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GLOBAL STABILITY ANALYSIS OF THE EFFECT OF VACCINATION AND TREATMENT IN CONTROLLING THE SPREAD OF HEPATITIS B VIRUS WITH INFECTIVE MIGRANTS.

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Abstract

In this study, we present a deterministic model on the effect of vaccination and treatment in controlling the spread of hepatitis b virus with infective migrants. The disease free equilibrium state is obtained and we compute the effective reproduction number from which we establish the endemic equilibrium state of the model. The global stability of endemic equilibrium state was analyzed using a lyapunov function and found to be stable. The public health implication is that HBV will be sustained if infective migrants are allowed and also, there is improper or no vaccination regiment, under steady state conditions. Hence the governing model can be applied for predicting the spread of HBV. However, effort should be undertaken that will help to maximize the long-term effectiveness of vaccination and treatment program in curtailing the spread of HBV with infective migrants.

Keywords: Hepatitis B Virus, migrant, vaccination, treatment, stability, Endemic equilibrium state.

1.0 Introduction

Hepatitis B virus (HBV) is one of the greatest and deadly global health concerns of modern times. It was estimated that 2 billion people acquire the disease resulting in 350 million cases of chronic active hepatitis [1] and 780,000 deaths per year [2]. This infection is accountable for 80% of all cases of primary liver cancer, which is one of the principal causes of death in Asia and Africa [3]. Therefore, HBV have created a global and security threat and have drawn the attention of WHO to declare war against the disease.

The disease can be transmitted through unprotected sex, accidental needle injury, birth among others [4, 5]. Moreover, the spread might become faster due to porous borders and risky practices of migration process. Therefore, as the epidemic spreads wider, the bond between migration and the spread of HBV is becoming stronger. Thus, prevention of transmission of HBV between infective migrants and the resident population appears to be an important step in reducing the global burden of HBV infection.

The prevention and control effort should be aimed at promoting optimum use of available therapy, where the disease is evident and vaccines for those susceptible to infection. Hence, cleaving to HBV therapies has > 95% effectiveness for sustaining utmost suppression [6, 7, and 8]. In additional, above 1.1 million deaths could be avoided by 2030, if global vaccination coverage improves [9, 10]. Unfortunately, many are not aware of the infection and as such they have no access to preventive or therapeutic interventions.

Sub-Saharan Africa and East Asia have being categorized among regions of the world that is highly endemic for hepatitis B virus infection. It is estimated that 2-5% of the general population are reportedly likely to be chronically infected [11].Considering the number of migrants from these regions who travel around the world on a daily basis. This is not just these regions public health problems but has a global consequence since HBV is not isolated geographically. Therefore, the prevalence rate also stands to hinder successes recorded by other regions (countries) on preventing chronic liver disease [12].

The prevalence of the disease due to population growth, drug- resistant strains, co-infection with HIV, re-infection and relapse, cultural factors, the collapse of public health programs [13, 14] is on the increase globally and is a challenge for health care services worldwide.

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Therefore, vaccination and treatment of HBV are needed to reduce the incidence rate and the total burden of liver disease worldwide. Vaccination helps to provide protection against HBV infection [15]. However, despite successes associated with the use of vaccines and supportive therapies for acute infection, the devastating effect of HBV has increased. Also, since vaccination alone does not eliminate infectivity or block the route of transplacental (vertical) transmission, the call for vaccination in conjunction with effective treatment becomes necessary.

Nevertheless, treatment as a control approach helps to reduce viral load depending on medication and genotype [16]. Most commonly used drugs include interferon and nucleoside such as lamivudine, adefovir dipivoxil, telbivudine [17]. Though, most patients with chronic HBV infection need long–term therapy [18]. However, treatment should be modified if failure to attain decline in viral load after 12weeks of therapy is identified. When using drugs with a low barrier to resistance, good adherence to anti-HBV therapies is important for sustaining maximal suppression of HBV replication. Notwithstanding, therapeutic efficacy of treatment can be hampered by development of adverse effects, poor patient compliance, previous treatment with suboptimal regimens, infection with drug- resistance viral strains, inadequate drug exposure because of pharmacologic properties of particular drug(s) and individual genetic variation [19,16,20,18and 21].

To improve better understanding on the dynamics of HBV infection, several mathematical models have been used extensively to study the transmission dynamics of HBV (see [22, 23, 24, 25] and the references therein).

This study is motivated by the work of [25], on the transmission model of hepatitis B virus with the migration effect. Their result suggests that migrants for short visit and students should be subjected to test to reduce the number of migrants with the disease. Therefore, guided by the work in [25] as mentioned above, the present study intends to extend their work by incorporating treatment class and its relapse effect. Hence, this study intends to investigate the global stability analysis of the effect of vaccination and treatment on HBV transmission with infective migrants.

2.0 Model Formulation

2.1 The Existing Model

We consider the following assumptions of the existing model in [25] below.

i. The population is compartmentalized into six groups namely: Susceptible individuals, S(t), Exposed individuals E(t), Acutely infected individuals, A(t), Chronic carriers, C(t), Immunised individuals, V(t), and Migrated individuals, M(t), all at time t.
ii. The population is mixed homogeneously, that is, all people are equally likely to be infected by the infectious individuals in case of contact.
iii. The newborns to carrier mothers infected at birth are latently infected individual.
iv. A proportion of susceptibles is vaccinated per unit time and the vaccinated individuals do not acquire permanent immunity.
v. They also considered γ_3 ,as the rate at which chronic carriers acquire immunity and move to the immunized class.
vi. There is a transmission rate from exposed to migrated class and vise–visa.
vii. There is a transmission rate from migrated class to susceptible class and migrated class to acutely infected class.
viii. There is a stable population with equal percapita birth and death rate δ (as disease- induced death rate is not considered in the system).

