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Analysis of a Nonautonomous HIV/AIDS Model

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Abstract. In this paper we have considered a nonlinear and nonautonomous stage-structured HIV/AIDS epidemic model with an imperfect HIV vaccine, varying total population size and distributed time delay to become infectious due to intracellular delay between initial infection of a cell by HIV and the release of new virions. 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 persons. 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. The aim of the analysis of this model is to trace the parameters of interest for further study, with a view to informing and assisting policy-maker in targeting prevention and treatment resources for maximum effectiveness.

Key words: 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. Worldwide, explosive population growth with expanding poverty and urban migration is going on, international travel and commerce are increasing, technology is changing

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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 a host of life threatening opportunistic infections, neurological disorders or unusual malignancies. It causes mortality, morbidity of millions of people and 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 occur , including 330,000 children [46]. 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 [11].

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 the presence of certain infections caused by Mycobacterium avium-intracellular, cytomegalovirus and Penicillium marneffei [32].

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 a larger scale of populations. It is well known that HIV virus has the 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 have 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 methods of prevention are based on avoiding exposure to the virus. There is a growing body of opinion that it requires an effective vaccine to curtail the global spread of HIV [17]. Several HIV vaccines are currently undergoing clinical trials [35, 52]. In 2007, HIV Vaccine Trials Network started the first large-scale HIV vaccine trials in Africa. These studies will last until 2011 and include up to 3000 participants [35]. In September 2009 it has been reported by several companies and organizations working on AIDS that two new AIDS antibodies have been discovered. These

antibodies are said to be very significant to develop a vaccine that will be working against many mutant strains of the virus [49]. Moreover, in September 2009, the results of a successful clinical trial in Thailand have been reported. The experiment involved 16,395 patients, 8197 of them were given a vaccine consisting of HIV types B and E (not C, which is most prevalent in Africa), while 8198 were given a placebo. The participants were examined for HIV every six months for a period of three years. After three years, those given the vaccine saw HIV infection rates reduced by more than thirty percent in compare with those who had been given a placebo. It gives the first successful HIV vaccine trial in history. However, these results could still be attributed to chance and the Thai study has yet to undergo peer review [5, 49]. The current expectation is that such a vaccine would be imperfect, i.e. it may be effective in some cases, but not all. It may give protection that wanes with time. The vaccine may also offer some therapeutic benefits by changing the clinical course of the disease [41].

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 [1,3,34], several refinements have been added into modelling frameworks, and specific issues have been addressed by workers [4,6,7,9,12,19,24,25,26,30,31,37,38,47,48]. According to clinical symptoms or viral load and $CD4^+\ T$ counts, 2-6 stages of infection before AIDS can be classified [24,42]. Elbasha and Gumel [16] analyzed an HIV vaccine model that considers both staged progression and transmission by AIDS patients. Gumel et al. [20] proposed an HIV vaccine model that considers possible vaccine induced bypass of primary infection and reversal from AIDS to chronic stage of infection together with staged progression and transmission by AIDS patients.

Time delays of one type or another have been considered into biological models by many researchers [8,14,18,29]. Time delay can arise for various practical reasons in epidemiology. Perelson et al. [39] 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. [22] incorporate a discrete delay to model the intracellular delay in a HIV model and show that the addition of a delay would substantially shorten the estimate for the half-life of free virus. Culshaw and Ruan [13] use 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. The nonautonomous phenomenon occurs mainly due to the seasonal variety, which makes the population to behave periodically. Since biological and environmental parameters are naturally subject to fluctuation in time, the effects of a periodically varying environment are considered as important se-

lective forces on systems in a fluctuating environment. To investigate this kind of phenomenon, in the model, the coefficients should be periodic functions, then 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 [23,40,44,45,50,51]. Therefore, the research on the nonautonomous epidemic dynamical models is also very important.

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. HIV infected individuals pass through sequential infectious stages, being highly infectious during primary infection (first few weeks of infection), having low infectivity in the asymptomatic stage (lasting many years) and becoming more infectious in the AIDS stage [20]. The whole dynamics of the spread of HIV/AIDS is too complex that we could not analyze it all at once. By considering the above facts, in this paper we have considered a nonlinear and nonautonomous stage-structured HIV/AIDS epidemic model with an imperfect HIV vaccine, varying total population size and distributed time delay to become infectious due to intracellular delay between initial infection of a cell by HIV and the release of new virions. The infected persons in the different stages have different ability of transmitting disease. It is assumed that an imperfect HIV vaccine could offer a therapeutic effect by converting vaccinees in the highly infectious AIDS stage into the less infectious asymptomatic stage. It is also assumed that the vaccine could induce a bypass of primary infection, where a proportion of vaccinated infectious individuals move straight to the asymptomatic (chronic) stage. In the proposed system all the coefficients are time-dependent, i.e., this system 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 behaviours in nonautonomous case. 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 persons with the help of inequality analytical technique. 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 system.

2. A nonautonomous HIV/AIDS epidemic model with distributed time delay

We consider a nonautonomous dynamical model of diseases that spread by HIV with distributed time delay which satisfies the following assumptions:

The underlying human population being studied is assumed to be small, high-risk subset of a larger population. It is assumed that the larger population is relatively free of HIV and provides a variable source of uninfected individuals entering the high-risk population. The model monitors the temporal dynamics of the high-risk population which is divided into the populations of unvac-

cinated ($S(t)$) and vaccinated ($J(t)$) susceptible individuals, HIV-infected individuals in primary ($I_1(t)$), secondary ($I_2(t)$) and AIDS ($I_3(t)$) stages of infection. The total high-risk population is $N(t) = S(t) + J(t) + I_1(t) + I_2(t) + I_3(t)$.

The unvaccinated susceptible population ($S(t)$) is increased by the recruitment of uninfected sexually active individuals from the larger embedding population (at a rate $\Lambda(t)$) and by waning of vaccinated immunity (at a per capita rate $\nu(t)$). The population is decreased by infection, which may be acquired through horizontal transfer from infected individuals in any of the three infected classes, by vaccination (at a per capita rate $\xi(t)$) and by natural death (at a per capita rate $\mu(t)$). The natural death rate also includes the rate at which individuals leave the high-risk population due to migration or other reasons not directly related to HIV infection.

The population of vaccinated susceptible individuals ($J(t)$) is generated by the vaccination of unvaccinated susceptible individuals (at the per capita rate $\xi(t)$) and diminished by infection, vaccine waning (at the per capita rate $\nu(t)$) and natural death rate (at the per capita rate $\mu(t)$). It is further assumed that a proportion ($p(t)$) of vaccinated infectious individuals move straight to the secondary infectious stage (by bypassing the primary infectious stage).

The population of individuals in the primary infectious stage ($I_1(t)$) is generated by the infection of susceptible individuals and decreased by progression to the secondary infectious stage (at a per capita rate $\sigma_1(t)$) and natural death (at the per capita rate $\mu(t)$).

