MATHEMATICAL MODEL ANALYSIS ON THE TRANSMISSION DYNAMICS OF CHOLERA

MSc. Thesis

By

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Hawassa, Ethiopia
October , 2024

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Declaration

I hereby declare that "A mathematical model on the transmission dynamics of cholera " is my own work, that it has not been done for any degree in any other universities, and that all the sources I have used have been indicated and acknowledged by complete references.

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ADVISORS' APPROVAL SHEET
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HAWASSA UNIVERSITY

This is to officially state that the study entitled "A mathematical model on the transmission dynamics of cholera" is an original work carried out by Alemayehu Animaw Nigussie, ID No mathk/052/09. under my guidance and supervision. This is a genuine work that has been done by Alemayehu Animaw Nigussie for the partial fulfillment of the award of the Degree of Master of Science in Mathematical and Statistical Modeling from Hawassa University. Daily acknowledgments are done during his course of investigation. Therefore, I recommend that it would be accepted as fulfilling the thesis requirements.

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We, the undersigned, members of the Board of Examiners of the final open defense by Alemayehu Animaw have read and evaluated his thesis entitled "Amathematical model on the transmission dynamics of cholera" and examined the candidate. This is therefore to certify that the thesis has been accepted in partial fulfillment of the requirement of the Degree of Master of Science in Mathematical and Statistical Modeling.

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Final approval and acceptance of the thesis is contingent upon the submission of the final copy of the thesis to the school of graduate studies (SGS) through the department /school graduate committee (DGC/SGS) of the candidate's department .

Stamp of SGS date

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Abstract

This research focuses on the development and analysis of a mathematical model to understand the transmission dynamics of cholera, a waterborne disease caused by Vibrio cholera. The model divides the population into five compartments: Susceptible (S), Symptomatic Infected (Is), Asymptomatic Infected (Ia), Recovered (R), and Contaminated Environment (B), considering both human-to-human and environment-to-human transmission routes. The threshold parameter $R_0 = \frac{k\delta\beta_1\lambda\psi+\epsilon_1\lambda e\lambda\psi}{\mu k\delta(\mu+\tau_1)} + \frac{k\delta\beta_2\lambda\phi+\epsilon_2\lambda e\lambda\phi}{\mu k\delta(\mu+\tau_2)}$ is calculated to assess whether cholera will spread in the population. It is found that if R_0 is less than 1, the disease-free equilibrium point is stable, suggesting that cholera can be eradicated under these conditions. Stability analysis of both disease-free and endemic equilibrium points shows that cholera can be controlled when certain conditions, such as reduced infection rates and environmental contamination, are met. Simulations using MATLAB's ODE45 solver confirm the theoretical results, demonstrating that controlling R_0 can effectively manage the disease dynamics. The study identifies key parameters influencing R_0, including the transmission rates and the impact of therapeutic treatments, providing valuable insights for intervention strategies. The model is based on a system of nonlinear ordinary differential equations that describe the dynamics of the disease in the population. It incorporates therapeutic treatment rates, environmental bacterial concentration, and different infection categories to represent a more realistic cholera transmission scenario. The research concludes that cholera transmission can be reduced by controlling the following conditions: Lowering the contact rates between susceptible individuals and infected individuals (both symptomatic and asymptomatic) significantly impacts R_0. Controlling environmental contamination from infected individuals is crucial in minimizing disease spread. Effective therapeutic treatments for symptomatic cases can reduce the spread and severity of the disease. This study provides a comprehensive framework for understanding the dynamics of cholera and offers actionable insights for public health strategies aimed at controlling and preventing outbreaks.

Key Words: Cholera, Bacteria Growth, Reproduction Number, Stability, Modeling, Sensitivity Analysis, Numerical Simulation.

Chapter 1
INTRODUCTION

Cholera, a severe diarrheal disease caused by the bacterium Vibrio cholerae, continues to pose a significant global health challenge, particularly in regions with poor access to clean water and sanitation. The World Health Organization (WHO) estimates that cholera affects 1.3 to 4 million people annually, resulting in 21,000 to 143,000 deaths worldwide. Cholera outbreaks are most common in areas where safe water, sanitation, and hygiene services are inadequate, especially in developing countries during humanitarian crises [23].

1.1 Background of the study

Cholera is an example of a bacterial disease whose primary mode of infection is indirect ; which is caused when individuals ingest fecal-contaminated water containing the bacteria V. cholera [42].Transmission between humans and reservoirs of pathogens implies that disease transmission includes an indirect route other than human-to-human contact. The last few years have witnessed many cholera outbreaks in developing countries, including India (2007), Congo (2008), Iraq (2008), Zimbabwe (2008–2009), Vietnam (2009), Nigeria (2010), and Haiti (2010). In the year of 2010 alone, it is estimated that cholera affects 3–5 million people and causes 100,000–130,000 deaths in the world annually [31]. In essence, Cholera is an infection of the small intestine caused by the gram-negative bacterium, Vibrio cholera .

Untreated individuals suffer severely from diarrhea and vomiting. The disease can cause a rapid dehydration and electrolyte imbalance, and can lead to death. Meanwhile, different transmission pathways are possible. For example, a cholera outbreak in a Singapore psychiatric hospital indicated that the direct human-to-human transmission was a driving force [16]. The dynamics of cholera involve multiple interactions between the human host, the pathogen, and the environment [31] , which contribute to both direct human-to-human and indirect environment-to-human transmission pathways. Due to its huge impact on public health, and social and economic development, cholera has been the subject of extensive studies in clinical, experimental and theoretical fields. It remains an important global cause of morbidity and mortality, capable of causing periodic epidemic disease [32].Typical at-risk areas include peri-urban slums, where basic infrastructure is not available, as well as camps for internally displaced people or refugees, where minimum requirements of clean water and sanitation are not met. Outcomes behind the disruption

of water and sanitation systems or the displacement of populations to inadequate and overcrowded camps can increase the risk of cholera transmission.

Cholera remains a global threat to public health and a key indicator of lack of social development. Recently, the reemergence of cholera has been noted in parallel with the ever increasing size of vulnerable populations living in unsanitary conditions [33] . Education, which is a key tool in disease control, is often overlooked [13]. It requires investment in people rather than in biomedical interventions, but it has the potential to lead to enormous benefits for relatively low cost. Conversely, a lack of information can have a severe impact on worsening the spread of the disease. Cholera-specific education includes advising people with symptoms to seek medical care promptly, and improving sanitation and hygienic practices [11]. Failures to provide health education can be traced to barriers at one of six sites: to be effective, messages have to(1) reach the intended audience, (2) gain attention, (3) be correctly understood, (4) be accepted, (5) result in changed behavior and (6) result in improvement in health [17]. During the 1994 cholera epidemic of Guinea-Bissau, health education demonstrated that local preventive rituals, radio and word-of-mouth communication were effective educational tools [11]. The firsit scintist to suggest disinfecting water with chlorine were Louis- Bernard Guyton de Morveau (in France) and William Cumberland Cruikshank (in England), both around the year 1800, as it was found that water that has been treated with chlorine is effective in preventing the spread of Water- borne diseases [35]. However, disinfection by chlorination can be problematic in some circumstances. Chlorine can react with naturally occurring organic compounds found in the water supply to produce disinfection by products (DBPs) such as trihalomethanes and haloacetic acids. Due to the potential carcinogenicity of these compounds, drinking water regulations across the developed world require regular monitoring of the concentration of these compounds in the distribution systems of municipal water systems.

The World Health Organization (WHO) has stated that risks to health from DBPs are extremely small in comparison with inadequate disinfection. Understanding the fundamental mechanism in the disease transmission is crucial for effective prevention and intervention strategies against a cholera outbreak. To this effect, mathematical modeling provides a unique approach to gain basic insights into the dynamics of infectious diseases. Therefore, by exploring the potential effects of disease control strategies such as water chlorination, mathematical modeling can predict the dynamics of explosive epidemics often associated with cholera out breaks. In an effort to gain deeper understanding of the complex dynamics of cholera, several mathematical models have been published. For example, Codeço in 2001 proposed a model [6] that explicitly accounted for the environmental component, i.e., the V. cholera concentration in the water supply, into a regular

SIR epidemiological model. The incidence (or, the infection force) was modeled by a logistic function to represent the saturation effect. [44] extended Codeço's work to include a hyper infectious state of the pathogen, representing the explosive" infectivity of freshly shed V. cholera, based on the laboratory observations [25]. This model was rigorously analyzed in [22]. Joh , Wang, Weiss et al. [18] in 2009Modified Code¸co's model by a threshold pathogen density for infection with a careful discussion on human environment contact and in-reservoir pathogen dynamics .

More recently , Mukandavire et al. [28] proposed a model to study the 2008–2009 cholera outbreaks in Zimbabwe. The model explicitly considered both human-to-human and environment-to-human transmission pathways. The results in this work demonstrated the importance of the human-to human transmission in cholera epidemics, especially in such places as Zimbabwe, a landlocked country in the middle of Africa. Moreover, Tien and Earn [40] in 2010 published a water-borne disease model which also included the dual transmission pathways, with bilinear incidence rates employed for both the environment-to-human and human-to human infection routes. No saturation effect was consider Tien and Earn's work. A rigorous global stability analysis was conducted in [38] for many of the aforementioned models. In addition, Neilan et al. [26] in 2010 modified the cholera model proposed by Hartley, Morris and Smith [14] and added several control measures into the model. They consequently analyzed the optimal intervention strategies and conducted numerical simulation based on their model. No human-to-human infection route is considered in this work.Jing Wang [22] considered three types of control : vaccination, therapeutic treatment (including hydration therapy, antibiotics, etc.), and water sanitation but he did not incorporate the role of education control strategy in their model, also they did not consider a logistic growth of vibrio cholera. This seventh cholera pandemic reached the African continent in 1970 were there were at least 2 independent introduction of the infection (department of Health 2002).The first one caused out breaks in the west(sierra leone ,Liberia Nigeria ,and other coastal countries)and the spread of the disease into the interior of the sub saharan states. The second route is thought to have originated in the middle East entering Africa from the eastern countries of Djibouti , Ethiopia ,and Somalia. Since 1970 parts of Ethiopia have been frequently affected by cholera ,acting as sources of infection for the dissemination of the 1985-1986 large scale epidemic in the horn of Africa (maimone et.,1986,coppet al.1995).From 1993 to1999,they were again system –atically involved as active focuses in the recurrent spreading of the disease in the region .In spite of the critical role of Ethiopia in the epidemic transmission of cholera, no scientific investigation have been carried out.

Addis Ababa and dire dawa were obtained from records kept at the regional health Bureau in the Ethiopia city of Harar. In 1998,they set up a surveillance system to investigate

directly the epidemiological clinical, and micro biological aspects of sever dehydrating diarrhea disease at the regional Health Bureau in the Ethiopia city of Harrer .other zones were they survey out breaks of Acute diarrhea when cholera break out in epidemic from where the Ethiopia states of Somali ,oromiyya , and southern people.

1.2 Statement of the problem

In resource-limited settings, efforts to control and prevent cholera transmission often intensify only during outbreaks. However, the development of vaccine-induced immunity requires a certain period, during which the population remains vulnerable. In such cases, mathematical modeling has become an essential tool for predicting the dynamics of epidemics and evaluating the effectiveness of various prevention strategies. Mathematical models provide quantitative insights that can assist in guiding public health policies, such as estimating direct and indirect contact rates and clarifying critical parameters and variables involved in disease transmission.In this context, the following research questions are raised to address the problem through the use of mathematical modeling:

- What conditions enhance the transmission of cholera?
- How can the stability analysis of equilibrium states be demonstrated?
- What are the most sensitive parameters influencing the transmission of the disease?