Table 1: Parameters of the Existing Model

The existing model in [25] has the following parameters:

Parameters	Description
δ	Equal per capita birth and death rate (as disease-induced death rate is not considered in the system)
π	The proportion of failure immunization or proportion without immunization
γ_1	Rate at which exposed individuals become infectious and move to the acute infected class.
γ_2	Rate at which acutely infected individuals move to the chronic carrier class
γ_3	Rate at which carriers acquire immunity and move to the immunized class
β	The transmission coefficient
k	The infectiousness of carrier relative to acute infections.
q	Proportion of acute infected individual that become carrier.
$1-q$	Proportion of acute infected individuals that move to the immunity class
δ_0	The loss of immunity from the immunized class to susceptible class.
P	Proportion of vaccinated susceptible per unit time.
ξ	The rate of flow from exposed to migrated class.
α	The flow from migrated to susceptible class.
μ_1	The transmission rate from migrated class to exposed class.
μ_2	The transmission rate from migrated class to acute infected class
η	Proportion of the unimmunized children born to carrier mothers
$\delta(1-\pi)$	The newborns that are successfully immunized
$\delta\pi(1-\eta C(t))$	Births flux into the susceptible class

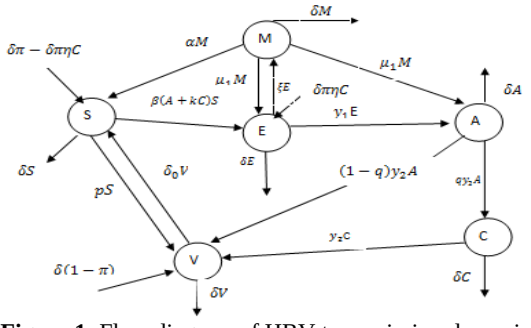

Figure 1: Flow diagram of HBV transmission dynamics for the existing model

With the above assumptions, parameters and flow diagram by [25], the following model equations were derived.

$$\frac{dS}{dt} = \delta\pi(1-\eta C) - \delta S - \beta(A+kC)S + \delta_0 V - pS + \alpha M$$
$$\frac{dE}{dt} = \beta(A+kC)S - \delta E + \delta\pi\eta C - \gamma_1 E + \mu_1 M - \xi E$$
$$\frac{dA}{dt} = \gamma_1 E - (\delta+\gamma_2)A + \mu_2 M \qquad (1)$$
$$\frac{dC}{dt} = q\gamma_2 A - \delta C - \gamma_3 C$$
$$\frac{dV}{dt} = \gamma_3 C + (1-q)\gamma_2 A - \delta_0 V - \delta V + \delta(1-\pi) + pS$$
$$\frac{dM}{dt} = \xi E - (\mu_1+\mu_2)M - \delta M - \alpha M$$

2.2 The Extended Model

In addition to the assumptions of the existing model, we make the following assumptions.

i. We assume that the chronic carriers do not acquire immunity accept they are treated [26] and recruited into the treated class. Whereas, not all treated individuals recovers and progress to the recovery class, some relapse to chronic if drug resistant mutants are present[27]. In addition, we change the notation of the immune class to vaccinated class and redefined the parameters of the extended model in table 2**.**

Table 2: Parameters of the Extended Model.

Parameters	Description
$T(t)$	Number of treated individuals at time t
$R(t)$	Number of recovered individuals at time t
δ_0	The loss of immunity from the vaccinated class to susceptible class
α_o	Proportion of chronic carriers that are treated per unit time.
γ_3	Rate of recovery of the treated individuals
φ	Rate at which treated individual relapse and proceed to the chronic class
$1-q$	Proportion of acute infected individual that move to the recovered class

The flow diagram for the existing model is now amended to obtain the flow diagram for the extended model as follows;

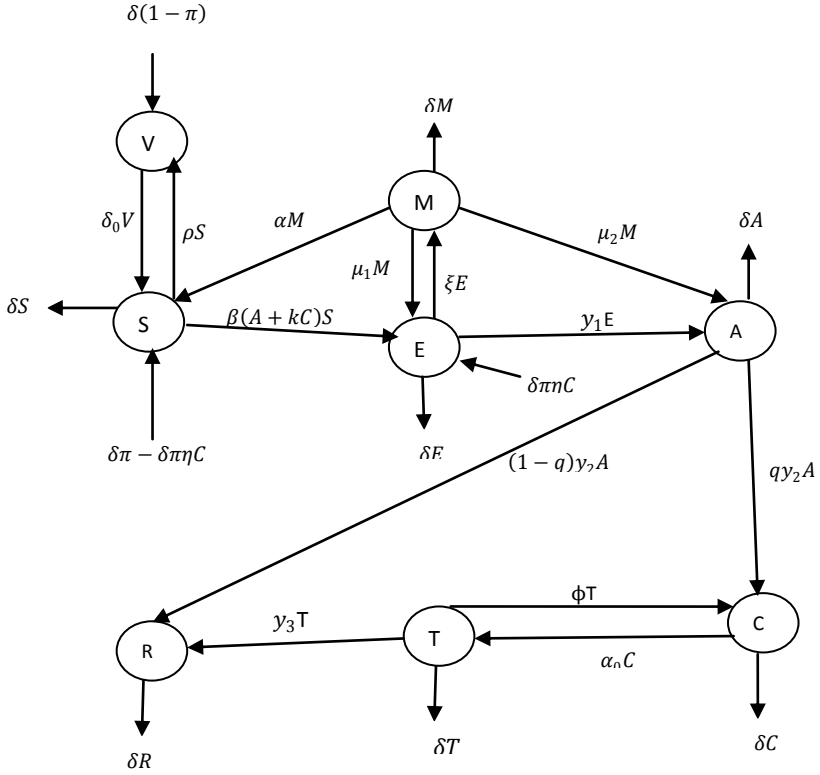

Figure 2: Flow Diagram of HBV transmission Dynamics for the Extended Model

The extended model equations are derived based on the above assumptions, parameters and flow diagram in figure 2.

$$\frac{dS}{dt} = \delta\pi(1-\eta C) - \delta S - \beta(A+kC) - pS + \delta_0 V + \alpha M$$
$$\frac{dE}{dt} = \beta(A+kC)S - (\delta+\xi+\gamma_1)E + \delta\pi\eta C + \mu_1 M$$
$$\frac{dA}{dt} = \gamma_1 E - (\delta+\gamma_2)A + \mu_2 M$$
$$\frac{dC}{dt} = q\gamma_2 A + \varphi T - (\delta+\alpha_0)C \qquad (2)$$
$$\frac{dT}{dt} = \alpha_0 C - (\delta+\varphi+\gamma_3)T$$
$$\frac{dR}{dt} = (1-q)\gamma_2 A + \gamma_3 T - \delta R$$
$$\frac{dM}{dt} = \xi E - (\mu_1+\mu_2+\delta+\alpha)M$$
$$\frac{dV}{dt} = \delta(1-\pi) + pS - (\delta+\delta_0)V,$$
$$S(0) > 0, E(0) \geq 0, A(0) \geq 0, C(0) \geq 0, T(0) \geq 0, R(0) \geq 0, M(0) \geq 0, V(0) \geq 0$$