The population of individuals in the secondary infectious stage (asymptomatic stage) ($I_2(t)$) is generated by the infection of some vaccinated susceptible individuals (proportion $p(t)$), the progression of individuals in the primary infectious stage (at the per capita rate $\sigma_1(t)$) and through vaccine-induced conversion of individuals in the AIDS stage to the asymptomatic stage (at the per capita rate $\eta(t)$). The secondary infectious stage is diminished by progression to the AIDS stage (at a per capita rate $\sigma_2(t)$) and natural death (at the per capita rate $\mu(t)$).

The population of individuals in the AIDS stage of infection ($I_3(t)$) is generated by the progression to AIDS class from the secondary infectious stage (at the per capita rate $\sigma_2(t)$). This population is diminished by the vaccine-induced therapeutic effect (at the per capita rate $\eta(t)$), natural death (at the per capita rate $\mu(t)$) and disease-induced death (at a per capita rate $\sigma_3(t)$).

Thus, a nonautonomous dynamical model of diseases that spread by HIV infection with distributed time delay can be written as:

$$\frac{dS(t)}{dt} = \Lambda(t) - \{\beta_1(t)\int_0^h I_1(t-s)d\omega(s) + \beta_2(t)\int_0^h I_2(t-s)d\omega(s)$$

$$+\beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}S(t) - (\xi(t)+\mu(t))S(t) + \nu(t)J(t),$$

$$\frac{dJ(t)}{dt} = \xi(t)S(t) - k(t)\{\beta_1(t)\int_0^h I_1(t-s)d\omega(s) + \beta_2(t)\int_0^h I_2(t-s)d\omega(s)$$

$$+\beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}J(t) - (\nu(t)+\mu(t))J(t),$$

$$\frac{dI_1(t)}{dt} = \{\beta_1(t)\int_0^h I_1(t-s)d\omega(s) + \beta_2(t)\int_0^h I_2(t-s)d\omega(s)$$

$$+\beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}[S(t)+(1-p(t))k(t)J(t)] - (\sigma_1(t)+\mu(t))I_1(t),$$

$$\frac{dI_2(t)}{dt} = p(t)k(t)\{\beta_1(t)\int_0^h I_1(t-s)d\omega(s) + \beta_2(t)\int_0^h I_2(t-s)d\omega(s) \tag{2.1}$$

$$+\beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}J(t) + \sigma_1(t)I_1(t) + \eta(t)I_3(t) - (\sigma_2(t)+\mu(t))I_2(t),$$

$$\frac{dI_3(t)}{dt} = \sigma_2(t)I_2(t) - \eta(t)I_3(t) - (\sigma_3(t)+\mu(t))I_3(t).$$

Here $N(t) = S(t) + J(t) + I_1(t) + I_2(t) + I_3(t)$ denotes the total number of high-risk human population at time t; $S(t), J(t), I_1(t), I_2(t), I_3(t)$ are the densities (or fractions) of the populations of unvaccinated susceptible individuals, vaccinated susceptible individuals, HIV-infected individuals in primary stage of infection, HIV-infected individuals in secondary stage of infection and AIDS stage of infection respectively at time t.

The quantities $\Lambda(t), \mu(t), \xi(t), \nu(t), \beta_1(t), \beta_2(t), \beta_3(t), k(t), p(t), \sigma_1(t), \sigma_2(t), \sigma_3(t), \eta(t)$ are:

$\Lambda(t)$: The recruitment rate function of unvaccinated susceptible population from the larger embedding population.

$\mu(t)$: The per capita natural death rate function.

$\xi(t)$: The per capita rate function at which unvaccinated susceptible individuals move into vaccinated class on account of vaccination.

$\nu(t)$: The per capita rate function at which individuals of vaccinated susceptible class are moved into unvaccinated susceptible class due to the wane of the vaccine with time.

$\beta_1(t)$: The transmission rate function of infection when unvaccinated susceptible individuals contact with infective in the primary infectious stage and the rate of transmission is of the form:

$$\beta_1(t)S(t)\int_0^h I_1(t-s)d\omega(s).$$

$\beta_2(t)$: The transmission rate function of infection when unvaccinated susceptible individuals contact with infective in the secondary infectious stage (asymptomatic stage) and the rate of transmission is of the form:

$$\beta_2(t)S(t)\int_0^h I_2(t-s)d\omega(s).$$

$\beta_3(t)$: The transmission rate function of infection when unvaccinated susceptible individuals contact with infective in the AIDS stage and the rate of transmission is of the form:

$$\beta_3(t)S(t)\int_0^h I_3(t-s)d\omega(s).$$

$k(t)$: $1-k(t)$ $(0 < k(t) < 1)$ accounts for the efficacy of the vaccine-induced protection against infection (for a vaccine that offers hundred percent protection, $k(t) = 0$; thus in reality $k(t) > 0$) [20]. The rate of transmission of infection when vaccinated susceptible individuals contact with infective in the primary infectious stage is of the form:

$$k(t)\beta_1(t)J(t)\int_0^h I_1(t-s)d\omega(s).$$

Similarly, the rates of transmission of infection when vaccinated susceptible individuals contact with infective in the secondary infectious stage and AIDS stage are respectively of the forms:

$$k(t)\beta_2(t)J(t)\int_0^h I_2(t-s)d\omega(s), \text{ and } k(t)\beta_3(t)J(t)\int_0^h I_3(t-s)d\omega(s).$$

Here we assume that the reduced infectivity of infected individuals in the secondary infection stage (due to their low viral load) and also we assume that the reduced infectivity of infected individuals in the AIDS stage due to stringent screening measures. Hence $\beta_2(t), \beta_3(t) \leq \beta_1(t)$. It is also assumed that there is a time lag due to intracellular delay between initial infection of a cell by HIV and the release of new virions. The nonnegative constant h is the time delay. The function $\omega(s) : [0, h] \to [0, \infty)$ is nondecreasing and has bounded variation such that:

$$\int_0^h d\omega(s) = \omega(h) - \omega(0) = 1.$$

$p(t)$: The proportion rate function at which vaccinated infectious individuals move straight to the secondary infectious stage (by bypassing the primary infectious stage) [20]. It is assumed that $0 < p(t) < 1$.

$\sigma_1(t)$: The per capita progression rate function to the secondary infectious stage from the primary infectious class.

$\sigma_2(t)$: The per capita progression rate function to the AIDS stage from the secondary infectious class.

$\sigma_3(t)$: The per capita additional death rate function in the AIDS class inflicted by disease.

$\eta(t)$: The vaccine-induced per capita conversion rate function of individuals in the AIDS stage to the asymptomatic stage (secondary infectious stage).

3. Permanence and extinction

In this section, we first introduce the following assumptions for system (2.1): functions $\Lambda(t), \mu(t), \xi(t), \nu(t), \beta_1(t), \beta_2(t), \beta_3(t), k(t)(< 1), p(t)(< 1), \sigma_1(t), \sigma_2(t), \sigma_3(t), \eta(t)$ are positive continuous bounded and have positive lower bounds. It is assumed that $\beta_2(t), \beta_3(t) \leq \beta_1(t)$ [20].

