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MATHEMATICAL MODEL FOR TRANSMISSION DYNAMICS OF HIV AND TUBERCULOSIS CO-INFECTION IN KOGI STATE, NIGERIA

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Abstract: In this work, we formulated a deterministic co-infection mathematical model made up of a system of non-linear differential equations and rigorously analyzed it so as to gain insight into the transmission dynamics of each of the diseases as they were co-circulating in the population. We investigated the existence and stability of equilibria of the co-infection model and we subjected the model to rigorous analysis. The analysis of the sub-models (HIV-only and TB-only models) and that of the co-infection model revealed that their disease-free equilibrium are locally and globally asymptotically stable when their reproduction numbers were each less than unity, showing that the diseases can be put under control under these conditions. We carried out sensitivity analysis of the co-infection model, using data relevant to Kogi state of Nigeria, which revealed that the top ranked parameters that drive the tuberculosis infection (with respect to the associated response function R_T) is (u_1) , the control measure, educational awareness for the susceptible to always cover their mouth when coughing, sneezing and the need for the infants to be inoculated against the disease, while the top ranked parameter that drive the HIV infection (with respect to the associated response function R_H) is (u_2) , the educational awareness campaign measure for the susceptible individuals to practice safe sexual activities, the need to avoid contacts with bodily fluids of infected patients and the

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prevention of vertical transmission of the disease. From the simulation of the co-infection model, the phenomenon of competitive exclusion occur where the disease with higher reproduction number drives out that with lesser one; furthermore, it was revealed that increasing the treatment rates of the individuals co-infected with TB and HIV could bring down the burden of the two diseases significantly, while increasing the control measures (u_1) and (u_2) leads to significant reduction in the cumulative co-infection new cases of mixed infection in the population.

Keywords: tuberculosis; HIV; co-infection; model; stability; simulations.

2010 AMS Subject Classification: 92D30, 37C75.

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) is a lenti-virus that causes the Acquired Immunodeficiency Syndrome (AIDs), [1]. The condition in which humans' immune system degrades gradually which allows life threatening opportunistic infections to invade and thrive in the decaying immune system of the infected human is as a result of the disease called AIDS [1, 2]. The HIV infection suppresses the body's resistant framework by diminishing the quantity CD4-T Cells [3,4,5,6]. HIV symptoms include chills, diarrhea that lasts for more than a week, tiredness, fever, profuse night sweats, mouth ulcers, muscle aches, rapid weight loss, sore throat [7,8]. The HIV virus can be transmitted through the exchange of a variety of fluids from infected individuals such as blood, breast milk, semen and vaginal secretions. Presently there is no cure and vaccine for HIV infection but effective treatment with antiretroviral drugs can control the virus so that people with HIV can live healthy [9, 10].

Tuberculosis (TB) is an infectious disease caused by mycobacterium tuberculosis bacteria [7]. It affects the lungs and virtually other parts of the human body; it can also affect any age group [5, 11]. Symptoms of the TB includes chronic cough with blood containing sputum fever, night sweat and weight loss [7]. When people who have active tuberculosis cough, spit, speak, sing or sneeze, they propel and expel tuberculosis germs [11, 12, 13, 14].

HIV and tuberculosis increase the challenge of public health, the synergy between tuberculosis and HIV co-infection in patients is bidirectional on one hand, HIV infection influences the

progression of active TB and on the other hand active TB worsen the Immunodeficiency of HIV patients, [3,15].

According to [12], infected HIV patients are bounded to be infected with tuberculosis. It is therefore important that adequate attention should be given to how the co-infection of HIV and tuberculosis can be controlled in a population.

Some authors have developed models to investigate the co infection of HIV and TB epidemics. [2] presented a dynamic model of a TB –HIV co infection with latent age where they discussed the significance of including the effects of each disease;[1] developed a simple mathematical model for HIV–TB co infection. The authors observed that the co infection equilibrium point exists only under same restrictions on the parameters provided. The co-infection equilibrium point was observed to be unstable

A mathematical model for TB-HIV co infection transmission mechanism was presented by [3]. Results from their model analysis show that individual experiencing incidence of HIV infection are at a risk of TB co infection compared with individuals without HIV infection .

An optimal treatment control of TB – HIV co-infection was presented by [9],their work focus on the effect of optimal control on the transmission dynamics of TB /HIV. Results from their model analysis shows that the combination of anti-TB and ARV treatments is the most effective tool to reduce the TB –HIV co infection. Models such as the ones in [5, 11, 16,17,18, 19] are veritable tools towards studying the transmission dynamics of infectious diseases.

Consequently, in this work, we formulated a mathematical model that can help gain insight into the transmission dynamics of HIV and Tuberculosis co-infection,co-circulating in a population, using Kogi state Nigeria as a case study.

2. MODEL FORMULATION

The two diseases, HIV/AIDS and Tuberculosis are assumed to be spreading in Kogi state, Nigeria of total population size ($N(t)$). We then classify the total population into six classes; the Susceptible $S(t)$, Individuals infected with Tuberculosis ($I_1(t)$), individuals infected with HIV

with TB ($I_2(t)$), individuals infected with TB that are on treatment ($T_1(t)$), individuals infected with HIV with TB infection that are on treatment ($T_2(t)$), individuals infected with AIDs ($A(t)$), this is as a result of the progression of individuals already infected with HIV that refuse to go for treatment and lastly individuals that recovered from tuberculosis infection ($R_1(t)$).

In modeling the co-infection of these two diseases, we make the following assumptions:

- (i) Only individuals infected with TB can be infected with HIV as finding shows that 80% of individuals infected with HIV are practically bound to be infected with TB [20].
- (ii) Those infected with TB and HIV are taken for treatment.
- (iii) While TB infected individuals are taken for treatment, only those that are treated can recover from the disease, though they are still susceptible to the disease.
- (iv) While some proportion of individuals infected with HIV accept to go for treatment, the remaining proportion that refused to go for treatment progress to the AIDs infected class.
- (v) Those individuals infected with TB, AIDs on treatment can die due to the diseases. However, the disease-induced death rate due to AIDs is higher as compared to the other. Due to higher efficacy of drugs for TB as compared to antiretroviral drugs available for HIV treatment, disease-induced death rate for TB is assumed to be lower.
- (vi) Natural death rate for individuals in all the classes are taken to be the same.
- (vii) The transmission rate for the individuals in the susceptible class to be infected with TB is reduced by a factor (u_1) which represents the awareness educational campaign measures available for them that they should always cover their mouth when coughing, sneezing and the need for the infants to be inoculated against the disease. Similarly, the transmission rate for the Susceptible to be infected with HIV is reduced by a factor (u_2), which represents awareness educational campaign measures that susceptible individuals practice safe sexual activities, the need to avoid contacts with infected body fluids and the prevention of mother to child transmission during child birth or breast feeding. Furthermore, infection of individuals with TB and HIV together can be reduced by a factor (u_3) which also represents

the awareness educational campaign measure available for the individuals infected with TB to refrain themselves from HIV infection with proper awareness campaign.

Based on the assumptions stated above, the schematic diagram for the co-infection model is as presented below:

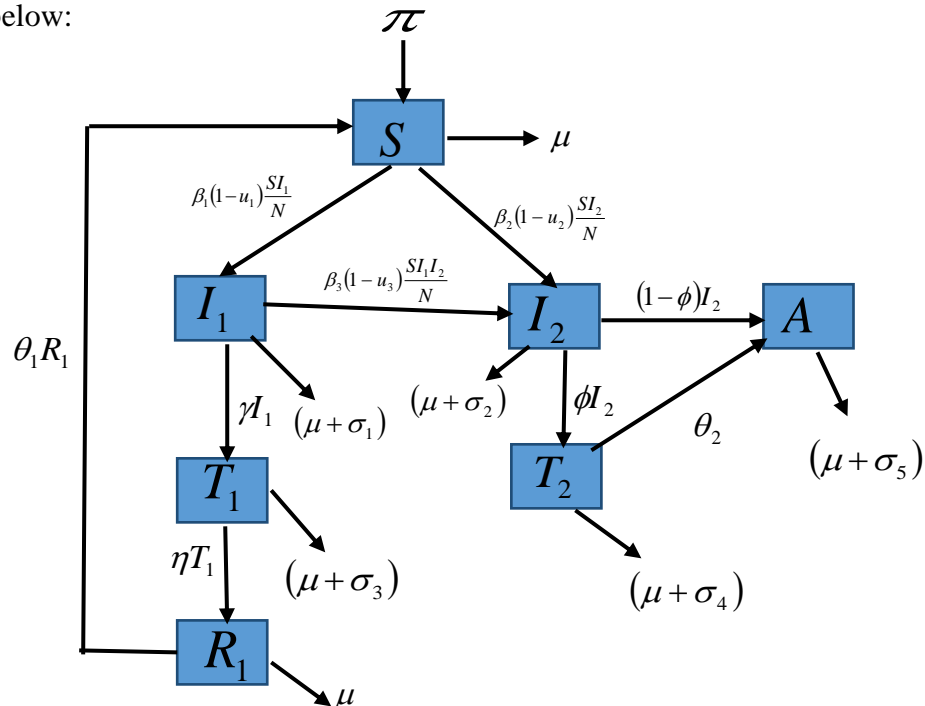


Fig 1: Schematic diagram for co-infection transmission

2.1 MODEL DESCRIPTION

Individuals are recruited into the Susceptible class at the rate (π), the population reduces at the rate (β_1), the rate at which individuals in the Susceptible class came in contact with Tuberculosis infected individuals in TB infected class (I_1), this rate is reduced by (u_1) which represents an awareness educational campaign measures for the individuals in the susceptible class to always cover their mouth when coughing, sneezing and the need to always inoculate the infants against TB. The individuals in Susceptible class also decreases at the rate by which individuals carelessness get exposed to HIV infected individuals in class (I_2) and became infected at the contact rate (β_2), this rate can be reduced by a factor (u_2) a control parameter that represents an awareness educational campaign measure available for the individuals in susceptible class to practice safe sexual activities, the need to avoid contact with bodily fluid of infected individuals

