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Estimation of Parameters for the Mathematical Model of the Spread of Hepatitis B in Burkina Faso Using Grey Wolf Optimizer

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Abstract. In this paper, we developed a mathematical model of differential susceptibility, taking into account vaccination and treatment, to simulate the transmission of the hepatitis B virus in the population of Burkina Faso. The existence and uniqueness of non-negative solutions are proved. The model has a globally asymptotically stable disease free equilibrium when the basic reproduction number $\mathcal{R}_0 < 1$ and an endemic equilibrium when $\mathcal{R}_0 > 1$. We estimated the parameters of the model based on hepatitis B cases from 1997 to 2020 by using a Grey Wolf Optimizer Algorithm (GWO). The results demonstrated the efficacy of the GWO algorithm in estimating the model parameters. A sensitivity analysis was carried out to determine the determining factors in the spread of hepatitis B in Burkina Faso. The estimated parameters were used to simulate the spread of hepatitis B in Burkina Faso from 1997 to 2020.

1. Introduction

Viral hepatitis B remains a major public health problem in the world, especially in Africa and particularly in Burkina Faso. HBV is second only to tobacco as a known human carcinogen. It damages the liver through acute and chronic infection. The chronic infection, through its complications such as cirrhosis and/or hepatocellular carcinoma (liver cancer), makes it a really serious pathology since it causes more than 5000 deaths per year in Burkina Faso [43]. It is well noted that one over four people with chronic HBV infection is likely to die prematurely of

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cirrhosis or liver cancer. Hepatitis B endemicity is defined as the seroprevalence of HBsAg carrier statusantigen in the general population. Burkina Faso is classified as a highly endemic country ([39], [6]). In addition, in the 2011 Demographic Health Survey, HBV seroprevalence was estimated at 9.1% [5]. Similarly, a study conducted in Ouagadougou (capital city of Burkina Faso) revealed a prevalence of 14.5% in the general population [7]. Thus, nearly 2 million people in Burkina Faso are infected with HBV, whether they know it or not [41]. In these highly endemic areas, transmission of hepatitis B virus occurs mainly by vertical transmission, that is, from infected mothers to their infants during the perinatal period, and the rate of chronic carriage is inversely proportional to the age at which the individual becomes infected ([6,39]). The three main axes of the fight against the spread of HBV in Burkina Faso are: vaccination, treatment, and awareness.

Mathematical models are valuable tools for understanding the dynamics of hepatitis B in the population. They can be used to assess the impact of measures taken to combat the disease. Edmunds et al. [19] proposed a mathematical model to study the transmission dynamics and control of hepatitis B virus in the Gambia. Kamyad et al. [22] Proposed a mathematical model for hepatitis b virus taking acount vaccination and treatment. Khan et al. [23] presented a model for the hepatitis B virus dynamic by dividing the infectious class into three sub-classes: acute, chronic and carrier. Horizontal and vertical transmissions have also been taken into account. Fall [9] proposed a differential susceptibility and infectivity mathematical model of Hepatitis B transmission to study the dynamic of virus in sub-Saharan Africa (case of Senegal).
Recently, a mathematical model for analysis of effective intervention strategies on transmission dynamics of hepatitis B virus has been proposed by Firaol et al. [20].

In this paper, a differential susceptibility mathematical model of Hepatitis B ([3], [9]) transmission taking acount vaccination and treatement was developed in order to simulate the potential spread of the Hepatitis B virus in the population of Burkina Faso presented. This depend on parameters. To identify these parameters, a cost function to minimize or maximize is built by using Burkina Faso hepatitis B cases for the period 1997 to 2020. Generally these functions have a complex structure with respect to the parameters, and sometimes they suffer from a lack of regularity. Thus, the minimization of these functions using classical methods becomes impossible, which is precisely the main problem encountered here. Hence, the remedy is to use meta-heuristic methods. Meta-heuristic optimization techniques are adapted better to the problems of optimization in which the size of the space of research is important, where the parameters interact in a complex way and where very little information on the function to be optimized is available [21]. In this work we used Grey Wolf Optimizer (GWO) algorithm, a meta-heuristic proposed by S. Mirjalili et al [21]. This algorithm is inspired by grey wolves. He mimics the leadership hierarchy and hunting mechanism of grey wolves in nature.

The remainder of this paper is organized as follows: section 2 is dedicated to the presentation of the proposed model. In Section 3, the mathematical analysis of the model is done focusing on uniqueness, existence, positivity and boundedness of the solutions, global stability of equilibriums.

We also determined the number of basic reproduction. Section 4 is devoted to the parameters estimation. After constructing the function to be minimized, we presented the algorithm used. The estimation result was presented. Data of hepatitis B cases for the period 2007 to 2020 of Burkina Faso are used. In Section 5, discussion of the obtained numerical results is presented. The conclusion is given in section 6.

2. Model Formulation

Here we formulate a deterministic mathematical model with differential susceptibility [3] *SVLACTR*, i.e. Susceptible-Vaccinated-Latent-Acute-Chronic-Treatment-Recovered, composed of nine ordinary differential equations (ODE) to illustrate the dynamics of HBV in Burkina Faso. The cumulative population at time t, represented by $N(t)$, is classified into nine different compartments, the meaning of each of which is given in Table 1. We draw the compartmental diagram given in Figure 1, from which we obtain the model 2.1 of hepatitis B transmission dynamics with vaccination and treatment in the Burkina Faso population. Table 2 contains the various parameters with their meanings.

Parameters	description
λ	birth rate of total population
λ_1	proportion of births infected by vertical transmission, from acute mothers.
λ_2	proportion of births infected by vertical transmission, from chronic mothers.
λ_3	proportion of births infected by vertical transmission, from treated mothers.
$\theta_i, i = 1,2,3$	transfer rate of $S_i, i = 1,2,3$ vaccinated individuals to the vaccinated class V
$\phi_i, i = 1,2,3$	transfer rate of vaccinated individuals and non-immunized to the susceptible S_i
p_1	proportion of S_1 individuals aged $0-1$ who grow up healthy enough to enterS_2
p_2	proportion of individuals aged $1-5$ years who grow up healthy to enter in S_3
β_1	adequate contact coefficient for a susceptible to be infected by a acute
β_2	adequate contact coefficient for a susceptible to be infected by a chronic
β_3	adequate contact coefficient for a susceptible to be infected by a treated
δ_1	proportion of latent who become acute infected A
δ_2	proportion of latent who become chronic C
τ	rate of reactivation of hbv infection after recovery
γ_a	proportion of acute cases that are recovered
γ_c	proportion of chronic cases that are recovered
γ_{tr}	proportion of treated cases that are recovered
ω_1	proportion of chronic patients who are treated
ω_2	proportion of chronic patients who are treated but still remain chronic
μ	natural mortality rate, i.e., mortality not caused by HBV
μ_a	mortality rate caused by acute HBV infection
μ_c	mortality rate caused by chronic HBV infection
μ_{tr}	HBV mortality rate in treated patients

Table 1. Parameters used in the model

In this work, we make these considerations:

(i) Susceptible individuals were subdivided into three age classes $S_i, i = 1, 2, 3$.

(ii) The high prevalence (> 8%) in Burkina Faso is mainly due to the vertical transmission, hence the choice of the vertical transmission model ([5]), [9]).

(iii) The general recruitment of the population i.e. $\lambda N - \lambda_1 A - \lambda_2 C - \lambda_3 Tr$.

(iv) A Part of the births from the acute and chronic HBV infections participate with an amount $\lambda_1 A + \lambda_2 C + \lambda_3 T$, which will move to the exposed compartments of both acute and chronic infections.

(v) Vertical transmission occurs in acutely infected, chronic carriers and treated.

(vi) The adequate contact β coefficient for a susceptible person to be infected with HBV, depends of infectious ([45], [3]) individuals i.e. the A, C, T_r. One has: $\beta = \dfrac{\beta_1 A + \beta_2 C + \beta_3 Tr}{N}$ the adequate coefficient of contact so that a susceptible S_i becomes contaminated by the HBV.

(vii) Acute infection includes fulminant hepatitis, which is very rare [40].

(viii) All individuals who do not die from HBV, i.e. individuals in compartments S_1, S_2, S_3, V, L, R have the same mortality rate μ.

(ix) The risk of hepatitis B virus reactivation in recovered individuals can be high in cases of immunosuppression ([31]), [32]).