The initial conditions of (2.1) are given as

$$S(\theta) = \varphi_1(\theta),\ J(\theta) = \varphi_2(\theta),\ I_1(\theta) = \varphi_3(\theta),\ I_2(\theta) = \varphi_4(\theta),\ I_3(\theta) = \varphi_5(\theta),\ -h \leq \theta \leq 0, \tag{3.1}$$

where $\varphi = (\varphi_1, \varphi_2, \varphi_3, \varphi_4, \varphi_5) \in C$ such that $\varphi_i(\theta) \geq 0$ $(i = 1, 2, 3, 4, 5),\ \forall\ \theta \in [-h, 0]$, and C denotes the Banach space $C([-h, 0], \mathbb{R}^5)$ of continuous functions mapping the interval $[-h, 0]$ into $\mathbb{R}^5$ and denote the norm of an element φ in C by $\|\varphi\| = \sup_{-h\leq\theta\leq 0}\{|\varphi_1(\theta)|, |\varphi_2(\theta)|, |\varphi_3(\theta)|, |\varphi_4(\theta)|, |\varphi_5(\theta)|\}$. For a biological meaning, we further assume that $\varphi_i(0) > 0,\ i = 1, 2, 3, 4, 5$, and also $\|\varphi\| \leq \sup_{t\geq 0} \frac{\Lambda(t)}{\mu(t)} = (\frac{\Lambda}{\mu})^u$.

Theorem 3.1. [21,27] *If the functions* $\Lambda(t), \mu(t), \xi(t), \nu(t), \beta_1(t), \beta_2(t), \beta_3(t), k(t), p(t), \sigma_1(t), \sigma_2(t), \sigma_3(t), \eta(t)$ *are continuous and bounded on* $[0, +\infty)$ *then there exists a unique solution of the system (2.1) with initial conditions (3.1) defined on* $[0, +\infty)$.

Here we wish to discuss the permanence of the system (2.1) with initial conditions (3.1), which demonstrates how the disease will be permanent 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: The system (2.1) is said to be permanent if there are positive constants v_i and M_i $(i = 1, 2, 3, 4, 5)$ such that:

$$
\begin{aligned}
v_1 \leq \liminf_{t\to\infty} S(t) \leq \limsup_{t\to\infty} S(t) \leq M_1,\\
v_2 \leq \liminf_{t\to\infty} J(t) \leq \limsup_{t\to\infty} J(t) \leq M_2,\\
v_3 \leq \liminf_{t\to\infty} I_1(t) \leq \limsup_{t\to\infty} I_1(t) \leq M_3,\\
v_4 \leq \liminf_{t\to\infty} I_2(t) \leq \limsup_{t\to\infty} I_2(t) \leq M_4,\\
v_5 \leq \liminf_{t\to\infty} I_3(t) \leq \limsup_{t\to\infty} I_3(t) \leq M_5,
\end{aligned}
$$

hold for any solution $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ of (2.1) with initial conditions (3.1). Here v_i and M_i $(i = 1, 2, 3, 4, 5)$ are independent of (3.1).

Theorem 3.2. *The system (2.1) with initial conditions (3.1) is permanent provided*

$$
\begin{aligned}
&R_0 = \{\frac{\Lambda}{(\beta_1 + \beta_2 + \beta_3)(\frac{\Lambda}{\mu})^u + \xi + \mu}\}^l\\
&\frac{\xi^l(\sigma_1 + \mu)^l}{(\nu + \mu)^u(\sigma_1 + \mu)^l + k^u(\beta_1^u)^2((\frac{\Lambda}{\mu})^u)^2(1 + (1 - p^l)k^u)} \frac{p^l k^l \beta_2^l}{(\sigma_2 + \mu)^u} > 1.
\end{aligned}
\tag{3.2}
$$

Proof. We will give the following Propositions 3.1-3.6 to complete the proof of this theorem. □

From biological consideration, we study the system (2.1) with initial conditions (3.1) in the closed set

$$\Omega = \{(S(t), J(t), I_1(t), I_2(t), I_3(t)) \in \mathbb{R}^5_+,$$

$$\text{such that } N(t) = S(t) + J(t) + I_1(t) + I_2(t) + I_3(t) \leq (\frac{\Lambda}{\mu})^u\}.$$

About the positive invariance of Ω, we have the following result.

Proposition 3.1. *If $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ is a solution of (2.1) with initial conditions (3.1) and $\|\varphi\| \leq (\frac{\Lambda}{\mu})^u$, then $(S(t), J(t), I_1(t), I_2(t), I_3(t)) \in \Omega$, for all $t \geq 0$.*

Proof. Since the functions $\Lambda(t), \mu(t), \xi(t), \nu(t), \beta_1(t), \beta_2(t), \beta_3(t), k(t), p(t), \sigma_1(t), \sigma_2(t), \sigma_3(t), \eta(t)$ are continuous and bounded on $[0, +\infty)$, the solution $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ of (2.1) with initial conditions (3.1) exists and is unique on $[0, +\infty)$. Firstly, we show that $S(t) > 0$ for all $t \in [0, +\infty)$. Otherwise, there exists a $t_1 \in (0, +\infty)$ such that $S(t_1) = 0,\ \dot{S}(t_1) \leq 0$ and $S(t) > 0$ for all $t \in [0, t_1)$. We claim that $J(t) > 0$ 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 $J(t) > 0$ on $[0, t_2)$. Integrating the second equation of system (2.1) from 0 to t_2, we have:

$$J(t_2) = J(0) \exp[-\int_0^{t_2} \{k(\theta)(\beta_1(\theta) \int_0^h I_1(\theta - s)d\omega(s) + \beta_2(\theta) \int_0^h I_2(\theta - s)d\omega(s)$$

$$+\beta_3(\theta) \int_0^h I_3(\theta - s)d\omega(s)) + \nu(\theta) + \mu(\theta)\}d\theta] + \int_0^{t_2} \xi(u)S(u) \exp[\int_{t_2}^u \{k(\theta)(\beta_1(\theta)$$

$$\int_0^h I_1(\theta - s)d\omega(s) + \beta_2(\theta) \int_0^h I_2(\theta - s)d\omega(s)$$

$$+\beta_3(\theta) \int_0^h I_3(\theta - s)d\omega(s)) + \nu(\theta) + \mu(\theta)\}d\theta]du > 0,$$

which is a contradiction with $J(t_2) = 0$. So $J(t) > 0,$ for all $t \in [0, t_1)$. Integrating the first equation of system (2.1) from 0 to t_1, we have:

$$S(t_1) = S(0) \exp[-\int_0^{t_1} \{\beta_1(\theta) \int_0^h I_1(\theta - s)d\omega(s) + \beta_2(\theta) \int_0^h I_2(\theta - s)d\omega(s)$$

$$+\beta_3(\theta) \int_0^h I_3(\theta - s)d\omega(s) + \xi(\theta) + \mu(\theta)\}d\theta] + \int_0^{t_1} (\Lambda(u) + \nu(u)J(u)) \exp[\int_{t_1}^u \{\beta_1(\theta)$$

$$\int_0^h I_1(\theta - s)d\omega(s) + \beta_2(\theta) \int_0^h I_2(\theta - s)d\omega(s)$$

$$+\beta_3(\theta)\int_0^h I_3(\theta-s)d\omega(s)+\xi(\theta)+\mu(\theta)\}d\theta]du>0,$$

which is a contradiction with $S(t_1)=0$. So $S(t)>0,$ for all $t\geq 0$ and hence $J(t)>0$, for all $t\geq 0$.