and also prevention of mother to child transmission through child bearing and breastfeeding. This susceptible population is increased by the rate at which those individuals that recovered from TB infection recover due to treatment and became Susceptible again. This Susceptible population finally decreases by natural death at the rate (μ) . The population of TB infected individuals in class (I_1) increases by the rate at which the susceptible individuals become infected and progresses to the class at the rate (β_1) . This population reduces by the contact rate (β_3) , the rate by which the TB infected individuals infects the already infected HIV individuals, this rate is however reduced by a factor (u_3) which is a control parameter that represents an awareness educational campaign measure available for the TB infected individuals to refrain themselves from HIV infected individuals through proper awareness campaign. The population is further reduced by the rate at which the TB infected individuals are taken for treatment at the rate (γ) , finally, this population is reduced through natural death and tuberculosis-induced death rate (μ) and (σ_3) respectively. The HIV infected population with tuberculosis (I_2) increases by the rate at which the susceptible individuals become infected with HIV at a contact rate (β_2) . This population also increases by the rate at which the TB infected individuals infects the HIV infected individuals with TB at the contact rate (β_3) . These contact rates (β_2) and (β_3) is reduced by factors (u_2) and (u_3) respectively.

When the control parameters $u_1 = u_2 = u_3 = 0$, this implies that the educational campaign measures are not accepted, but when $u_1 = u_2 = u_3 = 1$, it means that the educational campaign measures are accepted and the three disease transmission rates (β_1) , (β_2) and (β_3) are reduced and as such, the spread of these diseases could be effectively reduced. The HIV population with or without TB (I_2) can be reduced by the rate at which the infected individuals are taken for treatment at the rate (ϕ) , the remaining population of the HIV infected individuals with TB who refused to go for treatment progress to the AIDs infected class at the rate $(1 - \phi)$. This class is reduced by both disease-induced and natural death rates (σ_2) and (μ) respectively.

The TB infected individuals on treatment in class (I_1) increases at the rate (γ) and the class reduces by both disease-induced death rate and natural death rate (σ_2) and (μ) respectively. This class finally reduces at the rate by which the recovered individuals due to treatment becomes susceptible again.

The class of individuals infected with HIV with TB (I_2) increases at the rate (ϕ) and reduces at the rate (θ_2), this rate represents the rate at which the HIV treatment fails or the infected individuals refuse to take their drugs and thereby progress to AIDs class (A); this population is reduced by disease-induced death rate and natural death rate (σ_4) and (μ) respectively. Individuals are recruited into AIDs infected population (A) by the progression of HIV infected individuals with TB that refuse to go for treatment and secondly, due to treatment failure at rate (θ_2). This class finally reduces due to high disease-induced death rate (σ_5) and by natural death rate (μ). The tuberculosis recovered class (R_1) grows as a result of the incoming individuals that recovered after treatment at the rate (η); this class is reduced further by the individuals that become susceptible at the rate (θ_1) and by natural death.

Arising from above, the co-infection model for HIV/AIDs and Tuberculosis is given by the following systems of non-linear differential equations:

$$\left. \begin{aligned} \frac{dS}{dt} &= \pi - \beta_1(1-u_1)\frac{SI_1}{N} - \beta_2(1-u_2)\frac{SI_2}{N} + \theta_1R_1 - \mu S \\ \frac{dI_1}{dt} &= \beta_1(1-u_1)\frac{SI_1}{N} - \beta_3(1-u_3)\frac{I_1I_2}{N} - (\gamma + \sigma_1 + \mu)I_1 \\ \frac{dI_2}{dt} &= \beta_2(1-u_2)\frac{SI_2}{N} - \beta_3(1-u_3)\frac{I_1I_2}{N} - (1-\phi)I_2 - \phi I_2 - (\sigma_2 + \mu)I_2 \\ \frac{dT_1}{dt} &= \gamma I_1 - (\eta + \sigma_3 + \mu)T_1 \\ \frac{dT_2}{dt} &= \phi I_2 - (\theta_2 + \sigma_4 + \mu)T_2 \\ \frac{dA}{dt} &= (1-\phi)I_2 + \theta_2T_2 - (\sigma_5 + \mu)A \\ \frac{dR_1}{dt} &= \eta T_1 - (\theta_1 + \mu)R_1 \end{aligned} \right\} (1)$$

Where $0 \leq u_1 \leq 1$, $0 \leq u_2 \leq 1$ and $0 \leq u_3 \leq 1$.

Below is the model state variables and Parameters description:

Table 1: Model State variables and Parameters description

S/N	State Variables	Description
1.	$S(t)$	Susceptible class
2.	$I_1(t)$	Tuberculosis infected class
3.	$I_2(t)$	Dually infected individuals with HIV and TB class
4.	$T_1(t)$	Treatment class for individuals infected with Tuberculosis
5.	$T_2(t)$	Treatment class for individuals dually infected with HIV and TB infection
6.	$A(t)$	AIDs infected class
7.	$R_1(t)$	Tuberculosis Recovered class
	Parameters	Description
1.	β_1	Contact rate for TB
2.	β_2	Contact rate for HIV
3.	β_3	Transmission rate for tuberculosis infected individuals to contact HIV.
4..	u_1	Educational campaign measure for the susceptible individuals to always cover their mouth when coughing, sneezing and the need for the infants to be inoculated against tuberculosis.
5.	u_2	Educational campaign measure for the susceptible individuals to always practice safe sexual activities, the need to avoid contacts with infected bodily fluids and the prevention of mother to child transmission during birth or breast feeding.
6.	u_3	Educational campaign measure for the TB infected individuals to refrain themselves from HIV infection with proper awareness campaign.
7.	ϕ	Treatment rate of individuals infected with HIV infection

8.	$(1-\phi)$	Proportion of individuals infected with HIV infection that refuse to go for treatment and progressed to AIDs infected class.
9.	γ	Treatment rate for tuberculosis infected individuals.
10.	θ_1	Recovery rate of tuberculosis infected individuals on treatment who become susceptible again.
11.	θ_2	The rate at which individuals infected with HIV infection progress to AIDs infected class due to treatment failure.
12.	μ	Natural death rate which is the same in all classes.
13.	$\sigma_1 (\sigma_5)$	Disease-induced death rate due to TB (due to AIDs)
14.	σ_2	Disease-induced death rate due to co-infection with HIV and TB
15.	σ_3	Disease-induced death rate due to tuberculosis for individuals on treatment
16.	σ_4	Disease-induced death rate due to co-infection with HIV and TB infection for individuals on treatment
17.	η	Recovery rate for tuberculosis infected individuals
18.	π	Recruitment rate into Susceptible class

2.2 POSITIVITY OF SOLUTION

Considering the fact that model (1) is a monitor for human population, there is a compelling need that all its state variables and parameters remains positive for all time, t . Hence, the following non-negativity results for the state variables in model (1) is given rise to:

Theorem 2.1

Given that the initial data be $\{(S(0), I_1(0), I_2(0), T_1(0), T_2(0), A(0), R(0)) \geq 0\} \in R_+^7$. Then, the solution set $\{(S(t), I_1(t), I_2(t), T_1(t), T_2(t), A(t), R(t))\}$ of the model (1) with non-negative initial data, will remain non-negative for all time $t > 0$.