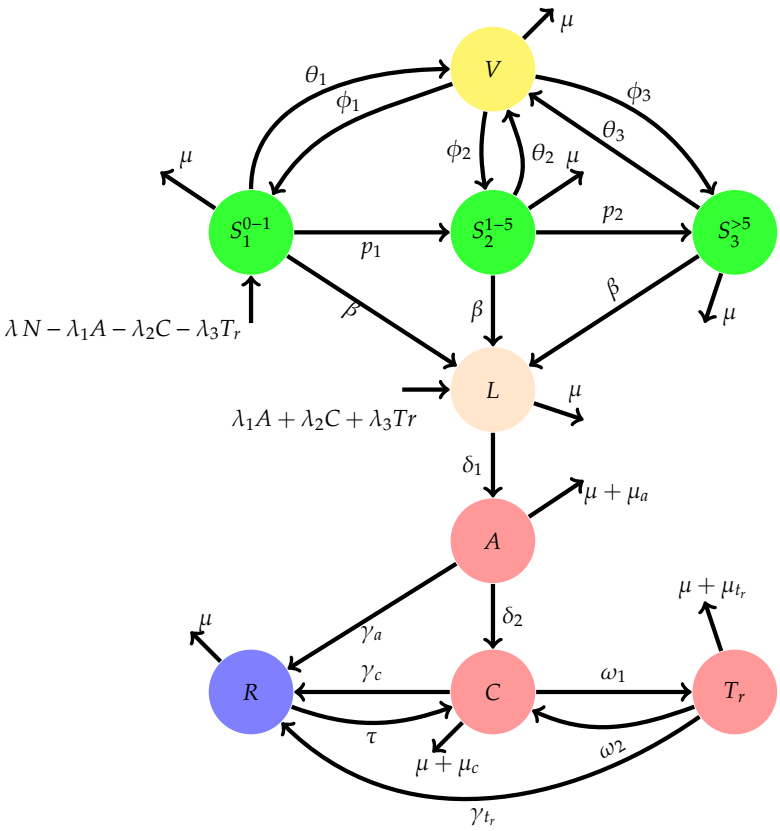

FIGURE 1. HBV model with vertical transmission, vaccination and treatment

Variables	Biological description
$S_1(t)$	babies aged 0-1 year susceptible to disease
$S_2(t)$	infants 1 to 5 years old susceptible to disease
$S_3(t)$	children over 5 years of age, adolescents and adults at risk of disease
$V(t)$	Vaccinated of all susceptible of the three age groups
$L(t)$	latently infected individuals
$A(t)$	acutely infected individuals
$C(t)$	Chronic carriers individuals
$Tr(t)$	Chronic patients who receive treatment
$R(t)$	Recovered individuals

TABLE 2. Description of variables used in the model

By doing a mass balance through the different considered compartments, one obtains the following system:

$$\begin{cases} \frac{dS_1}{dt} = \lambda N - \lambda_1 A - \lambda_2 C - \lambda_3 T + \phi_1 V - \frac{(\beta_1 A + \beta_2 C + \beta_3 T_r)}{N} S_1 - (\theta_1 + p_1 + \mu) S_1 \\ \frac{dS_2}{dt} = p_1 S_1 + \phi_2 V - \frac{(\beta_1 A + \beta_2 C + \beta_3 T)}{N} S_2 - (\theta_2 + p_2 + \mu) S_2 \\ \frac{dS_3}{dt} = p_2 S_2 + \phi_3 V - \frac{(\beta_1 A + \beta_2 C + \beta_3 T)}{N} S_3 - (\theta_3 + \mu) S_3 \\ \frac{dV}{dt} = \theta_1 S_1 + \theta_2 S_2 + \theta_3 S_3 - (\phi_1 + \phi_2 + \phi_3 + \mu) V \\ \frac{dL}{dt} = \lambda_1 A + \lambda_2 C + \lambda_3 T_r + \frac{(\beta_1 A + \beta_2 C + \beta_3 T_r)}{N} (S_1 + S_2 + S_3) - (\delta_1 + \mu) L \\ \frac{dA}{dt} = \delta_1 L - (\mu + \mu_a + \gamma_a) A \\ \frac{dC}{dt} = \delta_2 A + \omega_2 T_r + \tau R - (\gamma_c + \omega_1 + \mu + \mu_c) C \\ \frac{dT_r}{dt} = \omega_1 C - (\gamma_{t_r} + \omega_2 + \mu + \mu_t) T_r \\ \frac{dR}{dt} = \gamma_a A + \gamma_c C + \gamma_{t_r} T_r - (\tau + \mu) R \end{cases} \tag{2.1}$$

Let:

$$\begin{aligned} k_1 &= \theta_1 + p_1 + \mu \\ k_2 &= \theta_2 + p_2 + \mu \\ k_3 &= \theta_3 + \mu \\ k_4 &= \phi_1 + \phi_2 + \phi_3 + \mu \\ k_5 &= \delta_1 + \mu, \\ k_6 &= \mu + \mu_a + \gamma_a \\ k_7 &= \gamma_c + \omega_1 + \mu + \mu_c \\ k_8 &= \gamma_{tr} + \omega_2 + \mu + \mu_{tr} \\ k_9 &= \tau + \mu \end{aligned} \tag{2.2}$$

and

$$s_1 = \frac{S_1}{N},\ s_2 = \frac{S_2}{N},\ s_3\frac{S_3}{N},\ v = \frac{V}{N},\ l = \frac{L}{N},\ a = \frac{A}{N},\ c = \frac{C}{N},\ t_r = \frac{T_r}{N},\ r = \frac{R}{N} \tag{2.3}$$

The normalized model of the model 2.1 is given by:

$$\begin{cases} \frac{ds_1}{dt} = \lambda - \lambda_1 a - \lambda_2 c - \lambda_3 t_r + \phi_1 v - (\beta_1 a + \beta_2 c + \beta_3 tr)\, s_1 - k_1 s_1 \\ \frac{ds_2}{dt} = p_1 s_1 + \phi_2 v - (\beta_1 a + \beta_2 c + \beta_3 tr)\, s_2 - k_2 S_2 \\ \frac{ds_3}{dt} = p_2 s_2 + \phi_3 v - (\beta_1 a + \beta_2 c + \beta_3 tr)\, s_3 - k_3 s_3 \\ \frac{dv}{dt} = \theta_1 s_1 + \theta_2 s_2 + \theta_3 s_3 - k_4 v \\ \frac{dl}{dt} = \lambda_1 a + \lambda_2 c + \lambda_3 tr + (\beta_1 a + \beta_2 c + \beta_3 tr)\,(s_1 + s_2 + s_3) - k_5 l \\ \frac{da}{dt} = \delta_1 l - k_6 a \\ \frac{dc}{dt} = \delta_2 a + \omega_2 t_r + \tau\, r - k_7 c \\ \frac{dt_r}{dt} = \omega_1 c - k_8 t_r \\ \frac{dr}{dt} = \gamma_a a + \gamma_c c + \gamma_{tr} t_r - k_9 r \\ s_1(0) = s_{1,0},\ s_2(0) = s_{2,0},\ s_3(0) = s_{3,0},\ v(0) = v_0,\ l(0) = l_0, \\ a(0) = a_0,\ c(0) = c_0,\ t_r(0) = t_{r,0},\ r(0) = r_0 \end{cases} \tag{2.4}$$

3. Mathematical analysis

3.1. **Positivity, boundedness and global existence of solutions.**

Theorem 3.1. *Let the initial value* $(s_{1,0}, s_{2,0}, s_{3,0}, v_0, l_0, a_0, c_0, tr_0, r_0) \in \mathbb{R}^9_+$,

$$\text{such that} \quad s_{1,0} + s_{2,0} + s_{3,0} + v_0 + l_0 + c_0 + tr_0 + r_0 = 1,$$

and

$$\begin{aligned} &0 \le \lambda_1,\ \lambda_2,\ \lambda_3,\ \ p_1,\ p_2,\ \delta_1,\ \delta_2,\ \phi_1,\ \phi_2,\ \phi_3,\ \theta_1,\ \theta_2,\ \theta_3,\ \le 1 \\ &0 \le \lambda,\ \mu,\ \mu_a,\ \mu_c,\ \mu_t,\ \gamma_a,\ \gamma_c,\ \gamma_t,\ \omega_1,\ \omega_2,\ \beta_1,\ \beta_2,\ \beta_3,\ \le 1 \end{aligned} \tag{3.1}$$

then there exists a unique, nonnegative, bounded global solution to system 2.4.
Moreover for all $t \ge 0$

(i)

$$\Omega = \left\{ (s_1(t), s_2(t), s_3(t), v(t), l(t), a(t), c(t), t_r(t), r(t)) \mid\ 0 \le \Psi(t) \le \frac{\lambda}{\mu} + 1 \right\} \tag{3.2}$$

where

$$\Psi(t) = s_1(t) + s_2(t) + s_3(t) + v(t) + l(t) + a(t) + c(t) + t_r(t) + r(t)$$

(ii) *Moreover, if*

$$s_{1,0} \leq \left[\frac{\lambda}{k_1} + \frac{\phi_1 \lambda \left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right)}{k_1 \left[k_2 k_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3 \right]} \right]$$

$$s_{2,0} \leq \left[\frac{\lambda p_1}{k_1 k_2} + \frac{\left(p_1 \phi_1 + k_1 \phi_2 \right) \left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right) \lambda}{k_1 k_2 \left[\kappa_2 \kappa_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3 \right]} \right]$$

$$s_{3,0} \leq \left[\frac{\lambda \, p_1 p_2}{k_1 k_2 k_3} + \frac{\left(p_1 p_2 \phi_1 + p_2 k_1 \phi_2 + k_1 k_2 \phi_3 \right) \left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right) \lambda}{k_1 k_2 k_3 \left[k_2 k_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3 \right]} \right]$$

$$v_0 \leq \frac{\left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right) \lambda}{k_2 k_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3} \tag{3.3}$$

then

$$s_1(t) \leq s_{1,0}, \;\; s_2(t) \leq s_{2,0}, \;\; s_3(t) \leq s_{3,0}, \;\; v(t) \leq v_0 \tag{3.4}$$

Proof. (i) For the local existence, all the functions of system 2.4 are locally Lipschitz continuous. Thus, there exists a unique local solution on $t \in [T_0, T_{max})$, where T_{max} is the explosion time. The analysis of this kind of system is based on elementary methods of ordinary differential equations. The existence of unique solutions is guaranteed by various fixed point theorems on a maximal interval $[T_0, T_{max})$ [2]. By proving that the components of the solution vector $(s_1(t),\ s_2(t),\ s_3(t),\ v(t),\ l(t),\ a(t),\ c(t),\ t_r(t),\ r(t))$ are uniformly bounded on any bounded interval $[0, T_{max})$, one ensures that $T_{max} = \infty$. We remark that the components of the vector

$$F(s_1, s_2, s_3, v, l, a, c, t_r, r) = \begin{pmatrix} F_1(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_2(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_3(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_4(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_5(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_6(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_7(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_8(s_1, s_2, s_3, v, l, a, c, t_r, r) \\ F_9(s_1, s_2, s_3, v, l, a, c, t_r, r) \end{pmatrix} \tag{3.5}$$

