ISSN 0974 - 9373

Vol. 24 No. 3 (2020) **Journal of International Academy of Physical Sciences** pp. 263- 287

Mathematical Modeling and Analysis of an HIV/AIDS Model with Treatment and Time Delay

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(Received August 15, 2020)

Abstract: A nonlinear mathematical model to study the effect of treatment and time delay on the spread of HIV/AIDS in a population with variable size structure is proposed and analyzed. The model divides the population into four subclasses namely susceptibles, asymptomatic infectives, symptomatic infectives and AIDS population. The delay is used to represent the time from the start of treatment in the symptomatic stage until the treatment effects become visible. The analysis of the model is carried out using stability theory of differential equations. The model exhibits two equilibria, the disease - free and the endemic equilibrium. Some inferences have been drawn regarding disease spread by establishing the local and global asymptotic stability of the equilibria. Model analysis reveals that with increase in the treatment rate, the population of symptomatic infectives decreases

which results to increase the population of asymptomatic infectives. This decrease in symptomatic infectives population, as a result of treatment, ultimately decreases AIDS population. The time delay, however, produces oscillations which increases its amplitude with increase in delay period. Numerical analysis of the model is also performed to investigate the influence of certain key parameters on the spread of the disease and to support the analytical results.
Keywords: Mathematical model, HIV/AIDS, stability, treatment, delay, numerical simulation

1. Introduction

The extensive spread of Human Immuno-deficiency Virus (HIV) and the associated Acquired Immuno-deficiency Syndrome (AIDS), a dreaded disease, has reached the epidemic heights in the most of the countries and has affected people all over the world. At the end of 2019, an estimated 38 million people globally were living with HIV whereas 25.4 million people were accessing antiretroviral therapy (ART). Since the start of the epidemic 32.7 million people have died from AIDS related illness whereas 690000 people died from AIDS-related illnesses in 2019 itself. Worldwide 1.7 million people became newly infected with HIV in 2019. New HIV infections have been reduced by 40% since the peak in 1998[1]. A comprehensive National AIDS Control Programme (NACP) for prevention and control of HIV/AIDS in India was launched in 1992 and implemented successfully. India is estimated to have around 87.58 thousand new HIV infections in 2017, showing new HIV infection decline by 85% since the peak of 1995 and by 27% between 2010 - 2017. The total number of people living with HIV in India is estimated at 21.40 lakhs in 2017. Since 2005, when the number of AIDS related deaths started to show a declining trend, the annual number of AIDS related deaths has declined by almost 71%[2].

Mathematical models play an important role in the study of transmission of HIV and for short and long term prediction of HIV/AIDS incidence. Various modeling studies have been made to understand the transmission of HIV infection and specific issues have been addressed[3-13]. In particular, Hyman et al.[7] considered different levels of viral infectivity between individuals to study the impact of variations in infectiousness. Hsieh and Chen[8] studied a model for a sexually structured population consisting of commercial sex workers and sexually active male customers with different sexual activity levels. Tripathi et al.[10] proposed and analyzed a nonlinear model to study the effect of screening of unaware infectives on the spread of HIV/AIDS and concluded that the screening of unaware

infectives helps in reducing the spread of AIDS epidemic. Naresh et al.[12] highlighted the importance of contact tracing in reducing the spread of AIDS epidemic in a homogeneous population with constant inflow of susceptibles. The HIV/AIDS models that take into account the treatment of infectives have been studied by many investigators[14-26]. Kirschner and Webb[16] developed mathematical models for the chemotherapy of AIDS. They incorporated AZT chemotherapy as a weakly effective treatment and found that AZT treatment does not eliminate HIV, but only restrains its progress. Schmitz[17] considered a model of HIV/AIDS transmission in a homosexual community with genetic heterogeneity and found that neither treatment nor vaccination alone can eliminate the disease from the population, but that a combination of both vaccination and treatment can help eradicate or eliminate the disease provided the quality of vaccines is decent. Blower[19] has shown that incidence rates of HIV will fall as more HIV- positive individuals gain access to treatment (HAART), but the underlying assumption is that treated individuals would change their behavior and the level of risky behavior does not increase. Kgosimore and Lungu[20] proposed a model to study the effect of vaccination and treatment on the spread of HIV/AIDS. They have found threshold conditions for the existence and stability of equilibria in terms of effective reproduction number. The model considers exponential population growth by taking different birth and death rates and assumes that vaccine does not wane over time. Culshaw[21] presented a review and comparison of some models for treatment of HIV-1 infections in which treatment is expressed as a forcing function. Culshaw *et. al.*[22] proposed optimal control models of drug treatment of the HIV and described the interaction between HIV and specific immune responses as measured by levels of natural killer cells. Kgosimore and Lungu[23] developed a model that incorporates treatment of both juveniles who were infected with HIV/AIDS through vertical transmission and HIV/AIDS infected adults. Naresh et al.[24] studied the effect of vaccination on the spread of HIV/AIDS in a population with variable size structure and obtained a threshold quantity in terms of vaccine reproduction number which characterizes the disease eradication.

Since susceptibles become infected via sexual contacts with infectives, the infectives then proceed to develop end stage disease AIDS through several stages due to long incubation period of the disease in adults. It is possible that a patient infected with HIV may develop different epidemiological or clinical stages before developing full blown AIDS depending on the level of infection in an individual[26]. Due to long incubation period of the disease, the role of time delay becomes more

important in such studies. A very few studies have been made that include time delay in the HIV/AIDS transmission models[27-30]. For example, Mukandavire et al.[28] proposed a model with explicit incubation period as a system of discrete time delay and studied the impact of epidemic for Zimbabwe. Naresh et al.[29] studied a nonlinear model to see the effect of screening of infected individuals on the transmission dynamics of HIV/AIDS and incorporated time delay in the recruitment of infected persons and found that the introduction of time delay in the model has a destabilizing effect on the system and periodic solutions can arise by Hopf bifurcation.

It is pointed out here that the delay in starting the treatment of HIV infectives may cause the epidemic to continue for a long time. This aspect has not been taken into account in the above studies though it plays a very important role to capture realistic dynamics of the spread of HIV/AIDS[31]. In view of the above, in this paper we propose a nonlinear mathematical model to study the effect of treatment on the transmission dynamics of HIV in a variable size population by considering two stages according to clinical manifestation i.e. asymptomatic stage and the symptomatic stage. The delay is also incorporated to represent the time from the start of the treatment in the symptomatic stage until the treatment effects are visibly observed. Our objective is to investigate the qualitative and quantitative behavior of the model to see the effect of treatment and delay on disease dynamics.