Proof: From the first equation of the model:

$$\frac{dS}{dt} = \pi - \beta_1(1-u_1)\frac{SI_1}{N} - \beta_2(1-u_2)\frac{SI_2}{N} + \theta_1 R_1 - \mu S$$

$$dS/dt = \pi + \theta_1 R_1 - \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] S$$

$$dS/dt \geq - \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] S$$

By integrating both sides of this, we have:

$$\int dS/S \geq \int - \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] dt$$

$$\ln S \geq - \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] t + c_1$$

Taking the exponential of both sides of this, we have:

$$S(t) \geq e^{- \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] t + c_1} \Rightarrow S(t) \geq c_1 e^{- \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] t}$$

By applying the initial condition $t = 0$, $S(0) \geq c_1$, we have:

$$S(t) \geq S(0) e^{- \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] t} \geq 0, \quad \text{since } \left[\beta_1(1-u_1) \frac{I_1}{N} + \beta_2(1-u_2) \frac{I_2}{N} + \mu \right] > 0$$

Similarly, it can be shown that other state variables:

$$S(t) > 0, I_1(t) > 0, I_2(t) > 0, T_1(t) > 0, T_2(t) > 0, A(t) > 0, \text{ and } R(t) > 0$$

Consequently, for all non-negative initial conditions, all solutions of the model (1) remain positive.

2.3 INVARIANCE PROPERTY

For our model (1) to be meaningful epidemiologically, there is a need to show that all the state variables of model are positive for all time (t). In other words, the solutions of model (1) with non-negative initial data will remain non-negative for all $t \geq 0$; the proof of this is as follows:

Lemma 2.2 The region: $D = \left\{ S(t), I_1(t), I_2(t), T_1(t), T_2(t), A(t), R(t) \right\} \in R_+^7 : N \leq \pi/\mu$

is positively-invariant and attracts all the solution in R_+^7 .

Proof: By adding the equations in the model system (1), we have:

$$N(t) = S(t) + I_1(t) + I_2(t) + T_1(t) + T_2(t) + A(t)$$

$$\therefore \frac{dN(t)}{dt} = \pi - \mu N - \sigma_1 I_1 - \sigma_1 I_1 - \sigma_1 T_1 - \sigma_1 T_2 - \sigma_1 A \quad (2)$$

At steady state, when there is no infection in the system, (2) becomes:

$$\frac{dN(t)}{dt} = \pi - \mu N = 0 \quad \Rightarrow \pi - \mu N = 0$$

$$\therefore N = \frac{\pi}{\mu}$$

Thus, the region D is a positively-invariant set under the flow described by model (1) so that all the solutions are contained in the boundary of region D. Hence, this is the necessary and sufficient condition for the consideration of the dynamics of the model (1) in region D. Thus, in this region, we say that model (1) is epidemiologically and mathematically well posed.

3. ANALYSIS OF SUB MODELS

Before analysing full co-infection model (1), it is pertinent to gain some insights into the dynamics of the model with only tuberculosis appearing in the system and the case when only HIV is appearing in the system. This we do in this section.

3.1 TUBERCULOSIS-ONLY MODEL

From the general co-infection model (1), neglecting the interaction of HIV infected individuals by setting $I_2 = T_2 = A = 0$, we obtain tuberculosis-only infected model which is as presented below:

$$\left. \begin{aligned} \frac{dS}{dt} &= \pi - \beta_1(1-u_1)\frac{SI_1}{N} + \theta_1 R_1 - \mu S \\ \frac{dI_1}{dt} &= \beta_1(1-u_1)\frac{SI_1}{N} - (\gamma + \sigma_1 + \mu)I_1 \\ \frac{dT_1}{dt} &= \eta I_1 - (\eta + \sigma_3 + \mu)T_1 \\ \frac{dR_1}{dt} &= \eta T_1 - (\theta_1 + \mu)R_1 \end{aligned} \right\} (2)$$

The flow diagram for tuberculosis alone model is as presented below:

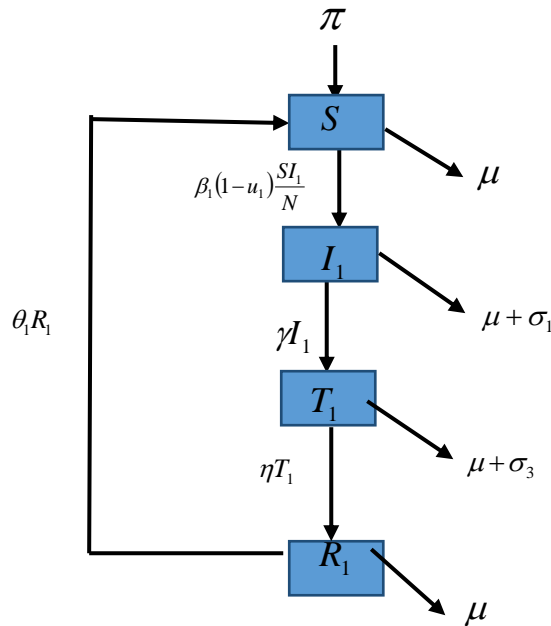


Fig 2: Schematic diagram for Tuberculosis-only transmission

3.1.1 LOCAL ASYMPTOTIC STABILITY OF DISEASE FREE EQUILIBRIUM OF TUBERCULOSIS-ONLY MODEL

The disease-free equilibrium (DFE) of the model (2) is given by:

$$D_1 = \left\{ (S^0, I_1^0, T_1^0, R_1^0) \in R_+^4 : N \leq \frac{\pi}{\mu} \right\}.$$

It is not difficult to show that the set D_1 is positively invariant, such that it will attract all positive solution of sub model (2). Consequently, in this region, the given model can be considered to be epidemiologically and mathematically well posed and it is sufficient to consider the dynamics of model (2) in D_1 .

We obtain the DFE of model (2) by setting the right hand side of the equations in the model to zero to obtain:

$$\varepsilon_0 = (S^0, I_1^0, T_1^0, R_1^0) = \left(\frac{\pi}{\mu}, 0, 0, 0 \right)$$

The local asymptotic stability (LAS) of the DFE is shown by using the next generation operator method on (2). By using related notations given by van den Driessche and Watmough in [21], the matrices F and V for the new infection terms and the remaining transfer terms, are, respectively, given by:

$$F = \begin{pmatrix} \beta_1(1-u_1) & 0 \\ 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} P_1 & 0 \\ -\gamma & P_1 \end{pmatrix}$$

Where, $P_1 = (\gamma + \mu + \delta_1)$ and $P_2 = (\eta + \mu + \delta_3)$

From here, it follows from van den Driessche and Watmough [21], that the reproduction number of model (2) is given by:

$$R_T = \rho(FV^{-1}) = \frac{\beta_1(1-u_1)}{(\gamma + \mu + \sigma_1)}$$

We Claim the result below from theorem (2) given by [21].

Lemma 3.1

The DFE, ε_0 , of model (2) is locally asymptotically stable (LAS) if $R_T < 1$ and unstable if $R_T > 1$.

This threshold R_T , the basic reproduction number for the tuberculosis-only model can be interpreted to be the product of the transmission rate β_1 with the control $(1-u_1)$ and the average duration $\frac{1}{(\gamma + \mu + \sigma_1)}$ spent in the infection compartment of the disease.

The implication of Lemma 3.1, epidemiologically and biologically speaking is that necessary and sufficient condition for the elimination of tuberculosis from the population is $R_T < 1$, if the initial sizes of the subpopulation of the sub model are in the region of attraction of ε_0 .

3.1.2 EXISTENCE AND LOCAL STABILITY OF ENDEMIC EQUILIBRIUM POINT (EEP) OF MODEL (2)

Let the endemic equilibrium of tuberculosis-only infection model (2) be represented by:

$$\varepsilon_1 = (S^{**}, I_1^{**}, T_1^{**}, R_1^{**})$$

By rewriting the equations in system (2) in terms of the force of infection written as

$$\lambda^{**} = \beta_1(1-u_1) \frac{I_1^{**}}{N^{**}} \quad (3)$$

and setting the right hand sides of the equations in model (2) to zero, solving for the state variables in terms of the force of infection at steady state we obtain:

$$S^{**} = \frac{\pi}{(\lambda^{**} + \mu)} + \frac{\eta\gamma\theta_1\lambda^{**}}{(\theta_1 + \mu)(\gamma + \mu + \sigma_1)(\eta + \mu + \sigma_3)(\lambda^{**} + \mu)}, \quad I_1^{**} = \frac{\lambda^{**}}{(\gamma + \sigma_1 + \mu)},$$

$$T_1^{**} = \frac{\gamma\lambda^{**}}{(\gamma + \sigma_1 + \mu)(\eta + \sigma_3 + \mu)}, \quad T_1^{**} = \frac{\eta\gamma\lambda^{**}}{(\theta_1 + \mu)(\eta + \sigma_3 + \mu)(\gamma + \sigma_1 + \mu)} \quad (4)$$

By substituting the expression for the endemic equilibrium point into the force of infection at steady state given in (3), we obtain:

$$F_2(\lambda^{**})^3 + F_1(\lambda^{**})^2 - F_0(R_H - 1)(\lambda^{**}) = 0 \quad (5)$$

Where

$$F_2 = (\theta_1 + \mu)(\eta + \sigma_3 + \mu) + \gamma(\theta_1 + \eta + \mu)$$

$$F_1 = (\theta_1 + \mu)(\eta + \sigma_3 + \mu)(\gamma + \sigma_1 + \mu)\mu + (\theta_1 + \mu)\mu\gamma + \eta\gamma\mu\theta_1 + \eta\gamma\mu - \beta_1(1-u_1)(\theta_1 + \mu)(\eta + \sigma_3 + \mu)$$

$$F_0 = (\theta_1 + \mu)(\gamma + \sigma_1 + \mu)(\gamma + \sigma_1 + \mu)\gamma\mu \quad (6)$$

It follows from (5) and (6) that the polynomial (6) has a unique positive solution whenever $R_T > 1$.

