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GLOBAL DYNAMICS OF A CHOLERA MODEL WITH AGE-OF-IMMUNITY STRUCTURE AND REINFECTION*

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Abstract To understand *Vibrio cholerae* transmission dynamics, in this paper, a mathematical model for the dynamics of cholera with reinfection is formulated, where we incorporate the duration time of the recovery individuals (age-of-immunity). The basic reproduction number $\Re_0$ for the proposed model is identified and the threshold property of $\Re_0$ is established. By applying the persistence theory for infinite-dimensional systems, we show that the disease is uniformly persistent if the basic reproductive number $\Re_0 > 1$. By constructing suitable Lyapunov functions, the global stability of the infection-free equilibrium in the system is obtained for $\Re_0 < 1$; the unique endemic equilibrium of the system is globally asymptotically stable for $\Re_0 > 1$.

Keywords Cholera model, duration time of immunity, Lyapunov functional, global stability.

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1. Introduction

Cholera is a water-borne disease caused by the bacterium *Vibrio cholerae*. It is typically transmitted through lack of safe water supply, poor sanitation conditions and the rainy season. Although infection is mostly mild, in some cases it may develop into severe diarrhea and vomiting, where the untreated population may lead to death within a few hours due to dehydration and electrolyte imbalance. The World Health Organization has estimated that each year there are 1.3 million to 4.0 million cases of cholera, and 21 000 to 143 000 deaths worldwide due to cholera [36]. In the past 200 years, seven cholera pandemics have occurred, with the seventh pandemic originating in Indonesia in 1961 [2]. In recent years, cholera outbreaks in Haiti, Zimbabwe have always led to a large number of infections and received worldwide attention [11, 24]. In particular, in October 2016, a cholera outbreak started in Yemen. It is surprising that the outbreak was apparently in decline by March 2017, however in April 2017, an outbreak resurged in Yemen [38].

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It is difficult to gauge the exact morbidity and mortality of cholera due to the surveillance systems in many developing countries are rudimentary. Many countries are hesitant to report cholera cases to the WHO because of the potential negative economic impact of the disease on trade and tourism [26].

Mathematical models have been developed to understand the dynamics of cholera and design and analyze control strategies. The earliest cholera mathematical model can be traced to the model formulated by Capasso in 1973 [4], where cholera epidemic occurred in the European Mediterranean region. Since then, the mathematical study of cholera transmission dynamics is continued. In 2001, Codeco [7] extended Capasso's model by describing the interaction between concentrations of cholera bacteria in water reservoirs and human hosts who consumed contaminated water. Codeco's model can be described by the following differential equations

$$\begin{aligned} \frac{dS(t)}{dt} &= \mu(H - S(t)) - \beta S(t)\frac{B(t)}{\kappa + B(t)}, \\ \frac{dI(t)}{dt} &= \beta S(t)\frac{B(t)}{\kappa + B(t)} - \gamma I(t), \\ \frac{dB(t)}{dt} &= \xi I(t) - mB(t), \end{aligned} \tag{1.1}$$

where, $S(t)$ and $I(t)$ refer to the population size of susceptible, infectious persons at time t, respectively. H is the total human population. $B(t)$ refers to the concentration of *Vibrio cholerae* in the water reservoir or supply at time t. μ is the new birth or natural death rate. β is the rate of contaminated water consumption; $\frac{B(t)}{\kappa+B(t)}$ reflects the probability that a person drinking the contaminated water will be infected by *V. cholera*, where κ is the half saturation concentration of environmental vibrio. γ is recovery rate of infected people. ξ is the rate at which infectious people contribute *Vibrio cholerae* to the water reservoir; m is the rate at which *Vibrio cholerae* are removed from the water reservoir. In paper [7], the obtained results show that the reproduction rate of cholera is a function of social and environmental factors, and seasonal variations of contact rates force a cyclical pattern of cholera outbreaks.

Model (1.1) has been extended by King [17] to assess the impact of "inapparent infections" in Bengal and concluded that these undiagnosed cholera cases could amplify the transmission and mortality caused by cholera epidemics. By further extending the basic model adapted from Codeco [7], Fung [12] formulated cholera transmission dynamics incorporating different hypotheses, including the importance of asymptomatic or inapparent infections, and hyperinfectious *Vibrio cholerae* and human-to-human transmission. The obtained results highlight important challenges of cholera modeling. More recently, many other modeling attempts have been made to describe and to predict the transmission dynamics of cholera and design future prevention strategies in the literature(*e.g.,* [1, 5, 13, 16, 26, 33]). However, recovery from a primary infection with cholera does not imply fully protectively immunity against reinfection. In paper [34], some instances of reinfection with clinical cholera have been described almost a century ago. It is estimated that the length of immunity in the literature [17, 18] ranges widely from several months to three to ten years. The loss of immunity to cholera is poorly understood. Recently, Pasetti and Levine [28] pointed out that the acquired immunity of Cholera may depend on both the duration and the intensity of past exposure to infection. Authors [8, 27] have investigated the vaccine-derived immunity in the case of ongoing oral cholera vaccine campaigns worldwide in Haiti, and Thailand. However, the mechanisms of immunity to cholera are not fully understood.

Our aim, in this paper, is to better understand cholera epidemiology and to predict the impact of age-of-immunity structure and reinfection on cholera transmission. In section 2, we formulate a dynamical system with an age-structured partial differential equations (PDEs), which is described the duration of immunity. The impact of reinfection in population due to loss of immunity is also included in our model. In section 3, with the fundamental mathematical analysis for the model, we determine the existence of all possible equilibria and the explicit formula for the reproductive number of system, which determines the stability of the all possible equilibria. In section 4, we investigate global dynamics of the proposed model. By applying the persistence theory for infinite-dimensional systems, we show that Cholera in population is uniformly persistent if the reproductive number $\Re_0 > 1$. The global stability of the infection-free equilibrium and the endemic equilibrium of the system is established by constructing Lyapunov functions. In Section 5 we summarize our results and give our conclusions.

2. Formulation of the Model

We assume that the size of the population at time t are divided into susceptible individuals $S(t)$, infected individuals $I(t)$, and recovered individuals $R(t)$. Let $B(t)$ be the concentration of *Vibrio cholerae* in the contaminated environment at time t. Due to the recovered individuals are not necessary completely immune to the disease, we here assume that their susceptibility depends on the time that has elapsed since their recovery. Similar to the work in paper [32], we stratify the recovered part of the population along recovery age, *i.e.,* the time τ that has passed since the recovered individuals from the infectious disease. Let

$$R(t) = \int_0^\infty r(t,\tau)d\tau,$$

where, $r(t,\tau)$ is the density of the recovered part of the human population at time t that is recovered at time $t-\tau$ (*i.e.,* τ is duration time of immunity.)

It is assumed that the susceptible population are recruited at a constant rate Λ and individuals die at constant rate μ. Infected individuals are treated and subsequently enter the recovered class at a rate γ, and appear in the recovered class with a boundary condition $r(t,0) = \gamma I(t)$. μ is the natural mortality rate of human population. For the disease incidence, we employ a saturation incidence [7,29] in the form of $\frac{\beta B(t)}{B(t)+\kappa}$ to describe the force of infection from the environment. Transmission of cholera usually stems from the waterborne bacteria *Vibrio cholerae*, and therefore the infection occurs as a result of an effective contact between a susceptible individual and the pathogenic *Vibrio cholerae*, reflected by the contact rate β. Infected individuals contribute to *Vibrio cholerae* in the aquatic environment at a constant rate α and *Vibrio cholerae* have a reduction rate m_0, which includes the natural death and other means of the removal of the pathogen in the environment. Since the fatality rates for cholera generally are very low (at or below 1%) [39], we assume that the cholera-induced mortality can be neglected in this study.