Next we prove that $I_1(t)>0$ for all $t\in[0,+\infty)$. Otherwise, there exists a $t_3\in(0,+\infty)$ such that $I_1(t_3)=0,\ \dot{I}_1(t_3)\leq 0$ and $I_1(t)>0$ for all $t\in[0,t_3)$. Hence there must have $I_2(t)>0$ for all $t\in[0,t_3)$. If this statement is not true, then there exists a $t_4\in(0,t_3)$ such that $I_2(t_4)=0$ and $I_2(t)>0$ on $[0,t_4)$. We claim that $I_3(t)>0$ for all $t\in[0,t_4)$. If this is not true, then there exists a $t_5\in(0,t_4)$ such that $I_3(t_5)=0$ and $I_3(t)>0$ on $[0,t_5)$. Integrating the fifth equation of system (2.1) from 0 to t_5, we have:

$$I_3(t_5)=I_3(0)\exp\{-\int_0^{t_5}(\eta(s)+\sigma_3(s)+\mu(s))ds\}$$

$$+\int_0^{t_5}\sigma_2(u)I_2(u)\exp\{\int_{t_5}^{u}(\eta(s)+\sigma_3(s)+\mu(s))ds\}du>0,$$

which is a contradiction with $I_3(t_5)=0$. So $I_3(t)>0,$ for all $t\in[0,t_4)$. Integrating the fourth equation of system (2.1) from 0 to t_4, we have:

$$I_2(t_4)=I_2(0)\exp\{-\int_0^{t_4}(\sigma_2(s)+\mu(s))ds\}+\int_0^{t_4}\int_0^h[p(u)k(u)J(u)\{\beta_1(u)I_1(u-s)$$

$$+\beta_2(u)I_2(u-s)+\beta_3(u)I_3(u-s)\}+\sigma_1(u)I_1(u)$$

$$+\eta(u)I_3(u)]\exp\{\int_{t_4}^{u}(\sigma_2(s)+\mu(s))ds\}d\omega(s)du>0,$$

which is a contradiction with $I_2(t_4)=0$. So $I_2(t)>0,$ for all $t\in[0,t_3)$ and hence $I_3(t)>0$, for all $t\in[0,t_3)$. Integrating the third equation of system (2.1) from 0 to t_3, we have:

$$I_1(t_3)=I_1(0)\exp\{-\int_0^{t_3}(\sigma_1(s)+\mu(s))ds\}+\int_0^{t_3}\int_0^h[S(u)+(1-p(u))k(u)J(u)]\{\beta_1(u)$$

$$I_1(u-s)+\beta_2(u)I_2(u-s)+\beta_3(u)I_3(u-s)\}\exp\{\int_{t_3}^{u}(\sigma(s)+\mu(s))ds\}d\omega(s)du>0,$$

which is a contradiction with $I_1(t_3)=0$. So $I_1(t)>0,$ for all $t\geq 0$ and hence $I_2(t)>0$, $I_3(t)>0$, for all $t\geq 0$.

Therefore, $S(t)>0, J(t)>0, I_1(t)>0, I_2(t)>0, I_3(t)>0,$ for all $t\geq 0$. Thus, for all $t\in[0,+\infty)$,

$$\dot{N}(t)\leq\Lambda(t)-\mu(t)N(t),\ \text{since, } \sigma_3(t)>0,\ \forall\, t\geq 0.$$

This differential inequality combined with $N(0) \leq (\frac{\Lambda}{\mu})^u$ imply that

$$N(t) = S(t) + J(t) + I_1(t) + I_2(t) + I_3(t) \leq (\frac{\Lambda}{\mu})^u, \text{ for all } t \geq 0. \tag{3.3}$$

Therefore, $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ is uniformly bounded on $[0, +\infty)$.

This completes the proof. □

Proposition 3.2. *The solution* $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ *of (2.1) with initial conditions (3.1) satisfies*

$$\liminf_{t\to\infty} S(t) \geq \{\frac{\Lambda}{(\beta_1 + \beta_2 + \beta_3)(\frac{\Lambda}{\mu})^u + \xi + \mu}\}^l \equiv v_1 > 0. \tag{3.4}$$

Proof. By Proposition 3.1, we have

$$I_1(t), I_2(t), I_3(t) \leq (\frac{\Lambda}{\mu})^u, \ \forall\, t \geq 0.$$

Thus, from the first equation of system (2.1), we have

$$\dot{S}(t) \geq \Lambda(t) - \{\beta_1(t) \int_0^h I_1(t-s)d\omega(s) + \beta_2(t) \int_0^h I_2(t-s)d\omega(s)$$

$$+\beta_3(t) \int_0^h I_3(t-s)d\omega(s) + \xi(t) + \mu(t)\}S(t)$$

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

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

This completes the proof. □

Proposition 3.3. *The solution* $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ *of (2.1) with initial conditions (3.1) satisfies*

$$\liminf_{t\to\infty} J(t) \geq \{\frac{\xi}{(\beta_1 + \beta_2 + \beta_3)k(\frac{\Lambda}{\mu})^u + \nu + \mu}\}^l v_1 \equiv v_2 > 0, \tag{3.5}$$

where $v_1 > 0$ *is given in the Proposition 3.2.*

Proof. From the second equation of system (2.1) and by Proposition 3.1 and Proposition 3.2, the result follows. □

Proposition 3.4. *Assume that $R_0 > 1$, then for any solution $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ of (2.1) with initial conditions (3.1) we have*

$$\liminf_{t\to\infty} I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)} \equiv v_3 > 0, \tag{3.6}$$

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

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

$$\begin{aligned}
&\frac{p^l k^l \beta_2^l}{(\sigma_2+\mu)^u}(\frac{v_1\xi^l}{G}) \to R_0 \text{ as } \alpha \to 0, \text{ where } G = \{(\nu+\mu)^u + k^u(\beta_1^u F + \beta_2^u \alpha + c\beta_3^u \alpha)\},\\
&F = \frac{\{\beta_1^u(\frac{\Lambda}{\mu})^u + (\beta_2^u + c\beta_3^u)\alpha\}(1 + (1-p^l)k^u)(\frac{\Lambda}{\mu})^u}{(\sigma_1+\mu)^l},\\
&c = (\frac{\sigma_2}{\eta+\sigma_3+\mu})^u \text{ and } v_1 = \{\frac{\Lambda}{(\beta_1+\beta_2+\beta_3)(\frac{\Lambda}{\mu})^u + \xi + \mu}\}^l,
\end{aligned} \tag{3.7}$$

then there exists two positive constants α and ρ such that

$$\frac{p^l k^l \beta_2^l}{(\sigma_2+\mu)^u}(\frac{v_1\xi^l}{G})[1 - \exp\{-G\rho\}] > 1. \tag{3.8}$$

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

$$\begin{aligned}
V(t) = I_2(t) + \int_0^h \int_{t-s}^t p(u+s)k(u+s)\{\beta_1(u+s)I_1(u)\\
+\beta_2(u+s)I_2(u) + \beta_3(u+s)I_3(u)\}J(u+s)dud\omega(s).
\end{aligned} \tag{3.9}$$

