Research Article

Parameter Estimation and Sensitivity Analysis of Dysentery Diarrhea Epidemic Model

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In this paper, dysentery diarrhea deterministic compartmental model is proposed. The local and global stability of the disease-free equilibrium is obtained using the stability theory of differential equations. Numerical simulation of the system shows that the backward bifurcation of the endemic equilibrium exists for $R_0 > 1$. The system is formulated as a standard nonlinear least squares problem to estimate the parameters. The estimated reproduction number, based on the dysentery diarrhea disease data for Ethiopia in 2017, is $R_0 = 1.1208$. This suggests that elimination of the dysentery disease from Ethiopia is not practical. A graphical method is used to validate the model. Sensitivity analysis is carried out to determine the importance of model parameters in the disease dynamics. It is found out that the reproduction number is the most sensitive to the effective transmission rate of dysentery diarrhea (β_h). It is also demonstrated that control of the effective transmission rate is essential to stop the spreading of the disease.

1. Introduction

Diarrheal disease is a common threat worldwide, particularly in developing countries. It is preventable and treatable. According to [1], diarrhea in its various forms is usually one of the five major causes of deaths in developing nations. It is the second leading cause of death in children under five years of age. Pneumonia and diarrhea are responsible for an estimated 40 percent of all child deaths each year. The authors [2] also reported that diarrhea causes 18% of all the deaths of children under the age of five. According to the study, more than 5000 children are dying every day as a result of diarrheal diseases. African and South-East Asian regions share 78% of all these deaths.

In most cases, diarrhea disease occurs in three forms and frequently occurs in children of under five years age [1, 3]. The first type of diarrhea is called dysentery diarrhea. This is diarrhea with the loose or watery stools with visible blood. Dysentery diarrhea is most often caused by shigella dysenteriae serotype 1 (bacillary dysentery) or Entamoeba histolytica (amoebic dysentery). The second form of diarrhea

is acute watery diarrhea. This form includes cholera and is associated with significant fluid loss and rapid dehydration in an infected individual. It usually lasts for several hours or days. This can be caused by the pathogens V. cholerae or E. coli bacteria and rotavirus. The last form of diarrhea is persistent diarrhea. This is diarrhea with or without blood that lasts at least 14 days. It is common in undernourished children and those with other illnesses, such as AIDS.

Stochastic and deterministic mathematical models are widely employed by public health practitioners in order to predict and control disease outbreak as well as determining the cost effectiveness of the available strategies [4–10]. In stochastic model, the disease transmission dynamics within a given population is based on the probabilistic analyses, while the deterministic models deals with the use of continuous functions to describe the time evolution of disease in a homogeneously mixed population [11]. Several authors [12–21] have made use of stability theory of differential equations in order to analysis deterministic compartmental models for both local and global dynamics

of diseases transmission in a within hosts and between hosts population such as HIV/AIDs, cholera, sheep brucellosis, influenza, typhoid, etc. In all these work, the threshold parameters for disease control and elimination were determined.

Epidemiologically speaking, it is important to have adequate knowledge of the physical characteristic of any given ailment or disease in order to provide accurate model that can be utilized to predict and control its outbreak effectively. The availability of relevant data for the disease will also enhance the model parameters estimation and the usefulness of the model with respect to the disease involved. Model parameters from epidemiological models can be easily estimated using methods involving ordinary least squares estimator, maximum likelihood estimator derivative approximation, moments estimator, Markov chain Monte Carlo (MCMC) strategy, derivative-free optimization algorithms, the Levenberg-Marquardt, and Trust-Region-Reflective [22–26]. Biegler and Grossmann [27] employed optimization technique based on the seasonal data with the SIRS epidemic model as a constraint in order to estimate the parameters of a generalized incidence rate function. Li [28] also made use of optimization method with difference equations associated with a given system as a constraint in order to estimate the values of embedded parameters. The SIR model parameters were numerically estimated by Capaldi et al. [29] using least squares method. Other authors [30–34] have made use of various parameter estimation techniques base on the available data to determine the effects of various epidemiological factors on the disease transmission and possible control strategy. However, there is still a need to estimate the parameters involved in the various epidemiological models in order to assess the relative influence of each input variable on the output variable.

To the best of our knowledge problem involving estimation of parameters in dysentery diarrhea epidemic model with sensitivity analysis of the basic reproduction number has been scarcely investigated. The main objective of this paper is to tackle this problem by employing constrained optimization technique in order to estimate the values of parameters involved in a deterministic compartmental model for dysentery diarrhea epidemic as a constraint. Real data based on the weekly dysentery diarrhea epidemic that occurred in Ethiopia in 2017 were used to estimate parameters which are not accessible from the characteristic of the disease. In addition, we establish the local and global stability of the disease-free equilibrium and perform the bifurcation analysis. Sensitivity and uncertainty of the basic reproduction number of the system are analyzed. The study estimates the reproduction number of Ethiopia using the estimated parameters to predict the disease spread in the community. In the following Section 2, we present the model and its analysis. The numerical approximation and parameter estimation methods are presented in Section 3. In Section 4, numerical simulation of the system and sensitivity analysis with given parameter values is performed. Brief discussion and conclusions are presented in the last section.

2. The Model and Its Analysis

The SIRSB (Susceptible-Infected-Recovered-Susceptible-Pathogen population) model for dysentery diarrhea proposed by same authors [35] consists of the following system of nonlinear ordinary differential equations:

$$\frac{dS}{dt} = \Lambda + \alpha R - (\lambda_h + \lambda_B + \mu) S,$$

$$\frac{dI}{dt} = (\lambda_h + \lambda_B) S - (\mu + \gamma + d) I,$$

$$\frac{dR}{dt} = \gamma I - (\mu + \alpha) R,$$

$$\frac{dB}{dt} = \epsilon I - \sigma B, \tag{1}$$

$$S(0) = S_0 \geq 0,$$

$$E(0) = I_0 \geq 0,$$

$$R(0) = R_0 \geq 0,$$

$$B(0) = B_0 \geq 0.$$

The standard (frequency dependent) incidence in the human to human interaction and the logistic incidence in the environment to human interaction are respectively given by

$$\lambda_h = \frac{\beta_h I}{N}$$

$$\text{and } \lambda_\beta = \frac{\beta_B B}{K + B}. \tag{2}$$

K is the shigella concentration that yields 50% chance of catching dysentery diarrhea [36]. β_B and β_h represent rates of ingesting shigella from the contaminated environment and through human to human interaction, respectively. It is assumed that the incidence $\lambda_B = \beta_B B/(K + B)$ is a nonlinear function in B. This incidence represents a Hill function. If $B \ll K$, λ_B grows linearly with B; if $B \gg K$, λ_B approaches a constant state, β_B, resulting in a saturation state. Therefore, this form is based on the assumption that the incidence has a saturation form. The pathogen population is diminished (at a rate of $\sigma_2 - \sigma_1 = \sigma > 0$) [17, 35, 36].

The corresponding flow diagram and the description of the parameters for the model are given in Figure 1 and Table 1, respectively.