Based on the above assumptions, the dynamics of the disease transmission are described by the following equations

$$\begin{aligned}
&\frac{dS(t)}{dt} = \Lambda - \frac{\beta B(t)S(t)}{B(t)+\kappa} - \mu S(t),\\
&\frac{dI(t)}{dt} = \frac{\beta B(t)S(t)}{B(t)+\kappa} + \int_0^{+\infty}\theta(\tau)r(t,\tau)d\tau - (\gamma+\mu)I(t),\\
&\frac{\partial r(t,\tau)}{\partial \tau} + \frac{\partial r(t,\tau)}{\partial t} = -(\mu+\theta(\tau))r(t,\tau),\\
&r(t,0) = \gamma I(t),\\
&\frac{dB(t)}{dt} = \alpha I(t) - m_0 B(t),
\end{aligned} \tag{2.1}$$

where, $\theta(\tau)$ stands for the rate that the waning immunity individuals revert to the infective individuals. System (2.1) is equipped with the following initial conditions:

$$S(0) = S_0,\ I(0) = I_0,\ r(0,\tau) = \psi(\tau),\ B(0) = B_0.$$

We assume that all the parameters take positive values. Moreover, the parameters satisfy the following assumption.

Assumption 2.1. *The parameter functions satisfy*

(1) The function $\theta(\tau) \in L^\infty(0,\infty)$.

(2) The function $\psi(\tau)$ is nonnegative and integrable.

If the total human population size is denoted by $N(t)$, we have

$$N(t) = S(t) + I(t) + \int_0^\infty r(t,\tau)d\tau.$$

From system (2.1), we have

$$\frac{dN(t)}{dt} \le \Lambda - \mu N(t).$$

Thus, we have

$$\limsup_{t\to\infty} N(t) \le \frac{\Lambda}{\mu}.$$

It follows from the last equation of system (2.1) that

$$\limsup_{t\to\infty} B(t) \le \frac{\alpha\Lambda}{\mu_0 m_0}.$$

Define the set Ω as

$$\{(S(t), I(t), r(t,.), B(t)) \in \mathbb{R}^+ \times \mathbb{R}^+ \times L^1(0,\infty) \times \mathbb{R}^+ | N(t) \le \frac{\Lambda}{\mu}, B(t) \le \frac{\alpha\Lambda}{\mu_0 m_0}\}.$$

Define the space of functions $X = \mathbb{R}^+ \times \mathbb{R}^+ \times L^1_+(0,\infty) \times \mathbb{R}^+$. The model (2.1) with assumption 2.1 is a well posed system of differential equations in the positive cone. Using semigroup theory and methods applied in paper [6, 19, 20], the well-posed of system (2.1) can be justified.

3. Equilibria and their local stability

In this section, we shall analyze the existence of equilibria and the reproduction number associated with system (2.1). For simplicity, we let $\kappa = 1$ (through a normalization).

It is easy to see that there always exists the equilibrium of infection-free $E_0(\frac{\Lambda}{\mu},0,0,0)$ in system (2.1). Let $E^*(S^*, I^*, r^*(\tau), B^*)$ be any endemic equilibrium in system (2.1). Thus, we have

$$\begin{aligned}
&\Lambda - \frac{\beta B^* S^*}{B^*+1} - \mu S^* = 0,\\
&\frac{\beta B^* S^*}{B^*+1} + \int_0^{+\infty} \theta(\tau) r^*(\tau) d\tau - (\gamma+\mu) I^* = 0,\\
&\frac{dr^*(\tau)}{d\tau} = -(\mu + \theta(\tau)) r^*(\tau),\\
&r^*(0) = \gamma I^*,\\
&\alpha I^* - m_0 B^* = 0.
\end{aligned} \tag{3.1}$$

From equation (3.1), by direct computing, the equilibrium satisfies the following equation

$$\begin{aligned}
S^* &= \frac{\Lambda(\alpha I^* + m_0)}{(\beta\alpha + \mu\alpha) I^* + \mu m_0}, \qquad I^* = \frac{\mu m_0}{\alpha(\beta+\mu)}(\Re_0 - 1),\\
r^*(\tau) &= \gamma I^* e^{-\int_0^\tau (\mu+\theta(s))ds}, \qquad B^* = \frac{\alpha I^*}{m_0},
\end{aligned} \tag{3.2}$$

where,

$$\Re_0 = \frac{\Lambda\beta\alpha}{\mu m_0(\gamma(1-K)+\mu)}, \quad K = \int_0^{+\infty} \theta(\tau)\rho(\tau) d\tau, \quad \rho(\tau) = e^{-\int_0^\tau (\mu+\theta(s))ds}.$$

It is easy to verify that $K \le \int_0^{+\infty} de^{-\int_0^\tau \theta(s)ds} = 1$. $\Re_0$ is positive and can be regarded as the control reproduction number of system (2.1), which has been introduced by paper [9]. Therefore, we have the following results

Theorem 3.1. *If* $\Re_0<1$*, system* (2.1) *has always infection-free equilibrium* $E_0(\frac{\Lambda}{\mu},0,0,0)$*; If* $\Re_0 > 1$*, there are two equilibria, infection-free equilibrium* $E_0(\dfrac{\Lambda}{\mu}, 0, 0, 0)$ *and endemic equilibrium* $E^*(S^*, I^*, r^*(\tau), B^*)$*, where* $S^*, I^*, r^*(\tau), B^*$ *can be determined by the expressions in* (3.2)*.*

Now we investigate the stability of the equilibria in system (2.1). We notice that for the structured model with unbounded domain, *i.e.*, $a \in [0, \infty)$, its linear stability analysis of the equilibrium is different from those of the models in ODEs, where the characteristic equation has only roots with negative real part, which directly leads to the conclusion that the corresponding equilibrium point is locally stable. Some analytical techniques in recent years have been established for the local stability of equilibrium solutions with the structured models (see, [6, 20]).

First, we consider the local stability of the infection free equilibrium $E_0(S^0,0,0,0)$, $S^0 = \dfrac{\Lambda}{\mu}$. Let $S(t) = S^0 + S_1(t), I(t) = I_1(t),\ r(t,\tau) = r_1(t,\tau), B(t) = B_1(t)$, and linearizing system (2.1) about E_0, we obtain the following system:

$$\begin{aligned}
\frac{dS_1(t)}{dt} &= -\mu S_1(t) - \beta S^0 B_1(t),\\
\frac{dI_1(t)}{dt} &= -(\mu+\gamma)I_1(t) + \int_0^\infty \theta(a) r_1(t,\tau)d\tau + \beta S^0 B_1(t)\\
\frac{\partial r_1(t,\tau)}{\partial t} + \frac{\partial r_1(t,\tau)}{\partial \tau} &= -(\mu+\theta(\tau))r_1(t,\tau),\\
\frac{dB_1(t)}{dt} &= \alpha I_1(t) - m_0 B_1(t),\\
r_1(t,0) &= \gamma I_1(t).
\end{aligned}$$

