MATHEMATICAL ANALYSIS OF THE ROLE OF DETECTION RATE IN THE DYNAMICAL SPREAD OF HIV-TB CO-INFECTION

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ABSTRACT

Human Immunodeficiency Virus (HIV) co-existing with Tuberculosis (TB) in individuals remains a major global health challenges, with an estimated 1.4 million patients worldwide. These two diseases are enormous public health burden, and unfortunately, not much has been done in terms of modeling the dynamics of HIV-TB co-infection at a population level. We formulated new fifteen (15) compartmental models to gain more insight into the effect of treatment and detection of infected undetected individuals on the dynamical spread of HIV- TB co-infection.

Sub models of HIV and TB only were considered first, followed by the full HIV-TB co-infection model. Existence and uniqueness of HIV and TB only model were analyzed quantitatively, and we shown that HIV model only and TB only model have solutions, moreover, the solutions are unique. Stability of HIV model only, TB model only and full model of HIV-TB co-infection were analyzed for the existence of the disease free and endemic equilibrium points. Basic reproduction number (R_0) was analyzed, using next generation matrix method (NGM), and it has been shown that the disease free equilibrium point is locally asymptotically stable whenever $R_0 < 1$ and unstable whenever this threshold exceeds unity. i.e. $R_0 > 1$, Numerical simulation was carried out by maple software using differential transformation method, to show the effect of treatment and detection of infected undetected individuals on the dynamical spread of HIV-TB co-infection.

Significantly, all the results obtained from this research show the importance of treatment and detection of infected undetected individuals on the dynamical spread of HIV-TB co-infection. Detection rate of infected undetected individuals reduce the spread of HIV-TB co-infections.

KEYWORDS: HIV; TB, Stability; Reproduction Number; Critical points; Co-infection

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1.0 INTRODUCTION

1.1 Human Immunodeficiency Virus (HIV) is the etiological agent that causes acquired Immunodeficiency Syndrome (AIDS) when left untreated. HIV weakens immune system by attacks many blood cells, it wrecks T-cell in the blood by destroying and decreasing their number leading to decline in body's immunity to fight infection [28]. The term AIDS refers to only the last stage of the HIV infection after which death occurs. The HIV epidemic is posing threat to the world both developed and developing nations as HIV has infected millions of people all over the world without any restriction of nationality, religion etc[25]. HIV infection in adults (75-80 percent) has been transmitted to one partner through unprotected sexual intercourse when the other partner is infected with HIV. The sexual transmission is believed globally responsible for the majority of new HIV infections [22, 24].

There are multiple modes of HIV transmission including Sexual intercourse, sharing needles and sharp objects with HIV infected persons, or via HIV-contaminated blood transfusions [30]. Infants may acquire HIV at birth or through breast feeding if the mother is HIV positive, this type of transmission is known as vertical transmission [8]. Mother to child transmission (vertical infection), accounts for more than 90 percent of global infection to infants and children. As HIV infection progresses, immunity declines and patients tend to become more susceptible to common infections. The absolute T-helper cell (CD4$^+$) count or percentage is used most often to evaluate the progression of HIV infection and to help clinicians make treatment decisions. [18].

1.2 TUBERCULOSIS (TB) is an airborne infectious disease caused by a bacterium called a MYCOBICTERIUM TUBERCULOSIS (Tubercle bacilli).It typically affects lung and other parts of the body. TB can be acquired when an individual is exposed to tubercle bacilli produced by an infective individual. The risk of infection with the tubercle bacilli is directly related to the degree of exposure and less to genetic or other host factors. In those with HIV, the risk of developing active TB increases to nearly 18% per year [3,7]. TB is one of the major global cause of death, especially in developing countries. Even in many countries where its overall incidence is low, TB remains a problem; there has been an outbreak in the New York in the recent past [5], and incidence is currently rising in the United Kingdom (UK) [16] . In 2004, TB caused an estimated 1.7 million deaths and 8.9 million new cases of infection [36], Worldwide, 9.15 million new infections occurred in the year 2006. In 2009, WHO estimated that there were 9.4 million incident cases of TB and 1.3 million deaths due to TB among HIV negative cases globally [35]. Over 95% of infections are in developing countries, where TB remains a dominant cause of morbidity and mortality [18].

Even today after the development of advanced screening, diagnostic and treatment method for the disease, it is shown that about one third of the world's population has been exposed and is infected with tuberculosis. [27]. anyone can become infected with T.B. bacteria, but people with HIV infectious disease suffers greater risk of getting infected with this disease. T.B. is the second leading cause of death among people with infectious disease after HIV [29].

TB infection occurs when droplet nuclei containing tubercle bacilli are inhaled into the lungs and deposited in the alveoli. It is spread when individuals with active TB disease cough, sneeze, sing, laugh or through interaction with infectious individual. [1] After a person becomes infected, the tuberculosis bacteria are controlled by the person's immune system and the infection becomes latent. The infection becomes active, when the bacteria spread out of control most especially when the tubercle bacilli overwhelm the immune system and break out of the tubercles in the alveoli and spread to the lungs and other parts of the body via bloodstream. [35]. If not treated active TB can be fatal. TB is curable disease by the implementation of antibiotics, which decrease the mortality of TB to a minimal level, for instance, a 70% reduction in TB related mortality was recorded in the United State of America (USA) between 1945-1955 [2]. Many doctors prefer to hospitalize the patient in order to observe him or her during treatment, the method is called Direct Observed Therapy Short Course (DOTS), huge success has been achieved by this method. [1].

2.0 A BRIEF BACKGROUND ON HIV AND TB CO-INFECTIONS

The synergetic effect produced by the interaction of mycobacterium tuberculosis (TB) and the human immune-deficiency syndrome (HIV) are well known [26, 19, 20, 34], where each accelerates the progression of the other. For instance, since its emergence in the 1980s, the HIV/AIDS pandemic continues to play a major role in the resurgence of TB disease which has greatly increased the morbidity and mortality rate of the disease worldwide. While HIV infections increase the risk of many opportunistic infections, the interactions between HIV and several infectious disease agents have caused particular medical and public health concern. [26]. For adults co-infected with HIV and latent TB, the life time risk of developing active TB disease rises from an estimated 10% up to 50%. This resulted in a parallel pandemic of HIV/AIDS and TB disease where HIV prevalence is high. [18]. Persons co-infected with TB and HIV may spread the disease not only to other HIV-infected persons, but also members of the general population who do not participate in any of the high risk behaviours associated with HIV. The largest increase in the number of TB cases has been in men aged 25-44. [33].

HIV fuels progression to active disease in people infected with TB [13]. Rate of recurrence of TB, both due to endogenous reactivation and exogenous re-infection, are increased among people infected with HIV, [18]. For instance, in many countries of eastern and southern Africa, the rates of TB notification have increased by five or more times as a result of HIV infection. Similarly, TB also fuels the progression of HIV infection in the patient to full blown AIDS after which death occurs. [37].

Currently, about 8% of global TB cases are linked to HIV infection, but this number is likely to increase in the future. For instance, the number of HIV positives in India is estimated to be 3.97 million cases, and almost 60% of the reported cases of AIDS had TB.

The interaction of TB and HIV/AIDS is on the increase and these infections occur mostly in poor economically regions of the world. The immunodeficiency caused by HIV infection reactivates latent TB infection and accelerates the progression of newly acquired TB [15].

The enormous public health burden inflicted by these two deadly diseases necessitates the use of mathematical modeling to gain insights into the effects of treatment on the infected detected individuals and detection of infected undetected individuals on the dynamical spread of the disease.

3.0 MATHEMATICAL MODEL FORMULATION

A non linear mathematical model is formulated and analyzed to study the effect of detection of undetected individuals on the dynamical spread of HIV- TB co-infection.

In modeling the dynamics, the total homogeneously mixing population at time t, denoted by N(t), is divided into (15) fifteen mutually–exclusive compartments of Susceptible (S(t)) individuals, Latently HIV $(L_H(t))$ individuals, HIV Undetected $(H_U(t))$ individuals, HIV Detected $(H_D(t))$ individuals, Treated HIV $(H_W(t))$ individuals, Latently TB induced HIV $(L_{TH}(t))$ individuals, Active TB Induced HIV $(A_{TH}(t))$ individuals, Latently HIV induced TB $(L_{HT}(t))$ individuals, Active HIV induced TB $(A_{HT}(t))$ individuals, Latent TB $(L_T(t))$ individuals, TB Undetected $(T_U(t))$ individuals, TB Detected $(T_D(t))$ individuals, Failed Treatment TB $(F_T(t))$ individuals, Recovered TB $(R_T(t))$ individuals, Recovered TB induced HIV $(R_{TH}(t))$ individuals. So that,

$$N(t) = S + L_H + H_U + H_D + H_W + L_{TH} + A_{TH} + L_{HT} + A_{HT} + L_T + T_U + T_D + F + R_T + R_{TH} \quad (1)$$

The Susceptible population is increased by the recruitment of individuals into the population at rate π. the population decrease by natural death rate μ and by both singly and dually-infected transmission individuals. Transmission by singly-infected individuals, we assumed that susceptible individuals acquire HIV infection, following effective contact with people infected with HIV only (i.e., those in the $(L_H, \eta_U H_U, \eta_{dH} H_D$ and $\eta_W H_W)$ classes at a rate λ_H, given by

$$\lambda_H = \beta_H \frac{(L_H + \eta_U H_U + \eta_{dH} H_D + \eta_W H_W)}{N} \quad (2)$$

Where, β_H is the effective contact rate for HIV transmission.

Similarly, susceptible individuals acquire TB infection from individuals with TB only. $(L_T, \eta_U T_U, \eta_{dT} T_D, \eta_{RT} R_T \text{ and } F_T)$ classes at a rate λ_T, given by

$$\lambda_T = \beta_T \frac{(L_T + \eta_U T_U + \eta_{dT} T_D + \eta_{RT} R_T + F_T)}{N} \quad (3)$$

Where, β_T is the effective contact rate for TB infection.

Dually-infected individuals are assumed capable of transmitting either HIV or TB, but not the mixed infection.

$$\lambda_{HT} = \beta_H \frac{(L_{HT} + \eta_H A_{HT})}{N} \quad (4)$$

$$\lambda_{TH} = \beta_T \frac{(L_{TH} + \eta_T A_{TH} + \eta_{RT} R_{TH})}{N} \quad (5)$$

Then,

$$\frac{dS}{dt} = \pi - \lambda_H S - \lambda_T S - \mu S - \lambda_{TH} S - \lambda_{HT} S \quad (6)$$

A fraction ε_1 of the newly infected individuals with HIV only are assumed to show no disease symptoms initially. These individuals (known as "slow progressor" for HIV) are moved to the latently HIV class (L_H). The remaining fraction, $(1 - \varepsilon_1)$ of the newly infected individuals are assumed to immediately display disease symptoms (Fast

progressors) and are moved to the undetected infectious class H_U. The population of latent class is decreased by the progression of latent HIV individual to active undetected HIV H_U (at a rate κ_H) and also reduced by natural death rate (μ) and finally increased by the fraction of Treated HIV at the rate (ϕ) that moves from treated class to latently HIV compartment. Thus,

$$\frac{dL_H}{dt} = \varepsilon_1 \lambda_H S - (\kappa_H + \mu)L_H + \phi H_W \tag{7}$$

The population of undetected infected individuals is increased by the infection of fast progressors (at the rate $(1-\varepsilon_1)\lambda$) and the development of symptoms by latently individual at the rate $(1-\omega_1)\kappa_H$ where ω_1 is the endogenous reactivation rate. This population is decreased by natural death rate (μ) and disease induced death (at a rate δ_{UH}) and further decreased by detection rate (γ_{UH}) of HIV undetected infected individuals. Hence

$$\frac{dH_U}{dt} = (1-\varepsilon_1)\lambda_H S + (1-\omega_1)\kappa_H L_H - (\gamma_{UH} + \mu + \delta_{UH})H_U \tag{8}$$

The population of Detected infected HIV individual increases by the fraction of latently individuals who develop disease symptoms (at the rate $\omega_1 \kappa_H$), where ω_1 is the endogenous reactivation rate and the detection of undetected individual at the rate γ_{UH}. The population later decreased by treatment rate (τ_1) for HIV detected individual and finally reduced by the natural death rate, induced mortality death rate at μ and δ_{UH} respectively. Hence we have.

$$\frac{dH_D}{dt} = \omega_1 \kappa_H L_H + \gamma_{UH} H_U - (\tau_1 + \mu + \delta_{UH})H_D \tag{9}$$

The population of Treated HIV individuals is increased by those that have received treatment from HIV detected infected individual at the rate (τ_1) this population reduces by fraction of treated individual that moved back to latently HIV individuals at the rate, (ϕ) since treatment does not completely clears the bacteria and finally reduced by natural death rate (μ).