The total population $N(t)$, therefore becomes

$$\frac{dN}{dt} = \delta(1-N) \qquad (3)$$

Using variable separable method, we have

$$\frac{dN}{(1-N)} = \delta dt$$

Integrating both side yield

$$\int \frac{dN}{(1-N)} = \int \delta dt$$
$$-In(1-N) = \delta t + C$$

Multiplying through by -1

$$In(1-N) = -\delta t - C$$

Taking exponential of both side

$1 - N = Ae^{-\delta t}$, where $A = e^{-c}$

$N(t) = 1 - Ae^{-\delta t}$,

At time $t = 0$, we have

$N(0) = N_0 = 1 - A$

$A = 1 - N_0$

$N(t) = 1 - (1-N_0)e^{-\delta t}$,

$N(t) \to 1$ as t $\to \infty$, it means that

Since $S + E + A + C + T + R + M + V = 1$, we have

$$R = 1 - S - E - A - C - T - M - V \qquad (4)$$

Hence, the governing equation becomes

$$\frac{dS}{dt} = \delta\pi(1-\eta C) - \delta S - \beta(A+kC)S + \delta_0 V - pS + \alpha M,$$
$$\frac{dE}{dt} = \beta(A+kC)S - \delta E + \delta\pi\eta C - \gamma_1 E - \xi E + \mu_1 M,$$
$$\frac{dA}{dt} = \gamma_1 E - (\delta+\gamma_2)A + \mu_2 M,$$
$$\frac{dC}{dt} = q\gamma_2 A + \varphi T - (\delta+\alpha_0)C \,, \qquad (5)$$
$$\frac{dT}{dt} = \alpha_0 C - (\delta+\varphi+\gamma_3)T$$
$$\frac{dM}{dt} = \xi E - (\mu_1+\mu_2+\delta+\alpha)M.$$
$$\frac{dV}{dt} = \delta(1-\pi) + pS - (\delta+\delta_0)V,$$

The initial conditions for the extended model are non-negative. $S(0) \geq 0, E(0) \geq 0, A(0) \geq 0, C(0) \geq 0, T(0) \geq 0, M(0) \geq 0, V(0) \geq 0,$

3 Model Analysis

The governing model equation (5) is biologically meaningful, epidemiologically well posed and has solutions which are contained in the region

$\Omega = \{(S, E, A, C, T, M, V): N(t) \leq 1\} \epsilon R_+^7$

Hence Ω is attracting and all the feasible solution of the model with initial condition in R_+^7 enters or stays in the region Ω.

3.1 The disease free equilibrium state

The disease-free equilibrium state when solved gives:

$$X_0 = (S^O, E^O, A^O, C^O, T^O, M^O, V^O) = \left(\frac{\delta\pi + \delta_0}{\delta + \delta_0 + p}, 0,0,0,0,0, \frac{(\delta + \rho) - \delta\pi}{\delta + \delta_0 + p}\right) \quad (6)$$

3.2 The effective reproduction number, R_{r^c}

The effective reproduction number is defined as the average number of new infection generated by a typical infectious individual in the presence of a control measure [28]. Effective reproduction number is the useful threshold for predicting outbreaks and evaluating control strategies that would reduce the spread of the disease in the population. If $R_{r^c} < 1$, the disease can be eliminated, however, when $R_{r^c} > 1$ it will persist or become endemic in the population.

The effective reproduction number for the model (5) is calculated using the next generation operator approach as described in [28]. Applying this approach, we rearrange our model in equation (5) in order of infected compartments followed by uninfected compartment. This gives

$$\begin{aligned}
\frac{dE}{dt} &= \beta(A + kC)S - \delta E + \delta\pi\eta C - \gamma_1 E - \xi E + \mu_1 M, \\
\frac{dA}{dt} &= \gamma_1 E - (\delta + \gamma_2)A + \mu_2 M, \\
\frac{dC}{dt} &= q\gamma_2 A + \varphi T - (\delta + \alpha_0)C, \\
\frac{dM}{dt} &= \xi E - (\mu_1 + \mu_2 + \delta + \alpha)M. \qquad (7) \\
\frac{dS}{dt} &= \delta\pi(1 - \eta C) - \delta S - \beta(A + kC)S + \delta_0 V \ - pS + \alpha M, \\
\frac{dT}{dt} &= \alpha_0 C - (\delta + \varphi + \gamma_3)T \\
\frac{dV}{dt} &= \delta(1 - \pi) + pS - (\delta + \delta_0)V,
\end{aligned}$$

From equation (7), we have the new infective and transfer terms from one compartment to another given as

$$f = \begin{pmatrix} \beta(A + KC)S \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad (8)$$

and

$$v = \begin{pmatrix} (\delta + \xi + \gamma_1)E - \delta\pi\eta C - \mu_1 M \\ (\delta + \gamma_2)A - \mu_2 M - \gamma_1 E \\ (\delta + \alpha_0)C - q\gamma_2 A - \varphi T \\ (\delta + \varphi + \gamma_3)T - \alpha_0 C \\ (\mu_1 + \mu_2 + \alpha + \delta)M - \xi E \end{pmatrix} \quad (9)$$

Therefore, taking the partial derivatives of (8) with respect to (E, A, C, T, M) at disease free equilibrium$\varepsilon_0 = S^0$, we obtain

$$F = Df(\varepsilon_0) = \begin{pmatrix} 0 & \beta S^0 & \beta K S^0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (10)$$

Similarly, the partial derivatives of (9) with respect to (E, A, C, T, M) at disease free equilibrium ε_0 gives

$$V = \begin{pmatrix} m_1 & 0 & -m_2 & 0 & -\mu_1 \\ -\gamma_1 & m_3 & 0 & 0 & -\mu_2 \\ 0 & -m_4 & m_5 & -\varphi & 0 \\ 0 & 0 & -\alpha_0 & m_6 & 0 \\ -\xi & 0 & 0 & 0 & m_7 \end{pmatrix} \quad (11)$$

where , $m_1 = (\delta + \xi + \gamma_1)$, $m_2 = \delta\pi\eta, m_3 = (\delta + \gamma_2), m_4 = q\gamma_2, m_5 = (\delta + \alpha_0)$, $m_6 = (\delta + \varphi + \gamma_3)$ and $m_7 = (\alpha + \delta + \mu_1 + \mu_2)$

