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Semi-Analytic Solution of HIV and TB Co-Infection Model

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ABSTRACT In this work we developed and analyzed a mathematical model of HIV and TB co-infection. The model is a first order Ordinary Differential Equations, in which the human population is divided into six mutually- exclusive compartments namely; TB- Susceptible individuals (S), TB-Infected individuals (I), TB-Recovered individuals (R), HIV-Infected individuals (P_1), Co- Infected individuals (P_2) and individuals with AIDS (A). The analytical solution is obtained using Homotopy Perturbation Method (HPM). The result of the numerical simulation shows that at high HIV and TB treatment rates; TB, AIDS and HIV/TB co-infection will be eradicated completely in the population. Also, early detection of HIV and TB cases and provision of early treatments can reduce the rate of infection, reduce the rate of progression of HIV infected individuals to AIDS and lowers co-infection. ©JASEM
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Tuberculosis (TB) and Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) constitute the main burden of infectious disease in resource-limited countries. Estimates by the World Health Organization (WHO) indicate that there are more than 9 million new active cases of TB and close to 2 million deaths per year WHO (2010). In the individual host the two pathogens, M. tuberculosis and HIV, potentiate one another, accelerating the deterioration of immunological functions and resulting in premature death if left untreated. About 14 million individuals worldwide are estimated to be dually infected. Both TB and HIV have profound effects on the immune system, as they are capable of disarming the host's immune responses through mechanisms that are not fully understood. HIV/TB co-infection is the most powerful known risk factor for progression of M. tuberculosis infection to active disease, increasing the risk of latent TB reactivation 20-fold Getahun *et al.,* (2010). Bolarin, 2012; in his work, formulated a sex-structured model to capture the effect of complacency on the dynamics of HIV/AIDS but did not include how TB will affect the mix. But, recently a lot of ground work has been covered in the mathematical modelling of co-infection of different pathogens though very little was done in the modelling of HIV/TB co infection. David, 2013; Nthiiri, 2015; Roeger *et al.,* (2009), Shah and Jyota (2013) have developed mathematical models of HIV/TB co-infection under TB treatment. Their work did not include anti-HIV treatment. Silver and Delfim (2015) developed a TB-HIV/AIDS co-infection model and optimal control treatment.

One of the most powerful methods to approximately solve linear and non-linear differential equations is the Homotopy Perturbation Method (HPM); see Abubakar *et al.,* (2013), (Jiya, 2010) for examples. The HPM method is based in the use of a power series, which transforms the original non-linear differential equation into a series of linear differential equations. Two continuous functions from one topological space to another are called homotopic if one can be “continuously deformed" into the other, such a deformation is called a homotopy between the two functions. The Homotopy Perturbation Method (HPM), which provides analytical approximate solution, is applied to various linear and non-linear equations (He, 1999). The Homotopy Perturbation Method (HPM) is a series expansion method used in the solution of non-linear partial differential equations (Jiya, 2010). The method employs a

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homotopy transform to generate a convergent series solution of differential equations. To illustrate the basic ideas of this method, the following non-linear differential equation was considered (He, 2000).

$A(u) - f(r) = 0, \; r \in \Omega,$ (1)

Subject to the boundary condition

$$B\left(U, \frac{\partial U}{\partial n}\right) = 0 \quad r \in \Gamma \tag{2}$$

Where A is a general differential operator, B a boundary operator, $f(r)$ is a known analytical function and Γ is the boundary of the domain Ω. The operator A can be divided into two parts L and N, where L is the linear part, and N is the nonlinear component. Equation (1) may therefore be written as:

$$L(U) + N(U) - f(r) = 0, \quad r \in \Omega \tag{3}$$

The Homotopy Perturbation structure is shown as follows;

$$H(V,h) = (1-h)\left[L(V) - L(U_0)\right] + h\left[A(V) - f(r)\right] = 0 \tag{4}$$

Where $V(r,P) : \Omega \in [0,1] \to R$

In equation (3) $P \in [0,1]$ is an embedding parameter and U_0 is the approximation that satisfies the boundary condition. It can be assumed that the solution of the equation (3) can be
Written as power series in h as follows:

$$V = V_0 + hV_1 + h^2 V_2 + \ldots \tag{5}$$

And the best approximation for the solution is:

$$U = \lim_{h \to 1} v = v_0 + hv_1 + h^2 v_2 + \ldots \tag{6}$$

The series (6) is convergent for most cases. However, the convergent rate depends on the nonlinear operator A (V)
The derivation and analysis of the HIV/TB co-infection model used in this work can be found in Bolarin and Omatola (2016). The main objective of this project is to develop a mathematical model for control and elimination of HIV and TB Co-Infection in the presence of HIV and TB treatments.

