Analysis of a Nonautonomous HIV/AIDS Epidemic Model with Distributed Time Delay

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Abstract. In this paper, we have considered a nonautonomous stage-structured HIV/AIDS epidemic model through vertical and horizontal transmissions of infections, having two stages of the period of infection according to the developing progress of infection before AIDS defined would be detected, with varying total population size and distributed time delay to become infectious (through horizontal transmission) due to intracellular delay between initial infection of a cell by HIV and the release of new virions. The infected people in the different stages have different ability of transmitting disease. We have established some sufficient conditions on the permanence and extinction of the disease by using inequality analytical technique. We have obtained the explicit formula of the eventual lower bounds of infected people. We have introduced some new threshold values R_0 and R^* and further obtained that the disease will be permanent when $R_0 > 1$ and the disease will be going to extinct when $R^* < 1$. By Lyapunov functional method, we have also obtained some sufficient conditions for global asymptotic stability of this model. Computer simulations are carried out to explain the analytical findings.

Keywords: HIV/AIDS; time delay; permanence; extinction; Lyapunov functional; global stability.

AMS Subject Classification: 92D25; 92D30; 34D23.

1 Introduction

The spectrum of infectious disease is changing rapidly in conjunction with dramatic social and environmental changes. Explosive population growth with expanding poverty and urban migration is going on worldwide, international travel and commerce are increasing, technology is changing rapidly, all of which are affecting the risk of exposure to infectious agents. The human immunodeficiency virus (HIV) infection which can lead to acquired immunodeficiency syndrome (AIDS), has become an important infectious disease in both the

developed and developing countries. It is a fatal disease which destroys the human's immune system, leaving the victim vulnerable to life threatening infections, neurological disorders and unusual malignancies. It causes mortality and morbidity of millions of people and recurs expenditure of enormous amount of money in health care and disease control. It was first recognized by the U.S. Centers for Disease Control and Prevention in 1981 and its cause (HIV) was identified in the early 1980s. In 2007, it was estimated that 33.2 million people lived with the disease worldwide, and estimated 2.1 million AIDS death occurred, including 330,000 children (WHO, [42]). Viral transmission occurs through direct contact of a mucous membrane or the bloodstream with a bodily fluid containing HIV, such as blood, semen, vaginal fluid, preseminal fluid, and breast milk (Centers for Disease Control and Prevention [13]).

HIV is a retrovirus that infects, among others the $CD4^+$ T lymphocytes, which are the most abundant white blood cells of the human immune system. It directly and indirectly destroys $CD4^+$ T cells. A person may advance through several infective stages before developing full blown AIDS. In a normal healthy individual's peripheral blood, $CD4^+$ T counts is between 800 and $1200/mm^3$. Once HIV has killed so many $CD4^+$ T cells that there are fewer than 200 of these cells per mm^3 of blood, cellular immunity is lost. Acute HIV infection progresses over time to clinical latent HIV infection and then to early symptomatic HIV infection and later to AIDS, which is identified either on the basis of the amount of $CD4^+$ T cells remaining in the blood and/or on the basis of the presence of certain infections caused by Mycobacterium avium-intracellulare, cytomegalovirus and Penicillium marneffei (Lipman et al., [26]).

In many countries in Africa, AIDS has been already a major cause of death. It is predicted by experts that it will soon become so in Asian countries having larger populations. It is well known that HIV virus has a long incubation and infectious period. In the absence of antiretroviral therapy, the median time of progression from HIV infection to AIDS is 9–10 years and the median survival time after developing AIDS is only 9.2 months. Moreover, the rate of clinical disease progression varies widely between individuals, from two weeks up to 20 years. Many factors affect the rate of progression. These include the factors that influence the body's ability to defend against HIV such as the infected person's general immune function; older people have weaker immune systems, and therefore are at a greater risk of rapid disease progression than younger people. Poor access to health care and the existence of coexisting infections such as tuberculosis also may accelerate people to faster disease progression. The infected individual's genetic inheritance plays an important role and some people are resistant to certain strains of HIV. HIV is genetically variable and exists as different strains, which cause different rates of clinical disease progression. There is currently no vaccine or cure for HIV or AIDS. The only known method of prevention are based on avoiding exposure to the virus.

From the theoretical point of view, the HIV/AIDS dynamics gives a large number of new problems to mathematicians, biologists and epidemiologists, because it has a lot of features different from traditional infectious diseases. Hence, the research of HIV/AIDS dynamics has stimulated the recent development of mathematical epidemiology. Mathematical models have been used

extensively to study the epidemiology of HIV/AIDS which help to improve our understanding of the major contributing factors to the pandemic. From the initial models of May and Anderson (Anderson et al., [3]; May and Anderson, [29]; Anderson, [1]), several refinements have been added into modelling frameworks and specific issues have been addressed by several authors (Hethcote and Van Ark, [19]; Brauer, [6]; Perelson and Nelson, [33]; Hsieh and Cooke, [21]; Blower, [5]; Greenhalgh et al., [15]; Li et al., [25]; Connell McCluskey, [30]; Leenheer and Smith, [24]; Bachar, [4]; Hsieh and Chen, [20]; Naresh et al., [32]; Wang and Li, [41]; Wang and Wang, [40]; Cai et al., [8], G. Magombedze et al.,[28]). According to clinical symptoms or viral load and $CD4^+$ T counts, 2–6 stages of infection before AIDS can be classified (Hethcote and Van Ark, [19]; Stoddart and Reyes, [36]). HIV infection spreads rapidly in populations through unprotected sexual interaction with an accompanying risk of vertical transmission. This is the main factor in many infectious diseases, including AIDS, chagas's disease and hepatitis B. Therefore, this aspect should also be considered in the modelling of AIDS especially in developing countries where the infection may be transmitted vertically at a very high rate. Vertical transmission can also be accomplished through transplacental transfer of disease agents. Busenberg and Cooke [7] discussed a variety of diseases that transmit both horizontally and vertically, and performed a comprehensive survey of the formulation and the mathematical analysis of compartmental models by using autonomous differential equations. Brauer [6] studied models for disease with vertical transmission and analyzed the stability of equilibria. Li et al. [25] considered a model for an infectious disease that spreads in the host population through horizontal and vertical transmissions. Naresh et al. [32] developed a model for transmission of HIV into a population with vertical transmission by using a system of autonomous ordinary differential equations.

Time delays of one type or another have been considered into biological models by many researchers (Cushing, [11]; Gopalsamy, [14]; Busenberg and Cooke, [7]; Kuang, [23]). Time delays can arise for various practical reasons in epidemiology. Perelson et al. [34] have considered two types of time delays: (i) pharmacological delay that occurs between the ingestion of drug and its appearance within cells and (ii) intracellular delay between initial infection of a cell by HIV and the release of new virions. Herz et al., [17] incorporated a discrete delay to model the intracellular delay in a HIV model and showed that the addition of a delay would substantially shorten the estimate for the half-life of free virus. Culshaw and Ruan [10] used the time delay between infection of a $CD4^+$ T cell and the emission of viral particles on a cellular level to investigate the effect of the time delay on the stability of the endemically infected equilibrium. Time delay is also used to model the gestation lag, the incubation time for a infectious vector etc. These delay differential equations exhibit much more complicated dynamics than ordinary differential equations since a time delay could cause a stable equilibrium to become unstable and cause the population to fluctuate.

