HIV Vertical Transmission DTSM Simulation Models - An Indian Based Study

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ABSTRACT:-The disease dynamics and progression of HIV-MTCT over a period of time and disease transmission and susceptible simulation model (DTSM-MODEL) were computed by different reproduction numbers for each time interval with set of fixed values of the parameters. As per the model, study found that placental absorption ,prolonged breast feeding and absence of ARV at the onset of birth or delivery, after six hours of birth ,prolonged breast feeding influenced factors for increase of MTCT of HIV infection (Karnataka).DTSM model achieved local asymptotically stabilization , globally disease Free endemic equilibrium ($R_0 > 1 \, \& R_0 < 1$) and consistently maintained endemic equilibrium E^*,

Key words:- MTCT, HIV, DTSM, AIDS, HAART, DBS, CD4, ARV

INTRODUCTION:

HIV continues to have a significant impact especially on children. In 2008, an estimated 2.1 million children were living with HIV worldwide; there were 4300,000 new HIV infections in children and 280, 000 HIV-related deaths among children[13]. According to these estimates, children constitute about 6% of all people living with HIV, 16% of new infections, and 14% of all AIDS-related mortality.1 The majority of children living with HIV are in Sub-Saharan Africa.13 HIV is also resulting in the stalling or reversal of gains in child survival in some countries in this region. In India approximately 80,000 are infected and 70% of the infected children are on HAART from 2004. It is a great burden in the present scenario. The programmatic interventions are needed for control of non curable diseases .The exact transmission rate is not known for implementation of new programmes at national level .In this situations Mathematical and statistical modeling can also play an important role in predicting the incidence, prevalence and effects of the programme on a variety of indicators and outcomes. The Main aim or purpose of this study is fitting mathematical simulation models and to develop understanding of the interplay between the variables that determine the course of the infection from mother to child.

EQUATIONS:

DISEASE TRANSMISSION AND SUSCEPTIBLE MODEL (DTSM-MODEL)

The year wise cohort retrospective data were collected from Government hospitals of Karnataka State, all patients met their inclusion criteria , demographic profile, laboratory parameters like CD4 count at base line ,WHO clinical staging, Serial CD4 count such as CD4 count at 6 months, 12 months ,36 months etc., were recorded.

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History of mothers , HAART details ,regimen , ARV – prophylaxis at the time of onset of birth or after six hours ,DBS –testing at 6 weeks and follow up record , course of breast feeding , duration of feeding , method of feeding were taken in to consideration. The collected data were analyzed by using Matlab-9.0 version. DTSM model was effectively demonstrated with different parameter values and significant inference of the model was drawn.

Model Variables Description: *N-* Total population, *S-* Susceptible class, *I-* Infectives class, *P-* Pre-AIDS class, *T-* Treated class, *A-* AIDS class.

Definitions of Symbols used frequently:

π − Rate of recruitment into susceptible population.

C -- **Average number of sexual partners per unit time**
β -- **Sexual contact rate**

δ − Rate of movement from infectious class

ε −Fraction of newborns infected with HIV who dies immediately after birth

θ − Rate of newborns infected with HIV

μ − Natural mortality rate

α − Induced death rate due to AIDS

$\sigma 1$ − Fraction of δ joining the pre − AIDS class

γ −Rate of movements of pre-AIDS class individuals into AIDS Class

$\sigma 2$ − Fraction of δ joining treated class

v − Rate at which AIDS group get treatment

m − Fraction of γ who get treatment

k − Rate at which treated group becomes full blown AIDS

FORMULATION OF MODELS:

Consider a population of size $N(t)$ at time t with constant inflow of susceptible with rate πN. The population size $N(t)$ is divided into five subclasses which are susceptible $S(t)$ infective $I(t)$ (also assumed to be infectious), pre-AIDS Patients $P(t)$ treated class $T(t)$ and AIDS patients $A(t)$ with natural mortality rate μ in all classes. $\propto$ is the

disease induced death rate in the AIDS patients and v the rate at which AIDS patients get treatment. In the model, it is assumed that the susceptible become HIV infected via sexual contacts with HIV-infected, which may also lead to the birth of infected children. It is assumed that a fraction of new born children are infected during birth and hence are directly recruited into the infective class with a rate $(1 - \varepsilon)\theta$ and others die effectively at birth $(0 \leq \varepsilon \leq 1)$. We do not consider direct recruitment of the infected persons but by vertical transmission only. It is assumed that some of the infectives join pre-AIDS class, depending on the viral counts, with a rate $\sigma 1 \delta$ and then proceed with a rate γ to develop full blown AIDS, it is also assumed that some of the infectives move to join treated class with a rate $\sigma 2 \delta$ and then proceed with a rate k to develop full blown AIDS while others with serious infection directly join the AIDS class with a rate $(1 - \sigma 1 - \sigma 2)\delta$. The interaction between susceptible and infectives is assumed to be of standard mass action type.

Now the system of equation was follows, we have obtained

$$\frac{di}{dt} = C_1\beta_1 is + C_3\beta_3 hs + (1 - \varepsilon)\theta i - [\pi + \delta - \alpha a + (1 - \varepsilon)\theta i]i$$

$$\frac{dp}{dt} = \sigma 1 \delta i - [\pi + \gamma - \alpha a + (1 - \varepsilon)\theta i]p \qquad (3.3)$$

$$\frac{dh}{dt} = \sigma 2 \delta i + m\gamma p + va - (\pi + k - \alpha a + (1 - \varepsilon)\theta i)h$$

$$\frac{da}{dt} = (1 - \sigma 1 - \sigma 2)\delta i + (1 - m)\gamma p + kh - [\pi + \gamma + \alpha - \alpha a + (1 - \varepsilon)\theta i]a,$$

Such that,

$$s + i + p + h + a += 1$$

POSITIVITY OF SOLUTIONS
For the model (3.3) to be epidemiological meaningful and well posed, we need to prove that all state variables are non-negative $\forall \geq 0.$

Theorem (1.0): Let

$\Omega = \{(s, i, p, h, a)\} \in \mathbb{R}+: s + i + p + h + a = 1\}$, then the solution $\{s(t), i(t), p(t), h(t), a(t)\}$ of the system 3.1.3 are the $\forall \geq 0.$

To P.V.T the theoram, we have to use the differential equation of the system (3.3) using the 1st equation, we have

$$\frac{ds}{dt} \leq \pi - \pi S$$

$$\frac{ds}{dt} + \pi s \leq \pi$$

We was find out the integrating factor

$$IF = e^{\pi} \int dt = e^{\pi t}.$$

$$\frac{d}{dt} = (s \, e^{\pi t}) \leq \pi e^{\pi t}$$

Intigrating both the side,

$$S(t) \leq 1 + Ce^{-\pi t}$$

Applaying initial condition ; when $t = 0, s(t)s(0), s(0) \leq 1 + C.$

$$s(t) \leq 1 + (s(o) - 1)e^{-\pi t}$$

When $t \to \infty, s(t) \leq 1$

There fore

$$0 \leq s(t) \leq 1$$

Similarly we had using the second of the system equation 3.30 we had get

$$\frac{di}{dt} \geq -(\delta + \pi)$$

$$IF = e \int (\delta + \pi) dt = e^{(-\delta + \pi)t}$$

$$\frac{d}{dt}\left(ie^{\delta + \pi t}\right) \geq 0$$

Integarating both sides $t = 0, i(t) = i(o), i(0) \geq 0$

$$i(t) \geq i(0)e^{(\delta + \pi)t}$$

$$t \to \infty, i(t) \geq 0$$

There fore,

$$i(t) \geq 0$$

Also in the third equation of the system (3.3)

$$\frac{dp}{dt} \geq -(\pi + \gamma p) \qquad (3.6)$$

$$\frac{dp}{p} \geq -(\pi + \gamma p)dt$$

Integrating both sides ,we get

$$p(t) \geq p(0)e^{-(\pi+\gamma)t}$$

Applaying initail conditions at $t = 0, p(t) \geq p(0)$.

When $t \to \infty, p(t) \geq 0$

Similarly ,using euation of the system (3.3) we have

$$\frac{dh}{dt} \geq -(\pi + k)h$$

$$\frac{dh}{h} \geq -(\pi + k)dt$$

Integarting both side we get

$$h(t) \geq h(o)e^{-(\pi+k)t}$$

Applaying initail conditions at $t = 0, h(t) \geq h(0)$

When, $t \to \infty, h(t) \geq 0$

Finally ,using equation of the system(3.3) we have

$$\frac{da}{dt} \geq (\pi + v + \alpha)a$$

$$\frac{da}{a} \geq -(\pi + v + \alpha)dt$$

Integarting both sides ,we get

$$a(t) \geq a(0)e^{-(\pi+\gamma+\alpha)t}$$

Applaying initail condition :at $t = 0, a(t) \geq a(0)$

When $t \to \infty, a(t) \geq 0$

3.3) Stability Analysis of the model. In this section ,we present the result of stability analysis of the equalibrium points

3.4) Equalibrium points of the model. The model (3.3) has two non negative equlibrium points which are ;the diseases free equalibrium point E_0,and endemic equalibrium E^*
At equalibrium points

$$\frac{ds}{dt} = \frac{di}{dt} = \frac{dp}{dt} = \frac{dh}{dt} = \frac{da}{dt} = 0.$$

Hence the following system of equation is solved for equalibrium points

$$0 = \pi - C_1\beta_1 is - C_3\beta_3 hs - (\pi - \alpha a + (1-\varepsilon)\theta i)s$$

$$0 = C_1\beta_1 is + C_3\beta_3 hs + (1-\varepsilon)\theta i - [\pi + \delta - \alpha a + (1-\varepsilon)\theta i]i$$

$$0 = \sigma 1\delta i - [\pi + \gamma - \alpha a + (1-\varepsilon)\theta i]p$$

$$0 = \sigma_2\delta i + m\gamma p + va - (\pi + k - \alpha a + (1-\varepsilon)\theta i)h$$

$$o = (1 - \sigma_1 - \sigma_2)\delta i + (1-m)\gamma p + kh - [\pi + v + \alpha - \alpha a + (1-\varepsilon)\theta i]a$$

For the diseases free equalibrium $i = p = h = a = 0$ when substituted above ,the system of the equation reduced to $\pi - s\pi = 0, hence\ s = 1$ There fore ,the disease free equalibrium E_0 is $(1,0,0,0,0)$. The linear stability of E_0 can be established by its basic reproduction number. It is determined by using next generation method on the equation (3.3) in the form of matrices F and V. Let F_i be the rate of appearance of new infection in compartment be the transfer of individuals out of compartment by another means X_0 be the disease free equilibrium

MODEL FORWARD BIFURCATION:
We analyzed the local asymptotic stability of endemic equilibrium by using the theorem of Centre manifold (Gumel *et al.,* 2008). The linearizion matrix has at least one eigen value with zero real part. Also we have described the possibility of forward bifurcation from the non hyperbolic equilibrium. To describe it, consider a general system of ODEs with F . This theory is convenient by changing variables.