2.1. Basic Reproduction Number and Existence of Equilibria. System equation (1) has one disease-free equilibrium $E_0 = (\Lambda/\mu, 0, 0, 0)$. The basic reproduction number (R_0) is utilized to quantify the transmission capability of a sickness. It is thought of as the quantity of secondary diseases delivered by a primary case of an infection in a population that is completely susceptible. It can in this manner be estimated by checking the quantity of secondary cases following the presentation of a disease into an absolutely susceptible population. R_0 decides if a pathogen can hold on in such a population, and it is important for evaluating control alternatives. At the
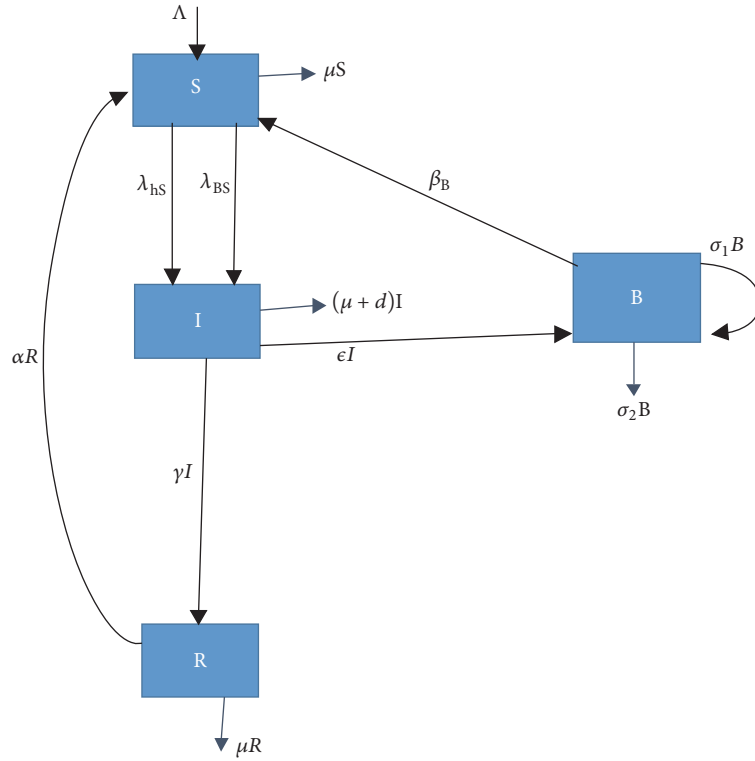
FIGURE 1: Schematic diagram for the flow of dysentery diarrhea infection.

TABLE 1: Description of parameters of the model equation (1).

Parameters	Interpretation	Units
Λ	Recruitment rate of susceptible population	Humans Time^{-1}
μ	Natural death rate of humans	Time^{-1}
γ	Natural recovery rate of diarrhea	Time^{-1}
α	Relapse rate of the recovered humans to the susceptible class	Time^{-1}
d	Disease induced death rate of dysentery diarrhea	Time^{-1}
K	Concentration of Shigella	cells
β_h	Effective transmission rate of diarrhea due to human to human interaction	Time^{-1}
β_B	Effective transmission rate of dysentery diarrhea due to environment to human interaction	Time^{-1}
ϵ	Pathogen shedding rate	Cells Human^{-1}Time^{-1}
σ_1	Shigella Pathogen growth rate	Time^{-1}
σ_2	Shigella Pathogen death rate	Time^{-1}
σ	Net death rate of Shigella Pathogen	Time^{-1}

point when R_0 is under 1, on average each infected individual infects less than one other individual, and the pathogen will cease to exist in the population. Conversely, when R_0 surpasses 1 there is an exponential ascent in the quantity of cases after some time and disease epidemic results [38]. Using the next generation approach of [39], the reproduction number is

$$R_0 = \frac{\beta_h}{(\mu + \gamma + d)} + \frac{\Lambda \beta_B \epsilon}{\mu (\mu + \gamma + d) K \sigma}. \tag{3}$$

The endemic equilibrium $E^* = (S^*, I^*, R^*, B^*)$ of the system is the solution of the algebraic equation

$$\Lambda - (\lambda_h + \lambda_B + \mu) S^* + \alpha R^* = 0,$$
$$(\lambda_h + \lambda_B) S^* - (\mu + d + \gamma) I^* = 0,$$
$$\gamma I^* - (\mu + \alpha) R^* = 0,$$
$$\epsilon I^* - \sigma B^* = 0. \tag{4}$$

That is,

$$B^* = \frac{\epsilon I^*}{\sigma},$$

$$R^* = \frac{\gamma I^*}{\alpha + \mu}, \tag{5}$$

$$S^* = \frac{\Lambda(\alpha + \mu) - (\mu(\mu + \gamma + d) + \alpha(\mu + d))I^*}{\mu(\alpha + \mu)} \text{ and}$$

I^* is the solution of the following quadratic equation:

$$AI^{*2} + BI^* + C = 0, \tag{6}$$

where

$$A = \epsilon\left((\mu\beta_h - \beta_B d)(\mu(\mu + d + \gamma) + \alpha(\mu + d))\right.$$
$$\left. - d(\mu + d + \gamma)\right),$$

$$B = \Lambda\epsilon(\alpha + \mu)(\beta_B d - \mu\beta_h) + (\mu(\mu + d + \gamma) + \alpha(\mu + d)) \tag{7}$$
$$\cdot (K\sigma + \epsilon\Lambda\beta_B) - (\mu + d + \gamma)(Kd\sigma + \epsilon\Lambda),$$

$$C = \mu\Lambda K\sigma(\alpha + \mu)(\mu + d + \gamma)(1 - R_0).$$

(i) System equation (1) always has the disease-free equilibrium.

(ii) If $R_0 > 1$ and $A < 0$, $B > 0$, then system equation (1) may has two endemic equilibria E_1 and E_2.

(iii) If $R_0 > 1$, and $A < 0$, $B < 0$, then system equation (1) may has a unique endemic equilibrium, E^*.

(iv) If $R_0 > 1$ and $A > 0$, $B < 0$, then system equation (1) may has a unique endemic equilibrium, E^*.

(v) If $R_0 > 1$ and $A > 0$, $B > 0$, then system equation (1) has no endemic equilibrium.

(vi) If $0 \le R_0 < 1$, there is no endemic equilibrium.

2.2. Stability of the Disease-Free Equilibrium. This section is devoted to analytic conditions for the stability of the disease-free equilibrium.

2.2.1. Local Stability of the Disease-Free Equilibrium

Theorem 1. *The disease-free equilibrium E_0 is locally asymptotically stable if $R_0 \le 1$ and is unstable if $R_0 > 1$.*

Proof. Local stability is analyzed by the Jacobian matrix of (1) at E_0. That is,

$$J(E_0) = \begin{bmatrix} -\mu & -\beta_h & \alpha & -\frac{\beta_B\Lambda}{K\mu} \\ 0 & \beta_h - (\mu + d + \gamma) & 0 & \frac{\beta_B\Lambda}{K\mu} \\ 0 & \gamma & -(\alpha + \mu) & 0 \\ 0 & \epsilon & 0 & -\sigma \end{bmatrix}. \tag{8}$$

The eigenvalues of this matrix are

$$\lambda_1 = -\mu,$$

$$\lambda_2 = -(\mu + \alpha)$$

and the solutions of $\lambda^2 + a_1\lambda + a_2 = 0$ (9)

where $a_1 = (\mu + d + \gamma + \sigma) - \beta_h$

and $a_2 = (\mu + d + \gamma)\sigma(1 - R_0)$.

If $R_0 < 1$, $a_1 < 0$ and $a_1 a_2 > 0$. Thus, according to the Hurwitz criterion, the quadratic equation, $\lambda^2 + a_1\lambda + a_2 = 0$, has negative real eigenvalues. Hence, E_0 is locally asymptotically stable. If $R_0 = 1$, one eigenvalue of the quadratic equation is 0 and it is simple. Hence, based on Hartman-Grobman Theorem [40], the disease-free equilibrium E_0 is a nonhyperbolic equilibrium. The loss of hyperbolicity of the equilibrium implies that the local behavior of the system cannot be described by the linearized system. And instead center manifold theory has to be used. The bifurcation analysis Theorem 3 below proves that E_0 is the only equilibrium at $R_0 = 1$ and hence E_0 is locally asymptotically stable. If $R_0 > 1$, then E_0 is unstable. $\square$

2.2.2. Global Stability of the Disease-Free Equilibrium. In this section, we use the method used in [36] to investigate the global asymptotic stability of the disease-free equilibrium. To do so, we write system equation (1) as

$$\frac{d\mathbf{X}}{dt} = F(\mathbf{X}, I),$$
$$\frac{d\mathbf{I}}{dt} = G(\mathbf{X}, \mathbf{I}), \quad G(\mathbf{X}, 0) = 0, \tag{10}$$

where $\mathbf{X} \in \mathbf{R}^m$ denotes the number of noninfectious individuals and $\mathbf{I} \in \mathbf{R}^n$ denotes the number of infected individuals. Let $U_0 = (\mathbf{X}^*, 0)$ denote the disease-free equilibrium of this system. Furthermore, suppose that the following assumptions are true:

(H_1) For $d\mathbf{X}/dt = F(\mathbf{X}, 0)$, $\mathbf{X}^*$ is globally asymptotically stable;

(H_2) $G(\mathbf{X}, \mathbf{I}) = A\mathbf{I} - \widehat{G}(\mathbf{X}, \mathbf{I}), \widehat{G}(\mathbf{X}, \mathbf{I}) \ge 0$ for $(\mathbf{X}, \mathbf{I}) \in A$,

where $A = D_\mathbf{I} G(\mathbf{X}^*, 0)$ is an M-matrix.