3.1.3 GLOBAL ASYMPTOTIC STABILITY OF THE DFE OF MODEL (2)

In order to show that system (2) does not undergo a backward bifurcation at $R_T = 1$, we now prove the global asymptotic stability of the DFE of model (2).

Theorem 3.1

The DFE of the tuberculosis-only model (2) is globally asymptotically stable if $R_T \leq 1$ and unstable if $R_T \geq 1$.

Proof: Consider the following Lyapunov function:

$$F = aI_1 + bT_1$$

With Lyapunov derivative (where a dot represents differentiation with respect to time)

$$\dot{F} = a\dot{I}_1 + b\dot{T}_1$$

With a little perturbation from the reproduction number we have: $a = \gamma$ and $b = (\gamma + \mu + \sigma_1)$

Therefore,

$$\begin{aligned} \dot{F} &= \gamma\dot{I}_1 + (\gamma + \mu + \sigma_1)\dot{T}_1 \\ &= \gamma \left[\beta_1(1-u_1) \frac{SI_1}{N} - (\gamma + \sigma_1 + \mu)I_1 \right] + (\gamma + \mu + \sigma_1) [\gamma I_1 - (\eta + \sigma_3 + \mu)T_1] \\ &= \gamma\beta_1(1-u_1) \frac{SI_1}{N} - \gamma(\gamma + \sigma_1 + \mu)I_1 + \gamma(\gamma + \sigma_1 + \mu)I_1 - \gamma(\gamma + \sigma_1 + \mu)(\eta + \sigma_3 + \mu)T_1 \\ &= \gamma\beta_1(1-u_1) \frac{SI_1}{N} - \gamma(\gamma + \sigma_1 + \mu)(\eta + \sigma_3 + \mu)T_1 \\ &= \gamma \left[\beta_1(1-u_1) \frac{SI_1}{N} - (\gamma + \sigma_1 + \mu)(\eta + \sigma_3 + \mu)T_1 \right] \\ &= \gamma \left[\frac{\beta_1(1-u_1)}{(\gamma + \sigma_1 + \mu)(\eta + \sigma_3 + \mu)T_1} \frac{SI_1}{N} - 1 \right] = \gamma \left[\frac{SI_1}{(\eta + \sigma_3 + \mu)T_1 N} R_0 - 1 \right] = \gamma[CR_0 - 1] \end{aligned}$$

$$\text{Where } C = \frac{SI_1}{(\eta + \sigma_3 + \mu)T_1 N} \quad \forall S \leq N$$

$$\Rightarrow \dot{F} = \gamma[CR_0 - 1] \leq 0 \quad \forall R_0 \leq 1$$

Since all the model parameters are non-negative, it follows that $\dot{F} \leq 0$ for $R_0 \leq 1$ with $\dot{F} = 0$ if and only if $I_1 = T_1 = 0$. Hence, F is a Lyapunov function in the invariant region. Therefore, by LaSalle's invariance principle, every solution to the equations in the treatment-free model, with condition in the invariant region, approaches ε_0 as $t \rightarrow \infty$.

Thus, the above theorem shows that the classical epidemiological requirement of $R_0 \leq 1$ is the necessary and sufficient condition for the elimination of the disease from the community.

3.2 HIV-ONLY MODEL

Also from the general co-infection model (1), by neglecting the interaction of tuberculosis infected individuals by setting $I_1 = T_1 = R_1 = 0$, we obtain HIV-only infected model which is as presented below:

$$\begin{aligned}
 \frac{dS}{dt} &= \pi - \beta_2(1-u_2)\frac{SI_2}{N} - \mu S \\
 \frac{dI_2}{dt} &= \beta_2(1-u_1)\frac{SI_2}{N} - (1-\phi)I_2 - \phi I_2 - (\sigma_2 + \mu)I_2 \\
 \frac{dT_2}{dt} &= \phi I_2 - (\theta_2 + \sigma_4 + \mu)T_2 \\
 \frac{dA}{dt} &= (1-\phi)I_2 - \theta_2 I_2 - (\sigma_5 + \mu)A
 \end{aligned}
 \tag{7}$$

The flow diagram for HIV-only model is as presented below.

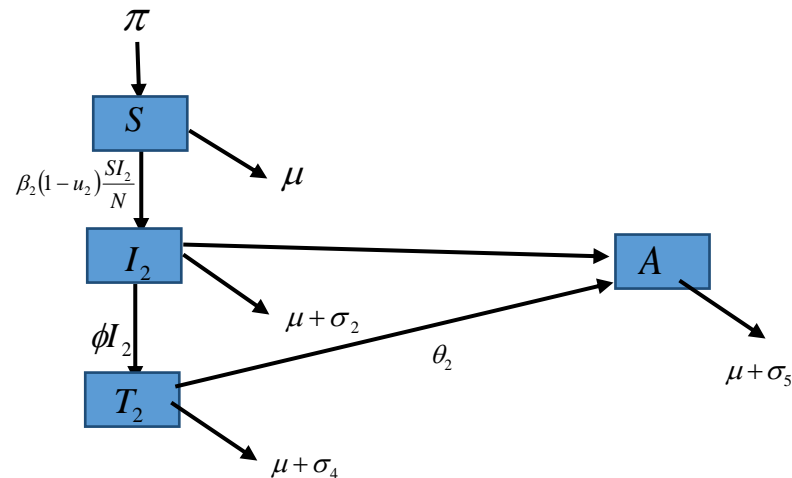


Fig 3: Schematic diagram for HIV-only transmission

3.2.1 LOCAL ASYMPTOTIC STABILITY OF DISEASE FREE EQUILIBRIUM OF HIV-ONLY MODEL

The disease-free equilibrium (DFE) of the model (7) is given by:

$$D_2 = \left\{ (S^0, I_2^0, T_2^0, A^0) \in R_+^4 : N \leq \frac{\pi}{\mu} \right\}.$$

It is not difficult to show that the set D_2 is positively invariant, such that it will attract all positive solution of sub model (7). Hence, in this region, the given model can be considered to be epidemiologically and mathematically well posed and it is sufficient to consider the dynamics of model (7) in D_2 .

We obtain the DFE of model (7) by setting the right hand side of the equations in the model to zero to obtain:

$$\varepsilon_{S_0} = (S^0, I_1^0, T_1^0, R_1^0) = \left(\frac{\pi}{\mu}, 0, 0, 0 \right)$$

The local asymptotic stability (LAS) of the DFE is shown by using the next generation operator method on (7). By using related notations given by van den Driessche and Watmough [21], the matrices F and V for the new infection terms and the remaining transfer terms, are, respectively, given by:

$$F = \begin{pmatrix} \beta_1(1-u_1) & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} P_1 & 0 & 0 \\ -\phi & P_2 & 0 \\ -(1-\phi) & -\theta_2 & P_3 \end{pmatrix}$$

Where, $P_1 = (1 + \mu + \delta_2)$, $P_2 = (\theta_2 + \mu + \delta_4)$ and $P_3 = (\mu + \delta_5)$

From here, it follows from [21] that the reproduction number of model (7) is given by:

$$R_H = \rho(FV^{-1}) = \frac{\beta_2(1-u_2)}{(1 + \mu + \sigma_2)}$$

We Claim the result below from theorem (7) given in [21].

Lemma 3.2

The DFE, ε_{S_0} , of model (7) is locally asymptotically stable (LAS) if $R_H < 1$ and unstable if

$$R_H > 1.$$

This threshold R_H , the basic reproduction number for the HIV-only model can be interpreted to be the product of the transmission rate β_2 with the control $(1-u_2)$ and the average duration

$\frac{1}{(1 + \mu + \sigma_2)}$ spent in the infection compartment of the disease.

The implication of Lemma 3.2, epidemiologically and biologically speaking is that necessary and sufficient condition for the elimination of HIV from the population is $R_H < 1$, if the initial sizes of the subpopulation of the sub model are in the region of attraction of ε_{S_0} .