Where

$$F_1(s_1,s_2,s_3,v,l,a,c,t_r,r) = \lambda - \lambda_1 a - \lambda_2 c - \lambda_3 tr + \phi_1 v - (\beta_1 a + \beta_2 c + \beta_3 tr)\, s_1 - k_1 s_1$$

$$F_2(s_1,s_2,s_3,v,l,a,c,t_r,r) = p_1 s_1 + \phi_2 v - (\beta_1 a + \beta_2 c + \beta_3 t_r)\, s_2 - k_2 s_2$$

$$F_3(s_1,s_2,s_3,v,l,a,c,t_r,r) = p_2 s_2 + \phi_3 v - (\beta_1 a + \beta_2 c + \beta_3 tr)\, s_3 - k_3 s_3$$

$$F_4(s_1,s_2,s_3,v,l,a,c,t_r,r) = \theta_1 s_1 + \theta_2 s_2 + \theta_3 s_3 - k_4 v$$

$$F_5(s_1,s_2,s_3,v,l,a,c,t_r,r) = \lambda_1 a + \lambda_2 c + \lambda_3 t_r + (\beta_1 a + \beta_2 c + \beta_3 t_r)\,(s_1 + s_2 + s_3) - k_5 l$$

$$F_6(s_1,s_2,s_3,v,l,a,c,t_r,r) = \delta_1 l - k_6 a$$

$$F_7(s_1,s_2,s_3,v,l,a,c,t_r,r) = \delta_2 a + \omega_2 tr + \tau\, r - k_7 c$$

$$F_8(s_1,s_2,s_3,v,l,a,c,t_r,r) = \omega_1 c - k_8 tr$$

$$F_9(s_1,s_2,s_3,v,l,a,c,t_r,r) = \gamma_a a + \gamma_c c + \gamma_t tr - k_9 r$$

are quasi-positive.

Consequently, since the initial conditions are non-negative, this implies that the solution components are non-negative for all $t \in [T_0, T_{max})$.

Now, let the function Ψ be defined as

$$\Psi(t) = s_1(t) + s_2(t) + s_3(t) + v(t) + l(t) + a(t) + c(t) + tr(t) + r(t)$$

By taking the sum of the first nine equations in 2.4, we observe

$$\begin{cases} \dfrac{d\Psi}{dt} \leq \lambda - \mu\Psi(t) \\ \Psi(0) = 1. \end{cases} \tag{3.6}$$

Integrating equation 3.6 over $(0,t)$ for all $t_0 < t < T$, one can get the following

$$\Psi(t)e^{\mu t} - 1 \leq \frac{\lambda}{\mu}(e^{\mu t} - 1),$$

which implies that

$$\Psi(t) \leq e^{-\mu t} + \frac{\lambda}{\mu}(1 - e^{-\mu t}).$$

Therefore

$$\Psi(t) \leq (1-\frac{\lambda}{\mu})e^{-\mu t}+\frac{\lambda}{\mu}.$$

Here, two different cases are distinguished. If $\frac{\lambda}{\mu} < 1$, then the following inequality is satisfied

$$\Psi(t) \leq 1-\frac{\lambda}{\mu}+\frac{\lambda}{\mu} \leq 1,$$

otherwise, if $\frac{\lambda}{\mu} \geq 1$ then

$$\Psi(t) \leq \frac{\lambda}{\mu}.$$

Finally, one can get the following which $\Psi(t) \geq 0$

$$0 \leq \Psi(t) \leq \frac{\lambda}{\mu}+1. \tag{3.7}$$

Hence, $T_{max} = \infty$ and the existence of unique, non-negative and bounded global solution are proved.

(ii) We remark that s_1 satisfies the following:

$$\begin{cases} \dfrac{ds_1}{dt} \leq \lambda+\phi_1\left[\dfrac{\lambda\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)}{k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3}\right]-k_1s_1(t) \\ s_1(0)=s_{1,0} \end{cases} \tag{3.8}$$

By integrating (11) over $[0,t]$ for all $t>0$,

we obtain:

$$s_1(t)e^{k_1(t)} \leq \frac{\lambda+\phi_1\left[\dfrac{\lambda\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)}{k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3}\right]}{k_1} \times\left(e^{k_1(t)}-1\right)+s_{1,0} \tag{3.9}$$

Since

$$s_{1,0} \leq \frac{\lambda+\phi_1\left[\dfrac{\lambda\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)}{k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3}\right]}{k_1} \tag{3.10}$$

which implies that $s_1(t) \leq s_{1,0}$.

The same reasoning is applied for $s_2(t)$, $s_3(t)$ and $v(t)$ which concludes the proof of this theorem.

□

3.2. **Disease free-equilibrium and Basic reproduction number.**

Theorem 3.2. *Consider the model 2.4 with the given parameters in 3.1 Then,*

(i) *The disease free equilibrium point (DFE) is*

$$\mathcal{E}^0 = (s_{1,0},\ s_{2,0},\ s_{3,0},\ v_0,\ 0,\ 0,\ 0,\ 0,\ 0) \tag{3.11}$$

which

$$\begin{aligned}
s_{1,0} &= \left[\frac{\lambda}{k_1} + \frac{\phi_1\lambda\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)}{k_1\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right] \\
s_{2,0} &= \left[\frac{\lambda p_1}{k_1k_2} + \frac{\left(p_1\phi_1 + k_1\phi_2\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2\left[\kappa_2\kappa_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right] \\
s_{3,0} &= \left[\frac{\lambda\, p_1p_2}{k_1k_2k_3} + \frac{\left(p_1p_2\phi_1 + p_2k_1\phi_2 + k_1k_2\phi_3\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2k_3\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right] \\
v_0 &= \frac{\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3}
\end{aligned} \tag{3.12}$$

(ii) *The basic reproduction number $\mathcal{R}_0$ of model is:*

$$\mathcal{R}_0 = \frac{\delta_1\left(H_1k_7k_8 - H_1\omega_1\omega_2 + H_2\delta_2k_8 + H_3\delta_2\omega_1\right)}{k_5k_6\left(k_7k_8 - \omega_1\omega_1\right)} \tag{3.13}$$

Where k_5, k_6, k_7, k_8 are given by 2.2 and H_1, H_2, H_3 are given by:

$$\begin{aligned}
H_1 = \lambda_1 &+ \beta_1\left[\frac{\lambda}{k_1} + \frac{\phi_1\lambda\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)}{k_1\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right] \\
&+ \beta_1\left[\frac{\lambda p_1}{k_1k_2} + \frac{\left(p_1\phi_1 + k_1\phi_2\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2\left[\kappa_2\kappa_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right] \\
&+ \beta_1\left[\frac{\lambda\, p_1p_2}{k_1k_2k_3} + \frac{\left(p_1p_2\phi_1 + p_2k_1\phi_2 + k_1k_2\phi_3\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2k_3\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]
\end{aligned} \tag{3.14}$$

$$H_2 = \lambda_2 + \beta_2\left[\frac{\lambda}{k_1} + \frac{\phi_1\lambda\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)}{k_1\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]$$

$$+ \beta_2\left[\frac{\lambda p_1}{k_1k_2} + \frac{\left(p_1\phi_1 + k_1\phi_2\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2\left[\kappa_2\kappa_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]$$

$$+ \beta_2\left[\frac{\lambda\, p_1p_2}{k_1k_2k_3} + \frac{\left(p_1p_2\phi_1 + p_2k_1\phi_2 + k_1k_2\phi_3\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2k_3\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]$$

$$H_3 = \lambda_3 + \beta_3\left[\frac{\lambda}{k_1} + \frac{\phi_1\lambda\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)}{k_1\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]$$

$$+ \beta_3\left[\frac{\lambda p_1}{k_1k_2} + \frac{\left(p_1\phi_1 + k_1\phi_2\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2\left[\kappa_2\kappa_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]$$

$$+ \beta_3\left[\frac{\lambda\, p_1p_2}{k_1k_2k_3} + \frac{\left(p_1p_2\phi_1 + p_2k_1\phi_2 + k_1k_2\phi_3\right)\left(\theta_1k_2k_3 + \theta_2k_3p_1 + \theta_3p_1p_2\right)\lambda}{k_1k_2k_3\left[k_2k_3\left(k_1k_4 - \theta_1\phi_1\right) - \phi_1p_1\left(\theta_2k_3 + \theta_3p_2\right) - \theta_3k_1\left(\phi_2p_1 + \phi_3k_2\right) - \theta_2\phi_2k_1k_3\right]}\right]$$

Proof. Here, we consider the proposed mathematical model 2.4 with nine homogeneous compartments. This model can be written as

$$\frac{d}{dt}(s_1,\ s_2,\ s_3,\ v,\ l,\ a,\ c,\ t_r,\ r)^T = F(s_1,\ s_2,\ s_3,\ v,\ l,\ a,\ c,\ tr,\ r)^T$$

Where F is defined by 3.5. The point $\mathcal{E}_0$ defined by 3.2 satisfies $F(\mathcal{E}_0) = 0$.