Hence,

$$\frac{dH_W}{dt} = \tau_1 H_D - (\phi + \mu)H_W \tag{10}$$

The population of latent TB induced HIV is increased by infection, which can be acquired following effective contact with infections individuals in the latent TB induced HIV (L_{TH}), Active TB induced HIV ($\eta_T A_{TH}$) or Recovered TB induced HIV ($\eta_{RT} R_{TH}$) categories at a rate λ given by

$$\lambda_{TH} = \beta_T \frac{(L_{TH} + \eta_T A_{TH} + \eta_{RT} R_{TH})}{N} \tag{11}$$

Where β_T represents the effective contact rate. The population reduced by progression from latent stage to active stage at the rate (κ_{TH}), and by natural death at the rate (μ). The population later increased by fraction of those that have been treated that moved from treated compartment at the rate (α_T). Then the rate of change of latent TB induced HIV population is given by;

$$\frac{dL_{TH}}{dt} = \lambda_{TH} S - (\kappa_{TH} + \mu)L_{TH} + \alpha_T R_{TH} \tag{12}$$

The population of active TB induced HIV is increased by the progression from latent stage to active stage at the rate (κ_{TH}), the population decreased by natural death, induced mortality due to disease at the rate (μ) and (δ) respectively, individual who recovered also moved to recovered TB induced HIV at the rate (σ_1).

Hence,

$$\frac{dA_{TH}}{dt} = \kappa_{TH} L_{TH} - (\mu + \sigma_1 + \delta A_{TH}) A_{TH} \tag{13}$$

The population of latent HIV induced TB is increased by infection, which can be acquired following effective contact with infectious individuals in the latent HIV induced TB (L_{HT}), or active HIV induced TB $(\eta_H A_{HT})$ categories at a rate λ given by

$$\lambda_{HT} = \beta_H \frac{(L_{HT} + \eta_H A_{HT})}{N} \tag{14}$$

Where β_H represents the effective contact rate. The population reduced by progression from latent stage to active stage at the rate (κ_{HT}) and by natural death rate. Hence, latent HIV induced TB population is given by

$$\frac{dL_{HT}}{dt} = \lambda_{HT} S - (\kappa_{HT} + \mu) L_{HT} \tag{15}$$

Active HIV induced TB (A_{HT}) population is increased by the progression from latent stage to active stage at the rate (κ_{HT}). The population decreased by natural death rate (μ) and disease induced mortality at the rate (δ). Hence the system of equation of Active HIV induced TB is given by

$$\frac{dA_{HT}}{dt} = \kappa_{HT} - (\mu + \delta A_{HT}) A_{HT} \tag{16}$$

A fraction ε_2 of the newly–infected individuals with TB only are assumed to show no disease symptoms initially. These individuals (Known as slow progressor for TB) moved to the latently TB class (L_T). The population decreased by progression rate (κ_T) from latent TB class to infected undetected class, natural death rate (μ) and exogenous re-infective (at a rate $\varphi \lambda_T$), where $\varphi < 1$ accounts for the assumption that latent individual have reduced infection rate, this is to account for the fact that individuals with latent TB infection have partial immunity against exogenous re-infection. [29].The population increased by natural recovery at the rate (υ), number of unsuccessful treated individuals who move to the latent TB individual at the rate $(\theta_1 \rho)$ and rate $(r\alpha)$ at which treated TB individual wanes off the treatment. Then the population is given by

$$\frac{dL_T}{dt} = \varepsilon_2 \lambda_T S - (\kappa_T + \varphi \lambda_T + \mu) L_T + \upsilon T_U + \theta_1 \rho F_T + r\alpha R_T \tag{17}$$

The population of undetected infectious individuals is increased by the infection of fast progressor at the rate $(1-\varepsilon_1)\lambda_T$ and the development of symptoms by latent individual at the rate $(1-\omega_2)\kappa_T$, where ω_2 is the fraction of exposed individuals who develop symptoms and are detected. It is further increased by the exogenous re-infection of expressed individual at the rate $(1-\omega_3)\varphi \lambda_T$, where ω_3 the fraction of is re-infected exposed individuals who are detected, and fraction of unsuccessful treated individuals that move from detected individuals to undetected individuals at the rate $(\theta_2 \rho)$. This population is decreased by natural recovery at a rate (υ), detection of undetected individual at a rate (γ_{UH}), natural death at the rate (μ) and disease induced death at a rate (δ_{UT}).

Hence,

$$\frac{dT_U}{dt} = (1-\varepsilon_2)\lambda_H S + (1-\omega_2)\kappa_T L_T + (1+\omega_3)\varphi \lambda_T L_T + \theta_2 \rho F_T - (\upsilon + \gamma_{UT} + \mu + \delta_{UT}) T_U \tag{18}$$

The population of detected infectious individual increases by the fraction of latent individuals who develop diseases symptoms at a rate $\omega_2 \kappa_T$, exogenous re-infection of latent individual, detection rate for undetected individual at the rate $(\omega_3 \varphi \lambda_T, \gamma_{UT}$ respectively) and numbers of unsuccessful treated individuals who move to latent and undetected individual at the rate (θ_1) and (θ_2) respectively. The population is decreased by those that are treated and recovered

who later moved to recovered compartment at the rate (σ_2), treatment rate (τ_1), natural death rate (μ) and disease induced death at a rate (δ_{dT}). This gives

$$\frac{dT_D}{dt} = \omega_2 \kappa_T L_T + \omega_3 \varphi \lambda_T L_T + \gamma_{UT} T_U + [1 - (\theta_1 + \theta_2)]\rho F_T - (\sigma_2 + \tau_2 + \mu + \delta_{dT})T_D \qquad (19)$$

The population of fail treatment compartment is generated by the failure of treated infected detected individuals at the rate $(1 - q_1)\tau_2$. The treatment failure could be due to a number of reasons, such as incomplete compliance to the specified treatment or drug resistance among others. The population decreased by fraction of treated individuals who lose their treatment the population decreased by the rate at which TB individuals who fail treatment move to other classes, the natural death and induced death at the rate $(\rho + \mu + \delta_F)$. Thus,

$$\frac{dF_T}{dt} = (1 - q_1)\tau_2 T_D + (1 - r)\alpha R_T - (\rho + \mu + \delta_F)F_T \qquad (20)$$

The population of TB recovered individual is increased by the treatment of detected individual at the rate $q_1 \tau_2$ and treated detected individual (at the rate σ_2), successfully– recovered individuals eventually move to the latent class (at the rate α). This population is further decreased by natural death and disease induced death (at a rate μ and δ_{RT}).

Hence

$$\frac{dR_T}{dt} = q_1 \tau_2 T_D - (\alpha + \mu + \delta_{RT})R_T + \sigma_2 T_D \qquad (21)$$

The population of TB induced HIV recovered individual is increased by the treatment of active TB at the (σ_1) and leather reduced by natural death rate at μ and rate (α_T), at which treated individual lose their treatment induced immunity. Then we have

$$\frac{dR_{TH}}{dt} = \sigma_1 A_{TH} - (\alpha_T + \mu)R_{TH} \qquad (22)$$

Hence, we have,

3.2 MATHEMATICAL MODEL OF HIV-TB

$$\frac{dS}{dt} = \pi - \lambda_H S - \lambda_T S - \mu S - \lambda_{TH} S - \lambda_{HT} S$$

$$\frac{dL_H}{dt} = \varepsilon_1 \lambda_H S - K_1 L_H + \phi H_W$$

$$\frac{dH_U}{dt} = (1 - \varepsilon_1) \lambda_H S + K_2 L_H - K_3 H_U$$

$$\frac{dH_D}{dt} = \omega_1 \kappa_H L_H + \gamma_{UH} H_U - K_4 H_D$$

$$\frac{dH_W}{dt} = \tau_1 H_D - K_5 H_W$$

$$\frac{dL_{TH}}{dt} = \lambda_{TH} S - K_6 L_{TH} + \alpha_T R_{TH}$$

$$\frac{dA_{TH}}{dt} = \kappa_{TH} L_{TH} - K_7 A_{TH}$$

$$\frac{dL_{HT}}{dt} = \lambda_{HT} S - K_8 L_{HT}$$

$$\frac{dA_{HT}}{dt} = \kappa_{HT} L_{HT} - K_9 A_{HT}$$

$$\frac{dL_T}{dt} = \varepsilon_2 \lambda_T S - K_{10} L_T + \upsilon T_U + \theta_1 \rho F_T + r\alpha R_T$$

$$\frac{dT_U}{dt} = (1 - \varepsilon_2) \lambda_H S + K_{11} L_T + K_{12} L_T + \theta_2 \rho F_T - K_{13} T_U$$

$$\frac{dT_D}{dt} = \omega_2 \kappa_T L_T + \omega_3 \varphi \lambda_T L_T + \gamma_{UT} T_U + K_{14} F_T - K_{15} T_D$$

$$\frac{dF_T}{dt} = K_{16} T_D + K_{17} R_T - K_{18} F_T$$

$$\frac{dR_T}{dt} = K_{19} T_D - K_{20} R_T$$

$$\frac{dR_{TH}}{dt} = \sigma_1 A_{TH} - K_{21} R_{TH}$$

(23)

Where

$K_1 = (\kappa_H + \mu)$, $\quad K_2 = (1 - \omega_1)\kappa_H$, $\quad K_3 = (\gamma_{UH} + \mu + \delta_{UH})$, $\quad K_4 = (\tau_1 + \mu + \delta_{dH})$, $K_5 = (\phi + \mu)$,

$K_6 = (\kappa_{TH} + \mu)$, $\quad K_7 = (\mu + \sigma_1 + \delta_{A_{TH}})$, $\quad K_8 = (\kappa_{HT} + \mu)$, $\quad K_9 = (\mu + \delta_{A_{HT}})$, $K_{10} = (\kappa_T + \varphi\lambda_T + \mu)$,

$K_{11} = (1 - \omega_2)\kappa_T$, $\quad K_{12} = (1 + \omega_3)\varphi\lambda_T$, $\quad K_{13} = (\upsilon + \gamma_{UT} + \mu + \delta_{UT})$, $\quad K_{14} = [1 - (\theta_1 + \theta_2)]\rho$,

$K_{15} = (\sigma_2 + \tau_2 + \mu + \delta_{dT})$, $\quad K_{16} = (1 - q_1)\tau_2$, $\quad K_{17} = (1 - r)\alpha$, $\quad K_{18} = (\rho + \mu + \delta_F)$, $\quad K_{19} = (q_1\tau_2 + \sigma_2)$,

$K_{20} = (\alpha + \mu + \delta_{RT})$, $\quad K_{21} = (\alpha_T + \mu)$

VARIABLES AND PARAMETERS DESCRIPTIONS

VARIABLES	DESCRIPTIONS
S	Susceptible individuals
L_H	Latent HIV individual
H_D	Detected HIV individual
H_U	Undetected HIV individual

L_{TH}	Latent TB induced HIV individual
A_{TH}	Active TB induced HIV individual
L_T	Latent TB individual
T_U	Undetected TB individual
T_D	Detected TB individual
F_T	TB treatment fail individual
R_T	TB recover individual
R_{TH}	TB induced HIV recover individual
H_W	Treated HIV individual
L_{HT}	Latent HIV induced TB
A_{HT}	Active HIV induced TB

PARAMETERS	DESCRIPTIONS
π	Recruitment rate
μ	Natural death rate
τ_1, τ_2	Treatment rate for Detected HIV and TB
θ_1	Number of unsuccessful treated individual who moves to latent TB
θ_2	Number of unsuccessful treated who moves to undetected TB
φ	Exogenous re-infection rate for TB
ε_1	Fast progressor for HIV
ε_2	Fast progressors for TB
κ_H	Progression rate of HIV.
κ_T	Progression rate of TB.
κ_{HT}	Progression rate of HIV induced TB
κ_{TH}	Progression rate of TB induced HIV
ω_2	Endogenous reactivation rate of TB
ω_3	Fraction of re-infected individuals that moves to detected class
γ_{UH}	Detection rate for undetected HIV
γ_{UT}	Detection rate for undetected TB
υ	Natural recovery rate of undetected TB individuals
α	Loss of immunity
r	Treated TB who move to Latent class after treatment wanes
ρ	Rate at which TB individuals fail treatment.
$\delta_{UT}, \delta_{dT}, \delta_F, \delta_{RT}$	Tuberculosis-induced mortality rate for classes T_U, T_D, F, R
ϕ	HIV treated individuals that moves to Latent individuals
σ_2	Recovery rate for TB detected individuals
σ_1	Recovery rate for active TB induced HIV individuals

β_T, β_H	Effective contact rate for TB and HIV
q_1	Detected individuals who are successfully treated
δ_{UH}, δ_{dH}	HIV-induced mortality rate for classes H_U, H_D respectively
$\eta_U, \eta_{dH}, \eta_W$	HIV Modification parameters for classes H_U, H_D, H_W respectively
$\eta_U, \eta_{dT}, \eta_{FT}, \eta_{RT}$	TB Modification parameters for classes T_U, T_D, F_T, R_T respectively

3.2   POSITIVITY OF SOLUTIONS

For HIV-TB model only to be epidemiologically meaningful and well posed, we need to prove that all state variables are non-negative for all $t > 0$

$$D_1 = \{(S, L_H, H_U, H_D, H_W, L_{TH}, A_{TH}, L_{HT}, A_{HT}, L_T, T_U, T_D, F_T, R_T, R_{TH}) \in R^{15}{}_+ : N \leq \pi/\mu\}$$

Lemma 1.