To analyze the asymptotic behavior of E_0, we look for solutions of the form $S_1(t) = \bar{x}e^{\lambda t}$, $I_1(t) = \bar{y}e^{\lambda t}$, $r_1(t,\tau) = \bar{r}_1(\tau)e^{\lambda t}$ and $B_1(t) = \bar{B}e^{\lambda t}$. Thus, we can consider the following eigenvalue problems:

$$\begin{aligned}
&\bar{x}\lambda = -\mu\bar{x} - \beta S^0 \bar{B},\\
&\bar{y}\lambda = -(\gamma+\mu)\bar{y} + \int_0^\infty \theta(\tau)\bar{r}_1(\tau)d\tau + \beta S^0\bar{B},\\
&\bar{r}_1(\tau)\lambda + \frac{d\bar{r}_1(\tau)}{d\tau} = -(\mu+\theta(\tau))\bar{r}_1(\tau),\\
&\bar{B}\lambda = \alpha\bar{y} - m_0\bar{B},\\
&\bar{r}_1(0) = \gamma\bar{y}.
\end{aligned}$$

By directly computing, we obtain the following characteristic equation

$$\lambda = -(\gamma+\mu) + K\gamma e^{-\lambda a} + \beta S^0 \frac{\alpha}{\lambda+m_0}. \tag{3.3}$$

Let

$$H(\lambda) = -\lambda - (\gamma+\mu) + K\gamma e^{-\lambda a} + \beta S^0 \frac{\alpha}{\lambda+m_0}.$$

It is easy to obtain for the expression $H(\lambda)$ that

$$H(+\infty) = -\infty, \quad H(0) = -(\gamma+\mu)+K\gamma+\frac{\beta\Lambda\alpha}{\mu m_0} = (\gamma+\mu-K\gamma)(\Re_0-1), \quad H'(\lambda) < 0.$$

Thus, if $\Re_0 < 1$, there are not any real roots for Eq.$H(\lambda) = 0$. That is, we have not any positive the characteristic values for λ. Therefore, every solution of Eq.$H(\lambda) = 0$ must have a negative real part. This implies that the infection-free equilibrium E_0 is locally asymptotically stable for $\Re_0 < 1$. From the above, we know that if $\Re_0 > 1$, $H(\lambda) = 0$ has at least a root with positive parts. Therefore, the infection-free equilibrium E_0 is unstable.

Summing up the above discussions, we have the following result:

Theorem 3.2. *The disease-free equilibrium E_0 of system* (2.1) *is locally asymptotically stable when $\Re_0 < 1$, and unstable when $\Re_0 > 1$.*

Now we investigate the stability of the endemic equilibrium $E^*(S^*, I^*, r^*(\tau), B^*)$ of system (2.1). We establish the following result

Theorem 3.3. *The endemic equilibrium $E^*(S^*, I^*, r^*(\tau), B^*)$ of of system* (2.1) *is locally asymptotically stable when it exists*

Proof. Let

$$S(t) = S_2(t) + S^*, I(t) = I_2(t) + I^*, r(t,\tau) = r_2(t,\tau) + r^*(\tau), B(t) = B_2(t) + B^*.$$

By linearizing system (2.1) about $E^*(S^*, I^*, r^*(\tau), B^*)$, we obtain the following system:

$$\begin{aligned}
\frac{dS_2(t)}{dt} &= -\mu S_2 - \frac{\beta B^*}{B^*+1}S_2(t) - \frac{\beta S^*}{(B^*+1)^2}B_2(t),\\
\frac{dI_2(t)}{dt} &= \frac{\beta B^*}{B^*+1}S_2(t) - (\gamma+\mu)I_2(t) + \int_0^\infty \theta(\tau)r_2(t,\tau)d\tau + \frac{\beta S^*}{(B^*+1)^2}B_2(t),\\
\frac{\partial r_2(t,\tau)}{\partial t} + \frac{\partial r_2(t,\tau)}{\partial \tau} &= -(\mu+\theta(\tau))r_2(t,\tau),\\
\frac{dB_2(t)}{dt} &= \alpha I_2(t) - m_0 B_2(t),\\
r_2(t,0) &= \gamma I_2(t).
\end{aligned} \tag{3.4}$$

We look for solutions of the following form in system (3.4).

$$S_2(t) = \bar{S}_2 e^{\lambda t}, \quad I_2(t) = \bar{I}_2 e^{\lambda t}, \quad r_2(t,\tau) = \bar{r}_2(\tau)e^{\lambda t}, \quad B_2(t) = \bar{B}_2 e^{\lambda t}.$$

Substituting the above expressions into system(3.4), we have

$$\begin{aligned}
\bar{S}_2\lambda &= -\mu\bar{S}_2 - \frac{\beta B^*}{B^*+1}\bar{S}_2 - \frac{\beta S^*}{(B^*+1)^2}\bar{B}_2,\\
\bar{I}_2\lambda &= \frac{\beta B^*}{B^*+1}\bar{S}_2 - (\gamma+\mu)\bar{I}_2 + \int_0^\infty \theta(\tau)\bar{r}_2(\tau)d\tau + \frac{\beta S^*}{(B^*+1)^2}\bar{B}_2,\\
\bar{r}_2(\tau)\lambda + \frac{d\bar{r}_2(\tau)}{d\tau} &= -(\mu+\theta(\tau))\bar{r}_2(\tau),\\
\bar{B}_2\lambda &= \alpha\bar{I}_2 - m_0\bar{B}_2,\\
\bar{r}_2(0) &= \gamma\bar{I}_2.
\end{aligned} \tag{3.5}$$

By directly computing, from system (3.5), we obtain the following characteristic equation

$$\begin{aligned}
\lambda + \frac{\beta B^*}{B^*+1}\frac{\frac{\beta S^*}{(B^*+1)^2}}{\lambda+\mu+\frac{\beta B^*}{B^*+1}}\frac{\alpha}{\lambda+m_0} + (\gamma+\mu) &= \int_0^\infty \theta(\tau)\gamma\rho(\tau)e^{-\lambda\tau}d\tau\\
&\quad + \frac{\beta S^*}{(B^*+1)^2}\frac{\alpha}{\lambda+m_0}.
\end{aligned} \tag{3.6}$$

Let

$$LHS \overset{def}{=} \lambda + \frac{\beta B^*}{B^*+1}\frac{\frac{\beta S^*}{(B^*+1)^2}}{\lambda+\mu+\frac{\beta B^*}{B^*+1}}\frac{\alpha}{\lambda+m_0} + (\gamma+\mu),$$

$$RHS \overset{def}{=} \int_0^\infty \theta(\tau)\gamma\rho(\tau)e^{-\lambda\tau}d\tau + \frac{\beta S^*}{(B^*+1)^2}\frac{\alpha}{\lambda+m_0}.$$

If we assume that there is one eigenvalue λ with $Re(\lambda) \geq 0$, it is easy to obtain that

$$\begin{aligned}
&|LHS| \geq \gamma + \mu,\\
&|RHS| \leq | \int_0^\infty \theta(\tau)\gamma\rho(\tau)e^{-\lambda\tau}d\tau \mid + \mid \frac{\beta S^*}{(B^*+1)^2}\frac{\alpha}{\lambda+m_0} \mid\\
&\qquad \leq \frac{\beta S^*}{B^*+1}\frac{\alpha}{m_0} + \int_0^\infty \theta(\tau)\gamma\rho(\tau)d\tau = \gamma + \mu.
\end{aligned}$$