To calculate the reproduction rate $\mathcal{R}_0$, let's use the next generation matrix method described in [1]. Thus let us consider only the infected and infectious compartments which satisfy the following order 4 system:

$$\frac{d}{dt}\begin{pmatrix} l \\ a \\ c \\ tr \end{pmatrix} = \begin{pmatrix} \lambda_1a + \lambda_2c + \lambda_3t_r + \left(\beta_1a + \beta_2c + \beta_3t_r\right)\left(s_1 + s_2 + s_3\right) - k_5l \\ \delta_1l - k_6a \\ \delta_2l + \omega_2t_r + \tau\, r - k_7c \\ \omega_1c - k_8t_r \end{pmatrix} \tag{3.15}$$

The rate of occurrence of new infection in the four compartments $(l,\ a,\ c,\ t_r)$ is represented by the vector F as follows

$$F = \begin{pmatrix} \lambda_1 a + \lambda_2 c + \lambda_3 t_r + (\beta_1 a + \beta_2 c + \beta_3 t_r)(s_1 + s_2 + s_3) \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{3.16}$$

and the transfer rate of individuals into and out of the infected compartments is given by the vector $\mathcal{G}$

$$G = \begin{pmatrix} k_5 l \\ -\delta_1 l + k_6 a \\ -\delta_2 l - \omega_2 t_r - \tau r + k_7 c \\ -\omega_1 c + k_8 t_r \end{pmatrix} \tag{3.17}$$

Thus, all the epidemiological events leading to new infections are incorporated into the model via the matrix $\mathcal{F}$, while all the other events are included in the matrix $\mathcal{G}$. Progression to either death or immunity ensures that G is invertible. By substituting the variables (s_1, s_2, s_3) with the free equilibrium point $\mathcal{E}_0$, we obtain the two matrices $\mathcal{F}$ and $\mathcal{G}$ which are expressed as follows:

$$\mathcal{F} = \begin{pmatrix} 0 & H_1 & H_2 & H_3 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.18}$$

Where $H_1,\ H_2,\ _3$ are given in 3.14

$$\mathcal{G} = \begin{pmatrix} k_5 & 0 & 0 & 0 \\ -\delta_1 & k_6 & 0 & 0 \\ 0 & -\delta_2 & k_7 & -\omega_2 \\ 0 & 0 & -\omega_1 & k_8 \end{pmatrix} \tag{3.19}$$

By calculating $\mathcal{G}^{-1}$, we obtain:

$$\mathcal{G}^{-1} = \begin{pmatrix} \frac{1}{k_5} & 0 & 0 & 0 \\ \frac{\delta_1}{k_5 k_7} & \frac{1}{k_6} & 0 & 0 \\ \frac{\delta_1 \delta_2 k_8}{k_5 k_6 (k_7 k_8 - \omega_1 \omega_2)} & \frac{\delta_2 k_8}{k_6 (k_7 k_8 - \omega_1 \omega_2)} & \frac{k_8}{k_7 k_8 - \omega_1 \omega_2} & \frac{\omega_2}{k_7 k_8 - \omega_1 \omega_2} \\ \frac{\delta_1 \delta_2 \omega_1}{k_5 k_6 (k_7 k_8 - \omega_1 \omega_2)} & \frac{\delta_2 \omega_2}{k_6 (k_7 k_8 - \omega_1 \omega_2)} & \frac{\omega_1}{k_7 k_8 - \omega_1 \omega_2} & \frac{k_7}{k_7 k_8 - \omega_1 \omega_2} \end{pmatrix} \tag{3.20}$$

We calculate the matrix of the new generation, we obtain:

$$\mathcal{F}\mathcal{G}^{-1} = \begin{pmatrix} M_1 & M_2 & M_3 & M_4 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.21}$$

Where

$$M_1 = \frac{\delta_1 H_1}{k_5 k_7} + \frac{\delta_1 \delta_2 k_8 H_2 + \delta_2 \omega_1 H_3}{k_5 k_6 (k_7 k_8 - \omega_1 \omega_2)}, M_2 = \frac{H_1}{k_6} + \frac{\delta_2 k_8 H_2 + \omega_1 \omega_2 H_3}{k_6 (k_7 K_8 - \omega_1 \omega_2)}, M_3 = \frac{k_8 H_2 + \omega_1 H_3}{k_7 k_8 - \omega_1 \omega_2}, M_4 = \frac{\omega_2 H_2 + k_7 H_3}{k_7 k_8 - \omega_1 \omega_2} \tag{3.22}$$

By the next generation matrix approach, $\mathcal{R}_0$ for the model. By calculating the spectral radius of the next generation matrix $\mathcal{F}\mathcal{G}^{-1}$, we get:

$$\mathcal{R}_0 = \frac{\delta_1 (H_1 k_7 k_8 - H_1 \omega_1 \omega_2 + H_2 \delta_2 k_8 + H_3 \delta_2 \omega_1)}{k_5 k_6 (k_7 k_8 - \omega_1 \omega_2)} \tag{3.23}$$

Where k_5, k_6, k_7, k_8 are given by 2.2 and H_1, H_2, H_3 are given by 3.14. □

3.3. **Endemic equilibria.** In presence of infected individuals, model 2.1 is said to be exhibiting an endemic equilibrium point
$\mathcal{E}^* = \left(S_1^*,\ S_2^*,\ S_3^*,\ V^*,\ L^*,\ A^*,\ C^*,\ T_r^*,\ R^*\right)$ where $S_1^*,\ S_2^*,\ S_3^*,\ V^*,\ L^*,\ A^*,\ C^*,\ T_r^*,\ R^*$ are given by:

$$
\begin{aligned}
S_1^* &= \frac{(\lambda N^* - \lambda_1 A^* - \lambda_2 C^* - \lambda_3 T_r^* + \phi_1 V^*)\, N^*}{k_1 N^* + \beta_1 L^* + \beta_2 A^* + \beta_3 C^* + \beta_4 T_r^*}, \quad S_2^* = \frac{\left(p_1 S_1^* + \phi_2 V^*\right) N^*}{k_2 N^* + \beta_1 A^* + \beta_2 C^* + \beta_3 T_r^*} \\
S_3^* &= \frac{\left(p_2 S_2^* + \phi_3 V^*\right) N^*}{k_3 N^* + (\beta_1 A^* + \beta_2 C^* + \beta_3 T^*)}, \quad V^* = \frac{\theta_1 S_1^* + \theta_2 S_2^* + \theta_3 S_3^*}{K_4} \\
L^* &= \frac{(\lambda_1 A^* + \lambda_2 C^* + \lambda_3 T_r^*)\, N^* + (\beta_1 A^* + \beta_2 C^* + \beta_3 T_r *) \left(S_1^* + S_2^* + S_3^*\right)}{k_5 N^*} \\
A^* &= \frac{\delta_1 L^*}{K_6}, \quad C^* = \frac{\delta_2 A^* + \omega_2 T * + \sigma R *}{K_7}, \quad T_r^* = \frac{\omega_1 C^*}{K_8}, \quad R^* = \frac{\gamma_a A^* \gamma_c C^* + \gamma_{t_r} T_r^*}{K_9}
\end{aligned}
\tag{3.24}
$$

3.4. **Global stability of disease-free equilibrium point $\mathcal{E}^0$.** In the section, the global stability analysis of the model for the disease free equilibrium is shown. In the following, we aim to provide a brief investigation of the Castillo Chavez technique ([15], [14], [10]) to prove the stability of system 2.4 in the global sense at the disease free equilibrium point.

Therefore, by applying the Castillo Chavez technique ([15], [10]), the given problem 2.4 is converted into the following sub-models:

$$
\begin{cases}
\dfrac{dX_1}{dt} = F(X_1, X_2), \\[2ex]
\dfrac{dX_2}{dt} = G(X_1, X_2), \\[2ex]
G(X_1, 0) = 0.
\end{cases}
\tag{3.25}
$$

Where X_1 and X_2 designate the population of uninfected individuals, and infected individuals, respectively.

The following conditions (H1) and (H2) must be satisfied to guarantee the local asymptotic stability.

(H1) If $\dfrac{dX_1}{dt} = F(X_1, 0)$ then $\mathcal{E}^0$ is globally asymptotically stable.

(H2) $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2)$.

Where $\hat{G}(X_1, X_2) \geq 0$ for $(X_1,\ X_2) \in \Omega$, the matrix A is a M-matrix whose off diagonal elements are nonnegative.

In the proposed system 2.4, $X_1 = (s_1, s_2, s_3, v, r) \in \mathbb{R}^5$ and $X_1 = (l, a, c, t_r) \in \mathbb{R}^4$. According to the results obtained in Section 3, the free disease equilibrium point (DFE) was denoted by $\mathcal{E}^0$, and is defined by:

$$\mathcal{E}^0 = (s_{1,0},\ s_{2,0},\ s_{3,0},\ v_0,\ 0,\ 0,\ 0,\ 0,\ 0)$$

In order to ensure the globally asymptotically stability of DFE point, the results given above [10] were applied.

Theorem 3.3. *If* $\mathcal{R}_0 < 1$

and

$$s_{1,0} \leq \left[\frac{\lambda}{k_1} + \frac{\phi_1 \lambda \left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right)}{k_1 \left[k_2 k_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3 \right]} \right]$$

$$s_{2,0} \leq \left[\frac{\lambda p_1}{k_1 k_2} + \frac{\left(p_1 \phi_1 + k_1 \phi_2 \right) \left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right) \lambda}{k_1 k_2 \left[\kappa_2 \kappa_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3 \right]} \right]$$

$$s_{3,0} \leq \left[\frac{\lambda \, p_1 p_2}{k_1 k_2 k_3} + \frac{\left(p_1 p_2 \phi_1 + p_2 k_1 \phi_2 + k_1 k_2 \phi_3 \right) \left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right) \lambda}{k_1 k_2 k_3 \left[k_2 k_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3 \right]} \right]$$

$$v_0 \leq \frac{\left(\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2 \right) \lambda}{k_2 k_3 \left(k_1 k_4 - \theta_1 \phi_1 \right) - \phi_1 p_1 \left(\theta_2 k_3 + \theta_3 p_2 \right) - \theta_3 k_1 \left(\phi_2 p_1 + \phi_3 k_2 \right) - \theta_2 \phi_2 k_1 k_3}$$

then the DFE point $\mathcal{E}^0$ of the model 2.4 is globally asymptotically stable.