Consider $s = x_1, i = x_2\ p = x_2, h = x_4, \alpha = x_5$. By using vector notation $X = (x_1, x_2, x_3, x_4, x_5)^T$ in the model (3.3) can be written in the form

$$\frac{dX}{dt} = F(x), \quad \text{Where}$$

by $F = (x_1, x_2, x_3, x_4, x_5)^T\ as\ follows$.

$$\frac{dx_1}{dt} = f_1 = \pi - c_1\beta_1 x_2 x_1 - c_3\beta_3 x_4 x_1 - [\pi - \alpha x_5 + (1-\varepsilon)\theta x_2]x_1$$

$$\frac{dx_2}{dt} = f_2 = \pi - c_1\beta_1 x_2 x_1 + c_3\beta_3 x_4 x_1 + x_1(1-\varepsilon)\theta x_2 - [\pi + \delta - \alpha x_5 + (1-\varepsilon)\theta x_2]x_2$$

$$\frac{dx_3}{dt} = f_3 = \sigma_1\delta\sigma_2[\pi + \delta - \alpha x_5 + (1-\varepsilon)\theta x_2]x_3 \quad \textbf{(3.1.5)}$$

$$\frac{dx_4}{dt} = f_4 = \sigma_1\delta\sigma_2 + m\gamma x_3 + vx_5[\pi + k - \alpha x_5 + (1-\varepsilon)\theta x_2]x_4$$

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$$\frac{dx_5}{dt} = f_5 = (1 - \sigma_1 - \sigma_2)\delta x_2 + (1 - m)\gamma x_3 + k x_4 - [\pi + v + \alpha - \alpha x_5 + (1 - \varepsilon)\theta x_2] x_5$$

Where,

$$R_0 = \frac{c_1 \beta_1}{\pi + \delta - \theta + \theta\varepsilon} + \frac{c_3 \beta_3 (\sigma_2 \pi^2 + \sigma_2 \pi\alpha + \pi_2 \gamma\alpha + \sigma_1 m\gamma\pi + \sigma_1 m\gamma\alpha + v\pi + v\gamma + \sigma_1 v\pi)\delta}{(\pi + \delta - \theta + \theta\varepsilon)(\pi + \gamma)(\alpha\pi + \pi k + \pi^2 + \alpha k + v\pi)}$$

Suppose $\beta_1 = \beta^*$ is the chosen bifurcation parameter and if we consider $R_0 = 1$ and solve for

$\beta_1 = \beta^*$ **gives.**

$$\beta^* = \frac{(\pi + \delta - \theta + \sigma\theta)(\pi + \gamma)(\alpha\pi + \pi k + \pi^2 + \alpha k + v\pi - c_3 \beta_3 \delta\emptyset)}{c_1(\pi + \gamma)(\alpha\pi + \pi k + \pi^2 + \alpha k + v\pi)} \rightarrow (3.1.7)$$

Where,

$$\emptyset = (\sigma_2 \pi^2 + \sigma_2 \pi\alpha + \sigma_2 \gamma\pi + \sigma_1 \gamma\alpha + \sigma_1 m\gamma\pi + \sigma_1 m\gamma\alpha + v\pi + v\gamma - \sigma_1 v\pi)$$

The system of the transformed equation with $\beta_1 = \beta^*$ has a simple zero eigen values .Hence the centre manifold theory can be used to analyze the dynamics of

$$\frac{dX}{dt} = F(x) = f(f_1, f_2, f_3, f_4, f_5)T$$ near $\beta_1 = \beta^*$ it can be shown that the Jacobeans' of $\frac{dX}{dt} = F(x) = F = (f_1, f_2, f_3, f_4, f_5)T$ at $\beta_1 = \beta^*$ has right eigen vector associated with the zero eigen values by $w = [w_1, w_2, w_3, w_4, w_5]T$

$$w_1 = \frac{(c_3 \beta_3 vn(-c_1 \beta_1 + (1 - \varepsilon)\theta + \Psi) + \alpha(\eta\varphi\Psi) - c_3 \beta_3 m v \sigma_1 \delta - c_3 \beta_3 \eta\sigma_2 \delta}{c_3 \beta_3 v\eta} w_2$$

$$w_3 = \frac{\sigma_1 \delta}{\eta} w_2$$

$$w_4 = \frac{-(c_1 \beta_1 + (1 - \varepsilon)\theta - \pi - \delta)}{c_3 \beta_3} w_2$$

$$w_5 = \frac{-[\eta\varphi(c_1 \beta_1 + (1 - \varepsilon)\theta - \pi - \delta] + c_3 \beta_3 m\gamma\sigma_1 \delta + c_3 \beta_3 n\sigma_2 \delta}{c_3 \beta_3 v\eta} w_2$$

$$w_2 > 0$$

Where,

$$\eta = (\pi + \gamma)$$

$$\varphi = (\pi + k)$$

$$\varpi = (\pi + v + \alpha)$$

$$\Psi = (c_1 \beta_1 + (1 - \varepsilon)\theta - (\pi + \delta))$$

The right Eigen vector of $J(E_0)$ associated with the zero Eigen values at $\beta_1 = \beta^*$ is given by

$$u = (u_1, u_2, u_3, u_4, u_5)T$$ When $u_1 = 0$

$$u_2 = \frac{-[\sigma_1 \delta(m\gamma\varpi + (1 - m)\gamma v) + \sigma_2 \delta\varpi\eta + (1 - \sigma_1 - \sigma_2)\delta\eta]}{\varpi\eta\Psi} u_4$$

$$u_3 = \frac{[m\gamma\varpi + (1 - m)\gamma v]}{\varpi\eta} u_4$$

$$u_5 = \frac{v}{\varpi} u_4$$

$$u_4 > u_5$$

Theorem 3: (Castillo-Chavez and Song, 2004) Consider the following general System of ordinary differential equations with a parameter $\emptyset$ such that

$$\frac{dx}{dt} = f(x, \emptyset), f: \mathbb{R}^n X\mathbb{R} \rightarrow \mathbb{R}^n \text{ and } f \in C^2 (\mathbb{R}^n X\mathbb{R})$$

Where "O" is an equilibrium point of the system that is $f(0, \emptyset) = 0$ for all $\emptyset$ and

1. $A = D_x f(0, \emptyset) = \left(\frac{\partial f_i}{\partial x_j}(0,0)\right)$ is the linearization matrix of the system around the equilibrium 0 with $\emptyset$ evaluated at 0.

2. Zero is a simple eigen value of A and all other eigen values of A have negative real parts.

3. Matrix A has a right eigenvectors ω and left eigenvector q corresponding to zero eigen values.

Let f_k be the kth component of f and

$$a = \sum_{k,i,j=1}^{n} u_k \omega_i \omega_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) \rightarrow 3.18$$

$$b = \sum_{k,i,j=1}^{n} u_k \omega_j \frac{\partial^2 f_k}{\partial x_j \partial_\beta}(0,0) \rightarrow 3.19$$

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The local dynamics of the system around the equilibrium point is totally determined by the signs of *a* and *b* particularly, if $a > 0 \; and \; b > 0$ then a backward bifurcation occurs at $\emptyset = 0$

1. $a > 0, b > 0$. When $\emptyset < 0$ with $|\emptyset||1,0$ is locally asymptotically stable, and there exist a positive unstable equilibrium; when $0 < \emptyset 1,0$ is unstable and there exists a negative and locally asymptotically stable equilibrium;

2. $a < 0, b < 0$. When $\emptyset < 0$ with $|\emptyset||1,0$ is unstable; when is locally $0 < \emptyset 1,0$ asymptotically stable, and there exists a positive unstable equilibrium

3 $a < 0, b < 0$. When $\emptyset < 0$ with $|\emptyset||1,0$ is unstable and there exists a locally $0 < \emptyset 1,0$ Asymptotically stable negative equilibrium; when stable and positive unstable equilibrium appears.

4. $a < 0, b < 0$. When $\emptyset$ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.