Thus, we obtain that $|LHS| > |RHS|$. This leads to a contradiction. From the above discussion, we can determine that the existing endemic equilibrium E^* is locally asymptotically stable. This concludes the proof. □

4. Global dynamics

Now we are in position to show the global stability of the equilibria in system (2.1). Inspired by recent works of Magal et al [19], McCluskey [22], Shuai and van den Driessche [31], and Martcheva and Li [21], we construct a suitable Lyapunov functional to establish the global stability of the equilibrium in system (2.1). One difficulty with the constructing Lyapunov functional is that it is not defined when the variables in system may be zero (see, [19]). To show that the constructing Lyapunov functionals of the system are valid, we need to show that the system is persistent. Thus, we first investigate the disease persistence for system (2.1). Integrating the third equation in system (2.1) along the characteristic lines, it its easy to obtain that

$$r(t,\tau) = \begin{cases} \gamma I(t-\tau)\rho(\tau), & 0 < \tau \leq t,\\ r_0(\tau - t)\dfrac{\rho(\tau)}{\rho(\tau-t)}, & 0 < t \leq \tau. \end{cases} \tag{4.1}$$

Applying the methods of paper [23] and using the expression (4.1), we restrict our attention to the following limiting system, which preserves the same dynamics of the model (2.1).

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - \frac{\beta B(t)S(t)}{B(t)+1} - \mu S(t),\\
\frac{dI(t)}{dt} &= \frac{\beta B(t)S(t)}{B(t)+1} + \gamma\int_0^\infty \theta(\tau)I(t-\tau)\rho(\tau)d\tau - (\gamma+\mu)I(t),\\
\frac{dB(t)}{dt} &= \alpha I(t) - m_0 B(t),
\end{aligned} \tag{4.2}$$

with the initial conditions to (4.2) take the form $S(0) = S_0, I(0) = \phi(s), B(0) = B_0$.

Notice that model(4.2) contains terms with infinite delay. Here following the standard procedure in paper [30], we denote the space UC_g of fading memory type with the norm C_Δ

$$\|\phi\| = \sup_{s\leq 0}\|\phi(s)e^{\delta s}\|.$$

Now we shall prove the uniform persistence and the existence of compact attractor by using results of Hale and Waltman [15]. Let $(X;\ d)$ be a complete metric space with metric d. We need to partition X as $X = X^0 \bigcup X_0$, where X^0 is an open subset of X. Let $\bar{\tau} = \sup\{\tau \in (0, \infty) : \theta(\tau) > 0\}$. Note that, possibly, $\bar{\tau} = +\infty$. Let $X^0 = \{(S(t), I(t), B(t)) : S(t) > 0, I(t) > 0, B(t) > 0, \theta(\tau) \in L^1_+(0, \infty) : \int_0^{\bar{\tau}} \theta(\tau)d\tau > 0\}$. Set $X_0 := X/\ X^0$. Clearly, X_0 is a closed subset of X. Denote by $T(t), t \geq 0$ the family of solution operators corresponding to system (4.2). We introduce some notations and terminology: the positive orbit $\gamma^+(x)$ through $x \in X$ is defined as $\gamma^+(x) = \bigcup_{t\geq 0}\{T(t)x\}$. The ω-limit set $\omega(x)$ of x consists of $y \in X$ such that there is a sequence $t_n \to \infty$ as $n \to \infty$ with $T(t_n)x \to y$ as $n \to \infty$. The semigroup $T(t)$ is said to be asymptotically smooth, if for any bounded subset U of X, for which $T(t)U \subset U$ for any $t \geq 0$, there exists a compact set X^0 such that $d(T(t)U, X^0) \to 0$ as $t \to \infty$. The following result is taken from ([15], Theorem 4.2):

Theorem 4.1. *Suppose that we have the following:*

(i) X^0 *is open and dense in* X *with* $X^0 \bigcup X_0 = X$ *and* $X_0 \bigcap X^0 = \phi$*;*

(ii) the solution operators $T(t)$ *satisfy*

$$T(t) : X^0 \to X^0; \quad T(t) : X_0 \to X_0;$$

(iii) $T(t)$ *is point dissipative in* X*;*

(iv) $\gamma^+(U)$ *is bounded in* X *if* U *is bounded in* X*;*

(v) $T(t)$ *is asymptotically smooth;*

(vi) $\mathcal{A} = \bigcup_{x\in A_b} \omega(x)$ *is isolated and has an acyclic covering* $\mathcal{N}$*, where* A_b *is the global attractor of* $T(t)$ *restricted to* X_0 *and* $\mathcal{N} = \bigcup_{i=1}^k N_i$*;*

(vii) for each $N_i \in \mathcal{N}$*,* $W^s(N_i) \bigcap X^0 = \phi$*, where* W^s *refers to the stable set. Then* $T(t)$ *is a uniform repeller with respect to* X^0*, i.e. there is an* $\eta > 0$ *such that for any* $x \in X^0$*,* $\liminf_{t\to\infty} d(T(t)x; X_0) \geq \eta$*.*

Theorem 4.2. *If* $\Re_0 > 1$*, then the disease is endemic; more precisely, there exists an* $\eta > 0$ *such that*

$$\lim\inf_{t\to\infty} I(t) \geq \eta.$$

Proof. Now we check all the conditions of the permanence theorem. It is straightforward to see that (i) is satisfied. The point dissipativity has been discussed in section 2. So we have (iii). In the following, we first show the conclusions (ii) hold. In fact, for X_0, suppose by way of contradiction that there exists $x \in X_0$ and $t_1 > 0$ such that $T(t_1)x \in X^0$. Let $\tau = \inf\{t > 0 : T(t)x \in X^0\}$. Since X^0 is an open set in X and by the continuity of the semigroup $T(t)$, we have $T(\tau)x \notin X^0$ and, hence, $T(\tau)x \in X_0$. Then $\dot{I}(\tau) = \dfrac{\beta B(\tau)S(\tau)}{B(\tau)+1} + \int_0^{\bar{a}} \theta(a)r(a,\tau)da - (\gamma+\mu)I(\tau) = 0$ and $r(\tau, a) = \gamma\rho(a)I(\tau-a)1_{\{\tau>a\}} + r_0(0, a-\tau)\dfrac{\rho(a)}{\rho(a-\tau)}1_{\{a>\tau\}} \in X_0$. and $\dot{B}(\tau) = \alpha I(\tau) - m_0B(\tau)$. For $t \geq 0$, define $x_2 = 0,\ x_3(t,a) = r_0(0, a-t)\dfrac{\rho(a)}{\rho(a-t)}1_{\{a>\tau+t\}},\ x_4 = 0$. Then, $f(t) := (S(t+\tau), x_2(t), x_3(t,a), x_4)$ is a solution to (4.2) with initial condition $f(0) = T(\tau)x$ and $\xi(t) \in X_0, \forall t \geq 0$. Then, by forward uniqueness of solutions, $T(t)x \in X_0, \forall t \geq 0$, which contradicts our assumption that $T(t_1)x \in X_0$. Thus X_0 is forward invariant. That is, $T(t) : X_0 \to X_0$. Now we show that X_0 also is forward invariant. Notice that $\dot{I}(t) \geq -(\gamma+\mu)I(t)$. Hence, $I(t) \geq I(0)e^{-(\gamma+\mu)t}$ for all $t \geq 0$. If $I(0) > 0$, the result obvious holds. If $I(0) = 0$, then $\int_0^{\infty} \theta(\tau)r(0,\tau)d\tau > 0$ (since

$x(0) \in X^0$) Then $\dot{I}(0) > 0$, so that $\exists \tau'$ such that $\forall t \in (0, \tau']$, we have $I(t) > 0$. In this case, we choose τ' such that $\int_0^\infty \theta(\tau')r(t,\tau')d\tau' > 0$ for all $t \in [0, \tau']$. Then, similar to above arguments, we have $I(t) \geq I(\tau')e^{-(\gamma+\mu)t}$ for $t \geq \tau'$. Hence we have $I(t) > 0, \forall t > 0$. Similarly, we have $B(t) > 0, \forall t > 0$ and from the expression of $r(t,\tau) \geq \gamma\rho(\tau)I(t-\tau)$, we can obtain $r(t,\tau) > 0$ for all $t > 0$. Therefore, we have $T(t) : X^0 \to X^0$. Thus we confirmed (iii). From the last discussed part in section 2, we can directly obtain (iv).