Theorem 2. *The fixed point $U_0 = (X^*, 0)$ is a globally asymptotic stable equilibrium of model equation (1) provided that $R_0 \le 1$ and that assumptions (H_1) and (H_2) hold.*

Proof. To prove this, we write (1) in the form of (10). That is, $\mathbf{X} = S$, $\mathbf{I} = (I, B)$. Furthermore,

$$F(\mathbf{X}, 0) = \begin{bmatrix} \Lambda - \mu S \\ 0 \end{bmatrix},$$

$$A = \begin{bmatrix} \beta_h - (\mu + \gamma + d) & \frac{\beta_B\Lambda}{K\mu} \\ \epsilon & -\sigma \end{bmatrix} \tag{11}$$

and

$$\widehat{G}(\mathbf{X}, \mathbf{I}) = \begin{bmatrix} \widehat{G_1}(\mathbf{X}, \mathbf{I}) \\ \widehat{G_2}(\mathbf{X}, \mathbf{I}) \end{bmatrix}$$

$$= \begin{bmatrix} \left(1 - \dfrac{S}{N}\right)\beta_h I + \left(\dfrac{\Lambda}{K\mu} - \dfrac{S}{K+B}\right)\beta_B B \\ 0 \end{bmatrix}. \tag{12}$$

Since $(1 - S/N) > 0$ and $(\Lambda/K\mu - S/(K + B)) > 0$, then $\widehat{G}(\mathbf{X}, \mathbf{I}) \geq 0$. It is also clear that $X^* = (\Lambda/\mu, 0)$ is a global stable equilibrium of the system $d\mathbf{X}/dt = F(\mathbf{X}, 0)$. Hence, the above theorem $U_0 = (X^*, 0)$ is globally stable. $\qquad\square$

2.3. Bifurcation Analysis

Theorem 3. *If $R_0 < 1$, the system exhibits a forward bifurcation at $R_0 = 1$.*

Proof. To investigate the type of bifurcation, let

$$\beta_B^* := \frac{\mu K \sigma}{\epsilon \Lambda} \left((\mu + d + \gamma) - \beta_h\right) \tag{13}$$

be a bifurcation parameter. The Jacobin matrix at E_0 with $\beta_B = \beta_B^*$ is

$$J(E_0) = \begin{bmatrix} -\mu & -\beta_h & \alpha & -\dfrac{\beta_B^* \Lambda}{K\mu} \\ 0 & \beta_h - (\mu + d + \gamma) & 0 & \dfrac{\beta_B^* \Lambda}{K\mu} \\ 0 & \gamma & -(\alpha + \mu) & 0 \\ 0 & \epsilon & 0 & -\sigma \end{bmatrix}. \tag{14}$$

The eigenvalues of the characteristics polynomial at $R_0 = 1$ are $\lambda_1 = -\mu$, $\lambda_2 = -(\alpha + \mu)$, $\lambda_3 = \beta_h(\Lambda/\mu) - (\mu + d + \gamma + \sigma)$, and $\lambda_4 = 0$. It can observe that the three eigenvalues are real and negative and one is 0 and simple. Now we denote by $\mathbf{w} = (w_1, w_2, w_3, w_4)^T$ the right eigenvector corresponding to $\lambda_4 = 0$. Direct calculation gives,

$$\mathbf{w} = \left(\frac{-(\alpha(\mu + d) + \mu(\mu + d + \gamma))}{\mu(\alpha + \mu)} w_2, w_2, \frac{\epsilon}{\sigma} w_2, \frac{\gamma}{\mu + \alpha} \right. $$
$$\left. \cdot w_2 \right)^T. \tag{15}$$

Moreover, the left eigenvector $\mathbf{v} = (v_1, v_2, v_3, v_4)^T$ that satisfy $\mathbf{v}.\mathbf{w} = 1$ is given by

$$-\mu v_1 = 0,$$

$$-\beta_h v_1 + (\beta_h - (\mu + d + \gamma)) v_2 + \gamma v_3 + \epsilon v_4 = 0,$$

$$\alpha v_1 - (\mu + \alpha) v_3 = 0, \tag{16}$$

$$-\frac{\sigma}{\epsilon}((\mu + d + \gamma) - \beta_h) v_1 + \frac{\sigma}{\epsilon}((\mu + d + \gamma) - \beta_h) v_2 - \sigma v_4$$

$$= 0.$$

Then, the left eigenvector $\mathbf{v}$ turns out to be

$$\mathbf{v} = \left(0, v_2, 0, \frac{(\mu + d + \gamma) - \beta_h}{\epsilon} v_2 \right)^T. \tag{17}$$

The equation $\mathbf{v}.\mathbf{w} = 1$ results in $v_2 w_2 + v_4 w_4 = 1$. Assume $w_2 = \epsilon(\mu + \alpha)$. Then

$$\mathbf{v} = \left(0, \frac{1}{\epsilon(\mu + \alpha) + (\gamma)(\mu + d + \gamma) - \beta_h)}, 0, \right.$$
$$\left. \frac{(\mu + d + \gamma) - \beta_h}{\epsilon(\epsilon(\mu + \alpha) + (\gamma)(\mu + d + \gamma) - \beta_h))} \right)^T.$$

$$\mathbf{w} = \left(\frac{-(\alpha(\mu + d) + \mu(\mu + d + \gamma))}{\mu} \epsilon, \epsilon(\mu + \alpha), \right.$$
$$\left. \frac{\epsilon^2}{\sigma}(\mu + \alpha), \frac{\gamma}{\epsilon} \right)^T. \tag{18}$$

Based on theoretical results in [40], we have to compute $\mathbf{a}$ and $\mathbf{b}$ where

$$\mathbf{a} = \sum_{k,i,j=1}^{3} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(E_0, \beta_B^*),$$

$$\mathbf{b} = \sum_{k,i=1}^{3} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta}(E_0, \beta_B^*). \tag{19}$$

Set $x_1 = S$, $x_2 = I$, $x_3 = R$, $x_4 = B$. Evaluating the partial derivatives at (E_0, β_B^*), we obtain

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_2}(E_0, \beta_B^*) = \frac{\partial^2 f_2}{\partial x_2 \partial x_1}(E_0, \beta_B^*) = \frac{\beta_h}{S_0},$$

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_4}(E_0, \beta_B^*) = \frac{\partial^2 f_2}{\partial x_4 \partial x_1}(E_0, \beta_B^*) = \frac{-\beta_B^*}{K} \tag{20}$$

$$\frac{\partial^2 f_2}{\partial x_4^2}(E_0, \beta_B^*) = \frac{-2\beta_B^*}{K^2}.$$