3.2.2 EXISTENCE AND LOCAL STABILITY OF ENDEMIC EQUILIBRIUM POINT (EEP) OF MODEL (7)

Let the endemic equilibrium of tuberculosis alone infection model (7) be represented by:

$$\varepsilon_2 = (S^{**}, I_2^{**}, T_2^{**}, A^{**})$$

By rewriting the equations in system (6) in terms of the force of infection and setting the right hand sides of the equations in it to zero, solving for the state variables in terms of the force of infection at steady state given as:

$$\lambda_1^{**} = \beta_2(1-u_2) \frac{I_2^{**}}{N^{**}} \quad (8)$$

we obtain:

$$S^{**} = \frac{\pi}{(\lambda_1^{**} + \mu)}, \quad I_2^{**} = \frac{\pi \lambda_1^{**}}{(1 + \sigma_2 + \mu)(\lambda_1^{**} + \mu)}, \quad T_2^{**} = \frac{\phi \pi \lambda^{**}}{(\lambda^{**} + \mu)(1 + \sigma_2 + \mu)(\theta_2 + \sigma_4 + \mu)},$$

$$A^{**} = \frac{(1 - \phi) \pi \lambda^{**}}{(\lambda^{**} + \mu)(1 + \sigma_2 + \mu)(\sigma_5 + \mu)} + \frac{\theta_2 \phi \pi \lambda^{**}}{(\lambda^{**} + \mu)(1 + \sigma_2 + \mu)(\theta_2 + \sigma_4 + \mu)} \quad (9)$$

By substituting this expression for the endemic equilibrium point into the force of infection at steady state given in (8), we obtain:

$$F_2(\lambda^{**})^2 - F_1(1 - R_H)\lambda^{**} = 0 \quad (10)$$

Where:

$$F_2 = (\theta_1 + \mu)(\eta + \sigma_3 + \mu) + \gamma(\theta_1 + \eta + \mu)$$

$$F_1 = \pi[\theta(\sigma_5 + \mu) + (1 - \phi)(\theta_2 + \mu + \sigma_4) + \theta_2\phi(\mu + \sigma_5)] \quad (11)$$

It follows from (10) and (11) that the quadratic equation (10) has a unique positive solution whenever $R_H < 1$.

3.2.3 GLOBAL ASYMPTOTIC STABILITY OF THE DFE OF HIV-ONLY MODEL (7)

In order to show that system (7) does not undergo a backward bifurcation at $R_H = 1$, we now prove the global asymptotic stability of the DFE of model (7). The approach illustrated in [22], Castillo Chaves to investigate the global asymptotic stability of disease-free equilibrium of epidemiological models becomes relevant here. By adopting the approach here, below are the

necessary and sufficient conditions to guarantee the global asymptotic stability of disease-free equilibrium of our HIV-only model (7):

(1) The system (7), the HIV-only model can be written in the form:

$$\begin{aligned}\frac{dU}{dt} &= F(U, V) \\ \frac{dV}{dt} &= G(U, V), G(U, 0) = 0\end{aligned}\quad (12)$$

Where $U \in R^m$ denotes its components, the number of uninfected individuals and $V \in R^m$ denotes its components, the number of infected individuals. Thus $U=S$ and $V = (I_2, T_2, A)$ with $U \in R_+^1$ denoting the number of susceptible individuals and $V \in R_+^3$ denoting the number of infected individuals. We now denote the disease-free equilibrium of this system (7) by:

$$\varepsilon_{s_0} = (U^*, 0), \text{ where } U^* = \left(\frac{\pi}{\mu} \right)$$

(2) In order to guarantee the local asymptotic stability of the model (7), the conditions (W1) and (W2) following must be satisfied:

$$(W1): \text{ For } \frac{dU}{dt} = P(U, 0), U^* \text{ is globally asymptotically stable (GAS).}$$

$$(W1): \text{ For } G(U, V) = AV - \hat{G}(U, V)V, \hat{G}(U, V) \geq 0 \text{ for } (U, V) \in \Omega$$

Where $A = D_V G(U^*, 0)$ is an M-matrix (where the off-diagonal elements of A are non-negative) and Ω is the region where the model makes biological sense. If system (7) satisfies the afore-stated necessary and sufficient conditions, then the following theorem holds:

Theorem 3.2

The disease-free equilibrium ε_{s_0} of the HIV-only model (7) is a globally asymptotic stable provided that $R_H < 1$ (LAS) and assumptions (W1) and (W2) are met.

Proof:

From theorem 3.2, we have that ε_{s_0} is locally asymptotically stable if $R_H < 1$. We now consider:

$$F(U, 0) = \begin{pmatrix} \pi - \mu S \\ 0 \end{pmatrix}$$

$$G(U, V) = AV - \hat{G}(U, V)$$

$$A = \begin{pmatrix} \beta_2 - (1 + \mu + \sigma_2) & 0 & 0 \\ \phi & -(\theta_2 + \mu + \sigma_4) & 0 \\ 1 - \phi & \theta_2 & -(\mu + \sigma_5) \end{pmatrix}$$

$$\hat{G}(U, V) = \begin{pmatrix} \hat{G}_1(U, V) \\ \hat{G}_2(U, V) \\ \hat{G}_3(U, V) \end{pmatrix} = \begin{pmatrix} \frac{\beta_2(1-u_2)}{N} \left(1 - \frac{S}{N}\right) \\ 0 \\ 0 \end{pmatrix} \quad \forall S \leq N$$

From the above, it is obvious that $\hat{G}_1(U, V) \geq 0$ and $\hat{G}_2(U, V) = \hat{G}_3(U, V) = 0$, which implies that $\hat{G}(U, V) \geq 0$. Consequently, since the given necessary and sufficient conditions stated above is met, then the disease-free equilibrium ε_{S_0} of the HIV-only model (7) is globally asymptotically stable when $R_H < 1$. This implies that the model (7) does not exhibit backward bifurcation.

4. ANALYSIS OF FULL HIV-TB CO-INFECTION MODEL

A major requirement of an epidemiological model is that it is stable (local and global asymptotic stability). Therefore, in this section, we do the analysis of model (1) for its stability property.

4.1 LOCAL STABILITY OF THE DFE OF HIV-TB CO-INFECTION MODEL (1)

In the absence of disease, otherwise called steady state, the Disease Free Equilibrium refers to a state when there is neither HIV/AIDs nor Tuberculosis infection in the system; as such, $I_1 = I_2 = T_1 = T_2 = A_1 = 0$. The disease-free equilibrium (DFE) of the co-infection (1) model is given by:

$$\xi_0 = (S^*, I_1^*, I_2^*, T_1^*, T_2^*, A^*, R_1^*) = \left(\frac{\pi}{\mu}, 0, 0, 0, 0, 0 \right)$$

Basic Reproduction Number

Using the matrices F and V , for the new infection and the remaining transmission terms respectively gives:

$$F = \begin{pmatrix} \beta_1(1-u_1) & 0 & 0 & 0 & 0 \\ 0 & \beta_2(1-u_2) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} P_1 & 0 & 0 & 0 & 0 \\ 0 & P_2 & 0 & 0 & 0 \\ -\gamma & 0 & P_3 & 0 & 0 \\ 0 & -\phi & 0 & P_4 & 0 \\ 0 & -(1-\phi) & 0 & -\theta_2 & P_5 \end{pmatrix}$$

Where

$$P_1 = (\gamma + \mu + \sigma_1), P_2 = (1 + \mu + \sigma_2), P_3 = (\eta + \mu + \sigma_3), P_4 = (\theta_2 + \mu + \sigma_4) \text{ and } P_5 = (\mu + \sigma_5)$$

Consequently, the reproduction number denoted by:

$$R_0^i = \rho(FV^{-1})$$

Where ρ the spectral radius or largest eigenvalue of FV^{-1} is given by:

$$R_T = \frac{\beta_1(1-u_1)}{(\gamma + \mu + \sigma_1)} \text{ and } R_H = \frac{\beta_2(1-u_2)}{(1 + \mu + \sigma_2)}$$

Where R_T the basic reproduction number of tuberculosis and R_H is the basic reproduction number of HIV.

When the basic reproduction numbers R_T and R_H are more than one, the disease invades the population under consideration while when it is kept less than one, the disease will be wiped out of the population with time.

4.2 LOCAL ASYMPTOTIC STABILITY ANALYSIS OF THE DISEASE FREE EQUILIBRIUM OF THE CO-INFECTION MODEL

In this section, we investigate the local stability of the co-infection model (1).

Theorem 4.2

The DFE of the co-infection model is locally asymptotically stable if $R_0^i < 1$ and unstable if $R_0^i > 1$.