2. Mathematical Model and Description

Consider a population of size $N(t)$ at time $t>0$ with constant recruitment of susceptibles at a rate Q_0. The population size $N(t)$ is divided into four subclasses of susceptibles $S(t)$, asymptomatic infectives $I(t)$, symptomatic infectives $J(t)$ and that of AIDS patients $A(t)$ with natural mortality rate d in all the classes. The susceptibles are assumed to become infected via sexual contacts with asymptomatic infectives, symptomatic infectives and with those in AIDS class. The total population $N(t)$ looses individuals at a higher rate from the class $A(t)$ than the others. It may be noted that the individuals in symptomatic infectives class and in AIDS class may also interact sexually owing to illiteracy, ignorance or other social factors especially in underdeveloped nations but the contact rate may be less in comparison to that of other infectives ($\beta_2 < \beta_1 < \beta_0$), where β_0, β_1 and β_2 are probabilities of disease transmission per contact by infectives in

asymptomatic, symptomatic and AIDS class respectively[32]. The constants c_0, c_1 and c_2 are the number of sexual partners of an individual infective in asymptomatic, symptomatic and AIDS class respectively per unit of time, k_1 and k_2 are transfer rate coefficients from the asymptomatic infectives class $I(t)$ to the symptomatic infectives class $J(t)$ and from symptomatic infectives class $J(t)$ to the AIDS class respectively. The coefficient μ is the treatment rate from the symptomatic infectives class $J(t)$ to the asymptomatic infectives class $I(t)$, α is the disease-related death rate of individuals in AIDS class and τ is the time from the start of treatment in the symptomatic stage $J(t)$ until the treatment effects become visible. It is assumed that a symptomatic infective individual is getting treatment at a time $t-\tau$. However, for the model to be biologically reasonable, it may be more realistic to assume that not all those symptomatic infectives getting treatment will survive after time τ units and this claim supports the introduction of the survival term $e^{-d\tau}$, where $0 < e^{-d\tau} \leq 1$[33].

With the above assumptions and considerations, the dynamics of the disease is assumed to be governed by the following system of nonlinear ordinary differential equations,

$$\frac{dS}{dt} = Q_0 - \frac{\beta_0 c_0 S(t) I(t)}{N(t)} - \frac{\beta_1 c_1 S(t) J(t)}{N(t)} - \frac{\beta_2 c_2 S(t) A(t)}{N(t)} - dS(t), \tag{2.1}$$

$$\frac{dI}{dt} = \frac{\beta_0 c_0 S(t) I(t)}{N(t)} + \frac{\beta_1 c_1 S(t) J(t)}{N(t)} + \frac{\beta_2 c_2 S(t) A(t)}{N(t)} - (d + k_1) I(t) + \mu e^{-d\tau} J(t-\tau), \tag{2.2}$$

$$\frac{dJ}{dt} = k_1 I(t) - (d + k_2) J(t) - \mu e^{-d\tau} J(t-\tau), \tag{2.3}$$

$$\frac{dA}{dt} = k_2 J(t) - (d + \alpha) A(t), \tag{2.4}$$

with $S(0) = S_0 > 0,\ I(0) = I_0 > 0,\ J(0) = J_0 \geq 0,\ A(0) = A_0 \geq 0$.

Since $N = S + I + J + A$, the above equations can be written as follows,

$$\frac{dN}{dt} = Q_0 - dN(t) - \alpha A(t), \tag{2.5}$$

$$\frac{dI}{dt} = \frac{(\beta_0 c_0 I(t) + \beta_1 c_1 J(t) + \beta_2 c_2 A(t))[N(t) - I(t) - J(t) - A(t)]}{N(t)} - (d + k_1) I(t) + \mu e^{-d\tau} J(t - \tau) , \tag{2.6}$$

$$\frac{dJ}{dt} = k_1 I(t) - (d + k_2) J(t) - \mu e^{-d\tau} J(t - \tau) , \tag{2.7}$$

$$\frac{dA}{dt} = k_2 J(t) - (d + \alpha) A(t) . \tag{2.8}$$

2.1 Positivity and Boundedness of Solutions: In order to find the bounds of dependent variables involved in the model system (2.5) - (2.8), we need the region of attraction which is stated in the form of following lemma without proof.

Lemma 2.1: *The set*

$$\Omega = \left\{ (N, I, J, A); 0 < N(t) \le \overline{N}; 0 \le I(t) + J(t) + A(t) \le \overline{I} \right\} \tag{2.9}$$

is a region of attraction which attracts all solutions initiating in the interior of the positive octant,
where,

$$\overline{N} = \frac{Q}{d}, \qquad \overline{I} = \frac{Q}{d}\left[\frac{c_0\beta_0 - d}{c_0\beta_0} \right],$$

In the following, we state a lemma to show the positivity of solutions of the model system (2.5) - (2.8).

Lemma 2.2: *Let the initial data be* $N(0) = N_0 \ge 0$, $I(0) = I_0 \ge 0$, $J(0) = J_0 \ge 0$ *and* $A(0) = A_0 \ge 0$ *for all* $t \ge 0$. *Then, the solution (*$N(t)$, $I(t)$, $J(t)$, $A(t)$*) of the model remain positive for all time* $t \ge 0$.

Proof: From equation (2.8), we have
$A'(t) \ge -(d + \alpha) A(t)$ and by applying a theorem on differential inequalities[34], we obtain
$A(t) \ge Ce^{-(d+\alpha)t} > 0$, where C is a constant of integration. A similar reasoning on the remaining equations shows that they are always positive in Ω for $t > 0$.

3. Computation of Basic Reproduction Number

The basic reproduction number R_0, defined as the effective number of secondary infections generated by a typical infected individual in an otherwise disease-free population. We calculate R_0 by closely following the approach in van den Driessche and Watmough[35]. We first compute the new infectious matrix F and transfer matrix V, according to formula

$$[F-V]=\begin{bmatrix} \frac{\partial(dI/dt)}{\partial I} & \frac{\partial(dI/dt)}{\partial J} & \frac{\partial(dI/dt)}{\partial A} \\ \frac{\partial(dJ/dt)}{\partial I} & \frac{\partial(dJ/dt)}{\partial J} & \frac{\partial(dJ/dt)}{\partial A} \\ \frac{\partial(dA/dt)}{\partial I} & \frac{\partial(dA/dt)}{\partial J} & \frac{\partial(dA/dt)}{\partial A} \end{bmatrix}, \tag{3.1}$$

To calculate F and V, we only consider equations (2.6), (2.7) and (2.8), which correspond to the infected groups (I, J, A) capable of transmitting the disease. The non-negative matrix F, corresponding to new infections in the population at disease-free equilibrium is,

$$F=\begin{bmatrix} c_0\beta_0 & c_1\beta_1 & c_2\beta_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \tag{3.2}$$

The non-singular matrix V, corresponding to the transfer of individuals into and out of the compartment is,

$$V=\begin{bmatrix} (d+k_1) & -\mu e^{-d\tau} & 0 \\ -k_1 & (d+k_2+\mu e^{-d\tau}) & 0 \\ 0 & -k_2 & (\alpha+d) \end{bmatrix}, \tag{3.3}$$

FV^{-1} is the next generation matrix of the system (2.5) - (2.8). It follows that the spectral radius of matrix FV^{-1} is

$$\rho(FV^{-1})=\frac{c_0\beta_0[d+k_2+\mu e^{-d\tau}](\alpha+d)+c_1\beta_1k_1(\alpha+d)+c_2\beta_2k_1k_2}{(d+k_1)(d+k_2)(\alpha+d)+d(\alpha+d)\mu e^{-d\tau}}. \tag{3.4}$$

Thus, the basic reproduction number of the system (2.5)-(2.8) is

$$R_0 = \frac{c_0\beta_0[d+k_2+\mu e^{-d\tau}](\alpha+d)+c_1\beta_1k_1(\alpha+d)+c_2\beta_2k_1k_2}{(d+k_1)(d+k_2)(\alpha+d)+d(\alpha+d)\mu e^{-d\tau}}. \tag{3.5}$$

If $R_0<1$, then an infected individual produces less than one infected individual over the course of its infectious period and infection cannot grow. Conversely, if $R_0>1$ then an infected individual produces more than one new infection and the disease can invade the population.