Therefore, we have

$$V^{-1} = \begin{pmatrix} B_1 & B_2 & B_3 & B_4 & B_5 \\ C_1 & C_2 & C_3 & C_4 & C_5 \\ D_1 & D_2 & D_3 & D_4 & D_5 \\ E_1 & E_2 & E_3 & E_4 & E_5 \\ F_1 & F_2 & F_3 & F_4 & F_5 \end{pmatrix} \quad (12)$$

such that

$$FV^{-1} = (N_1 \quad N_2), \quad (13)$$

where

$$N_1 = \begin{pmatrix} (\beta S^0 C_1 + \beta K S^0 D_1) & (\beta S^0 C_2 + \beta K S^0 D_2) & (\beta S^0 C_3 + \beta K S^0 D_3) \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad (14)$$

$$N_2 = \begin{pmatrix} (\beta S^0 C_4 + \beta K S^0 D_4) & (\beta S^0 C_5 + \beta K S^0 D_5) \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix} \quad (15)$$

From which we obtain

$$R_{r^c} = \rho(FV^{-1}) = \beta S^0 C_1 + \beta K S^0 D_1 \ , \quad (16)$$

where

$$D_1 = \left(\frac{m_4 m_6(\gamma_1 m_7 + \xi\mu_2)}{\theta}\right)$$

$$C_1 = \left(\frac{(m_5 m_6 - \varphi\alpha_0)(\gamma_1 m_7 + \xi\mu_2)}{\theta}\right)$$

and

$$\theta = \varphi\alpha_0 m_3(m_1 m_7 + \xi\mu_1) - \xi m_6(m_2 m_4 \mu_2 + m_3 m_5 \mu_1) - m_6 m_7(m_2 m_4 \gamma_1 - m_1 m_3 m_5)$$

Thus, the effective reproduction number (16) can be rewritten as

$$R_{r^c} = \frac{\left[\beta S^0\left(c + Kq\gamma_2(\delta + \varphi + \gamma_3)\right) + e(\delta + \varphi + \gamma_3)\right](\mu_2\xi + \gamma_1 a) + \xi\mu_1 bc}{dbca} \quad (17)$$

3.3 Existence of endemic equilibrium

At endemic equilibrium the forth equation of the model (5) gives

$$C = \frac{qy_2A + \varphi T}{\delta + \alpha_0} \quad (18)$$

From the third equation of the model system (5) we have

$$E = \frac{(\delta+\gamma_2)A-\mu_2 M}{\gamma_1} \quad (19)$$

Also, the sixth equation of the model (5) gives

$$M = \frac{\xi E}{\mu_1 + \mu_2 + \delta + \alpha} \quad (20)$$

Substitute equation (19) into (20), we have

$$M = \frac{\xi(\delta+\gamma_2)A}{\xi\mu_2+\gamma_1(\mu_1+\mu_2+\delta+\alpha)} \quad (21)$$

Substitute (21) in equation(19), we have

$$E = \frac{(\delta + y_2)A - \frac{\xi\mu_2(\delta+\gamma_2)A}{(\xi\mu_2+\gamma_1(\mu_1+\mu_2+\delta+\alpha))}}{\gamma_1}$$

$$E = \frac{(\delta + \gamma_2)(\mu_1 + \mu_2 + \delta + \alpha)A}{\left(\xi\mu_2 + \gamma_1(\mu_1 + \mu_2 + \delta + \alpha)\right)} = \Delta_1 A \quad (22)$$

At equilibrium state the fifth equation of the model (5) results to

$$T = \frac{\alpha_0 C}{\delta + \varphi + \gamma_3} \quad (23)$$

Substitute (18) in equation(23), we have

$$T = \frac{\alpha_0 q\gamma_2 A}{(\delta+\alpha_0)(\delta+\gamma_3)+\delta\varphi} \quad (24)$$

Substitute (24) in equation(18), we have

$$C = \frac{q\gamma_2 A(\delta + \varphi + \gamma_3)}{(\delta + \alpha_0)(\delta + \gamma_3) + \delta\varphi} = \Delta_2 A \quad (25)$$

At equilibrium state the seventh equation of the model (5) results to

$$V = \frac{\delta(1 - \pi) + pS}{(\delta + \delta_0)} \quad (26)$$

At equilibrium state the second equation of the model (5) is given by

$\beta AS + \beta kCS - (\delta + \xi + \gamma_1)E + \delta\pi\eta C + \mu_1 M = 0$

where,

$$C = \frac{q\gamma_2 A(\delta + \varphi + \gamma_3)}{(\delta + \alpha_0)(\delta + \gamma_3) + \delta\varphi} = \Delta_2 A, M = \frac{\xi(\delta + \gamma_2)A}{\xi\mu_2 + \gamma_1(\mu_1 + \mu_2 + \delta + \alpha)} = \Delta_3 A\,, E = \frac{(\delta + \gamma_2)(\mu_1 + \mu_2 + \delta + \alpha)A}{\left(\xi\mu_2 + \gamma_1(\mu_1 + \mu_2 + \delta + \alpha)\right)} = \Delta_1 A$$

we have,

$$\beta AS + \frac{\beta kSq\gamma_2(\delta + \varphi + \gamma_3)A}{(\delta + \alpha_0)(\delta + \gamma_3) + \delta\varphi} - \frac{(\delta + \xi + \gamma_1)(\delta + \gamma_2)(\mu_1 + \mu_2 + \delta + \alpha)A}{\left(\xi\mu_2 + \gamma_1(\mu_1 + \mu_2 + \delta + \alpha)\right)} + \frac{\delta\pi\eta q\gamma_2(\delta + \varphi + \gamma_3)A}{(\delta + \alpha_0)(\delta + \gamma_3) + \delta\varphi} + \frac{\mu_1\xi(\delta + \gamma_2)A}{\xi\mu_2 + \gamma_1(\mu_1 + \mu_2 + \delta + \alpha)} = 0$$

Let,

$a = (\alpha + \delta + \mu_1 + \mu_2), b = (\delta + \gamma_2), c = (\delta + \alpha_0)(\delta + \gamma_3) + \delta\varphi, d = (\delta + \xi + \gamma_1),$ and $e = \delta\pi\eta q\gamma_2$

By factorizing yields

$$\left(\beta S + \frac{\beta kSq\gamma_2(\delta + \varphi + \gamma_3)}{c} - \frac{dba}{\xi\mu_2 + \gamma_1 a} + \frac{e(\delta + \varphi + \gamma_3)}{c} + \frac{\mu_1\xi b}{\xi\mu_2 + \gamma_1 a}\right)A = 0 \quad (27)$$