The closed set

$$D_1 = \{(S, L_H, H_U, H_D, H_W, L_{TH}, A_{TH}, L_{HT}, A_{HT}, L_T, T_U, T_D, F_T, R_T, R_{TH}) \in R^{15}{}_+ : N \leq \pi/\mu\} \text{ is}$$
positively-invariant and attracting with respect to the model (23)

Proof: Consider the biologically-feasible region D, defined above. The rate of change of the total population, obtained by adding all equations of the model (23), is given by

$$\frac{dN}{dt} = \pi - \mu N - \delta_{UH} - \delta_{dH} - \delta A_{TH} - \delta A_{HT} - \delta_{UT} - \delta_{dT} - \delta_{RT} - \delta_F. \qquad (24)$$

It follows that $\dfrac{dN}{dt} < 0$ whenever $N > \dfrac{\pi}{\mu}$. Furthermore, since $\dfrac{dN}{dt} \leq \pi - \mu N$, it is clear that $N(t) \leq \dfrac{\pi}{\mu}$ if

$N(0) \leq \dfrac{\pi}{\mu}$. Therefore, all solutions of the model with initial conditions in D remain in D for all $t > 0$ (i.e., the ω-limits

sets of the system (13) are contained in D). Thus, D is positively-invariant and attracting. In this region, the model can be considered as been epidemiologically and mathematically well posed

3.3   ANALYSIS OF SUB MODEL

Before analyzing the full model (23), it is pertinent to gain insights into the dynamics of the models for HIV only and TB only.

3.4   HIV MODEL ONLY

$$\frac{dS}{dt} = \pi - \lambda_H S - \mu S$$

$$\frac{dL_H}{dt} = \varepsilon_1 \lambda_H S - K_1 L_H + \phi H_W$$

$$\frac{dH_U}{dt} = (1 - \varepsilon_1)\lambda_H S + K_2 L_H - K_3 H_U \qquad (25)$$

$$\frac{dH_D}{dt} = \omega_1 \kappa_H L_H + \gamma_{UH} H_U - K_4 H_D$$

$$\frac{dH_W}{dt} = \tau_1 H_D - K_5 H_W$$

Where $\lambda_H = \beta_H \dfrac{(L_H + \eta_U H_U + \eta_{dH} H_D + \eta_W H_W)}{N} \qquad (26)$

For this model, it can be shown that the region,

$$D_1 = \{(S + L_H + \eta_U H_U + \eta_{dH} H_D + \eta_W H_W) \in R^5_+ : N \le \pi / \mu \tag{27}$$

3.4.1 DERIVATION OF BASIC REPRODUCTION NUMBER (R_O) FOR HIV ONLY

The Next Generation Matrix ($F.V^{-1}$) Method

One of fundamental questions of mathematical epidemiology is to find the threshold conditions that determine whether an infectious disease will spread in a population when the disease is introduced into the population [14].

The basic reproduction number of the model (25) R_H is calculated by using the next generation matrix [31]. Using their approach [31], we have,

$$F_i = \begin{pmatrix} F1 \\ F2 \\ F3 \\ F4 \end{pmatrix} = \begin{pmatrix} \varepsilon_1 \lambda_H S \\ (1-\varepsilon_1) \lambda_H S \\ 0 \\ 0 \end{pmatrix} \quad and \quad V_i = \begin{pmatrix} V1 \\ V2 \\ V3 \\ V4 \end{pmatrix} = \begin{pmatrix} (K_H + \mu)L_H - \phi H_W \\ (1-\omega_1)K_H L_H + (\gamma_{UH} + \mu + \delta_{UH})H_U \\ -\omega_1 K_H L_H - \gamma_{UH} H_U + (\tau_1 + \mu + \delta_{UH})H_D \\ -\tau_1 H_D + (\phi + \mu)H_W \end{pmatrix}$$

After taking partial derivative F and V, we have

$$F = \begin{pmatrix} \varepsilon_1 \beta_H & \varepsilon_1 \beta_H \eta_U & \varepsilon_1 \beta_H \eta_{dH} & \varepsilon_1 \beta_H \eta_W \\ (1-\varepsilon_1)\beta_H & (1-\varepsilon_1)\beta_H \eta_U & (1-\varepsilon_1)\beta_H \eta_{dH} & (1-\varepsilon_1)\beta_H \eta_W \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{28}$$

$$V = \begin{pmatrix} K_1 & 0 & 0 & -\phi \\ K_2 & K_3 & 0 & 0 \\ -\omega_1 K_H & -\gamma_{UH} & K_4 & 0 \\ 0 & 0 & -\tau_1 & K_5 \end{pmatrix} \tag{29}$$

Thus,

$$R_H = \left\{ \left(\frac{1}{\phi\tau_1 K_2 \gamma_{UH} + \phi\tau_1 \omega_1 K_H K_3 - K_4 K_5 K_1 K_3} \right) \begin{pmatrix} \beta_H(-(1-\varepsilon_1)\gamma_{UH}\phi\tau_1 + (1-\varepsilon_1)\eta_U \phi\tau_1 \omega_1 \kappa_H \\ -(1-\varepsilon_1)\eta_U K_5 K_4 K_1 - (1-\varepsilon_1)\gamma_{UH} \eta_{dH} K_5 K_1 \\ -(1-\varepsilon_1)\gamma_{UH} \eta_W \tau_1 K_1 - \varepsilon_1 K_4 K_5 K_3 - \varepsilon_1 K_4 K_5 K_2 \eta_U \\ -\eta_{dH} \omega_1 \kappa_H \varepsilon_1 K_5 K_3 - \eta_{dH}\gamma_{UH}\varepsilon_1 K_5 K_2 - \tau_1 \omega_1 \kappa_H \varepsilon_1 \eta_W K_3 \\ -\eta_W \gamma_{UH} \varepsilon_1 \tau_1 K_2 \end{pmatrix} \right\} \tag{30}$$

The threshold quantity R_H is the basic reproduction number of the normalized model system (25) for HIV infection in a population. It measures the average number of new secondary infections generated by a single infected individual in his or her infectious period in a susceptible population [1].

3.4.2 DISEASE FREE EQUILIBRIUM

For critical points, we set

$$\frac{dS}{dt} = \frac{dL_H}{dt} = \frac{dH_U}{dt} = \frac{dH_D}{dt} = \frac{dH_W}{dt} = 0 \tag{31}$$

At disease free equilibrium, it is assumed that there is no infection, Hence (DFE) is given as

$$\varepsilon_0 = (S, L_H, H_U, H_D, H_W) = \left(\frac{\pi}{\mu}, 0, 0, 0, 0 \right)$$

3.4.3 GLOBAL STABILITY OF DISEASE FREE EQUILIBRIUM (HIV)

Here, the global asymptotic stability (GAS) property of the DEF of the HIV model only will be explored.

Theorem3.4: The disease free-equilibrium of the system (25) is globally asymptotically stable whenever $R_H < 1$ and unstable if $R_H > 1$.

Proof: It follows that $S = N^* - L_H - H_U - H_D - H_W$ at steady state. The proof is based on using the comparison method [21] to prove the global stability.

Using comparison method, we have,

$$\begin{pmatrix} \dfrac{dL_H}{dt} \\ \dfrac{dH_U}{dt} \\ \dfrac{dH_D}{dt} \\ \dfrac{dH_W}{dt} \end{pmatrix} = (F - V) \begin{pmatrix} L_H \\ H_U \\ H_D \\ H_W \end{pmatrix} - Fi \begin{pmatrix} L_H \\ H_U \\ H_D \\ H_W \end{pmatrix}$$

Where

$$F - V = \begin{pmatrix} \varepsilon_1 \beta_H - K_1 & \varepsilon_1 \beta_H \eta_U & \varepsilon_1 \beta_H \eta_{dH} & \varepsilon_1 \beta_H \eta_W + \phi \\ (1 - \varepsilon_1)\beta_H + K_2 & (1 - \varepsilon_1)\beta_H \eta_U - K_3 & (1 - \varepsilon_1)\beta_H \eta_{dH} & (1 - \varepsilon_1)\beta_H \eta_W \\ \omega_1 \kappa_H & \gamma_{UH} & -K_4 & 0 \\ 0 & 0 & \tau_1 & -K_5 \end{pmatrix}$$

According to [6, 31], all eigen values of the matrix (F - V) have negative real parts.

Hence, we have

$$\begin{bmatrix} ((\varepsilon_1 \beta_H - K_1) - \lambda)((1 - \varepsilon_1)\beta_H \eta_U - K_3 - \lambda)(-K_4 - \lambda)(-K_5 - \lambda) \\ -(\varepsilon_1 \beta_H \eta_U)((1 - \varepsilon_1)\beta_H + K_2)(-K_4 - \lambda)(-K_5 - \lambda) + (\varepsilon_1 \beta_H \eta_{dH})((1 - \varepsilon_1)\beta_H + K_2)(\gamma_{UH}(-K_5 - \lambda)) \\ -(\varepsilon_1 \beta_H \eta_W + \phi)((1 - \varepsilon_1)\beta_H + K_2)(\gamma_{UH} + \tau_1) \end{bmatrix} = 0 \qquad (32)$$