Proof:

From co-infection model (1), the Jacobian matrix expression of the DFE (ε_0) is given by:

$$J_0 = \begin{pmatrix} -\mu & -\beta_1(1-u_1) & -\beta_2(1-u_2) & 0 & 0 & 0 & \theta_1 \\ 0 & [\beta_1(1-u_2) - \beta_3(1-u_3) - (\mu + \sigma_5)] & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -[\beta_2(1-u_2) - (1 + \mu + \sigma_2)] & 0 & 0 & 0 & 0 \\ 0 & \gamma & 0 & -(\eta + \mu + \sigma_4) & 0 & 0 & 0 \\ 0 & 0 & \phi & 0 & -(\theta_2 + \mu + \sigma_4) & 0 & 0 \\ 0 & 0 & (1 - \phi) & 0 & \theta_2 & -(\mu + \sigma_5) & 0 \\ 0 & 0 & 0 & \eta & 0 & 0 & -(\theta_1 + \mu) \end{pmatrix} \text{ by}$$

rewriting J_0 in terms of R_T and R_H we have:

$$J_0 = \begin{pmatrix} -\mu & -\beta_1(1-u_1) & -\beta_2(1-u_2) & 0 & 0 & 0 & \theta_1 \\ 0 & [(\gamma + \mu + \sigma_1)(R_T - 1) - \beta_3(1-u_3)] & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & [(1 + \mu + \sigma_2)(R_H - 1) - \beta_3(1-u_3)] & 0 & 0 & 0 & 0 \\ 0 & \gamma & 0 & -(\eta + \mu + \sigma_4) & 0 & 0 & 0 \\ 0 & 0 & \phi & 0 & -(\theta_2 + \mu + \sigma_4) & 0 & 0 \\ 0 & 0 & (1 - \phi) & 0 & \theta_2 & -(\mu + \sigma_5) & 0 \\ 0 & 0 & 0 & \eta & 0 & 0 & -(\theta_1 + \mu) \end{pmatrix}$$

The eigen values of the above Jacobian matrix are: $-\mu$, $[(\gamma + \mu + \sigma_1)(R_T - 1) - \beta_3(1-u_3)]$, $[(1 + \mu + \sigma_2)(R_H - 1) - \beta_3(1-u_3)]$, $-(\eta + \mu + \sigma_4)$, $-(\theta_2 + \mu + \sigma_4)$, $-(\mu + \sigma_5)$, $-(\theta_1 + \mu)$.

Clearly, all the eigen values will have negative real parts if $R_T < 1$ & $R_H < 1$ in the second and third eigen value; this implies that the disease free equilibrium of the co-infection model (1) is locally asymptotically stable. On the other hand, the DFE of the co-infection model (1) will be unstable when $R_T > 1$ and $R_H > 1$.

Remark:

The epidemiological implication of theorem 4.1 is that the two diseases HIV and TB, co-circulating in the given population, can be effectively eradicated from the population when the threshold, reproduction numbers $R_T < 1$ and $R_H < 1$, if the initial sizes of the sub-populations of the model (1) are in the basin of attraction of the disease-free equilibrium. Consequently, a small influx of HIV-infected or TB-infected individuals into the population will not generate large outbreaks of the diseases, and the diseases will die out in time.

4.3 GLOBAL STABILITY OF DISEASE FREE EQUILIBRIUM OF CO-INFECTION MODEL

Theorem 4.3

The DFE of the co-infection model (1) is globally asymptotically stable if $R_T < 1$ and $R_H < 1$; otherwise, it will be unstable when $R_T > 1$ and $R_H > 1$.

Proof:

Let us define $U(I_1, I_2, T_1, T_2, A) = I_1 + I_2 + T_1 + T_2 + A$

Then the time derivative of U along the solution of the system (1) is given by:

$$\begin{aligned} \dot{U} &= \dot{I}_1 + \dot{I}_2 + \dot{T}_1 + \dot{T}_2 + \dot{A} \\ &= \left[\frac{\beta_1(1-u_1)S}{N} - (\gamma + \mu) \right] I_1 + \left[\frac{\beta_2(1-u_2)S}{N} - (\phi + (1-\phi) + \mu) \right] I_2 \\ &\quad - (\eta + \mu)T_1 - (\theta_2 + \mu)T_2 - \mu A \\ &= \frac{(\gamma + \mu)I_1}{N} [(1 - R_H) + I_1 + I_2 + T_1 + T_2 + A] - \\ &\quad \frac{(\phi + (1-\phi) + \mu)I_2}{N} [(1 - R_T)S + I_1 + I_2 + T_1 + T_2 + A] \\ &\quad - (\eta + \mu)T_1 - (\theta_2 + \mu)T_2 - \mu A \end{aligned}$$

Since all the parameters of the model are positive and state variables are non-negative, it follows that $U(I_1, I_2, T_1, T_2, A) \leq 0$ for $R_T < 1$ and $R_H < 1$. And $U(I_1, I_2, T_1, T_2, A) = 0$ if and only if $I_1 = I_2 = T_1 = T_2 = A = 0$. Consequently, u is a Lyapunov function.

Also for $R_T < 1$ and $R_H < 1$, from the second and third equations of system (1), we have:

$$\lim_{t \rightarrow \infty} I_1 = 0,$$

And from the 1st, 4th, 5th and 6th equations of the system (1), we get $\lim_{t \rightarrow \infty} I_1 = \frac{\pi}{\mu}$, $\lim_{t \rightarrow \infty} T_1 = 0$,

$\lim_{t \rightarrow \infty} T_2 = 0$ and $\lim_{t \rightarrow \infty} A = 0$. Hence, the largest compact invariant set in

$\{(I_1, I_2, T_1, T_2, A) \in D : \dot{U} = 0\}$ is the singleton $\left\{ \frac{\pi}{\mu}, 0, 0, 0, 0 \right\}$ in D.

By using LaSalle's invariance principle [23], the infection free equilibrium ε_0 is globally asymptotically stable for $R_T < 1$ and $R_H < 1$. Consequently, from the above theorem, the necessary and sufficient condition for the elimination of the disease from the population is the classical requirement that $R_T < 1$ and $R_H < 1$.

4.4 ENDEMIC EQUILIBRIUM POINT

In this section we investigate the existence of endemic equilibrium for the co-infection model (1). At the Endemic Equilibrium, there is presence of HIV and tuberculosis in the given system. Thus, we obtain endemic equilibrium when $(I_1, I_2, T_1, T_2, A) \neq 0$.

Theorem 4.4

The co-infection model (2) has the following endemic equilibrium points:

$$\varepsilon_3 = (S^{**}, I_1^{**}, I_2^{**}, T_1^{**}, T_2^{**}, A^{**}, R_1^{**}).$$

Where,

$$\begin{aligned} I_1^{**} &= \frac{(1 + \mu + \sigma_2)(R_H - 1)}{\beta_3(1 - u_3)}, & I_2^{**} &= \frac{(\gamma + \mu + \sigma_1)(R_T - 1)}{\beta_3(1 - u_3)}, \\ T_1^{**} &= \frac{\gamma(1 + \mu + \sigma_2)(R_H - 1)}{\beta_3(1 - u_3)(\eta + \mu + \sigma_3)}, & T_2^{**} &= \frac{\phi(\gamma + \mu + \sigma_1)(R_T - 1)}{\beta_3(1 - u_3)(\theta_2 + \mu + \sigma_4)}, \\ A^{**} &= \frac{(1 - \phi)(\gamma + \sigma_1 + \mu)(R_T - 1)}{\beta_3(1 - \mu_3)(\theta_2 + \sigma_4 + \mu)(\mu + \sigma_5)} + \frac{\theta_2\phi(\gamma + \sigma_1 + \mu)(R_T - 1)}{\beta_3(1 - \mu_3)(\theta_2 + \sigma_4 + \mu)(\mu + \sigma_5)}, \\ R_1^{**} &= \frac{\eta\gamma(1 + \mu + \sigma_2)(R_H - 1)}{\beta_3(1 - u_3)(\eta + \sigma_4 + \mu)(\theta_1 + \mu)}, \\ S^{**} &= \frac{\pi}{\mu} - \frac{\beta_1(1 - u_1)(1 + \mu + \sigma_2)(R_H - 1)}{\mu\beta_3(1 - u_3)} + \\ &\quad \frac{\beta_3(1 - u_2)(\gamma + \mu + \sigma_2)(R_T - 1)}{u\beta_3(1 - u_3)} + \frac{\theta_1\eta\gamma(1 + \mu + \sigma_2)(R_H - 1)}{u\beta_3(1 - u_3)(\eta + \sigma_4 + \mu)(\theta_1 + \mu)} \end{aligned}$$

Lemma 4.4

The endemic equilibrium ε_3 of model (1) exists and is unique if and only if $R_H > 1$ and $R_T > 1$.

Proof:

It is enough to show that the components of each of I_1^{**} , T_1^{**} and R_1^{**} are positive when $R_H > 1$; likewise, the component of each of I_2^{**} , T_2^{**} and A^{**} are positive when $R_T > 1$; and the components of S^{**} are positive when $R_T > 1$ and $R_H > 1$.