Nonautonomous phenomenon often occurs in many realistic epidemic models. It occurs mainly due to the seasonal variety, which makes the population to behave periodically. Since biological and environmental parameters are nat-

urally subject to fluctuation in time, the effects of a periodically varying environment are considered as important selective forces on systems in a fluctuating environment. To investigate this kind of phenomenon in the model, the coefficients should be periodic functions, in which case, the system is called periodic system. The nonautonomous epidemic models can be regarded as an extension of the periodic epidemic models. To the best of our knowledge, the research works on the nonautonomous epidemic dynamical models are very few (Thieme, [38, 39]; Herzong and Redheffer, [18]; Zhang and Teng, [43, 44]; Samanta, [35]). Therefore, the research on the nonautonomous epidemic dynamical models is also very important.

Researches on epidemic models that incorporate time dependent biological and environmental parameters, disease related death, varying total population and time delay are becoming one of the important areas in the mathematical theory of epidemiology. The whole dynamics of the spread of HIV/AIDS is too complex to be analyzed by a single model. By considering the above facts, in this paper we have considered a nonlinear and nonautonomous stage-structured HIV/AIDS epidemic model through vertical and horizontal transmissions of infections, having two stages of the period of infection according to the developing progress of infection before AIDS would be detected, i.e., the asymptomatic and the symptomatic stages, with varying total population size and distributed time delay to become infectious (through horizontal transmission) due to intracellular delay between initial infection of a cell by HIV and the release of new virions. The infected people in different stages have different abilities to transmit the disease. It is assumed that the infective and people in full-blown AIDS group are capable of producing children; the infected babies are born to increase the growth of infective (asymptomatic stage) population directly. Here, we have established some sufficient conditions on the permanence and extinction of the disease by using inequality analytical technique. We have obtained the explicit formula of the eventual lower bounds of infected people. We have introduced some new threshold values R_0 and R^* and further obtained that the disease will be permanent when $R_0 > 1$ and the disease will be going to extinct when $R^* < 1$. By Lyapunov functional method, we have also obtained some sufficient conditions for global asymptotic stability of this model. Our analytical results are validated through numerical simulations. The aim of the analysis of this model is to identify the parameters of interest for further study, with a view to informing and assisting policy-makers in targeting prevention and treatment resources for maximum effectiveness.

2 A Nonautonomous HIV/AIDS Epidemic Model with Distributed Time Delay

We divide the total population into a susceptible class (S), infectious class before the onset of AIDS and a full-blown AIDS group (A). Based on the facts that the infectious period is very long (≥ 9 years), we divide the infectious period into two stages, namely, the asymptomatic stage (I) and the symptomatic stage (J) (Hethcote and Van Ark, [19]; Stoddart and Reyes, [36]). It is assumed that infective and people in full-blown AIDS group are capable of producing

children, the infected babies are born to increase the growth of infective population directly. Our mathematical model is formulated as the following system of nonautonomous delay differential equations:

$$\frac{dS(t)}{dt} = \Lambda(t) - \Big\{ \beta_1(t) \int_0^h I(t-s)\,d\eta(s) + \beta_2(t) \int_0^h J(t-s)\,d\eta(s)$$

$$+ \beta_3(t) \int_0^h A(t-s)\,d\eta(s) \Big\} S(t) - \mu(t)S(t),$$

$$\frac{dI(t)}{dt} = \Big\{ \beta_1(t) \int_0^h I(t-s)\,d\eta(s) + \beta_2(t) \int_0^h J(t-s)\,d\eta(s) + \beta_3(t)$$

$$\times \int_0^h A(t-s)d\eta(s) \Big\} S(t) - (\mu(t)+p_1(t))I(t) + \xi(t)\Big(I(t) + J(t) + A(t) \Big),$$

$$\frac{dJ(t)}{dt} = p_1(t)I(t) - (\mu(t)+p_2(t))J(t), \qquad (2.1)$$

$$\frac{dA(t)}{dt} = p_2(t)J(t) - \mu_1(t)A(t).$$

Here $N(t) = S(t) + I(t) + J(t) + A(t)$ denotes the total number of high-risk human population at time t; $S(t), I(t), J(t), A(t)$ are the densities (or fractions) of susceptible, first stage (asymptomatic stage) infective, second stage (symptomatic stage) infective, and full-blown AIDS individuals, respectively at time t. The function $\Lambda(t)$ defines the recruitment rate function of the susceptible, $\beta_1(t)$ the horizontal transmission rate function of infection when susceptible humans contact with infective in the first stage (asymptomatic stage) and the rate of transmission is of the form $\beta_1(t)S(t)\int_0^h I(t-s)d\eta(s)$, $\beta_2(t)$ defines the horizontal transmission rate function of infection when susceptible humans contact with infective in the second stage (symptomatic stage) and the rate of transmission is of the form $\beta_2(t)S(t)\int_0^h J(t-s)d\eta(s)$, $\beta_3(t)$ denotes the horizontal transmission rate function of infection when susceptible humans contact with infective in the full-blown AIDS class and the rate of transmission is of the form $\beta_3(t)S(t)\int_0^h A(t-s)d\eta(s)$. The nonnegative constant h is the time delay. The function $\eta(s) : [0,h] \to [0,\infty)$ is nondecreasing and has bounded variation such that $\int_0^h d\eta(s) = \eta(h) - \eta(0) = 1$. The time delay is due to intracellular delay between initial infection of a cell and the release of new virions. Those infected at time $t-s$ become infectious at time $s(0 \le s \le h)$ later with different probabilities. Here we assume that the second stage (symptomatic stage) infective and full-blown AIDS class contribute less viral transmission horizontally due to stringent measures, i.e., $\beta_2(t), \beta_3(t) \le \beta_1(t)$.

Function $\mu(t)$ defines the instantaneous per capita mortality rate function of susceptible and infective population, $\mu_1(t)$ the instantaneous per capita mortality rate function of full-blown AIDS group. It is natural biologically to assume that $\mu(t) \le \mu_1(t)$ (that is, disease will increase the death rates of the full-blown AIDS group). Function $p_1(t)$ defines the progression rate function to the second stage (symptomatic stage) infectious class from first stage (asymptomatic stage) infectious class, $p_2(t)$ denotes the progression rate function to the full-blown AIDS class from the second stage (symptomatic stage) infectious class,

$\xi(t)$ denotes the instantaneous vertical transmission rate function, i.e., the rate of recruitment of new borne infected children into the first stage (asymptomatic stage) infectious class. It is natural to assume that $\xi(t) < \mu(t)$.

3   Permanence and Extinction

In this section, we first introduce the following assumptions for system (2.1): functions $\Lambda(t), \beta_1(t), \beta_2(t), \beta_3(t), \mu(t), \mu_1(t), p_1(t), p_2(t), \xi(t)$ are positive continuous bounded and have positive lower bounds. Here we assume that the second stage (symptomatic stage) infective and full-blown AIDS class contribute less viral transmission horizontally due to stringent measures, i.e., $\beta_2(t), \beta_3(t) \leq \beta_1(t), \forall t \geq 0$. It is natural biologically to assume that $\mu(t) \leq \mu_1(t), \forall t \geq 0$ that is, disease will increase the death rates of the full-blown AIDS group. It is also natural to assume that $\xi(t) < \mu(t), \forall t \geq 0$.