Previous epidemiological models, such as [37], have provided foundational insights into disease dynamics by focusing on broad population compartments, typically considering only susceptible (S), infected (I), recovered (R), and environmental factors like bacterial load (B). However, these models often treat the infected population as a homogenous group, with no distinction between symptomatic and asymptomatic cases. This simplification may limit our understanding of transmission dynamics, particularly in diseases where asymptomatic carriers play a significant role in disease spread [15].

Additionally, existing models frequently overlook the differentiated contributions of symptomatic and asymptomatic infections to environmental contamination, which may affect bacterial load dynamics. For instance, in the initial model, bacterial contributions from the infected population (I) are lumped together, assuming identical contributions from all infected individuals. This can lead to inaccuracies in predicting disease outbreaks, as asymptomatic carriers might have a lower or different shedding rate compared to symptomatic individuals.

To address these gaps, the modified model differentiates between symptomatic (I_s) and asymptomatic (I_a) infection compartments, as well as their unique contributions to infection spread and bacterial load. By incorporating separate infection rates (β_1 for I_s

and β_2 for I_a) and bacterial contributions ($\epsilon_1 I_s$ and $\epsilon_2 I_a$), the modified model provides a more detailed framework for understanding how different infected subpopulations affect both direct and environmental transmission. This allows for more accurate predictions and potentially more effective control strategies, especially in cases where asymptomatic individuals are significant contributors to transmission.

1.3 Objectives of the Study

1.3.1 General Objective

The general objective of this study is to develop and analyze a mathematical model that describes the transmission dynamics of cholera :providing insights for better understanding,prevention and control of the disease .

1.3.2 Specific Objectives

This study holds substantial significance in several key areas:

1. **Identify influential or sensitive parameters:**

   This allows the researcher to prioritize interventions or factors that have the greatest impact on cholera transmission, such as the transmission rate or recovery rate. These parameters may represent real-world quantities like infection rates or environmental contamination levels.

2. **Determine mechanisms for cholera treatment:**

   This relates to practical, real-world approaches to reducing the disease's spread. It could involve medical treatments like antibiotics or oral rehydration therapy, and infrastructure improvements like clean water access.

3. **Identify conditions for the existence and stability of disease-free and endemic equilibrium points:**

   Disease-free equilibrium (DFE) represents a situation where cholera is no longer spreading, while endemic equilibrium indicates a persistent, stable presence of the disease in the population. This helps in assessing the effectiveness of control measures.

4. **Find conditions that enhance the transmission of cholera:**

   This could involve identifying factors like poor sanitation, overcrowding, or lack of treatment, which facilitate higher transmission rates. Understanding these factors is key to designing preventive strategies.

5. **Determine the basic reproduction number (R_0) using the next generation matrix:**

   R_0 represents the average number of secondary cases generated by an infected individual in a completely susceptible population. If $R_0 > 1$, an epidemic is likely; if $R_0 < 1$, the disease will die out.

6. **Investigate stability analysis of disease-free and endemic equilibrium points:**

   Stability analysis ensures that the population will not fluctuate wildly or unpredictably under normal conditions. It helps in understanding whether cholera control measures are effective in maintaining low transmission rates.

7. **Identify the most sensitive parameters:**

   This provides insights into the specific areas where interventions (like reducing transmission rates or improving treatment access) will have the greatest impact on reducing cholera transmission.

1.4 Significance of the study

This study holds substantial significance in several key areas:

By developing a mathematical model that intricately describes the transmission dynamics of cholera, this research provides crucial insights that can inform further investigations by researchers, facilitating a deeper understanding of the disease's mechanisms and spread. The findings from this study can serve as a foundational resource for public health administrations, enabling them to devise more effective control strategies tailored to the dynamics of cholera transmission. This is particularly relevant in regions prone to cholera outbreaks, where timely interventions can save lives.

The study not only formulates a mathematical model but also analyzes its equilibrium points and stability. This analytical approach allows for a comprehensive interpretation of the model's solutions, contributing to the scientific discourse on cholera dynamics. Through sensitivity analysis, this research identifies the most critical parameters that influence the spread of cholera. Understanding these parameters is essential for prioritizing public health interventions and resource allocation effectively.

The recommendations derived from the model's findings can guide policymakers in implementing evidence-based strategies aimed at cholera prevention and control, ultimately reducing the incidence and impact of this disease on vulnerable populations.

The study thus not only advances academic knowledge but also has practical implications for improving public health outcomes related to cholera.

1.5 Organization of the Thesis

The thesis is organized as follows:

- **Chapter 1:** This chapter contains an introduction to the topic at hand. It outlines the background of the study, providing context and rationale for the research. Additionally, it presents the statement of the problem, clearly defining the issues that the study aims to address. The chapter also details the objectives of the research, articulating the goals it seeks to achieve. Furthermore, it highlights the significance of the study, explaining its relevance and potential contributions to the field. Lastly, the organization of the thesis is outlined, offering a roadmap of the subsequent chapters and their contents.

- **Chapter 2:** In this chapter, we examine various studies that employ deterministic (compartmental) models, which serve as important guides and references for our work.

- **Chapter 3:** This chapter presents some epidemiological preliminaries and the methodology of the study .

- **Chapter 4:** This chapter outlines and formulates both existing and modified mathematical models. It also discusses the underlying assumptions of these models, the calculation of the reproduction number, and the sensitivity analysis conducted to assess their reliability including definition on sensitivity analysis.

- **Chapter 5:** This chapter discusses the mathematical simulation of the model using ODE45 in MATLAB software.

- **Chapter 6:** The final chapter presents the concluding observations based on the work done in the previous chapters. It includes a summary of the overall objectives of the research study and concludes with an appendix.

Chapter 2
LITRATURE RIVIEW

In 1927, Kermack and Mckendrick [[19]] introduced a prominent compartmental model to analyze the plague disease in Mumbai and succeeded in revealing its epidemiology. After that mathematical modeling have been playing a significant role in analyzing the spread and control of different infectious diseases [[5], [24]].

[7] was one of the first to integrate the environmental component of cholera transmission into a classical SIR epidemiological model. The model incorporated the concentration of Vibrio cholera in water supplies and highlighted how the bacterial load could impact the transmission rate. This model utilized a logistic function to represent the saturation effect of the pathogen in the environment, helping to understand how the environmental reservoir of the bacteria contributes to epidemic outbreaks and the spread of cholera.

[29] focused on modeling cholera outbreaks in Zimbabwe by considering both human-to-human and environment-to-human transmission pathways. Their model emphasized the importance of human-to-human transmission, especially in landlocked regions with limited access to clean water and sanitation. The study demonstrated that in settings like Zimbabwe, reducing the rate of human-to-human transmission could be more critical in controlling the disease than managing environmental factors alone.

[30] modified existing cholera models by incorporating control measures, including vaccination, therapeutic treatments, and sanitation. They analyzed the optimal strategies for reducing cholera transmission, using numerical simulations to explore how these interventions could be applied during outbreaks. Their study emphasized the potential of combining multiple control strategies to reduce the impact of cholera, especially in resource-limited settings where healthcare infrastructure is minimal

[41] proposed a cholera model that included dual transmission pathways—environment-to-human and human-to-human. They used bilinear incidence rates for both routes but did not account for the saturation effect of the pathogen in the environment. Their analysis showed that human-to-human transmission played a significant role in cholera dynamics, but they noted that the environmental transmission pathway remained essential in sustaining cholera outbreaks, particularly when hygiene and sanitation conditions

were poor.

[45] extended the work of earlier models by incorporating the hyper-infectious nature of freshly shed Vibrio cholera in water supplies, which is known to significantly increase the pathogen's effectivity. Their model accounted for pathogen density thresholds required for infection and included the potential for explosive outbreaks. By analyzing these dynamics, the study contributed to a better understanding of the rapid spread of cholera in environments with high pathogen loads, thus providing more targeted intervention strategies.

Mathematical models constructed for epidemic diseases is to study the nonlinear process involves in the dynamics of infectious diseases. The mathematical models which is often constructed in Ordinary and Partial differential equations, and now the concept of fractional differential equations that generalize these models are considered and are considered much effective. For example, the Hepatitis E disease modeling in fractional derivative [31], the use of two variables in modeling the real world problems [12], the new fractional derivative to epidemic model [16], the piece-wise differential equations and its applications [32]. To better understand the model related to infectious diseases, it is first formulated in ordinary differential equations and then it is generalized to form a fractional order system. Among other infectious diseases, the Buruli ulcer (BU) is a disease that can also be known as necrotizing skin disease, and it is the Mycobacterium ulcer [6] that cause this infection. In the current situation, the disease has been identified around the globe in several countries where the high infection includes is the tropical region.

The most frequent occurrence can be found in most West Africans countries including Ghana, Cote d'Ivoire, Benin and Cameroon, which made up of about 80% of the entire global reported cases In each endemic country the disease is commonly found in foci, which unfortunately affects the people within such environment which usually is highly impoverished and have serious challenges to access quality medical care within the communities [13].The only proper way of controlling the BU infection spread, is the disease early identification and the application of antibiotics, that include the streptomycin and rifampicin for at least eight weeks [1]. In an advanced situation the lesion may demand debridement or usually grafting which will help improve the healing process and eventually could prevent deformities [10]-[11]. BU is characterized by long duration stay in hospital which economically brings cost to the patients and the state [17]. In Ghana, for instance, around 1200 cases of BU have been identified in the era 1993–1998, by the first proper surveillance system undertaken in the entire country; and interestingly in the era 2004–2014 more than 9000 cases have been recorded nationwide [13].

The most endemic district is the Amansle West and is found in Ashanti Region of Ghana,

which is highly associated with artisanal mining popularly known as galamsey. Due to uncovered pit holes in these communities cholera outbreak is very common. The illegal mining activities create conducive environment for the Mycobacterium ulcer to thrive. This eventually exposes arsenic into the environment and weakens the immune system of children whose immune systems are not fully developed [39], and hence they become susceptible to may diseases commonly among them is cholera due to poor sanitation because of the level of poverty in the communities. Cholera in modern times was identified by John Snow in the 19thcentury.

Cholera is very common in Sub-Saharan Africa while the West Africa Guinea is considered to be the first country that recorded this disease [15]. On the first day of September, 1970, the first case of cholera reported when a Togolese national was diagnosed at the Kotoka International Airport [16]. There have been five major cholera cases in Ghana and the worse of them occurred in 2014 with record 243 death (n).The disease is estimated that each year they affect in the range of 3 to 5 million people, where the particular cases occurred from Asian and African regions [14]. This cholera infection is associated with an acute diarrheal caused by infection of the intestine with the bacterium Vibrio cholera. The nature of the infection can be described as asymptomatic, mild or severe and nearly 1 in 20 infected people exhibits severe option [25]. The individual with cholera is characterized by watery diarrhea and vomiting and these individuals lose water and turn to be dehydrated. When the desired treatment is not given, the effect is devastating and the individual life is at risk.