MATERIALS AND METHODS

HIV/TB Model

$$\frac{ds}{dt} = \Lambda + rR - (\lambda_T + \lambda_H + \mu)S \tag{7}$$

$$\frac{dI}{dt} = \lambda_T S - (\lambda_H + a + d_T + \mu)I \tag{8}$$

$$\frac{dR}{dt}=aI-(\lambda_H+r+\mu)R \quad (9)$$

$$\frac{dP_1}{dt}=(S+R)\lambda_H+(b_1+b_2)P_2-(\lambda_T+e+d_H+\mu)P_1 \quad (10)$$

$$\frac{dP_2}{dt}=\lambda_H I+\lambda_T P_1-(b_1+b_2+d+d_{H1}+\mu)P_2 \quad (11)$$

$$\frac{dA}{dt}=eP_1+dP_2-(d_A+\mu)A \quad (12)$$

Where

$N=S+I+R+P_1+P_2+A$

N total population

S number of susceptible (that is no infection)

I number of persons with active TB

R number of persons recovered from TB

P_1 number of persons with HIV infection

P_2 number of persons with both HIV and TB infection

A number of persons with AIDS

W number of active population

Λ Constant recruitment rate

β_T Probability of transmission of TB infection from an active to a susceptible Per contact per unit time

β_H Probability of transmission of HIV infection from an infected person to an uninfected person per contact per unit time

c per capita contact rate for TB

δ per capita contact rate for HIV

μ Natural death rate

a treatment rate of active TB individuals

b_1 treatment rate of infectious TB in HIV individuals

b_2 HIV treatment rate

d AIDS progression rate for individuals in P_2

e AIDS progression rate for individuals in P_1

r rate at which TB recovered individuals become susceptible to TB

d_T active TB induced death rate

d_{H1} death rate due to both HIV and TB infection

d_H HIV induced death rate

d_A AIDS induced death rate

Solution of the Model Equations

$$\frac{dS}{dt}+(\lambda_T+\lambda_H+\mu)S-rR-\Lambda=0 \tag{13}$$

$$\frac{dI}{dt}+(\lambda_H+a+d_T+\mu)S-\lambda_T S=0 \tag{14}$$

$$\frac{dR}{dt}+(\lambda_H+r+\mu)R-aI=0 \tag{15}$$

$$\frac{dP_1}{dt}+(\lambda_T+e+d_H+\mu)P_1-(S+R)\lambda_H-(b_1+b_2)P_2=0 \tag{16}$$

$$\frac{dP_2}{dt}+(b_1+b_2+d+d_{H1}+\mu)P_2-\lambda_H I-\lambda_T P_1=0 \tag{17}$$

$$\frac{dA}{dt}+(d_A+\mu)A-eP_1-dP_2=0 \tag{18}$$

With the following initial conditions $S(0)=S_0$, $I(0)=I_0$, $R(0)=R_0$, $P_1(0)=P_1o$,

$P_2(0)=P_2o$ And $A(0)=A_0$

Let

$$S=c_0+hc_1+h^2c_2+\ldots \tag{19}$$

$$I=e_0+he_1+h^2e_2+\ldots \tag{20}$$

$$R=w_0+hw_1+h^2w_2+\ldots \tag{21}$$

$$P_1=x_0+hx_1+h^2x_2+\ldots \tag{22}$$

$$P_2=y_0+hy_1+h^2y_2+\ldots \tag{23}$$

$$A=z_0+hz_1+h^2z_2+\ldots \tag{24}$$

Applying HPM to (13)

$$(1-h)\frac{dS}{dt}+h\left[\frac{dS}{dt}+(\lambda_T+\lambda_H+\mu)S-rR-\Lambda\right]=0 \tag{25}$$