Now we show $T(t)$ is asymptotically smooth in (v). Let $K > \Lambda/d$, $0 < \delta < \gamma+\mu$ and

$$\mathcal{D} := \{\phi \in C_\Delta : \sup_{s\leq 0} \phi(s)e^{\delta s} \leq K\}.$$

From Lemma 3.2 of [3], we have $\mathcal{D}$ is compact in C_Δ. Consider an arbitrary bounded set $U \subset X$, and let $I_t(s)(I_t(s) := I(t+s), s \leq 0)$ be the segment of a solution with $I_0 \in U$. By the above discussion, we know that there exists a $T > 0$ such that $I(T) \leq K$ for $t \geq T$ and $I(T) = K$ or $I(t) < K$ for all t. It is easy to follow our results for the case $I(t) < K$ for all t. Now we consider the first case. Let M be the maximum of $I(t)$ on $[0,T]$ and define for $t > T$ the function $\varphi^t(s)$ such that

$$\varphi^t(s) := \begin{cases} I(t+s)e^{-\delta/2s}, & \text{if } T-t \leq s \leq 0, \\ Ke^{-\delta/2s} & \text{if } s \leq T-t. \end{cases}$$

Obviously, $\varphi^t(s) \in \mathcal{D}$, and $d(I_t, \mathcal{D}) \leq d(I_t, \varphi^t(s)) = \sup_{s\leq 0} |I_t(s) - \varphi^t(s)|e^{\delta s}$. By separating the interval $(-\infty, 0)$ into $[T-t, 0], [-t, T-t], (-\infty, -t]$, we have

$$\sup_{T-t\leq s\leq 0} |I_t(s) - \varphi^t(s)|e^{\delta s} = 0,$$

$$\sup_{-t\leq s\leq T-t} |I_t(s) - \varphi^t(s)|e^{\delta s} \leq (Me^{\delta T} + Ke^{\delta/2T})e^{-\delta/2t},$$

and

$$\sup_{s\leq -t} |I_t(s) - \varphi^t(s)|e^{\delta s} \leq (\|I_0\| + M)e^{-\delta t}.$$

Therefore, we have

$$\lim_{t\to\infty} d(I_t, \mathcal{D}) = 0,$$

$T(t)$ is asymptotically smooth. Thus, we confirmed the condition (v) holds. Regarding (vi) , Obviously, $\mathcal{A} = \{E_0\}, (E_0 = (\Lambda/\mu, 0, 0) \in X)$ and isolated. The covering is simply $\mathcal{N} = \{E_0\}$, which is acyclic.

At last, we show that $W^s(E_0) \bigcap X^0 = \phi$. Suppose the contrary, there is a solutions $\varphi_t \in X^0$ such that

$$\lim_{t\to\infty} S(t) = \frac{\Lambda}{\mu}, \quad \lim_{t\to\infty} I(t) = 0, \quad \lim_{t\to\infty} B(t) = 0.$$

Thus, there exists an $\varepsilon_0 > 0$ such that $S(t) > \dfrac{\Lambda}{\mu} - \varepsilon_0$ and $B(t) < \varepsilon_0$ for $t \geq t_0 - \tau$. Since $\Re_0 > 1$, we can choose the above sufficiently small ε_0, such that

$$\left(\frac{\Lambda}{\mu} - \varepsilon_0\right) \frac{\beta\alpha}{(\gamma(1-K)+\mu)(1+\varepsilon_0)m_0} > 1. \tag{4.3}$$

From system(4.2), we have

$$\begin{aligned}\frac{dI(t)}{dt} &\leq \frac{\beta B(t)}{(1+\varepsilon_0)}\left(\frac{\Lambda}{\mu}-\varepsilon_0\right)+\gamma\int_0^{\infty}\theta(\tau)\rho(\tau)I(t-\tau)d\tau-(\gamma+\mu)I(t),\\ \frac{dB(t)}{dt} &= \alpha I(t)-m_0B(t).\end{aligned} \tag{4.4}$$

Consider the following matrix M_ε defined by

$$M_\varepsilon=\begin{pmatrix}-\gamma(1-K)-\mu & \dfrac{\beta}{1+\varepsilon_0}\left(\dfrac{\Lambda}{\mu}-\varepsilon\right)\\ \alpha & -m_0\end{pmatrix}. \tag{4.5}$$

Since M_ε admits positive off-diagonal element, the Perron-Frobenius Theorem [14] implies that there is a positive eigenvector $v=(v_1,v_2)$ for the maximum eigenvalue λ^* of M_ε. From (4.5), we see that the maximum eigenvalue λ^* is positive. Let us consider the following system:

$$\begin{aligned}\frac{du_1(t)}{dt} &= \frac{\beta}{1+\varepsilon_0}\left(\frac{\Lambda}{\mu}-\varepsilon\right)u_2(t)-(\gamma(1-K)+\mu)u_1(t),\\ \frac{du_2(t)}{dt} &= \alpha u_1(t)-m_0u_2(t).\end{aligned} \tag{4.6}$$

Let $u(t)=(u_1(t),u_2(t))$ be a solution of (4.6) through (lv_1,lv_2) at $t=t_0$, where $l>0$ satisfies $lv_1<I(t_0), lv_2<B(t_0)$. Since the semi flow of (4.6) is monotone and $M_\varepsilon v>0$, it follows that $u_i(t)$ are strictly increasing and $u_i(t)\to+\infty$ as $t\to+\infty$, contradicting the eventual boundedness of positive solutions of system (4.6). Thus, $W^s(E_0)\bigcap X^0=\phi$. By Theorem 4.1, we conclude our conclusion. □

Now we first investigate the global stability of the uninfected equilibrium E_0 by constructing Lypunov function. We have the following result

Theorem 4.3. *The disease-free equilibrium $E_0(\frac{\Lambda}{\mu},0,0,0)$ of system (2.1) is globally asymptotically stable when $\Re_0<1$, and unstable when $\Re_0>1$.*