In recent times, authors in [38] proposed a cholera model to explore human to human and environment-to-human transmission pathways and obtained a result that sought to implicate human-to-human transmission in a country such as Zimbabwe which is a landlocked country in East Africa. Furthermore, authors in [38] developed a cholera model and incorporated a dual transmission path ways with bilinear incident cerates on both human-to-human paths and environmental-to-human infection without taking into account the saturation effect. In [26] the authors modified model in [28] by adding some controls measures in to the proposed model which numerically analyzed to determine the best strategy to minimize the spread of cholera. The authors in [8] proposed to analyze the dual infection dynamics of cholera and malaria by incorporating several time reproduction controls (Rc) to examine the best strategy to reduce the co-infection of the diseases. The authors proposed a set of useful combinations of controls to minimize possibly the infection in both the diseases and its confection. There are some mathematical models on BU epidemiology that studied this infection. For example, the authors in [39], considered an SIR structure model and concluded that the spread of BU increases with the arsenic environments and the biting of the water bugs. In [9], the authors proposed a

model that sought to capture the transmission dynamics of BU via two routes: the direct contact with Mycobacterium ulcer in the environment and the biting by the water bugs which serves as a reservoir of MU.

Chapter 3
METHODOLOGY

We used a deterministic compartmental model and the model is formulated by using a system of non-linear ordinary differential equation, which is well known to describe the epidemiology of symptomatic and asymptomatic infection diseases. The model sub divides the human population into five compartments depending on the epidemiological status of individuals. The compartments are susceptible, symptomatic, asymptomatic, contaminated on water and food and recover . The parameters of the model are incorporated using death rate, birth rate, environment-to- human transmission rate, recover rate, the growth rate of vibrio cholera bacteria in the environment etc. We analyzed the local stability behavior of equilibrium using the Routh-Hurwitz stability criteria and the global stability of equilibrium using the Castillo-Chavez theorem . We used the next generation matrix to determine the basic reproductive number. Mathematical software such as MATLAB code 45 is used to in order to identify the impact of different parameters on the dynamics of cholera diseases.

3.1 Differential equations

A differential equation is an equation that involves derivatives of an unknown function. When the unknown function depends on a single variable, the equation is classified as an ordinary differential equation (ODE).

3.2 System of Differential Equations (Autonomous system of ordinary differential equations)

An autonomous n-dimensional system of ordinary differential equation has the form

$$\begin{aligned} \frac{dx}{dt} &= f(x(t)) \\ x(t_0) &= x_0 \end{aligned} \tag{3.1}$$

where $x_0, x \in D \subset \mathbb{R}$ and $f : \mathbb{R}^n \to \mathbb{R}^n$, with f continuous at $x \in D \subset \mathbb{R}^n$.

Definition 3.1 ([[46]]). ***Well-posedness***

An initial value problem (IVP) given in 3.1 is mathematically said to be well-posed if the following conditions hold:

i. Its solution exists,

ii. Its solution is unique.

iii. Its solution continuously depends on the initial conditions.

Since in epidemiology we are dealing with populations, the following two additional conditions are quite important:

iv. The solution should be non-negative over time,

v. The solution should be bounded.

Theorem 3.1 ([27]). *Picard's theorem*

Consider the initial value problem given in (3.1.1). If the function f is continuous and all its partial derivatives $\frac{\partial f_i}{\partial x_j}$, for $i, j = 1, 2, 3, \ldots, n$, are continuous for x in some open connected set $D \subset \mathbb{R}^n$, then for $x_0 \in D$, the problem (3.1.1) has a solution $x(t)$ on some time interval $(-\tau, \tau)$, $\tau > 0$, about $t = 0$, and the solution is unique.

Definition 3.1.2 ([[43]]). *Positivity of solution*

The solution of a given autonomous system of (3.1.1) is said to be positive if all trajectories $x(t)$ are positive for any $t \geq 0$.

Definition 3.1.3 ([[34]]). *Boundedness of solution*

The positive solution given in (3.3) of an autonomous system of (3.1) is said to be bounded if any solution $x(t, t_0, x_0)$ satisfies

$$\|x(t, t_0, x_0)\| \leq C(\|x_0\|, t_0),$$

for all $t \geq t_0$, where $C : \mathbb{R}^+ \times \mathbb{R}^+ \to \mathbb{R}^+$ is a constant that depends on t_0 and x_0.

Theorem 3.2 ([[21]]).

Let a linear ordinary differential equation be given by

$$\dot{y}(x) + p(x)y = q(x). \tag{3.2}$$

Then, using the integrating factor method, the integrating factor and its general solution are given, respectively, by

$$I_f(x) = e^{\int p(x)\,dx}, \tag{3.3a}$$

$$y(x) = e^{-\int p(x)\,dx}\left[C + \int q(x)e^{\int p(\tau)\,d\tau}dx\right], \tag{3.3b}$$

where C is an arbitrary constant of integration.

Theorem 3.4 ([[4]]).

Let A be a constant matrix. The solution of the system

$$\dot{x} = Ax + f(t),$$

with initial conditions $x(t_0) = x_0$, is given by

$$x(t) = \phi(t)\phi^{-1}(t_0)x_0 + \int_{t_0}^{t} \phi(t - s + t_0)\phi^{-1}(t_0)f(s)\, ds, \tag{3.5}$$

where $\phi(t)$ is

3.3 Equilibrium Point

The equilibrium points or steady states to a system of the first order differential equation are the points at which the first derives are equal to zero that is for the system

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1(X_1, X_2, \ldots, X_k) \\
\frac{dx_2}{dt} &= f_2(X_1, X_2, \ldots, X_k) \\
&\vdots \\
\frac{dx_k}{dt} &= f_k(X_1, X_2, \ldots, X_k)
\end{aligned}$$

Here $f_1, f_2, \ldots f_k$ are distinct functions representing different dynamics for each variable.

$$\begin{aligned}
f_1(X_1, X_2, \ldots, X_k) &= 0 \\
f_2(X_1, X_2, \ldots, X_k) &= 0 \\
f_3(X_1, X_2, \ldots, X_k) &= 0 \\
&\vdots \\
f_k(X_1, X_2, \ldots, X_k) &= 0
\end{aligned} \tag{r}$$

This equation represents an equilibrium condition, where f_i is a function of the state variables that equals zero at steady state points. Usually the system of equation exhibits two type of equilibrium points .these are disease free and endemic equilibrium points ([36]).

3.3.1 Disease free Equilibrium Point (DFE) of the Modified Model

The disease free equilibrium of the model system 4.1 is obtained by set

$\frac{dS}{dt} = \frac{dI_s}{dt} = \frac{dI_a}{dt} = \frac{dR}{dt} = \frac{dB}{dt} = 0$ and in the absence of disease,$I_a = I_s = B = 0$ so that Stephen Edwards.

3.3.2 Endemic Equilibrium Point of the Model

The endemic equilibrium state is the state where the disease can not totally eradicated but remains in the population and the nonlinear differential equation equal to zero .

3.4 The basic Reproduction Number, R_0

The basic reproduction number R_o is a threshold parameter defined as the average number of secondary infections produced by a single infected individual in a completely susceptible population. It is also the basic reproduction ratio or basic reproductive rate. To calculate R_o , It is important to identify new infections from all other changes in the population and it can be determined using the method of next generation matrix.

3.5 The next Generation matrix

Next Generation matrix is a method used to drive the basic reproduction number for a compartment models of the spread of infectious diseases. To compute R_o , It is important to use the next generation matrix theory presented by [20] which consists to finding the spectra radios (the dominant Eigenvalue) of the next generation matrix. The next generation matrix is given by $R_0 = p(K) = \mathbb{P}(FV^{-1})$ where F and V^{-1}) are transmission and transition matrix, respectively. In addition, P denotes the spectra radius (The dominant eigenvalue) of the matrix, FV^{-1} . Here R_o is the Eigenvalue of largest magnitude , or spectra radius of matrix FV^{-1} where:

- $F_i(x)$ be the rate of appearance of new Infection in compartment i
- $V_i(t)$ be the rate of transfer of individual in and out of the compartment by another mean $V_i = V_i^- - V_i^+$.
- V_i^- be the rate of transfer of individuals out of compartments i
- V_i^+ be the rate of transfer of individuals in to compartment i.

Then $R_0 = P(FV^{-1})$ and FV^{-1} is given by $FV^{-1} = \left(\frac{\partial f_i(E_0)}{\partial t_i}\right)\left(\frac{\partial V_i(E_0)}{\partial t_i}\right)^{-1}$

Based on the value of R_o we have the following conclusions:-

- ✓ If $R_0 < 1$, then on the average, an Infected individual produces less than one new infected individual over the course its infections period, and the infection cannot be spread.
- ✓ If $R_0 > 1$, then each Infected individuals produce on the average, more than one new infection and the disease can invade the population.
- ✓ If $R_0 = 1$, the disease remains the population at the constant rate.

3.6 Stability Analysis of Equilibrium points

Given the autonomous system, a state X^* is said to be an equilibrium point of the system if F(X) = 0 the solution X^* is said to be stable if for every $\epsilon > 0$, there exists a $\delta = \delta(\epsilon)$ such that $|X^* - X0| < \delta \implies |X^* - X(t)| < \epsilon$, $t > t_0 \in \mathbb{R}$ for every solution X (t) of with $X(t_0) = X_0$.

Alternatively, an equilibrium point determines whether solution nearby the equilibrium point remains nearby, get closer or get further a ways is known as stability.

An equilibrium point X* is said to be globally as asymptotically stable if it is asymptotically stable for all initial condition $X_0 \in \mathbb{R}$, An equilibrium point X^* is globally stable if all trajectories converge to X^* i. e $\lim_{x \to a} f(x) = X^*$

3.7 Sensitivity analysis

Sensitivity analysis is used to determine the relative importance of model to disease transmission . We perform the analysis by calculating the sensitivity indices of the basic reproduction number R_o is important to understand how change in various parameter affects the stability of the model.

3.8 Castillo – Chavez theorem [5]

Assume that the system 3.1 can be rewriting the form

$$\begin{aligned} \frac{dh_1}{dt} &= F(h_1, h_2) \\ \frac{dh_2}{dt} &= G(h_1, h_2), \quad \text{where} \quad G(h_1, 0) \end{aligned}$$

where $h_1, h_2 \in \mathbb{R}^m$, h_1 represents the class of non- infected Individuals and h_2 represents the class of infected individuals . Assume that G (h_1, 0) = 0 and $h_0 = (h_1^*, 0)$ be the disease free equilibrium point of 3.1.

If the Following conditions are satisfied.

I. For the system $\frac{dh_1}{dt} = F(h_1, h_2)$ the steady state $h1^*$ is globally asymptotically stable.

II. $G(h_1, h_2) = Ah_1 - \hat{G}(h_1, h_2)$ and $\hat{G}(h_1, h_2) \geq 0$

for $(h_1, h_2) \in \Pi$ where A is the off diagonal element of A are non – negative and Π is the region of the model makes biological sense. Then the steady state$h_0 = (h_1^*, 0)$ is globally stable for the system provided that basic reproduction number of the model is less than one.

3.9 ROUTH – Hurwitz criteria [3]

ROUTH- Hurwitz criteria is an important criteria that given necessary and sufficient condition for all coefficients) to have negative real parts. It is used to determine the symptomatic and asymptomatic stability of an equilibrium point for non – liner system of differential equations consider the characteristic equation of degree n, given:

The characteristic equation is:

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + a_2\lambda^{n-2} + \cdots + a_n, \quad a_i > 0$$

For i= 1, 2, 3,.....n . Where the a_i coefficients are real constants, we define the $n \times n$ matrix using the coefficients a_i of the characteristic polynomial:

$$H_1 = \begin{vmatrix} a_1 \end{vmatrix}$$

$$H_2 = \begin{vmatrix} a_1 & 1 \\ 0 & a_2 \end{vmatrix}$$

$$\vdots$$

$$\begin{vmatrix} a_1 & 1 & 0 & \dots & 0 \\ a_3 & a_2 & a_1 & \dots & 0 \\ a_5 & a_4 & a_3 & \dots & 0 \\ \vdots & \vdots & \vdots & \dots & \vdots \\ 0 & 0 & 0 & \dots & 0 \end{vmatrix}$$

Where a_j =0 if $j > 0$. All the roots of the polynomial $P(\lambda)$ are negative have negative real part if and only if the determinants of all Hurwitz matrices are positive . That is det(H_j) >0 for all j= 1,2,3,....n.