The initial conditions of (2.1) are given as

$$S(\theta) = \varphi_1(\theta), \ I(\theta) = \varphi_2(\theta), \ J(\theta) = \varphi_3(\theta), \ A(\theta) = \varphi_4(\theta), \ -h \leq \theta \leq 0, \ (3.1)$$

where $\varphi = (\varphi_1, \varphi_2, \varphi_3, \varphi_4)^T \in C$ such that $\varphi_i(\theta) \geq 0, \ (i = 1, 2, 3, 4), \forall \theta \in [-h, 0]$, and C denotes the Banach space $C([-h, 0], \mathbb{R}^4)$ of continuous functions mapping the interval $[-h, 0]$ into $\mathbb{R}^4$. Let us denote the norm of an element φ in C by

$$\|\varphi\| = \sup_{-h \leq \theta \leq 0} \{|\varphi_1(\theta)|, |\varphi_2(\theta)|, |\varphi_3(\theta)|, |\varphi_4(\theta)|\}.$$

For a biological meaning, we further assume that $\varphi_i(0) > 0, \ i = 1, 2, 3, 4$.

Here we want to discuss the permanence of the system (2.1), this means that the long-term survival of all components of the system (2.1), with initial conditions (3.1). It demonstrates how the disease will not vanish in time under some conditions. Also, we discuss how the disease in the community will be going to die out under some conditions.

Let $f^l = \inf_{t \geq 0} f(t)$, $f^u = \sup_{t \geq 0} f(t)$, for a continuous and bounded function $f(t)$ defined on $[0, +\infty)$.

DEFINITION 1. The system (2.1) is said to be permanent, i.e., we have the long-term survival of all components of the system (2.1), if there are positive constants v_i and M_i $(i = 1, 2, 3, 4)$ such that:

$$v_1 \leq \liminf_{t \to \infty} S(t) \leq \limsup_{t \to \infty} S(t) \leq M_1, \ v_2 \leq \liminf_{t \to \infty} I(t) \leq \limsup_{t \to \infty} I(t) \leq M_2,$$

$$v_3 \leq \liminf_{t \to \infty} J(t) \leq \limsup_{t \to \infty} J(t) \leq M_3, \ v_4 \leq \liminf_{t \to \infty} A(t) \leq \limsup_{t \to \infty} A(t) \leq M_4$$

hold for any solution $(S(t), I(t), J(t), A(t))$ of (2.1) with initial conditions (3.1). Here v_i and M_i $(i = 1, 2, 3, 4)$ are independent of (3.1).

Theorem 1. *The system* (2.1) *with initial conditions* (3.1) *is permanent provided*

$$R_0 = \frac{\beta_1^l}{(\mu - \xi + p_1)^u} \left(\frac{\Lambda^l}{\mu^u}\right) > 1.$$

Proof. We will give the following Propositions 1–5 to complete the proof of this theorem. □

Proposition 1. *The solution* $(S(t), I(t), J(t), A(t))$ *of* (2.1) *with initial conditions* (3.1) *is positive for all* $t \geq 0$, *and*

$$\limsup_{t \to \infty} N(t) \leq \left(\frac{\Lambda}{\mu - \xi}\right)^u.$$

Proof. Since the right hand side of system (2.1) is completely continuous and locally Lipschitzian on C, the solution $(S(t), I(t), J(t), A(t))$ of (2.1) with initial conditions (3.1) exists and is unique on $[0, \alpha)$, where $0 < \alpha \leq +\infty$ (Hale, [16]). Now,

$$S(t) = S(0) \exp\left[-\int_0^t \left\{\beta_1(\theta) \int_0^h I(\theta - s)\, d\eta(s) + \beta_2(\theta) \int_0^h J(\theta - s)\, d\eta(s)\right.\right.$$

$$\left. + \beta_3(\theta) \int_0^h A(\theta - s) d\eta(s) + \mu(\theta)\right\} d\theta\right] + \int_0^t \Lambda(u) \exp\left[\int_t^u \left\{\beta_1(\theta) \int_0^h I(\theta - s) d\eta(s)\right.\right.$$

$$\left. + \beta_2(\theta) \int_0^h J(\theta - s) d\eta(s) + \beta_3(\theta) \int_0^h A(\theta - s) d\eta(s) + \mu(\theta)\right\} d\theta\right] du > 0, \ \forall t \geq 0.$$

Let us show that $I(t) > 0$ for all $t \in [0, \alpha)$, where $0 < \alpha \leq +\infty$. Otherwise, there exists a $t_1 \in (0, \alpha)$ such that $I(t_1) = 0$ and $I(t) > 0$ for all $t \in [0, t_1)$. Hence there must have $J(t) > 0$ for all $t \in [0, t_1)$. If this statement is not true, then there exists a $t_2 \in (0, t_1)$ such that $J(t_2) = 0$ and $J(t) > 0$ at $[0, t_2)$. Now,

$$J(t_2) = J(0) \exp\left\{-\int_0^{t_2} \left(\mu(s) + p_2(s)\right) ds\right\}$$

$$+ \int_0^{t_2} p_1(u) I(u) \exp\left\{\int_{t_2}^u \left(\mu(s) + p_2(s)\right) ds\right\} du > 0,$$

which is a contradiction with $J(t_2) = 0$. So $J(t) > 0$ for all $t \in [0, t_1)$. We also claim that $A(t) > 0$ for all $t \in [0, t_1)$. If this is not true, then there exists $t_3 \in (0, t_1)$ such that $A(t_3) = 0$ and $A(t) > 0$ in $[0, t_3)$. From the fourth equation of (2.1), we have

$$A(t_3) = A(0) \exp\left\{-\int_0^{t_3} \mu_1(s) ds\right\} + \int_0^{t_3} p_2(u) J(u) \exp\left\{\int_{t_3}^u \mu_1(s) ds\right\} du > 0,$$

which is a contradiction with $A(t_3) = 0$. So $A(t) > 0$ for all $t \in [0, t_1)$. Integrating the second equation of system (2.1) from 0 to t_1, we have:

$$I(t_1) = I(0) \exp\left\{-\int_0^{t_1} \left(\mu(s) - \xi(s) + p_1(s)\right) ds\right\}$$

$$+ \int_0^{t_1} \int_0^h \left\{\left(\beta_1(u) I(u - s) + \beta_2(u) J(u - s) + \beta_3(u) A(u - s)\right) S(u)\right.$$

$$\left. + \xi(u)(J(u) + A(u))\right\} \exp\left\{\int_{t_1}^u \left(\mu(s) - \xi(s) + p_1(s)\right) ds\right\} d\eta(s) du > 0,$$

which is a contradiction with $I(t_1) = 0$. So $I(t) > 0$, $\forall t \geq 0$, and hence $J(t) > 0$, $A(t) > 0$, $\forall t \geq 0$. Thus $\forall t \in [0, +\infty)$, because $\mu(t) \leq \mu_1(t)$, we get:

$$\dot{N}(t) \leq \Lambda(t) - \big(\mu(t) - \xi(t)\big)N(t) \quad \Rightarrow \quad \limsup_{t \to \infty} N(t) \leq \Big(\frac{\Lambda}{\mu - \xi}\Big)^u.$$

That is, $(S(t), I(t), J(t), A(t))$ is uniformly bounded on $[0, +\infty)$. $\square$

Proposition 2. *The solution* $(S(t), I(t), J(t), A(t))$ *of* (2.1) *with initial conditions* (3.1) *satisfies*

$$\liminf_{t \to \infty} S(t) \geq \Big\{ \frac{\Lambda}{(\beta_1 + \beta_2 + \beta_3)(\frac{\Lambda}{\mu - \xi})^u + \mu} \Big\}^l \equiv v_1 > 0.$$

Proof. By Proposition 1, for any $\epsilon > 0$, there exists a $t_1 > 0$ such that:

$$I(t), J(t), A(t) \leq \Big(\frac{\Lambda}{\mu - \xi}\Big)^u + \epsilon, \text{ as } t \geq t_1.$$