Substituting equations (19) and (21) into equation (25)

$$(1-h)\left(c_0'+hc_1'+h^2c_2'+\ldots\right)$$
$$+h\begin{bmatrix}\left(c_0'+hc_1'+h^2c_2'+\ldots\right)+(\lambda_T+\lambda_H+\mu)\left(c_0+hc_1+h^2+\ldots\right)\\ -r\left(w_0+hw_1+h^2w_2+\ldots\right)-\Lambda\end{bmatrix}=0 \tag{26}$$

Expanding and collecting the coefficients of the powers of h, we have

$$h^0 : c_1^{'} = 0 \tag{27}$$

$$h^{'} : c_1^{'} + (\lambda_T + \lambda_H + \mu)c_0 - rw_0 - \Lambda = 0 \tag{28}$$

$$h^2 : c_2^{'} + (\lambda_T + \lambda_H + \mu)c_1 - rw_1 = 0 \tag{29}$$

$$h^3 : (\lambda_T + \lambda_H + \mu)c_2 - rw_2 = 0 \tag{30}$$

Applying (H P M) to (14)

$$(1-h)\frac{dI}{dt} + h\left[\frac{dI}{dt} + (\lambda_H + a + d_T + \mu)I - \lambda_T S\right] = 0 \tag{31}$$

Substitute equation (19) and (20) into equation (31)

$$e_0^{'} + he_1^{'} + h^2 e_2^{'} + \ldots + h\begin{bmatrix}(\lambda_H + a + d_T + \mu)(e_0 + he_1 + h^2 e_2 + \ldots) \\ -\lambda_T (c_0 + hc_1 + h^2 c_2 + \ldots)\end{bmatrix} \tag{32}$$

Collecting the coefficient of the powers of h, we have

$$h^0 : e_0^{'} = 0 \tag{33}$$

$$h^1 : e_1^{'} + (\lambda_H + a + d_T + \mu)e_0 - \lambda_T c_0 = 0 \tag{34}$$

$$h^2 : e_2^{'} + (\lambda_H + a + d_T + \mu)e_1 - \lambda_T c_1 = 0 \tag{35}$$

$$h^3 : (\lambda_H + a + d_T + \mu)e_2 - \lambda_T c_2 = 0 \tag{36}$$

Applying H P M to (15)

$$(1-h)\frac{dR}{dt} + h\left[\frac{dR}{dt} + (\lambda_H + r + \mu)R - aI\right] = 0 \tag{37}$$

Substitute equation (20) and (21) into equation (37)

$$(1-h)(w_0^{'} + hw_1^{'} + h^2 w_2^{'} + \ldots) + h\begin{bmatrix}(w_0^{'} + hw_1^{'} + h^2 w_2^{'} + \ldots) + (\lambda_H + r + \mu)(w_0 + hw_1 + h^2 w_2 + \ldots) \\ -a(e_0 + he_1 + h^2 e_2 + \ldots)\end{bmatrix} = 0 \tag{38}$$

Expanding and collecting the coefficients of the power of h, we have

$$h^0 : w_0^{'} = 0 \tag{39}$$

$$h^1 : w'_1 + (\lambda_H + r + \mu)w_0 - ae_0 = 0 \tag{40}$$

$$h^2 : w'_2 + (\lambda_H + r + \mu)w_1 - ae_1 = 0 \tag{41}$$

$$h^3 : (\lambda_H + r + \mu)w_2 - ae_2 = 0 \tag{42}$$

Applying HPM to (16)

$$\frac{dP_1}{dt} + (\lambda_T + e + d_H + \mu)P_1 - (S+R)\lambda_H - (b_1 + b_2)P_2 = 0 \tag{43}$$

Substitute equation (19), (21), (22) and (23) into equation (43)

$$\begin{aligned}&(1-h)\left(x'_0 + hx'_1 + h^2 x'_2 + \ldots\right)\\ &h\begin{bmatrix}\left(x'_0 + hx'_1 + h^2 x'_2 + \ldots\right)\\ +(\lambda_T + e + d_H + \mu)\left(x_0 + hx_1 + h^2 x_2 + \ldots\right)\\ -\left(c_0 + hc_1 + h^2 c_2 + \ldots + w_0 + hw_1 + h^2 w_2\right)\lambda_H - b_1\left(y_0 + hy_1 + h^2 y_2 + \ldots\right)\end{bmatrix} = 0\end{aligned} \tag{44}$$