Bifurcation Parameters a and b calculation.
From model (3.15), the associated none zero partial derivatives of *F* at the disease free equilibrium are given by,

$$\frac{\partial^2 f_2}{\partial x^2_2} = \frac{\partial^2 f_2}{\partial x_5 \partial x_5} = \frac{\partial^2 f_3}{\partial x_2 \partial x_3} = \frac{\partial^2 f_3}{\partial x_3 \partial x_5} = \frac{\partial^2 f_4}{\partial x_2 \partial x_4} = \frac{\partial^2 f_4}{\partial x_4 \partial x_5} = \frac{\partial^2 f_5}{\partial x_2 \partial x_5} = \frac{\partial^2 f_5}{\partial x^2_5} = 0$$

$$\frac{\partial^2 f_2}{\partial x^2_2} = -2(1-\varepsilon)\theta, \quad \frac{\partial^2 f_2}{\partial x_5 \partial x_5} = \alpha, \quad \frac{\partial^2 f_3}{\partial x_3 \partial x_5} = -(1-\varepsilon)\theta, \quad \frac{\partial^2 f_3}{\partial x_3 \partial x_5} = \alpha$$

$$\frac{\partial^2 f_4}{\partial x_2 \partial x_4} = -(1-\varepsilon)\theta, \quad \frac{\partial^2 f_4}{\partial x_4 \partial x_5} = \alpha \quad \frac{\partial^2 f_5}{\partial x_2 \partial x_5} = -(1-\varepsilon)\theta \quad \frac{\partial^2 f_5}{\partial x^2_5} = 2\alpha$$

It follows from above expressions that,

$$a = u_2 \sum w_i w_j \frac{\partial^2 f_2}{\partial x_i \partial x_j} + u_3 \sum w_i w_j \frac{\partial^2 f_3}{\partial x_i \partial x_j} + u_4 \sum w_i w_j \frac{\partial^2 f_3}{\partial x_i \partial x_j} + u_5 \sum w_i w_j \frac{\partial^2 f_5}{\partial x_i \partial x_j} \quad (3.2.0)$$

$$u_2[\alpha w_2 w_5 + 2(1-\varepsilon)\theta w^2_2] - u_3[\alpha w_3 w_5 + (1-\varepsilon)\theta w_2 w_3] + u_4$$
$$[\alpha w_4 w_5 + (1-\varepsilon)\theta w_2 w_4] + u_5[2\alpha w^2_5 + (1-\varepsilon)\theta \, w_2 w_5]$$

Therefore a>0, if

$$[\alpha w_3 w_5 + (1-\varepsilon) \, w_2 w_5] < \frac{q_1}{u_3}$$

Where q_1

$$u_2[\alpha w_2 w_5 + 2(1-\varepsilon)\theta w^2_2] - u_3[\alpha w_3 w_5 + (1-\varepsilon)\theta w_2 w_3] + u_4$$
$$[\alpha w_4 w_5 + (1-\varepsilon)\theta w_2 w_4] + u_5[2\alpha w^2_5 + (1-\varepsilon)\theta \, w_2 w_5]$$

Hence a>0,if

$$\frac{\alpha \sigma_1 \delta}{\eta}\left[\frac{\eta\varphi\Psi + c_3\beta_3 m\gamma\sigma_1 \delta + c_3\beta_3 \eta\sigma_2 \; \delta + c_3\beta_3 v\sigma_1 (1-\varepsilon)\theta}{c_3\beta_3 \, v \, \eta\sigma_2}\right] < \frac{\varpi n \Theta}{m\gamma\varpi + (1-m)\gamma v}$$

Where,

$$\Theta = \frac{\alpha\Psi}{c_3\beta_3}\left(\frac{\eta\varphi\Psi + c_3\beta_3 \, m\gamma\sigma_1\delta + c_3\beta_3 \, \eta\sigma_2\delta}{c_3\beta_3 \, v\eta}\right) + \frac{v_2\alpha}{\varpi}\left(\frac{\eta\varphi\psi + c_3\beta_3 \, m\gamma\sigma_1\delta + c_3\beta_3 \, m\gamma\sigma_1\delta}{c_3\beta_3 \, v\eta}\right)2$$

$$+ \frac{(1-\varepsilon)\theta\Psi}{c_3\beta_3} + \left(\frac{\sigma_1\delta(m\gamma\varpi + (1-m)\gamma v) + \sigma_2\delta\varpi\eta + (1-\sigma_1-\sigma_2)\delta_n}{\varpi\eta\Psi}\right) +$$

$$v(1-\varepsilon)\theta\left(\frac{\eta\varphi\Psi + c_3\beta_3 \, m\gamma\sigma_1\delta + c_3\beta_3 \eta\sigma_2 \; \delta}{\varpi c_3\beta_3 \, v\eta}\right) + \alpha\left(\frac{\eta\varphi\Psi + c_3\beta_3 \, m\gamma\sigma_1\delta + c_3\beta_3 \eta\sigma_2\delta}{c_3\beta_3 \, v\eta}\right) +$$

$$2(1-\varepsilon)\theta$$

For the sign of "b" it can be shown that the associated non vanishing partial derivatives of $\frac{\partial^2 f^2_2}{\partial\beta_1\partial x_2} = c_1$, So that

$$b = u_2 \sum w_i \frac{\partial^2 f_2}{\partial\beta_1 \partial x_i} = u_2 w_2 c_1$$

$$-\frac{[\partial_1\delta(m\gamma\varpi + (1-m)\gamma v + \sigma_2\gamma\varpi\eta + (1-\sigma_1-\sigma_2)\delta\eta}{\varpi\eta\Psi}$$

Therefore, *b* < 0, hence, we have established the following result. Since b<0 and a>0 if the inequality satisfies, and then there exists a forward bifurcation.

3.9 Global Stability of the Endemic Equilibrium
Theorem 4: *If the endemic equilibrium E^* exist, then it is globally asymptotically stable provided that* $R_0 > 1$

Consider the following positive definite function about E^*

$$V(s^*, i^*, p^*, h^*, a^*) = s\left(s - s^* - s\log\frac{s^*}{s}\right) + \left(i - i^* - i\log\frac{i^*}{i}\right) + \left(p - p^* - p\log\frac{p^*}{p}\right)$$

$$+ \left(h - h^* - h\log\frac{h^*}{h}\right) + \left(a - a^* - a\log\frac{a^*}{a}\right) - - - (3.2.2)$$

By the direct calculation of the derivation of V along the solution of (3.3) can be written as

$$\frac{dV}{dt} = \left(\frac{s - s^*}{s}\right)\frac{ds}{dt} + \left(\frac{i - i^*}{i}\right)\frac{di}{dt} + \left(\frac{p - p^*}{p}\right)\frac{dp}{dt} + \left(\frac{h - h^*}{h}\right)\frac{dh}{dt} + \left(\frac{a - a^*}{a}\right)\frac{da}{dt}$$

$$\frac{ds}{dt} = \pi - c_1\beta_1\, is - c_3\beta_3\, hs - [\pi - \alpha a + (1-\varepsilon)\theta_i]s$$

$$\frac{di}{dt} = \pi - c_1\beta_1\, is + c_3\beta_3\, hs + (1-\varepsilon)\theta_i - [\pi + \delta - \alpha a + (1-\varepsilon)\theta_i]i$$

$$\frac{dp}{dt} = \sigma_i\,\delta_i - [\pi + \delta - \alpha a + (1-\varepsilon)\theta_i]p$$

$$\frac{dh}{dt} = \sigma_2\,\delta_i + m\gamma p + va - [\pi + k - \alpha a + (1-\varepsilon)\theta_i]h$$

$$\frac{da}{dt} = (1-\sigma_1-\sigma_2)\delta_i + (1-m)\gamma p + kh - [\pi + v + \alpha - \alpha a + (1-\varepsilon)\theta_i]a$$

It can now be written as

$$\frac{dV}{dt} = \left(\frac{s-s^*}{s}\right)\Big[\pi - c_1\beta_1\, is - c_3\beta_3\, hs - [\pi - \alpha a + (1-\varepsilon)\theta_i]s+\Big] + \left(\frac{i-i^*}{i}\right)$$

$$c_1\beta_1\, is + c_3\beta_3\, hs + (1-\varepsilon)\theta_i - [\pi + \delta - \alpha a + (1-\varepsilon)\theta_i]i + \left(\frac{p-p^*}{p}\right)\sigma_i\delta_i - [\pi + \delta - \alpha a + (1-\varepsilon)\theta_i]p$$

$$+\left(\frac{h-h^*}{h}\right)\sigma_2\delta_i + m\gamma p + va - [\pi + k - \alpha a + (1-\varepsilon)\theta_i]h + \left(\frac{a-a^*}{a}\right)(1-\sigma_1-\sigma_2)\delta_i + (1-m)\gamma p$$

$$+ kh - [\pi + v + \alpha - \alpha a + (1-\varepsilon)\theta_i]a$$

Therefore, substitute

$$s = s - s^*, i = i - i^*, p = p - p^*, h = h - h^* \text{ and } a = a - a^*$$

After some algebraic calculation we get,

$$\frac{dV}{dt} = [c_1\beta_1\, i^* + c_3\beta_3\, h^* + \alpha a + \theta i + \varepsilon\theta i]\left(\frac{s-s^*}{s}\right)^2 + [c_1\beta_1\, s + \theta + \alpha a]\left(\frac{i-i^*}{i}\right)^2 + [\alpha a + \theta i^* + \varepsilon\theta i]$$

$$\left(\frac{p-p^*}{p}\right)^2 + [\alpha a + \theta i^* + \varepsilon\theta i] + \left(\frac{h-h^*}{h}\right)^2 + [\theta i^* + \varepsilon\theta i]\left(\frac{a-a^*}{a}\right)^2 + \theta\frac{i^{*3}}{i} + c_3\beta_3\, h^*\frac{i^*}{i} + \sigma1\delta i^*\frac{p^*}{p} + \sigma2\delta i$$

$$\frac{h^*}{h} + m\gamma p^*\frac{h^*}{h} + va\frac{h^*}{h} + \sigma1\delta_i\frac{a^*}{a} + \gamma p^*\frac{a^*}{a} + m\gamma p\frac{a^*}{a} + kh^*\frac{a^*}{a} + 3\theta ii^* + \varepsilon\theta i^2 + 3\varepsilon\theta i^{*2}$$

$$+ \pi + c_3\beta_3\, h + \sigma1\delta i + \sigma2\delta i + m\gamma p + va + \alpha a^2 + 3\alpha a^* + \delta i\sigma1\delta i^* + \sigma2\delta i^* + \gamma p + m\gamma p^* + kh$$

$$[c_1\beta_1\, i + c_3\beta_3\, h + \pi + \alpha a^* + \theta i + \varepsilon\theta i^*]\left(\frac{h-h^*}{h}\right)^2 - [\pi + \gamma + \alpha + \theta i + \varepsilon\theta i^*]\left(\frac{p-p^*}{p}\right)^2 -$$

$$[\pi + k\alpha a^* + \theta i + \varepsilon\theta i^*]\left(\frac{h-h^*}{h}\right)^2 - [\pi + \gamma + \alpha + \theta i + \varepsilon\theta i^*]\left(\frac{a-a^*}{a}\right)^2 - \pi\frac{s^*}{s} - c_3\beta_3\, h\frac{i^*}{i} -$$