5. SENSITIVITY ANALYSIS

Sensitivity analysis shows how sensitive a model is to changes in the values of the parameters of the model and the variation in the structure of the model [18]. Sensitivity analysis is required to know which parameter should be targeted towards control intervention strategies.

Sensitivity index of a parameter say (β_1) depends on the differentiable (R_T) which is expressed as:

$$S_{\beta_1}^{R_T} = \frac{\partial R_T}{\partial \beta_1} \times \frac{\beta_1}{R_T} \quad (10)$$

The sensitivity index for other parameters can be expressed likewise. The values of sensitivity index corresponding to each of the reproduction numbers for each of the diseases is as presented in the table below.

Table 2: Numerical values of sensitivity index corresponding to R_T

S/N	Parameter	Parameter values	Sensitivity Index
1.	β_2	0.1	1.00000
2.	u_2	0.8	-0.71878
3.	μ	0.013	-0.01168
4.	σ_2	0.1	-0.08985

Table 3: Numerical Values of sensitivity values index corresponding to R_H

S/N	Parameter	Parameter values	Sensitivity Index
1.	β_1	0.1	1.00000
2.	u_1	0.8	-1.00883
3.	γ	0.7	-0.88272
4.	μ	0.013	-0.01639
5.	σ_1	0.08	-0.10088

Sensitivity analysis results shows that parameters with positive sensitivity indexes increase the endemicity of the diseases, while parameters with negative sensitivity indexes decrease the endemicity of the two diseases. From table 2, parameters with negative sensitivity indexes will have significant impact on the reduction of the basic reproduction number of tuberculosis R_T to a value less than 1 and as such, these parameters should be targeted in controlling the spread of the tuberculosis in the given population under consideration. Observe that from the sensitivity indexes result, it is evident that educational measure for the susceptible individuals to always cover their mouth when coughing, sneezing and the need for infants to be vaccinated against tuberculosis which is represented by u_1 should be given greater attention towards reduction in the spread of the disease as it has the highest negative sensitivity index -1.00883, this is to be followed by treatment rate of the infected individuals whose index is -0.88272. From table 3 likewise, parameters with negative indexes will have significant impact on the reduction of the reproduction number of HIV with tuberculosis infection to a value less than 1 and as such it should be targeted towards controlling the spread of the disease. It is also obvious that educational campaign measure for the susceptible individuals to practice safe sexual activities, the need to avoid contact with bodily fluids of infected individuals which is represented by u_2 whose sensitivity index is the highest with -0.71878 will have greater impact on the reduction of the burden of the disease.

5.1 ASSESSMENT OF THE EFFECTS OF CONTROL MEASURES ON THE TRANSMISSION DYNAMICS OF CO-INFECTION OF HIV/AIDS AND TUBERCULOSIS

Using the reproduction numbers of HIV/AIDS and tuberculosis with control as derived earlier given by:

$$R_H = \frac{\beta_2(1-u_1)}{(1+\mu+\sigma_2)} \text{ and } R_T = \frac{\beta_1(1-u_1)}{(\gamma+\mu+\sigma_1)}$$

respectively, and the ones without control, given by:

$$R_{WH} = \frac{\beta_2}{(1+\mu+\sigma_2)} \text{ and } R_{WT} = \frac{\beta_1}{(\gamma+\mu+\sigma_1)}$$

By computing the reproduction number using each of the above and parameter values in table 4; it is observed that reproduction numbers with control measures gives lesser reproduction number for each of the diseases as compared to that of without control measures (as would be expected). On the other hand, for the co-infection model, addition of reproduction numbers with control measures $(R_H + R_T)$ when computed gives a reproduction number (0.043) which is less than 1, while the one computed for without control measures $(R_{WH} + R_{WT})$ gives a reproduction number (1.1648) which is greater than 1, showing that co-infection of these diseases will invade the given population in this scenario. From the foregoing, it is clear that as $(R_H + R_T) < 1$, the control intervention strategies when adequately implemented would be sufficient enough to reduce and help eliminate the tuberculosis-only infection, HIV-only infection such that the burden of co-infection of both diseases will be greatly put under control so long as R_H , R_T , and $(R_H + R_T)$ are each less than 1. However, in the absence of control measures, tuberculosis-only infection and the co-infection of both diseases will invade the population as it is evident (as shown) that R_{WT} and $(R_{WH} + R_{WT})$ are each greater than 1.

6. NUMERICAL SIMULATION AND DISCUSSION

We carried out numerical simulations of the co-infection model to illustrate some of the theoretical results obtained in this study. This was done using MATLAB code solver. Variables and parameters values used in the simulations are as presented in the table 4 below:

Table 4: Parameter values of the co-infection model (1) with the total population of Kogi State Nigeria as of 1st January 2021 estimated at 4,434,624 (data obtained from National Population Commission of Nigeria).

S/N	Parameters	Values	Sources
1.	β_1	0.1	[1]
2.	β_2	0.1	[1]
3.	β_3	0.07	Inferred from [1]
4..	u_1	0.8	[1]
5.	u_2	0.8	Inferred from [3]
6.	u_3	0.8	Inferred from [3]
7.	ϕ	0.8	Estimated
8.	γ	0.7	Estimated
9.	θ_1	0.2	[5]
10.	θ_2	0.3	[5]
11.	μ	0.013	[3]
12.	$\sigma_1 (\sigma_5)$	0.08(0.8)	Inferred from [3]
13.	σ_2	0.1	Estimated
14.	σ_3	0.03	Estimated
15.	σ_4	0.05	Estimated
16.	η	0.7	[11]
17.	π	5,0000	[3]

The results from the simulations are as presented in the figures below:

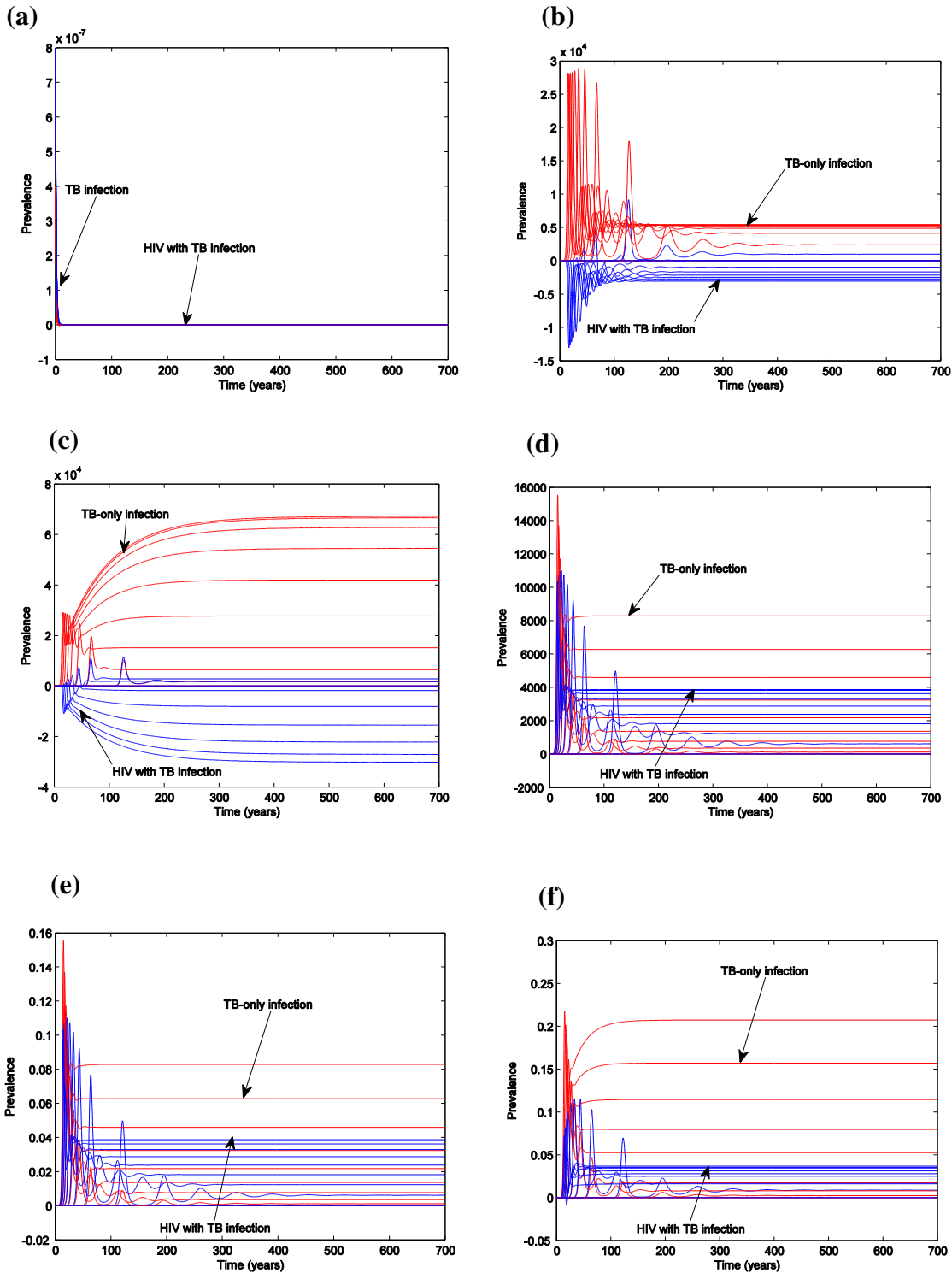


Figure 4. Prevalence (total number of infected individuals divided by the total population) as a function of time for the co-infection model (1).