Furthermore,

$$\frac{\partial^2 f_2}{\partial x_3 \partial \beta_B^*}(E_0, \beta_B^*) = \frac{\Lambda}{\mu K} \tag{21}$$

and all the other second order partial derivatives are zero. It follows that

$$\mathbf{a} = 2v_2 \left(w_1 w_2 \frac{\partial^2 f_2}{\partial x_1 \partial x_2}(E_0, \beta_B^*) + w_1 w_4 \frac{\partial^2 f_2}{\partial x_1 \partial x_4}(E_0, \beta_B^*) \right.$$
$$\left. + \frac{w_4^2}{2} \frac{\partial^2 f_2}{\partial x_4^2}(E_0, \beta_B^*) \right) \tag{22}$$

and

$$\mathbf{b} = v_2 w_4 \frac{\partial^2 f_2}{\partial x_4 \partial \beta_B^*}(E_0, \beta_B^*). \tag{23}$$

Substituting the eigenvectors and the partial derivatives into $\mathbf{a}$ and $\mathbf{b}$, we get

$$\mathbf{a} = -\frac{2\epsilon(\mu+\alpha)}{\Lambda(\epsilon(\mu+\alpha)+\gamma(\mu+d+\gamma)-\beta_h))}a_0 \tag{24}$$

$$\text{where } a_o = (\alpha(\mu+d)+\mu(\mu+d+\gamma))\beta_h + \left((\alpha(\mu+d)+\mu(\mu+d+\gamma)+\frac{\gamma}{\alpha+\mu}\right)\left(\frac{\sigma}{\epsilon}\right)\left(\frac{\gamma}{\alpha+\mu}\right)(\mu+d+\gamma-\beta_h)$$

and

$$\mathbf{b} = \frac{1}{\epsilon(\mu+\alpha)+\gamma(\mu+d+\gamma-\beta_h)}\frac{\gamma}{\epsilon}\frac{\Lambda}{\mu K}. \tag{25}$$

□

If $R_0 < 1$, then $(\mu+d+\gamma)-\beta_h > 0$, $\mathbf{a} < 0$ and $\mathbf{b} > 0$. This scenario indicates that the system exhibits transcritical bifurcation at $\beta_B = \beta_B^*$. Its biological meaning is that as long as $R_0 < 1$ the dysentery epidemic can be eliminated from the population. If parameters change and result in $R_0 > 1$, a small endemic state may occur.

3. Numerical Methods

3.1. Parameter Estimation. In this manuscript we solve a dynamics parameter estimation problem. It aims to solve for the unknown parameters of a dynamic model supplied as a system of ordinary differential equations. The problem is setup as a standard nonlinear least squares problem; however the nonlinear function to be fitted involves solving ordinary differential equations using a numerical integration scheme. Least squares are a special case of maximum likelihood in which it is assumed that the data are drawn from a normal distribution with mean given by the solution to the ODE. System equation (1) is formulated as a standard dynamic model in the following form:

$$
\begin{aligned}
y' &= f(t, y, \vartheta), \\
y(t_0) &= y_0,
\end{aligned} \tag{26}
$$

where y is the vector of dependent variables and ϑ is the vector of unknown parameters. The error is sum-of-squares error and is represented by

$$\psi(\vartheta) = \sum_{i=1}(y_i - \overline{y_i})^2 \tag{27}$$

in which $\overline{y_i}$ is the real data and $y_i = y(t_i, \vartheta)$ is the solution to (26) at time t_i for a given ϑ. The aim is to minimize the objective function

$$
\begin{aligned}
\min_{\vartheta} \quad & \psi(\vartheta) \\
\text{subject to} \quad & Eq.\ (26)
\end{aligned} \tag{28}
$$

to obtain our parameter estimates. The parameter estimation algorithm based on [25] with some modification is summarized below.

Algorithm

Result: Optimal estimated parameter values ω.

(1) Guess initial parameter values ω_0. Set $\omega = \omega_0$.

(2) Using MATLAB **ode45** routine, solve (26) using ω to find the solution y_i.

(3) Evaluate error using (27).

(4) Minimize (28) using an optimization algorithm **lsqnonlin** along with **Trust-Region-Reflective** to find bounded estimated parameters $\widehat{\omega}$. Update $\omega = \widehat{\omega}$.

(5) Check convergence criteria. If not converged, go to (2).

(6) On convergence, set $\omega = \widehat{\omega}$ to current parameter values.

4. Numerical Simulations and Discussion

In this section, we first present the existence and nonexistence of the endemic equilibria. Secondly, fitting the data of dysentery diarrhea cases in Ethiopia is performed to estimate the parameters. Next, the sensitivity of the R_0 to the system parameters is analyzed. Finally, the uncertainty analysis is presented using the estimated parameters.

4.1. The Disease-Free and Endemic Equilibria. It is proved in Theorem 2 that the disease does not exist in the community so long as the reproduction number is less than unity and the disease is endemic in the community if the reproduction number is greater than unity. It is depicted in Figure 2(a). The disease-free equilibrium is globally stable if $R_0 \leq 1$. However, there exists a possibility of multiple equilibria for $R_0 > 1$ (Figure 2(b)).

4.2. Dysentery Diarrhea Data. Dysentery diarrhea is one of the most dangerous types of diarrhea which is endemic in Ethiopia. It is reported weekly under Integrated Disease Surveillance and Response System (IDSR) in the Ministry of Health. Ethiopian Weekly Epidemiological Bulletin [41] reports National Surveillance Data Summary of diseases in Ethiopia. For instance, dysentery surveillance data of week 10 of 2018 is 5,345. There is an increment of 614 as compared to week 9, 2018. However, the number of cases reported during this week is lower than the same weeks of the previous two years. The data of dysentery diarrhea reported cases in 2017 used in this simulation are presented in (Table 2). Time series graphs of data given in (Table 2) are shown in Figure 3. As shown in Figure 3, the infected cases have maximum amplitude in the sixteenth week.
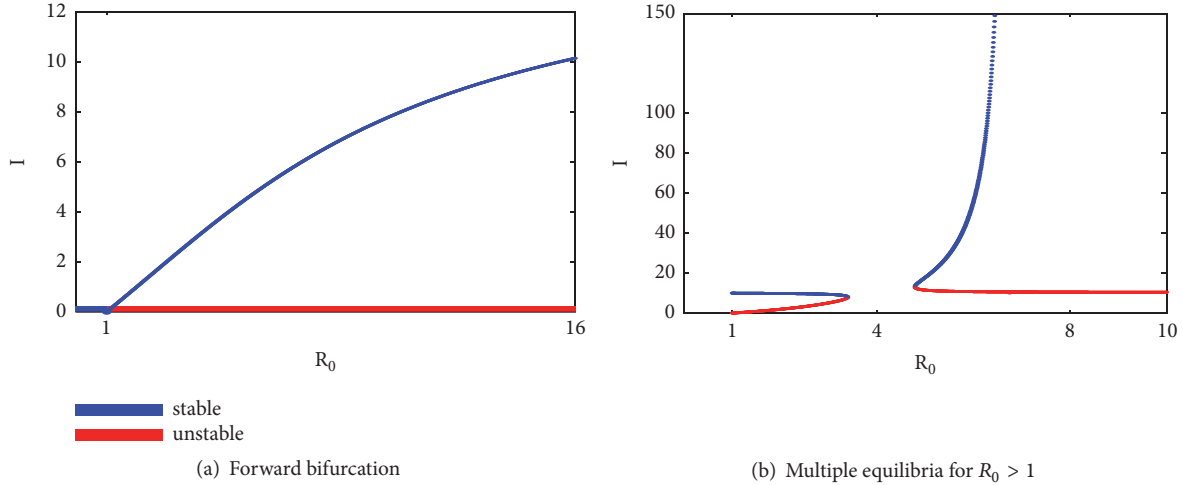
(a) Forward bifurcation

(b) Multiple equilibria for $R_0 > 1$

FIGURE 2: (a) Forward bifurcation graph for $\Lambda = 0.5$, $\beta_B = 0.4$, $K = 1$, $\mu = 0.2$, $\epsilon = 0.05$, $d = 0.1$, $\gamma = 0.1$, $\sigma = 3$, $\alpha = 1$, and β_h varies $\beta_h = 0.001 : 0.01 : 15$. (b) Multiple equilibria for $\Lambda = 2$, $\beta_B = 5$, $K = 1$, $\mu = 0.5$, $\epsilon = 0.05$, $d = 0.8$, $\gamma = 0.1$, $\sigma = 3$, $\alpha = 1$, and β_h varies $\beta_h = 0 : 0.001 : 50$.
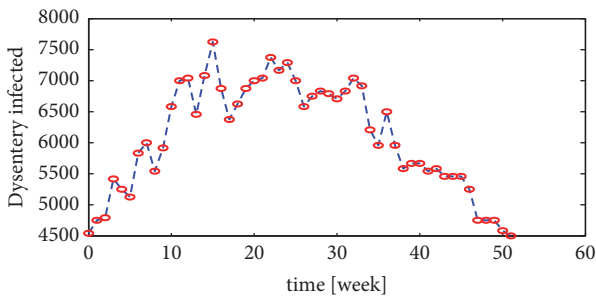

FIGURE 3: Weekly time series of dysentery diarrhea data in Ethiopia 2017.