4. Equilibrium and Stability Analysis

4.1 Equilibria of the Model: The model (2.5)-(2.8) has two non-negative equilibria namely,

(i) $E_0\left(Q_0/d, 0, 0, 0\right)$, the disease-free equilibrium, which exists without any condition. This equilibrium implies that in the absence of any infection, the total population size remains at its equilibrium value Q_0/d.

(ii) $E^*\left(N^*, I^*, J^*, A^*\right)$, the endemic equilibrium. The equilibrium values of different variables are obtained by setting right hand side of equations in model system (2.5)-(2.8) equal to zero to give,

$$N^* = \frac{(c_0\beta_0a_1+c_1\beta_1a_2+c_2\beta_2)d(1+a_1+a_2)Q_0}{b}, \quad I^* = a_1A^*, \quad J^* = a_2A^*,$$

$$A^* = \frac{[(c_0\beta_0a_1+c_1\beta_1a_2+c_2\beta_2)-\{(d+k_1)a_1-\mu e^{-d\tau}a_2\}]Q_0}{b},$$

where

$$a_1 = \frac{(d+k_2+\mu e^{-d\tau})}{k_2}a_2, \quad a_2 = \frac{(\alpha+d)}{k_2}$$

and

$$b = (c_0\beta_0a_1+c_1\beta_1a_2+c_2\beta_2)d((1+a_1+a_2)+[(c_0\beta_0a_1+c_1\beta_1a_2+c_2\beta_2)$$
$$-\{(d+k_1)a_1-\mu e^{-d\tau}a_2\}]\alpha.$$

These values are all positive when

$$(c_0\beta_0 a_1 + c_1\beta_1 a_2 + c_2\beta_2) > [(d + k_1)a_1 - \mu e^{-d\tau} a_2].$$

i.e. $$\frac{(c_0\beta_0 a_1 + c_1\beta_1 a_2 + c_2\beta_2)}{(d + k_1)a_1 - \mu e^{-d\tau} a_2} > 1, \text{ which is } R_0 > 1$$

4.2 Local Stability of the Equilibria without Delay ($\tau = 0$): To determine the local stability of E_0, the following Jacobian matrix of the model system (2.5)-(2.8) is computed about E_0 as,

$$J(E_0) = \begin{bmatrix} -d & 0 & 0 & -\alpha \\ 0 & \beta_0 c_0 - (k_1 + d) & \beta_1 c_1 + \mu & \beta_2 c_2 \\ 0 & k_1 & -(\mu + k_2 + d) & 0 \\ 0 & 0 & k_2 & -(\alpha + d) \end{bmatrix},$$

One root of the characteristic equation of above matrix is $\lambda = -d$ where as other three roots are determined by the following cubic equation,

$$f(\lambda) = \lambda^3 + A\lambda^2 + B\lambda + C = 0,$$

where,

$$A = 3d + \alpha + k_1 + k_2 + \mu - c_0\beta_0,$$

$$B = d(2d + \alpha + k_2 + \mu) + k_1(2d + \alpha + k_2) + (d + \alpha)(d + k_2 + \mu)$$
$$-c_0\beta_0(2d + \alpha + k_2 + \mu) - c_1\beta_1 k_1,$$

$$C = [(d + k_1)(d + k_2) + d\mu](\alpha + d) - [c_0\beta_0(d + \alpha)$$
$$\times(d + \alpha + k_2) + c_1\beta_1 k_1(d + \alpha) + c_2\beta_2 k_1 k_2],$$

From equation (3.5), we get reproduction number R_0 for disease- free equilibrium with $\tau = 0$ as follows,

$$\frac{c_0\beta_0[d + k_2 + \mu](\alpha + d) + c_1\beta_1 k_1(\alpha + d) + c_2\beta_2 k_1 k_2}{(d + k_1)(d + k_2)(\alpha + d) + d(\alpha + d)\mu} < 1$$

from which we get,

$$[(d+k_1)(d+k_2)+d\mu](\alpha+d) > c_0\beta_0[d+k_2+\mu] \times(\alpha+d)+c_1\beta_1k_1(\alpha+d)+c_2\beta_2k_1k_2, \tag{4.1}$$

showing that $C>0$. It can easily be proved that $A>0$, $B>0$ and $AB>C$

Thus, the disease - free equilibrium E_0 is locally asymptotically stable for $R_0<1$ which corresponds to inequality (4.1). Therefore, the disease dies out and infection does not persist in the population. If $R_0>1$, it is unstable and the endemic equilibrium E^* exists and the disease always persists in the population.

The equilibrium value of I in terms of basic reproduction number R_0 can be written as follows with $\tau=0$,

$$I^* = \frac{a_1Q_0[(d+k_1)(d+\alpha)(d+k_2)+\mu d(\alpha+d)](R_0-1)}{\alpha[(d+k_1)(d+\alpha)(d+k_2)+\mu d(\alpha+d)](R_0-1) +(c_0\beta_0a_1+c_1\beta_1a_2+c_2\beta_2)d(1+a_1+a_2)}, \tag{4.2}$$

where a_1 and a_2 are defined as above with $\tau=0$.

The basic reproduction number for $\tau=0$ can be obtained from equation (3.5) as follows,

$$R_0 = \frac{c_0\beta_0[d+k_2+\mu](\alpha+d)+c_1\beta_1k_1(\alpha+d)+c_2\beta_2k_1k_2}{(d+k_1)(d+k_2)(\alpha+d)+d(\alpha+d)\mu e}. \tag{4.3}$$

From figure 1, we observe that the basic reproduction number $R_0=1$ is the bifurcation point which changes the stability behavior between disease - free equilibrium and endemic equilibrium. It is noted that the disease - free equilibrium is always stable for $R_0<1$ and in this case there is no possibility for endemic equilibrium to exist and thus the disease is eradicated from the population.

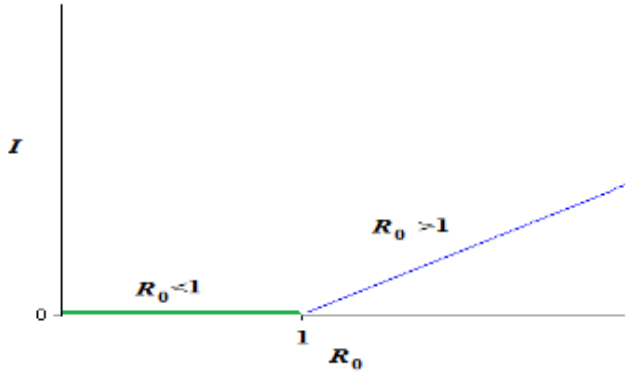

Figure 1. Bifurcation diagram

The system shows a forward bifurcation if reproduction number R_0 slightly exceeds one and disease - free equilibrium becomes unstable and an endemic equilibrium appears. Thus, it is observed that the HIV infection can be eradicated from the population if we reduce the reproduction number R_0 below one successfully and in that case the endemic equilibrium does not exist for $R_0<1$.