$$\sigma1\delta i\frac{p^*}{p} - \sigma2\delta i\frac{h^*}{h} - m\gamma p\frac{h^*}{h} - 3\varepsilon\theta\frac{i^*}{i} - \alpha\frac{a^{*3}}{a} - \delta i\frac{a^*}{a} - \sigma1\delta i^*\frac{a^*}{a} - \sigma2\delta i^*$$

$$\frac{a^*}{a} - \gamma p\frac{a^*}{a} - kh\frac{a^*}{a} - 3\varepsilon\theta ii^* - 3\alpha\alpha a^* - \theta i^* - 3\theta i^* - c_3\beta_3\, h^* - \sigma1\delta i^* - m\gamma p^* - \gamma a - \sigma1\delta i$$

$$- - \sigma2\delta i - \delta i^* - \gamma p^* - m\gamma p - kh$$

Hence the sufficient condition for $\frac{dV}{dt}$ to be negative definite is that $Z - Y < 0$, where

$$Y = -\Big[c_1\beta_1\, i + c_3\beta_3\, h + \pi + \alpha a^* + \theta i + \varepsilon\theta i^*\Big]\left(\frac{s-s^*}{s}\right)^2 - \Big[c_1\beta_1\, s^* + \varepsilon\theta + \pi + \delta + \alpha a\Big]$$

$$\left(\frac{i-i^*}{i}\right)^2 - [\pi + \gamma + \alpha a^* + \theta i + \varepsilon\theta i^*]\left(\frac{p-p^*}{p}\right)^2 - [\pi + k + \alpha a^* + \theta i + \varepsilon\theta i^*]\left(\frac{h-h^*}{h}\right)^2$$

$$-[\pi + v + \alpha + \theta i + \varepsilon\theta i^*]\left(\frac{a-a^*}{a}\right)^2 - \pi\frac{s^*}{s} - c_3\beta_3\, h\frac{i^*}{i} - \sigma1\delta i\frac{p^*}{p} - \sigma2\delta i\frac{h^*}{h} - m\gamma p\frac{h^*}{h} - va\frac{h^*}{h} -$$

$$-3\varepsilon\theta\frac{i^*}{i} - \alpha\frac{a^{*3}}{a} - \delta i\frac{a^*}{a} - \sigma1\delta i^*\frac{a^*}{a} - \sigma2\delta i^*\frac{a^*}{a} - \gamma p\frac{a^*}{a} - m\gamma p^*\frac{a^*}{a} - kh\frac{a^*}{a} - 3\varepsilon\theta ii^* -$$

$$-3\alpha\alpha a^* - \theta i^* - 3\theta i^* - c_3\beta_3\, h^* - \sigma1\delta i^* - \sigma2\delta i^* - m\gamma p^* - va - \sigma1\delta i - \sigma2\delta i - \delta i^* - \gamma p^* - m\gamma p - kh^*$$

Therefore, the largest compact invariant set in $\left\{(s^*, i^*, p^*, h^*, a^*) \in \Omega : \frac{dV}{dt} = 0\right\}$ is the single $\{E^*\}$, where E^* is the endemic equilibrium of the normalized model system (3.3) By LaSalle's invariant principle, it implies that E^* is globally asymptotically stable in Ω if $Z < Y$ this completes the proof of theorem.

Tables and Graphs:
Tab(1): Parameters of the DTSM-Model.

SI	Name of the Parameters	Values	Name of the Parameters	Value
01.	θ	0.30	k	0.08
02.	ε	0.20	γ	0.90
03.	v	0.10	c_1	3.00
04.	β_1	0.40	c_3	1.00
05.	β_3	0.05	m	0.40
06.	σ_1	0.20	π	0.40
07.	σ_2	0.01	δ	0.60
08.			α	1.00

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Parameters of the model were considered based on the proportion of the population infected and incidence rate of MTCT in Bangalore city, Karnataka State.
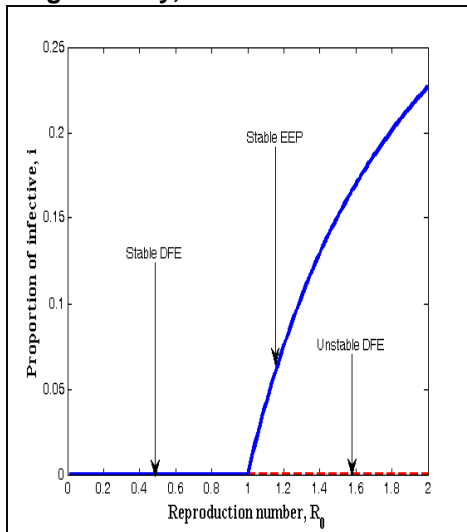

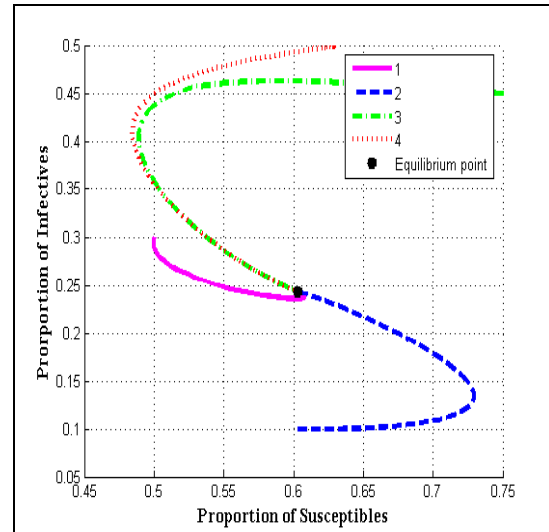Figure 3.2 Forward Bifurcation of the model (3.3).

Figure 4.1(a).EPIS

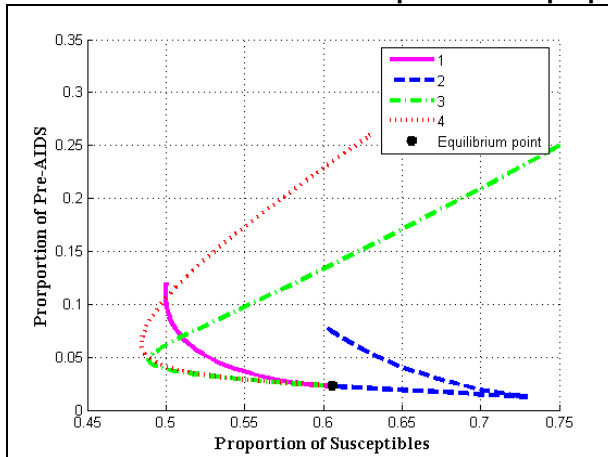**EPIS: Endemic equilibrium of proportion of infectives with Susceptibles.**
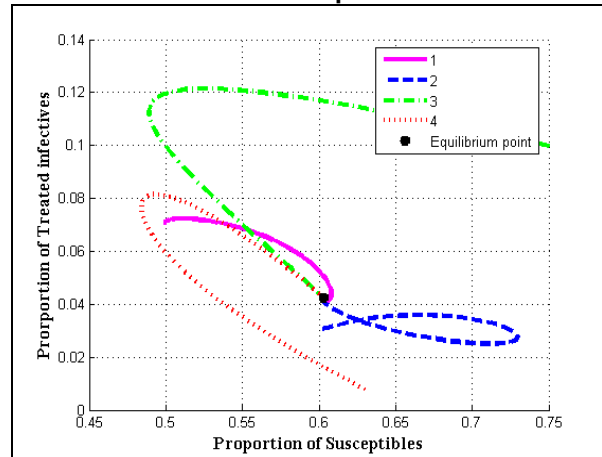

Figure 4.1(b)

Figure 4.1(c)

**Figure 4.1(b). Endemic equilibrium of proportion of Pre-AIDS population
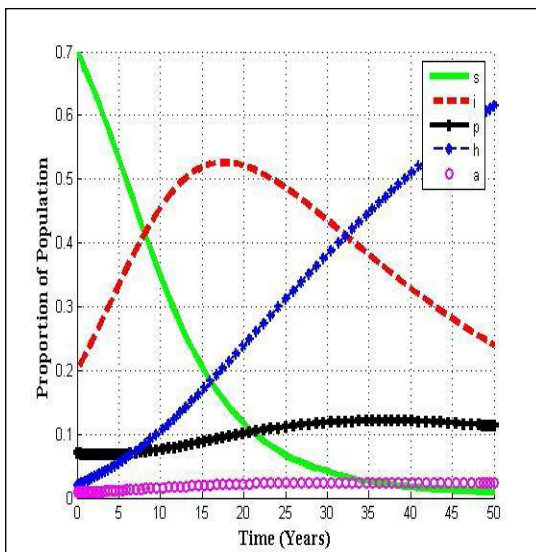Figure 4.1(c). Endemic equilibrium of proportion of treated group.**

Figure 4.2(a)
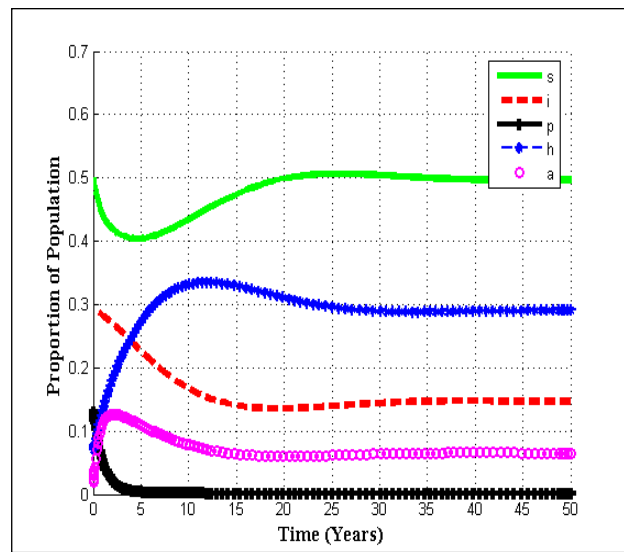
Figure 4.2(b)

Figure 4.2(a) Variation of population in different groups for $\pi = 0$ and $\theta = 0$.

