(\beta_3 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \right)$$

$$\chi_3 = d\beta_3(\gamma_1 + \gamma_2) + d\beta_1 + d\beta_1(\beta_3 - \beta_4) \frac{I_1^*}{N^*}$$

$$\chi_4 = \gamma_1\gamma_2\beta_3 - \beta_1\beta_2\beta_4 \frac{I_1^*}{N^*} \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} + \beta_1\beta_2(\beta_3 + \beta_5) \frac{I_1^*}{N^*} \frac{I_2^*}{N^*} + \beta_1(\beta_3 - \beta_4)\gamma_2 \frac{I_1^*}{N^*}$$

$$\chi_5 = \beta_3\gamma_2 + \beta_1(\beta_3 - \beta_4) \frac{I_1^*}{N^*} + 2\beta_2(\beta_3 + \beta_5) \frac{I_2^*}{N^*}$$

$$\phi_1 = d\gamma_1(d + \alpha) \left((\beta_2 + \beta_5)(\beta_3 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} - \gamma_2\gamma_3 \right)$$

$$\phi_2 = (\beta_3 - \beta_4)(\beta_1\beta_5 - \beta_2\beta_4) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \frac{I_1^*}{N^*}$$

$$\phi_3 = (\beta_1\beta_2(\beta_4 - \beta_3 - \beta_5)) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \frac{I_1^*}{N^*} - \gamma_1\gamma_2\beta_3 - \beta_2(\beta_3 + \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} - \gamma_2\beta_1(\beta_3 - \beta_4) \frac{I_3^*}{N^*} \frac{I_1^*}{N^*}$$

$$\phi_4 = (\beta_3 + \beta_4 - \beta_5) \frac{I_2^*}{N^*} \frac{I_3^*}{N^*} \frac{I_1^*}{N^*} - \gamma_1\gamma_2\beta_3 \frac{I_3^*}{N^*} + \gamma_1\beta_2(\beta_3 - \beta_4) \frac{I_3^*}{N^*} \frac{I_2^*}{N^*} + \gamma_2\beta_1(\beta_3 - \beta_4) \frac{I_3^*}{N^*} \frac{I_1^*}{N^*}$$

$$\gamma_1 = \beta_1 - (d + \lambda_1) - \beta_1 \frac{2I_1^* + I_2^* + I_3^* + A^*}{N^*} - \beta_4 \frac{I_3^*}{N^*}$$

$$\gamma_2 = \beta_2 - (d + \lambda_2) - \beta_2 \frac{2I_2^* + I_1^* + I_3^* + A^*}{N^*} - \beta_5 \frac{I_3^*}{N^*}$$

$$\gamma_3 = \beta_3 - (d + \varepsilon) - \beta_3 \frac{2I_3^* + I_1^* + I_2^* + A^*}{N^*} + \beta_4 \frac{I_1^*}{N^*} + \beta_5 \frac{I_2^*}{N^*}$$

The coefficients of above equation give all roots with negative real part. Routh-Hurwitz conditions are: $c_i (i=1,3,4,5) > 0$

$$\text{and } (c_1c_4 - c_5)(c_1c_2c_3 - c_3^2 - c_1^2 - c_1^2c_4) > c_5(c_1c_2 - c_3)^2 + c_1c_5^2$$

For these conditions the equilibrium point P_7 is locally stable.

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Stability and Numerical Analysis of Malaria-mTB-HIV/AIDS Co-infection

TECHNICAL
NOTE

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در این مقاله، برای بررسی پویایی انتقال مالاریای قابل درمان، سل قابل علاج، و اچ آی وی / ایدز غیرقابل درمان و عفونت‌های همزمان با آنها یک مدل ریاضی می‌سازیم. با توجه به مهاجرت مبتلایان، اندازه‌ی جامعه‌ی مورد بررسی را متغیر در نظر می‌گیریم. کل جمعیت به پنج زیر شاخه تحت عنوان‌های: مستعد، آلوده به مالاریا، مسلول، دارای عفونت اچ آی وی و مبتلا به ایدز با فرض عفونت همزمان در میان آنها، تقسیم شده است. این مدل دارای دو بخش اساسی، کیفی و کمی است. در بخش کیفی، ما به تجزیه و تحلیل پویایی انتقال این عفونت همزمان با استفاده از تجزیه و تحلیل تعادل و ثبات می‌پردازیم. در بخش عددی، جریان انتقال بیماری در میان طبقات مختلف به از شبیه سازی محاسباتی استفاده شده است. تجزیه و تحلیل حساسیت نیز انجام شده است.

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