4.3. Estimation of Parameters.

In this model we have ten parameter values to be estimated. Among these parameters, the value of μ, natural mortality rate is obtained from the local demography of Ethiopia. The parameter γ, the duration of infectiousness, is also found from dysentery diarrhea characteristics [37]. The initial infectious individuals are taken as the number of infected ones in the first week of 2017. Furthermore, the shigella concentration that yields $25 - 50\%$ chance of catching dysentery diarrhea is 200 [37]. Thus, the initial parameter values for estimation is $\omega_0 = (\Lambda, \beta_h, \beta_B, K, \mu, \gamma, d, \alpha, \epsilon, \sigma) = (2500, 0.0158, 0.052, 200, 0.000457, 0.1106, 0.0103, 0.018, 0.01, 0.3319)$ and the initial population is $(S_0, I_0, R_0, B_0) = (416253, 4542, 200, 2000)$. Using the algorithm in Section 3.1 the estimated parameter values are given in Table 3.

The reproduction number based on the Ethiopian data is therefore $R_0 = R_2 + R_1 = 1.0476 + 0.0732 = 1.1208$. R_2 is the reproduction number due to the human to human interaction and R_1 is the reproduction number due to the environment to human interaction.

4.4. Sensitivity Analysis.

The sensitivity analysis reveals how imperative every parameter is to illness transmission. It is regularly used to decide the robustness of model expectations to parameter values since there are errors in data collection and assumed parameter values [42]. The perturbation of fixed point estimation of model parameters and the uncertainty in the model parameter estimation are the two most commonly used techniques for sensitivity analysis. The sensitivity of a variable with respect to system parameters is usually measured by sensitivity index. Sensitivity indices enable us to quantify the relative change in a variable when a parameter changes. The normalized forward sensitivity index of a variable regarding a parameter is the proportion of the relative change in the variable to the relative change in the parameter. When the variable is a differentiable function of the parameter, the sensitivity index might be on the other hand defined utilizing partial derivatives.

Definition 4 (see [42, 43]). The normalized forward sensitivity index of R_0 that depends differentiably on a parameter ρ is defined by

$$\varphi_\rho^{R_0} = \frac{\partial R_0}{\partial \rho} \frac{\rho}{|R_0|}. \tag{29}$$

For instance, $\varphi_\rho^{R_0} = 1$ implies an increase (decrease) of ρ by $y\%$ increases (decreases) R_0 by the same percentage. On the other hand, $\varphi_\rho^{R_0} = -1$ indicates an increase (decrease) of ρ by $y\%$ decreases (increases) R_0 by $y\%$. In this case, ρ is called a highly sensitive parameter.

Proposition 5. *Given*

$$R_0 = \frac{\beta_h}{(\mu + \gamma + d)} + \frac{\Lambda \beta_B \epsilon}{\mu (\mu + \gamma + d) K \sigma}. \tag{30}$$

TABLE 2: Weekly dysentery diarrhea reports in Ethiopia, 2017.

Weeks	Infected	Weeks	Infected	Weeks	Infected	Weeks	Infected	Weeks	Infected
1	4542	12	7000	23	7375	33	7042	43	5583
2	4750	13	7042	24	7167	34	6917	44	5458
3	4792	14	6458	25	7292	35	6208	45	5458
4	5417	15	7083	26	7000	36	5958	46	5458
5	5250	16	7625	27	6583	37	6500	47	5250
6	5125	17	6875	28	6750	38	5958	48	4750
7	5833	18	6375	29	6833	39	5583	49	4750
8	6000	19	6625	30	6792	40	5667	50	4750
9	5542	20	6875	31	6708	41	5667	51	4583
10	5917	21	7000	32	6833	42	5542	52	4500
11	6583	22	7042							

TABLE 3: Estimated parameter values.

Parameter	Value	Bounds	Source
Λ	462	$[0, 84388.8700]$	Estimated
β_h	0.69864	$[0.2175, 1.1798]$	Estimated
β_B	0.04465	$[0, 2.4170]$	Estimated
K	200		[36]
μ	0.000457		[36]
γ	0.1106		[37]
d	0.55602	$[0.0581, 1.0540]$	Estimated
α	0.0211	$[0, 1.0588]$	Estimated
ϵ	0.01		Assumed
σ	46.2086	$[0, 2520.3600]$	Estimated
S_0	216253	$[91252, 341254]$	Estimated
I_0	3152	$[0, 58153]$	Estimated
R_0	165	$[0, 25288]$	Estimated
B_0	1356	$[0, 4520]$	Estimated

Let

$$R_2 = \frac{\beta_h}{(\mu + \gamma + d)}$$

$$\text{and } R_1 = \frac{\Lambda \beta_B \epsilon}{\mu (\mu + \gamma + d) K \sigma}.$$

(31)

The normalized forward sensitivity index of R_0 with respect to the given parameters is given by

$$\varphi_{\beta_h}^{R_0} = \frac{R_2}{R_0},$$

$$\varphi_d^{R_0} = -\frac{d}{\mu + d + \gamma},$$

$$\varphi_\gamma^{R_0} = -\frac{\gamma}{\mu + d + \gamma},$$

$$\varphi_\mu^{R_0} = -\left(\frac{\mu^2}{\mu + d + \gamma} + \frac{R_1}{R_0} \right),$$

$$\varphi_{\beta_B}^{R_0} = \varphi_\epsilon^{R_0} = \varphi_\Lambda^{R_0} = \frac{R_1}{R_0},$$

$$\varphi_K^{R_0} = \varphi_\sigma^{R_0} = -\frac{R_1}{R_0}.$$

(32)