Thus, from the first equation of system (2.1), when $t \geq t_1 + h$,

$$\dot{S}(t) \geq \Lambda(t) - \Big\{ \big(\beta_1(t) + \beta_2(t) + \beta_3(t)\big)\Big(\big(\frac{\Lambda}{\mu - \xi}\big)^u + \epsilon\Big) + \mu(t) \Big\} S(t)$$

$$\Rightarrow \liminf_{t \to \infty} S(t) \geq \Big\{ \frac{\Lambda}{(\beta_1 + \beta_2 + \beta_3)((\frac{\Lambda}{\mu - \xi})^u + \epsilon) + \mu} \Big\}^l.$$

Since $\epsilon > 0$ can be made arbitrarily small, the result of this proposition is valid. $\square$

Proposition 3. *Assume that* $R_0 > 1$, *then for any solution* $(S(t), I(t), J(t), A(t))$ *of* (2.1) *with initial conditions* (3.1) *we have*

$$\liminf_{t \to \infty} I(t) \geq \alpha e^{-(\mu - \xi + p_1)^u(h + \rho)} \equiv v_2 > 0,$$

where $\alpha > 0$ *and* $\rho > 0$ *will be given in the proof.*

Proof. Since $R_0 > 1$, and it is obvious that

$$\frac{\Lambda^l}{G} \to \frac{\Lambda^l}{\mu^u} \text{ as } \alpha \to 0, \text{ where } G = \mu^u + \alpha(\beta_1^u + c_1\beta_2^u + c_2\beta_3^u),$$

$$c_1 = \Big(\frac{p_1}{\mu + p_2}\Big)^u \text{ and } c_2 = \Big(\frac{p_2}{\mu_1}\Big)^u c_1, \tag{3.2}$$

then there exists two positive constants α and ρ such that

$$\frac{\Lambda^l}{G}\Big[1 - \exp\{-G\rho\}\Big]\frac{\beta_1^l}{(\mu - \xi + p_1)^u} > 1. \tag{3.3}$$

Let us consider the following differential function $V(t)$,

$$V(t) = I(t) + \int_0^h \int_{t-s}^t \Big\{ \beta_1(u + s)I(u) + \beta_2(u + s)J(u)$$

$$+ \beta_3(u + s)A(u) \Big\} S(u + s)\, du d\eta(s).$$

The derivative of $V(t)$ along solution of (2.1) is

$$\dot{V}(t) = \left[\int_0^h \beta_1(t+s)S(t+s)\,d\eta(s) - (\mu(t) - \xi(t) + p_1(t)) \right] I(t)$$

$$+ \int_0^h \left\{ J(t)\beta_2(t+s) + A(t)\beta_3(t+s) \right\} S(t+s)\,d\eta(s) + \xi(t)\big(J(t) + A(t) \big)$$

$$\geq \left[\beta_1^l \int_0^h S(t+s)\,d\eta(s) - (\mu - \xi + p_1)^u \right] I(t). \tag{3.4}$$

We claim that it is impossible that $I(t) \leq \alpha$, $\forall t \geq t'$ (t' is any nonnegative constant). Suppose the contrary, then from the third and fourth equations of (2.1), we have, $\exists t_1 > t'$, such that $J(t) \leq c_1\alpha$, $A(t) \leq c_2\alpha$, $\forall t \geq t_1$, where c_1, c_2 are given in (3.2). Therefore, as $t \geq t_1 + h$,

$$\dot{S}(t) \geq \Lambda(t) - \big(\mu(t) + \alpha(\beta_1^u + c_1\beta_2^u + c_2\beta_3^u) \big) S(t) \geq \Lambda^l - GS(t),$$

where G is given in (3.2). For $t > t_1 + h$, integrating the above inequality from $t_1 + h$ to t, we obtain

$$S(t) \geq S(t_1 + h) \exp \left(\int_t^{t_1+h} G\,ds \right) + \int_{t_1+h}^t \Lambda^l \exp \left(\int_t^s G\,d\theta \right) ds$$

$$\geq \Big(\frac{\Lambda^l}{G} \Big) \frac{\int_{t_1+h}^t G \exp(\int_0^s G\,d\theta)\,ds}{\exp(\int_0^t G\,d\theta)}.$$

Hence, $S(t) \geq \Big(\dfrac{\Lambda^l}{G} \Big) \Big[1 - \exp\big\{ - G(t - t_1 - h) \big\} \Big]$. Therefore,

$$S(t) \geq \Big(\frac{\Lambda^l}{G} \Big) \Big[1 - \exp\big\{ - G\rho \big\} \Big] \equiv S^\Delta, \quad \forall\, t \geq t_1 + h + \rho \equiv t_2. \tag{3.5}$$

From (3.4) and (3.5), we have

$$\dot{V}(t) \geq \big(\mu - \xi + p_1 \big)^u \Big[\frac{\beta_1^l S^\Delta}{(\mu - \xi + p_1)^u} - 1 \Big] I(t), \quad \forall\, t \geq t_2. \tag{3.6}$$

Let us take $\underline{i} = \min_{t_2 \leq t \leq t_2 + h} I(t)$. Next we shall prove that $I(t) \geq \underline{i}$, $\forall t \geq t_2$. Suppose that it is not true, then $\exists T \geq 0$, such that $I(t) \geq \underline{i}$, for all $t_2 \leq t \leq t_2 + h + T$, $I(t_2 + h + T) = \underline{i}$ and $\dot{I}(t_2 + h + T) \leq 0$. On the other hand, by the second equation of (2.1), as $t = t_2 + h + T$,

$$\dot{I}(t) \geq \beta_1(t)S(t) \int_0^h I(t-s)\,d\eta(s) - \big(\mu(t) - \xi(t) + p_1(t) \big) I(t)$$

$$\geq \big\{ \beta_1^l S^\Delta - (\mu - \xi + p_1)^u \big\} \underline{i} = \big(\mu - \xi + p_1 \big)^u \Big[\frac{\beta_1^l S^\Delta}{(\mu - \xi + p_1)^u} - 1 \Big] \underline{i} > 0,$$

since from (3.3), we have $\beta_1^l S^\Delta / (\mu - \xi + p_1)^u > 1$. This is a contradiction. Hence, $I(t) \geq \underline{i}$, $\forall t \geq t_2$. Consequently from (3.6), we have

$$\dot{V}(t) \geq \big(\mu - \xi + p_1 \big)^u \Big[\frac{\beta_1^l S^\Delta}{(\mu - \xi + p_1)^u} - 1 \Big] \underline{i} > 0, \quad \forall\, t \geq t_2,$$

which implies $V(t) \to +\infty$ as $t \to +\infty$. From Proposition 1, $V(t)$ is bounded. This is a contradiction. Hence, the claim is proved.

From this claim, we will discuss the following two possibilities:

(i) $I(t) \geq \alpha$ for all large t.

(ii) $I(t)$ oscillates about α for all large t.