Now the Jacobian matrix corresponding to endemic equilibrium E^* is given by,

$$J(E^*)=\begin{bmatrix} -d & 0 & 0 & -\alpha \\ m_{21} & -m_{22} & -m_{23} & -m_{24} \\ 0 & k_1 & -(\mu+k_2+d) & 0 \\ 0 & 0 & k_2 & -(\alpha+d) \end{bmatrix},$$

where

$$m_{21}=pq,\ m_{22}=p+\beta_0 c_0 q+(d+k_1)-\beta_0 c_0,$$

$$m_{23}=p+\beta_1 c_1 q+\mu-\beta_1 c_1,\quad m_{24}=p+\beta_2 c_2 q-\beta_2 c_2$$

and

$$p=\frac{\beta_0 c_0 I^*+\beta_1 c_1 J^*+\beta_2 c_2 A^*}{N^*}>0,\ q=\frac{I^*+J^*+A^*}{N^*}>0.$$

The characteristic equation corresponding to $J(E^*)$ is given by,

$$f(\lambda) = \lambda^4 + P\lambda^3 + Q\lambda^2 + R\lambda + S = 0,$$

where

$$P = 3d + \alpha + \mu + k_2 + m_{22},$$

$$Q = (\alpha + 2d)(\mu + k_2 + d) + d(\alpha + d) + m_{22}(\alpha + \mu + k_2 + 3d) - m_{23}k_1,$$

$$R = d(\alpha + d)(\mu + k_2 + d) + m_{22}[(\alpha + 2d)(\mu + k_2 + d) + d(\alpha + d)]$$
$$+ m_{24}k_1k_2 - m_{23}k_1(\alpha + 2d),$$

$$S = m_{22}d(\alpha + d)(\mu + k_2 + d) + m_{24}k_1k_2d + m_{21}\alpha k_1k_2 - m_{23}k_1d(\alpha + d),$$

Thus, E^* is locally asymptotically stable if the conditions of the Routh - Hurwitz criteria are satisfied i.e. $P>0$, $Q>0$, $R>0$, $S>0$, $PQ>R$ and $R(PQ-R)-P^2S>0$.

4.3. Global Stability of the Endemic Equilibrium: The global stability of the equilibrium E^* is established using Liapunov method and the result obtained is stated in the following theorem.

Theorem 4.1: *If the endemic equilibrium E^* exists, then it is globally asymptotically stable provided the following sufficient conditions are satisfied in Ω ,*

(4.4) $$\frac{27m_{26}^{\ 2}}{8(\alpha + d)m_{27}} < \frac{(k_2 + \mu + d)m_{28}}{k_2^{\ 2}k_1},$$

(4.5) $$\frac{27\alpha^2}{8(\alpha + d)^2 d^2} < \frac{(k_2 + \mu + d)m_{27}m_{28}}{k_2^{\ 2}k_1m_{25}^{\ 2}},$$

where

$$m_{25} = \left(\frac{c_0\beta_0\bar{I}}{N^*} + \frac{c_0\beta_0(J^* + A^*)I^*(\alpha + d)}{Q_0N^*} + \frac{c_1\beta_1(J^* + A^*)J^*(\alpha + d)}{Q_0N^*} \right.$$

$$+\frac{c_0\beta_0(J^*+A^*)A^*(\alpha+d)}{Q_0N^*}\Bigg),$$

$$m_{26}=\left(\frac{c_0\beta_0I^*(\alpha+d)}{Q_0}+\frac{c_1\beta_1J^*(\alpha+d)}{Q_0}+\frac{c_2\beta_2I^*(\alpha+d)}{Q_0}+c_2\beta_2+\frac{c_1\beta_1A^*(\alpha+d)}{Q_0}\right),$$

$$m_{27}=-c_0\beta_0+(d+k_1)+\frac{c_0\beta_0I^*}{N^*},$$

$$m_{28}=\left(-c_1\beta_1-\mu+\frac{c_0\beta_0I^*}{N^*}+\frac{c_1\beta_1I^*}{N^*}+\frac{c_0\beta_0J^*}{N^*}\right)$$

and $A_2k_1=A_1m_{28}$

Proof: Consider the following positive definite function about E^*,

(4.6) $$V=\frac{1}{2}(N-N^*)^2+\frac{1}{2}A_1(I-I^*)^2+\frac{1}{2}A_2(J-J^*)^2+\frac{1}{2}A_3(A-A^*)^2,$$

where A_i,(i = 1, 2, 3) are positive constants to be chosen appropriately. Differentiating V with respect to t, we get

$$\frac{dV}{dt}=(N-N^*)\frac{dN}{dt}+A_1\left(\frac{I-I^*}{I}\right)\frac{dI}{dt}+A_2(J-J^*)\frac{dJ}{dt}+A_3(A-A^*)\frac{dA}{dt}.$$

Using model equations (2.5) - (2.8) and simplifying, we get

$$\frac{dV}{dt}=-d(N-N^*)^2-\alpha(N-N^*)(A-A^*)$$
$$A_1\left(\frac{c_0\beta_0I^2+c_1\beta_1J^2+c_2\beta_2A^2}{NN^*}+\frac{c_0\beta_0(J^*+A^*)I^*}{NN^*}+\frac{c_1\beta_1(I^*+A^*)J^*}{NN^*}\right.$$
$$\left.+\frac{c_0\beta_0(J^*+I^*)A^*}{NN^*}\right)(N-N^*)(I-I^*)-A_1\left(-c_0\beta_0+(d+k_1)+\frac{c_0\beta_0(I+I^*)}{N^*}\right.$$
$$\left.+\frac{c_0\beta_0(J+A)}{N}+\frac{c_1\beta_1J}{N}+\frac{c_2\beta_2A}{N}\right)(I-I^*)^2-A_1\left(-c_1\beta_1-\mu+\frac{c_0\beta_0I^*}{N}+\frac{c_1\beta_1I^*}{N}\right.$$

$$+\frac{c_1\beta_1 A}{N^*}+\frac{c_2\beta_2 A}{N}+\frac{c_1\beta_1(J+J^*)}{N^*}\Bigg)(J-J^*)(I-I^*)$$
$$-A_1\left(-c_2\beta_2+\frac{c_0\beta_0 I^*}{N}+\frac{c_1\beta_1 J^*}{N}+\frac{c_2\beta_2 I^*}{N}+\frac{c_2\beta_2 I}{N}+\frac{c_1\beta_1(A+A^*)}{N}\right)$$
$$\times(A-A^*)(I-I^*)+A_2k_1(J-J^*)(I-I^*)$$
$$-A_2(d+k_2+\mu)(J-J^*)^2+A_3k_2(J-J^*)(A-A^*)-A_3(\alpha+d)(A-A^*)^2.$$

After little algebraic calculations, we get the following conditions for *dV*/*dt* to be negative definite,