Proof. This follows immediately from Definition 4. □

The sensitivity indices of $\varphi_\Lambda^{R_0}$, $\varphi_{\beta_h}^{R_0}$, $\varphi_{\beta_B}^{R_0}$, $\varphi_\epsilon^{R_0}$ are positive and the remaining are negative. Since all indices are the functions of other parameters the sensitivity indices will change with the change in other parameter values. The parameter values in Table 3 are used to calculate the sensitivity indices. The normalized sensitivity of the basic reproduction number with respect to the estimated parameters is given in Table 4. For example, $\varphi_{\beta_h}^{R_0}$ = 0.9901115761; the physical meaning is that increasing (or decreasing) β_h by 10% increases (or decreases) R_0 by 9.9%. A highly sensitive parameter should be carefully estimated, because a small variation in that parameter will lead to large quantitative changes. As can be seen from Table 4, the basic reproduction number is most sensitive to the effective transmission rate of dysentery
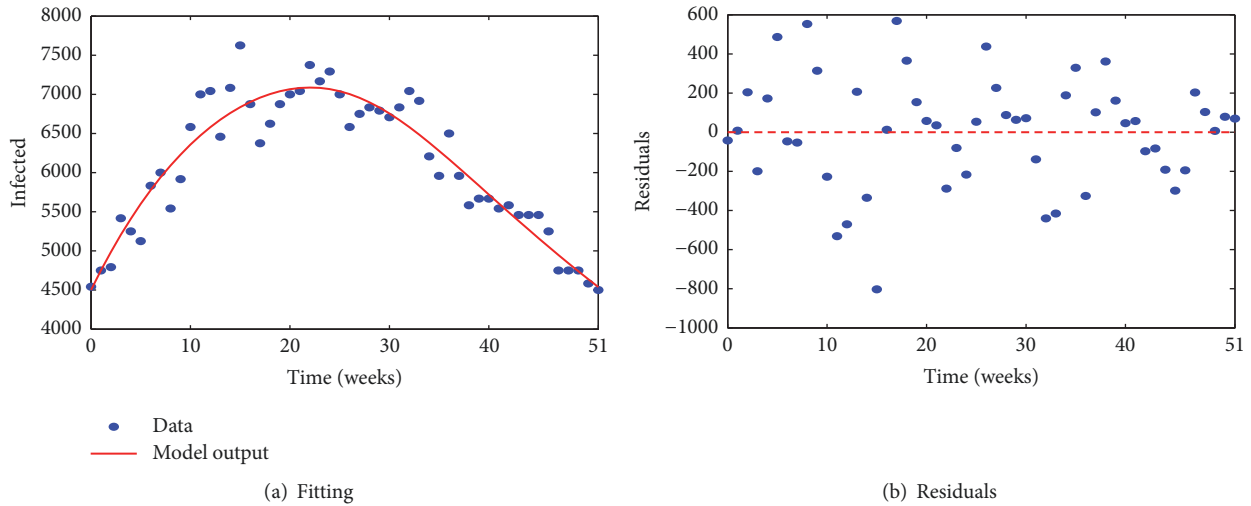
(a) Fitting

(b) Residuals

FIGURE 4: Fitting of the model equation (1) to the reported data in Table 2 and residual analysis using the estimated parameters.

TABLE 4: Estimated parameters.

Parameter	Sensitivity indices of R_0
Λ	$\varphi_\Lambda^{R_0} = 0.009888424079$
β_h	$\varphi_{\beta_h}^{R_0} = 0.9901115761$
β_B	$\varphi_{\beta_B}^{R_0} = 0.009888424076$
K	$\varphi_K^{R_0} = -0.009888424073$
μ	$\varphi_\mu^{R_0} = -0.01466434116$
γ	$\varphi_\gamma^{R_0} = -0.1651192337$
d	$\varphi_d^{R_0} = -0.8301048495$
ϵ	$\varphi_\epsilon^{R_0} = 0.009888424080$
σ	$\varphi_\sigma^{R_0} = -0.009888424073$

diarrhea (β_h). The implication of this is that an increase in the transmission rate increases the spread of the disease in the community.

4.5. Model Validation. Once a model is developed, we use real data to validate it. There are many statistical techniques applied for model validation. The two most frequently used methods are graphical and numerical techniques. Graphical methods demonstrate a comprehensive range of complex features of the relationship between the model and the real data. A numerical technique for model validation, on the other hand, tends to be narrowly targeted on a specific side of the connection between the model and the observed data.

4.5.1. Graphical Method. The residuals from a fitted model are the differences between the real data and the solution to the model. If the model fits the real data appropriately, the residuals approximate the random errors that make the association with the real data and the solution to the system [44]. As a result, if the residuals seem to behave randomly, it is sound to say that the model fits the real data. On the contrary, if nonrandom arrangement is visible in the residuals, the model fails to depict the true representation of

the real data. Keeping in mind the goal to check the validity of the model to the given information, Figure 4(a) has been drawn. Figure 4(a) demonstrates the results of fitting the SIRSB model in (1) to the dysentery data in Table 2. For this figure, the continuous line represents the model output and the points represent the real data points. There are a few data points that fit poorly with the model outcome. However, overall the model solution and data agree well.

Residuals plots for the model and the real data in Table 2 are given in Figure 4(b). As given in Figure 4(b), the residuals seem to be random and the standard errors are generally small for the model. In this manner the estimates acquired here are reasonable.

The residual analysis is determined by computing autocorrelations for the residuals at varying time Lags. Residual analysis includes two tests: the whiteness test and the independence test. The whiteness test is about autocorrelation function of the residuals for each output. Based on this test, the residual autocorrelation function of a good model is inside the confidence interval of the corresponding estimates, showing that the residuals are uncorrelated. On the other hand, the independence test checks the cross-correlation between the input and the residuals for each input output pair. The independence test makes evident that a good model has the residuals uncorrelated with past inputs. In this case, correlation shows that the model does not describe how part of the output relates to the corresponding input.

The autocorrelation function plot for the residuals shows that most of the residuals are not statistically significant (Figure 5) which directly follows that the residuals are not highly correlated. Except for one major downturn, the residuals between week one and the last week do not show any particular form. They fluctuate randomly around zero. The independence of the residuals obtained suggests that the parameter estimates obtained are reliable. It is easy to see from the plot that almost all of the autocorrelations except the fifth Lag fall within the 99% confidence limits. One Lag outside the 99% confidence limits does not necessarily show
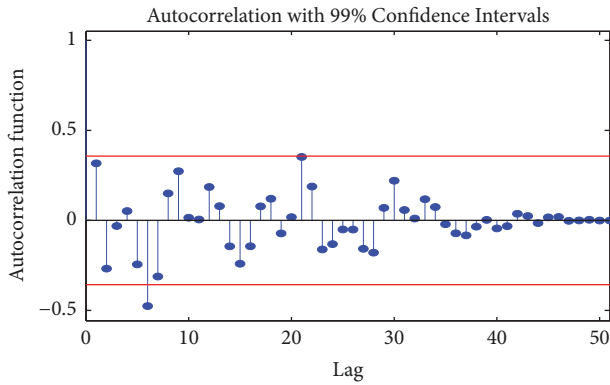
FIGURE 5: Correlation of residuals for the infected individuals $\Lambda = 462$, $\mu = 0.003199$, $\beta_h = 0.69864$, $\beta_B = 0.04465$, $K = 200$, $\alpha = 0.0211$, $\epsilon = 0.01$, $\gamma = 0.1106$, $\sigma = 46.2086$, and $K = 0.1$.

nonrandomness. Furthermore, adjacent observations do not correlate.

4.5.2. Uncertainties Analysis. In the process of parameter estimation, it is reasonable to assume that the parameters are dependent. Particularly, the parameters could be thought to vary together or covary. Covariance is the measure of how the parameter y_i is associated with y_j. In the analysis of model parameters a covariance matrix approximates the uncertainties in the model parameters and the possible disorders in the outputs. The diagonal elements of the matrix contain the variances of the parameters and the off-diagonal elements contain the covariances between all potential pairs of parameter. This matrix Σ is positive semidefinite and symmetric. The interrelations between the estimated elements in this are based on the signs. If the covariance between any two estimated parameters is positive, then the parameters values tend to vary in a positive way. If the covariance between any two estimated parameters is 0, then the two parameters are unrelated. On the other hand, if the covariance between any two parameters is negative, then the parameters values tend to move in opposite directions. The covariance matrix Σ for the model is represented below.

$$
\Sigma = \begin{bmatrix}
 & \beta_h & \beta_B & d & \Lambda & \alpha & \sigma \\
\beta_h & 0.23 & 0.16 & 0.24 & 34654 & -0.42 & 160 \\
\beta_B & 0.16 & 5.63 & 0.15 & 52.17 & 0.022 & 5869.23 \\
d & 0.24 & 0.15 & 0.25 & 36864.41 & -0.45 & 153.64 \\
\Lambda & 34654 & 521.65 & 36864.40 & 7043651412.80 & -87035.24 & -762050.23 \\
\alpha & -0.42 & 0.022094 & -0.45 & -87035.24 & 1.08 & 39.46 \\
\sigma & 160 & 5869.23 & 153.64 & -762050.22 & 39.46 & 6121430.51
\end{bmatrix}. \tag{33}
$$

The variance in descending order are recruitment rate of susceptible population, Λ (7043651412.8), the net death rate of shigella pathogen, σ (6121430.51), effective transmission rates of dysentery diarrhea due to the environment to human interaction, β_B (5.63), relapse rate of the recovered ones to susceptible, α (1.08), disease induced death rate of dysentery diarrhea, d (0.23), and effective transmission rates of diarrhea due to the human to human interaction, β_h (0.23).