- (4) (a) $R_H < R_T < 1$ ($\beta_1 = 2.9$ and $\beta_2 = 1.9$) (b) $R_T < R_H < 1$ ($\beta_1 = 1.9$ and $\beta_2 = 3.9$)
 (c) $R_T > 1 > R_H$ ($\beta_1 = 14.9$ and $\beta_2 = 2.9$) (d) $R_H > 1 > R_T$ ($\beta_1 = 2.9$ and $\beta_2 = 9.9$)
 (e) $R_H < R_T > 1$ ($\beta_1 = 14.9$ and $\beta_2 = 2.9$) (f) $R_T < 1 < R_H$ ($\beta_1 = 2.9$ and $\beta_2 = 6.9$)

The co-infection model (1) was simulated by using the parameters in table 4, with $\beta_1 = 2.9$ and $\beta_2 = 1$ it follows that the reproduction numbers $R_H = 0.3414$ and $R_T = 0.7314$, so that $R_0 = 0.7314 < 1$. Thus by theorem 1, the diseases free equilibrium of the system (1) is globally asymptotically stable. Figure 4 (a) depicts simulation of the model under this scenario with various initial conditions; this is a confirmation of global asymptotic stability (GAS) property of the DFE of the co-infection model. Additional simulations of the co-infection model was carried out for $R_i > R_j$ with $R_j > 1$ ($i, j = H, T$) and $i \neq j$, the strain with higher reproduction numbers drives out the other in line with competitive exclusion principle; the results is as shown in figures (b)-(f).

6.1 TREATMENT STRATEGY

We carried out the simulation of the co-infected model (1) for dually infected individuals with HIV-TB on treatment while varying parameter u_1 : Educational campaign measure for the susceptible individuals to always cover their mouth when coughing, sneezing and the need for the infants to be inoculated against tuberculosis at different values between 0 and 0.5, the simulation is as shown in figure 5 (a) where the cumulative number of new cases drop in value as u_1 increases, showing that a combination of treatment of dually infected individuals with HIV-TB while intensifying the awareness campaign u_1 is a good strategy to reducing the burden of the co-infection of the diseases. Likewise, the co-infection model was simulated for dually infected individuals with HIV-TB on treatment while varying parameter u_2 and u_3 , the simulation is as shown in figure 4 (b) and (c) respectively producing the same result as that in figure 5 (a).

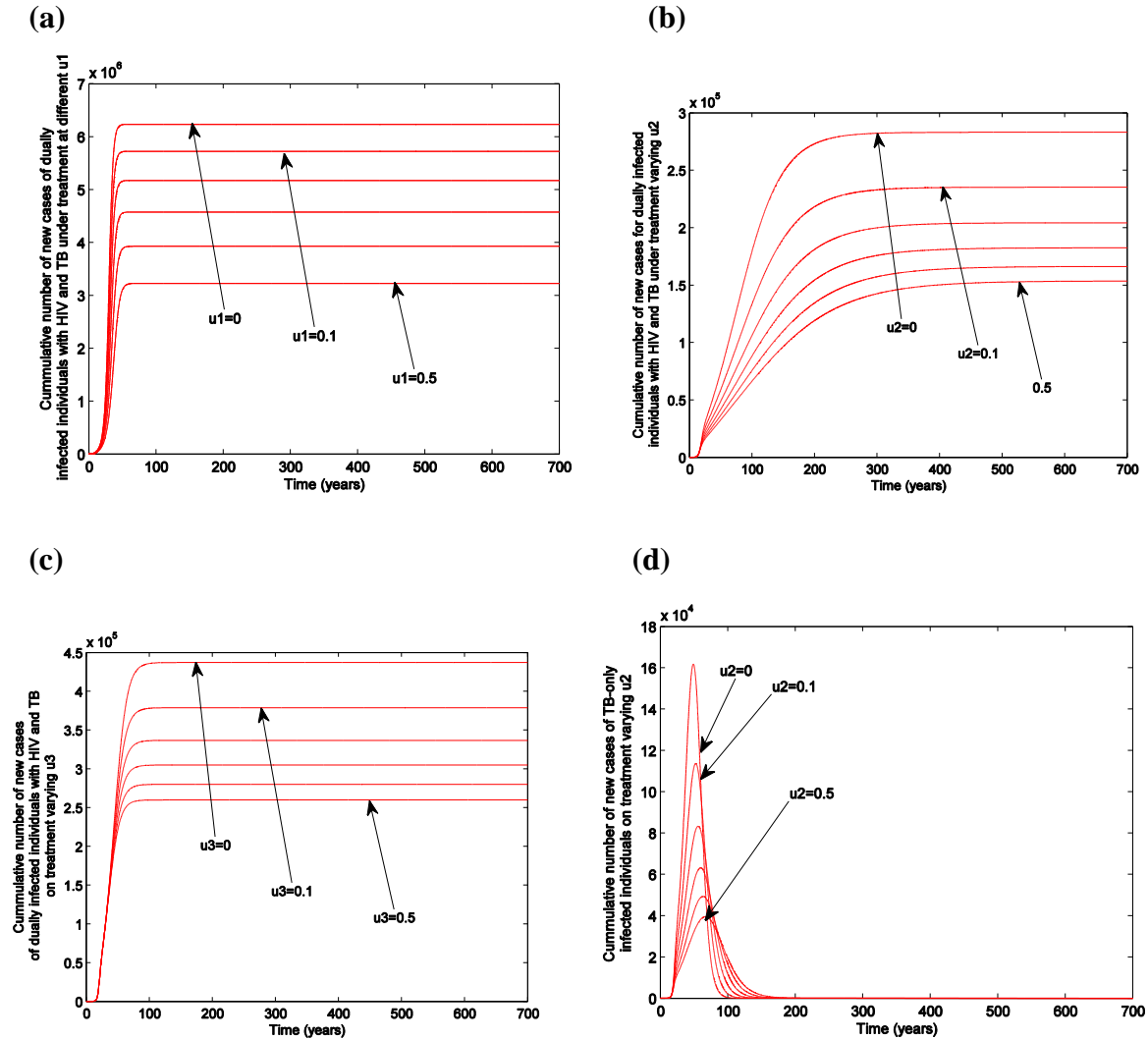


Figure 5. (a)-(c) Cumulative number of new cases of co-infection of dually infected individuals with HIV-TB as a function of time for the co-infection model (1).

(d) Cumulative number of new cases of TB-only infected individuals.

7. CONCLUSION

In this study, we formulated a system of non-linear differential equations to gain insight into the transmission dynamics of HIV-TB in a population where they are co-circulating. The sub models (TB-only and HIV-only models) were rigorously analyzed. Each of them has their disease-free equilibrium locally asymptotically stable when their reproduction number were each less than unity; each of them were globally asymptotically stable too when their reproduction number

were each less than unity. For the co-infection model, the disease-free equilibrium was locally and globally asymptotically stable, confirming that the disease will be kept in check so long that the epidemiological threshold, (reproduction number) is less than unity. We carried out sensitivity analysis of the co-infection model, using data relevant to Kogi state of Nigeria, which revealed that the top ranked parameters that drive the tuberculosis infection (with respect to the associated response function R_T) is (u_1) , the control measure, educational awareness for the susceptible to always cover their mouth when coughing, sneezing and the need for the infants to be inoculated against the disease, while the top ranked parameter that drive the HIV infection (with respect to the associated response function R_H) is (u_2) , the educational awareness campaign measure for the susceptible individuals to practice safe sexual activities, the need to avoid contacts with bodily fluids of infected patients and the prevention of vertical transmission of the disease. To confirm some of the analytical results, we carried out the simulation of the sub-models and the co-infection model. From the simulation, it was revealed that the phenomenon of competitive exclusion occur where the strain with higher reproduction numbers drives out the other; further, simulation of the co-infection model revealed that increasing the treatment rates of the individuals dually infected with HIV and TB could bring down the burden of the two diseases significantly, while increasing the control measures (u_1) and (u_2) leads to significant reduction in the cumulative co-infection new cases of mixed infection in a population.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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