(4.7) $$A_1\left(\frac{c_0\beta_0 I^2+c_1\beta_1 J^2+c_2\beta_2 A^2}{NN^*}+\frac{c_0\beta_0(J^*+A^*)I^*}{NN^*}+\frac{c_1\beta_1(I^*+A^*)J^*}{NN^*}\right.$$
$$\left.+\frac{c_0\beta_0(J^*+I^*)A^*}{NN^*}\right)^2<\frac{2}{3}d\left(-c_0\beta_0+(d+k_1)+\frac{c_0\beta_0(I+I^*)}{N^*}\right.$$
$$\left.+\frac{c_0\beta_0(J+A)}{N}+\frac{c_1\beta_1 J}{N}+\frac{c_2\beta_2 A}{N}\right),$$

(4.8) $$\alpha^2<\frac{2d}{3}A_3(\alpha+d),$$

(4.9) $$\left[A_2k_1-A_1\left(-c_1\beta_1-\mu+\frac{c_0\beta_0 I^*}{N}+\frac{c_1\beta_1 I^*}{N}+\frac{c_1\beta_1 A}{N^*}+\frac{c_2\beta_2 A}{N}+\frac{c_1\beta_1(J+J^*)}{N^*}\right)\right]$$
$$<\frac{2}{3}A_1A_2(k_2+\mu+d)\left(-c_0\beta_0+(d+k_1)+\frac{c_0\beta_0(I+I^*)}{N^*}\right.$$
$$\left.+\frac{c_0\beta_0(J+A)}{N}+\frac{c_1\beta_1 J}{N}+\frac{c_2\beta_2 A}{N}\right),$$

(4.10) $$A_1\left(-c_2\beta_2+\frac{c_0\beta_0 I^*}{N}+\frac{c_1\beta_1 J^*}{N}+\frac{c_2\beta_2 I^*}{N}+\frac{c_2\beta_2 I}{N}+\frac{c_1\beta_1(A+A^*)}{N}\right)^2$$
$$<\frac{4}{9}A_3(\alpha+d)\left(-c_0\beta_0+(d+k_1)+\frac{c_0\beta_0(I+I^*)}{N^*}\right.$$

$$+\frac{c_0\beta_0(J+A)}{N}+\frac{c_1\beta_1 J}{N}+\frac{c_2\beta_2 A}{N}\Bigg),$$

(4.11) $$A_3k_2^2<\frac{2}{3}A_2(\alpha+d)(k_2+\mu+d).$$

After maximizing the LHS and minimizing the RHS of the above, the stability conditions as given in the statement of the theorem are obtained. Thus, *dV*/*dt* will be negative definite showing that *V* is a Liapunov function. Hence, the endemic equilibrium E^* is globally asymptotically stable inside the region of attraction Ω.

5. Local Stability of the Endemic Equilibrium with Delay ($\tau \neq 0$)

Since the disease-free equilibrium E_0 is unstable when $\tau=0$ and $R_0>1$, incorporation of delay will not change the instability. Thus, E_0 is unstable when $\tau>0$ and $R_0>1$. Now we establish the local stability of endemic equilibrium E^* with delay.

The Jacobian matrix $M(E^*)$ corresponding to endemic equilibrium E^* is obtained as follows,

$$M(E^*)=\begin{bmatrix} -d & 0 & 0 & -\alpha \\ l & -m & -n+\mu e^{-(\lambda+d)\tau} & -r \\ 0 & k_1 & -(\mu e^{-(\lambda+d)\tau}+k_2+d) & 0 \\ 0 & 0 & k_2 & -(\alpha+d) \end{bmatrix},$$

where,

$$l=pq,\quad m=p+\beta_0c_0q+(d+k_1)-\beta_0c_0,\quad n=p+\beta_1c_1q-\beta_1c_1,$$

$$r=p+\beta_2c_2q-\beta_2c_2\quad p=\frac{\beta_0c_0I^*+\beta_1c_1J^*+\beta_2c_2A^*}{N^*}>0,$$

and $q=\dfrac{I^*+J^*+A^*}{N^*}>0.$

The characteristic equation corresponding to $M(E^*)$ is given as,

(5.1) $$P(\lambda)+Q(\lambda)e^{-\lambda\tau}=0\ ,$$

where

$$P(\lambda)=\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4,$$

$$Q(\lambda)=b_1\lambda^3+b_2\lambda^2+b_3\lambda+b_4.$$

The equation (5.1) can be written as,

(5.2) $$\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4+e^{-\lambda\tau}(b_1\lambda^3+b_2\lambda^2+b_3\lambda+b_4)=0,$$

where

$$a_1=3d+k_2+\alpha+m>0,$$

$$a_2=\alpha m+(m+d)(\alpha+2d+k_2)+(\alpha+d)(d+k_2)+k_1n>0,$$

$$a_3=dm(\alpha+2d+k_2)+(k_2+d)(\alpha+d)(m+d)+rk_1k_2+k_1n(\alpha+2d)>0,$$

$$a_4=d(\alpha+d)[m(d+k_2)+k_1n]+k_1k_2(dr+\alpha l)>0,$$

$$b_1=\mu e^{-d\tau},$$

$$b_2=\mu(\alpha+m+2d-k_1)e^{-d\tau},$$

$$b_3=[d(\alpha+d)+(\alpha+2d)(m-k_1)]e^{-d\tau},$$

$$b_4=\mu d(\alpha+d)(m-k_1)e^{-d\tau}.$$

When $\tau=0$, the equation (5.2) reduces to

(5.3) $$\lambda^4+(a_1+c_1)\lambda^3+(a_2+c_2)\lambda^2+(a_3+c_3)\lambda+(a_4+c_4)=0,$$

where c_1, c_2, c_3 and c_4 can be found by putting $\tau=0$ in b_1, b_2, b_3 and b_4 respectively. Roots of this equation (5.3) has already been discussed in Section 4.2.

Now we will investigate the distribution of roots of equation (5.2) when $\tau>0$. The transcendental equation (5.2) has roots with positive real parts if and only if it has purely imaginary roots[7]. We determine if equation (5.2) has purely imaginary roots, from which we shall be able to find conditions for all eigenvalues to have negative real parts.

Let $\lambda = u(\tau)+iv(\tau)$ $(v > 0)$, be the eigenvalue of characteristic equation (5.2), where $u(\tau)$ and $v(\tau)$ depend on the delay τ. If $\tau>0$ is sufficiently small, we shall assume that $u(\tau) < 0$ and E^* is stable. Also $u(\tau_0) = 0$, for certain value of $\tau_0>0$ so that $\lambda = iv$ is purely imaginary root of equation (5.2), then the steady state E^* loses stability and eventually becomes unstable when $u(\tau)$ becomes positive. In other words, if such $v(\tau_0)$ does not exist, that is if the characteristic equation (5.2) does not have purely imaginary roots for all delays, then the steady state E^* is always stable. The main purpose here is to study the stability behavior of E^* in the case when $\tau \neq 0$. When $R_0>1$, $\tau>0$, without loss of generality, assuming $\lambda = iv$ with $v>0$ and substituting in equation (5.2) we get,

$$v^4 - a_2v^2 + a_4 + i(-a_1v^3 + a_3v) + [(-v^3b_1 + vb_3)\sin v\tau + (-v^2b_2 + b_4)\cos v\tau] + i[(-v^3b_1 + vb_3)\cos v\tau + (v^2b_2 - b_4)\sin v\tau] = 0 . \tag{5.4}$$