For polynomials of degree n= 2,3,4 and 5, the Routh- Hurwitz criteria are summarized as follows:

$$
\begin{aligned}
n = 2: &\quad a_1 > 0, a_2 > 0, \quad \text{and} \quad (a_1 a_2) > 0 \\
n = 3: &\quad a_1 > 0, a_3 > 0 \quad \text{and}\, (a_1 a_2 > a_3) \\
n = 4: &\quad a_1 > 0, a_3 > 0, a_4 > 0 \quad \text{and} \quad (a_1 a_2 a_3 > a_3^2 + a_1^2 a_4) \\
n = 5: &\quad a_i > 0, i = 1, 2, 3, 4, 5; \left(a_1 a_2 a_3 > a_3^2 + a_1^2 a_4\right) \\
&\qquad \text{and} \quad (a_1 a_4 - a_5)\left(a_1 a_2 a_3 - a_3^2 - a_1^2 a_4\right) > \left(a_5 (a_1 a_2 - a_3)^2 + a_1 a_5^2\right)
\end{aligned}
$$

Chapter 4
MATHEMATICAL MODEL FORMULATION AND ANALYSIS

In this chapter, we explore a mathematical framework for analyzing the cholera model. We derive the formula for the basic reproduction number and examine the existence and stability of both the disease-free equilibrium point and the local endemic equilibrium point. Additionally, we conduct a sensitivity analysis of the reproduction number to better understand its implications

4.1 The Existing model formulation [37]

The SIR model is widely recognized as the most prevalent epidemiological framework for studying infectious diseases. In this context, the SIR-B model serves as a valuable tool for modeling general epidemics, enabling us to understand disease transmission within a specific population and explore potential control strategies. To effectively analyze the dynamics of the SIR-B model, we adopt a logistic approach reminiscent of the Michaelis-Menten kinetics. The existing work aims to investigate the foundational aspects of the model by categorizing the total population into four distinct compartments: Susceptible (S), Infected (I), Recovered (R), and Contaminated (B), which represents water and food sources in the environment. The SIR-B epidemic model is particularly significant as it lays the groundwork for further exploration into the SIs-Ia-R-B model. Consequently, at any given time t, the total population can be comprehensively analyzed through this structured framework .

- γ is the recovery rate .
- λ is natural birth rate .
- The contact rate between the susceptible population with symptomatic infection is β_1 .
- The contact rate between the susceptible population with asymptomatic infection is β_2 .
- The rate that a therapeutic treatment is τ_1

- The symptomatic Infected group contributed to the contaminated food and water is ϵ_1
- The asymptomatic infected group contributed to the contaminated food and water is ϵ_2
- μ is natural death rate .
- Concentration of vibrio cholera in food and water that yield 50% chance of catching cholera disease K.
- The decay rate of vibrio cholera is δ .
- The environment-to- human transmission rate is λ_e.
- The human-to -human transmission rate is B_h.

The following flow diagram figure 4.1 illustrates the structure of the SIR-B model, highlighting how various compartments interact and the roles of critical parameters in disease transmission and recovery.

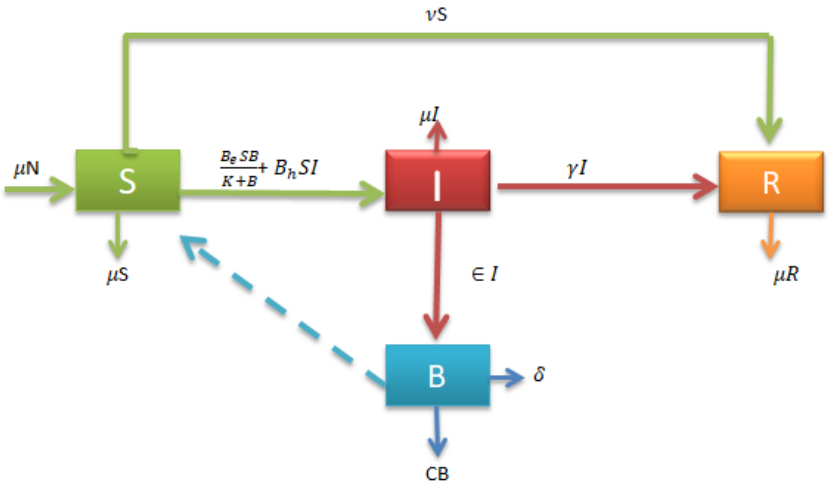

Figure 4.1: Flow diagram of the existing mathematical model

The Dynamic equation of the initial model

$$\frac{dS}{dt} = \mu N - \left(B_e S\frac{B}{K+B} + B_h SI\right) - \mu S - vS$$
$$\frac{dI}{dt} = B_e S\frac{B}{K+B} + B_h SI - (\gamma + \mu)I$$
$$\frac{dR}{dt} = \gamma I - \mu R + vS$$
$$\frac{dB}{dt} = \epsilon I - \delta B - CB$$

With initial conditions $S(0) > 0$, $I(0) > 0$, $B(0) > 0$ and $R(0) > 0$. Here all parameter values of the model must be positive .

4.2 The modified Mathematical model formulation and Analysis

In this thesis, we modified the existing SIR-B model [37] to study the dynamic transmission of cholera within a population. Our model extends the original SIR-B model by including both symptomatic and asymptomatic infections, as well as considering treatment for symptomatic cases. This modification allows us to analyze the effects of treatment on the disease's spread over time. The model divides the population into five compartments based on their epidemiological status: Susceptible (S), Symptomatic Infected (Is), Asymptomatic Infected (Ia), Recovered (R), and Contaminated Environment (B). This SIsIaR-B model is formulated using a system of differential equations to describe the transmission dynamics of cholera. It is assumed that the population size in each compartment is differentiable with respect to time, and the process is deterministic.

We have incorporated several key factors into the model, including the rate of therapeutic treatment (τ_1), the recruitment rate (Λ), the natural death rate (μ), the recovery rate (γ), and the contribution of symptomatic and asymptomatic infected individuals to environmental contamination (ϵ_1 and ϵ_2, respectively). Additionally, the model accounts for the decay rate of Vibrio cholerae in the environment (δ), human-to-human transmission rate (B_h), environment-to-human transmission rate (λ_e), and the concentration of Vibrio cholerae in food and water that leads to a 50% chance of infection (K). Furthermore, the contact rates between susceptible individuals and both symptomatic (β_1) and asymptomatic (β_2) infected individuals are considered.

This modified model provides a more realistic representation of cholera transmission dynamics, incorporating treatment strategies and varying levels of infection, making it a useful tool for understanding and controlling cholera outbreaks.

4.3 The modified Mathematical model assumption

1. The total population at any point of time is constant i.e N=$S + I_a + I_s + R$.
2. The population under this study are divided into five compartments and consider the contaminate food or water.
3. Some of Individual in symptomatic and asymptomatic infected group becomes Infections and the remain becomes the recovered group.

4. The populations are under study is heterogeneous .

5. The natural death rates are the same for all compartments except concentration of vibrio cholera in the environment.

6. All the parameters of the model are positive.

7. Our modified model is an $SI_sI_aR - B$ model.

4.4 The Variables and Parameters of the Model

The variables and parameters used in this new model are described in detail in Tables 4.1 . These tables provide a comprehensive overview of the essential components that influence the dynamics of the SIR-B model, facilitating a deeper understanding of disease transmission and recovery processes.

Table 4.1: The description of the variables in $SI_sI_aR - B$ mathematical model

Variables	Descriptions
S(t)	Susceptible individual at time t
$I_s(t)$	Symptomatic infected at time t
B(t)	Concentration of vibrio cholera in the environment at time t
$I_a(t)$	Asymptomatic infected at time t
R(t)	Recovered individuals at time t
N(t)	Total population at time t

Table 4.2: The description of the parameters in $SI_sI_aR - B$ model

Parameters	Descriptions
μ	Natural death rate ,Recruitment rate
τ_1	The rate that a therapeutic treatment I_s
τ_2	Natural recovery rate
ϵ_1	The symptomatic infected group contributed to the contaminated food and water
ϵ_2	The asymptomatic infected group contributed to the contaminated food and water
$(1-p)\Pi$	The rate of susceptible individual contact with symptomatic infected becomes symptomatic and asymptomatic infected
δ	The decay rate of vibrio cholera bacteria due to sanitary measures
λ_e	Environment-to-Human transmission rate
$p\Pi$	The rate of susceptible individual contact with asymptomatic infected becomes symptomatic and asymptomatic infected
K	Concentration of vibrio cholera in food and water that yield 50% chance of catching cholera disease
β_1	The contact rate between the susceptible population with symptomatic infected
β_2	The contact rate between the susceptible populations with asymptomatic infected

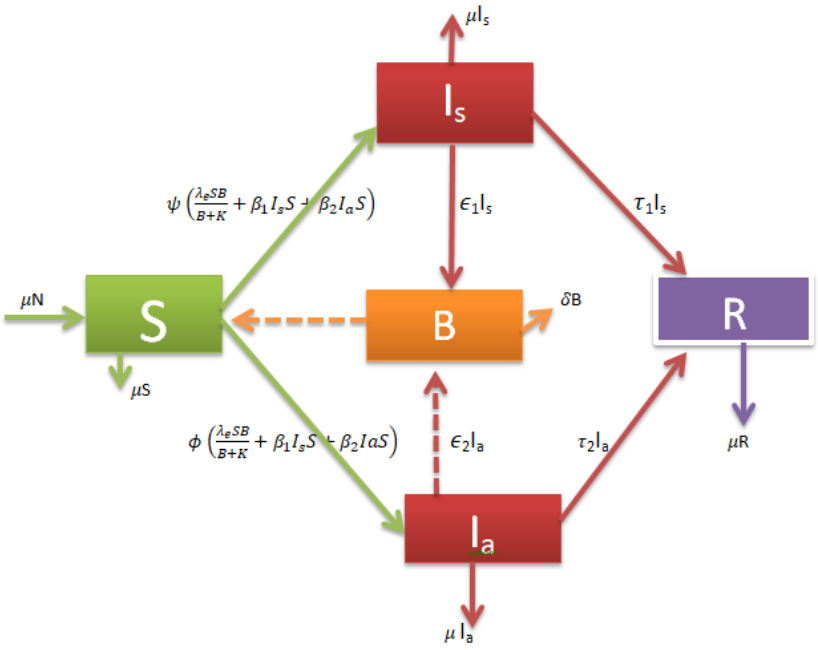

Figure 4.2: The flow chart representation of the modified model

Let $\psi = (1-p)\Pi$ and $\phi = p\Pi$

The non-linear differential equations of the modified model

$$\frac{dS}{dt} = \mu N - \Pi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu S$$

$$\frac{dI_s}{dt} = \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s$$

$$\frac{dI_a}{dt} = \phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_2 I_a \tag{4.1}$$

$$\frac{dB}{dt} = \epsilon_1 I_s + \epsilon_2 I_a - \delta B$$

$$\frac{dR}{dt} = \tau_1 I_s + \tau_2 I_a - \mu R$$

With in the population $S + I_s + I_a + R = N$

All state variables remain non-negative all the time because this study based on human population, therefore the model is restricted is given by :-

$S(0) = S_o > 0$,$R(0) = R_o > 0$, $I_s(0) = I_{s0} > 0$, $I_a(0) = I_{a0} > 0$, B(0)=$B_0 > 0$

4.5 Well-posedness

Since all the functions on the right hand side of the system (4.1) are continuously differentiable. Thus, the existence and uniqueness of the solutions is established by the Picard's theorem (3.1). Now, we show the positivity and boundedness of solutions.