Therefore, from equation (27), if $A \neq o$ it implies that

$$S^* = \frac{dbca - \left[e\left(\xi\mu_2 + \gamma_{1_a}\right)(\delta + \varphi + \gamma_3) + \xi\mu_1 bc\right]}{\beta\left(c + kq\gamma_2(\delta + \varphi + \gamma_3)\right)(\xi\mu_2 + \gamma_1 a)} \quad (28)$$

At endemic equilibrium the first equation of the model (5) is re-written as

$$0 = \delta\pi(1 - \eta\Delta_2 A) - S^*\beta A^* - S^*(\delta + \beta k\Delta_2 A^* + p) + \delta_0\left(\frac{\delta(1 - \pi) + pS}{(\delta + \delta_0)}\right) + \alpha\Delta_3 A^*$$

from which we obtain

$$A^*K = \delta\left(\delta\pi + \delta_0 - S^*(\delta + \delta_0 + p)\right)$$

giving as

$$A^* = \frac{\delta(\delta+\delta_0+p)S^*}{K}\left(\frac{S^O}{S^*}-1\right)$$

with

$$K = (\delta\pi\eta\Delta_2 + S^*\beta + S^*\beta k\Delta_2 - \alpha\Delta_3)(\delta+\delta_0), \qquad K>0$$

Since$R_r^c = \frac{S^O}{S^*} > 1$, it follows that

$$A^* = \frac{\delta(\delta+\delta_0+p)S^*}{K}(R_r^c - 1), \qquad R_r^c > 1 \tag{29}$$

Therefore, at endemic equilibrium $\varepsilon_1 = (S^*, E^*, A^*, C^*, T^*, M^*, V^*)$, substitute (29) in equation (22, 24 , 25 and 21) we have Therefore, $\varepsilon_1 = (S^*, E^*, A^*, C^*, T^*, M^*, V^*)$ is the endemic equilibrium state of the system (25) given by

$$S^* = \frac{dbca - \left[e\left(\xi\mu_2 + \gamma_{1_a}\right)(\delta+\varphi+\gamma_3) + \xi\mu_1 bc\right]}{\beta\left(c + kq\gamma_2(\delta+\varphi+\gamma_3)\right)(\xi\mu_2+\gamma_1 a)} \tag{30}$$

$$E^* = \frac{\delta(\delta+\gamma_2)(\mu_1+\mu_2+\delta+\alpha)(\delta+\delta_0+p)S^*}{K\left(\xi\mu_2+\gamma_1(\mu_1+\mu_2+\delta+\alpha)\right)}(R_r^c-1), \quad R_r^c>1 \tag{31}$$

$$A^* = \frac{\delta(\delta+\delta_0+p)S^*}{K}(R_r^c-1), \quad R_r^c>1 \tag{32}$$

$$C^* = \frac{\delta q\gamma_2(\delta+\varphi+\gamma_3)(\delta+\delta_0+p)S^*}{K((\delta+\alpha_0)(\delta+\gamma_3)+\delta\varphi)}(R_r^c-1), \qquad R_r^c>1 \tag{33}$$

$$T^* = \frac{\delta\alpha_0 q\gamma_2\,(\delta+\delta_0+p)S^*}{K\left((\delta+\alpha_0)(\delta+\gamma_3)+\delta\varphi\right)}(R_r^c-1), \qquad R_r^c>1 \tag{34}$$

$$M^* = \frac{\delta\xi(\delta+\gamma_2)(\delta+\delta_0+p)S^*}{K(\xi\mu_2+\gamma_1(\mu_1+\mu_2+\delta+\alpha))}(R_r^c-1), \qquad R_r^c>1 \tag{35}$$

$$V^* = \frac{\delta(1-\pi)+\rho s^*}{(\delta+\delta_0)} \tag{36}$$

Therefore, at the endemic equilibrium state $\varepsilon_1 = (S^*, E^*, A^*, C^*,\ T^*, M^*, V^*)$ of the system (5), is given by equation $(30-36)$respectively.

Thus, the following result is established

Proposition 1: The endemic equilibrium state exists whenever $R_r^c > 1$

3.4 Global Stability of the Endemic Equilibrium State

We present the global stability of endemic equilibrium state of the model (5) by constructing the Lyapunov function. Though, there is no general method to construct a Lyapunov function which proves the stability of equilibrium. However, similar to the approach in [30], we state the following theorem.

Proposition 2: The endemic equilibrium state ε_1 of the model (5) is globally asymptotically stable on Ω if $R_r^c > 1$ and given that $\frac{A^*}{T^*} = \frac{\varphi}{q\gamma_2}$, $\frac{M^*}{E^*} = \frac{\gamma_1}{\mu_2}$ and $\delta_0 = \alpha = \rho = 0$.

Proof: The global stability of the endemic equilibrium can be determined by constructing a volterra-like Lyapunov function $L(t)$ similar to the one explored in [31] given by $L(t) = \sum_{k=1}^{n} d_k(x_k - x_k{}^* \ln x_k)$

Which is positive definite for all positive values of x.

At endemic equilibrium, $\varepsilon_1 = (S^*, E^*, A^*, C^*, T^*, M^*, V^*)$, we have

$$L = \sum_{k=1}^{7} d_k(x_k - x_k{}^* \ln x_k)$$

$$= \alpha_1(x_1 - x_1{}^*\ln x_1) + \alpha_2(x_2 - x_2{}^*\ln x_2) + \alpha_3(x_3 - x_3{}^*\ln x_3) + \alpha_4(x_4 - x_4{}^*\ln x_4)$$

$$+\alpha_5(x_5 - x_5{}^*\ln x_5) + \alpha_6(x_6 - x_6{}^*\ln x_6) + +\alpha_7(x_7 - x_7{}^*\ln x_7)$$

Let $x_1 = S, x_2 = E, x_3 = A, x_4 = C, x_5 = T, x_6 = M, x_7 = V$

Therefore,

$$L(t) = d_1(S - S^*\ln S) + d_2(E - E^*\ln E) + d_3(A - A^*\ln A) + d_4(C - C^*\ln C) + d_5(T - T^*InT) + d_6(M - M^*InM)$$
$$+ d_7(V - V^*InV)$$

The time derivative of $v(t)$ along the solutions of the model (5) is given by

$$L' = d_1\left(1-\frac{S^*}{S}\right)S' + d_2\left(1-\frac{E^*}{E}\right)E' + d_3\left(1-\frac{A^*}{A}\right)A' + d_4\left(1-\frac{C^*}{C}\right)C'$$
$$+d_5\left(1-\frac{T^*}{T}\right)T' + d_6\left(1-\frac{M^*}{M}\right)M' + d_7\left(1-\frac{V^*}{V}\right)V' \quad (37)$$