Collecting the coefficients of the powers of h

$$h^0 : x'_0 = 0 \tag{45}$$

$$h^1 : x'_1 + (\lambda_T + e + d_H + \mu)x_0 - (c_0 + w_0)\lambda_H - by_0 \tag{46}$$

$$h^2 : x'_2 + (\lambda_T + e + d_H + \mu)x_1 - (c_1 + w_1)\lambda_H - by_1 \tag{47}$$

$$h^3 : (\lambda_T + e + d_H + \mu)x_2 - (c_2 + w_2)\lambda_H - by_2 \tag{48}$$

Applying HPM to (17)

$$(1-h)\frac{dP_2}{dt} + h\left[\frac{dP_2}{dt} + (b_1 + b_2 + d + dH_1 + \mu)P_2 - \lambda_H I - \lambda_T P_1\right] = 0 \tag{49}$$

Substitute equations (20), (22) and (23) into equation (49)

$$\begin{aligned}&(1-h)\left(y'_0 + hy'_1 + h^2 y'_2 + \ldots\right)\\ &+h\begin{bmatrix}\left(y'_0 + hy'_1 + h^2 y'_2 + \ldots\right) + (b_1 + b_2 + d + d_H + \mu)\left(y_0 + hy_1 + h^2 y_2 + \ldots\right)\\ -\left(e_0 + he_1 + h^2 e_2 + \ldots\right)\lambda_H - \lambda_T\left(j_0 + hj_1 + h^2 j_2 +\right)\end{bmatrix} = 0\end{aligned} \tag{50}$$

Collecting the coefficient of the powers of h

$$h^0 : y'_0 = 0 \tag{51}$$

$$h' : y'_1 + (b_1 + b_2 + d + d_{H1} + \mu)y_0 - e_0\lambda_H - x_0\lambda_T \tag{52}$$

(53)

$$h^2 : y'_2 + \left(b_1 + b_2 + d + d_{H1} + \mu\right) y_1 - e_1\lambda_H - x\lambda_T$$

$$h^3 : \left(b_1 + b_2 + d + d_{H1} + \mu\right) y_2 - e_2\lambda_H - x_2\lambda_T$$

(54)

Applying HPM to (18)

$$(1-h)\frac{dA}{dt} + h\left[\frac{dA}{dt} + \left(d_A + \mu\right)A - eP_1 - dP_2\right] = 0 \tag{55}$$

Substitute equation (22), (23) and (24) into equation (55)

$$\begin{aligned}&(1-h)\left(z'_0 + hz'_1 + h^2 z^1_2 + \ldots\right)\\ &+h\begin{bmatrix}\left(z_0 + hz'_1 + h^2 z^1_2 + \ldots\right)\\ +\left(d_A + \mu\right)\left(z_0 + hz_1 + h^2 z_2 + \ldots\right)\\ -e\left(x_0 + hx_1 + h^2 x_2 + \ldots\right)\\ -d\left(y_0 + hy_1 + h^2 y_2 + \ldots\right)\end{bmatrix} = 0\end{aligned} \tag{56}$$

Collecting the coefficients of the powers of h,
We have

$$h^0 : z'_0 = 0 \tag{57}$$

$$h^1 : z'_1 + \left(d_A + \mu\right) z_0 - ex_0 - dy_0 = 0 \tag{58}$$

$$h^2 : z'_2 + \left(d_A + \mu\right) z_1 - ex_1 - dy_1 = 0 \tag{59}$$

$$h^3 : \left(d_A + \mu\right) z_2 - ex_2 - dy_2 = 0 \tag{60}$$

Solving equations (27), (28), (29) and (30) we have:

$$\begin{aligned}&S(t) = S_0 + (rR_0 + \Lambda - \left(\lambda_T + \lambda_H + \mu\right)S_0)t\\ &+\begin{bmatrix}r(aI_0 - \left(\lambda_H + r + \mu\right)R_0\\ -\left(\lambda_T + \lambda_H + \mu\right)(rR_0 + \Lambda - \left(\lambda_T + \lambda_H + \mu\right)S_0\end{bmatrix}\frac{t^2}{2}\end{aligned} \tag{61}$$