4.6 Positivity of the solution

In order to show that the general model equations 4.1 are to be epidemiological meaning full and well passed, it is needed to prove that all the state variables are non-negative $\forall t \geq 0$ .This fact has been stated as a theorem and proved in what follows.

Theorem 4.6.1. *If the initial conditions* $\{S(0) = S_o > 0, R(0) = R_o > 0, I_s(0) = I_s0 > 0, I_a(0) = I_a0 > 0, B(0) = B_0 > 0\} \in G$ *, then the solution* $(S(t), R(t), I_s(t), I_a(t), B(t))$ *of the system of the equation 4.1 are non- negative* $\forall t \geq 0$ *.*

Proof. to show that the positivity of the solution for the dynamical system of the equations (3.1), we have to consider each differential equation and show that their solution is positive. From the differential equation of dynamical system (s) we have . □

From the differential equation of the dynamical system 4.1 we have

$$\frac{dS}{dt} = \mu N - \Pi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu S$$

$$\frac{dS}{dt} \geq -\Pi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu S \quad \text{since } \mu\text{N is constant}$$

$$= -\left(\Pi\lambda_e\frac{B}{K+B} + \Pi\beta_1 I_s + \Pi\beta_2 I_s + \mu\right) S$$

Separate by variables and integrating both sides gives

$$\int \frac{dS}{S} \geq -\int \left[\pi\lambda_e \frac{B}{K+B} + \pi B_1 I_s + \pi B_2 I_a + \mu\right] dt$$

$$\int \frac{dS}{S} \geq -\int g(t)dt, \quad \text{where} \quad g(t) = \pi\lambda_e \frac{B}{K+B} + \pi B_1 I_s + \pi B_2 I_a + \mu$$

$$\ln S = -f(t)t + c_1, \quad f(t) = \int g(t)dt$$

$$S(t) \geq e^{-f(t)t+c_1}$$

$$S(t) \geq e^{-f(t)t} \cdot e^{c_1}$$

$$S(t) \geq e^{-f(t)t} q, \quad q = e^{c_1}$$

$$S(t) \geq qe^{-f(t)t}$$

Using the initial condition t =0 we have S(0) = q , Which implies that S(t)$\geq e^{-f(t)}$

Therefore S(t)≥ 0 $\forall$t ≥ 0

From the differential equation of the dynamical system (2) we have

$$\begin{aligned}\frac{dI_s}{dt} &= \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s \\ &\geq \left(\psi\beta_1 S - \tau_1 - \mu\right) I_s\end{aligned}$$

since $\dfrac{B}{K+B}$ doesn't directly involve I_s

By rearranging and Integrate both sides of the inequality ;

$$\int \frac{dI_s}{I_s} \geq \int (\psi\beta_1 S - \tau_1 - \mu)dt$$

$$\ln I_s \geq (\psi\beta_1 S - \mu - \tau_1)t + c_2$$

$$I_s(t) \geq e^{(\psi\beta_1 S - \mu - \tau_1)t + c_2}$$

$$I_s(t) \geq e^{(\Psi\beta_1 S - \mu - \tau_1)t} \cdot e^{c_2}$$

$$I_s(t) \geq e^{(\psi\beta_1 S - \mu - \tau_1)t} \cdot k_1, \quad k_1 = e^{c_2}$$

$$\text{Therefore} \quad I_s(t) \geq k_1 e^{(\Psi\beta_1 S - \mu - \tau_1)t}$$

$$\text{At } t = 0 \text{ we have } I_s(0) = k_1$$

$$\text{Hence } I_s(t) \geq I_s(0) \cdot e^{(\psi\beta_1 S - \mu - \tau_1)t}$$

Which implies that $I_s(\mathrm{t}) \geq 0$ $\forall \mathrm{t} \geq 0$.
From the differential equation of the dynamical system (3) We have

$$\begin{aligned}\frac{dI_a}{dt} &= \phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_2 I_a \\ &\geq \phi\beta_2 I_a S - \mu I_a - \tau_1 I_a\end{aligned}$$

By rearranging and Integrate both sides of the inequality we have :

$$\int \frac{dI_a}{I_a} \geq \int (\phi\beta_2 S - \mu - \tau_2)dt$$

$$\ln I_a \geq (\phi\beta_2 S - \mu - \tau_2)t + c_3$$

$$I_a(t) \geq e^{(\phi\beta_2 S - \mu - \tau_2)t + c_3}$$

$$I_a(t) \geq e^{(\phi\beta_2 S - \mu - \tau_2)t} \cdot e^{c_3}$$

$$I_a(t) \geq e^{(\phi\beta_2 S-\mu-\tau_2)t} \cdot k_3, \quad k_3 = e^{c_3}$$

$$\text{Therefore } I_a(t) \geq k_3 e^{(\phi\beta_2 S-\mu-\tau_2)t}$$

$$\text{At } t = 0 \text{ we have } I_a(0) = k_3$$

$$\text{Hence } I_a(t) \geq I_a(0) \cdot e^{(\phi\beta_2 S-\mu-\tau_2)t}$$

$$\text{Which implies that } I_a(t) \geq 0 \text{ for } \forall t \geq 0.$$

From the differential equation of the dynamical system (4) We have

$$\frac{dB}{dt} = \epsilon_1 I_s + \epsilon_2 I_a - \delta B$$

This can be rewritten as:

$$\frac{dB}{dt} \geq -\delta B$$

By rearranging, we have:

$$\frac{dB}{B} \geq -\delta dt$$

Integrating both sides of the inequality:

$$\int \frac{dB}{B} \geq \int -\delta dt$$

$$\ln B \geq -\delta t + C_4$$

$$B(t) \geq e^{-\delta t + C_4}$$

$$B(t) \geq e^{-\delta t}(e^{C_4})$$

$$B(t) \geq e^{-\delta t}(k_4), \quad k_4 = e^{C_4}$$

Therefore $B(t) \geq k_4 e^{-\delta t}$

At t=0 we have B(0) $=k_4$

Hence

$$B(t) \geq B(0)e^{-\delta t}$$

Which implies that ; $B(t) \geq 0 \quad \forall t \geq 0$.

From the differential equation of the dynamical system (5)

$$\frac{dR}{dt} = I_s\tau_1 + I_a\tau_2 - \mu R$$

This can be rewritten as:

$$\frac{dR}{dt} \geq -\mu R$$

By rearranging, we have:

$$\frac{dR}{R} \geq -\mu dt$$

Integrating both sides of the inequality:

$$\int \frac{dR}{R} \geq \int -\mu dt$$

$$\ln R \geq -\mu t + C_5$$

$$R(t) \geq e^{-\mu t + C_5}$$

$$R(t) \geq e^{-\mu t}(e^{C_5})$$

$$R(t) \geq e^{-\mu t}(k_5), \quad k_5 = e^{C_5}$$

Therefore $R(t) \geq k_5 e^{-\mu t}$
At t=0 we have $R(0) = K_5$
Hence $R(t) \geq R(0)e^{-\mu t}$
Which implies that $R(t) \geq 0 \quad \forall t \geq 0$
All the state variables are positive for all time t. The solutions are therefore non negative for $\forall t \geq 0$ and are bounded in the invariant region Ω and thus the model is mathematically well posed and biologically meaningful in the feasible region Ω.

Theorem 4.6.2 (**Boundedness**). *There exists a positively invariant region Ω in which the solution $(S(t), I_s(t), I_a(t), R(t))$ of the dynamical system (4.1) is bounded.*

Proof. The positivity has already been established by Theorem (4.3). For this model the total population is

$$N(t) = S(t) + I_s(t) + I_a(t) + R(t).$$

Total Population Dynamics Differentiating $N(t)$ with respect to t, we sum the equations for $\frac{dS}{dt}$, $\frac{dI_s}{dt}$, $\frac{dI_a}{dt}$, and $\frac{dR}{dt}$:

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_s}{dt} + \frac{dI_a}{dt} + \frac{dR}{dt}.$$

Substituting the right-hand sides of the equations:

$$\frac{dN}{dt} = \mu N - \mu S - \mu I_s - \mu I_a - \mu R.$$

This simplifies to:

$$\frac{dN}{dt} = \mu N - \mu N.$$

Solving for $N(t)$ The differential equation for $N(t)$ is:

$$\frac{dN}{dt} = (\mu - \mu)N = 0.$$

This is a linear differential equation and its solution is :

$$N(t) = c \quad \text{where c is constant.}$$

This implies that the total population remains constant:

$$N(t) = c = N(0).$$

From the model, the dynamics within each compartment ensure non-negativity ($S, I_s, I_a, R \geq 0$).

Boundedness of $B(t)$

The equation for $\frac{dB}{dt}$ is given by :

$$\frac{dB}{dt} = \epsilon_1 I_s + \epsilon_2 I_a - \delta B.$$

Since I_s and I_a are bounded (as subsets of $N(t)$), the input term $\epsilon_1 I_s + \epsilon_2 I_a$ is bounded. By solving the differential equation, we see $B(t)$ approaches a steady state as $t \to \infty$:

$$B(t) \leq \frac{\epsilon_1 \max(I_s) + \epsilon_2 \max(I_a)}{\delta}.$$

The system defined by (4.1) is bounded. The solutions remain within a positively invariant region:

$$\Omega = \left\{ (S, I_s, I_a, B, R) \in \mathbb{R}^5_+ : N(t) = c = N(0), B(t) \leq \frac{\epsilon_1 \max(I_s) + \epsilon_2 \max(I_a)}{\delta} \right\}.$$

Thus, the total population $N(t)$ and bacterial load $B(t)$ are both bounded over time.

4.7 Qualitative analysis of the model

4.7.1 Disease Free Equilibrium Point (DFE)

The disease free equilibrium points are steady state solution of mathematical model indicating that there is no disease. Any epidemiological model has point at which the population remains in the absence of the disease. The disease free equilibrium points are found by setting the right hand side of the model equations equal to zero.