Now on separating the real and imaginary parts of equation (5.4) we get,

$$[(-v^2b_2 + b_4)\cos v\tau + (-v^3b_1 + vb_3)\sin v\tau] = -(v^4 - a_2v^2 + a_4) , \tag{5.5}$$

$$[(-v^3b_1 + vb_3)\cos v\tau + (v^2b_2 - b_4)\sin v\tau] = -(-a_1v^3 + a_3v) . \tag{5.6}$$

On squaring and adding both the equations (5.5) and (5.6) we obtain,

$$v^8 + (a_1^2 - 2a_2 - b_1^2)v^6 + (a_2^2 + 2a_4 - 2a_1a_3 + 2b_1b_3 - b_2^2)v^4 + (a_3^2 - 2a_2a_4 - 2b_2b_4 - b_3^2)v^2 + (a_4^2 - b_4^2) = 0 . \tag{5.7}$$

Let $v^2 = z$, $d_1 = a_1^2 - 2a_2 - b_1^2$, $d_2 = a_2^2 + 2a_4 - 2a_1a_3 + 2b_1b_3 - b_2^2$, $d_3 = a_3^2 - 2a_2a_4 - 2b_2b_4 - b_3^2$ and $d_4 = a_4^2 - b_4^2$, we get

$$z^4 + d_1z^3 + d_2z^2 + d_3z + d_4 = 0 . \tag{5.8}$$

The following results on the distribution of roots of equation (5.8) are denoted as,

$$m_1 = \frac{1}{2}d_2 - \frac{3}{16}d_1^{\,2},\ n_1 = \frac{1}{32}d_1^{\,3} - \frac{1}{8}d_1 d_2 + d_3,$$

$$\Delta = \left(\frac{n_1}{2}\right)^3 + \left(\frac{m_1}{2}\right)^3,\ \eta = \frac{-1 + i\sqrt{3}}{2},$$

$$y_1 = \sqrt[3]{-\frac{n_1}{2} + \sqrt{\Delta}} + \sqrt[3]{-\frac{n_1}{2} - \sqrt{\Delta}},$$

$$y_2 = \eta \sqrt[3]{-\frac{n_1}{2} + \sqrt{\Delta}} + \eta^2 \sqrt[3]{-\frac{n_1}{2} - \sqrt{\Delta}},$$

$$y_3 = \eta^2 \sqrt[3]{-\frac{n_1}{2} + \sqrt{\Delta}} + \eta \sqrt[3]{-\frac{n_1}{2} - \sqrt{\Delta}},$$

$$z_i = y_i - \frac{3d_1}{4},\ i = 1, 2, 3.$$

Lemma 5.1: *For the polynomial equation (5.8)*

(i) If $d_4 < 0$, *then equation (5.8) has at least one positive real root, thus the equilibrium is unstable.*

(ii) If $d_4 \geq 0$ *and* $\Delta \geq 0$, *then equation (5.8) has positive roots if and only if* $z_1 > 0$ *and* $H(z_1) < 0$.

(iii) If $d_4 \geq 0$ *and* $\Delta < 0$, *then equation (5.8) has positive roots if and only if there exists at least one* $z^* \in \{z_1, z_2, z_3\}$ *such that* $z^* > 0$ *and* $H(z^*) \leq 0$, *where* $H(z) = z^4 + d_1 z^3 + d_2 z^2 + d_3 z + d_4$.

Let $\lambda = u(\tau) + iv(\tau)$ be the eigenvalue of equation (5.2) such that $u(\tau) = 0$, $v(\tau) = 0$. From equations (5.5) and (5.6), we get the corresponding $\tau_k > 0$ such that the characteristic equation (5.2) has a pair of imaginary roots,

$$\tau_k = \frac{1}{v_0}\cos^{-1}\left[\frac{\begin{array}{l}(b_2 + a_1b_1)v_0^{\,6} - (a_1b_3 + b_1a_3 + b_2a_2 + b_4)v_0^{\,4} \\ +(a_3b_3 + a_2b_4 + b_2a_4)v_0^{\,2} - a_4b_4\end{array}}{\begin{array}{l}b_1^{\,2}v_0^{\,6} + (b_2^{\,2} - 2b_1b_3)v_0^{\,4} + (b_3^{\,2} - 2b_2b_4)v_0^{\,2} \\ +b_4^{\,2}\end{array}}\right] + \frac{2k\pi}{v_0}. \tag{5.9}$$

Here, k = 0,1, 2, ….. and we have the following transversality condition,

$$\left.\frac{d(\mathrm{Re}(\lambda\tau))}{d\tau}\right|_{\tau=\tau_k} > 0. \tag{5.10}$$

Thus, Hopf bifurcation occurs at $\tau = \tau_k$ and the endemic equilibrium E^* is asymptotically stable when $\tau < \tau_k$,

1. The endemic equilibrium E^* is asymptotically stable for $\tau \in [0, \tau_k)$.
2. There exists $\tau = \tau_k$ satisfying $\left.\frac{d(\mathrm{Re}(\lambda\tau))}{d\tau}\right|_{\tau=\tau_k} > 0$. This signifies that there exists at least one eigenvalue with positive real part for $\tau > \tau_k$. The endemic equilibrium E^* of system undergoes a Hopf bifurcation as τ passes through τ_k.

6. Numerical Simulation

To see the dynamical behavior of the model system, the system (2.5) - (2.8) is integrated numerically by fourth order Runge - Kutta method using the following set of parameters values,

Q_0 = 2000, d = 0.02, α = 1, c_0 = 5, β_0 = 0.32, β_1 = 0.22,

c_1 = 4, c_2 = 3, β_2 = 0.12, μ = 0.1, k_1 = 0.5, k_2 = 0.7,

with initial values $N(0)$ = 10000, I(0) = 2000, J(0) = 1000 and A(0) = 200. The equilibrium values of different variables are computed as,

N^* = 10816, I^* = 4262, J^* = 2599 and A^* = 1784.

The eigenvalues corresponding to endemic equilibrium E^* are obtained as,

$$-0.6443596291 \pm 0.3655557399i,\ -0.3692482209,\ -1.202314984.$$

Since all the eigenvalues are either negative or have negative real parts, the endemic equilibrium E^* is locally asymptotically stable.

The computer simulations are performed for different initial starts and results are displayed in the Figs. 2-3. We see from these figures that for any initial start, the solution trajectories tend to the endemic equilibrium E^* showing that the equilibrium E^* is globally asymptotically stable. In figs. (4) - (6), the variation of asymptomatic infectives, symptomatic infectives and AIDS population, respectively has been shown with time t for different delay periods τ, which represents the time period from the start of treatment in the symptomatic stage until the treatment effects become visible to join the asymptomatic class. It is observed that as delay period increases, the population of asymptomatic infectives decreases (fig.4). This decrease in the population of asymptomatic infectives results to increase the population of symptomatic infectives and hence the disease remain endemic in the population (fig.5). As a consequence of increased population of symptomatic infectives, the AIDS population also increases (fig.6). These populations, however, reach their steady states as time increases. It is also noted from these figures that time delay produces oscillations in the beginning which increases its amplitude with increase in delay period τ.