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

$$\begin{aligned}
\dot{V}(t) &\geq I_2(t)\int_0^h p(t+s)k(t+s)\beta_2(t+s)J(t+s)d\omega(s) - (\sigma_2(t)+\mu(t))I_2(t)\\
&\geq p^l k^l \beta_2^l I_2(t)\int_0^h J(t+s)d\omega(s) - (\sigma_2+\mu)^u I_2(t).
\end{aligned} \tag{3.10}$$

We claim that it is impossible that $I_2(t) \leq \alpha$, $\forall\ t \geq t'$ (t' is any nonnegative constant). Suppose the contrary, then from the third and fifth equations of (2.1), we have,

$$\exists\, t_1' > t', \text{ such that } I_1(t) \leq F,\ I_3(t) \leq c\alpha,\ \forall\, t \geq t_1', \text{ where } c \text{ and } F \text{ are given in (3.7).}$$

From the first equation of (2.1), we have,

$$\exists\, t_2' > t', \text{ such that } S(t) \geq v_1,\ \forall\, t \geq t_2', \text{ where } v_1 \text{ is given in (3.7). Let, } t_1 = \max\{t_1', t_2'\}.$$

Therefore, as $t \geq t_1 + h$,

$$\dot{J}(t) \geq v_1\xi^l - GJ(t), \text{ where } v_1 \text{ and } G \text{ are given in (3.7).} \tag{3.11}$$

For $t > t_1 + h$, integrating the above inequality from $t_1 + h$ to t, we obtain

$$\begin{aligned} J(t) &\geq J(t_1+h)\exp(\int_t^{t_1+h} Gds) + \int_{t_1+h}^{t} v_1\xi^l \exp(\int_t^s Gd\theta)ds \\ &\geq (\frac{v_1\xi^l}{G})\frac{\int_{t_1+h}^{t} G\exp(\int_0^s Gd\theta)ds}{\exp(\int_0^t Gd\theta)}. \end{aligned} \tag{3.12}$$

Hence, $J(t) \geq (\frac{v_1\xi^l}{G})[1 - \exp\{-G(t - t_1 - h)\}]$.

Therefore, $J(t) \geq (\frac{v_1\xi^l}{G})[1 - \exp\{-G\rho\}] \equiv J^{\Delta}$, $\forall\, t \geq t_1 + h + \rho \equiv t_2$.

From (3.12) and the fourth equation of (2.1), we have,

$$\begin{aligned} \dot{I}_2(t) &\geq p(t)k(t)\beta_2(t)J(t)\int_0^h I_2(t-s)d\omega(s) - (\sigma_2(t) + \mu(t))I_2(t) \\ &\geq p^l k^l \beta_2^l J^{\Delta}\int_0^h I_2(t-s)d\omega(s) - (\sigma_2 + \mu)^u I_2(t). \end{aligned} \tag{3.13}$$

Let us take $\underline{i} = \min_{t_2 \leq t \leq t_2+h} I_2(t)$. Next we shall prove that $I_2(t) \geq \underline{i}$, $\forall\, t \geq t_2$. Suppose that it is not true, then $\exists T \geq 0$, such that $I_2(t) \geq \underline{i}$, for all $t_2 \leq t \leq t_2 + h + T$, $I_2(t_2 + h + T) = \underline{i}$ and $\dot{I}_2(t_2 + h + T) \leq 0$. On the other hand, by (3.13), as $t = t_2 + h + T$,

$$\dot{I}_2(t) \geq (\sigma_2 + \mu)^u[\frac{p^l k^l \beta_2^l J^{\Delta}}{(\sigma_2 + \mu)^u} - 1]\underline{i} > 0, \text{ since from (3.8), we have } \frac{p^l k^l \beta_2^l J^{\Delta}}{(\sigma_2 + \mu)^u} > 1. \tag{3.14}$$

This is a contradiction. Hence, $I_2(t) \geq \underline{i}$, $\forall\, t \geq t_2$.

Therefore, from (3.10) and (3.12), we have,

$$\dot{V}(t) \geq (\sigma_2 + \mu)^u[\frac{p^l k^l \beta_2^l J^{\Delta}}{(\sigma_2 + \mu)^u} - 1]I_2(t) \geq (\sigma_2 + \mu)^u[\frac{p^l k^l \beta_2^l J^{\Delta}}{(\sigma_2 + \mu)^u} - 1]\underline{i} > 0,\ \forall\, t \geq t_2, \tag{3.15}$$

which implies $V(t) \to +\infty$ as $t \to +\infty$. From Proposition 3.1, $V(t)$ is bounded. This is a contradiction. Therefore, the claim is proved. From this claim, we will discuss the following two possibilities:

(i) $I_2(t) \geq \alpha$ for all large t.

(ii) $I_2(t)$ oscillates about α for all large t.

Finally, we will show that $I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$ for sufficiently large t. Evidently, we only need to consider the case (ii). Let t_1 and t_2 be sufficiently large times satisfying:

$I_2(t_1) = I_2(t_2) = \alpha$,

$I_2(t) < \alpha$ as $t \in (t_1, t_2)$.

If $t_2 - t_1 \leq h + \rho$, since $\dot{I}_2(t) \geq -(\sigma_2 + \mu)^u I_2(t)$ and $I_2(t_1) = \alpha$ which implies $I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$, $\forall\, t \in [t_1, t_2]$. If $t_2 - t_1 > h + \rho$, then it is obvious that $I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$, for all t in $[t_1, t_1 + h + \rho]$. By (3.12), we have $J(t) \geq J^\Delta$, $\forall\, t \in [t_1 + h + \rho, t_2]$. Thus, proceeding exactly as the proof of the above claim, we see that $I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$, $\forall\, t \in [t_1 + h + \rho, t_2]$. If it is not true, then there exists a $T^* \geq 0$ such that $I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$, $\forall\, t \in [t_1, t_1 + h + \rho + T^*]$, $I_2(t_1 + h + \rho + T^*) = \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$ and $\dot{I}_2(t_1 + h + \rho + T^*) \leq 0$. Using (3.13), as $t = t_1 + h + \rho + T^*$, we have

$$\begin{aligned} &\dot{I}_2(t) \geq (\sigma_2 + \mu)^u [\frac{\beta_2^l J^\Delta}{(\sigma_2 + \mu)^u} - 1] \alpha e^{-(\sigma_2+\mu)^u(h+\rho)} > 0, \\ &\text{since from (3.8), we have } \frac{p^l k^l \beta_2^l J^\Delta}{(\sigma_2 + \mu)^u} > 1. \end{aligned} \tag{3.16}$$

This is a contradiction. Therefore, $I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)}$, $\forall\, t \in [t_1, t_2]$. Hence,

$$\liminf_{t\to\infty} I_2(t) \geq \alpha e^{-(\sigma_2+\mu)^u(h+\rho)} \equiv v_3 > 0.$$

This completes the proof of Proposition 3.4. □

Proposition 3.5. *Assume that $R_0 > 1$, then for any solution $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ of (2.1) with initial conditions (3.1) we have*

$$\liminf_{t\to\infty} I_3(t) \geq \{\frac{\sigma_2}{\eta + \sigma_3 + \mu}\}^l v_3 \equiv v_4 > 0, \tag{3.17}$$

where $v_3 > 0$ is given in the Proposition 3.4.