Figure 4.2(b) Variation of population in different groups for $\pi = 0.10$ and $\theta = 0.20$
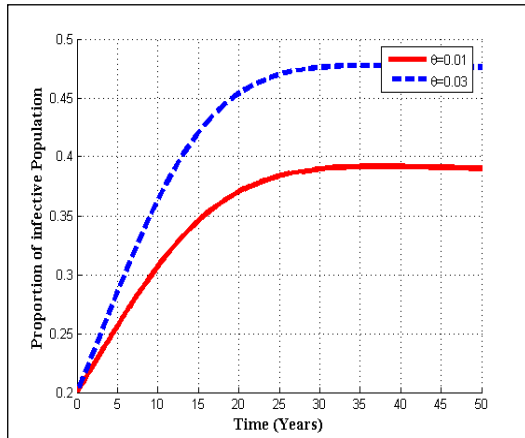
Figure 4.3(a)
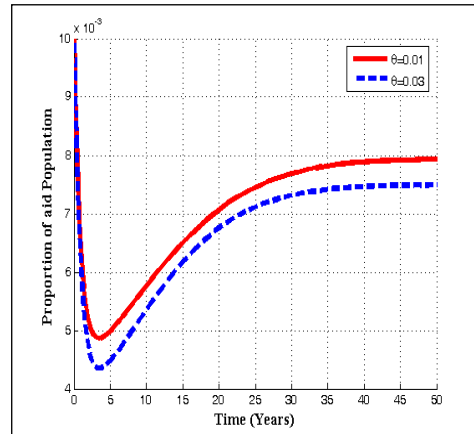
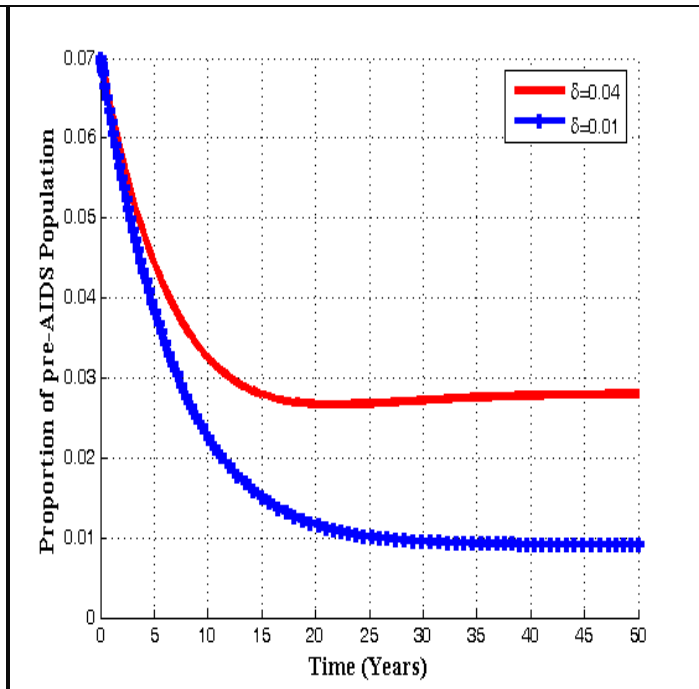Figure 4.3(b)
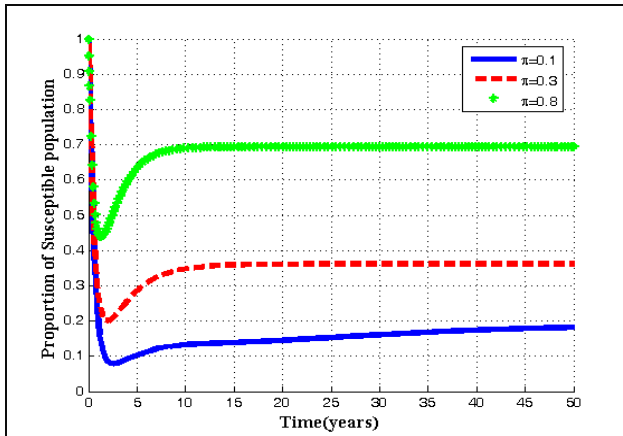
Figure 4.3(c)
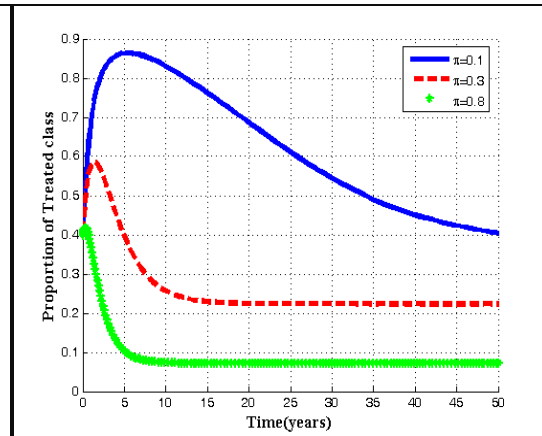
Figure 4.4(a)

Figure 4.3(a) Variation of infected population for different values of θ

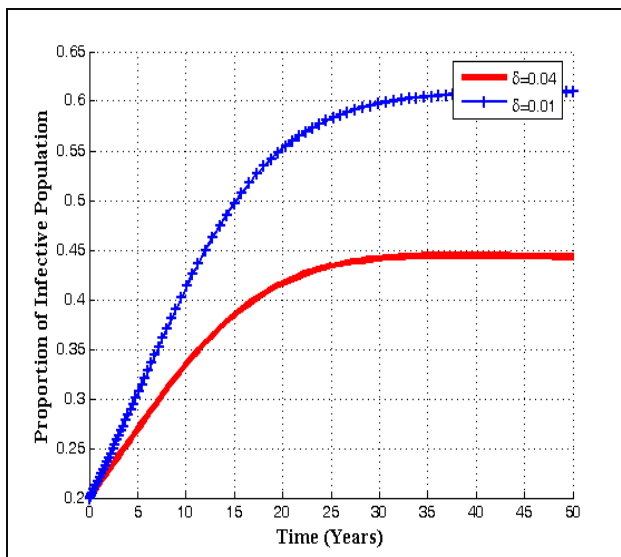**Figure 4.3(b) Variation of AIDS population for different values of θ**

Figure 4.3(c) Variation of Treated group for different values of θ

Figure 4.4(a) Variation of Susceptible group for different values of π.
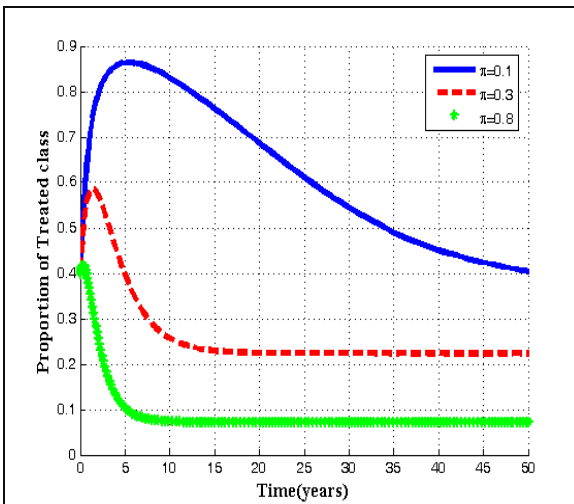
Figure 4.4(b)

Figure 4.4(c)

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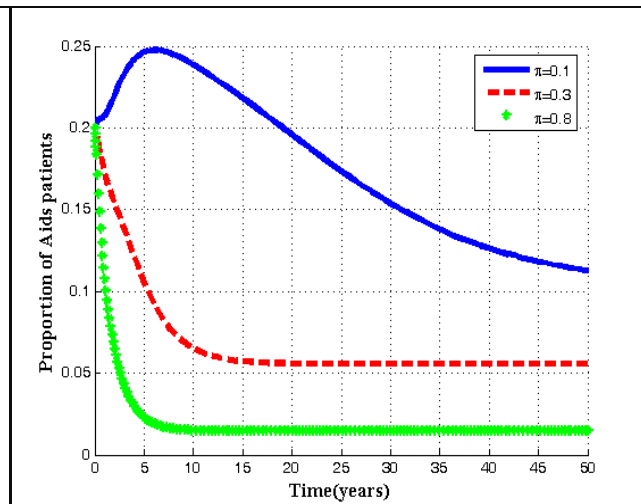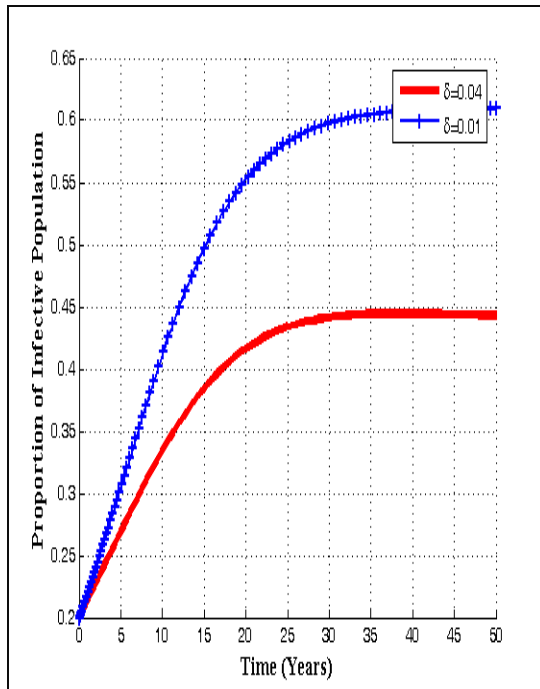
Figure 4.5(a)   Figure 4.5(b)

Figure 4.4(b) Variation of Treated population for different values of π
Figure 4.4(c) Variation of AIDS population for different values of π