Proof. Let

$$V(t)=I(t)+\int_0^{+\infty}\Delta(\tau)r(\tau,t)d\tau+\frac{\gamma+\mu-K\gamma}{\alpha}B(t),$$

where, $\Delta(\tau)=\displaystyle\int_\tau^{+\infty}\theta(v)e^{-\int_\tau^v\alpha(s)ds}dv$, $\quad\alpha(\tau)=\mu+\theta(\tau)$. By calculating the time derivatives of $V(t)$ along system (2.1), we obtain

$$\begin{aligned}\frac{dV(t)}{dt} &= \frac{dI(t)}{dt}+\int_0^{+\infty}\Delta(\tau)\frac{\partial r}{\partial t}d\tau+\frac{\gamma+\mu-K\gamma}{\alpha}\frac{dB(t)}{dt}\\ &= \frac{\beta B(t)S(t)}{B(t)+1}+\int_0^{+\infty}\theta(\tau)r(\tau,t)d\tau-(\gamma+\mu)I(t)\\ &\quad+\int_0^{+\infty}\Delta(\tau)[-(\mu+\theta(\tau))r(\tau,t)-\frac{\partial r}{\partial\tau}]d\tau+\frac{\gamma+\mu-K\gamma}{\alpha}(\alpha I(t)-m_0B(t))\\ &= \frac{\beta B(t)S(t)}{B(t)+1}+\int_0^{+\infty}\theta(\tau)r(\tau,t)d\tau-(\gamma+\mu)I(t)-\int_0^{+\infty}\Delta(\tau)\alpha(\tau)r(\tau,t)d\tau\end{aligned}$$

$$\begin{aligned}
&-\int_0^{+\infty}\Delta(\tau)\frac{\partial r}{\partial \tau}d\tau+\frac{\gamma+\mu}{\alpha}\alpha I(t)-\frac{K\gamma}{\alpha}\alpha I(t)-\frac{\gamma+\mu-K\gamma}{\alpha}m_0B(t)\\
&=\frac{\beta B(t)S(t)}{B(t)+1}+\int_0^{+\infty}\theta(\tau)r(\tau,t)d\tau-\int_0^{+\infty}\Delta(\tau)\alpha(\tau)r(\tau,t)d\tau\\
&\quad+\int_0^{+\infty}\Delta'(\tau)r(\tau,t)d\tau-\Delta(\tau)r(\tau,t)\big|_0^{+\infty}-K\gamma I(t)-\frac{\gamma+\mu-K\gamma}{\alpha}m_0B(t).
\end{aligned} \tag{4.7}$$

It is easy from the expression $\Delta(\tau)$ to obtain that

$$\Delta'(\tau)=\Delta(\tau)\alpha(\tau)-\theta(\tau),\quad K=\Delta(0).$$

Noting that $r(0,t)=\gamma I(t),\ S(t)\le\frac{\Lambda}{\mu}$. Thus, from Eq.(4.7), we have

$$\begin{aligned}
\frac{dV(t)}{dt}&=\Big(\frac{\beta S(t)}{B(t)+1}-\frac{\gamma+\mu-K\gamma}{\alpha}m_0\Big)B(t)\\
&\le\Big(\beta\frac{\Lambda}{\mu}-\frac{\gamma+\mu-K\gamma}{\alpha}m_0\Big)B(t)\\
&=\frac{(\gamma+\mu-K\gamma)\mu m_0(\Re_0-1)}{\mu\alpha}B(t).
\end{aligned} \tag{4.8}$$

The equality $\frac{dV(t)}{dt}=0$ holds if and only if $B(t)=0$. Thus, from system (2.1), it is easy to obtain that $S(t)\to\frac{\Lambda}{\mu}$ and $I(t)=0$ when $t\to\infty$. Along the characteristic lines, from system (2.1), we have that $r(\tau,t)=0$ for all $t>\tau$. It is easy to show that $\{E_0\}$ is the maximal compact invariant set. From the LaSalle invariant principle ([14],Theorem 5.3.1), we have that the disease-free equilibrium E_0 of system (2.1) is globally stable for $\Re_0\le 1$. □

Now we investigate the global stability of the infected equilibrium E^*. By using the function $g(x)=x-1-\ln x>0, x\ge 0$, we construct the suitable Lyapunov functions and establish the following result

Theorem 4.4. *The unique endemic equilibrium $E^*(S^*,I^*,r^*(\tau),B^*)$ of system* (2.1) *is globally asymptotically stable when $\Re_0>1$.*

Proof. Let

$$L(t)=L_1(t)+L_2(t)+L_3(t)+L_4(t),$$

where

$$\begin{aligned}
L_1(t)&=S(t)-S^*-S^*\ln\frac{S(t)}{S^*},\\
L_2(t)&=I^*g\Big(\frac{I(t)}{I^*}\Big),\\
L_3(t)&=\int_0^{+\infty}\Delta(\tau)r^*(\tau)g\Big(\frac{r(t,\tau)}{r^*(\tau)}\Big)d\tau,\\
L_4(t)&=\frac{\gamma+\mu-K\gamma}{\alpha}B^*g\Big(\frac{B(t)}{B^*}\Big).
\end{aligned} \tag{4.9}$$

By calculating the time derivatives of $L_1(t)$ along system (2.1), we obtain

$$\begin{aligned}
\frac{dL_1(t)}{dt} &= \frac{dS}{dt}(1-\frac{S^*}{S(t)})\\
&= [\Lambda - \frac{\beta B(t)S(t)}{B(t)+1} - \mu S(t)](1-\frac{S^*}{S(t)})\\
&= [\frac{\beta B^*S^*}{B^*+1} - \frac{\beta B(t)S(t)}{B(t)+1} + \mu(S^*-S(t))](1-\frac{S^*}{S(t)})\\
&= \frac{-\mu(S^*-S(t))^2}{S(t)} + \frac{\beta B^*S^*}{B^*+1}(1-\frac{S^*}{S(t)}) - \frac{\beta B(t)S(t)}{B(t)+1} + \frac{\beta B(t)S(t)}{B(t)+1}\frac{S^*}{S(t)}\\
&= \frac{-\mu(S^*-S(t))^2}{S(t)} - \frac{\beta B^*S^*}{B^*+1}g(\frac{S^*}{S(t)})\\
&\quad - \frac{\beta B^*S^*}{B^*+1}ln\frac{S^*}{S(t)} - \frac{\beta B(t)S(t)}{B(t)+1} + \frac{\beta B(t)S^*}{1+B(t)}.
\end{aligned}$$