Proof. In System 2.4, one can set the following

$$F(X_1, X_2) = \begin{pmatrix} \lambda - \lambda_1 a - \lambda_2 c - \lambda_3 t_r + \phi_1 v - \left(\beta_1 a + \beta_2 c + \beta_3 t_r \right) s_1 - k_1 s_1 \\ p_1 s_1 + \phi_2 v - \left(\beta_1 a - \beta_2 c - \beta_3 t_r \right) s_2 - k_2 s_2 \\ p_2 s_2 + \phi_3 v - \left(\beta_1 a + \beta_2 c + \beta_3 t_r \right) s_3 - k_3 s_3 \\ \phi_1 s_1 + \phi_2 s_2 + \phi_3 s_3 - k_4 V \\ \gamma_a a + \gamma_c c + \gamma_{t_r} t_r - k_9 r \end{pmatrix} \tag{3.26}$$

and

$$G(X_1, X_2) = \begin{pmatrix} G_1(X_1, X_2) \\ G_2(X_1, X_2) \\ G_3(X_1, X_2) \\ G_4(X_1, X_2) \end{pmatrix}$$

Where each component is defined by the following sense

$$\begin{aligned} G_1(X_1, X_2) &= \lambda_1 a + \lambda_2 c + \lambda_3 t_r + \left(\beta_1 a + \beta_2 c + \beta_3 t_r \right) \left(s_1 + s_2 + s_3 \right) - k_5 L \\ G_2(X_1, X_2) &= \delta_1 l - k_6 a \\ G_3(X_1, X_2) &= \delta_2 l + \omega_2 t_r + \sigma \, r - k_7 c \\ G_4(X_1, X_2) &= \omega_1 c - k_8 t_r \end{aligned}$$

At the DFE point, it is clear that $G(X_1, 0) = 0$.
To derive the condition (A_2), we first calculate the matrix $A = D_{X_2}G(X_0)$ at the DFE point.

$$A = \begin{pmatrix} -k_5 & H_1 & H_2 & H_3 \\ \delta_1 & -k_6 & 0 & 0 \\ 0 & \delta_2 & -k_7 & \omega_2 \\ 0 & 0 & \omega_1 & -k_8 \end{pmatrix} \tag{3.27}$$

It is clear that the matrix A given above is an M-matrix.
Now, one can calculate the following function:

$$\bar{G}(X_1, X_2) = \begin{pmatrix} \bar{G}(X_1, X_2) \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{3.28}$$

Where

$$\begin{aligned} \bar{G}_1(X_1, X_2) = &-s_1 (\beta_1 a + \beta_2 c + \beta_3 t_r) - s_2 (\beta_1 a + \beta_2 c + \beta_3 t_r) - \\ &-s_3 (\beta_2 a + \beta_2 c + \beta_3 t_r) + H_1 a + H_2 c + H_3 t_r - \lambda_1 a - \lambda_2 c - \lambda_3 t_r \end{aligned} \tag{3.29}$$

By replacing H_1, H_2, H_3 by their expressions given in 3.14, one obtain the following result:

$$\begin{aligned} \bar{G}_1(X_1, X_2) = &\beta_1 a \left[\left[\frac{\lambda}{k_1} + \frac{\phi_1 \lambda (\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2)}{k_1 [k_2 k_3 (k_1 k_4 - \theta_1 \phi_1) - \phi_1 p_1 (\theta_2 k_3 + \theta_3 p_2) - \theta_3 k_1 (\phi_2 p_1 + \phi_3 k_2) - \theta_2 \phi_2 k_1 k_3]} \right] - s_1 \right] \\ &+ \beta_1 a \left[\left[\frac{\lambda p_1}{k_1 k_2} + \frac{(p_1 \phi_1 + k_1 \phi_2) (\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2) \lambda}{k_1 k_2 [\kappa_2 \kappa_3 (k_1 k_4 - \theta_1 \phi_1) - \phi_1 p_1 (\theta_2 k_3 + \theta_3 p_2) - \theta_3 k_1 (\phi_2 p_1 + \phi_3 k_2) - \theta_2 \phi_2 k_1 k_3]} \right] - s_2 \right] \\ &+ \beta_1 a \left[\left[\frac{\lambda p_1 p_2}{k_1 k_2 k_3} + \frac{(p_1 p_2 \phi_1 + p_2 k_1 \phi_2 + k_1 k_2 \phi_3) (\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2) \lambda}{k_1 k_2 k_3 [k_2 k_3 (k_1 k_4 - \theta_1 \phi_1) - \phi_1 p_1 (\theta_2 k_3 + \theta_3 p_2) - \theta_3 k_1 (\phi_2 p_1 + \phi_3 k_2) - \theta_2 \phi_2 k_1 k_3]} \right] - s_3 \right] \\ &+ \beta_2 c \left[\left[\frac{\lambda}{k_1} + \frac{\phi_1 \lambda (\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2)}{k_1 [k_2 k_3 (k_1 k_4 - \theta_1 \phi_1) - \phi_1 p_1 (\theta_2 k_3 + \theta_3 p_2) - \theta_3 k_1 (\phi_2 p_1 + \phi_3 k_2) - \theta_2 \phi_2 k_1 k_3]} \right] - s_1 \right] \\ &+ \beta_2 c \left[\left[\frac{\lambda p_1}{k_1 k_2} + \frac{(p_1 \phi_1 + k_1 \phi_2) (\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2) \lambda}{k_1 k_2 [\kappa_2 \kappa_3 (k_1 k_4 - \theta_1 \phi_1) - \phi_1 p_1 (\theta_2 k_3 + \theta_3 p_2) - \theta_3 k_1 (\phi_2 p_1 + \phi_3 k_2) - \theta_2 \phi_2 k_1 k_3]} \right] - s_2 \right] \\ &+ \beta_2 c \left[\left[\frac{\lambda p_1 p_2}{k_1 k_2 k_3} + \frac{(p_1 p_2 \phi_1 + p_2 k_1 \phi_2 + k_1 k_2 \phi_3) (\theta_1 k_2 k_3 + \theta_2 k_3 p_1 + \theta_3 p_1 p_2) \lambda}{k_1 k_2 k_3 [k_2 k_3 (k_1 k_4 - \theta_1 \phi_1) - \phi_1 p_1 (\theta_2 k_3 + \theta_3 p_2) - \theta_3 k_1 (\phi_2 p_1 + \phi_3 k_2) - \theta_2 \phi_2 k_1 k_3]} \right] - s_3 \right] \end{aligned}$$

$$+\beta_3 t_r\left[\left[\frac{\lambda}{k_1}+\frac{\phi_1\lambda\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)}{k_1\left[k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3\right]}\right]-s_1\right]$$

$$+\beta_3 t_r\left[\left[\frac{\lambda p_1}{k_1k_2}+\frac{\left(p_1\phi_1+k_1\phi_2\right)\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)\lambda}{k_1k_2\left[\kappa_2\kappa_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3\right]}\right]-s_2\right]$$

$$+\beta_3 t_r\left[\left[\frac{\lambda\, p_1p_2}{k_1k_2k_3}+\frac{\left(p_1p_2\phi_1+p_2k_1\phi_2+k_1k_2\phi_3\right)\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)\lambda}{k_1k_2k_3\left[k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3\right]}\right]-s_3\right]$$

Thanks to Theorem 1, (ii) , one gets the folllowing result:

$$\left[\frac{\lambda}{k_1}+\frac{\phi_1\lambda\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)}{k_1\left[k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3\right]}\right]-s_1\geq 0$$

$$\left[\frac{\lambda p_1}{k_1k_2}+\frac{\left(p_1\phi_1+k_1\phi_2\right)\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)\lambda}{k_1k_2\left[\kappa_2\kappa_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3\right]}\right]-s_2\geq 0$$

$$\left[\frac{\lambda\, p_1p_2}{k_1k_2k_3}+\frac{\left(p_1p_2\phi_1+p_2k_1\phi_2+k_1k_2\phi_3\right)\left(\theta_1k_2k_3+\theta_2k_3p_1+\theta_3p_1p_2\right)\lambda}{k_1k_2k_3\left[k_2k_3\left(k_1k_4-\theta_1\phi_1\right)-\phi_1p_1\left(\theta_2k_3+\theta_3p_2\right)-\theta_3k_1\left(\phi_2p_1+\phi_3k_2\right)-\theta_2\phi_2k_1k_3\right]}\right]-s_3\geq 0 \tag{3.30}$$

Since Theorem3.1, the following result is obtained $\bar{G}(X_1,X_2)\geq 0$.
Consequently, the hypothesis (H_1) and (H_2) are satisfied.
Moreover, one uses Castillo Chavez technique ([10], [15], [13]) to conclude that If $\mathcal{R}_0<1$, the Disease free-equilibrium point is globally asymptotically stable. □

3.5. **Global stability of endemic equilibrium point $\mathcal{E}^*$.** In this subsection, by constructing suitable Lyapunov function, we will prove the global asymptotic stability of the endemic equilibrium point $\mathcal{E}^*$.