Proof. From the fifth equation of system (2.1) and by Proposition 3.4, the result follows. □

Proposition 3.6. *Assume that $R_0 > 1$, then for any solution $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ of (2.1) with initial conditions (3.1) we have*

$$\liminf_{t\to\infty} I_1(t) \geq \frac{\{v_1 + (1 - p^u)k^l v_2\}(\beta_2^l v_3 + \beta_3^l v_4)}{(\sigma_1 + \mu)^u} \equiv v_5 > 0, \tag{3.18}$$

where $v_1 > 0, v_2 > 0, v_3 > 0, v_4 > 0$ are given in the Propositions 3.2-3.5 respectively.

Proof. From the third equation of system (2.1) and by Propositions 3.2-3.5, the result follows. □

Thus, the system (2.1) with initial conditions (3.1) is permanent provided (3.2) holds.

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

Lemma 3.1. *Consider an autonomous delay differential equation*

$$\dot{x}(t) = a_1 \int_0^h x(t-s)d\eta(s) - a_2 x(t), \tag{3.19}$$

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:

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

Then the time derivative along system (3.19) is given by

$$\dot{V}(t) = a_1 \int_0^h x(t)x(t-s)d\eta(s) + \frac{a_1}{2}\int_0^h \{x^2(t) - x^2(t-s)\}d\eta(s) - a_2x^2(t)$$

$$= -\frac{a_1}{2}\int_0^h \{x(t) - x(t-s)\}^2 d\eta(s) + a_1x^2(t) - a_2x^2(t) \leq -(a_2 - a_1)x^2(t).$$

$$\text{Therefore, } \lim_{t\to\infty} x(t) = 0.$$

□

Theorem 3.3. *If $\beta_2(t), \beta_3(t) \leq \beta_1(t),\ 0 < k(t), p(t) < 1$, and*

$$R^* = (\frac{\beta_1^u}{\mu^l})(\frac{\Lambda}{\mu})^u < 1, \tag{3.20}$$

then $\lim_{t\to\infty}\{I_1(t) + I_2(t) + I_3(t)\} = 0$, i.e. the disease in system (2.1) will be going to extinction.

Proof. Let $U(t) = I_1(t) + I_2(t) + I_3(t)$. Adding third, fourth and fifth equations of system (2.1), assuming $\beta_2(t), \beta_3(t) \leq \beta_1(t),\ 0 < k(t), p(t) < 1$, and by Proposition 3.1, we have

$$\frac{dU(t)}{dt} \leq \mu^l[(\frac{\beta_1^u}{\mu^l})(S(t) + J(t))\int_0^h U(t-s)d\omega(s) - U(t)]$$

$$\leq \mu^l[(\frac{\beta_1^u}{\mu^l})(\frac{\Lambda}{\mu})^u \int_0^h U(t-s)d\eta(s) - U(t)],\ \forall\, t \geq 0.$$

Using the comparison theorem of functional differential equations and Lemma 3.1, we have

$$\lim_{t\to\infty} U(t) = \lim_{t\to\infty}\{I_1(t) + I_2(t) + I_3(t)\} = 0.$$

□

From (3.20) we conclude that the spread of the HIV infection should be controlled by way of effective protections to reduce the value of $\beta_1(t)$ 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^*. We have observed that vaccination has no effect on the extinction of the disease since R^* does not contain $\xi(t), k(t)$ and $p(t)$.

4. Global asymptotic stability

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

Definition[51]. System (2.1) with initial conditions (3.1) is said to be globally asymptotically stable if

$$\lim_{t\to\infty} \mid S(t) - S'(t) \mid = 0,\ \lim_{t\to\infty} \mid J(t) - J'(t) \mid = 0,\ \lim_{t\to\infty} \mid I_1(t) - I_1'(t) \mid = 0,$$

$$\lim_{t\to\infty} \mid I_2(t) - I_2'(t) \mid = 0,\ \lim_{t\to\infty} \mid I_3(t) - I_3'(t) \mid = 0,$$

hold for any two solutions $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ and $(S'(t), J'(t), I_1'(t), I_2'(t), I_3'(t))$ of (2.1) with different initial conditions satisfying (3.1).

Assume that $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ is a solution of (2.1). By Proposition (3.1), we have

$$0 \le S(t) \le A,\ 0 \le J(t) \le A,\ 0 \le I_1(t) \le A,\ 0 \le I_2(t) \le A,$$

$$0 \le I_3(t) \le A,\ \forall\, t \ge 0,\ \text{where } A = (\frac{\Lambda}{\mu})^u.$$

Let us define,

$$\begin{aligned}
B_1(t) &= c_1\mu(t) - c_2A(\beta_1(t) + \beta_2(t) + \beta_3(t)),\\
B_2(t) &= c_1\mu(t) - c_2Ak(t)(\beta_1(t) + \beta_2(t) + \beta_3(t)),\\
B_3(t) &= c_2\mu(t) - (c_1 + c_2)A\int_0^h \beta_1(t+s)(1 + k(t+s))d\omega(s),\\
B_4(t) &= c_2\mu(t) + (c_2 - c_3)\sigma_2(t) - (c_1 + c_2)A\int_0^h \beta_2(t+s)(1 + k(t+s))d\omega(s),
\end{aligned} \tag{4.1}$$

$$B_5(t) = c_3(\eta(t) + \sigma_3(t) + \mu(t)) - c_2\eta(t) - (c_1 + c_2)A\int_0^h \beta_3(t+s)(1 + k(t+s))d\omega(s).$$

Theorem 4.1. *If there exist $c_1 > 0, c_2 > 0$ and $c_3 > 0$ such that the functions $B_i(t), i = 1, 2, 3, 4, 5$, given by (4.1) 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 $i, j = 1, 2, \ldots$ 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.*

Proof. Assume that $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ and $(S'(t), J'(t), I_1'(t), I_2'(t), I_3'(t))$ are any two solutions of system (2.1) with different initial conditions satisfying (3.1).