Solving equations (33), (34), (35) and (36) we have:

$$\begin{aligned}&I(t) = I_0 + \left(\lambda_T S_0 - \left(\lambda_H + a + d_T + \mu\right)I_0\right)t\\ &+\begin{bmatrix}\lambda_T\left(rR_0 + \Lambda - \left(\lambda_H + \lambda_T \mu\right)S_0\right) -\\ \left(\lambda_H + a + d_T + \mu\right)\left(\lambda_T S_0 - \left(\lambda_H + a + d_T + \mu\right)I_0\right)\end{bmatrix}\frac{t^2}{2}\end{aligned} \tag{62}$$

Solving equations (39), (40), (41) and (42) we have:

$$R(t) = R_0 + (aI_0 - (\lambda_H + r + \mu)R_0)t + [a(\lambda_T S_0 - (\lambda_H + a + d_T + \mu)I_0) \\ -(\lambda_H + r + \mu)(aI_0 - (\lambda_H + r + \mu)R_0)]\frac{t^2}{t} \tag{63}$$

Solving equations (45), (46), (47) and (48) we have:

$$P_1(t) = P_1o + ((S_0 + R_0)\lambda_H + (b_1 + b_2)P_2o - (\lambda_T + e + d_H + \mu)P_1o)t + \\ \begin{bmatrix} (rR_0 + \Lambda - (\lambda_T + \lambda_H + \mu)S_0 + (aI_0 - (\lambda_H + r + \mu)R_0)\lambda_H \\ +(b_1 + b_2)(I_0\lambda_H + P_1o\lambda_T - (b_1 + b_2 + d + d_{H1} + \mu)P_2o) \\ -(\lambda_T + e + d_H + \mu)((S_0 + R_0)\lambda_H + \\ (b_1 + b_2)P_2o - (\lambda_T + e + d_H + \mu)P_1o) \end{bmatrix}\frac{t^2}{2} \tag{64}$$

Solving equations (51), (52), (53) and (54) we have:

$$P_2(t) = P_2o + (I_0\lambda_H + P_1o\lambda_T - (b_1 + b_2 + d + d_{H1} + \mu)P_2o)t \\ +[(\lambda_T S_0 - (\lambda_H + a + d_T + \mu)I_0)\lambda_H + \lambda_H((S_0 + R_0)\lambda_H \\ +(b_1 + b_2)P_2o] - (\lambda_T + e + d_H + \mu)P_1o - (b_1 + b_2 + d + d_{H1} + \mu) \\ (I_0\lambda_H + P_1o\lambda_T - (b_1 + b_2 + d + d_{H1} + \mu)P_2o)]\frac{t^2}{2} \tag{65}$$

Solving equations (57), (58), (59) and (60) we have:

$$A(t) = A_0 + (eP_1o + dP_2o - (d_A + \mu)A_0)t + \\ [e((S_0 + R_0)\lambda_H + bP_2o - (\lambda_T + e + d_H + \mu)P_1o) + \\ d(I_0\lambda_T + P_1o\lambda_T - (b + d + d_{H1} + \mu)P_2o) \\ -(d_A + \mu)(eP_1o + dP_2o - (d_A + \mu)A_0)]\frac{t^2}{2} \tag{66}$$

RESULTS AND DISCUSSION

In this section, we use maple software to plot the graph of semi-analytic solution of our model equations. Since, most of the parameters were not readily available; therefore we assumed them and obtain the rest from the papers we reviewed just for the purpose of illustration. The Table below shows the set of parameter values and the state variables which were used. The total number of the population of sample considered is 30000. In order to support the analytical results, graphical representations showing the time graphs of different state variables are provided.

Parameters and State Variables	**Value**	**Source**
a	0.30	Assumed
b_1	0.30	Assumed
c	1	(Nthiiri, 2015).
d	0.20	Assumed
e	0.20	Assumed
N	30000	Silver and Delfim (2015).
d_A	1.00	Shah and Jyota, (2013).
d_H	0.3	(Nthiiri, 2015).
d_{H1}	0.24	Assumed
d_T	0.24	Shah and Jyota (2013).
λ_T	0.65	Calculated
λ_H	0.03	Calculated
μ	0.02	Shah and Jyota (2013).
Λ	430	Silver and Delfim (2015).
S_0	16500	Assumed
I_0	9250	Assumed
R_0	3000	Assumed
P_1o	500	Assumed
P_2o	500	Assumed
A_0	250	Assumed
δ	0.03	Shah and Jyota (2013).