Figure 4.5(a) Variation of Infective population for different values of δ

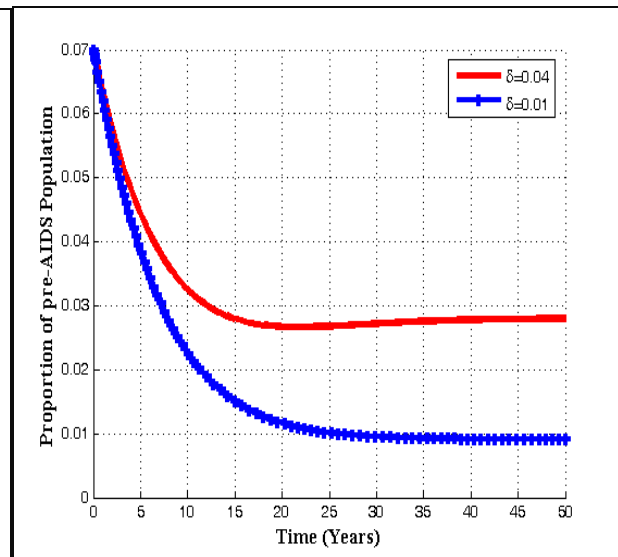**Figure 4.5(b) Variation of pre-AIDS population for different values of δ**

Figure 4.5(a)   Figure 4.5(b)
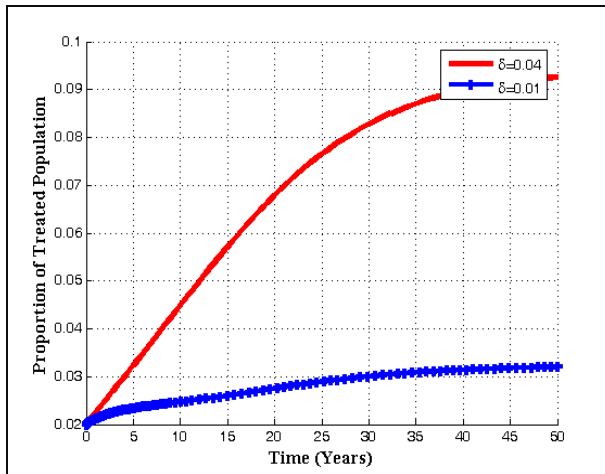
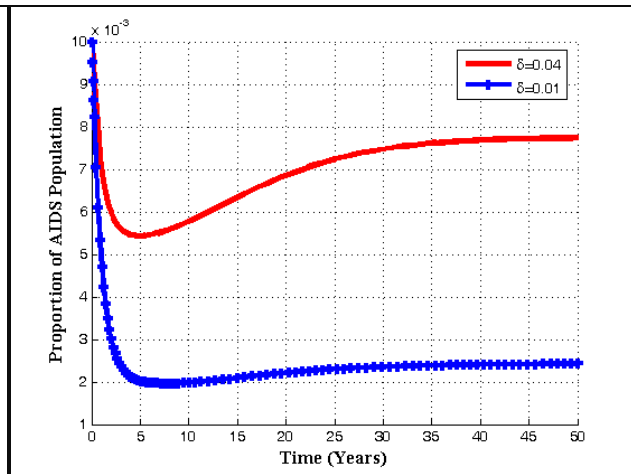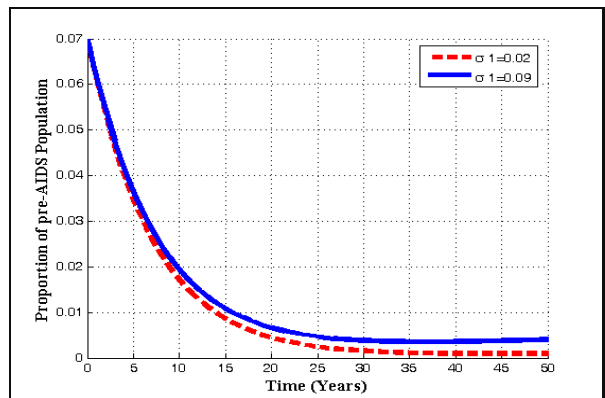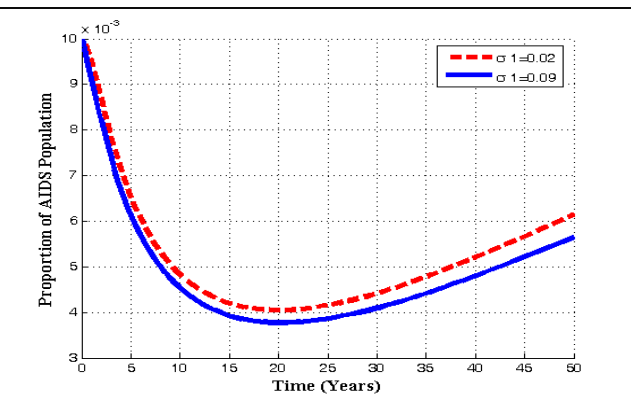Figure 4.5(c)   Figure 4.5(d)

Figure 4.6(a)   Figure 4.6(b)

Figure 4.5(a) Variation of Infective population for different values of δ

Figure 4.5(b) Variation of pre-AIDS population for different values of δ

Figure 4.5(c) Variation of Treated group for different values of δ

Figure 4.5(d) Variation of AIDS population for different values of δ

Figure 4.6(a) Variation of pre-AIDS population for different values of σ_1

Figure 4.6(b) Variation of AIDS population for different values of σ_1

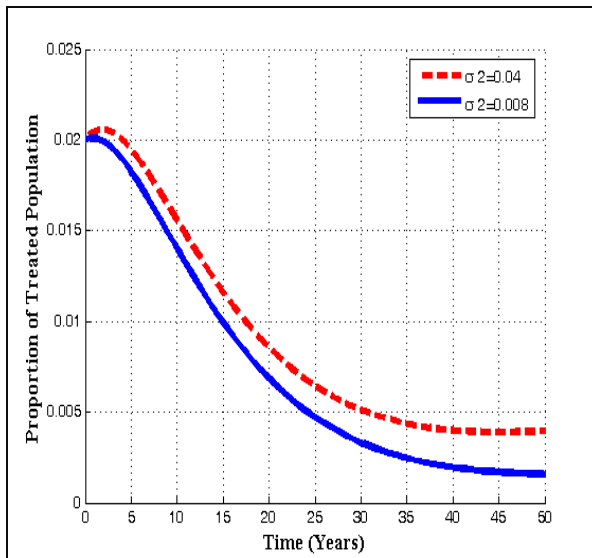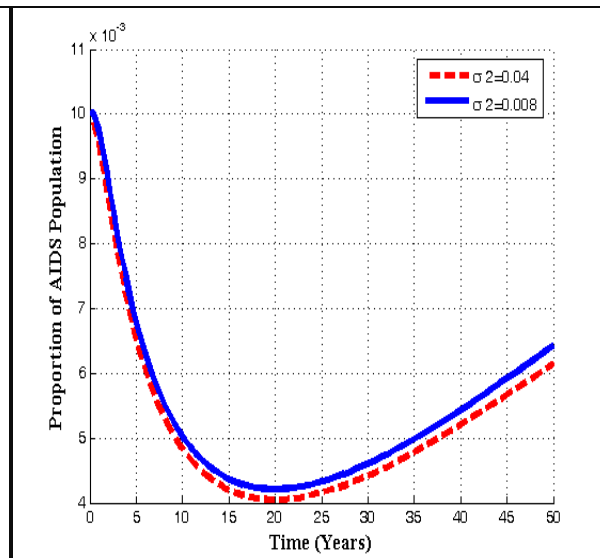
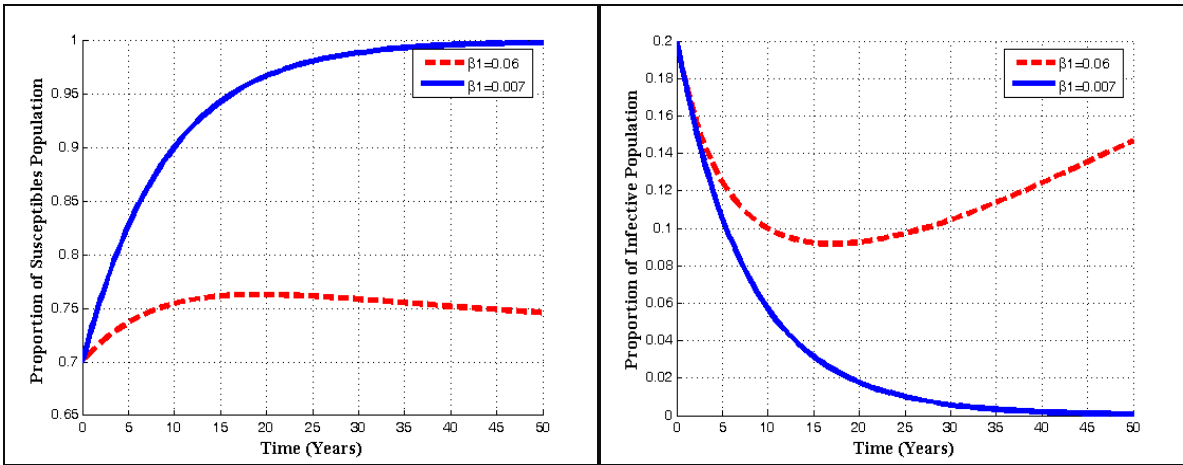Figure 4.6(c)   Figure 4.6(d)

Figure 4.7(a)

Figure 4.7(b)