Define $V_1(t) =\mid S(t) - S'(t) \mid$. Then the right-upper derivative of $V_1(t)$ along the solution of system (2.1) and (3.1) is given by

$$\begin{aligned}
D^+V_1(t) &= sgn(S(t) - S'(t))[-(S(t) - S'(t))\{\beta_1(t)\int_0^h I_1(t-s)d\omega(s)\\
&+\beta_2(t)\int_0^h I_2(t-s)d\omega(s) + \beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}\\
&+S'(t)\{\beta_1(t)\int_0^h (I_1'(t-s) - I_1(t-s))d\omega(s)\\
&+\beta_2(t)\int_0^h (I_2'(t-s) - I_2(t-s))d\omega(s) + \beta_3(t)\int_0^h (I_3'(t-s) - I_3(t-s))d\omega(s)\}\\
&-(\xi(t) + \mu(t))(S(t) - S'(t)) + \nu(t)(J(t) - J'(t))]\\
&\leq -(\xi(t) + \mu(t)) \mid S(t) - S'(t) \mid +\nu(t) \mid J(t) - J'(t) \mid\\
&+\beta_1(t)A\int_0^h \mid I_1(t-s) - I_1'(t-s) \mid d\omega(s)\\
&+\beta_2(t)A\int_0^h \mid I_2(t-s) - I_2'(t-s) \mid d\omega(s) + \beta_3(t)A\int_0^h \mid I_3(t-s) - I_3'(t-s) \mid d\omega(s).
\end{aligned} \tag{4.2}$$

Define $V_2(t) =\mid J(t) - J'(t) \mid$. Then the right-upper derivative of $V_2(t)$ along the solution of system (2.1) and (3.1) is given by

$$D^+V_2(t) = sgn(J(t) - J'(t))[\xi(t)(S(t) - S'(t)) - k(t)(J(t) - J'(t))\{\beta_1(t)\int_0^h I_1(t-s)d\omega(s)$$

$$+\beta_2(t)\int_0^h I_2(t-s)d\omega(s)+\beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}$$

$$+k(t)J'(t)\{\beta_1(t)\int_0^h (I_1'(t-s)-I_1(t-s))d\omega(s)+\beta_2(t)\int_0^h (I_2'(t-s)-I_2(t-s))d\omega(s)$$

$$+\beta_3(t)\int_0^h (I_3'(t-s)-I_3(t-s))d\omega(s)\}-(\nu(t)+\mu(t))(J(t)-J'(t))]$$

$$\leq -(\nu(t)+\mu(t))\mid J(t)-J'(t)\mid +\xi(t)\mid S(t)-S'(t)\mid$$

$$+k(t)\beta_1(t)A\int_0^h \mid I_1(t-s)-I_1'(t-s)\mid d\omega(s)+k(t)\beta_2(t)A\int_0^h \mid I_2(t-s)$$

$$-I_2'(t-s)\mid d\omega(s)+k(t)\beta_3(t)A\int_0^h \mid I_3(t-s)-I_3'(t-s)\mid d\omega(s). \tag{4.3}$$

Define $V_3(t) =\mid I_1(t)-I_1'(t)\mid$. Calculating the right-upper derivative of $V_3(t)$ along the solution of system (2.1) and (3.1), we have

$$D^+V_3(t)=sgn(I_1(t)-I_1'(t))[\{(S(t)-S'(t))+k(t)(1-p(t))(J(t)-J'(t))\}$$

$$\{\beta_1(t)\int_0^h I_1(t-s)d\omega(s)+\beta_2(t)\int_0^h I_2(t-s)d\omega(s)+\beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}$$

$$+\{S'(t)+k(t)(1-p(t))J'(t)\}\{\beta_1(t)\int_0^h (I_1(t-s)-I_1'(t-s))d\omega(s)$$

$$+\beta_2(t)\int_0^h (I_2(t-s)-I_2'(t-s))d\omega(s)+\beta_3(t)\int_0^h (I_3(t-s)-I_3'(t-s))d\omega(s)\}$$

$$-(\sigma_1(t)+\mu(t))(I_1(t)-I_1'(t))]$$

$$\leq -(\sigma_1(t)+\mu(t))\mid I_1(t)-I_1'(t)\mid$$

$$+A\{\mid S(t)-S'(t)\mid +k(t)(1-p(t))\mid J(t)-J'(t)\mid\}(\beta_1(t)+\beta_2(t)+\beta_3(t))$$

$$+A(1+k(t)(1-p(t)))\{\beta_1(t)\int_0^h \mid I_1(t-s)-I_1'(t-s)\mid d\omega(s)$$

$$+\beta_2(t)\int_0^h \mid I_2(t-s)-I_2'(t-s)\mid d\omega(s)+\beta_3(t)\int_0^h \mid I_3(t-s)-I_3'(t-s)\mid d\omega(s)\}. \tag{4.4}$$

Define $V_4(t) = \mid I_2(t) - I_2'(t) \mid$. Calculating the right-upper derivative of $V_4(t)$ along the solution of system (2.1) and (3.1), we have

$$D^+V_4(t) = sgn(I_2(t) - I_2'(t))[k(t)p(t)(J(t) - J'(t))\{\beta_1(t)\int_0^h I_1(t-s)d\omega(s)$$

$$+\beta_2(t)\int_0^h I_2(t-s)d\omega(s) + \beta_3(t)\int_0^h I_3(t-s)d\omega(s)\}$$

$$+k(t)p(t)J'(t)\{\beta_1(t)\int_0^h (I_1(t-s) - I_1'(t-s))d\omega(s)$$

$$+\beta_2(t)\int_0^h (I_2(t-s) - I_2'(t-s))d\omega(s) + \beta_3(t)\int_0^h (I_3(t-s) - I_3'(t-s))d\omega(s)\}$$

$$+\sigma_1(t)(I_1(t) - I_1'(t)) + \eta(t)(I_3(t) - I_3'(t)) - (\sigma_2(t) + \mu(t))(I_2(t) - I_2'(t))]$$

$$\leq -(\sigma_2(t) + \mu(t)) \mid I_2(t) - I_2'(t) \mid +\sigma_1(t) \mid I_1(t) - I_1'(t) \mid +\eta(t) \mid I_3(t) - I_3'(t) \mid$$

$$+Ak(t)p(t) \mid J(t) - J'(t) \mid (\beta_1(t) + \beta_2(t) + \beta_3(t))$$

$$+Ak(t)p(t)\{\beta_1(t)\int_0^h \mid I_1(t-s) - I_1'(t-s) \mid d\omega(s)$$

$$+\beta_2(t)\int_0^h \mid I_2(t-s) - I_2'(t-s) \mid d\omega(s) + \beta_3(t)\int_0^h \mid I_3(t-s) - I_3'(t-s) \mid d\omega(s)\}. \tag{4.5}$$

Define $V_5(t) = \mid I_3(t) - I_3'(t) \mid$. Calculating the right-upper derivatives of $V_5(t)$ along the solution of system (2.1) and (3.1), we have

$$D^+V_5(t) = sgn(I_3(t) - I_3'(t))\{\sigma_2(t)(I_2(t) - I_2'(t)) - (\eta(t) + \sigma_3(t) + \mu(t))(I_3(t) - I_3'(t))\}$$

$$\leq \sigma_2(t) \mid I_2(t) - I_2'(t) \mid -(\eta(t) + \sigma_3(t) + \mu(t)) \mid I_3(t) - I_3'(t) \mid . \tag{4.6}$$

Define $V_6(t)$ as

$$V_6(t) = \int_0^h \int_{t-s}^t A(1 + k(u+s))\{\beta_1(u+s) \mid I_1(u) - I_1'(u) \mid$$

$$+\beta_2(u+s) \mid I_2(u) - I_2'(u) \mid +\beta_3(u+s) \mid I_3(u) - I_3'(u) \mid\}dud\omega(s).$$