Thus, from equation (32), the characteristic equation is given by

$$\lambda^4 + a_4 \lambda^3 + a_3 \lambda^2 + a_2 \lambda - a_1$$

Where

$$a_4 = (-\eta_U \beta_H (1 - \varepsilon_1) - \varepsilon_1 \beta_H + K_4 K_5 K_1 K_3)$$

$$a_3 = (-(1 - \varepsilon_1)K_5 \eta_U \beta_H - K_5 \varepsilon_1 \beta_H + K_5 K_1 + K_5 K_3 + K_4 K_5 - \eta_{dH} \omega_1 \kappa_H \varepsilon_1 \beta_H - (1 - \varepsilon_1)\gamma_{UH} \eta_{dH} \beta_H \\ - (1 - \varepsilon_1)K_4 \eta_U \beta_H - K_4 \varepsilon_1 \beta_H + K_4 K_1 + K_4 K_3 - (1 - \varepsilon_1)K_1 \eta_U \beta_H - \varepsilon_1 K_2 \eta_U \beta_H - \varepsilon_1 K_3 \beta_H + K_1 K_3)$$

$$a_2 = (-\tau_1 \omega_1 \kappa_H \varepsilon_1 \eta_W \beta_H - (1 - \varepsilon_1)\gamma_{UH} \eta_W \tau_1 \beta_H - \phi \tau_1 \omega_1 \kappa_H - \eta_{dH} \omega_1 \kappa_H \varepsilon_1 K_5 \beta_H - (1 - \varepsilon_1)\gamma_{UH} \eta_{dH} K_5 \beta_H \\ - (1 - \varepsilon_1)\eta_U K_5 K_4 \beta_H - K_4 K_5 \varepsilon_1 \beta_H + K_4 K_5 K_1 + K_4 K_5 K_3 - (1 - \varepsilon_1)\eta_U \beta_H K_5 K_1 - \varepsilon_1 K_2 K_5 \eta_U \beta_H \\ - \varepsilon_1 K_3 K_5 \beta_H + -K_3 K_2 K_5 - \eta_{dH} \gamma_{UH} \varepsilon_1 K_2 \beta_H - (1 - \varepsilon_1)K_1 \gamma_{UH} \eta_{dH} \beta_H - \eta_{dH} \kappa_H \varepsilon_1 K_3 \beta_H \omega_1 \\ - (1 - \varepsilon_1)\eta_U \beta_H K_4 K_1 - \eta_U \varepsilon_1 K_2 K_4 \beta_H - \varepsilon_1 K_3 K_4 \beta_H + K_4 K_1 K_3)$$

$$a_1 = (-(-\phi \tau_1 \omega_1 \kappa_H K_3 - \varepsilon_1 K_4 K_5 K_3 \beta_H - \phi \tau_1 K_2 \gamma_{UH} + K_4 K_5 K_1 K_3 - (1 - \varepsilon_1)\gamma_{UH} \eta_W \tau_1 K_1 \beta_H \\ - (1 - \varepsilon_1)\gamma_{UH} \eta_{dH} K_5 K_1 \beta_H - (1 - \varepsilon_1)\eta_U K_5 K_4 K_1 \beta_H + (1 - \varepsilon_1)\eta_U \phi \tau_1 \omega_1 \kappa_H \beta_H - (1 - \varepsilon_1)\gamma_{UH} \phi \tau_1 \beta_H \\ - \eta_{dH} \gamma_{UH} \varepsilon_1 K_5 K_2 \beta_H - \varepsilon_1 K_4 K_5 K_2 \eta_U \beta_H - \eta_W \gamma_{UH} \varepsilon_1 \tau_1 K_2 \beta_H - \tau_1 \omega_1 \kappa_H \varepsilon_1 \eta_W K_3 \beta_H - \eta_{dH} \omega_1 \kappa_H \varepsilon_1 K_5 K_3))$$

Applying Routh-Hurwitz criteria of order 4;

$n = 4 : a_1 > 0 , a_3 > 0, a_4 > 0, and \ a_1 a_2 a_3 > a_3^2 + a_1^2 a_4.$

Then for $a_1 > 0$ we have

$$-\begin{pmatrix} \beta_H (-(1-\varepsilon_1)\gamma_{UH}\phi\tau_1 + (1-\varepsilon_1)\eta_U\phi\tau_1\omega_1\kappa_H \\ -(1-\varepsilon_1)\eta_U K_5 K_4 K_1 - (1-\varepsilon_1)\gamma_{UH}\eta_{dH} K_5 K_1 \\ -(1-\varepsilon_1)\gamma_{UH}\eta_W\tau_1 K_1 - \varepsilon_1 K_4 K_5 K_3 - \varepsilon_1 K_4 K_5 K_2 \eta_U \\ -\eta_{dH}\omega_1\kappa_H\varepsilon_1 K_5 K_3 - \eta_{dH}\gamma_{UH}\varepsilon_1 K_5 K_2 - \tau_1\omega_1\kappa_H\varepsilon_1\eta_W K_3 \\ -\eta_W\gamma_{UH}\varepsilon_1\tau_1 K_2) \end{pmatrix} + (\phi\tau_1 K_2\gamma_{UH} + \phi\tau_1\omega_1 K_H K_3 - K_4 K_5 K_1 K_3) > 0,$$

Hence

$$\frac{\begin{pmatrix} \beta_H (-(1-\varepsilon_1)\gamma_{UH}\phi\tau_1 + (1-\varepsilon_1)\eta_U\phi\tau_1\omega_1\kappa_H - (1-\varepsilon_1)\eta_U K_5 K_4 K_1 \\ -(1-\varepsilon_1)\gamma_{UH}\eta_{dH} K_5 K_1 - (1-\varepsilon_1)\gamma_{UH}\eta_W\tau_1 K_1 - \varepsilon_1 K_4 K_5 K_3 - \varepsilon_1 K_4 K_5 K_2 \eta_U - \\ \eta_{dH}\omega_1\kappa_H\varepsilon_1 K_5 K_3 - \eta_{dH}\gamma_{UH}\varepsilon_1 K_5 K_2 - \tau_1\omega_1\kappa_H\varepsilon_1\eta_W K_3 - \eta_W\gamma_{UH}\varepsilon_1\tau_1 K_2) \end{pmatrix}}{(\phi\tau_1 K_2\gamma_{UH} + \phi\tau_1\omega_1 K_H K_3 - K_4 K_5 K_1 K_3)} < 1,$$

Hence, we have established that the disease free equilibrium is globally asymptotically stable whenever $R_H < 1$ and unstable $R_H > 1$.

3.4.4   EXISTENCE OF ENDEMIC EQUILIBRIUM (EE)

Where $\varepsilon_0^{**} = (S^{**}, L_H^{**}, H_U^{**}, H_D^{**}, H_W^{**})$ are the endemic equilibrium points.

Equation (25) becomes

$$\frac{dS}{dt} = \pi - \lambda_H S - \mu S \tag{33.1}$$

$$\frac{dL_H}{dt} = \varepsilon_1 \lambda_H S - K_1 L_H + \phi H_W \tag{33.2}$$

$$\frac{dH_U}{dt} = (1-\varepsilon_1)\lambda_H S + K_2\kappa_H L_H - K_3 H_U \tag{33.3}$$

$$\frac{dH_D}{dt} = \omega_1\kappa_H L_H + \gamma_{UH} H_U - K_4 H_D \tag{33.4}$$

$$\frac{dH_W}{dt} = \tau_1 H_D - K_5 H_W \tag{33.5}$$

Solving at steady state, from equation $(33.1 - 33.5)$, we have;

$$\pi - (\lambda_H - \mu)S = 0$$

$$S^{**} = \frac{\pi}{(\lambda_H + \mu)} \tag{33.6}$$

$$L_{H^{**}} = \frac{\varepsilon_1 \lambda_H S^{**} + \phi H_{W^{**}}}{K_1} \tag{33.7}$$

$$H_{U^{**}} = \frac{(1-\varepsilon_1)\lambda_H S^{**} + K_2 \kappa_H L_H}{K_3} \tag{33.8}$$

$$H_{D^{**}} = \frac{\omega_1 \kappa_H L_H^{**} + \gamma_{UH} H_{U^{**}}}{K_4} \tag{33.9}$$

$$H_{W^{**}} = \frac{\tau_1 H_{D^{**}}}{K_5} \tag{33.10}$$

Substitute (33.10) into (33.7), we have

$$L_{H^{**}} = \frac{\varepsilon_1 \lambda_{H^{**}} S^{**}}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)\lambda_H^{**} S^{**}}{Y}$$

$$L_{H^{**}} = \rho_1 \lambda_H^{**} S^{**} \tag{33.14}$$

$$H_{U^{**}} = \frac{(1-\varepsilon_1)\lambda_H^{**} S^{**}}{K_3} + \frac{K_{12} K_H P_1 \lambda_H^{**} S^{**}}{K_3} . = P_2 \lambda_H^{**} S^{**} \tag{33.15}$$

$$H_{D^{**}} = \frac{\omega_1 K_H P_1 \lambda_H^{**} S^{**}}{K_4} + \frac{\gamma_{UH} P_2 \lambda_H^{**} S^{**}}{K_4} . = P_3 \lambda_H^{**} S^{**} \tag{33.16}$$

$$H_W = \frac{\tau_1 P_3 \lambda_H^{**} S^{**}}{K_5} . = P_4 \lambda_H^{**} S^{**} \tag{33.17}$$

Where

$$P_1 = \frac{\varepsilon_1}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)}{Y}$$

$$P_2 = \frac{(1-\varepsilon_1)}{K_3} + \frac{K_2 \kappa_H}{K_3}\left[\frac{\varepsilon_1}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)}{Y}\right]$$

$$P_3 = \frac{\omega_1 \kappa_H}{K_4}\left[\frac{\varepsilon_1}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)}{Y}\right] + \frac{\gamma_{UH}}{K_4}\left[\frac{(1-\varepsilon_1)}{K_2} + \frac{K_2 \kappa_H}{K_3}\left[\frac{\varepsilon_1}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)}{Y}\right]\right]$$

$$P_4 = \frac{\tau_1}{K_5} . \frac{\omega_1 \kappa_H}{K_4}\left[\frac{\varepsilon_1}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)}{Y}\right] + \frac{\gamma_{UH}}{K_4}\left[\frac{(1-\varepsilon_1)}{K_2} + \frac{K_{12} \kappa_H}{K_3}\left[\frac{\varepsilon_1}{X} + \frac{\phi \tau_1 \gamma_{UH}(1-\varepsilon_1)}{Y}\right]\right]$$

Where

$$X = K_1\left(1 - \frac{\phi \tau_1 w_1 \kappa_H}{K_1 K_4 K_5} - \frac{\phi \tau_1 \gamma_{UH} K_{12}\kappa_H}{K_1 K_4 K_5 K_3}\right)$$

$$Y = K_1 K_4 K_5 K_3\left(1 - \frac{\phi \tau_1 \omega_1 K_H}{K_1 K_4 K_5} - \frac{\phi \tau_1 \gamma_{UH} K_{12} K_H}{K_1 K_4 K_5 K_3}\right)$$

$$\lambda_H^{**} = \frac{\beta_H\left[L_H^{**} + \eta_U H_U^{**} + \eta_{dH} H_D^{**} + \eta_W H_W^{**}\right]}{N} \tag{33.18}$$

Substituting the expressions in $(33.14 - 33.17)$ into (33.18) we have

$$\lambda_H^{**}\left[S^{**} + P_1 \lambda_H^{**} S^{**} + P_2 \lambda_H^{**} S^{**} + P_3 \lambda_H^{**} S^{**} + P_4 \lambda_H^{**} S^{**}\right] = \beta \lambda_H^{**} S^{**}\left[P_1 + \eta_U P_2 + \eta_{dH} P_3 + \eta_W P_4\right] \tag{33.19}$$

Divide each term in (33.19) by $\lambda_H^{**} S^{**}$

$$1 + P_5 \lambda^{**} = \beta\left[P_1 + \eta_U P_2 + \eta_{dH} P_3 + \eta_W P_4\right]$$

Where $P_5 = P_1 + P_2 + P_3 + P_4 \geq 0$

So that

$$1 + P_5 \lambda_H^{**} = \frac{\beta}{K_1 K_3 K_4 K_5} \left[\frac{\varepsilon_1 (K_3 K_4 K_5)}{K_1 A} + \frac{\phi \tau_1 \gamma_{UH} (1 - \varepsilon_1)}{(A)} + (1 - \varepsilon_1) K_1 K_4 K_5 \right.$$

$$+ \frac{K_2 K_H \varepsilon_1 K_4 K_5}{A} + \frac{\phi \tau_1 \gamma_{UH} (1 - \varepsilon_1)}{A} + \frac{\omega_1 K_H \varepsilon_1 K_3 K_5}{A} + \frac{\phi \tau_1 \gamma_{UH} (1 - \varepsilon_1)}{A} + \gamma_{UH} (1 - \varepsilon_1) K_1 K_5$$

$$+ \frac{\gamma_{UH} K_2 \varepsilon_1 K_H K_5}{A} + \frac{\gamma_{UH} K_2 K_H \phi \tau_1 \gamma_{UH} (1 - \varepsilon_1)}{K_{14} K_{13} A} + \frac{\tau_1 \omega_1 K_H \varepsilon_1 K_3}{A} + \frac{\tau_1 \omega_1 K_H \phi \tau_1 \gamma_{UH} (1 - \varepsilon_1)}{K_{15} K_1 + A} + \gamma_{UH} (1 - \varepsilon_1) K_1 K_5$$

$$+ \frac{\gamma_{UH} K_2 K_H \varepsilon_1 K_5}{A} + \frac{\gamma_{UH} K_2 K_H \phi \tau_1 \gamma_{UH} (1 - \varepsilon_1)}{K_4 K_3 A}$$

$$= R_H + Q \quad where$$

$$Q = \frac{\beta}{K_1 K_3 K_4 K_5} \left[\frac{\varepsilon_1 K_3 K_5}{A} \left(K_4 + \omega_1 K_H \right) + \frac{\varepsilon_1 K_2 K_5 K_H}{A} \left(K_4 + 2\gamma_{UH} \right) + \frac{\varepsilon_1 \tau_1 \omega_1 K_H K_3}{A} \right.$$

$$\left. + 3 \frac{\phi \tau_1 \gamma_{UH} (1 - \varepsilon)}{A} + \frac{(1 - \varepsilon_1) 2 \gamma_{UH} K_H}{A K_4 K_3} \left(K_2 \phi \tau_1 + K_2 \phi \tau_1 \right) + (1 - \varepsilon_1) \gamma_{UH} \left(\frac{2 \tau_1 \omega_1 K_H \phi}{K_5 K_4 A} + 2 K_1 K_5 + K_1 K_4 K_5 \right) \right]$$