Finally, we will show that $I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$ for sufficiently large t. Evidently, we only need to consider the case (ii). Let t_1 and t_2 be sufficiently large times satisfying:

$$I(t_1) = I(t_2) = \alpha, \quad I(t) < \alpha \quad \text{as } t \in (t_1, t_2).$$

If $t_2 - t_1 \leq h + \rho$, since $\dot{I}(t) \geq -(\mu - \xi + p_1)^u I(t)$ and $I(t_1) = \alpha$ which implies $I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$, $\forall t \in [t_1, t_2]$. If $t_2 - t_1 > h + \rho$, then it is obvious that $I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$, $\forall t \in [t_1, t_1 + h + \rho]$. By (3.5), we have $S(t) \geq S^\Delta$, $\forall t \in [t_1+h+\rho, t_2]$. Thus, proceeding exactly as the proof of the above claim, we see that $I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$, $\forall t \in [t_1+h+\rho, t_2]$. If it is not true, then there exists a $T^* \geq 0$ such that $I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$, $\forall t \in [t_1, t_1 + h + \rho + T^*]$, $I(t_1 + h + \rho + T^*) = \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$ and $\dot{I}(t_1 + h + \rho + T^*) \leq 0$. Using the second equation of system (2.1), as $t = t_1 + h + \rho + T^*$, we have

$$\dot{I}(t) \geq \beta_1(t)S(t)\int_0^h I(t-s)\,d\eta(s) - \big(\mu(t) - \xi(t) + p_1(t)\big)I(t)$$

$$\geq \Big\{\beta_1^l S^\Delta - (\mu - \xi + p_1)^u\Big\}\alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$$

$$= \big(\mu - \xi + p_1\big)^u\Big[\frac{\beta_1^l S^\Delta}{(\mu - \xi + p_1)^u} - 1\Big]\alpha e^{-(\mu-\xi+p_1)^u(h+\rho)} > 0,$$

since from (3.3), we have $\beta_1^l S^\Delta/(\mu - \xi + p_1)^u > 1$. This is a contradiction. Therefore, $I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)}$, $\forall\, t \in [t_1, t_2]$. Hence,

$$\liminf_{t\to\infty} I(t) \geq \alpha e^{-(\mu-\xi+p_1)^u(h+\rho)} \equiv v_2 > 0.$$

This completes the proof of Proposition 3 $\square$

Proposition 4. *Assume that $R_0 > 1$, then for any solution $(S(t), I(t), J(t), A(t))$ of (2.1) with initial conditions (3.1) we have*

$$\liminf_{t\to\infty} J(t) \geq \Big\{\frac{p_1}{\mu + p_2}\Big\}^l v_2 \equiv v_3 > 0,$$

where $v_2 > 0$ is given in the Proposition 3.

Proof. From the third equation of (2.1) and by Propositions 3, the required result follows. $\square$

Proposition 5. *Assume that $R_0 > 1$, then for any solution $(S(t), I(t), J(t), A(t))$ of (2.1) with initial conditions (3.1) we have*

$$\liminf_{t\to\infty} A(t) \geq \left(\frac{p_2}{\mu_1}\right)^l v_3 \equiv v_4 > 0,$$

where $v_3 > 0$ is given in the Proposition 4.

Proof. From the fourth equation of (2.1) and by Propositions 4, the result follows. □

Thus, the system (2.1) with initial conditions (3.1) is permanent provided

$$R_0 = \frac{\beta_1^l}{(\mu - \xi + p_1)^u} \left(\frac{\Lambda^l}{\mu^u}\right) > 1.$$

Next, we shall use the following lemma to discuss the extinction of the disease.

Lemma 1. *Consider an autonomous delay differential equation*

$$\dot{x}(t) = a_1 \int_0^h x(t-s)\, d\eta(s) - a_2 x(t), \tag{3.7}$$

where a_1, a_2 are two constants. If $0 \leq a_1 < a_2$, then for any solution $x(t)$ with initial condition $\varphi(\theta) \geq 0$, $\theta \in [-h, 0]$, we have $\lim_{t\to\infty} x(t) = 0$.

Proof. Let us define the following Lyapunov functional:

$$V(t) = \frac{x^2(t)}{2} + \frac{a_1}{2} \int_0^h \int_{t-s}^t x^2(u)\, du\, d\eta(s).$$

Then the time derivative along system (3.7) is given by

$$\dot{V}(t) = a_1 \int_0^h x(t)x(t-s)\, d\eta(s) + \frac{a_1}{2} \int_0^h \left\{x^2(t) - x^2(t-s)\right\} d\eta(s) - a_2 x^2(t)$$

$$= -\frac{a_1}{2} \int_0^h \left\{x(t) - x(t-s)\right\}^2 d\eta(s) + a_1 x^2(t) - a_2 x^2(t)$$

$$\leq -(a_2 - a_1)x^2(t) \ \Rightarrow \ \lim_{t\to\infty} x(t) = 0.$$

□

Theorem 2. *If*

$$R^* = \frac{\beta_1^u}{(\mu - \xi)^l} \left(\frac{\Lambda}{\mu - \xi}\right)^u < 1, \tag{3.8}$$

then $\lim_{t\to\infty} \{I(t) + J(t) + A(t)\} = 0$, i.e. the disease in system (2.1) will extinct.

Proof. Let $U(t) = I(t) + J(t) + A(t)$. Adding the second, third and fourth equations of system (2.1) and assuming $\beta_2(t), \beta_3(t) \le \beta_1(t)$, $\mu(t) \le \mu_1(t)$, we have

$$\frac{dU(t)}{dt} \le \beta_1(t)S(t)\int_0^h U(t-s)\,d\eta(s) - \Big(\mu(t) - \xi(t)\Big)U(t). \qquad (3.9)$$

By condition (3.8), there exists a small enough $\epsilon > 0$ such that:

$$\frac{\beta_1^u}{(\mu - \xi)^l}\Big\{\Big(\frac{\Lambda}{\mu - \xi}\Big)^u + \epsilon\Big\} < 1.$$

By Proposition 1, for any given $\epsilon > 0$ there exists a $t_1 > 0$ such that:

$$S(t) \le \Big(\frac{\Lambda}{\mu - \xi}\Big)^u + \epsilon, \text{ as } t \ge t_1.$$

Therefore, it follows from (3.9) that:

$$\frac{dU(t)}{dt} \le \Big(\mu - \xi\Big)^l\Big[\frac{\beta_1^u}{(\mu - \xi)^l}\Big\{\Big(\frac{\Lambda}{\mu - \xi}\Big)^u + \epsilon\Big\}\int_0^h U(t-s)\,d\eta(s) - U(t)\Big], \ \forall\, t \ge t_1.$$

Using Lemma 1 and the comparison theorem of functional differential equations, we have

$$\lim_{t\to\infty} U(t) = \lim_{t\to\infty}\big\{I(t) + J(t) + A(t)\big\} = 0.$$

□

From (3.8) we conclude that the spread of the HIV infection should be controlled by effective protections to reduce the values of $\beta_1(t)$ (horizontal transmission rate function of infection when susceptible humans contact with infective in the asymptomatic stage), $\xi(t)$ (vertical transmission rate function) and thereby to decrease R^*. If the rate of migration or recruitment is restricted into susceptible community, the spread of the disease can also be kept under control by reducing $\Lambda(t)$ and thereby decreasing R^*.

4 Global Asymptotic Stability

In this section, we derive sufficient conditions for global asymptotic stability of system (2.1) with initial conditions (3.1). First, we state a definition of global asymptotic stability of solutions of system (2.1).

DEFINITION 2. System (2.1) with initial conditions (3.1) is said to be globally asymptotically stable if

$$\lim_{t\to\infty}\big|S_1(t) - S_2(t)\big| = 0, \quad \lim_{t\to\infty}\big|I_1(t) - I_2(t)\big| = 0,$$
$$\lim_{t\to\infty}\big|J_1(t) - J_2(t)\big| = 0, \quad \lim_{t\to\infty}\big|A_1(t) - A_2(t)\big| = 0,$$

hold for any two solutions $(S_1(t), I_1(t), J_1(t), A_1(t))$ and $(S_2(t), I_2(t), J_2(t), A_2(t))$ of (2.1) with initial conditions of type (3.1).