Let $E_0 = (S^0, I_s^0, I_a^0, B^0, R^0)$ represents the disease free equilibrium point of the modified model SI_sI_aR-B. Any epidemiological model has point at which the population remains in the absence of the disease . Hence in the absence of the disease we have $I_s = I_a = B = 0$. Then the disease equilibrium point E^0 can be obtained as :
From the dynamical system of the differential equation 4.1 we have :

$$\frac{dS}{dt} = \mu N - \Pi\left(\Lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu S$$

$$\mu N - \Pi\left(\lambda_e S^0\frac{B}{K+B} + \beta_1 I_s S^0 + \beta_2 I_a S^0\right) - \mu S^0 = 0$$

By Substituting $I_s = I_a = B = 0$ we get :

$$\mu N - \mu S^0 = 0$$

$$S^0 = \frac{\mu N}{\mu} = N(t)$$

For $\frac{dI_s}{dt} = \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s$

$$\psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s = 0$$

$$I_s^0 = 0$$

$$\text{For} \quad \frac{dI_a}{dt} = \phi\left(\frac{\lambda eSB}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_2 I_a = 0$$

$$\implies \phi\left(\frac{\lambda_e SB}{K+B} + \beta_1 I_s S + \beta_2 I_a^* S\right) - \mu I_a^* - \tau_2 I_a^* = 0$$

$$\implies \phi\beta_2 I_a^* S - \mu I_a^* - \tau_2 I_a^* = 0$$

$$\implies I_a^* \left(\phi\beta_2 S - \mu - \tau_2\right) = 0$$

$$I_a^* = \frac{0}{\phi\beta_2 S - \mu - \tau_2} = 0$$

$$I_a^* = 0$$

$$\text{For} \quad \frac{dB}{dt} = \epsilon_1 I_s + \epsilon_2 I_a - \delta B$$

$$\implies B^* = \frac{0}{-\delta} = 0$$

$$\implies B^* = 0$$

$$\text{For} \quad \frac{dR}{dt} = \tau_1 I_s + \tau_2 I_a - \mu R$$

$$\implies I_s\tau_1 + I_a\tau_2 - \mu R^* = 0$$

$$\implies -\mu R^* = 0$$

$$\implies R^* = 0$$

Thus ,the disease free equilibrium point of the system (E_0) is given by

$$E_0 = \left(S^0, I_s^0, I_a^0, B^0, R^0\right) = (N, 0, 0, 0, 0)$$

4.7.2 The Basic Reproduction number (R_0)

The basic reproduction number R_0 is a threshold parameter defined as the average number of secondary infections produced by a single infected individual in a completely susceptible population . it is very important parameter , which helps to determine whether the disease spread in the population or it dies out . To calculate R_0 ,it is important to

identify new infections from all other changes in the population and it can be determined using the method of next generation matrix . The next generation matrix is given by : $R_0 = P(K) = P(FV^{-1})$ Where F and V^{-1} are transmission and transition matrices, respectively .In addition, P denotes the spectra radius (dominate' Eigenvalue) of the matrix,$P(FV^{-1})$.

Here R_0 is the eigenvalue of largest magnitude or spectra radius of matrix $P(FV^{-1})$. Where

- $f_i(x)$ be the rate of appearance of new infection in compartment i .
- $V_i(t)$ be the rate of transfer of individuals in and out of the compartment by another means . $V_i(t) = v_i(t)^- - v_i(t)^+$
- $v_i(t)^-$ be the rate of transfer of individuals out of compartment i
- $v_i(t)^+$ be the rate of transfer of individuals in to compartment i

To calculate F and V , we will only consider the infected groups I_s , I_a and B as they alone are capable of transmitting the disease .
From the dynamical system 4.1 we have :

$$\frac{dI_s}{dt} = \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s$$

$$\frac{dI_a}{dt} = \phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_1 I_a$$

$$\frac{dB}{dt} = \epsilon_1 I_s + \epsilon_2 I_a - \delta B$$

From the given system, new infections are generated in I_s, I_a, and B through contact with B, I_s, and I_a.

For I_s and I_a:

$$F_1 = \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right)$$

$$F_2 = \phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right)$$

For B, new bacteria are generated from I_s and I_a: $F_3 = 0$

For I_s: $V_1 = (\mu + \tau_1)I_s$

For I_a: $V_2 = (\mu + \tau_2)I_a$

For B: $V_3 = \delta B$

We now construct the matrices F and V and then compute the next-generation matrix $\mathcal{K} = FV^{-1}$.

The new infections matrix F captures the rates at which new infections are introduced into the system from each of the infected compartments.

$$\mathbf{F} = \begin{bmatrix} F_1 \\ F_2 \\ F_3 \end{bmatrix} = \begin{bmatrix} I_s \\ I_a \\ B \end{bmatrix} = \begin{bmatrix} \frac{\partial F_1}{\partial I_s} & \frac{\partial F_1}{\partial I_a} & \frac{\partial F_1}{\partial B} \\ \frac{\partial F_2}{\partial I_s} & \frac{\partial F_2}{\partial I_a} & \frac{\partial F_2}{\partial B} \\ \frac{\partial F_3}{\partial I_s} & \frac{\partial F_3}{\partial I_a} & \frac{\partial F_3}{\partial B} \end{bmatrix} = \begin{pmatrix} \frac{\beta_1 \lambda \psi}{\mu} & \frac{\beta_2 \lambda \psi}{\mu} & \frac{\lambda_e \lambda \psi}{\mu K} \\ \frac{\phi \beta_1 \lambda}{\mu} & \frac{\phi \beta_2 \lambda}{\mu} & \frac{\lambda_e \lambda \phi}{\mu K} \\ 0 & 0 & 0 \end{pmatrix}$$

The transition matrix V describes how individuals or bacteria transition out of the infected compartments.

$$\mathbf{V} = \begin{bmatrix} \frac{\partial V_1}{\partial I_s} & \frac{\partial V_1}{\partial I_a} & \frac{\partial V_1}{\partial B} \\ \frac{\partial V_2}{\partial I_s} & \frac{\partial V_2}{\partial I_a} & \frac{\partial V_2}{\partial B} \\ \frac{\partial V_3}{\partial I_s} & \frac{\partial V_3}{\partial I_a} & \frac{\partial V_3}{\partial B} \end{bmatrix} = \begin{bmatrix} \mu + \tau_1 & 0 & 0 \\ 0 & \mu + \tau_2 & 0 \\ -\epsilon_1 & -\epsilon_2 & \delta \end{bmatrix}$$

$$V = \begin{pmatrix} \mu + \tau_1 & 0 & 0 \\ 0 & \mu + \tau_2 & 0 \\ -\epsilon_1 & -\epsilon_2 & \delta \end{pmatrix}$$

To find R_0, we compute the dominant eigenvalue (spectral radius) of the next-generation matrix $\mathcal{K} = FV^{-1}$.

Solution

First find the cofactor, then adj A:

$$A_{11} = (-1)^{1+1} \begin{vmatrix} \mu + \tau_2 & 0 \\ -\epsilon_2 & \delta \end{vmatrix} = \delta\,(\mu + \tau_2)$$

$$A_{12} = (-1)^{1+2} \begin{vmatrix} 0 & 0 \\ -\epsilon_1 & \delta \end{vmatrix} = 0$$

$$A_{13} = (-1)^{1+3} \begin{vmatrix} 0 & \mu + \tau_2 \\ -\epsilon_1 & -\varepsilon_2 \end{vmatrix} = \varepsilon_1\,(\mu + \tau_2)$$

$$A_{21} = (-1)^{2+1} \begin{vmatrix} 0 & 0 \\ -\varepsilon_2 & \delta \end{vmatrix} = 0$$

$$A_{22} = (-1)^{2+2} \begin{vmatrix} \mu + \tau_1 & 0 \\ -\varepsilon_1 & \delta \end{vmatrix} = \delta\,(\mu + \tau_1)$$

$$A_{23} = (-1)^{2+3}\begin{vmatrix} \mu+\tau_1 & 0 \\ -\varepsilon_1 & -\varepsilon_2 \end{vmatrix} = \varepsilon_2\,(\mu+\tau_1)$$

$$A_{31} = (-1)^{3+1}\begin{vmatrix} 0 & 0 \\ \mu+\tau_2 & 0 \end{vmatrix} = 0$$

$$A_{32} = (-1)^{3+2}\begin{vmatrix} \mu+\tau_1 & 0 \\ 0 & 0 \end{vmatrix} = 0$$

$$A_{33} = (-1)^{3+3}\begin{vmatrix} \mu+\tau_1 & 0 \\ 0 & \mu+\tau_2 \end{vmatrix} = (\mu+\tau_1)(\mu+\tau_2)$$

$$\text{CoFA} = \begin{bmatrix} \delta(\mu+\tau_2) & 0 & \epsilon_1(\mu+\tau_2) \\ 0 & \delta(\mu+\tau_1) & \epsilon_2(\mu+\tau_1) \\ 0 & 0 & (\mu+\tau_1)(\mu+\tau_2) \end{bmatrix}$$

$$\text{Hence adj } A = \begin{bmatrix} \delta(\mu+\tau_2) & 0 & 0 \\ 0 & \delta(\mu+\tau_1) & 0 \\ \varepsilon_1(\mu+\tau_2) & \varepsilon_2(\mu+\tau_1) & (\mu+\tau_1)(\mu+\tau_2) \end{bmatrix}$$

Next find $\det V$ =?

$$|V| = \begin{vmatrix} \mu+\tau_1 & 0 & 0 \\ 0 & \mu+\tau_2 & 0 \\ -\varepsilon_1 & -\varepsilon_2 & \delta \end{vmatrix} = (\mu+\tau_1)(\mu+\tau_2)\delta$$

Since matrix V is lower triangular, then after $V^{-1} = \frac{\text{adj}(V)}{\det(V)}$

$$V^{-1} = \frac{1}{(\mu+\tau_1)(\mu+\tau_2)\delta}\begin{bmatrix} \delta(\mu+\tau_2) & 0 & 0 \\ 0 & \delta(\mu+\tau_1) & 0 \\ \varepsilon_1(\mu+\tau_2) & \varepsilon_2(\mu+\tau_1) & (\mu+\tau_1)(\mu+\tau_2) \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu+\tau_1} & 0 & 0 \\ 0 & \frac{1}{\mu+\tau_2} & 0 \\ \frac{\varepsilon_1}{\delta(\mu+\tau_1)} & \frac{\varepsilon_2}{\delta(\mu+\tau_2)} & \frac{1}{\delta} \end{bmatrix}$$

Then we compute the product of both matrix F and V^{-1}. After some computation it gives

$$K = FV^{-1} = \begin{bmatrix} \frac{\beta_1\Lambda\psi}{\mu} & \frac{\beta_2\Lambda\psi}{\mu} & \frac{\lambda e\Lambda\psi}{\mu k} \\ \frac{\phi\beta_1\Lambda}{\mu} & \frac{\phi\beta_2\Lambda}{\mu} & \frac{\lambda e\Lambda\phi}{\mu k} \\ 0 & 0 & 0 \end{bmatrix}\begin{bmatrix} \frac{1}{\mu+\tau_1} & 0 & 0 \\ 0 & \frac{1}{\mu+\tau_2} & 0 \\ \frac{\varepsilon_1}{\delta(\mu+\tau_1)} & \frac{\varepsilon_2}{\delta(\mu+\tau_2)} & \frac{1}{\delta} \end{bmatrix}$$

$$= \begin{bmatrix} \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda e \Lambda \psi}{\delta(\mu+\tau_1)\mu k} & \frac{\beta_2 \Lambda \psi}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_2)} & \frac{\lambda_e \Lambda \psi}{\delta \mu k} \\ \frac{\phi \beta_1 \Lambda}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda e \Lambda \phi}{\mu k \delta(\mu+\tau_1)} & \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda e \lambda \phi}{\mu k \delta(\mu+\tau_2)} & \frac{\lambda_e \Lambda \phi}{\delta \mu k} \\ 0 & 0 & 0 \end{bmatrix}$$

The basic reproduction number is the eigenvalue of largest magnitude, i.e., the spectral radius of the next generation matrix, and we compute the eigenvalues of the next generation matrix FV^{-1} by finding the values of λ which satisfy the characteristic equation of the matrix, namely those values of λ for which

$$\det(FV^{-1} - \lambda I) = 0$$

Where λ and I are eigenvalues and identity matrix respectively.