Where $A = \left(1 - \frac{\phi \tau_1 w_1 K_H}{K_1 K_4 K_5} - \frac{\phi \tau_1 \gamma_{uH} K_{12} K_H}{K_1 K_4 K_5 K_3} \right)$

Therefore, $1 + P_5 \lambda^{**} = R_H + Q$

$$\lambda^{**} = \frac{R_H + Q - 1}{P_5} > 0 \text{ Whenever } R_H > 1 \tag{34}$$

Therefore, there exist an endemic equilibrium

3.5   TB MODEL ONLY

$$\left. \begin{aligned}
\frac{dS}{dt} &= \pi - \lambda_T S - \mu \\
\frac{dL_T}{dt} &= \varepsilon_2 \lambda_T S - K_{10} L_T + \upsilon T_U + \theta_1 \rho F_T + r \alpha R_T \\
\frac{dT_U}{dt} &= (1 - \varepsilon_2) \lambda_H S + K_{11} L_T + K_{12} L_T + \theta_2 \rho F_T - K_{13} T_U \\
\frac{dT_D}{dt} &= \omega_2 \kappa_T L_T + \omega_3 \varphi \lambda_T L_T + \gamma_{UT} T_U + K_{14} F_T - K_{15} T_D \\
\frac{dF_T}{dt} &= K_{16} T_D + K_{17} R_T - K_{18} F_T \\
\frac{dR_T}{dt} &= q_1 \tau_2 T_D - K_{19} R_T + \sigma_2 T_D
\end{aligned} \right\} \tag{35}$$

Where $\lambda_T = \beta_T \dfrac{(L_T + \eta_U T_U + \eta_{dT} T_D + \eta_{RT} R_T + \eta_{FT} F_T)}{N}$ \hfill (36)

For this model, it can be shown that the region,

$$D_1 = \{ (S + L_T + \eta_U T_U + \eta_{dT} T_D + \eta_{RT} R_T + \eta_{FT} F_T) \in R^6_+ : N \leq \pi / \mu \tag{37}$$

3.5.1 DERIVATION OF BASIC REPRODUCTION NUMBER (R_O) FOR TB ONLY

Using the same approach in HIV only model, we have,

$$Fi = \begin{pmatrix} F1 \\ F2 \\ F3 \\ F4 \\ F5 \end{pmatrix} = \begin{pmatrix} \varepsilon_2 \lambda_T S \\ (1-\varepsilon_2)\lambda_T S \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad and \quad Vi = \begin{pmatrix} V1 \\ V2 \\ V3 \\ V4 \\ V5 \end{pmatrix} = \begin{pmatrix} K_{10}L_T - \upsilon T_U - \theta_1 \rho F_T - r\alpha R_T \\ -K_{11}L_T - \theta_2 \rho F_T + K_{13}T_U \\ -\omega_2 \kappa_T L_T - \gamma_{UT}T_U - K_{14}F_T + K_{15}T_D \\ -K_{16}T_D - K_{17}R_T + K_{18}F_T \\ -K_{19}T_D + K_{20}R_T \end{pmatrix} \quad (38)$$

After taking partial derivative F and V, we have

$$F = \begin{pmatrix} \varepsilon_2 \beta_T & \varepsilon_2 \beta_T \eta_U & \varepsilon_2 \beta_T \eta_{dT} & \varepsilon_2 \beta_T \eta_{RT} & \varepsilon_2 \beta_T \eta_{FT} \\ (1-\varepsilon_2)\beta_T & (1-\varepsilon_2)\beta_T \eta_U & (1-\varepsilon_2)\beta_T \eta_{dT} & (1-\varepsilon_2)\beta_T \eta_{RT} & (1-\varepsilon_2)\beta_T \eta_{FT} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (39)$$

$$V = \begin{pmatrix} K_{10} & -\upsilon & 0 & -\theta_1 \rho & -r\alpha \\ -K_{11} & K_{13} & 0 & -\theta_2 \rho & 0 \\ -\omega_2 \kappa_T & -\gamma_{UT} & K_{15} & -K_{14} & 0 \\ 0 & 0 & -K_{16} & K_{18} & K_{17} \\ 0 & 0 & -K_{19} & 0 & K_{20} \end{pmatrix} \quad (40)$$

$$R_T = \left(\frac{B_1 + B_2 + B_3}{M} \right) \quad (41)$$

Where

$$M = \begin{bmatrix} \upsilon K_{20}K_{18}K_{15}K_{11} + \gamma_{UT}\alpha r K_{19}K_{18}K_{11} - \gamma_{UT}\theta_1 \rho K_{19}K_{17}K_{11} + \gamma_{UT}\theta_1 \rho K_{20}K_{16}K_{11} \\ -\upsilon K_{19}K_{17}K_{14}K_{11} + \gamma_{UT}\theta_2 \rho K_{19}K_{17}K_{10} + \upsilon\omega_2\theta_2\kappa_T \rho K_{19}K_{17} + K_{20}K_{16}K_{14}K_{13}K_{10} \\ -K_{20}K_{18}K_{15}K_{13}K_{10} + \omega_2\theta_1\kappa_T \rho K_{19}K_{17}K_{13} - \gamma_{UT}\theta_2 \rho K_{20}K_{16}K_{10} + \upsilon K_{20}K_{16}K_{14}K_{11} \\ -\omega_2\kappa_T r\alpha K_{19}K_{18}K_{13} - \upsilon\omega_2\theta_2\kappa_T \rho K_{20}K_{16} - \omega_2\theta_1\kappa_T \rho K_{20}K_{16}K_{13} - K_{19}K_{17}K_{14}K_{13}K_{10} \end{bmatrix}$$

$B_1 = (\beta_T (r\alpha K_{19}K_{18}\gamma_{UT} + K_{20}K_{18}K_{15}\upsilon + K_{20}K_{14}K_{16}\upsilon - K_{19}K_{16}K_{14}\upsilon + \gamma_{UT}\theta_1 \rho K_{19}K_{17} - \gamma_{UT}\theta_1 \rho K_{20}K_{16}$

$-\varepsilon_2 \eta_U K_{19}K_{17}K_{14}K_{11} + \varepsilon_2 \eta_{dT}K_{18}K_{20}\gamma_{UT} + \varepsilon_2 \eta_{RT}K_{11}K_{16}K_{20}\gamma_{UT} - \varepsilon_2 \eta_{RT}K_{11}K_{19}K_{17}\gamma_{UT} + \varepsilon_2 \eta_{FT}K_{11}K_{18}K_{19}\gamma_{UT}$

$-\varepsilon_2 r\alpha K_{19}K_{18}\gamma_{UT} - \varepsilon_2 \eta_U K_{10}K_{16}K_{14}K_{20} + \varepsilon_2 \eta_U K_{19}K_{17}K_{14}K_{10} - \varepsilon_2 \eta_U K_{15}K_{20}K_{10}K_{18} - \varepsilon_2 \eta_{dT}K_{10}K_{18}K_{20}\gamma_{UT}))$

$B_2 = (\beta_T (\varepsilon_2 \eta_{RT}K_{10}K_{19}K_{17}\gamma_{UT} - \varepsilon_2 \eta_{RT}K_{10}K_{15}K_{20}\gamma_{UT} - \varepsilon_2 \rho K_{20}K_{16}\theta_2\gamma_{UT} + \varepsilon_2 \rho K_{19}K_{17}\theta_2\gamma_{UT}$

$+\varepsilon_2 \eta_U K_{11}K_{15}K_{18}K_{20} + \varepsilon_2 \eta_U K_{11}K_{14}K_{16}K_{20} + \omega_2\eta_U \kappa_T \theta_1 K_{16}K_{20} - \omega_2\eta_U \kappa_T \theta_1 K_{19}K_{17} + \omega_2\eta_{RT}\kappa_T \upsilon K_{16}K_{20}$

$-\omega_2\eta_{RT}\kappa_T \upsilon K_{17}K_{19} + \omega_2\eta_{dT}\kappa_T \upsilon K_{18}K_{20} + \omega_2\eta_{FT}\kappa_T \upsilon K_{18}K_{19} - \varepsilon_2\omega_2\eta_U \kappa_T \theta_1 K_{16}K_{20} + \varepsilon_2\omega_2\eta_U \kappa_T \theta_1 K_{19}K_{17}$

$-\varepsilon_2\omega_2\eta_{dT}\kappa_T \upsilon K_{18}K_{20} - \varepsilon_2\omega_2\eta_{RT}\kappa_T \upsilon K_{16}K_{20} + \varepsilon_2\omega_2\eta_{RT}\kappa_T \upsilon K_{17}K_{19} - \varepsilon_2\omega_2\eta_{FT}\kappa_T \upsilon K_{18}K_{19}$

$+\varepsilon_2\omega_2\eta_{dT}\kappa_T K_{13}K_{18}K_{20}))$

$B_3 = (\beta_T (\varepsilon_2\omega_2\eta_{RT}\kappa_T K_{13}K_{16}K_{20} - \varepsilon_2\omega_2\eta_{RT}\kappa_T K_{13}K_{19}K_{13} + \varepsilon_2\omega_2\eta_{FT}\kappa_T K_{13}K_{18}K_{19} - r\alpha\omega_2\eta_U \kappa_T K_{19}K_{18}$

$-\varepsilon_2 \upsilon K_{15}K_{18}K_{20} - \varepsilon_2 \upsilon K_{14}K_{16}K_{20} + \varepsilon_2 \upsilon K_{14}K_{17}K_{19} + \varepsilon_2 K_{20}K_{16}\theta_1\gamma_{UT} - \varepsilon_2 K_{19}K_{17}\theta_1\gamma_{UT} + \varepsilon_2 K_{20}K_{16}K_{13}K_{14}$

$-\varepsilon_2 K_{19}K_{17}K_{13}K_{14} + \varepsilon_2 K_{20}K_{15}K_{13}K_{18} + \eta_U K_{20}K_{16}K_{10}K_{14} - \eta_U K_{19}K_{17}K_{10}K_{14} + \eta_U K_{20}K_{14}K_{10}K_{18}$

$+\eta_{RT}K_{10}K_{16}K_{20}\gamma_{UT} - \eta_{RT}K_1 K_{17}K_{19}\gamma_{UT} + \eta_{dT}K_{10}K_{18}K_{20}\gamma_{UT} + \eta_{FT}K_{10}K_{18}K_{19}\gamma_{UT} + \varepsilon_2 r\alpha\omega_2\eta_U \kappa_T K_{19}K_{18}$

$+\eta_U \varepsilon_2 \rho K_{20}K_{16}\theta_2\omega_2\kappa_T - \eta_U \varepsilon_2 \rho K_{19}K_{17}\theta_2\omega_2\kappa_T))$

The threshold quantity R_T is the basic reproduction number of the normalized model system (35) for HIV infection in a population. It measures the average number of new secondary infections generated by a single infected individual in his or her infectious period in a population [1].

3.5.2 DISEASE FREE EQUILIBRIUM

For critical points, we set

$$\frac{dS}{dt} = \frac{dL_T}{dt} = \frac{dT_U}{dt} = \frac{dT_D}{dt} = \frac{dF_T}{dt} = \frac{dR_T}{dt} = 0 \qquad (42)$$

At this free equilibrium, it is assumed that there is no infection, Hence the (DFE) is given as

$$\varepsilon_0 = (S, L_T, T_U, T_D, F_T, R_T) = \left(\frac{\pi}{\mu}, 0,0,0,0,0\right)$$

3.5.3 GLOBAL STABILITY OF DISEASE FREE EQUILIBRIUM (TB)

Theorem3.5: The disease free-equilibrium of the system (35) is globally asymptotically stable whenever $R_T < 1$ and unstable if $R_T > 1$.