At endemic equilibrium state $\varepsilon_1 = (S^*, E^*, A^*, C^*, T^*, M^*, V^*) \neq 0$, the model satisfy the following relation

$$S' = \beta(A^* + KC^*)S^* + (\delta\pi\eta)C^* - \delta_0 V + (\delta + P)S^* - \alpha M^* - \beta(A + KS)$$

$$-(\delta\pi\eta)C + \delta_0 V \quad -(\delta + P)S + \alpha M = 0 \quad (38)$$

$$E' = \beta(A + KS)S + \delta\pi\eta C + \mu_1 M - \left(\frac{\beta(A^* + KC^*)S^*}{E^*} + \frac{\delta\pi\eta C^*}{E^*} + \frac{\mu_1 M^*}{E^*}\right)E \quad (39)$$

$$A' = \gamma_1 E + \mu_2 M - \left(\frac{\gamma_1 E^*}{A^*} + \frac{\mu_2 M^*}{A^*}\right)A \quad (40)$$

$$C' = q\gamma_2 A + \varphi T^* - \left(\frac{q\gamma_2 A^*}{C^*} + \frac{\varphi T^*}{C^*}\right)C \quad (41)$$

$$T' = \alpha_0 - \frac{\alpha_0 C^*}{T^*}C \quad (42)$$

$$M' = \xi E - \left(\frac{\xi E^*}{M^*}\right)M \quad (43)$$

$$V' = (\delta + \delta_0)V^* - pS^* + \rho S - (\delta + \delta_0)V \quad (44)$$

Substitute equations $(38-44)$ into (37), we have

$$L' = d_1\left(1-\frac{S^*}{S}\right)(\beta(A^* + KC^*)S^* + \delta\pi\eta C^* + \delta_0 V + (\delta + P)S^* - \alpha M^*$$
$$-\beta(A + KC)S - \delta\pi\eta C \quad -\delta_0 V - (\delta + P)S + \alpha M)$$

$$+d_2\left(1-\frac{E^*}{E}\right)\left(\beta(A + KC)S + \delta\pi\eta C + \mu_1 M - \left(\frac{\beta(A^* + KC^*)S^*}{E^*} + \frac{\delta\pi\eta C^*}{E^*} + \frac{\mu_1 M^*}{E^*}\right)E\right)$$
$$+d_3\left(1-\frac{A^*}{A}\right)\left(\gamma_1 E + \mu_2 M - \left(\frac{\gamma_1 E}{A^*} + \frac{\mu_2 M^*}{A^*}\right)A\right)$$
$$+d_4\left(1-\frac{C^*}{C}\right)\left(q\gamma_2 A + \varphi T - \left(\frac{qy_2 A^*}{C^*} + \frac{\varphi T}{C^*}\right)C\right)$$
$$+d_5\left(1-\frac{T^*}{T}\right)\left(\alpha_0 C - \left(\frac{\alpha_0 C^*}{T^*}\right)T\right)$$
$$+d_6\left(1-\frac{M^*}{M}\right)\left(\xi E - \left(\frac{\xi E^*}{M^*}\right)M\right) \quad (45)$$
$$+d_7\left(1-\frac{V^*}{V}\right)\left((\delta + \delta_0)(V^* - V) + \rho(S - S^*)\right)$$

Upon simplification of equation(45), we have

$$L' = -(\delta + P)d_1\frac{(S - S^*)^2}{S} + d_1\left(1-\frac{S^*}{S}\right)\left(\beta\left(A^*S^*\left(1-\frac{AS}{A^*S^*}\right) + KC^*S^*\left(1-\frac{CS}{C^*S^*}\right)\right)\right.$$
$$\left.+\delta_{\pi\eta}C^*\left(1-\frac{C^*}{C}\right) + \delta_0(V - V^*) + \alpha M^*(M - M^*)\right) + d_5\alpha_0 C^*\left(1-\frac{T^*}{T}\right)\left(\frac{E}{E^*} - \frac{M}{M^*}\right)$$
$$+d_2\left(1-\frac{E}{E^*}\right)\left(\beta A^*S^*\left(\frac{AS}{A^*S^*} - \frac{E}{E^*}\right) + \beta KC^*S^*\left(\frac{CS}{C^*S^*} - \frac{E}{E^*}\right) + \delta_{\pi\eta}C^*\left(\frac{C}{C^*} - \frac{E}{E^*}\right)\right.$$
$$\left.+\mu_1 M^*\left(\frac{M}{M^*} - \frac{E}{E^*}\right)\right) + d_3\left(1-\frac{A^*}{\mathrm{A}}\right)\left(\gamma_1 E\left(\frac{E}{E^*} - \frac{A}{A^*}\right) + \mu_2 M^*\left(\frac{M}{M^*} - \frac{A}{A^*}\right)\right)$$
$$+d_4\left(1-\frac{C^*}{C}\right)\left(q\gamma_2 A^*\left(\frac{A}{A^*} - \frac{C}{C^*}\right) + \varphi T^*\left(\frac{T}{T^*} - \frac{C}{C^*}\right)\right) + d_7(\delta + \delta_0)\frac{(V - V^*)^2}{V}$$
$$+d_6\left(1-\frac{M^*}{M}\right)\left(\varepsilon E^*\left(\frac{E}{E^*} - \frac{M}{M^*}\right)\right) + d_7\rho\left(1-\frac{V^*}{V}\right)(S - S^*) \quad (46)$$

where,

$$L^{'} = -(\delta + p)d_1\frac{(S-S^*)^2}{S} + d_7(\delta+\delta_0)\frac{(V-V^*)^2}{V} + F(x,y,z,w,p,q,v) \qquad (47)$$

Setting

$$\frac{S}{S^*} = x, \frac{E}{E^*} = y, \frac{A}{A^*} = z, \frac{C}{C^*} = w, \frac{T}{T^*} = q\,, \frac{M}{M^*} = p, \frac{V}{V^*} = v$$