$$\det(FV^{-1} - \lambda I) = \begin{vmatrix} \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda_e \Lambda \psi}{\delta(\mu+\tau_1)\mu K} - \lambda & \frac{\beta_2 \Lambda \psi}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda_e \Lambda \psi}{\mu k \delta(\mu+\tau_2)} & \frac{\lambda_e \Lambda \psi}{\delta \mu k} \\ \frac{\phi \beta_1 \Lambda}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda_e \Lambda \phi}{\mu k \delta(\mu+\tau_1)} & \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda_e \Lambda \phi}{\mu k \delta(\mu+\tau_2)} - \lambda & \frac{\lambda_e \Lambda \phi}{\delta \mu k} \\ 0 & 0 & -\lambda \end{vmatrix} = 0$$

$$\left(\frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda e \Lambda \psi}{\delta(\mu+\tau_1)\mu k} - \lambda \right) \begin{bmatrix} \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda_e \Lambda \phi}{\mu k \delta(\mu+\tau_2)} - \lambda & \frac{\lambda_e \Lambda \phi}{\delta \mu k} \\ 0 & -\lambda \end{bmatrix} - \left(\frac{\beta_2 \Lambda \psi}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda_e \Lambda \psi}{\mu k \delta(\mu+\tau_2)} \right)$$

$$\begin{bmatrix} \frac{\phi \beta_1 \Lambda}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda_e \Lambda \phi}{\mu k \delta(\mu+\tau_1)} & \frac{\lambda_e \Lambda \phi}{\delta \mu k} \\ 0 & -\lambda \end{bmatrix} + \frac{\lambda_e \Lambda \psi}{\delta \mu k} \begin{bmatrix} \frac{\beta_1 \Lambda \phi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda_e \Lambda \phi}{\mu k \delta(\mu+\tau_1)} & \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda_e \Lambda \phi}{\mu k \delta(\mu+\tau_2)} - \lambda \\ 0 & 0 \end{bmatrix} = 0$$

multiplying both sides by negative sign we get :

$$\lambda^3 - \frac{\beta_1 \Lambda \psi \lambda^2}{\mu(\mu+\tau_1)} - \frac{\epsilon_1 \lambda e \Lambda \psi \lambda^2}{\mu k \delta(\mu+\tau_1)} - \frac{\phi \beta_2 \Lambda \lambda^2}{\mu(\mu+\tau_2)} - \frac{\epsilon_2 \lambda e \Lambda \phi \lambda^2}{\mu k \delta(\mu+\tau_2)} = 0$$

Simplified form after dividing both sides by λ^2:

$$\lambda - \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} - \frac{\epsilon_1 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_1)} - \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} - \frac{\epsilon_2 \lambda e \phi \Lambda}{\mu k \delta(\mu+\tau_2)} = 0$$

Now solving for λ_2:

$$\lambda_2 - \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} - \frac{\epsilon_1 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_1)} - \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} - \frac{\epsilon_2 \lambda e \phi \Lambda}{\mu k \delta(\mu+\tau_2)} = 0$$

Rearranging for λ_2:

$$\lambda_2 = \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_1)} + \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda e \phi \Lambda}{\mu k \delta(\mu+\tau_2)}$$

Finally, the basic reproduction number R_0 is:

$$R_0 = \rho(FV^{-1}) = \max(\lambda_1, \lambda_2)$$

$$R_0 = max\left(0, \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_1)} + \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda e \phi \Lambda}{\mu k \delta(\mu+\tau_2)}\right)$$

$$R_0 = \frac{\beta_1 \Lambda \psi}{\mu(\mu+\tau_1)} + \frac{\epsilon_1 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_1)} + \frac{\phi \beta_2 \Lambda}{\mu(\mu+\tau_2)} + \frac{\epsilon_2 \lambda e \phi \Lambda}{\mu k \delta(\mu+\tau_2)}$$

$$R_0 = \frac{k\delta\beta_1 \Lambda \psi + \epsilon_1 \lambda e \Lambda \psi}{\mu k \delta(\mu+\tau_1)} + \frac{k\delta\beta_2 \Lambda \phi + \epsilon_2 \lambda e \Lambda \phi}{\mu k \delta(\mu+\tau_2)}$$

4.7.3 Endemic Equilibrium Point

In this sub-section, we consider a situation in which all the disease states coexist in the equilibrium. We denote ($E^* = S^*, I_s^*, I_a^*, B^*, R^*$) as the endemic equilibrium of the system 4.1. The disease persists in the population called endemic equilibrium point (EEP). Endemic equilibrium points are steady state solutions where the disease cannot be totally eradicated remains but remains in the population. Unlike the disease free equilibrium, an endemic equilibrium point (EEP) is a steady state in which at least one of its coordinates in the infected compartment is non-zero. An endemic equilibrium point exists if and only if it can be obtained by setting each differential equation of the system equals to zero. An endemic equilibrium point exists if and only if $R_0 > 1$ it can be obtained by setting each differential equation of the system equal to zero.

$$\Lambda N - \Pi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu S = 0 \tag{4.2}$$

$$\psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s = 0 \tag{4.3}$$

$$\phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_1 I_a = 0 \tag{4.4}$$

$$\epsilon_1 I_s + \epsilon_2 I_a - \delta B = 0 \tag{4.5}$$

$$\tau_1 I_s + \tau_2 I_a - \mu R = 0 \tag{4.6}$$

From equation 4.3 , we get

$$S^* = \frac{\tau_1 I_s^* + \mu I_s^*}{\psi\left(\frac{\lambda_e B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)} \quad \text{where} \quad m = \frac{\lambda_e B^*}{K+B^*}$$

From equation 4.5:

$$I_s^* = \frac{\delta B^* - \epsilon_2 I_a^*}{\epsilon_1}$$

Expression for S^*:

$$S^* = \frac{\tau_1\left(\frac{\delta B^* - \epsilon_2 I_a^*}{\epsilon_1}\right) + \mu\left(\frac{\delta B^* - \epsilon_2 I_a^*}{\epsilon_1}\right)}{\psi\left(m + \beta_1\left(\frac{\delta B^* - \epsilon_2 I_a^*}{\epsilon_1}\right) + \beta_2 I_a^*\right)}$$

For the expressions based on equation 4.4:
Initial expression for S^*:

$$S^* = \frac{\tau_2 I_a^* + \mu I_a^*}{\phi\left(m + \beta_1 I_s^* + \beta_2 I_a^*\right)}$$

Substitute $I_s^* = \frac{\delta B^* - \epsilon_2 I_a^*}{\epsilon_1}$:

$$S^* = \frac{\tau_2 I_a^* + \mu I_a^*}{\phi\left(m + \beta_1\left(\frac{\delta B^* - \epsilon_2 I_a^*}{\epsilon_1}\right) + \beta_2 I_a^*\right)}$$

Final expression for S^*:

$$S^* = S^*$$

$$\frac{\tau_1\left(\delta B^* - \varepsilon_2 I_a^*\right) + \mu\left(\delta B^* - \varepsilon_2 I_a^*\right)}{\psi\left(m\varepsilon_1 + \beta_1\left(\delta B^* - \varepsilon_2 I_a^*\right) + \varepsilon_1\beta_2 I_a^*\right)} = \frac{\varepsilon_1\left(\tau_2 I_a^* + \mu I_a^*\right)}{\phi\left(m\varepsilon_1 + \beta_1\left(\delta B^* - \epsilon_2 I_a^*\right) + \epsilon_1\beta_2 I_a^*\right)}$$

$$\frac{\tau_1\delta B^* - \tau_1\varepsilon_2 I_a^* + \mu\delta B^* - \mu\varepsilon_2 I_a^*}{\psi m\varepsilon_1 + \psi\beta_1\delta B^* - \psi\beta_1\varepsilon_2 I_a^* + \psi\varepsilon_1\beta_2 I_a^*} = \frac{\varepsilon_1\tau_2 I_a^* + \varepsilon_1\mu I_a^*}{\phi m\varepsilon_1 + \phi\beta_1\delta B^* - \phi\beta_1\varepsilon_2 I_a^* + \phi\varepsilon_1\beta_2 I_a^*}$$

Where a_0, a_1, and a_2:

$$a_0 = \tau_1 \delta B^* + \mu \delta B^*$$

$$a_1 = \psi m \varepsilon_1 + \Psi \beta_1 \delta B^*$$

$$a_2 = \varphi m \varepsilon_1 + \phi \beta_1 \delta B^*$$

Then the modified equation using a_0, a_1, and a_2 becomes:

$$\frac{a_0 - I_a^*(\tau_1 \varepsilon_2 + \mu \varepsilon_2)}{a_1 - I_a^*(\Psi \beta_1 \varepsilon_2 - \psi \varepsilon_1 \beta_2)} = \frac{I_a^*(\varepsilon_1 \tau_2 + \varepsilon_1 \mu)}{a_2 - I_a^*(\phi \beta_1 \varepsilon_2 - \phi \varepsilon_1 \beta_2)}$$

$$(a_0 - I_a^*(a_3))\,(a_2 - I_a^*(a_4)) = I_a^*(a_5)\,(a_1 - I_a^*(a_6))$$

Where a_3, a_4, a_5, and a_6:

$$a_3 = \tau_1 \epsilon_2 + \mu \varepsilon_2$$

$$a_4 = \phi \beta_1 \epsilon_2 - \phi \epsilon_1 \beta_2$$

$$a_5 = \epsilon_1 \tau_2 + \epsilon_1 \mu$$

$$a_6 = \psi \beta_1 \epsilon_2 - \psi \epsilon_1 \beta_2$$

$$a_0 a_2 - a_0 a_4 I_a^* - a_2 a_3 I_a^* + a_3 a_4 (I_a^*)^2 = a_1 a_5 I_a^* - a_5 a_6 (I_a^*)^2$$

$$(a_3 a_4 + a_5 a_6)(I_a^*)^2 - (a_0 a_4 + a_2 a_3 + a_1 a_5) I_a^* + a_0 a_2 = 0$$

$$I_a^* = \frac{a_0 a_4 + a_2 a_3 + a_1 a_5 \pm \sqrt{(a_0 a_4 + a_2 a_3 + a_1 a_5)^2 - 4\,(a_3 a_4 + a_5 a_6)\,(a_0 a_2)}}{2\,(a_3 a_4 + a_5 a_6)}$$

$$I_a^* = \frac{C \pm \sqrt{C^2 - 4ED}}{2D}$$

Where C, D, and E are:

$$C = a_0 a_4 + a_2 a_3 + a_1 a_5$$

$$D = a_3 a_4 + a_5 a_6$$

$$E = a_0 a_2$$

Substitute equation 4.4 in to 4.3

$$I_s^* = \frac{\delta B^* - \varepsilon_2 I_a^*}{\varepsilon_1}$$

$$I_s^* = \frac{2\delta B^*(a_3a_4 + a_5a_6) - \varepsilon_2\left(a_0a_4 + a_2a_3 + a_1a_5 \pm \sqrt{(a_0a_4 + a_2a_3 + a_1a_5)^2 - 4a_0a_2(a_3a_4 + a_5a_6)}\right)}{2\varepsilon_1(a_3a_4 + a_5a_6)}$$

$$\text{Where} \qquad C = a_0a_4 + a_2a_3 + a_1a_5$$

$$D = a_3a_4 + a_5a_6$$

$$E = a_0a_2$$

$$I_s^* = \frac{2\delta B^* D - \varepsilon_2\left(C \pm \sqrt{C^2 - 4ED}\right)}{2\varepsilon_1 D}$$

substitute equation 4.3 and 4.4 in to 4.6

$$R^* = \frac{\tau_1 I_s^* + \tau_2 I_a^*}{\mu}$$

$$R^* = \frac{2\tau_1\delta B^* D - \tau_1\varepsilon_2 C \pm \tau_1\varepsilon_2\sqrt{C^2 - 4ED} + \tau_2\varepsilon_1 C \pm \tau_2\varepsilon_1\sqrt{C^2 - 4ED}}{2\mu\varepsilon_1 D}$$

Substitute equation 4.3 and 4.4 in to 4.1

$$S^* = \frac{\Lambda N}{(m + \beta_1 I_s^* + \beta_2 I_a^* + \mu)\pi}$$

$$S^* = \frac{2\Lambda N\varepsilon_1 D}{\left(2\varepsilon_1 Dm + \beta_1\left(2\delta B^* D - \varepsilon_2\left(C \pm \sqrt{C^2 - 4ED}\right)\right) + \beta_2\varepsilon_1\left(C \pm \sqrt{C^2 - 4ED}\right) + 2\mu\varepsilon_1 D\right)\pi}$$

4.8 Stability Analysis of Equilibrium Point

4.8.1 Local Stability of the Disease Free Equilibrium Point

In this section we investigate the local stability of the DFE. local stability is concerned with the behavior of the model solution near an equilibrium point. Mathematically the stability of equilibrium can be analyzed using the linearized system at the equilibrium or in other words the Jacobean matrix of first derivative of the right hand side of the differential equation of system 3.1 .