Figure 4.6(c) Variation of Treated population for different values of σ_2
Figure 4.6(d) Variation of AIDS population for different values of σ_2
Figure 4.7(a) Variation of Susceptible population for different values of β_1
Figure 4.7(b) Variation of Infectives population for different values of β_1
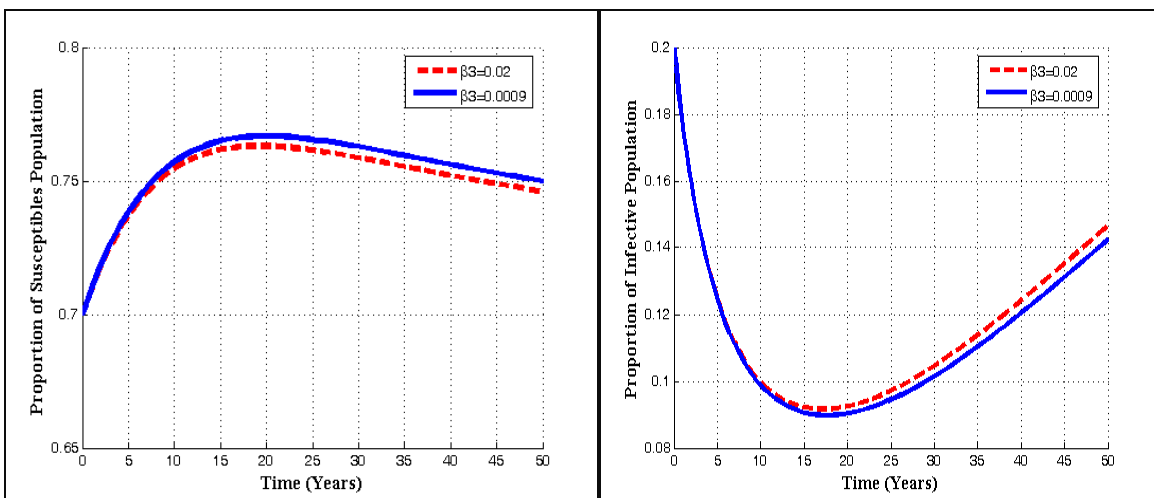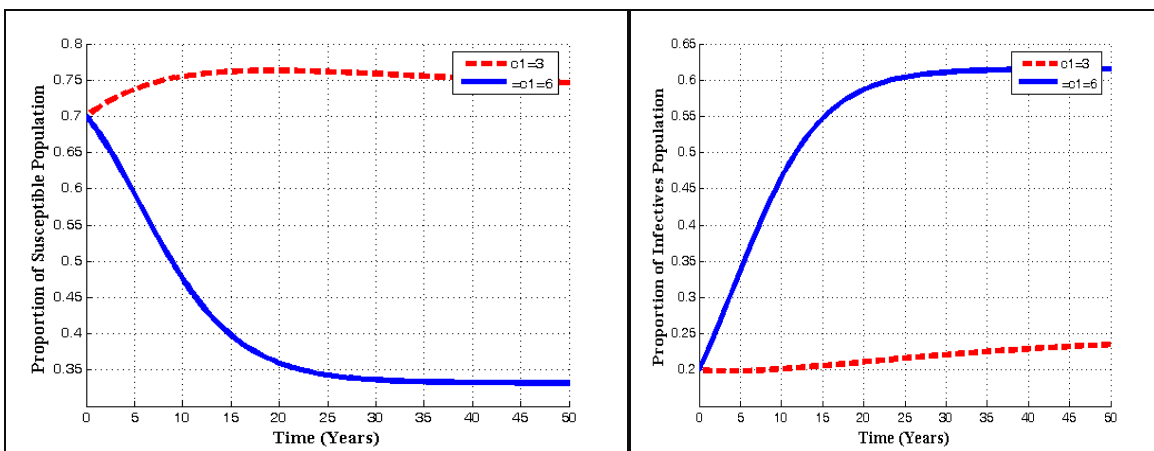

Figure 4.7(c)

Figure 4.7(d)

Figure 4.8(a)

Figure 4.8(b)
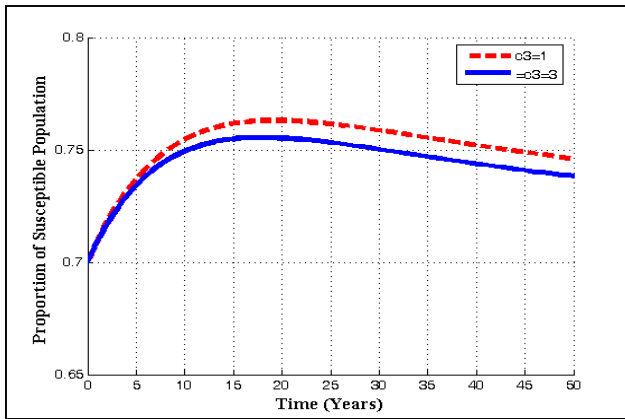
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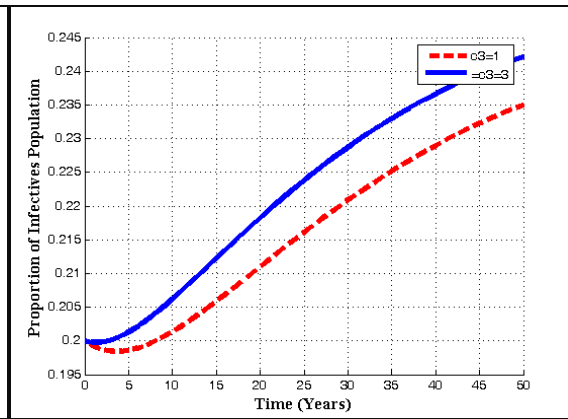
Figure 4.8(c)   Figure 4.8(d)

F**igure 4.7(c) Variation of Susceptible population for different values of** $\beta 3$
Figure 4.7(d) Variation of Infectives population for different values of β_3
Figure 4.8(a) Variation of Susceptible population for different values of c_1
Figure 4.8(b) Variation of Infectives population for different values of c_1
Figure 4.8(c) Variation of Susceptibles population for different values of c_3
Figure 4.8(d) Variation of Infectives population for different values of c_3
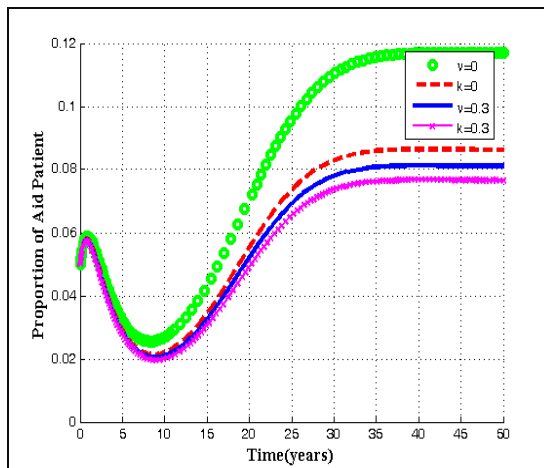

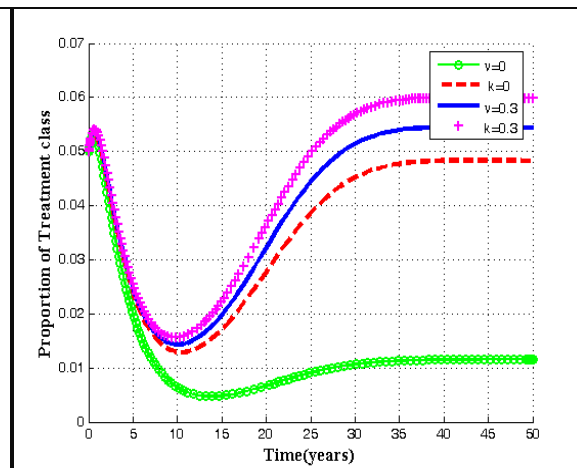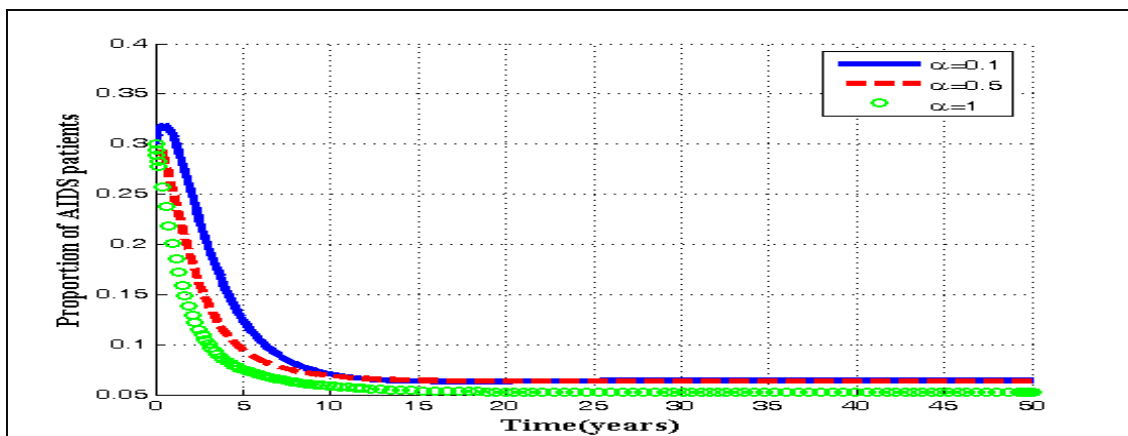Figure 4.9(a)   Figure 4.9(a)

Figure 4.10

Figure 4.9(a) Variation of AIDS patients for different values of $k\ and\ v$
Figure 4.9(a) Variation of AIDS patients for different values of $k\ and\ v$
Figure 4.10 Variation of AIDS populations for different values of α

PROOF AND NUMERICAL SIMULATION OF THE DTSM -MODEL

The dynamic behaviour of the model (3.3) demonstrated numerically that , the system is integrated by using Runge-Kutta method with the following set of parameter values:

We see from the figures that for any initial start of the curve, the solution curve tends to be equilibrium E^*. Hence, we infer that the system (3.3) may be globally stable about this endemic   equilibrium   pointE^*.   (The   computed   values

$$s^* = 0.6028, i^* = 0.243, p^* = 0.228, h^* = 0.0423, a^* = 0.0892$$

). The results of numerical simulation are shown graphically in Figures 4.2. In figure 4.2 (a) the distribution of proportion of population with time is shown in different classes with neither new infected children into the population nor recruitments i.e. $\pi = 0$ and $\theta = 0$. It is seen that in the absence of vertical transmission into the community, the proportion of susceptible population decreases continuously as the population is closed which results in an increase in proportion of infective population first and then it decreases as all infectives subsequently develop full blown AIDS and die out by natural or disease-induced death rate. The proportion of treated class increase continuously since the total population is being constant in this case.