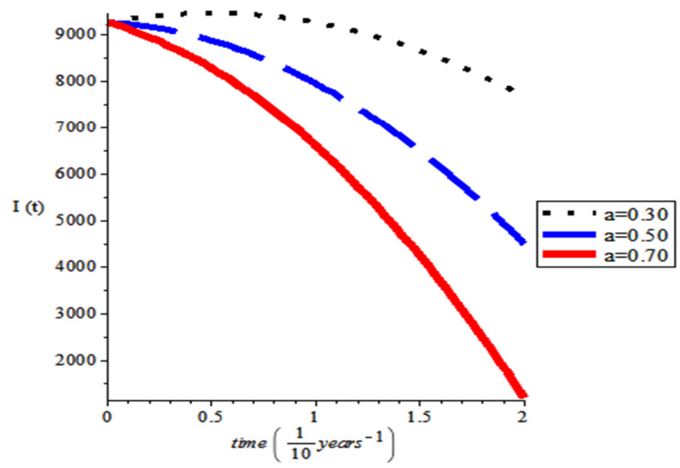

Fig 1: TB infected individuals against time

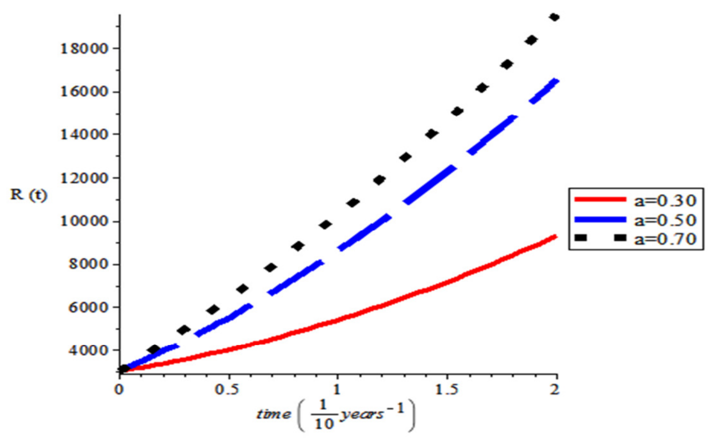

Fig 2: TB Recovered individuals against time (Low, Moderate and High treatments rate)

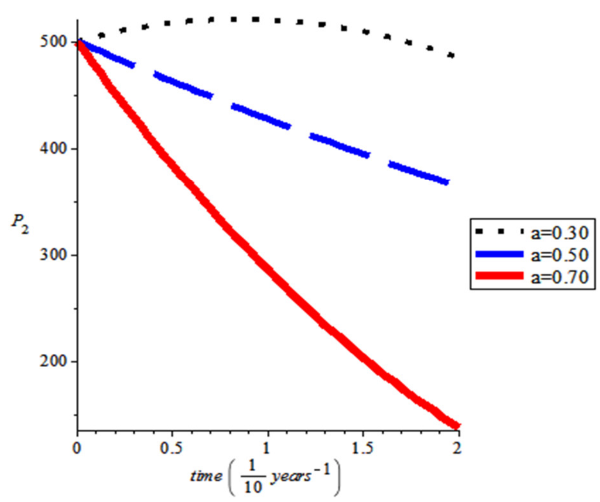

Fig 3: Low, Moderate and High treatments rate on the TB in HIV and TB co-infected individuals against time.

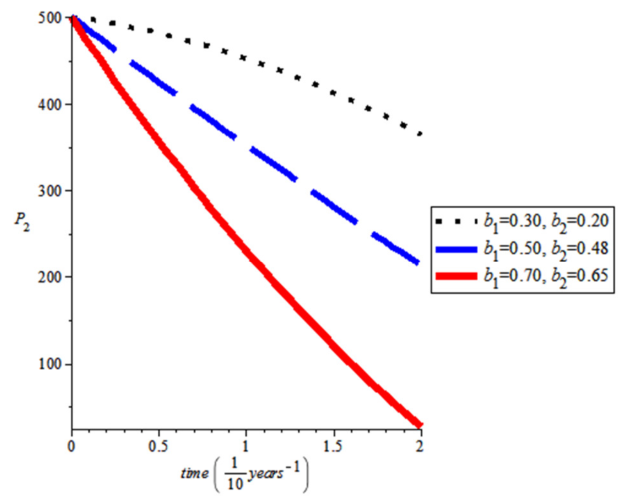

Fig 4: Co-infected individuals against time (Low, Moderate and High treatments rate)