Therefore upon simplification of $F(x,y,z,w,p,q,v)$, we have,

$$\left.\begin{aligned} &F(x,y,z,w,p,q,v) \\ &= \beta A^*S^*\left(d_1\left(1-\frac{1}{x}+z-xz\right)+d_2\left(xz-y-\frac{xz}{y}-1\right)\right) \\ &+\delta\pi\eta C^*\left(d_1\left(1-\frac{1}{x}-w+xw\right)+d_2\left(1+w-y-\frac{w}{y}\right)\right)+d_1\delta_0V^*\left(v-1-\frac{v}{x}+\frac{1}{x}\right) \\ &+d_1\alpha M^*\left(p-1-\frac{p}{x}+\frac{1}{x}\right)+d_2\mu_1M^*\left(p-\frac{p}{y}-y+1\right)+d_3\gamma_1E^*\left(y-\frac{y}{z}-z+1\right) \\ &+d_3\mu_2M^*\left(p-\frac{p}{z}-z+1\right)+d_4q\gamma_2A^*\left(z-\frac{z}{w}-w+1\right)+d_4\varphi T^*\left(q-\frac{q}{w}-w+1\right) \\ &+d_5\alpha_0C^*\left(w-\frac{w}{q}-q+1\right)+d_6\xi E^*\left(y-\frac{y}{p}-p+1\right)+d_7\rho s^*\left(x-\frac{x}{v}+\frac{1}{v}-1\right) \end{aligned}\right\} \qquad (48)$$

From (48) we can obtain the coefficients of the variables

$$y: -d_2\left(\beta S^*(A^*+KC^*)-d_2\delta_{\pi\eta}C^*+\mu_1M^*\right)+d_3\gamma_1E^*+d_6\xi E^* \qquad (49)$$

$$w: \beta KC^*S^*d_1-d_1\delta_{\pi\eta}C^*+d_2\delta_{\pi\eta}C^*-d_4q\gamma_2A^*-d_4\varphi T^*+d_5\alpha_0C^* \qquad (50)$$

$$z: \beta A^*S^*d_1-d_3\mu_1M^*-d_3\gamma_1E^*+d_4q\gamma_2A^* \qquad (51)$$

$$p: d_1\alpha M^*+d_2\mu_1M^*+d_3\mu_2M^*-d_6\xi E^* \qquad (52)$$

$$q: d_4\varphi T^*-d_5\alpha_0C^* \qquad (53)$$

$$xz: \beta A^*S^*(d_2-d_1) \qquad (54)$$

$$xw: d_1\delta_{\pi\eta}C^*-\beta KC^*S^*d_1+\beta KC^*S^*d_2 \qquad (55)$$

Therefore by setting the expression (49-55) to zero and solving yields

$$d_2 = d_1, d_3 = d_1\left(\frac{\beta[A^*+KC^*]S^*}{\gamma_1E^*+\mu_2M^*}\right), d_4 = d_1\left(\frac{\beta KC^*S^*}{q\gamma_2A^*}\right), d_5 = d_1\frac{\varphi T^*}{\alpha_0C^*}\left(\frac{\beta KC^*S^*}{q\gamma_2A^*}\right)$$

$$d_6 = d_1\frac{M^*}{\xi E^*}\left(\alpha+\mu_1+\frac{\mu_{2\beta[A^*+KC^*]S^*}}{(\gamma_1E^*+\mu_2M^*)}\right)$$

Furthermore

$$\begin{aligned} &F(x,y,z,w,p,q,v) \\ &= d_1\delta\pi\eta C^*\left(2-\frac{1}{x}-\frac{w}{y}\right)+d_1\beta A^*S^*\left(2-\frac{1}{x}-\frac{xz}{y}\right)+d_1\beta KC^*S^*\left(2-\frac{1}{x}-\frac{xw}{y}\right) \\ &+d_1\delta_0V^*\left(v-1-\frac{v}{x}+\frac{1}{x}\right)+d_1\alpha M^*\left(\frac{1}{x}-\frac{p}{x}-1\right)+d_2\mu_1M^*\left(1-\frac{p}{y}\right) \\ &+d_3\gamma_1E^*\left(1-\frac{y}{z}\right)+d_3\mu_2M^*\left(1-\frac{p}{z}\right)+d_4q\gamma_2A^*\left(1-\frac{z}{w}\right) \\ &+d_4\varphi T^*\left(1-\frac{q}{w}\right)+d_5\alpha_0C^*\left(1-\frac{w}{q}\right)+d_6\xi E^*\left(1-\frac{y}{p}\right) \qquad (56) \\ &+d_7\rho s^*\left(x-\frac{x}{v}+\frac{1}{v}-1\right) \end{aligned}$$

where,

$$F(x,y,z,w,p,q,v) = F_1 + F_2$$

and

$$F_1 = d_1\delta\pi\eta C^*\left(2-\frac{1}{x}-\frac{w}{y}\right)+d_1\beta A^*S^*\left(2-\frac{1}{x}-\frac{xz}{y}\right)+d_1\beta KC^*S^*\left(2-\frac{1}{x}-\frac{xw}{y}\right)$$

$$F_2 = d_1\delta_0 V^*\left(v-1-\frac{v}{x}+\frac{1}{x}\right)+d_1\alpha M^*\left(\frac{1}{x}-\frac{p}{x}-1\right)+d_2\mu_1 M^*\left(1-\frac{p}{y}\right)$$
$$+d_3\gamma_1 E^*\left(1-\frac{y}{z}\right)+d_3\mu_2 M^*\left(1-\frac{p}{z}\right)+d_4\varphi T^*\left(1-\frac{q}{w}\right)+d_5\alpha_0 C^*\left(1-\frac{w}{q}\right)$$
$$+d_6\xi E^*\left(1-\frac{y}{p}\right)+d_7\rho s^*\left(x-\frac{x}{v}+\frac{1}{v}-1\right)$$