The right-upper derivative of $V_6(t)$ along the solution of system (2.1) and (3.1) is given below:

$$D^+V_6(t) = \int_0^h A(1 + k(t+s))\{\beta_1(t+s) \mid I_1(t) - I_1'(t) \mid$$

$$+\beta_2(t+s) \mid I_2(t) - I_2'(t) \mid +\beta_3(t+s) \mid I_3(t) - I_3'(t) \mid\} d\omega(s)$$

$$-A(1+k(t)) \int_0^h \{\beta_1(t) \mid I_1(t-s) - I_1'(t-s) \mid \tag{4.7}$$

$$+\beta_2(t) \mid I_2(t-s) - I_2'(t-s) \mid +\beta_3(t) \mid I_3(t-s) - I_3'(t-s) \mid\} d\omega(s).$$

Let $V(t) = c_1(V_1(t)+V_2(t))+c_2(V_3(t)+V_4(t))+c_3V_5(t)+(c_1+c_2)V_6(t)$, then by using (4.2)-(4.7), we have

$$\begin{aligned} D^+V(t) &\leq -B_1(t) \mid S(t) - S'(t) \mid -B_2(t) \mid J(t) - J'(t) \mid \\ &-B_3(t) \mid I_1(t) - I_1'(t) \mid -B_4(t) \mid I_2(t) - I_2'(t) \mid -B_5(t) \mid I_3(t) - I_3'(t) \mid, \ \forall\, t \geq h, \end{aligned} \tag{4.8}$$

where $B_i(t),\ (i = 1, 2, 3, 4, 5)$ are defined in (4.1).

Integrating (4.8) from h to t, we have

$$\begin{aligned} &\int_h^t \{B_1(t) \mid S(t) - S'(t) \mid +B_2(t) \mid J(t) - J'(t) \mid +B_3(t) \mid I_1(t) - I_1'(t) \mid \\ &+B_4(t) \mid I_2(t) - I_2'(t) \mid +B_5(t) \mid I_3(t) - I_3'(t) \mid\} dt \leq V(h) - V(t) \\ \Rightarrow &\int_h^t \{B_1(t) \mid S(t) - S'(t) \mid +B_2(t) \mid J(t) - J'(t) \mid +B_3(t) \mid I_1(t) - I_1'(t) \mid \\ &+B_4(t) \mid I_2(t) - I_2'(t) \mid +B_5(t) \mid I_3(t) - I_3'(t) \mid\} dt < \infty. \end{aligned} \tag{4.9}$$

By assumptions about $B_i(t), i = 1, 2, 3, 4, 5$, and the boundedness of $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ and $(S'(t), J'(t), I_1'(t), I_2'(t), I_3'(t))$ on $[0, \infty)$, we obtain from system (2.1) that $\mid S(t) - S'(t) \mid$, $\mid J(t) - J'(t) \mid$,$\mid I_1(t) - I_1'(t) \mid$, $\mid I_2(t) - I_2'(t) \mid$ and $\mid I_3(t) - I_3'(t) \mid$ are bounded and uniformly continuous on $[0, \infty)$. It follows from (4.9) that,

$$\lim_{t\to\infty} \mid S(t) - S'(t) \mid = 0, \ \lim_{t\to\infty} \mid J(t) - J'(t) \mid = 0, \ \lim_{t\to\infty} \mid I_1(t) - I_1'(t) \mid = 0,$$

$$\lim_{t\to\infty} \mid I_2(t) - I_2'(t) \mid = 0, \ \lim_{t\to\infty} \mid I_3(t) - I_3'(t) \mid = 0.$$

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

Corollary 4.1. *If there exist $c_1 > 0, c_2 > 0$ and $c_3 > 0$ such that $\liminf_{t\to\infty} B_i(t) > 0$, for $i = 1, 2, 3, 4, 5$; where $B_i(t)$ are given by (4.1) then system (2.1) with initial conditions (3.1) is globally asymptotically stable.*

From the results of the Theorem 4.1 and Corollary 4.1, we observe that the vaccination and time delay both has an effect on the global asymptotic stability of the proposed model since $B_2(t)$

contains $k(t)$ and $B_i(t),\ i = 3, 4, 5$; contain h and $k(t)$, where $1 - k(t)$ $(0 < k(t) < 1)$ accounts for the efficacy of the vaccine-induced protection against infection. Therefore, we conclude that the vaccination programme may rule out any complicated behaviour (eg. limit cycles) under the restrictions specified on $B_i(t)$ in Theorem 4.1 and Corollary 4.1.

From our everyday experience we know that the biological and environmental parameters are subject to fluctuation 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 4.2. [43] *If system (2.1) is $\psi-$periodic and there are positive constants v_i and M_i $(i = 1, 2, 3, 4, 5)$ such that:*

$$v_1 \leq \liminf_{t\to\infty} S(t) \leq \limsup_{t\to\infty} S(t) \leq M_1,$$
$$v_2 \leq \liminf_{t\to\infty} J(t) \leq \limsup_{t\to\infty} J(t) \leq M_2,$$
$$v_3 \leq \liminf_{t\to\infty} I_1(t) \leq \limsup_{t\to\infty} I_1(t) \leq M_3,$$
$$v_4 \leq \liminf_{t\to\infty} I_2(t) \leq \limsup_{t\to\infty} I_2(t) \leq M_4,$$
$$v_5 \leq \liminf_{t\to\infty} I_3(t) \leq \limsup_{t\to\infty} I_3(t) \leq M_5,$$

hold for any solution $(S(t), J(t), I_1(t), I_2(t), I_3(t))$ of (2.1) with initial conditions (3.1), then system (2.1) has a unique positive periodic solution with period ψ.

Using Theorem 4.2, we have the following corollary.

Corollary 4.2. *If system (2.1) is $\psi-$periodic and conditions in Theorems 3.2 and 4.1 are valid, then there exists a unique positive $\psi-$periodic solution which is globally asymptotically stable.*

5. 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 [23,40,44,45,50,51]. In this paper we have considered a nonlinear and nonautonomous stage-structured HIV/AIDS epidemic model with an imperfect HIV vaccine, varying total population size and distributed time delay to become infectious due to intracellular delay between initial infection of a cell by HIV and

the release of new virions. The infected persons in the different stages have different ability of transmitting disease. It is assumed that an imperfect HIV vaccine could offer a therapeutic effect by converting vaccinees in the highly infectious AIDS stage into the less infectious asymptomatic stage. It is also assumed that the vaccine could induce a bypass of primary infection, where a proportion of vaccinated infectious individuals move straight to the asymptomatic (chronic) stage. 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. [2,10,15,28,33,36]. In this article, 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 persons. We have introduced some new threshold values R_0, R^* given by (3.2) and (3.20) respectively 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 mathematical analysis suggests that the spread of the HIV infection should be controlled by way of promoting the condom use or other effective protections to decrease R^* (since this process reduces the value of $\beta_1(t)$) and thereby to keep overall infective population under control. Since due to migration susceptible population increases continuously and therefore infection becomes more endemic and always persists in the population. Our analysis also suggests that 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^*. We have observed that vaccination has no effect on the extinction of the disease (since R^* does not contain $\xi(t), k(t)$ and $p(t)$) but it has an effect on the permanence and global asymptotic stability of this model. We have also observed that the time delay has no effect on the permanence of the system (since R_0 does not contain time delay h) but it has an effect on the global asymptotic stability of this model. 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-maker in targeting prevention and treatment resources for maximum effectiveness.

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