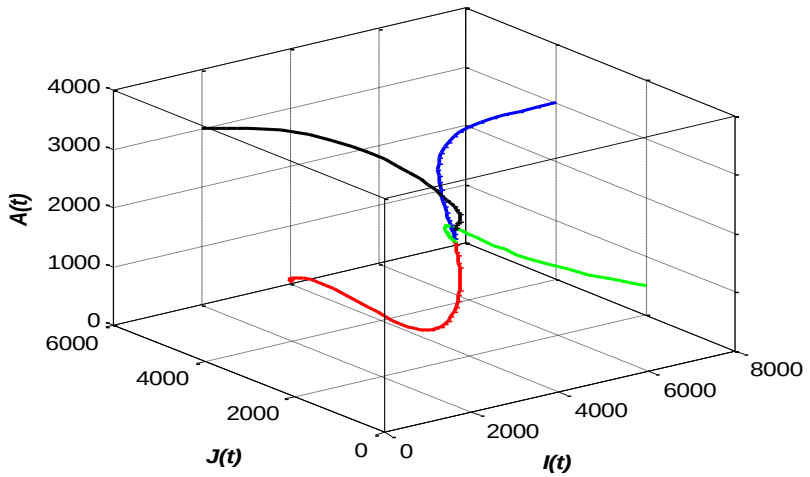

Figure 2. Global stability in I - J - A plane for $\tau = 0$

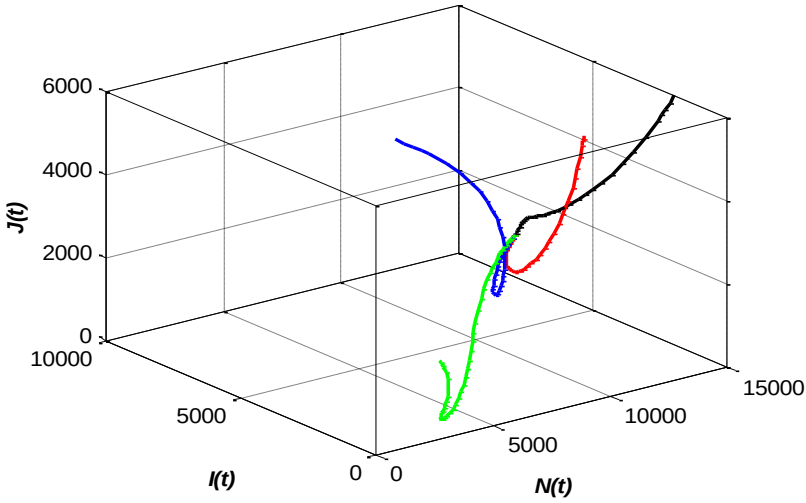

Figure 3. Global stability in N - I - J plane for $\tau = 0$

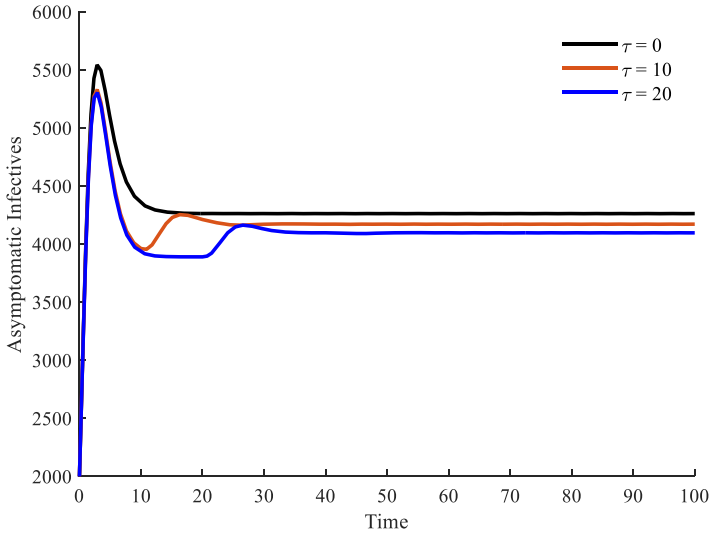

Figure 4. Variation of asymptomatic infectives with time for different values of τ .

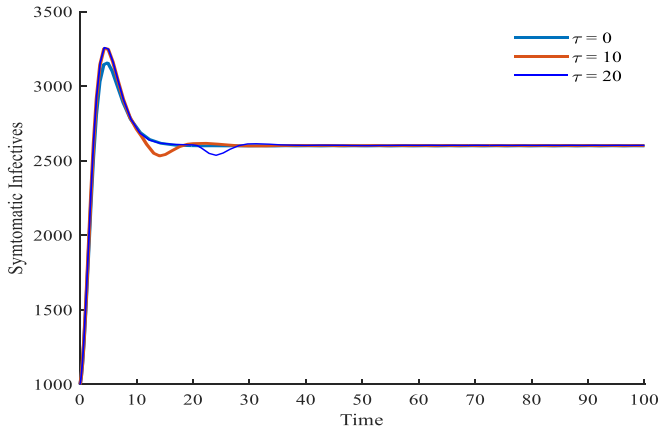

Figure 5. Variation of symptomatic infectives with time for different values of τ .

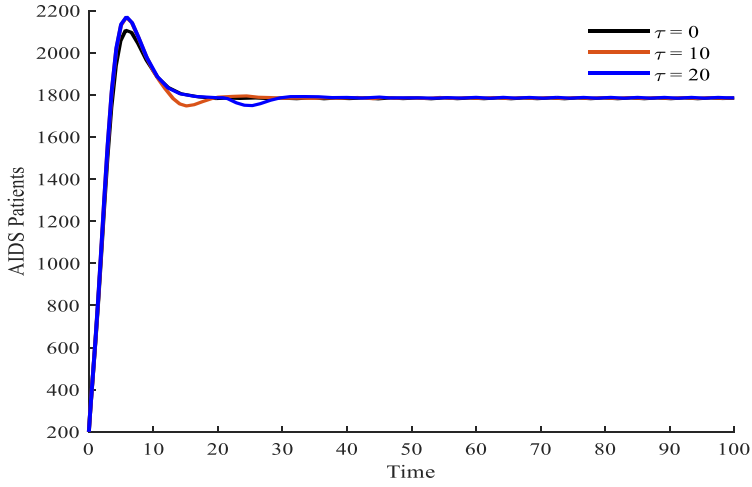

Figure 6. Variation of AIDS population with time for different values of τ .

7. Conclusions

In this paper, a nonlinear mathematical model has been proposed and analyzed to study the effect of treatment and time delay on the spread of HIV/AIDS in a population with variable size structure. In the modeling process. the total population is divided into four subclasses namely susceptibles, asymptomatic infectives, symptomatic infectives and AIDS

population. The delay incorporated in the model represents the time from the start of treatment in the symptomatic stage until the treatment effects become visible. The model has been analyzed qualitatively using stability theory of differential equations and computer simulations. The model exhibits two equilibria namely, the disease-free and the endemic equilibrium. The local and global stability results of these equilibria have been established. Analysis of the model shows that with increase in the treatment rate of symptomatic infectives, its population decreases which results to increase the population of asymptomatic infectives. The decline in the symptomatic infectives population, as a result of treatment, ultimately decreases the AIDS population. It is observed that as delay period increases, the population of asymptomatic infectives decreases which makes the population of symptomatic infectives to increase and as a consequence the AIDS population also increases. It is noted that delay makes the system unstable. As time delay increases, the amplitude of oscillations increases while in absence of delay the model system approaches to steady state without oscillations.