The covariance between transmission coefficient (β_h) and transmission coefficient (β_B), recruitment rate of susceptible population (Λ), disease induced death rate of dysentery diarrhea (d), and net death rate of shigella pathogen (σ) is positive. The covariance between transmission coefficient, β_B and recruitment rate of susceptible population (Λ), disease induced death rate of dysentery diarrhea (d), net death rate of shigella pathogen (σ), and relapse rate of the recovered ones to susceptible (α) is positive. The covariance between recruitment rate of susceptible population (Λ) and disease induced death rate of dysentery diarrhea (d) is positive. The possible implication of this is that if one parameter is increased, the other parameter must also be increased to achieve a similar fit to the data. On the other hand, the covariance between the relapse rate of the recovered ones to susceptible class (α) and transmission coefficient (β_h),

disease induced death rate of dysentery diarrhea (d), and recruitment rate of susceptible population (Λ) is negative. The covariance between transmission coefficient (β_h) and the relapse rate of the recovered ones to susceptible class (α) is negative. The covariance between recruitment rate of susceptible population (Λ) and the relapse rate of the recovered ones to susceptible class (α) and net death rate of shigella pathogen (σ) is negative. The physical implication of this is that if one parameter is increased, the other parameter must be decreased to achieve a similar fit to the data. Table 5 shows the summary of covariance of the model parameters.

5. Discussion and Conclusions

In this paper, we have proposed a deterministic compartmental dysentery diarrhea model. We have proved the global stability of the disease-free equilibrium. It is established in Theorem 2 that the basic reproduction number R_0 is a sharp threshold parameter and it completely determines the global stability of the disease-free equilibrium for $R_0 < 1$. The possible implication of this is that to eliminate the disease from the community, policymakers have to work on reducing the reproduction number to below unity.

TABLE 5: Covariance of the parameters.

Covariance	Direction	Covariance	Direction	Covariance	Direction
C_{β_h,β_B}	+ve	$C_{\beta_B,d}$	+ve	$C_{\alpha,d}$	-ve
$C_{\beta_h,d}$	+ve	$C_{\beta_B,\Lambda}$	+ve	$C_{\alpha,\Lambda}$	-ve
$C_{\beta_h,\Lambda}$	+ve	$C_{\beta_B,\alpha}$	+ve	$C_{\alpha,\sigma}$	+ve
$C_{\beta_h,\alpha}$	-ve	$C_{\beta_B,\sigma}$	+ve	$C_{\beta_h,\sigma}$	+ve
$C_{\sigma,d}$	+ve	$C_{\sigma,\Lambda}$	-ve		

The authors [17] have reported that the contribution of each transmission pathway in a disease outbreak is separable to focus on the control efforts of the infectious humans or the contaminated environment. Accordingly, R_0 could be written as

$$R_0 = \frac{\beta_h}{(\mu + d + \gamma)} + \frac{\Lambda \beta_B \epsilon}{\mu (\mu + d + \gamma) K \sigma_2 (1 - \sigma_1/\sigma_2)}. \quad (34)$$

Using Taylor's series expansion, we have

$$\left(1 - \frac{\sigma_1}{\sigma_2}\right)^{-1}$$
$$= \left(1 + \frac{\sigma_1}{\sigma_2} + \left(\frac{\sigma_1}{\sigma_2}\right)^2 + \text{higher order terms}\right). \quad (35)$$

Thus,

$$R_0 = R_{01} + R_{02} + R_{03} + \text{higher order terms.} \quad (36)$$

where $R_{01} = \beta_h/(\mu + d + \gamma)$, $R_{02} = (\epsilon\Lambda/\mu)(1/(\mu + d + \gamma))(\beta_B/K)(1/\sigma_2)$, and $R_{03} = (\epsilon\Lambda/\mu)(1/(\mu + d + \gamma))(\beta_B/K)(1/\sigma_2)(\sigma_1/\sigma_2)$.

R_{01} can be expressed as a primary case in the human population makes an infectious contact with humans at a rate of β_h over the mean infectious period of $1/(\mu + d + \gamma)$. R_{02} can be interpreted as a primary case in the human population makes an infectious contact with the environment at a rate of $\epsilon\Lambda/\mu$ over the mean infectious period of $1/(\mu + d + \gamma)$ and a primary case in the environment makes an infectious contact with humans at a rate of β_B/K over the mean infectious period of $1/\sigma_2$. R_{03} is interpreted as a primary case in the human population makes an infectious contact with the environment at a rate of $\epsilon\Lambda/\mu$ over the mean infectious period of $1/(\mu + d + \gamma)$ and a primary case in the environment makes an infectious contact with humans at a rate of β_B/K over the mean infectious period of $1/\sigma_2$, a fraction σ_1/σ_2 of which survive and become infectious.

Therefore, $R_0 = R_{01} + R_{02} + R_{03}$ represents the total contribution to the infectious class and the pathogen population class made by the hosts and pathogens of original case. The higher order terms represent the contribution through direct human to human and environment to human in the higher generation.

As an application, we have used our system to simulate the reported dysentery diarrhea cases in Ethiopia in 2017 (Table 2) and obtained reasonable matches. To solve the optimization problem, the Runge-Kutta method (**ode45**) has been used as a solver of a system of nonlinear differential equations along with **Trust-Region-Reflective** (to find optimum bounded parameter values) and **lsqnonlin** methods for the sum of squared residuals. The results indicate that simulations of our system can provide a match to the infectious cases in 2017. More importantly, we estimate that the basic reproduction number for dysentery transmission in Ethiopia is $R_0 = 1.1208$. The implication of this is that dysentery diarrhea is endemic in country. The estimated reproduction number is near to one. If control and treatment measures are implemented, with this value of R_0, the disease will be eliminated in short time.

The values of parameters describing the system have been estimated by fitting the integrals of the system to the field data on dysentery diarrhea epidemic. Estimation of parameters, in this case, is a challenging task because of missing a large part of the infectious process. One difficulty is that depending on the initially specified parameter values a local minimum may occur and the minimal value of the sum of squared residuals may be different. In such case, the parameter estimation should be repeated with different initial parameter guesses to achieve a better estimate of the global minimum (rather than local) of the sum of squared residuals.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] United Nations International Children's Emergency Fund, *Diarrhea: Why Children Are Still Dying and What Can Be Done*, 2009.

[2] M. Farthing, M. A. Salam, G. Lindberg et al., "Acute diarrhea in adults and children: a global perspective," *Journal of Clinical Gastroenterology*, vol. 47, no. 1, pp. 12–20, 2013.

[3] C. A. Bopp, A. A. Ries, and J. G. Wells, *Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera*, 1999.

[4] A. Hugo, O. D. Makinde, S. Kumar, and F. F. Chibwana, "Optimal control and cost effectiveness analysis for Newcastle disease eco-epidemiological model in Tanzania," *Journal of Biological Dynamics*, vol. 11, no. 1, pp. 190–209, 2017.

[5] S. Olaniyi, "Dynamics of Zika virus model with nonlinear incidence and optimal control strategies," *Applied Mathematics & Information Sciences*, vol. 12, no. 5, pp. 969–982, 2018.

[6] R. M. Anderson and R. M. May, "Age-related changes in the rate of disease transmission: Implications for the design of vaccination programmes," *Epidemiology & Infection*, vol. 94, no. 3, pp. 365–436, 1985.

[7] M. G. Roberts and M. I. Tobias, "Predicting and preventing measles epidemics in New Zealand: Application of a mathematical model," *Epidemiology and Infection*, vol. 124, no. 2, pp. 279–287, 2000.