Assume that $(S(t), I(t), J(t), A(t))$ is a solution of (2.1). By the uniform boundedness of solutions of (2.1), there is an $L > 0$ (in fact, $L = (\frac{\Lambda}{\mu-\xi})^u + \epsilon$ where $\epsilon > 0$ can be made arbitrarily small) independent of initial conditions (3.1) such that $0 \leq S(t) \leq L$, $0 \leq I(t) \leq L$, $0 \leq J(t) \leq L$, $0 \leq A(t) \leq L$, for large enough t. Without a loss of generality, we may assume that these inequalities are satisfied for $\forall t \geq 0$.

Theorem 3. *If there exist $k_1 > 0, k_2 > 0$, $k_3 > 0$, $k_4 > 0$ such that the functions $B_i(t)$ $(i = 1, 2, 3, 4)$ are nonnegative on $[0, \infty)$ and for any interval sequence $\{[a_i, b_i]\}_1^\infty$, $[a_i, b_i] \cap [a_j, b_j] = \phi$ and $b_i - a_i = b_j - a_j > 0$, for all $i, j = 1, 2, \dots$ and $i \neq j$, one has $\sum_{k=1}^{\infty} \int_{a_k}^{b_k} B_i(t)\, dt = \infty$, then system (2.1) with initial conditions (3.1) is globally asymptotically stable. Here,*

$$B_1(t) = k_1\mu(t) - k_2 L(\beta_1(t) + \beta_2(t) + \beta_3(t)), \tag{4.1}$$

$$B_2(t) = k_2\mu(t) + (k_2 - k_3)p_1(t) - k_2\xi(t) - (k_1 + k_2)L \int_0^h \beta_1(t+s)\, d\eta(s),$$

$$B_3(t) = k_3\mu(t) + (k_3 - k_4)p_2(t) - k_2\xi(t) - (k_1 + k_2)L \int_0^h \beta_2(t+s)\, d\eta(s),$$

$$B_4(t) = k_4\mu_1(t) - k_2\xi(t) - (k_1 + k_2)L \int_0^h \beta_3(t+s)\, d\eta(s).$$

Proof. Assume that $(S_1(t), I_1(t), J_1(t), A_1(t))$ and $(S_2(t), I_2(t), J_2(t), A_2(t))$ are any two solutions of system (2.1) with initial conditions of type (3.1). Define $V_1(t) = |S_1(t) - S_2(t)|$. Then the right-upper derivative of $V_1(t)$ along the solution of system (2.1) and (3.1) is given by

$$
\begin{aligned}
D^+V_1(t) = \operatorname{sgn}(S_1(t) - S_2(t)) \Big\{ &- \beta_1(t)(S_1(t) - S_2(t)) \int_0^h I_1(t-s)\, d\eta(s) \\
&+ \beta_1(t)S_2(t) \int_0^h (I_2(t-s) - I_1(t-s))\, d\eta(s) - \beta_2(t)(S_1(t) - S_2(t)) \\
&\times \int_0^h J_1(t-s)\, d\eta(s) + \beta_2(t)S_2(t) \int_0^h (J_2(t-s) - J_1(t-s))\, d\eta(s) \\
&- \beta_3(t)(S_1(t) - S_2(t)) \int_0^h A_1(t-s)\, d\eta(s) + \beta_3(t)S_2(t) \\
&\times \int_0^h (A_2(t-s) - A_1(t-s))\, d\eta(s) - \mu(t)(S_1(t) - S_2(t)) \Big\} \\
\leq &-\beta_1(t)|S_1(t) - S_2(t)| \int_0^h I_1(t-s)\, d\eta(s) + \beta_1(t)S_2(t) \\
&\times \int_0^h |I_1(t-s) - I_2(t-s)|\, d\eta(s) - \beta_2(t)|S_1(t) - S_2(t)| \int_0^h J_1(t-s)\, d\eta(s) \\
&+ \beta_2(t)S_2(t) \int_0^h |J_1(t-s) - J_2(t-s)|\, d\eta(s)
\end{aligned}
$$

$$- \beta_3(t)|S_1(t) - S_2(t)| \int_0^h A_1(t-s)d\eta(s)$$

$$+ \beta_3(t)S_2(t) \int_0^h |A_1(t-s) - A_2(t-s)|d\eta(s) - \mu(t)|S_1(t) - S_2(t)|,$$

then it follows that

$$D^+V_1(t) \le -\mu(t)|S_1(t) - S_2(t)| + \beta_1(t)L \int_0^h |I_1(t-s) - I_2(t-s)|d\eta(s) \qquad (4.2)$$

$$+ \beta_2(t)L \int_0^h |J_1(t-s) - J_2(t-s)|d\eta(s) + \beta_3(t)L \int_0^h |A_1(t-s) - A_2(t-s)|d\eta(s).$$

Let us define $V_2(t) = |I_1(t) - I_2(t)|$. Calculating the right-upper derivative of $V_2(t)$ along the solution of system (2.1) and (3.1), we have

$$D^+V_2(t) = \mathrm{sgn}(I_1(t) - I_2(t))\{\beta_1(t)(S_1(t) - S_2(t))\int_0^h I_1(t-s)\,d\eta(s) \qquad (4.3)$$

$$+ \beta_1(t)S_2(t)\int_0^h (I_1(t-s) - I_2(t-s))d\eta(s) + \beta_2(t)(S_1(t) - S_2(t))$$

$$\times \int_0^h J_1(t-s)\,d\eta(s) + \beta_2(t)S_2(t)\int_0^h \left(J_1(t-s) - J_2(t-s)\right)d\eta(s)$$

$$+ \beta_3(t)\left(S_1(t) - S_2(t)\right)\int_0^h A_1(t-s)\,d\eta(s) + \beta_3(t)S_2(t)$$

$$\times \int_0^h \left(A_1(t-s) - A_2(t-s)\right)d\eta(s) - \left(\mu(t) - \xi(t) + p_1(t)\right)\left(I_1(t) - I_2(t)\right)$$

$$+ \xi(t)(J_1(t) - J_2(t)) + \xi(t)(A_1(t) - A_2(t))\},$$

then we get

$$D^+V_2(t) \le \beta_1(t)L|S_1(t) - S_2(t)| + \beta_1(t)L \int_0^h |I_1(t-s) - I_2(t-s)|d\eta(s)$$

$$+ \beta_2(t)L|S_1(t) - S_2(t)| + \beta_2(t)L \int_0^h |J_1(t-s) - J_2(t-s)|d\eta(s)$$

$$+ \beta_3(t)L|S_1(t) - S_2(t)| + \beta_3(t)L \int_0^h |A_1(t-s) - A_2(t-s)|d\eta(s)$$

$$- (\mu(t) - \xi(t) + p_1(t))|I_1(t) - I_2(t)| + \xi(t)|J_1(t) - J_2(t)| + \xi(t)|A_1(t) - A_2(t)|.$$

Define $V_3(t) = |J_1(t) - J_2(t)|$. Calculating the right-upper derivative of $V_3(t)$ along the solution of system (2.1) and (3.1), we have

$$D^+V_3(t) = \mathrm{sgn}(J_1(t) - J_2(t))\{p_1(t)(I_1(t) - I_2(t)) - (\mu(t) + p_2(t))(J_1(t) - J_2(t))\}$$
$$D^+V_3(t) \le p_1(t)|I_1(t) - I_2(t)| - (\mu(t) + p_2(t))|J_1(t) - J_2(t)|.$$