References

1. UNAIDS, *www.unaids.org (Fact Sheet)*, 2020.

2. NACO, *http://naco.gov.in/hiv-facts-figures*, 2020.

3. R. M. Anderson, G. F. Medley, R. M. May and A. M. Johnson, A Preliminary Study of the Transmission Dynamics of the Human Immunodeficiency Virus (HIV), the Causative Agent of AIDS, *IMA J. Math. Appl. Med. Biol*., **3** (1986), 229-263.

4. R. M. Anderson, The Role of Mathematical Models in the Study of HIV Transmission and the Epidemiology of AIDS, *J. AIDS*., **1** (1988), 241-256.

5. H.W. Hethcote and J. W. Van Ark, *Modeling HIV Transmission and AIDS in the United States, Lecture Notes in Biomathematics*, Vol. 95, Springer, Berlin, 1992.

6. X. Lin, H. W. Hethcote and P. van den Driessche, An Epidemiological Model for HIV/AIDS with Proportional Recruitment, *Math. Biosc*., **118** (1993), 181-195.

7. J. M. Hyman, J. Li and E. A Stanley, The Differential Infectivity and Staged Progression Models for the Transmission of HIV, *Math. Biosc*., **55** (1999), 77-109.

8. Y. H. Hsieh and C. H. Chen, Modeling the Social Dynamics of a Sex Industry: Its Implications for Spread of HIV/AIDS, *Bull. Math. Biol*., **66** (2004), 143-166.

9. B. D. Corbett, S. M. Moghadas and A. B. Gumel, Subthreshold Domain of Bistable Equilibria for a Model of HIV Epidemiology, *Int. J. Math. Math. Sc*,. **58** (2003), 3679-3698.

10. A. Tripathi, R. Naresh and D. Sharma, Modelling the Effect of Screening of Unaware Infectives on the Spread of HIV Infection, *Appl. Math. Comp*., **184** (2007), 1053-1968.

11. G. Magombedze, Z. Mukandavire, C. Chiyaka and G. Musuka, Optimal Control of a Sex-Structured HIV/AIDS Model With Condom Use, *Math. Model. Anal*., **14(4)** (2009), 483–494.

12. R. Naresh, A. Tripathi and D. Sharma, A Nonlinear HIV/AIDS Model with Contact Tracing, *Appl. Math. Comp*., **217** (2011), 9575-9591.

13. A. Tripathi and R. Naresh, Modelling the Role of Media Awareness Programs on the Spread of HIV/AIDS, *World J. Model. Simul*., **15(1)** (2019), 12-24.

14. Y. H. Hsieh, A Two Sex Model for Treatment of HIV and Behavior Change in a Population of Varying Size, *IMA J. Math. Appl. Med. Biol*., **13** (1996), 151-173.

15. J. X. Velasco-Hernandez and Y. H. Hsieh, Modelling the Effect of Treatment and Behavioral Change in HIV Transmission Dynamics, *J. Math. Biol.*, **32** (1994), 233-249.

16. D. E. Kirschner and G. F. Webb, A Model for Treatment Strategy in the Chemotherapy of AIDS, *Bull. Math. Biol*., **58** (1996), 367-390.

17. H. Schmitz, The Effects of Treatment or/and Vaccination on HIV Transmission in Homosexuals with Genetic Heterogeneity, *Math. Biosc*., **167** (2000), 1-18.

18. Y. H. Hsieh and S. P. Sheu, The Effect of Density-Dependent Treatment and Behavior Change on the Dynamics of HIV Transmission, *J. Math. Biol*., **43** (2001), 69-80.

19. S. Blower, Calculating the Consequences: HAART and Risky Sex, *AIDS*, **15** (2001), 1309-131.

20. M. Kgosimore and E. M. Lungu, The Effects of Vaccination and Treatment on the Spread of HIV/AIDS, *J. Biol. Sys*., **12(4)** (2004), 399-417.

21. R. V. Culshaw, Review of HIV Models: The Role of the Natural Immune Response and Implications for Treatment, *J. Biol. Sys*., **12** (2004), 123-135.

22. R. V. Culshaw, S. Ruan and R. J. Spiteri, Optimal HIV Treatment by Maximizing Immune Response, *J. Math. Biol*., **48** (2004), 545-562.

23. M. Kgosimore and E. M. Lungu, The Effects of Vertical Transmission on the Spread of HIV/AIDS in the Presence of Treatment, *Math. Biosc. Engg*., **3(2)** (2006), 297-312.

24. R. Naresh, A. Tripathi, J. Biazar and D. Sharma, Analysis of the Effect of Vaccination on the Spread of AIDS Epidemic Using Adomian Decomposition Method, *J. Nature Sci. Sust. Tech*., **2(1/2)** (2008), 183-213.

25. H. F. Huo, R. Chen and X. Y. Wang, Modelling and Stability of HIV/AIDS Epidemic Model with Treatment, *Appl. Math. Model*., **40** (2016), 6550-6559.

26. Hai-Feng Huo and Li-Xiang Feng, Global Stability for an HIV/AIDS Epidemic Model with Different Latent Stages and Treatment, *Appl. Math. Model*., **37** (2013), 1480-1489.

27. S. Kovacs, Dynamics of an HIV/AIDS Model -the Effect of Time Delay, *Appl. Math. Comp*., **188** (2007), 1597-1609.

28. Z. Mukandavire, W. Garira and C. Chiyaka, Asymptotic Properties of an HIV/AIDS Model with a Time Delay, *J. Math. Anal. Appl*., **330** (2007), 916-933.

29. R. Naresh, A. Tripathi and D. Sharma, A Nonlinear AIDS Epidemic Model with Screening and Time Delay, *Appl. Math. Comp*., **217** (2011), 4416-4426.

30. A. Tripathi, R. Naresh, Jean M. Tchuenche and D. Sharma, Modeling the Spread of HIV/AIDS with Infective Immigrants and Time Delay, *Int. J. Nonlinear Sc*., **16** (2013), 313-322.

31. L. Cai, X. Li, M. Ghosh and B. Guo, Stability Analysis of HIV/AIDS Epidemic Model with Treatment, *J. Comp. Appl. Math.*, **229** (2009), 313-323.

32. Z. Mukandavire, P. Das, C. Chiyaka and F. Nyabadza, Global Analysis of an HIV/AIDS Epidemic Model, *World. J. Model. Simul*., **6(3)** (2010), 231-240.

33. R. Naresh and D. Sharma, An HIV/AIDS Model with Vertical Transmission and Time Delay, *World. J. Model. Simul*., **7(3)** (2011), 230-240.

34. G. Birkhoff and G. C. Rota, *Ordinary Differential Equations*, Ginn, 1982.

35. P. van den Driessche and J. Watmough, Reproduction Numbers and Sub-Threshold Endemic Equilibria for Compartmental Models of Disease Transmission, *Math. Biosc*.**, 180** (2002), 29-48.