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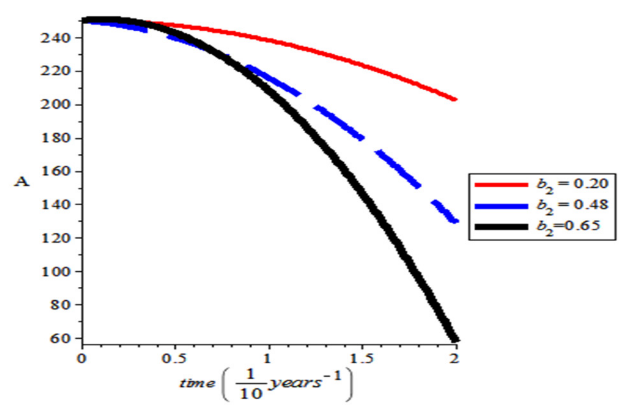

Fig 5: AIDS Infected Individuals against time for different treatment rates for HIV (Low, Moderate and High treatment rates)

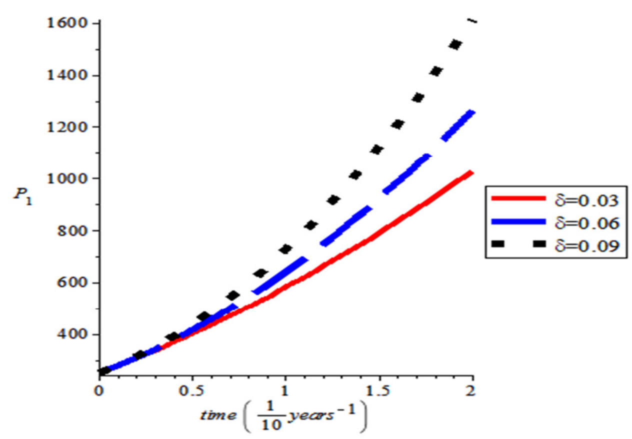

Fig 6: HIV Infected Individuals against time with different contact rates

Figure 1 is the graph of Infected TB individuals I (t) against time for different values of a. It is observed that the number of infected TB individuals decrease as the TB treatment parameter increases. This means, the TB can be eradicated completely in the population at time (t) =20years when the treatment is high i.e a=0.70.

Figure 2 displays the graph of Recovered TB individuals R (t) against time for different values of a. It is seen that the number of TB recovered individuals increase as the TB treatment parameter a increases.

Figure 3 is the graph of TB treatment in HIV/TB co-infected individuals (P_2) against time for different values of b_1. It is observed that the number of co-infected HIV/TB individuals decrease as the TB treatment parameter b_1 increases and brought down the number of HIV/TB co infected individuals to zero at high TB treatment rate. This means, the TB can be eradicated completely in the population at time (t) =20 years.

Figure 4 is the graph of co-treatment of HIV/TB co-infected individuals against time for different values of b_1 and b_2. It is observed that the number of co-infected HIV/TB individuals decrease as the TB and HIV treatment parameters b_1 and b_2 increases and brought down the number of HIV/TB infected individuals to zero at high HIV and TB treatment rates. This means the HIV/TB co-infection can be eradicated completely in the population.

Figure 5 is the graph of AIDS Infected individuals (A) against time for different values of b_2. It is seen that the number of AIDS infected individuals decrease as the HIV treatment parameter e increases and brought down the number of individuals infected with AIDS to zero when the HIV treatment rate is high.

Figure 6 shows the graph of HIV infected individuals P_1 against time for different contact rates. It is seen that the number of HIV infected individuals' increases as the HIV contact parameter δ increases.

Conclusion: The model has shown importance of TB and HIV treatments in preventing HIV and TB co-infection. It was realized that at high HIV and TB treatment rates; TB, AIDS and HIV/TB co-infection will be eradicated completely in the population. The model strongly indicated that the spread of a disease largely depend on the contact rates with infected individuals within a population. Therefore, early detection of HIV and TB cases and provision of early treatments can reduce the rate of infection, reduce the rate of progression of HIV infected individuals to AIDS and lowers co-infection.

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