By calculating the time derivatives of $L_2(t)$ along system (2.1), we obtain

$$\begin{aligned}
\frac{dL_2(t)}{dt} &= (1-\frac{I^*}{I(t)})\frac{dI(t)}{dt}\\
&= (1-\frac{I^*}{I(t)})[\frac{\beta B(t)S(t)}{B(t)+1} + \int_0^{+\infty}\theta(\tau)r(\tau,t)d\tau - (\gamma+\mu)I(t)]\\
&= (1-\frac{I^*}{I(t)})[\frac{\beta B(t)S(t)}{B(t)+1} - \frac{\beta B^*S^*}{B^*+1} + \int_0^{+\infty}\theta(\tau)r(\tau,t)d\tau - \int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau\\
&\quad + (\gamma+\mu)I^* - (\gamma+\mu)I(t)]\\
&= \frac{\beta B(t)S(t)}{B(t)+1} - \frac{\beta B(t)S(t)}{B(t)+1}\frac{I^*}{I(t)} + \frac{\beta B^*S^*}{B^*+1}(\frac{I^*}{I(t)}-1)\\
&\quad + (1-\frac{I^*}{I(t)})\int_0^{+\infty}\theta(\tau)r^*(\tau)(\frac{r(\tau,t)}{r(\tau)^*}-1)d\tau + (1-\frac{I^*}{I(t)})(\gamma+\mu)I^*(1-\frac{I(t)}{I^*})\\
&= \frac{\beta B(t)S(t)}{B(t)+1} - \frac{\beta B^*S^*}{B^*+1}\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)} + \frac{\beta B^*S^*}{B^*+1}g(\frac{I^*}{I(t)}) + \frac{\beta B^*S^*}{B^*+1}\ln\frac{I^*}{I(t)}\\
&\quad + \int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau[g(\frac{r(\tau,t)}{r^*(\tau)}) - g(\frac{I^*r(t,\tau)}{I(t)r^*(\tau)}) + g(\frac{I^*}{I(t)})]\\
&\quad + (\gamma+\mu)I^*[-g(\frac{I(t)}{I^*}) - g(\frac{I^*}{I(t)})]\\
&= \frac{\beta B(t)S(t)}{B(t)+1} - \frac{\beta B^*S^*}{B^*+1}g(\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)}) - \frac{\beta B^*S^*}{B^*+1}\\
&\quad - \frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)} + \frac{\beta B^*S^*}{B^*+1}g(\frac{I^*}{I(t)}) + \frac{\beta B^*S^*}{B^*+1}\ln\frac{I^*}{I(t)}\\
&\quad + \int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau[g(\frac{r(\tau,t)}{r^*(\tau)}) - g(\frac{I^*r(\tau,t)}{I(t)r^*(\tau)}) + g(\frac{I^*}{I(t)})]\\
&\quad + (\gamma+\mu)I^*[-g(\frac{I(t)}{I^*}) - g(\frac{I^*}{I(t)})]\\
&= \frac{\beta B(t)S(t)}{B(t)+1} - \frac{\beta B^*S^*}{B^*+1}g(\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)}) - \frac{\beta B^*S^*}{B^*+1}
\end{aligned}$$

$$
\begin{aligned}
&-\frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)}+\frac{\beta B^*S^*}{B^*+1}\ln\frac{I^*}{I(t)}\\
&+\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau[g(\frac{r(\tau,t)}{r^*(\tau)})-g(\frac{I^*r(\tau,t)}{I(t)r^*(\tau)})]-(\gamma+\mu)I^*g(\frac{I(t)}{I^*}).
\end{aligned}\tag{4.10}
$$

By calculating the time derivatives of $L_3(t)$ along system (2.1), we obtain

$$
\begin{aligned}
\frac{dL_3(t)}{dt}&=\int_0^{+\infty}\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})\frac{\partial r(t,\tau)}{\partial t}d\tau\\
&=\int_0^{+\infty}\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})(-(\mu+\theta(\tau))r(\tau,t)-\frac{\partial r(t,\tau)}{\partial \tau})d\tau.
\end{aligned}\tag{4.11}
$$

By direct calculating the derivative of the expression $\Delta(\tau)r^*(\tau)g\left(\frac{r(t,\tau)}{r^*(\tau)}\right)$ for τ,

$$
\begin{aligned}
&[\Delta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})]'\\
=&\Delta'(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})+\Delta(\tau)r'^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})\\
&+\Delta(\tau)r^*(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})(\frac{\frac{\partial r(t,\tau)}{\partial\tau}r^*(\tau)-\frac{dr^*(\tau)}{d\tau}r(\tau,t)}{(r^*(\tau))^2})\\
=&\Delta'(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}))+\Delta(\tau)r'^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})\\
&+\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})\frac{\partial r(t,\tau)}{\partial\tau}-\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})\frac{dr^*(\tau)}{d\tau}\frac{r(t,\tau)}{r^*(\tau)}\\
=&(\Delta(\tau)\alpha(\tau)-\theta(\tau))r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})+\Delta(\tau)(-\alpha(\tau))r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}\\
&+\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})\frac{\partial r(t,\tau)}{\partial\tau}+\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})\alpha(\tau)r(\tau,t)\\
=&-\theta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})+\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})(\frac{\partial r(t,\tau)}{\partial\tau}+(\mu+\theta(\tau))r(t,\tau)).
\end{aligned}
$$

From (4.11), we obtian

$$
\begin{aligned}
&\int_0^{+\infty}\Delta(\tau)(1-\frac{r^*(\tau)}{r(t,\tau)})(-(\mu+\theta(\tau))r(\tau,t)-\frac{\partial r(t,\tau)}{\partial\tau})d\tau\\
=&\int_0^{+\infty}-\theta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})d\tau-(\Delta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}))\big|_0^{+\infty}\\
=&\int_0^{+\infty}-\theta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})d\tau-(\Delta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}))\big|_0^{+\infty}+K\gamma I^*g(\frac{I(t)}{I^*})\\
=&\int_0^{+\infty}-\theta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)})d\tau-(\Delta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}))\big|_0^{+\infty}+\int_0^{+\infty}\theta(\tau)r^*(\tau)g(\frac{I(t)}{I^*})d\tau.
\end{aligned}\tag{4.12}
$$

By calculating the time derivatives of $L_4(t)$ along system (2.1), we obtain

$$\begin{aligned}
\frac{dL_4(t)}{dt} &= \frac{\gamma+\mu-K\gamma}{\alpha}(1-\frac{B^*}{B(t)})\frac{dB}{dt} = \frac{\gamma+\mu-K\gamma}{\alpha}(1-\frac{B^*}{B(t)})(\alpha I(t)-m_0B(t))\\
&= \frac{\gamma+\mu-K\gamma}{\alpha}(1-\frac{B^*}{B(t)})(\alpha I(t)-\alpha I^*+\alpha I^*-\frac{\alpha I^*}{B^*}B(t))\\
&= \frac{\gamma+\mu-K\gamma}{\alpha}(1-\frac{B^*}{B(t)})\alpha I^*(\frac{I(t)}{I^*}-1+1-\frac{B(t)}{B^*})\\
&= \frac{\gamma+\mu}{\alpha}(1-\frac{B^*}{B(t)})\alpha I^*(\frac{I(t)}{I^*}-\frac{B(t)}{B^*})-\frac{K\gamma}{\alpha}(1-\frac{B^*}{B(t)})\alpha I^*(\frac{I(t)}{I^*}-\frac{B(t)}{B^*})\\
&= (\gamma+\mu)I^*(1-\frac{B^*}{B(t)})(\frac{I(t)}{I^*}-\frac{B(t)}{B^*})-\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau(1-\frac{B^*}{B(t)})(\frac{I(t)}{I^*}-\frac{B(t)}{B^*})\\
&= (\gamma+\mu)I^*[g(\frac{I(t)}{I^*})-g(\frac{B(t)}{B^*})-g(\frac{I(t)B^*}{I^*B(t)})]\\
&\quad -\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau[g(\frac{I(t)}{I^*})-g(\frac{B(t)}{B^*})-g(\frac{I(t)B^*}{I^*B(t)})]\\
&= (\gamma+\mu)I^*g(\frac{I(t)}{I^*})-\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau g(\frac{I(t)}{I^*})+\frac{\beta B^*S^*}{B^*+1}[-g(\frac{B(t)}{B^*})-g(\frac{I(t)B^*}{I^*B(t)})].
\end{aligned}$$