Theorem 3.4. *If $\mathcal{R}_0>1$, the endemic equilibrium point $\mathcal{E}^*$ of system 2.1 is globally asymptotically stable.*

Proof. When $\mathcal{R}_0>1$, one defines the following Lyapunov function as in ([17], [12] , [16], [11], [47]):

$$\begin{aligned}\Gamma=&\left(S_1-S_1^*\right)+\left(S_2-S_2^*\right)+\left(S_3-S_3^*\right)+\left(V-V^*\right)+\left(L-L^*\right)+\left(A-A^*\right)\\&+\left(C-C^*\right)+\left(T_r-T_r^*\right)+\left(R-R^*\right)-\left(S_1^*+S_2^*+S_3^*+V^*+L^*+A^*+C^*+T_r^*+R^*\right)\\&\times ln\left(\frac{S_1+S_2+S_3+V+L+A+C+T_r+R}{S_1^*+S_2^*+S_3^*+V^*+L^*+A^*+C^*+T_r^*+R^*}\right)\end{aligned} \tag{3.31}$$

As $N=S_1+S_2+S_3+V+L+I+C+T_r+R$, one can set

$$N^*=S_1^*+S_2^*+S_3^*+V^*+L^*+A^*+C^*+T_r^*+R^*$$

Then, the Lyapunov function can also be rewriten as follows:

$$\begin{aligned}\Gamma &= N - N^* - N^* ln\frac{N}{N^*}\\ \Gamma &= N^*\left(\frac{N}{N^*} - 1 - ln\frac{N}{N^*}\right)\end{aligned} \tag{3.32}$$

We shall use the family of Volterra-type Lyapunov function defined by
$g(x) = x - 1 - ln(x)$, $x \in \mathbf{R}^+$ which admits a global mimnimun at $x = 1$, and satisfies $g(1) = 0$. Since $S_1(t) > 0,\ S_2(t) > 0,\ S_3(t) > 0,\ V(t) > 0,\ L(t) > 0,\ A(t) > 0,$
$C(t) > 0,\ T_r(t) > 0,\ R(t) > 0$, then one can obtain the following

$$\Gamma = N - N^* - N^* ln\frac{N}{N^*} > 0 \tag{3.33}$$

Therefore, the Lyapunov function V derivative is given by the following sense

$$\frac{d\Gamma}{dt} = \left(1 - \frac{N^*}{N}\right)\frac{dN}{dt} \tag{3.34}$$

Note that according to system (1)

$$\frac{dN}{dt} = \Lambda - \mu_a A - \mu_c C - \mu_{t_r} T_r - \mu N \tag{3.35}$$

As at the endemic equilibrium point $\frac{dN}{dt} = 0$, then one obtains

$$\Lambda = \mu_a A^* + \mu_c C^* + \mu_{t_r} T_r^* + \mu N^* \tag{3.36}$$

From 2.1, 2.2, and by assuming that
$N - N^* \geq 0,\ \ A - A^* \geq 0,\ \ C - C^* \geq 0,\ \ T_r - T_r^* \geq 0$, one has

$$\begin{aligned}\frac{d\Gamma}{dt} &= \left(1 - \frac{N^*}{N}\right)(\mu_a A^* + \mu_c C^* + \mu_{t_r} T_r^* + \mu N^* - \mu_a A - \mu_c C - \mu_t T - \mu N)\\ \frac{d\Gamma}{dt} &= -\left(\frac{N - N^*}{N}\right)[\mu_a (A - A^*) + \mu_c (C - C^*) + \mu_t (T_r - T_r^*)\, \mu (N - N^*)]\\ \frac{d\Gamma}{dt} &\leq 0\end{aligned} \tag{3.37}$$

From (2.4) and by using the fact that $\frac{dV}{dt} = 0$ if and only if
$S_1 = S_1^*,\ S_2 = S_2^*,\ S_3 = S_3^*,\ V = V^*,\ L = L^*,\ A = A^*,\ C = C^*, T_r = T_r^*,\ R = R^*$, then $\frac{dV}{dt}$ converges in positive region Ω as t $\longrightarrow \infty$.
Thanks to LaSalle's invariance principle theorem [47], the endemic equilibrium point $\uparrow^*$ is said to be globally asymptotically stable when $\mathcal{R}_0 > 1$ ([17], [46]). □

4. Parameters estimation

4.1. **Problem to solve.** Let thus M observations of values of infected $I_{obs}(t_j)$ at the moments t_j, $j = 1, \ldots, M$.

At the problem 2.1, we associate the functional J defined by

$$J(U) = \int_{t_i}^{t_f} (I(t) - I_{obs}(t))^2 dt \tag{4.1}$$

$U = (\lambda_1, \lambda_2, \lambda_3, \phi_1, \phi_2, \phi_3, \theta_1, \theta_2, \theta_3, p_1, p_2, \beta_1, \beta_2, \beta_3, \delta_1, \delta_2, \gamma_a, \gamma_c, \gamma_t, \omega_1, \omega_2)$ is the vector of parameters to determinate.
t_i the initial time and t_f the final time.
$I(t) = A(t) + C(t) + T(t)$ and $I_{obs}(t) = A_{obs}(t) + C_{obs}(t) + T_{obs}(t)$.
The parameters estimation problem consists in solving

$$\min_{U \subset \mathcal{D}} J(U) \tag{4.2}$$

where $\mathcal{D} = [0,1]^{21}$ a bounded subset of $\mathbb{R}^{21}$.

Theorem 4.1. *The problem defined by* (4.2) *has a unique solution denoted by*
$U^* = (\lambda_1^*, \lambda_2^*, \lambda_3^*, \phi_1^*, \phi_2^*, \phi_3^*, \theta_1^*, \theta_2^*, \theta_3^*, p_1^*, p_2^*, \beta_1^*, \beta_2^*, \beta_3^*, \delta_1^*, \delta_2^*, \gamma_a^*, \gamma_c^*, \gamma_t^*, \omega_1^*, \omega_2^*)$

Proof. Let be the functions

$$\begin{aligned} B :& \mathcal{D} \to L^2(T_i, T_f) \\ & U \to Y_U(t) := (S_1(t),\ S_2(t),\ S_3(t),\ V(t),\ L(t),\ A(t),\ C(t),\ T_r(t),\ R(t)) \end{aligned}$$

where $Y_U(t)$ is the unique solution of the system 4.2 for a given U.
and

$$\begin{aligned} H :& L^2(t_i, t_f) \to \mathbb{R} \\ & Y_U(t) \to \int_{t_i}^{t_f} (I_U(t) - I_{obs}(t))^2 dt \end{aligned}$$

The function J is then written as a composition of functions H and Y_U. Since H and Y_U are continuous, J is also continuous on the compact $\mathcal{D} = [0,1]^{21}$. Moreover, since J is convex, it admits a unique global minimum:
$U^* = (\lambda_1^*, \lambda_2^*, \lambda_3^*, \phi_1^*, \phi_2^*, \phi_3^*, \theta_1^*, \theta_2^*, \theta_3^*, p_1^*, p_2^*, \beta_1^*, \beta_2^*, \beta_3^*, \delta_1^*, \delta_2^*, \gamma_a^*, \gamma_c^*, \gamma_t^*, \omega_1^*, \omega_2^*)$ □

4.2. **Grey Wolf Optimizer algorithm (GWO) description.** The GWO algorithm we used to solve the problem (4.2) is a meta-heuristic which mimics the leadership hierarchy and hunting mechanism of grey wolves in nature proposed by S. Mirjalili et al [21]. Four types of grey wolves are employed for the simulating the leadership hierarchy (see figure 2):

- the leader of the group called alpha (α) which is mostly responsible for making decisions about hunting.
- the leader alpha is assisted by the beta (β) that help the alpha in decision-making or other pack activities.
- the third level in the hierarchy is delta (δ). Delta wolves have to submit to alphas and betas, but they dominate the omega (ω) wolves that occupy the last level.

- the omega wolves always have to submit to all the other dominant wolves.

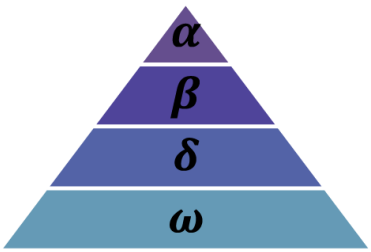

FIGURE 2. Hierarchy of grey wolf [21].

To model mathematically the hunting mechanism of grey wolves, three steps were considered:

- Tracking, chassing and approaching the prey.
- Pursuing, encircling and harassing the prey until it stops moving.
- Attacking the prey.

To respect the hierarchy, the best solution is alpha, the second solution is beta and the third delta. The optimum being the position of the prey. The grey wolves encircle prey during the hunt. The mathematical model is given:

$$\begin{cases} \vec{D} = |\vec{C}.\vec{X}_p(t) - \vec{X}(t)| \\ \vec{X}(t+1) = \vec{X}_p(t) - \vec{A}.\vec{D} \end{cases} \tag{4.3}$$

where t indicates the current iteration, $\vec{A} = 2a.\vec{r_1}$, $\vec{C} = 2.\vec{r_1}$; $\vec{a}$ are linearly decreased from 2 to 0 over the course of iterations and $\vec{r_1}$, $\vec{r_2}$ are random vectors in $[0, 1]$. $\vec{X}_p$ is the position vector of the prey, and $\vec{X}$ indicates the position vector of a grey wolf.
For better exploration of candidate solutions which tend to diverge when $|\vec{A}| > 1$ and to converge when $|\vec{A}| < 1$.
Grey wolves have the ability to recognize the location of prey and encircle them. Over the course of iterations, the first three fittest solutions we obtain so far are considered as α, β and δ respectively, which guide the optimization process (the hunting) and are assumed to take the position of the optimum (the prey). To model this process, we adapt the positions of population using the following formula:

$$\begin{cases} \vec{D_\alpha} = |\vec{C_1}.\vec{X_\alpha} - \vec{X}| \\ \vec{D_\beta} = |\vec{C_2}.\vec{X_\beta} - \vec{X}| \\ \vec{D_\delta} = |\vec{C_3}.\vec{X_\delta} - \vec{X}| \end{cases} \tag{4.4}$$

where:

- $\vec{C_1}$,$\vec{C_2}$ and $\vec{C_3}$ are random vectors.
- $\vec{X_\alpha}$, $\vec{X_\alpha}$ and $\vec{X_\delta}$, the positions of alpha, beta and delta respectively.