Figure 4.2(b) shows the variation of proportion of population in all classes with both recruitment of susceptible and fraction of new born children who are infected at birth. It is found that susceptibility first decreases with time after using ARV, they prolong life and increase   life span, to reach the equilibrium position.   Due to vertical transmission from infected mother to child , susceptible population increase continuously therefore infection becomes more endemic, following that $R_0 > 0$

The role of vertical transmission in the model i.e. the rate of recruitment of infected children directly into infective class is explicitly shown in figures 4.3(a) - 4.3(c). It is seen that in figure 4.3(a) as the rate of infected children born θ increases, the proportion of   infective population also increases. It may be noted here that the birth of infected children make the infective population increase. In figure 4.3(b) if we increase the value of θ the proportion of AIDS population decreases with time then it increases until it reaches its equilibrium position. Thus, if the birth of infected children is controlled by treatment, the overall infective population will remain under Control. This will help in reducing the AIDS population. In 4.3(c) it is found that as the rate of infected children born increases, the treated population decreases.

Figure 4.4(a) – 4.4(c) shows the impact of recruitment rate for Susceptible, Treated class and AIDS patients for different values of π. It is seen that as recruitment rate increases the susceptible population increases rather than decrease rate π .Since the inflow of susceptible increases, the treated population and AIDS population decrease with

time till it reaches equilibrium and then decreases continuously due to treatment in the dynamics of HIV.

Figures 4.5(a) – 4.5(d) depict the variation of infectives, pre-AIDS, Treated and AIDS population respectively with time for different values of movement rate (δ) of individuals from infective class to pre-AIDS, Treated or AIDS, depending upon viral counts. It is seen that with increase in the value of movement rate, the infected population decreases which inturn increase the Treated population. Also if we increase movement rate δ , the Pre-AIDS and AIDS population decreases with time until it reaches the equilibrium stabilization model.

Figure 4.6(a) – 4.6(b) shows the Variation of population in the classes with fraction of movement rate from infectious classσ . It is seen that from the figures when σ_1 increases, the pre-AIDS population also decreases continuously it might be because of HAART treatment which is provided to the patients, but for the AIDS class this is different, it is found that as σ_1 increases, the AIDS population decreases with time then reaches its equilibrium and starts to increase. This is caused by ARV.Treated population initially increase, as time goes on   then it decreases, but in AIDS patients they decrease continuously up to equilibrium then they increase because disease still exists.

Figure 4.7(a) – 4.7(d) predict the Variation of the contact rates of susceptible with infectives β_1 and susceptible with treated   class β_3 in   the   susceptible   and   infective population. The figures show that as the contact rate β_1 increase   the   susceptible   decrease,   infectives   class decrease and treatment class increase Also as the contact rates of susceptible with treated population$\beta_3$increase the susceptible initially increase with time and then it reaches its equilibrium position,

Figure 4.8(a) – 4.8(b) shows the variation of susceptible and infective population for different values of number of sexual partners of susceptible with infectives c_1,and between susceptible   to treated population c_3, It is seen that as the number of sexual partners of susceptible to infective c_1, increases with time, susceptible decreases continuously and infective increases continuously. Also it is seen that if the number of sexual partners of susceptible to treated population c_3,increases with time, susceptibles first increase than decrease with time as shown in fig. 4.8(c) due to loss of immunity . But for infectives it seen that as c_3, increases also infectives increases, thus in order to reduce the spread of the disease, the number of sexual partners as well as unsafe sexual intercourse   with an infective is to be restricted.

Figure 4.9(a) and 4.9(b) shows the variation of treatment rates in treated class and AIDS population. It is found that if the treatment rate is zero, the disease increases with time

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whereas, treatment population decreases. Also the graphs show that as the rate of treatment increases, the AIDS patients decrease due to treatment measures which increases the immune system function and prolongs life of AIDS population, therefore this increases the treated class In figure 4.10 the effect of disease induced death rate α is shown and it is found that as α increases, the population of AIDS patient decreases. It is found that the AIDS induced death rate α , can be controlled by providing antiretroviral drugs (ARVs) to AIDS patients or by advising AIDS patients to follow healthy regulation about the AIDS disease. From the figures, it can also be seen that the respective populations are tending to the equilibrium level. This has also been observed for different initial values of the variables. Hence the endemic equilibrium E^* is globally asymptotically stable for the above set of parameter values.

DISCUSSION:

In this study, a non linear model has been proposed and analyzed to study the dynamics of HIV/AIDS model with treatment and vertical transmission. The disease free and endemic equilibria are obtained and their stability are investigated. A numerical study of the model has been conducted to see the impact of certain key parameters on the spread of HIV disease. It is observed that an increase in infection through vertical transmission would lead to increase in the population of infectives which in turn increases the pre-AIDS, treated class and AIDS population. AIDS can be eradicated after some fixed years if we can reduce the value of R_0 to less than unity i.e. $R0 >1$. In the case $R0 >1$, all the infected classes which are infectives, pre-AIDS and AIDS populations decrease with time. When this is attained, immediately the treated class increases since the infective class starts decreasing, and then follows the pre-AIDS class and finally the AIDS can be eradicated. The following measures can be exercised in order to decrease the value of R_0 to be less than one so as to decrease the infections, which can lead to the eradication of HIV/AIDS disease. Women who have reached the advanced stages of HIV disease require combinations of antiretroviral drugs, which is also highly effective at preventing mother to-child transmission (PMTCT). The most effective PMTCT therapy involves a combination of three antiretroviral drugs taken during the later stages of pregnancy and during labour. This therapy is essentially identical to the treatment taken by HIV positive people; except that it is taken only for a few months and the choice of drugs may be slightly different. Triple therapy is usually recommended to women in developed countries, and its use is becoming more widespread in the rest of the world also; this is reflected by WHO 2009 Guidelines. Effective prevention of mother-to-child transmission (PMTCT) requires a three-fold strategy (UNAIDS/WHO, 2005).Preventing HIV infection among prospective parents, making HIV testing and other prevention interventions available, in services related to sexual health such as antenatal and postpartum care. Avoiding unwanted pregnancies among HIV positive women-by providing appropriate counseling and support to women living with HIV to enable them to make informed decisions about their reproductive lives. Preventing the transmission of HIV from HIV positive mothers to their infants during pregnancy, labour, delivery and breastfeeding. Integration of HIV care, treatment and support for women found to be positive and their families. Also it is needed to control the vertical transmission of HIV by suppressing horizontal transmission; including condom use and other safer sexual practices. From numerical simulation it is found that an increase in the number of sexual partners further increases the susceptible population by way of spreading the disease. Thus in order to reduce the spread of the disease, the number of sexual partners should be restricted as well, and consequently the equilibrium values of infective, treated and AIDS population can be maintained at desired levels. When a mother is HIV positive a cesarean section may be done to protect the baby from direct contact with her blood and other bodily fluids. There are indications that cesarean birth decreases the risk of mother-to-child transmission (Newell, 1998). If the mother is taking combination antiretroviral therapy then a cesarean section will often not be recommended because the risk of HIV transmission will be very low.Cesarean delivery may be recommended if the mother has a high level of HIV in her blood. Safer Infant Feeding by HIV Positive Mothers- a number of studies have shown that the protective benefits of drugs is diminished when babies continue to be exposed to HIV through breastfeeding (Lu L. *etal.,* 2009). Mothers with HIV are advised not to breastfeed whenever the use of breast milk substitutes (formula) is acceptable, feasible, affordable, sustainable and safe. For HIV positive women who choose to breastfeed, exclusive breastfeeding is recommended for the first months of an infant's life and should be discontinued once an alternative form of feeding becomes feasible (UNAIDS, 2005). Mixed feeding is not recommended because studies suggest it carries a higher risk than exclusive breastfeeding. This is because mixed feeding damages the lining of the baby's stomach and intestines and thus makes it easier for HIV in breast milk to infect the baby. However, since ARV have been more available, the risk from mixed feeding is reduced. Indirect evidence suggest that keeping the period of transmission from exclusive breastfeeding to alternative feeding as short as possible may reduce the risk of transmission. Unfortunately, the best duration for this is not yet known and may vary according to the infant's age and/or the environment (UNAIDS 2005).

CONCLUSIONS

In this research, a non-linear mathematical model is proposed and analyzed to study the transmission of HIV/AIDS in a population of varying size with treatments and vertical transmission under the assumption that due to sexual intercourse of susceptible with infection, the infected babies are born to increase the growth of infective population directly. By analyzing the model, we have found a threshold parameter $R0$. It is noted that when $R0 < 1$ then the disease dies out and when $R0 > 1$ the disease becomes endemic. The model has two non-negatives Equilibrium namely the disease-free equilibrium, $E_0(1,0,0,0,0)$ and the endemic equilibrium $E^* s^*, i^*, p^*, h^* a^*$ It is found that the disease-free equilibrium E_0 is locally asymptotically stable if $R0 < 1$ and for $R0 > 1$, it is unstable and the infection is maintained in the population. The endemic equilibrium E^*,

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which exists only when $R0 > 1$, is always locally asymptotically stable. The equilibrium is also shown to be globally asymptotically stable under certain conditions. It is found that an increase in the rate of vertical transmission leads to increase in the population of infectives which in turn increases the pre-AIDS and AIDS population. Thus, the vertical spread of the disease should be controlled by effective treatment and promoting the condom use to keep the overall infective population under control. This will help in reducing the AIDS population as well. Also by simulation it is shown that by controlling the rate of vertical transmission, the spread of the disease can be reduced significantly Consequently the equilibrium values of infectives, treatment and AIDS population can be maintained at desired levels. It is also found that the increase in the number of sexual partners further increases the total infective population by way of spreading the disease. Thus, in order to reduce the spread of the disease, the number of sexual partners as well as unsafe sexual intercourse with an infected is to be restricted. From the analysis, it may also be speculated that if the HIV infection is suppressed at an early stage by effectively treating the infectives, the progression to the AIDS can be slowed down and the life span of HIV infected can be prolonged.

FUTURE WORK:
HIV/AIDS at present has no cure and no effective vaccine available as yet. As the number of reported cases of AIDS continues to swell, the magnitude and severity of the problem becomes increasingly evident and the need to develop effective strategies to prevent and control HIV infection is becoming even more urgent.

ACKNOWLEDGEMENTS:

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