Proof: It follows that $S = N^* - L_T - T_u - T_D - F_T - R_T$ at steady state. The proof is based on using the comparison method.[21]

$$\begin{pmatrix} \dfrac{dL_T}{dt} \\ \dfrac{dT_U}{dt} \\ \dfrac{dT_D}{dt} \\ \dfrac{dF_T}{dt} \\ \dfrac{dR_T}{dt} \end{pmatrix} = (F - V) \begin{pmatrix} L_T \\ T_U \\ T_D \\ F_T \\ R_T \end{pmatrix} - Fi \begin{pmatrix} L_T \\ T_U \\ T_D \\ F_T \\ R_T \end{pmatrix} \qquad (43)$$

$$F - V = \begin{pmatrix} \varepsilon_2\beta_T - K_{10} & \varepsilon_2\beta_T\eta_U + \upsilon & \varepsilon_2\beta_T\eta_{dT} & \varepsilon_2\beta_T\eta_{RT} + \theta_1\rho & \varepsilon_2\beta_T\eta_{FT} + r\alpha \\ (1-\varepsilon_2)\beta_T + K_{11} & (1-\varepsilon_2)\beta_T\eta_U - K_{13} & (1-\varepsilon_2)\beta_T\eta_{dT} & (1-\varepsilon_2)\beta_T\eta_{RT} + \theta_2\rho & (1-\varepsilon_2)\beta_T\eta_{FT} \\ \omega_2\kappa_T & \gamma_{UT} & K_{15} & -K_{14} & 0 \\ 0 & 0 & K_{16} & -K_{18} & -K_{17} \\ 0 & 0 & K_{19} & 0 & -K_{20} \end{pmatrix} \qquad (44)$$

Then,

According to [6, 31], all eigenvalues of the matrix

(F - V) have negative real parts.

Thus, we have

$$\begin{bmatrix} ((\varepsilon_2\beta_T - K_{10}) - \lambda)((1-\varepsilon_2)\beta_T\eta_U - K_{13} - \lambda)(K_{15} - \lambda)((-K_{18} - \lambda)(-K_{20} - \lambda)) - ((\varepsilon_2\beta_T\eta_U + \upsilon) \\ ((1-\varepsilon_2)\beta_T + K_{11})(K_{15} - \lambda)(-K_{18} - \lambda)(-K_{20} - \lambda)) + ((\varepsilon_2\beta_T\eta_{dT})((1-\varepsilon_2)\beta_T + K_{11})(\gamma_{UT}) \\ (-K_{18} - \lambda)(-K_{20} - \lambda)) - ((\varepsilon_2\beta_T\eta_{RT} + \theta_2\rho)((1-\varepsilon_2)\beta_T + K_{11})(\gamma_{UT})(-K_{20} - \lambda)(K_{16}) + K_{17}K_{19}) \\ + ((\varepsilon_2\beta_T\eta_{FT} + r\alpha)((1-\varepsilon_2)\beta_T + K_{11})(\gamma_{UT})(-K_{18} - \lambda)(K_{19}) \end{bmatrix} \qquad (45)$$

Thus from equation (45), the characteristic equation is given by

$$\lambda^5 + a_5\lambda^4 + a_4\lambda^3 + a_3\lambda^2 + a_2\lambda + a_1 = 0 \qquad (46)$$

Thus according to Routh Hurwitz Criteria for order five (5),

$$a_5 > 0 \;\; a_4 > 0 \;\; a_3 > 0 \;\; a_2 > 0 \;\; a_1 > 0$$

Then for $a_1 > 0$ we have

$$-\beta_T(B_1 + B_2 + B_3) > -M$$

Hence

$$\frac{\beta_T(B_1 + B_2 + B_3)}{M} < 1,$$

Implying that

$$R_T < 1.$$

Hence, we have established that the disease free equilibrium is globally asymptotically stable whenever $R_T < 1$ and unstable $R_T > 1$.

3.5.4 EXISTENCE OF ENDEMIC FOR TB MODEL ONLY

Where $\varepsilon_0^{**} = (S^{**}, L_T^{**}, T_U^{**}, T_D^{**}, F_T^{**}, R_T^{**})$ are the endemic equilibrium points.

Equation (35) becomes

$$\frac{dS}{dt} = \pi - \lambda_T S - \mu S \qquad (47.1)$$

$$\frac{dL_T}{dt} = \varepsilon_2 \lambda_T S - K_{10} L_T \qquad (47.2)$$

$$\frac{dT_U}{dt} = (1 - \varepsilon_2)\lambda_T S + K_{11} L_T - K_{13} T_U \qquad (47.3)$$

$$\frac{dT_D}{dt} = \omega_2 \kappa_T L_T + \gamma_{UT} T_U - K_{15} T_D \qquad (47.4)$$

$$\frac{dR_T}{dt} = K_{19} T_D - \mu R_T + \sigma_2 T_D \qquad (47.5)$$

For a special case of TB-only model, when $q_1 = 1$ and $\upsilon_1, \theta_1, \theta_2 \;\; \varphi \; and \; \alpha$ are very small (negligible). Then, solving at steady state;

$$S^{**} = \frac{\pi}{\lambda_T^{**} + \mu} \qquad (47.6)$$

$$L_T^{**} = \frac{\varepsilon_2 \lambda_T^{**} S^{**}}{K_{10}} \qquad (47.7)$$

$$T_U^{**} = \frac{(1 - \varepsilon_2)\lambda_T^{**} S^{**} + K_{11}\kappa_T L_T^{**}}{K_{13}} \qquad (47.8)$$

$$T_D^{**} = \frac{\omega_2 \kappa_T L_T^{**} + \gamma_{UT} T_U^{**}}{K_{15}} \qquad (47.9)$$

$$R_T^{**} = \frac{K_{19} T_D^{**}}{\mu} \qquad (47.10)$$

The expression for λ_T at the endemic steady-state, denoted by λ^{**} is given by

$$\lambda_T^{**} = \frac{\beta_T\left[\eta_U T_U^{**} + \eta_{dT} T_D^{**} + \eta_{RT} R_T^{**} + \eta_{FT} F_T^{**} + L_T^{**}\right]}{N^{**}} \tag{47.11}$$

$$\left.\begin{aligned}
L_T^{**} &= \frac{\varepsilon_2 \lambda_T^{**} S^{**}}{K_{10}} \\[2mm]
T_u^{**} &= \frac{(1-\varepsilon_2)\lambda_T^{**} S^{**}}{K_{13}} + \frac{K_{11}\kappa_T \varepsilon_2 \lambda_T^{**} S^{**}}{K_{13}K_{10}} = P_1 \lambda^{**} S^{**} \\[2mm]
T_D^{**} &= \frac{\omega_2 \kappa_T \varepsilon_2 \lambda_T^{**} S^{**}}{K_{10}K_{15}} + \frac{\gamma_{UT} P_1 \lambda^{**} S^{**}}{K_{15}} = P_2 \lambda^{**} S^{**} \\[2mm]
R_T^{**} &= \frac{K_{19}}{\mu}\left[\frac{\omega_2 \kappa_T \varepsilon_2 \lambda_T^{**} S^{**}}{K_{10}K_{15}} + \frac{\gamma_{UT} P_1 \lambda^{**} S^{**}}{K_{15}}\right] = P_3 \lambda^{**} S^{**}
\end{aligned}\right\} \tag{47.12}$$

$$\left.\begin{aligned}
P_1 &= \frac{(1-\varepsilon_2)}{K_{13}} - \frac{K_{11}\kappa_T \varepsilon_2}{K_{10}K_{13}} \\[2mm]
P_2 &= \frac{\omega_2 \kappa_T \varepsilon_2}{K_{10}K_{15}} + \frac{\gamma_{UT}}{K_{15}}\left[\frac{(1-\varepsilon_2)}{K_{13}} - \frac{K_{11}\kappa_T \varepsilon_2}{K_{10}K_{13}}\right] \\[2mm]
P_3 &= \frac{K_{19}}{\mu}\left[\frac{\omega_2 \kappa_T \varepsilon_2}{K_{10}K_{15}} + \frac{\gamma_{UT}}{K_{15}}\left(\frac{(1-\varepsilon_2)}{K_{13}} - \frac{K_{11}\kappa_T \varepsilon_2}{K_{10}K_{13}}\right)\right]
\end{aligned}\right\} \tag{47.13}$$

Substituting the expression in (47.12) into (47.11)

$$\lambda^{**}\left[S^{**} + \frac{\varepsilon_2 \lambda_T^{**} S^{**}}{K_{10}} + P_1 \lambda^{**} S^{**} + P_2 \lambda^{**} S^{**} + P_3 \lambda^{**} S^{**}\right] = \beta \lambda_T^{**} S^{**}\left[\eta_U P_1 + \eta_{dT} P_2 + \eta_{RT} P_3\right] \tag{47.14}$$

Divide each term in (47.14) by $\lambda_T^{**} S^{**}$

$$1 + P_4 \lambda^{**} = \beta\left[\eta_U P_1 + \eta_{dT} P_2 + \eta_{RT} P_3\right]$$

Where $P_4 = \dfrac{\varepsilon_2}{K_{10}} + P_1 + P_2 + P_3 \geq 0$

So that

$$1 + P_4 \lambda^{**} = \frac{\beta_T}{K_{10}K_{13}K_{15}}\Big[\eta_U (1-\varepsilon_2)K_{10}K_{15} + \eta_U K_{11}\kappa_T \varepsilon_2 K_{13} + \eta_{dT}\omega_2 \kappa_T \varepsilon_2 K_{13}$$

$$+ \eta_{dT}\gamma_{UT}\left[(1-\varepsilon_2)K_{10} + K_{11}\kappa_T \varepsilon_2\right] + \eta_{RT}\frac{K_{19}}{\mu}\omega_2 \kappa_T \varepsilon_2 K_{13} + \eta_{RT}\frac{K_{19}}{\mu}\gamma_{UT}$$

$$\left[(1-\varepsilon_2)K_{10} + K_{11}\kappa_T \varepsilon_2\right] = R_T + Q$$

Where

$$Q = \frac{\beta_T}{K_{11}K_{12}K_{13}}\left[(1-\varepsilon_2)K_{11}\left[\eta_U K_{13} + \eta_{dT}\gamma_{UT} + \eta_{RT}\frac{(\sigma_2 + \tau_2)}{\mu}\right] + \right.$$

$$\left. (1-\omega_2)\kappa_T\varepsilon_2\left[\eta_U K_{12} + \eta_{dT}\gamma_{UT} + \eta_{RT}\gamma_{UT}\frac{(\sigma_2 + \tau_2)}{\mu}\right] + \omega_2\kappa_T\varepsilon_2 K_{12}\left[\eta_{dT} + \eta_{RT}\frac{(\sigma_2 + \tau_2)}{\mu}\right]\right]$$

Therefore $1 + P_4\lambda_T^{**} = R_T + Q$

$$\lambda_T^{**} = \frac{R_T + Q - 1}{P_4} > 0 \text{ ,whenever } R_T > 1 \qquad (48)$$

Therefore, there exist an endemic equilibrium whenever $R_T > 1$

3.6 ANALYSIS OF THE FULL MODEL

Consider the Co-infection model (23) of HIV-TB

3.6.1 DISEASE FREE EQUILIBRIUM

For critical points, we set

$$\frac{dS}{dt} = \frac{dL_H}{dt} = \frac{dH_U}{dt} = \frac{dH_D}{dt} = \frac{dH_W}{dt} = \frac{dL_{TH}}{dt} = \frac{dA_{TH}}{dt} = \frac{dL_{HT}}{dt} = \frac{dA_{HT}}{dt} = \frac{dL_T}{dt} \frac{dT_U}{dt} = \frac{dT_D}{dt} = \frac{dF_T}{dt} = \frac{dR_T}{dt} = \frac{dR_{TH}}{dt} = 0$$