- $\vec{X}$ the position of prey(current solution).

The next position of the best solution is given by:

$$\vec{X}(t+1) = \frac{\vec{X}_1 + \vec{X}_2 + \vec{X}_3}{3} \tag{4.5}$$

where

$$\begin{cases} \vec{X}_1 = \vec{X}_\alpha - \vec{A}_1.\vec{D}_\alpha \\ \vec{X}_2 = \vec{X}_\beta - \vec{A}_2.\vec{D}_\beta \\ \vec{X}_3 = \vec{X}_\delta - \vec{A}_3.\vec{D}_\delta \end{cases} \tag{4.6}$$

$\vec{A}_1$,$\vec{A}_2$ and $\vec{A}_3$ are random vectors.

To accelerate convergence, we take

$$\vec{X}(t+1) = 0.7 \times \vec{X}_1 + 0.2 \times \vec{X}_2 + 0.1 \times \vec{X}_3 \tag{4.7}$$

4.3. **Problem solving algorithm.** In summary the resolution of our problem by GWO algorithm is given by the algorithm below:

Algorithm 4.1 Algorithm

Initialize the input parameters for GWO $(N_p, d, lb, ub, Maxiter)$
Initialize Alpha, Beta and Delta Position and Score.
Initialize the random position of search agents.
$k \leftarrow 0$
while $k < Maxiter$ **do**
  for i=1 to N **do**
    solving direct problem (2.1)
    evaluate the score of each search agent using objective function (4.2)
    if $fitness < AlphaScore$ **then**
      Update alpha
    end if
    if $fitness > AlphaScore$ and $fitness < BetaScore$ **then**
      Update beta
    end if
    if $fitness > AlphaScore$ and $fitness > BetaScore$ and $fitness < DeltaScore$ **then**
      Update delta
    end if
  end for
  for i=1 to N_p **do**
    Update the Position of search agents including omegas using equation (4.4-4.6)
    Update the position of prey using equation(4.7)
  end for
  $k \leftarrow k + 1$
end while
Return the position of *Alpha* as the fittest optimum

5. Results and discussion

5.1. **Results of parameter estimation.** The data used were obtained using the evolution of hepatitis B prevalence and population trends in Burkina Faso from 1997 to 2020 [25,42].
The initial values used are $S_1(0) = 236764, S_2(0) = 1304902, S_3(0) = 5327470, V(0) = 18258, L(0) = 1355550, A(0) = 756067, C(0) = 457206, T(0) = 126802, R(0) = 886318$
. The parameters values used are given in the table below:

Parameters	description	Values	references
λ	birth rate of total population	0.048	[42]
μ	natural mortality rate	0.0165	[42]
μ_a	acute HBV related mortality rate	0.005	[42]
μ_c	acute HBV related mortality rate	0.02	[42]
μ_{tr}	treated patients related mortality rate	0.008	[42]
τ	rate of reactivation of hbv infection after recovery	0.0002	Assumed

Table 3. Parameters Value used in the model

The values of the other parameters were obtained by solving the problem 4.2. The following table shows the values obtained.

Parameters	ranges	references	estimated values
λ_1	$[0.01 - 0.8]$	[19,26,27]	$0,616912562$
λ_2	$[0.1 - 0.3]$	[19,20,26]	$0,209089581$
λ_3	$[0.01 - 0.1]$	assumed	$0,088845642$
ϕ_1	$[0.1 - 0.2]$	assumed	$0,120102694$
ϕ_2	$[0.1 - 0.2]$	assumed	$0,128915991$
ϕ_3	$[0.1 - 0.2]$	assumed	$0,15$
θ_1	$[0.2 - 0.3]$	assumed	$0,202492745$
θ_2	$[0.2 - 0.3]$	assumed	$0,251868343$
θ_3	$[0.1 - 0.2]$	assumed	$0,173427178$
p_1	$[0.7 - 0.9]$	assumed	$0,801097162$
p_2	$[0.7 - 0.9]$	assumed	$0,822901736$
β_1	$[0.1 - 0.9]$	[28–30]	$0,2$
β_2	$[0.1 - 0.3]$	[28–30]	$0,089274624$
β_3	$[0.002 - 0.01]$	[20,30,48]	$0,002009163$
δ_1	$[0.1 - 0.3]$	assumed	$0,230350944$
δ_2	$[0.05 - 0.1]$	[33,34]	$0,052127596$
γ_a	$[0.02 - 0.6]$	[9,20,35,48]	$0,500171105$
γ_c	$[0.003 - 0.1]$	[9,20,35,48]	$0,07512413$
γ_{tr}	$[0.002 - 0.2]$	[35,36,48]	$0,134158668$
ω_1	$[0.002 - 0.3]$	[20,35,48]	$0,247359489$
ω_2	$[0.01 - 0.3]$	[20,35,48]	$0,15$

Table 4. Estimated parameters

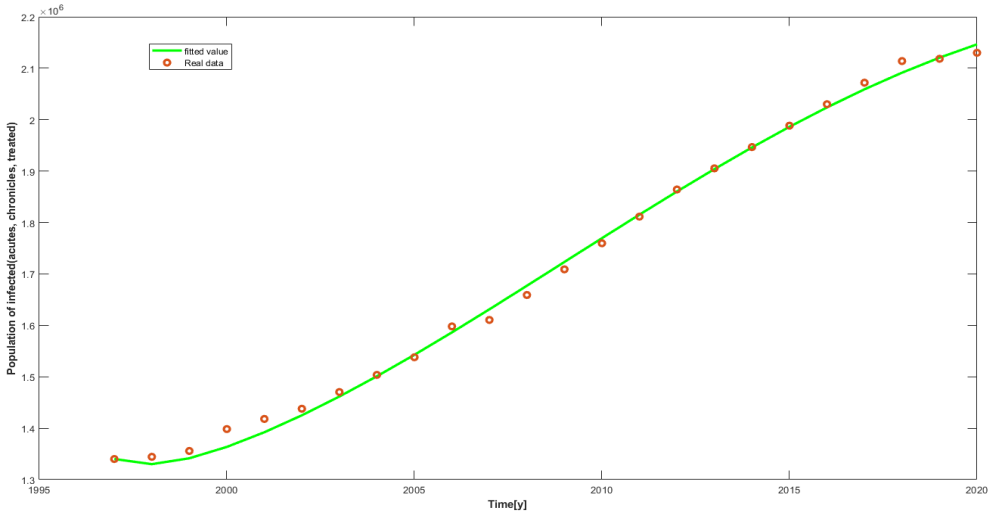

FIGURE 3. The yearly Hepatitis B cases time series in Burkina Faso from 1997 to 2020 and the proposed model best fitted curve

The figure (3) shows the observed data and the estimated data. This demonstrates the robustness of the Gray Wolf Optimizer (*GWO*) algorithm.

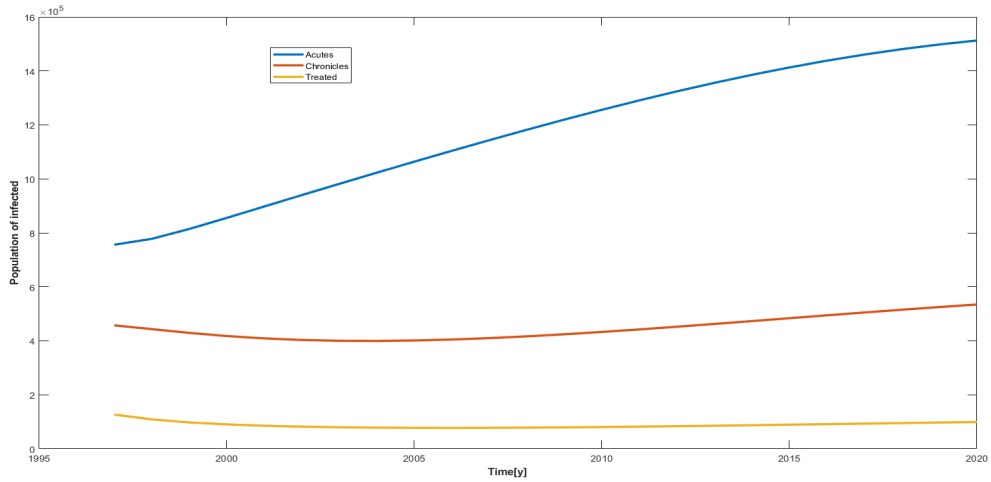

FIGURE 4. Evolution of acute, chronic and treated individuals

The numerical simulation based on the estimated parameters provides, on one hand, the figure (4), illustrating the increasing trend in the number of acute infections, chronic carriers, and individuals treated chronically in the population of Burkina Faso. On the other hand, the obtained value for the basic reproduction number is $\mathcal{R}_0 = 2.5088 > 1$. These results confirm the current trend in the endemic dynamics of hepatitis B in Burkina Faso.