[8] L. Li, C.-H. Wang, S.-F. Wang et al., "Hemorrhagic fever with renal syndrome in China: mechanisms on two distinct annual peaks and control measures," *International Journal of Biomathematics*, vol. 11, no. 2, Article ID 1850030, 2018.

[9] R. M. Anderson and R. M. May, *Infectious Diseases of Humans: Dynamics and Contro*, Oxford University Press, 1992.

[10] M. Choisy, J. F. Gugan, and P. Rohani, *Mathematical Modeling of Infectious Diseases Dynamics*, Institute of Ecology, University of Georgia, Athens, GA, USA, 2007.

[11] F. Brauer and C. Castillo-Chavez, *Mathematical Models in Population Biology and Epidemiology*, Texts in Applied Mathematics, Springer, 1st edition, 2012.

[12] G. Lu and Z. Lu, "Geometric approach to global asymptotic stability for the SEIRS models in epidemiology," *Nonlinear Analysis: Real World Applications*, vol. 36, pp. 20–43, 2017.

[13] M. C. Eisenberg, S. L. Robertson, and J. H. Tien, "Identifiability and estimation of multiple transmission pathways in cholera and waterborne disease," *Journal of Theoretical Biology*, vol. 324, pp. 84–102, 2013.

[14] S. Liao and W. Yang, "On the dynamics of a vaccination model with multiple transmission ways," *International Journal of Applied Mathematics and Computer Science*, vol. 23, no. 4, pp. 761–772, 2013.

[15] J. H. Tien and D. J. Earn, "Multiple transmission pathways and disease dynamics in a waterborne pathogen model," *Bulletin of Mathematical Biology*, vol. 72, no. 6, pp. 1506–1533, 2010.

[16] G.-Q. Sun and Z.-K. Zhang, "Global stability for a sheep brucellosis model with immigration," *Applied Mathematics and Computation*, vol. 246, pp. 336–345, 2014.

[17] M. Bani-Yaghoub, R. Gautam, Z. Shuai, P. van den Driessche, and R. Ivanek, "Reproduction numbers for infections with free-living pathogens growing in the environment," *Journal of Biological Dynamics*, vol. 6, no. 2, pp. 923–940, 2012.

[18] A. K. Misra, A. Gupta, and E. Venturino, "Cholera dynamics with bacteriophage infection: a mathematical study," *Chaos, Solitons & Fractals*, vol. 91, pp. 610–621, 2016.

[19] L. Li, "Monthly periodic outbreak of hemorrhagic fever with renal syndrome in China," *Journal of Biological Systems*, vol. 24, no. 4, pp. 519–533, 2016.

[20] W. A. Woldegerima, M. I. Teboh-Ewungkem, and G. A. Ngwa, "The impact of recruitment on the dynamics of an immune-suppressed within-human–host model of the plasmodium falciparum parasite," *Bulletin of Mathematical Biology*, pp. 1–56, 2018.

[21] F. K. Mbabazi, J. Mugisha, and M. Kimathi, "Modeling the within-host co-infection of influenza A virus and pneumococcus," *Applied Mathematics and Computation*, vol. 339, pp. 488–506, 2018.

[22] K. Schittkowski, *Numerical Data Fitting in Dynamical Systems*, vol. 77 of *Applied Optimization*, Kluwer Academic Publishers, 2002.

[23] R. M. Kristensen, *Parameter Estimation in Nonlinear Dynamical System [MSc thesis]*, Department of Chemical Engineering, Technical University of Denmark, 2004.

[24] M. U. Lei, *Parameter estimation methods for biological systems, [MSc thesis]*, Department of Chemical Engineering, University of Saskatchewan, Saskatoon, Canada, 2010.

[25] M. Samsuzzoha, M. Singh, and D. Lucy, "Parameter estimation of influenza epidemic model," *Applied Mathematics and Computation*, vol. 220, pp. 616–629, 2013.

[26] M. A. Capistran, M. A. Moreles, and B. Lara, "Parameter estimation of some epidemic models. The case of recurrent epidemics caused by respiratory syncytial virus," *Bulletin of Mathematical Biology*, vol. 71, no. 8, pp. 1890–1901, 2009.

[27] L. T. Biegler and I. E. Grossmann, "Retrospective on optimization," *Computers & Chemical Engineering*, vol. 28, no. 8, pp. 1169–1192, 2004.

[28] Z. Li, "Parameter estimation of ordinary differential equations," *IMA Journal of Numerical Analysis (IMAJNA)*, vol. 25, no. 2, pp. 264–285, 2005.

[29] A. Capaldi, S. Behrend, B. Berman, J. Smith, J. Wright, and A. L. Lloyd, "Parameter estimation and uncertainty quantification for an epidemic model," *Mathematical Biosciences and Engineering*, vol. 9, no. 3, pp. 553–576, 2012.

[30] J. A. Yorke and W. P. London, "Recurrent outbreaks of measles, chickenpox and mumps," *American Journal of Epidemiology*, vol. 98, no. 6, pp. 469–482, 1973.

[31] M. Kalivianakis, S. L. J. Mous, and J. Grasman, "Reconstruction of the seasonally varying contact rate for measles," *Mathematical Biosciences*, vol. 124, no. 2, pp. 225–234, 1994.

[32] I. M. Longini, J. S. Koopman, A. S. Monto, and J. P. Fox, "Estimating household and community transmission parameters for influenza," *American Journal of Epidemiology*, vol. 115, no. 5, pp. 736–751, 1982.

[33] M. D. Samsuzzoha, M. Singh, and D. Lucy, "Uncertainty and sensitivity analysis of the basic reproduction number of a vaccinated epidemic model of influenza," *Applied Mathematical Modelling*, vol. 37, no. 3, pp. 903–915, 2013.

[34] O. B. Ojo, S. Lougue, and W. A. Woldegerima, "Bayesian generalized linear mixed modeling of Tuberculosis using informative priors," *PLoS ONE*, vol. 12, no. 3, Article ID e0172580, 2017.

[35] H. W. Berhe, O. D. Makinde, and D. M. Theuri, "Optimal control and cost-effectiveness analysis for dysentery epidemic model," *Applied Mathematics and Information Sciences*, vol. 12, pp. 1183–1195, 2018.

[36] H. W. Berhe, O. D. Makinde, and D. M. Theuri, "Co-dynamics of measles and dysentery diarrhea diseases with optimal control and cost-effectiveness analysis," *Applied Mathematics and Computation*, vol. 347, pp. 903–921, 2019.

[37] J. P. S. Cabral, "Water microbiology. Bacterial pathogens and water," *International Journal of Environmental Research and Public Health*, vol. 7, no. 10, pp. 3657–3703, 2010.

[38] Z. T. Melese, S. M. Mwalili, and G. O. Orwa, "Threshold dynamics of the transmission of antibiotic-resistant infections," *Biosystems*, vol. 171, pp. 80–92, 2018.

[39] P. van den Driessche and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Mathematical Biosciences*, vol. 180, no. 1-2, pp. 29–48, 2002.

[40] C. Castillo-Chavez and B. Song, "Dynamical models of tuberculosis and their applications," *Mathematical Biosciences and Engineering*, vol. 1, no. 2, pp. 361–404, 2004.

[41] Z. Assefa and M. Bancha, "Ethiopian public health institute center for public health emergency management," *Ethiopian Weekly Epidemiological Bulletin*, vol. 4, no. 10, pp. 6-7, 2018.

[42] N. Chitnis, J. M. Hyman, and J. M. Cushing, "Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model," *Bulletin of Mathematical Biology*, vol. 70, no. 5, pp. 1272–1296, 2008.

[43] C. J. Silva and D. F. M. Torres, "Optimal control for a tuberculosis model with reinfection and post-exposure interventions," *Mathematical Biosciences*, vol. 244, no. 2, pp. 154–164, 2013.

[44] W. Guthrie, *NIST/SEMATECH e-Handbook of Statistical Methods*, National Institute of Standards and Technology, 2000.