At disease free equilibrium, it is assumed that there is no infection. Then, the disease free equilibrium of the full model is given by

$$\varepsilon_1 = \left(S^*, L_H^*, H_U^*, H_D^*, H_W^*, L_{TH}^*, A_{TH}^*, L_{HT}^*, A_{HT}^*, L_T^*, T_U^*, T_D^*, F^*, R_T^*, R_{TH}^*\right)$$

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

3.6.2 DERIVATION OF BASIC REPRODUCTION NUMBER (R_O) FOR HIV-TB CO-INFECTION

The associated matrices F and V, are given, respectively, by

$$F = \begin{bmatrix} F_1 & F_2 \\ F_3 & F_4 \end{bmatrix} \qquad (49)$$

Where,

$$F_1 = \begin{pmatrix}
\varepsilon_1\beta_H & \varepsilon_1\beta_H\eta_U & \varepsilon_1\beta_H\eta_{dH} & \varepsilon_1\beta_H\eta_W & \varepsilon_1\beta_T & \varepsilon_1\beta_T\eta_T & \varepsilon_1\beta_H \\
(1-\varepsilon_1)\beta_H & (1-\varepsilon_1)\beta_H\eta_U & (1-\varepsilon_1)\beta_H\eta_{dH} & (1-\varepsilon_1)\beta_H\eta_W & (1-\varepsilon_1)\beta_T & (1-\varepsilon_1)\beta_T\eta_T & (1-\varepsilon_1)\beta_H \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\beta_H & \beta_H\eta_U & \beta_H\eta_{dH} & \beta_H\eta_W & \beta_T & \beta_T\eta_T & \beta_H \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\beta_H & \beta_H\eta_U & \beta_H\eta_{dH} & \beta_H\eta_W & \beta_T & \beta_T\eta_T & \beta_H
\end{pmatrix} \qquad (50)$$

$$F_2 = \begin{pmatrix} \varepsilon_1\beta_H\eta_H & \varepsilon_1\beta_T & \varepsilon_1\beta_H\eta_U & \varepsilon_1\beta_T\eta_{dT} & \varepsilon_1\beta_T\eta_{FT} & \varepsilon_1\beta_T\eta_{RT} & \varepsilon_1\beta_T\eta_{RT} \\ (1-\varepsilon_1)\beta_H\eta_H & (1-\varepsilon_1)\beta_T & (1-\varepsilon_1)\beta_T\eta_U & (1-\varepsilon_1)\beta_T\eta_{dT} & (1-\varepsilon_1)\beta_T\eta_{FT} & (1-\varepsilon_1)\beta_T\eta_{RT} & (1-\varepsilon_1)\beta_T\eta_{RT} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \beta_H\eta_H & \beta_T & \beta_T\eta_U & \beta_T\eta_{dT} & \beta_T\eta_{FT} & \beta_T\eta_{RT} & \beta_T\eta_{RT} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \beta_H\eta_H & \beta_T & \beta_T\eta_U & \beta_T\eta_{dT} & \beta_T\eta_{FT} & \beta_T\eta_{RT} & \beta_T\eta_{RT} \end{pmatrix} \tag{51}$$

$$F_3 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \varepsilon_2\beta_H & \varepsilon_2\beta_H\eta_U & \varepsilon_2\beta_H\eta_{dH} & \varepsilon_2\beta_H\eta_W & \varepsilon_2\beta_T & \varepsilon_2\beta_T\eta_T \; \varepsilon_2\beta_H \\ (1-\varepsilon_2)\beta_H & (1-\varepsilon_2)\beta_H\eta_U & (1-\varepsilon_2)\beta_H\eta_{dH} & (1-\varepsilon_2)\beta_H\eta_W & (1-\varepsilon_2)\beta_T & (1-\varepsilon_2)\beta_T\eta_T & (1-\varepsilon_2)\beta_H \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{52}$$

$$F_4 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \varepsilon_2\beta_H\eta_H & \varepsilon_2\beta_T & \varepsilon_2\beta_T\eta_U & \varepsilon_2\beta_T\eta_{dT} & \varepsilon_2\beta_T\eta_{FT} & \varepsilon_2\beta_T\eta_{RT} & \varepsilon_2\beta_T\eta_{RT} \\ (I-\varepsilon_2)\beta_H\eta_H & (I-\varepsilon_2)\varepsilon_2\beta_T & (I-\varepsilon_2)\beta_T\eta_U & (I-\varepsilon_2)\beta_T\eta_{dT} & (I-\varepsilon_2)\beta_T\eta_{FT} & (I-\varepsilon_2)\beta_T\eta_{RT} & (I-\varepsilon_2)\beta_T\eta_{RT} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{53}$$

And, $V = \begin{bmatrix} V_1 & V_2 \\ V_3 & V_4 \end{bmatrix}$ \tag{50}

Where,

$$V_1 = \begin{pmatrix} K_1 & 0 & 0 & -\phi & 0 & 0 & 0 \\ K_2 & K_3 & 0 & 0 & 0 & 0 & 0 \\ -\omega_1 K_H & -\gamma_{UH} & K_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\tau_1 & K_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & K_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & -K_{TH} & K_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & K_8 \end{pmatrix} \tag{54}$$

$$V_2 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\alpha T \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{55}$$

$$V_3 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\sigma_1 & 0 \end{pmatrix} \tag{56}$$

$$V_4 = \begin{pmatrix} K_9 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & K_{10} & -\upsilon & 0 & -\theta_1\rho & -r\alpha & 0 \\ 0 & K_{11} & K_{13} & 0 & -\theta_2\rho & 0 & 0 \\ 0 & -\omega_2 & -\gamma_{UT} & K_{14} & K_{15} & 0 & 0 \\ 0 & 0 & 0 & K_{16} & K_{17} & K_{18} & 0 \\ 0 & 0 & 0 & K_{19} & 0 & K_{20} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & K_{21} \end{pmatrix} \tag{57}$$

$$F.V^{-1} = \begin{bmatrix} F_1.V_1^{-1} & F_2.V_2^{-1} \\ F_3.V_3^{-1} & F_4.V_4^{-1} \end{bmatrix} \tag{58}$$

$$R_1 = F_1.V_1^{-1} \tag{59}$$

$$\left. \begin{aligned} R_1 &= \frac{\beta_H \varepsilon_1}{A}\left[K_5 K_4 K_3 + \eta_U \phi\tau_1\gamma_{UH} + \eta_{dH}\phi\tau_1 K_3 + \eta_W \phi K_4 K_3 \right] \\ &+ \frac{\beta_H(1-\varepsilon_1)}{A}\left[-K_5 K_4 K_2 - \eta_U(K_5 K_4 K_1 - \phi\tau_1\omega_1\kappa_H) - \eta_{dH}\phi\tau_1 K_2 + \eta_W\phi K_4 K_2 \right] + \frac{\beta_T}{K_8} \end{aligned} \right\} \tag{60}$$

$$A = K_5 K_4 K_3 K_1 - \tau_1\phi\omega_1 K_4 K_3 + \tau_1\phi\gamma_{UH} K_2 \tag{61}$$

$$R_2 = F_4 V_4^{-1} \tag{62}$$

$$R_2 = \frac{P_1 + P_2 + P_3 + P_4 + P_5 + P_6 + P_7 + P_8 + P_9 + P_{10}}{B}$$

$$P_1 = \frac{-\left(\varepsilon_2\beta_T(K_{20}K_{16}\rho\gamma_{UT}\theta_2 - K_{20}K_{16}K_{13}K_{15} + K_{19}K_{15}K_{13}K_{18} + K_{14}K_{20}K_{13}K_{17} - K_{19}K_{18}\rho\gamma_{UT}\theta_2)\right)}{B}$$

$$P_2 = \frac{\left(\varepsilon_2\beta_T\delta_U(K_{11}K_{14}K_{17}K_{20} - K_{11}K_{15}K_{16}K_{20} + K_{11}K_{15}K_{18}K_{19} + K_{20}K_{16}\rho\omega_2\theta_2 - K_{19}K_{18}\rho\omega_2\theta_2)\right)}{B}$$

$$P_3 = \frac{\left(\varepsilon_2\beta_T\beta\delta_{dT}K_{17}K_{20}(K_{11}\gamma_{UT} - K_{13}\omega_2)\right)}{B}$$

$$P_4 = \frac{\left(\varepsilon_2\beta_T\delta_{FT}(K_{16}K_{20} - K_{18}K_{19})(K_{11}\gamma_{UT} - K_{13}\omega_2)\right)}{B}$$

$$P_5 = \frac{-\left(\varepsilon_2\beta_T\delta_{RT}K_{17}K_{19}(K_{11}\gamma_{UT} - K_{13}\omega_2)\right)}{B}$$

$$P_6 = \frac{\begin{pmatrix}(1-\varepsilon_2)\beta_T(-\upsilon K_{14}K_{17}K_{20} + \upsilon_{15}K_{16}K_{20} - \upsilon K_{15}K_{18}K_{19} + K_{20}K_{16}\rho\gamma_{UT}\theta_1 + r\alpha K_{19}K_{17}\gamma_{UT}\\ - K_{19}K_{18}\rho\gamma_{UT}\theta_1\end{pmatrix}}{B}$$

$$P_7 = \frac{-(1-\varepsilon_2)\beta_T\delta_U(K_{14}K_{20}K_{10}K_{17} - K_{20}K_{16}K_{18}K_{15} + K_{19}K_{15}K_{10}K_{18} - K_{19}K_{18}\rho\omega_2\theta_1 + K_{20}K_{16}\rho\theta_1 + r\alpha K_{19}K_{17}\omega_2))}{B}$$

$$P_8 = \frac{-((1-\varepsilon_2)\beta_T\delta_{dT}K_{17}K_{19}(\upsilon\omega_2 + K_{10}\gamma_{UT})}{B}$$

$$P_9 = \frac{((1-\varepsilon_2)\beta_T\delta_{FT}(K_{16}K_{20} - K_{18}K_{19}(\upsilon\omega_2 + K_{10}\gamma_{UT}))}{B}$$

$$P_{10} = \frac{((1-\varepsilon_2)\beta_T\delta_{RT}K_{17}K_{19}(\upsilon\omega_2 + K_{10}\gamma_{UT}))}{B}$$

Where;

$$B = (\upsilon K_{11}K_{20}K_{16}K_{15} - \upsilon K_{11}K_{20}K_{17} - \upsilon K_{11}K_{19}K_{15}K_{18} - \upsilon K_{20}K_{16}\rho\omega_2\theta_2 + \upsilon K_{14}\rho\omega_2\theta_2 K_{18} +$$
$$K_{11}K_{20}\rho\omega_2\theta_2 K_{18} + K_{11}K_{20}K_{16}\rho\gamma_{UT}\theta_1 + K_{11}K_{19}r\alpha\gamma_{UT}K_{17} - K_{11}K_{19}\rho\gamma_{UT}\theta_2 - K_{19}r\alpha\omega_2$$
$$- K_{20}K_{16}\gamma_{UT}K_{10}\theta_2 + K_{19}\omega_2\theta_1\rho K_{12}K_{18} + K_{19}\rho\gamma_{UT}K_{10}\theta_2 K_{18})$$

Hence it is shown that the associated Reproduction number is given by

$$R_C = \max[R_1, R_2].$$

3.7 NUMERICAL SIMULATIONS

Table 1. Parameter Values used in Numerical Simulations

Parameters	Value	Source
π	2000	[23]
μ	0.02	[4]
τ_1, τ_2	0.20619, 0.20619	Assumed
$\varepsilon_1, \varepsilon_2$	0.7, 0.7	[26]
κ_H, κ_T	0.2522, 0.2522	[10]
ω_1, ω_2	0.2, 0.2	[26]
γ_{UH}, γ_{UT}	0.2, 0.2	Assumed
ϕ	0.7	[32]
β_H, β_T	0.1, 0.1	[9]
δ_{UH}, δ_{dH}	0.3, 0.1	[9]
$\eta_U, \eta_{dH}, \eta_W$	0.001, 0.001, 0.001	[26]
θ_1, θ_2	0.1, 0.1	[11]
φ	0.85	Assumed

κ_{HT},κ_{TH}	0.2522, 0.2522	[10]
ω_2,ω_3	0.7, 0.7	[23]
υ	0.2	[11]
α	5	[11]
r	0.8	Assumed
ρ	0.1	Assumed
$\delta_{UT},\delta_{dT},\delta_F,\delta_{RT}$	0.3, 0.1	[10]
σ_1,σ_2	0.2	[17]
q_1	0.7	[32]
$\eta_U,\eta_{dT},\eta_{FT},\eta_{RT}$	0.001, 0.001, 0.001, 0.001	[26]