Define $V_4(t) = |A_1(t) - A_2(t)|$. Calculating the right-upper derivative of $V_4(t)$ along the solution of system (2.1) and (3.1), we have

$$D^+V_4(t) \le p_2(t)|J_1(t) - J_2(t)| - \mu_1(t)|A_1(t) - A_2(t)|. \qquad (4.4)$$

Define $V_5(t)$ as

$$V_5(t) = \int_0^h \int_{t-s}^t \beta_1(u+s)L\big|I_1(u) - I_2(u)\big|du\, d\eta(s) + \int_0^h \int_{t-s}^t \beta_2(u+s)L$$

$$\times \big|J_1(u) - J_2(u)\big|du\, d\eta(s) + \int_0^h \int_{t-s}^t \beta_3(u+s)L\big|A_1(u) - A_2(u)\big|du\, d\eta(s).$$

The right-upper derivative of $V_5(t)$ along the solution of system (2.1) and (3.1) is given below:

$$D^+V_5(t) = L\big|I_1(t) - I_2(t)\big| \int_0^h \beta_1(t+s)d\eta(s) - \beta_1(t)L \int_0^h \big|I_1(t-s) - I_2(t-s)\big|d\eta(s)$$

$$+ L\big|J_1(t) - J_2(t)\big| \int_0^h \beta_2(t+s)d\eta(s) - \beta_2(t)L \int_0^h \big|J_1(t-s) - J_2(t-s)\big|d\eta(s)$$

$$+ L\big|A_1(t) - A_2(t)\big| \int_0^h \beta_3(t+s)d\eta(s) - \beta_3(t)L \int_0^h \big|A_1(t-s) - A_2(t-s)\big|d\eta(s).$$
(4.5)

Let $V(t) = k_1 V_1(t) + k_2 V_2(t) + k_3 V_3(t) + k_4 V_4(t) + (k_1 + k_2)V_5(t)$, then by using (4.2)–(4.5), we have

$$D^+V(t) \le -B_1(t)\big|S_1(t) - S_2(t)\big| - B_2(t)\big|I_1(t) - I_2(t)\big|$$
$$- B_3(t)\big|J_1(t) - J_2(t)\big| - B_4(t)\big|A_1(t) - A_2(t)\big|, \quad \forall\, t \ge h,$$
(4.6)

where $B_i(t)$, $(i = 1, 2, 3, 4)$ are defined in (4.1). Integrating (4.7) from h to t, we get

$$\int_h^t \big\{B_1(t)\big|S_1(t) - S_2(t)\big| + B_2(t)\big|I_1(t) - I_2(t)\big| + B_3(t)\big|J_1(t) - J_2(t)\big|$$
$$+ B_4(t)\big|A_1(t) - A_2(t)\big|\big\}dt \le V(h) - V(t) < \infty.$$
(4.7)

By assumptions about $B_i(t)$, $(i = 1, 2, 3, 4)$ and the boundedness of $(S_1(t),$ $I_1(t), J_1(t), A_1(t))$ and $(S_2(t), I_2(t), J_2(t), A_2(t))$ on $[0, \infty)$, we obtain from system (2.1) that $\big|S_1(t) - S_2(t)\big|$, $\big|I_1(t) - I_2(t)\big|$, $\big|J_1(t) - J_2(t)\big|$ and $\big|A_1(t) - A_2(t)\big|$ are bounded and uniformly continuous on $[0, \infty)$. It follows from (4.7) that,

$$\lim_{t\to\infty} \big|S_1(t) - S_2(t)\big| = 0, \quad \lim_{t\to\infty} \big|I_1(t) - I_2(t)\big| = 0,$$
$$\lim_{t\to\infty} \big|J_1(t) - J_2(t)\big| = 0, \quad \lim_{t\to\infty} \big|A_1(t) - A_2(t)\big| = 0.$$

This shows that system (2.1) with initial conditions (3.1) is globally asymptotically stable. □

Corollary 1. If there exist $k_1 > 0$, $k_2 > 0$, $k_3 > 0$ and $k_4 > 0$ such that $\liminf_{t\to\infty} B_i(t) > 0$, for $i = 1, 2, 3, 4$, where $B_i(t)$ are given by (4.1) then system (2.1) with initial conditions (3.1) is globally asymptotically stable.

We observe that the lower values of $\beta_1(t)$ (horizontal transmission rate function of infection when susceptible humans contact with infective in the asymptomatic stage), $\xi(t)$ (vertical transmission rate function) and $\Lambda(t)$ (recruitment rate function of the susceptible) are leading to make $B_i(t) > 0$ $(i = 1, 2, 3, 4)$ which also keep the spread of the epidemic under control. The results of the Theorem 3 and Corollary 1 indicate that these parametric functions and also time delay have an effect on the global asymptotic stability, which may rule out any complicated behaviour (e.g. limit cycles, chaos) of the proposed model.

From our everyday experience we know that the biological and environmental parameters are subject to fluctuations in time, the effects of a periodically varying environment have an important selective forces on systems in a fluctuating environment. To investigate this kind of phenomenon, in the model, the coefficients should be periodic functions of time. Let us state a theorem related to this.

Theorem 4. [37] *If system* (2.1) *is ψ-periodic and there are positive constants v_i and M_i $(i = 1, 2, 3, 4)$ such that for any solution $(S(t), I(t), J(t), A(t))$ of* (2.1) *with initial conditions* (3.1), *the following estimates*

$$v_1 \leq \liminf_{t \to \infty} S(t) \leq \limsup_{t \to \infty} S(t) \leq M_1, \quad v_2 \leq \liminf_{t \to \infty} I(t) \leq \limsup_{t \to \infty} I(t) \leq M_2,$$

$$v_3 \leq \liminf_{t \to \infty} J(t) \leq \limsup_{t \to \infty} J(t) \leq M_3, \quad v_4 \leq \liminf_{t \to \infty} A(t) \leq \limsup_{t \to \infty} A(t) \leq M_4$$

hold, then system (2.1) *has positive periodic solution with period ψ.*

Corollary 2. If system (2.1) is ψ-periodic and conditions in Theorems 1 and 3 are valid, then there exists a unique positive ψ-periodic solution which is globally asymptotically stable.

5 Numerical Simulation

In this section we present computer simulation of some solution of the system (2.1) using MATLAB.

Example 1. Let $\Lambda(t) = 50 + 2 \sin t$, $\beta_1(t) = 0.02 + 0.00001 \sin t$, $\beta_2(t) = \beta_3(t) = 0.001 + 0.0001 \sin t$, $\mu(t) = 0.7 + 0.2 \sin t$, $p_1(t) = p_2(t) = 0.02 + 0.002 \cos t$, $\xi(t) = 0.01 + 0.001 \sin t$, $\mu_1(t) = 0.8 + 0.2 \sin t$, $\eta(s) = \dfrac{s}{h}$, $h = \dfrac{\pi}{2}$. In this case $R_0 > 1$ and $R^* > 1$. Therefore, system (2.1) is permanent. Fig. 1, Fig. 2, Fig. 3 and Fig. 4 show trajectories of $S(t), I(t), J(t)$ and $A(t)$ respectively for different initial conditions.