5.2. **Sensitivity analysis.** For hepatitis B virus transmission, the impact of each parameter on the endemic threshold was described in the sensitivity analysis. Sensitivity analysis is an essential method for complex systems, and has been used to determine the strength of model parameters 2.4. The parameter with higher sensitivity index magnitude is more influential than that with smaller magnitude of sensitive index. The sign of the sensitivity indices of $\mathcal{R}_0$ with respect to the parameters shows the positive or negative impact of the parameters. Here, we calculate sensitivity index for each parameter included in effective reproduction number using the parameters given on Table 3 above. The standard equation for the sensitivity index of a parameter Υ for $\mathcal{R}_0$ is given in 5.2 [37,38]:

$$\chi_{\Upsilon}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \Upsilon} \times \frac{\partial \Upsilon}{\mathcal{R}_0} \tag{5.1}$$

Given the complexity of the expression for $\mathcal{R}_0$, we have used numerical differentiation. Thus the numerical values of the sensitivity indices are given in table (5).

Sensitivity index	value
$\chi_{\theta_1}^{\mathcal{R}_0} = (\partial R_0/\partial\theta_1) \times (\theta_1/R_0)$	-0.002178
$\chi_{\theta_2}^{\mathcal{R}_0} = (\partial R_0/\partial\theta_2) \times (\theta_2/R_0)$	-0.003047
$\chi_{\theta_3}^{\mathcal{R}_0} = (\partial R_0/\partial\theta_3) \times (\theta_3/R_0)$	-0.047155
$\chi_{\phi_1}^{\mathcal{R}_0} = (\partial R_0/\partial\phi_1) \times (\phi_1/R_0)$	0.015579
$\chi_{\phi_2}^{\mathcal{R}_0} = (\partial R_0/\partial\phi_2) \times (\phi_2/R_0)$	0.017361
$\chi_{\phi_3}^{\mathcal{R}_0} = (\partial R_0/\partial\phi_3) \times (\phi_3/R_0)$	0.017574
$\chi_{\beta_1}^{\mathcal{R}_0} = (\partial R_0/\partial\beta_1) \times (\beta_1/R_0)$	0.256382
$\chi_{\beta_2}^{\mathcal{R}_0} = (\partial R_0/\partial\beta_2) \times (\beta_2/R_0)$	0.220346
$\chi_{\beta_3}^{\mathcal{R}_0} = (\partial R_0/\partial\beta_3) \times (\beta_3/R_0)$	0.000786
$\chi_{\delta_1}^{\mathcal{R}_0} = (\partial R_0/\partial\delta_1) \times (\delta_1/R_0)$	0.031261
$\chi_{\delta_2}^{\mathcal{R}_0} = (\partial R_0/\partial\delta_2) \times (\delta_2/R_0)$	0.458423
$\chi_{p_1}^{\mathcal{R}_0} = (\partial R_0/\partial p_1) \times (p_1/R_0)$	0.000250
$\chi_{p_2}^{\mathcal{R}_0} = (\partial R_0/\partial p_2) \times (p_2/R_0)$	-0.000280
$\chi_{\lambda_1}^{\mathcal{R}_0} = (\partial R_0/\partial\lambda_1) \times (\lambda_1/R_0)$	0.285195
$\chi_{\lambda_2}^{\mathcal{R}_0} = (\partial R_0/\partial\lambda_2) \times (\lambda_2/R_0)$	0.235145
$\chi_{\lambda_3}^{\mathcal{R}_0} = (\partial R_0/\partial\lambda_3) \times (\lambda_3/R_0)$	0.002146
$\chi_{\omega_1}^{\mathcal{R}_0} = (\partial R_0/\partial\omega_1) \times (\omega_1/R_0)$	-0.153987
$\chi_{\omega_2}^{\mathcal{R}_0} = (\partial R_0/\partial\omega_2) \times (\omega_2/R_0)$	0.116475
$\chi_{\gamma_a}^{\mathcal{R}_0} = (\partial R_0/\partial\gamma_a) \times (\gamma_a/R_0)$	-0.965469
$\chi_{\gamma_c}^{\mathcal{R}_0} = (\partial R_0/\partial\gamma_c) \times (\gamma_c/R_0)$	-0.066392
$\chi_{\gamma_{tr}}^{\mathcal{R}_0} = (\partial R_0/\partial\gamma_{tr}) \times (\gamma_{tr}/R_0)$	-0.124634

TABLE 5. Sensitivity indices of the model parameters

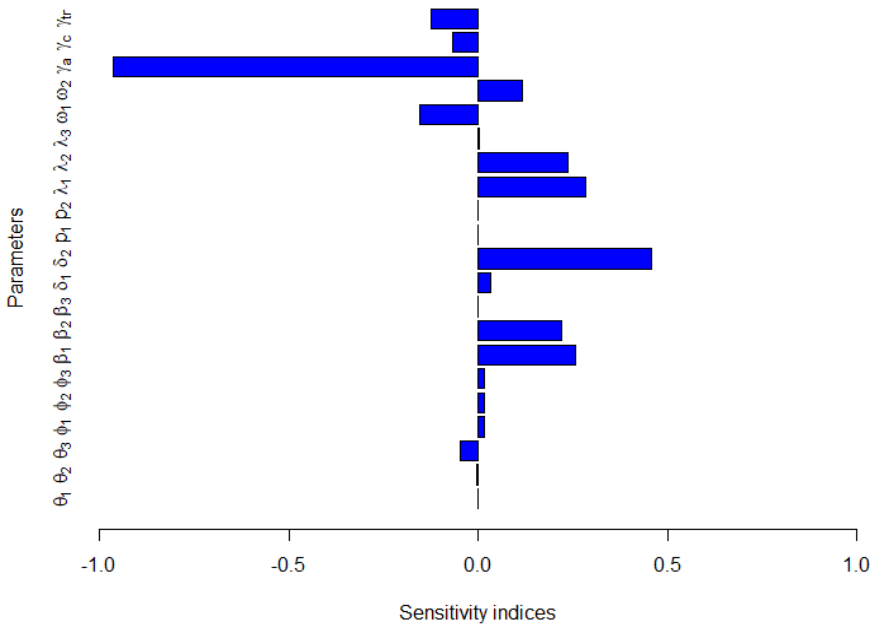

FIGURE 5. sensitivity indices of model parameters

The diagram of Figure 5 clearly shows the impact of each parameter on the endemic threshold. The most positive sensitive parameters are $\chi_{\beta_2}^{\mathcal{R}_0} = 0.220346$, $\chi_{\lambda_2}^{\mathcal{R}_0} = 0.235145$, $\chi_{\beta_1}^{\mathcal{R}_0} = 0.256382$, $\chi_{\lambda_1}^{\mathcal{R}_0} = 0.285195$, $\chi_{\delta_2}^{\mathcal{R}_0} = 0.458423$ for $\mathcal{R}_0 = 2.5088$. Which show on the one hand that infectious contacts with acutely infected people and carriers as well as infected births from acute and chronic mothers, on the other hand, the evolution of acutely infected people towards chronicity, strongly contribute to the increase in the endemic threshold and therefore the spread of the disease. The most negative sensitive parameter is $\chi_{\gamma_a}^{\mathcal{R}_0} = -0.965469$ with basic reproduction number $\mathcal{R}_0 = 2.5088$, which proves that all strategies that can help reduce the number of acute infections in the population can prevent the spread of the disease. In addition to vaccination, which will significantly reduce infectious contacts, we recommend mass screening of the population and early treatment of acute infections.

6. CONCLUSION

In this work, a mathematical model of hepatitis B virus transmission with differential susceptibility according to three age groups, including vertical transmission from acutely, chronically, and treated infected mothers, was developed and applied to the case of Burkina Faso. This model took into account the vaccination of the three susceptible groups and the treatment of chronically ill people. Our modeling process first began with the study of some biological aspects of the disease that enabled us to better approach the modeling problem. Mathematical analysis of the model

shows that the course of the disease is governed by the basic reproduction number $\mathcal{R}_0 < 1$. Indeed, when $\mathcal{R}_0$ the disease disappears from the population giving a disease-free equilibrium which has been proved to be and globally asymptotically stable. Moreover, when $\mathcal{R}_0$ exceeds 1, the disease persists and leads to an endemic state which is also and globally asymptotically stable.

Using data on acutely, chronically, and treated infected individuals in Burkina Faso from 1997 to 2020, we successfully estimated the optimal parameters of our model by solving a global optimization problem using the Grey Wolf Optimizer algorithm. The numerical simulation which showed a strong increase in infectious individuals in the population with a basic reproduction number $\mathcal{R}_0 = 2.5088 > 1$, which confirms the high endemicity of hepatitis B in Burkina Faso.

Furthermore, the sensitivity analysis of $\mathcal{R}_0$ highlighted the influence of each parameter on the dynamics of hepatitis B in Burkina Faso.Thus, the most positively sensitive parameters include, on the one hand, the appropriate contact coefficients for a susceptible to be infected by an acutely ill individual β_1 or by a chronically infected carrier β_2, and, on the other hand, the proportions λ_1 and λ_2 of births infected through vertical transmission from acutely and chronically infected mothers, respectively.

To reverse the current trend of the endemic dynamics of hepatitis B virus infection in Burkina Faso, we recommend:

- The rigorous implementation of systematic vaccination for children at birth, especially in this period of security crisis accompanied by a massive displacement of populations (majority of whom are women and children), in order to break the chain of transmission. This would significantly reduce the proportions of infected births λ_1 and λ_2.
- Mass screening of populations, so that those who test negative for hepatitis B virus infection can be vaccinated, and those who test positive can take measures to avoid being a reservoir of infection or undergo treatment to reduce their infectivity or achieve recovery. The goal here would be to reduce the appropriate contact coefficients β_1 and β_2.

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