From the Eq.(4.12),(4.12) and (4.13), we have

$$\begin{aligned}
\frac{dL(t)}{dt} &= \frac{dL_1(t)}{dt}+\frac{dL_2(t)}{dt}+\frac{dL_3(t)}{dt}+\frac{dL_4(t)}{dt}\\
&= \frac{-\mu(S^*-S(t))^2}{S(t)}-\frac{\beta B^*S^*}{B^*+1}g(\frac{S^*}{S(t)})-\frac{\beta B^*S^*}{B^*+1}\ln\frac{S^*}{S(t)}-\frac{\beta B(t)S(t)}{B(t)+1}+\frac{\beta BS^*}{1+B(t)}\\
&\quad +\frac{\beta B(t)S(t)}{B(t)+1}-\frac{\beta B^*S^*}{B^*+1}g(\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)})-\frac{\beta B^*S^*}{B^*+1}\\
&\quad -\frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)}+\frac{\beta B^*S^*}{B^*+1}\ln\frac{I^*}{I(t)}\\
&\quad +\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau[g(\frac{r(t,\tau)}{r^*(\tau)})-g(\frac{I^*r(t,\tau)}{I(t)r^*(\tau)})]-(\gamma+\mu)I^*g(\frac{I(t)}{I^*})\\
&\quad +\int_0^{+\infty}-\theta(\tau)r^*(\tau)d\tau g(\frac{r(t,\tau)}{r^*(\tau)})-(\Delta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}))\Big|_0^{+\infty}\\
&\quad +\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau g(\frac{I(t)}{I^*})+(\gamma+\mu)I^*g(\frac{I(t)}{I^*})\\
&\quad -\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau g(\frac{I(t)}{I^*})+\frac{\beta B^*S^*}{B^*+1}[-g(\frac{B(t)}{B^*})-g(\frac{I(t)B^*}{I^*B(t)})]\\
&= \frac{-\mu(S^*-S(t))^2}{S(t)}-\frac{\beta B^*S^*}{B^*+1}g(\frac{S^*}{S(t)})-\frac{\beta B^*S^*}{B^*+1}g(\frac{B^*+1}{B(t)+1}\frac{B(t)S(t)I^*}{B^*S^*I(t)})\\
&\quad -\int_0^{+\infty}\theta(\tau)r^*(\tau)d\tau g(\frac{I^*r(t,\tau)}{I(t)r^*(\tau)})-(\Delta(\tau)r^*(\tau)g(\frac{r(t,\tau)}{r^*(\tau)}))\Big|_0^{+\infty}\\
&\quad -\frac{\beta B^*S^*}{B^*+1}g(\frac{I(t)B^*}{I^*B(t)})+\frac{\beta B(t)S^*}{1+B(t)}-\frac{\beta B^*S^*}{B^*+1}\\
&\quad -\frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)}{B^*}-\frac{\beta B^*S^*}{B^*+1}g(\frac{B(t)}{B^*}).
\end{aligned}\tag{4.13}$$

Let

$$H(t) = \frac{\beta B(t)S^*}{1+B(t)} - \frac{\beta B^*S^*}{B^*+1} - \frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)}{B^*} - \frac{\beta B^*S^*}{B^*+1}g(\frac{B(t)}{B^*}).$$

By direct calculating, we obtain that following

$$\begin{aligned}
H(t) &= \frac{\beta B(t)S^*}{1+B(t)} - \frac{\beta B^*S^*}{B^*+1} - \frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)}{B^*} - \frac{\beta B^*S^*}{B^*+1}g(\frac{B(t)}{B^*})\\
&= \frac{\beta B(t)S^*}{1+B(t)} - \frac{\beta B^*S^*}{B^*+1} - \frac{\beta B^*S^*}{B^*+1}\ln\frac{B^*+1}{B(t)+1}\frac{B(t)}{B^*} + \frac{\beta B^*S^*}{B^*+1}\ln\frac{B(t)}{B^*} - \frac{\beta B^*S^*}{B^*+1}(\frac{B(t)}{B^*}-1)\\
&= \frac{\beta B(t)S^*}{1+B(t)} - \frac{\beta B^*S^*}{B^*+1} + \frac{\beta B^*S^*}{B^*+1}\ln\frac{B(t)+1}{B^*+1} - \frac{\beta B^*S^*}{B^*+1}(\frac{B(t)}{B^*}-1)\\
&= \frac{\beta B(t)S^*}{1+B(t)} - \frac{\beta B^*S^*}{B^*+1} - \frac{\beta B^*S^*}{B^*+1}g(\frac{B(t)+1}{B^*+1}) - \frac{\beta B^*S^*}{B^*+1} + \frac{\beta B^*S^*}{B^*+1}\frac{B(t)+1}{B^*+1}\\
&\quad - \frac{\beta B^*S^*}{B^*+1}(\frac{B(t)}{B^*}-1)\\
&= -\frac{\beta B^*S^*}{B^*+1}g(\frac{B(t)+1}{B^*+1}) + \frac{\beta B^*S^*}{B^*+1}[\frac{1+B^*}{1+B(t)}\frac{B(t)}{B^*} - 1 + \frac{B(t)+1}{B^*+1} - \frac{B(t)}{B^*}]\\
&= -\frac{\beta B^*S^*}{B^*+1}g(\frac{B(t)+1}{B^*+1}) - \frac{\beta S^*(B(t)-B^*)^2}{(1+B(t))(1+B^*)^2} \leq 0. \qquad (4.14)
\end{aligned}$$

From (4.13),(4.14),and using $g(x) = x - 1 - \ln x > 0, x \geq 0$, we obtain that $\frac{dL(t)}{dt} \leq 0$ for $S(t), I(t), r(t,\tau)$, and $B(t) > 0$. Moreover, $\frac{dL(t)}{dt} = 0$ if and only if $S(t) = S^*, I(t) = I^*, r(t,\tau) = r^*(\tau)$, and $B(t) = B^*$, for all $t \geq 0$. The largest compact invariant set in

$$\Omega = \{(S(t), I(t), r(t,\tau), B(t)|\dot{L}(t) = 0\}$$

is $\{E^*\}$. By LaSalle's invariance principle, we can conclude that the endemic equilibrium E^* of system (2.1) is globally asymptotically stable for $\Re_0 > 1$. □

5. Concluding Remarks

Loss of immunity is considered to be one of the sources causing recurrence of infectious disease dynamics observed in many epidemics. This recurrence of disease is an important feature of some infectious diseases, for example, tuberculosis (TB), Cholera, and Herpes. In recent years, several disease transmission models [10, 25, 40, 41] with temporary immunity have been investigated, where numerical simulations and the theoretical results are presented that there are not any evidence of sustained oscillatory solutions for recurrence of diseases. In this paper, a cholera epidemic model with age-of-immunity structure has been discussed, where recovered individuals may relapse with reactivation of latent infection and revert back to the infective class. By mathematical analysis for the model, we have established a threshold dynamics, which is completely determined by the basic reproduction number. It is shown that when the reproduction number $\Re_0 > 1$, then the endemic equilibrium is globally asymptotically stable and the disease persists in the human population. The infection free equilibrium is globally asymptotically stable and the cholera is disappeared if the reproduction number $\Re_0 < 1$. From the obtained expression of the reproduction number $\Re_0$, it can be observed that host immunity, pathogen hyperinfectivity and phages are all factors that can be leveraged for outbreak control. Recently, the cholera outbreak in Yemen [37] is shaped by the interplay of biological, environmental, socioeconomic, and climatic factors. To better understand cholera epidemiology retrospectively and to predict the impact of interventions in the future, further developments on cholera modeling demand a systematic study that incorporate all these components.

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