Example 2. Let $\Lambda(t) = 24 + 2 \sin t$, $\beta_1(t) = 0.0015 + 0.00001 \sin t$, $\beta_2(t) = \beta_3(t) = 0.001 + 0.0001 \sin t$, $\mu(t) = 0.7 + 0.2 \sin t$, $p_1(t) = p_2(t) = 0.02 + 0.002 \cos t$, $\xi(t) = 0.01 + 0.001 \sin t$, $\mu_1(t) = 0.8 + 0.2 \sin t$, $\eta(s) = \dfrac{s}{h}$, $h = \dfrac{\pi}{2}$. In this case $R_0 < 1$ and $R^* < 1$. Therefore, system (2.1) is not permanent and the disease in system (2.1) will be going to extinction. Fig. 5, Fig. 6, Fig. 7 and Fig. 8 show trajectories of $S(t), I(t), J(t)$ and $A(t)$ respectively for different initial conditions.
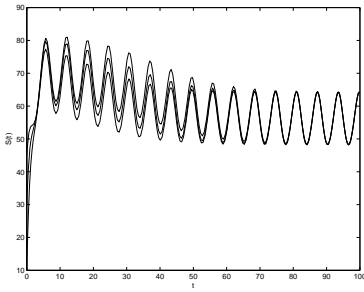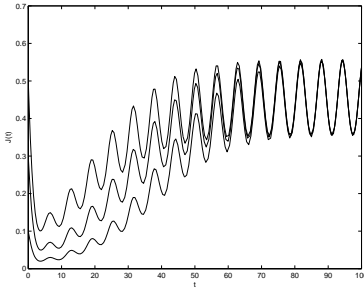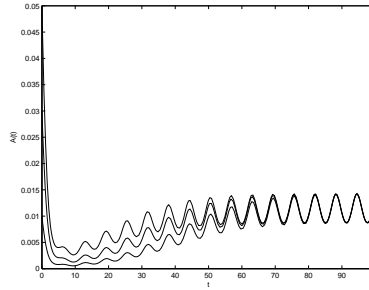
Figure 1. Trajectories of S(t) for different initial conditions.
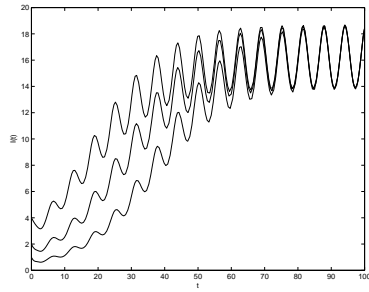
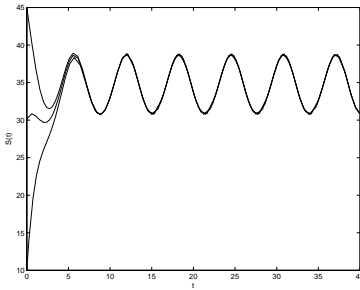**Figure 2.** Trajectories of I(t) for different initial conditions.

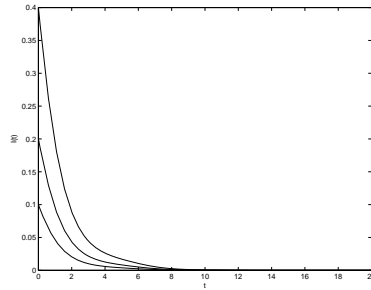**Figure 3.** Trajectories of J(t) for different initial conditions.

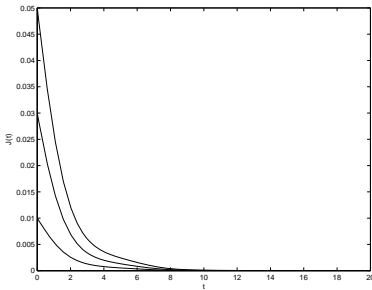**Figure 4.** Trajectories of A(t) for different initial conditions.

6 Conclusions

Research on epidemic models that incorporates time dependent biological and environmental parameters, disease related death, varying total population, and time delay is becoming one of the important areas in the mathematical theory of epidemiology. To the best of our knowledge, the research works on the nonautonomous epidemic dynamical models are very few (Thieme, [38, 39]; Herzong and Redheffer, [18]; Zhang and Teng, [43, 44]; Samanta, [35]). In this paper we have considered a nonlinear and nonautonomous stage-structured HIV/AIDS epidemic model through vertical and horizontal transmissions of infections, having two stages of the period of infection according to the developing progress of infection before AIDS would be detected, i.e., the asymptomatic and the symptomatic stages, with varying total population size and distributed time delay to become infectious (through horizontal transmission) due to intracellular delay between initial infection of a cell by HIV and the release of new virions. The infected people in the different stages have a different ability to transmit the disease. It is assumed that infective and people in full-blown AIDS group are able to produce children; the infected babies are born to increase the growth of infective (asymptomatic stage) population directly. The most basic and important questions to ask for the systems in the theory of mathematical epidemiology are the persistence, extinctions, the existence of periodic solutions, global stability, etc. (Kermark and Mckendrick, [22]; Anderson and May, [2];
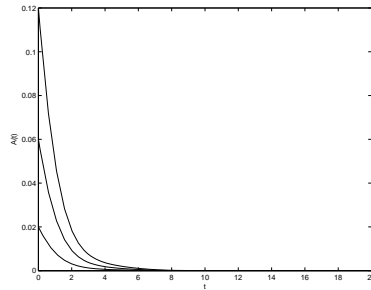
Figure 5. Trajectories of S(t) for different initial conditions.

Figure 6. Trajectories of I(t) for different initial conditions.

Figure 7. Trajectories of J(t) for different initial conditions.

Figure 8. Trajectories of A(t) for different initial conditions.

Capasso, [9]; Diekmann and Heesterbeek, [12]; Ma et al., [27, 29]; Meng et al., [31]). Here, we have established some sufficient conditions on the permanence and extinction of the disease by using inequality analytical technique.

We have obtained the explicit formula of the eventual lower bounds of infected people and introduced some new threshold values

$$R_0 = \frac{\beta_1^l}{(\mu - \xi + p_1)^u}\Big(\frac{\Lambda^l}{\mu^u}\Big), \quad R^* = \frac{\beta_1^u}{(\mu - \xi)^l}\Big(\frac{\Lambda}{\mu - \xi}\Big)^u$$

and further obtained that the disease will be permanent when $R_0 > 1$ and the disease will be going to extinct when $R^* < 1$. By Lyapunov functional method, we have also obtained some sufficient conditions for global asymptotic stability of this model. We conclude that the spread of the disease should be controlled with the help of suitable protective measures of the society to reduce the values of $\beta_1(t)$ (horizontal transmission rate function of infection when susceptible humans contact with infective in the asymptomatic stage), $\xi(t)$ (vertical transmission rate function) and $\Lambda(t)$ (recruitment rate function of the susceptible) and thereby to decrease R^*. We have observed that the time delay has no effect on the permanence of the system but it has an effect on the global asymptotic stability of this model. Our analytical results are illustrated through computer simulations. The aim of the analysis of this model is to identify the parameters of interest for further study, with a view to informing

and assisting policy-makers in targeting prevention and treatment resources for maximum effectiveness.

Here, all the coefficients in system (2.1) are time-dependent, i.e., system (2.1) is nonautonomous. Usually, such systems have not any disease-free equilibrium and endemic equilibrium. There are many methods to deal with autonomous systems, but they may not be suitable to nonautonomous systems. Therefore, it is more difficult to study the dynamical behaviour in nonautonomous case. By improving the Lyapunov functionals, we have studied global stability behaviour of system (2.1). Furthermore, by using the inequality analytical technique, we have obtained the ultimate lower bounds of the infected individuals.

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