Further simplification gives

$$F_2 = d_1\left(\frac{\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M}\right)\left(\gamma_1 E^*\left(1-\frac{y}{z}\right)+\mu_2 M^*\left(1-\frac{p}{z}\right)\right)$$
$$+d_1\left(\frac{\beta KC^*S^*}{q\gamma_2 A^*}\right)\left(q\gamma_2 A^*\left(1-\frac{z}{w}\right)+\varphi T^*\left(1-\frac{q}{w}\right)\right)+d_1\frac{\varphi T^*}{\alpha_0 C^*}\left(\frac{\beta KC^*S^*}{q\gamma_2 A^*}\right)\left(\alpha_0 C^*\left(1-\frac{w}{q}\right)\right)$$
$$+d_1\frac{\xi E^* M^*}{\xi E^*}\left(1-\frac{y}{p}\right)\left(\alpha+\mu_1+\frac{\mu_{2\beta[A^*+KC^*]S^*}}{(\gamma_1 E^*+\mu_2 M^*)}\right)+d_7\rho s^*\left(x-\frac{x}{v}+\frac{1}{v}-1\right)$$
$$+d_1\delta_0 V^*\left(v-1-\frac{v}{x}+\frac{1}{x}\right)+d_1\alpha M^*\left(\frac{1}{x}-\frac{p}{x}-1\right)+d_1\mu_1 M^*\left(1-\frac{p}{y}\right)$$
$$= d_1\frac{\varphi T^*\beta KC^*S^*}{q\gamma_2 A^*}\left(2-\frac{q}{w}-\frac{w}{q}\right)+d_1\mu_2 M^*\left(\frac{\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M}\right)\left(2-\frac{p}{z}-\frac{y}{p}\right)$$
$$+d_1\left(\frac{\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M}\right)\gamma_1 E^*\left(1-\frac{y}{z}\right)+d_1\beta KC^*S^*\left(1-\frac{z}{w}\right)+d_1 M^*(\alpha+\mu_1)\left(1-\frac{y}{p}\right)$$
$$+d_1\delta_0 V^*\left(v-1-\frac{v}{x}+\frac{1}{x}\right)+d_1\alpha M^*\left(\frac{1}{x}-\frac{p}{x}-1\right)+d_1\mu_1 M^*\left(1-\frac{p}{y}\right)$$
$$+d_7\rho s^*\left(x-\frac{x}{v}+\frac{1}{v}-1\right)=d_1\varphi T^*\beta KC^*S^*\left(\frac{1}{q\gamma_2 A^*}\left(2-\frac{q}{w}-\frac{w}{q}\right)+\frac{1}{\varphi T^*}\left(1-\frac{z}{w}\right)\right)$$
$$+\frac{d_1\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M^*}\left(\mu_2 M^*\left(2-\frac{p}{z}-\frac{y}{p}\right)+\quad\gamma_1 E^*\left(1-\frac{y}{z}\right)\right)+d_1\mu_1 M^*\left(2-\frac{p}{y}-\frac{y}{p}\right)$$
$$+d_1\alpha M^*\left(\frac{1}{x}-\frac{p}{x}-\frac{y}{p}\right)+d_1\delta_0 V^*\left(v-1-\frac{v}{x}+\frac{1}{x}\right)+\quad d_7\rho s^*\left(x-\frac{x}{v}+\frac{1}{v}-1\right)$$

If $\frac{A^*}{T^*}=\frac{\varphi}{q\gamma_2}$, $\frac{M^*}{E^*}=\frac{\gamma_1}{\mu_2}$ and $\delta_0=\alpha=\rho=0$

$$F_2 = d_1\varphi T^*\beta KC^*S^*\left(3-\frac{q}{w}-\frac{w}{q}-\frac{z}{w}\right)+\frac{d_1\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M^*}\left(3-\frac{p}{z}-\frac{y}{p}-\frac{y}{z}\right)+d_1\mu_1 M^*\left(2-\frac{p}{y}-\frac{y}{p}\right)$$

Thus,

$$F(x,y,z,w,p,q,v)=F_1+F_2$$
$$= d_1\delta\pi\eta C^*\left(2-\frac{1}{x}-\frac{w}{y}\right)+d_1\beta A^*S^*\left(2-\frac{1}{x}-\frac{xz}{y}\right)+d_1\beta KC^*S^*\left(2-\frac{1}{x}-\frac{xw}{y}\right)$$
$$+d_1\varphi T^*\beta KC^*S^*\left(3-\frac{q}{w}-\frac{w}{q}-\frac{z}{w}\right)+\frac{d_1\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M^*}\left(3-\frac{p}{z}-\frac{y}{p}-\frac{y}{z}\right)$$
$$+d_1\mu_1 M^*\left(2-\frac{p}{y}-\frac{y}{p}\right)$$

Now

$$L' = -d_1\delta\frac{(S-S^*)^2}{S}-d_7\delta\frac{(V-V^*)^2}{V}+d_1\delta\pi\eta C^*\left(2-\frac{1}{x}-\frac{w}{y}\right)+d_1\beta A^*S^*\left(2-\frac{1}{x}-\frac{xz}{y}\right)$$
$$+d_1\beta KC^*S^*\left(2-\frac{1}{x}-\frac{xw}{y}\right)+d_1\varphi T^*\beta KC^*S^*\left(3-\frac{q}{w}-\frac{w}{q}-\frac{z}{w}\right)$$
$$+\frac{d_1\beta(A^*+KC^*)S^*}{\gamma_1 E^*+\mu_2 M^*}\left(3-\frac{p}{z}-\frac{y}{p}-\frac{y}{z}\right)+d_1\mu_1 M^*\left(2-\frac{p}{y}-\frac{y}{p}\right) \qquad (57)$$

By arithmetic and geometric mean inequality [32], we have

$$2\le\frac{1}{x}+\frac{w}{y},2\le\frac{1}{x}+\frac{xz}{y},2\le\frac{1}{x}+\frac{xw}{y},3\le\frac{q}{w}+\frac{w}{q}+\frac{z}{w},3\le\frac{p}{z}+\frac{y}{p}+\frac{y}{z}\ and\ 2\le\frac{p}{y}+\frac{y}{p}$$

This implies that $F(x, y, z, w, p, q, v) \leq 0$
Therefore, $L' \leq 0 \; in \; \Omega \; if \; \rho = \delta_0 = \alpha = 0$
The equality $L' = 0$ holds only for $x = y = z = w = p = q = v = 1$.Thus, the model system (5) has a unique endemic equilibrium state $\varepsilon_1$which is the only positively invariant set in the feasible region $\Omega = (S^*, E^*, A^*, C^*, T^*, M^*, V^*)$Therefore, in [33], it implies that the endemic equilibrium state is globally asymptotically stable in Ω if R_r^c >1.

Conclusion

The endemic equilibrium state was found to be stable. The public health implication is that HBV will be sustained if susceptible migrants are restricted (that is, if infective migrants are allowed into the system), there is permanent immunity(improper vaccination) or no vaccination regiment and provided the transmission rate from migrated to acutely infected class is equal to that from exposed to acutely infected class; and the transmission from acutely infected class to chronic carrier class is equal to the rate at which the treated individual relapse to chronic carrier class (that is, under steady state condition).Hence the governing model can be applied for predicting the spread of HBV. However, to attain the desired goal, further research on the effect of vaccination and treatment may convey existing new information in controlling the spread of hepatitis b virus with infective migrants.

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