The new fifteen (15) compartmental non linear differential equations were designed to gain more insight on the effect of epidemiological features on the dynamical spread of HIV-TB co-infection. Numerical simulation of the model was carried out by maple software, using differential transformation method as to be able to determine the dynamical spread pattern of the disease in the community. Graphs and tables feature prominently in the discussion of results.
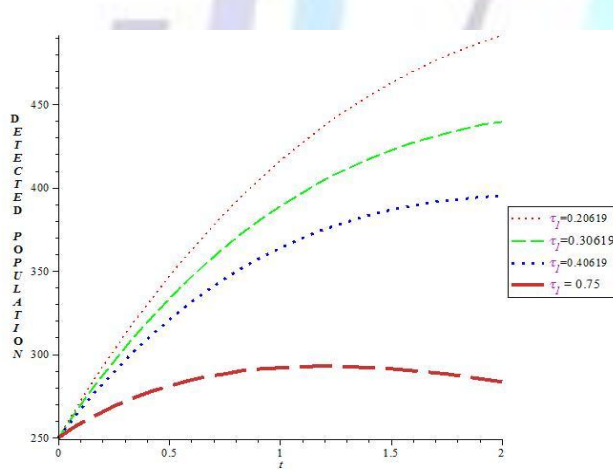
Fig. 1
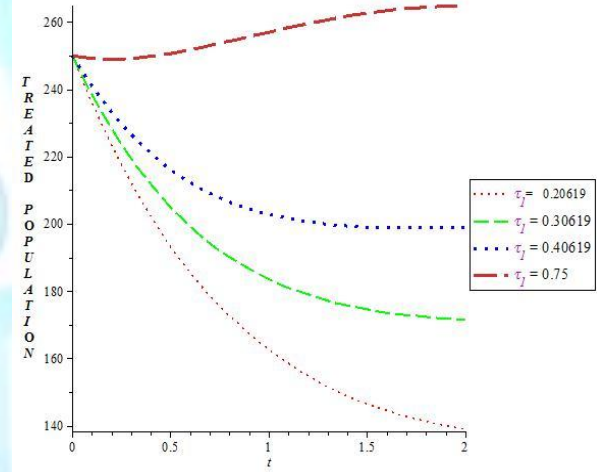
Fig. 2
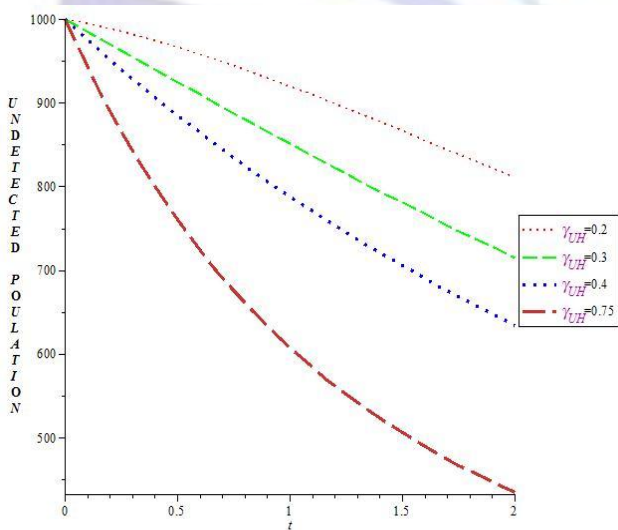
Fig. 3
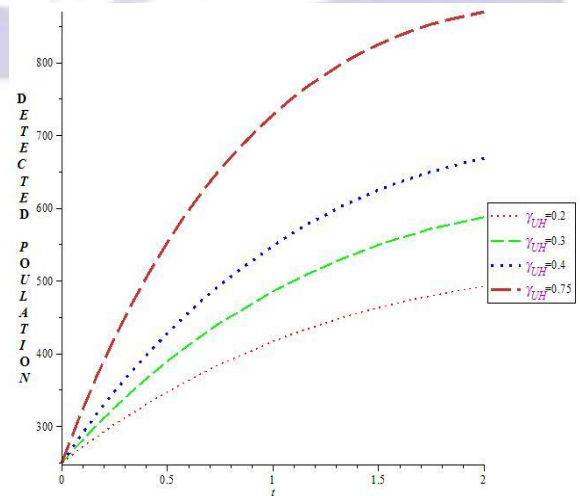
Fig. 4
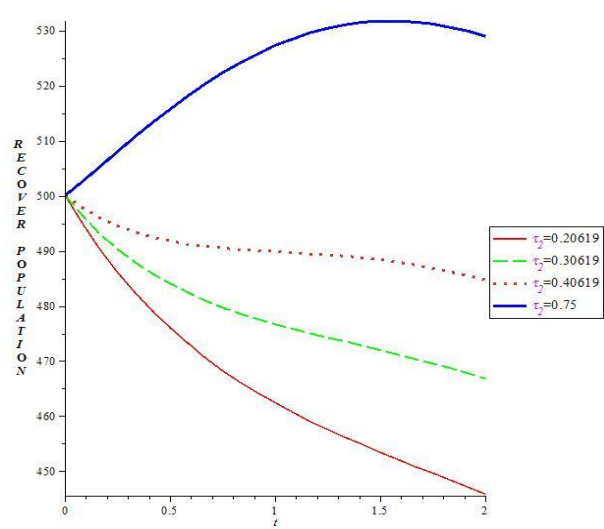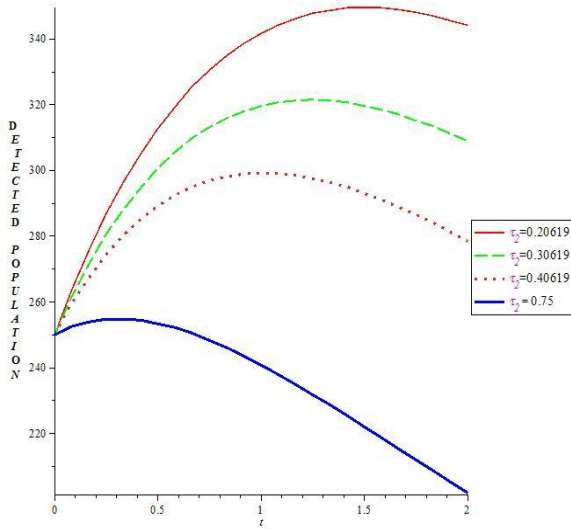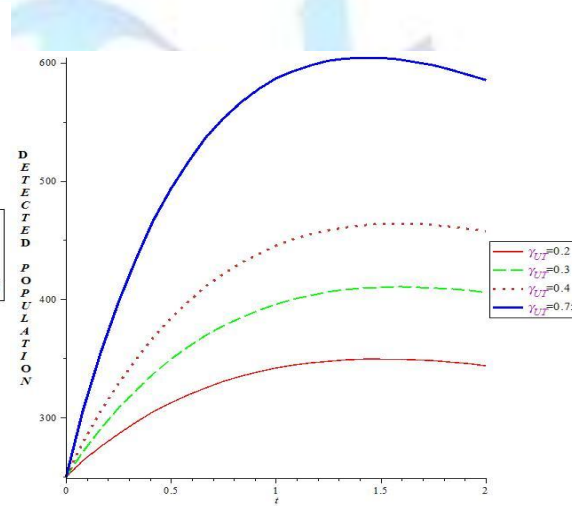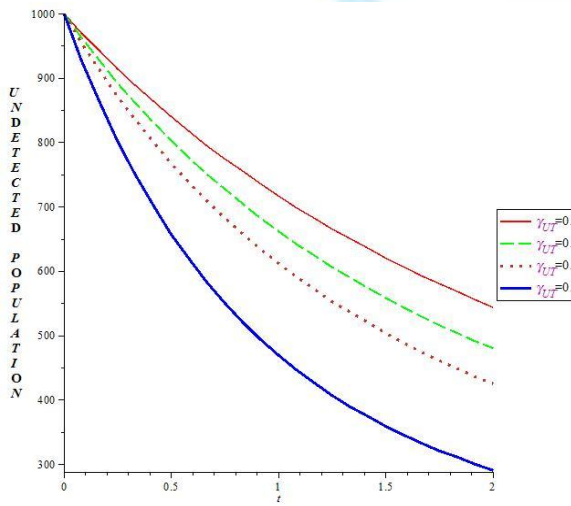
Fig. 5
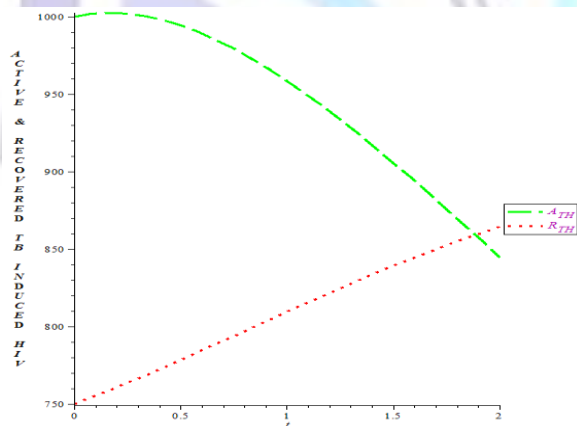

Fig. 6

Fig. 7

Fig. 8

Fig. 9

4.1 DISCUSSION

Figure 1and 2 Show the effect of treatment on HIV infected detected and recovered individuals. It shows a decrease in the numbers of infected detected individuals and also increases the number of recovered individuals. It reduces infected detected individuals from 500 to 275 when the treatment rate τ_1 is about 75% effective. **Figure 3 and 4** has shown that detection rate has pronounced effect on HIV undetected infected and detected infected individuals. It shows that the higher the detection rate, the higher the infected detected individuals and the lower the undetected infected individuals. It reduces it to a minimal level when the detection rate γ_{UH} is about 0.7. **Figure 5 and 6** Shown that treatment of TB has pronounced effect on TB infected detected individuals. It reduces the numbers of infected detected individuals and shows the increase in recovered individuals especially when the treatment rate τ_2 is about 75% effective. **Figure 7 and 8** Shown that the detection of TB infected undetected individuals reduces the spread of the disease in the community, it reduces the population of infected undetected individuals from 1000 to around 10 when the detection rate γ_{UT} is about 0.7. This suggests that, detection of infected undetected TB individuals plays a vital role in the control of TB disease.

Figure 9 Shows the pronounce effect of treatment on active TB induced HIV individuals, it reduces active TB induced HIV from 1000 to 840 individuals and increases recovered individuals due to the efficacy of the drugs.

5.1 CONCLUSION

This work deals with the formulation and analysis of mathematical model to have better understanding of detection of infected undetected individuals and treatment strategies on the dynamical spread of HIV-TB co-infection.

In this paper, a mathematical model showing the effect of detection rate of HIV, TB and HIV-TB co-infection has been analyzed separately. Both qualitative and numerical analysis of each model was carried out. Qualitative analysis of each model reveals well posedness and uniqueness of their solutions. Basic reproduction number (R_0) was computed by next generation matrix as well as the stability of model equilibrium. It was established that each model has two equilibrium points, namely; disease free equilibrium which is locally asymptotically stable whenever $R_0 < 1$ and unstable endemic equilibrium whenever $R_0 > 1$.

In numerical analysis, detection of infected undetected individuals γ_{UH} and γ_{UT} plays a vital role in the control of HIV-TB co-infection; it was observed that the detection of undetected individuals reduced the spread of disease, the disease becomes more endemic due to the increment in the numbers of infected undetected individuals. It was also shown that TB fuels the progression of HIV into full blown AIDS in the absence of proper treatment, likewise HIV increases latent TB to active TB in the absence of treatment. The results shown that in the presence of treatment, the rate of Active TB and HIV decreases as the treatment increases and consequently, the recover TB and HIV individuals increase rapidly.

In conclusion, epidemiological features such as detection rate of infected undetected individuals and treatment rate of infected detected individuals play vital roles in the control of the spread of HIV- TB co-infection disease in the community. Medical practitioners and policy health makers need to increase the rate at which infected undetected individuals are detected for proper and timely treatment, also, drugs should be made available at a cheaper rate for the consumers.

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