Theorem 4.8.1. *For a disease transmission model (4.1), the disease free equilibrium point E_o is locally asymptotically stable if $R_0 < 1$ but unstable if $R_0 > 1$.*

Proof: It is enough to show that disease free equilibrium point of our system is stable if and only if trace and determinant of Jacobean matrix at (E_0) are negative and positive respectively. Our Jacobean matrix evaluated at disease free equilibrium point is given by:

$$\mathbf{J(E_0)} = \begin{bmatrix} \frac{\partial F_1}{\partial S} & \frac{\partial F_1}{\partial I_s} & \frac{\partial F_1}{\partial I_a} & \frac{\partial F_1}{\partial B} & \frac{\partial F_1}{\partial R} \\ \frac{\partial F_2}{\partial S} & \frac{\partial F_2}{\partial I_s} & \frac{\partial F_2}{\partial I_a} & \frac{\partial F_2}{\partial B} & \frac{\partial F_2}{\partial R} \\ \frac{\partial F_3}{\partial S} & \frac{\partial F_3}{\partial I_s} & \frac{\partial F_3}{\partial I_a} & \frac{\partial F_3}{\partial B} & \frac{\partial F_3}{\partial R} \\ \frac{\partial F_4}{\partial S} & \frac{\partial F_4}{\partial I_s} & \frac{\partial F_4}{\partial I_a} & \frac{\partial F_4}{\partial B} & \frac{\partial F_4}{\partial R} \\ \frac{\partial F_5}{\partial S} & \frac{\partial F_5}{\partial I_s} & \frac{\partial F_5}{\partial I_a} & \frac{\partial F_5}{\partial B} & \frac{\partial F_5}{\partial R} \end{bmatrix}$$

$$|J(E_0)| = \begin{bmatrix} -\mu & \frac{-\pi\beta_1\Lambda}{\mu} & \frac{-\pi\beta_2\Lambda}{\mu} & \frac{-\pi\Lambda\epsilon\Lambda}{\mu K} & 0 \\ 0 & \frac{\beta_1\psi\Lambda}{\mu} - (\tau_1+\mu) & \frac{\beta_2\psi\Lambda}{\mu} & \frac{\beta_2\psi\lambda_e}{\mu K} & 0 \\ 0 & \frac{\beta_1\phi\Lambda}{\mu} & \frac{\beta_2\phi\Lambda}{\mu} - (\tau_2+\mu) & 0 & 0 \\ 0 & \epsilon_1 & \epsilon_2 & -\delta & 0 \\ 0 & \tau_1 & \tau_2 & 0 & -\mu \end{bmatrix} = 0$$

This Jacobian matrix can be written as :

$$\begin{vmatrix} -\mu-\lambda & \frac{-\pi\beta_1\Lambda}{\mu} & \frac{-\pi\beta_2\Lambda}{\mu} & \frac{-\pi\Lambda\epsilon\Lambda}{\mu K} & 0 \\ 0 & \frac{\beta_1\phi\Lambda}{\mu} - (\tau_1+\mu) - \lambda & \frac{\beta_2\psi\Lambda}{\mu} & \frac{\beta_2\psi\lambda_e}{\mu} & 0 \\ 0 & \frac{\beta_1\phi\Lambda}{\mu} & \frac{\beta_2\phi\Lambda}{\mu} - (\tau_2+\mu) - \lambda & \frac{\beta_2\phi\lambda_e}{\mu} & 0 \\ 0 & \epsilon_1 & \epsilon_2 & -\delta-\lambda & 0 \\ 0 & \tau_1 & \tau_2 & 0 & -\mu-\lambda \end{vmatrix} = 0$$

$$\begin{vmatrix} -\mu-\lambda & -K_1 & -K_2 & -K_3 & 0 \\ 0 & \psi K_1 - K_4 - \lambda & \psi K_2 & \psi K_3 & 0 \\ 0 & \phi K_1 & \phi K_2 - K_5 - \lambda & \phi K_3 & 0 \\ 0 & \epsilon_1 & \epsilon_2 & -\delta-\lambda & 0 \\ 0 & \tau_1 & \tau_2 & 0 & -\mu-\lambda \end{vmatrix} = 0$$

where $K_1 = \dfrac{\pi\beta_1\Lambda}{\mu}, \quad K_2 = \dfrac{\pi\beta_2\Lambda}{\mu}, \quad K_3 = \dfrac{\pi\lambda_e\Lambda N}{\mu K}, \quad K_4 = \tau_1 + \mu, \quad K_5 = \tau_2 + \mu$

$$\text{Hence} \quad (-\mu-\lambda)\begin{vmatrix} -\psi K_1 - K_4 - \lambda & -\psi K_2 & -\psi K_3 \\ -\phi K_1 & -\phi K_2 - K_5 - \lambda & -\phi K_3 \\ \epsilon_1 & \epsilon_2 & -\delta-\lambda \end{vmatrix} = 0$$

$$(-\mu-\lambda)(-\mu-\lambda)\begin{vmatrix} -\psi K_1 - K_4 - \lambda & -\psi K_2 & -\psi K_3 \\ -\phi K_1 & -\phi K_2 - K_5 - \lambda & -\phi K_3 \\ \epsilon_1 & \epsilon_2 & -\delta-\lambda \end{vmatrix} = 0$$

$$(-\mu-\lambda)(-\mu-\lambda)\left(-\psi K_1-K_4-\lambda\right)\begin{vmatrix}-\phi K_2-K_5-\lambda & -\phi K_3\\ \epsilon_2 & -\delta-\lambda\end{vmatrix}+\psi K_2\begin{vmatrix}-\phi K_1 & -\phi K_3\\ \epsilon_1 & -\delta-\lambda\end{vmatrix}$$

$$-\psi K_3\begin{vmatrix}-\phi K_1 & -\phi K_2-\lambda\\ \epsilon_1 & \epsilon_2\end{vmatrix}=0$$

Hence, $\lambda_{1,2}=-\mu<0$.

The parameter value μ is positive. From the above equation, we conclude that the eigenvalues $\lambda_{1,2}$ are real, distinct, and negative.

$$-\psi\phi K_1K_2\delta-\psi\phi K_1K_2\lambda-\psi K_1K_5\delta-\psi K_1\lambda^2-\psi\phi K_1K_3\epsilon_2-\phi K_2K_4\delta-\phi K_2K_4\lambda-K_4K_5\delta-K_4\lambda^2$$

$$-\phi K_3K_4\epsilon_2-\phi K_2\delta\lambda-\phi K_2\lambda^2-K_5\delta\lambda-\lambda^3-\phi K_3\epsilon_2\lambda+\psi\phi K_1K_2\delta+\psi\phi K_1K_2\lambda$$

$$+\psi\phi K_2K_3\epsilon_1+\psi\phi K_1K_3\epsilon_2-\psi\phi K_2K_3\epsilon_1-\psi K_3\epsilon_1\lambda=0$$

$$-\lambda^3+(-\psi K_1-\phi K_2-K_4)\lambda^2+(-\psi\phi K_1K_2-\phi K_2K_4-\phi K_2\delta-K_5\delta-\phi K_3\epsilon_2$$

$$+\psi\phi K_1K_2-\psi K_3\epsilon_1)\lambda+(-\psi\phi K_1K_2\delta-\psi K_1K_5\delta-\psi\phi K_1K_3\epsilon_2-\phi K_2K_4\delta-K_4K_5\delta-\phi K_3K_4\epsilon_2$$

$$+\psi\phi K_1K_2\delta+\psi\phi K_2K_3\epsilon_1+\psi\phi K_1K_3\epsilon_2-\psi\phi K_2K_3\epsilon_1)=0$$

$$-\lambda^3-(\psi K_1+\phi K_2+K_4)\lambda^2-(\psi\phi K_1K_2+\phi K_2K_4+\phi K_2\delta+K_5\delta+\phi K_3\epsilon_2-\psi\phi K_1K_2+\psi K_3\epsilon_1)\lambda$$

$$-(\psi\phi K_1K_2\delta+\psi K_1K_5\delta+\psi\phi K_1K_3\epsilon_2+\phi K_2K_4\delta+K_4K_5\delta+\phi K_3K_4\epsilon_2$$

$$+\psi\phi K_2K_3\epsilon_1-\psi\phi K_1K_2\delta-\psi\phi K_2K_3\epsilon_1-\psi\phi K_1K_3\epsilon_2)=0$$

Consider the characteristic equation:

$$\lambda^3+(\psi K_1+\phi K_2+K_4)\lambda^2+(\psi\phi K_1K_2+\phi K_2K_4+\phi K_2\delta+K_5\delta+\phi K_3\epsilon_2-\psi\phi K_1K_2+\psi K_3\epsilon_1)\lambda$$

$$+(\psi\phi K_1K_2\delta+\psi K_1K_5\delta+\psi\phi K_1K_3\epsilon_2+\phi K_2K_4\delta+K_4K_5\delta+\phi K_3K_4\epsilon_2+\psi\phi K_2K_3\epsilon_1-\psi\phi K_1K_2\delta$$

$$-\psi\phi K_2K_3\epsilon_1-\psi\phi K_1K_3\epsilon_2)=0$$

Consider the polynomial:

$$P(K) = \lambda^n + a_1\lambda^{n-1} + a_2\lambda^{n-2} + \cdots + a_k$$

where $a_i > 0$ and the coefficients a_i are real constants for $i = 1, 2, \ldots, k$.

The k Hurwitz matrices, defined using the coefficients a_i of the characteristic polynomial, are given by the following structure .

1. First Hurwitz matrix H_1:

$$H_1 = \begin{bmatrix} a_1 \end{bmatrix}$$

2. Second Hurwitz matrix H_2:

$$H_2 = \begin{bmatrix} a_1 & 1 \\ 0 & a_2 \end{bmatrix}$$

3. Third Hurwitz matrix H_3:

$$H_3 = \begin{bmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & 0 & a_3 \end{bmatrix}$$

For polynomial of degree K=2, 3 ,4 and 5 the Routh –Hurwith criteria are summarized as :

For $K = 2$:

$$a_1 > 0, \quad a_2 > 0, \quad \text{and} \quad a_1 a_2 > 0$$

For $K = 3$:

$$a_1 > 0, \quad a_3 > 0, \quad \text{and} \quad a_1 a_2 > a_3$$

By Routh-Hurwitz criteria for order polynomial leads to n= 3 ; the coefficient of the characteristics polynomial $p(\lambda)$ are

$a_1 = \psi k_1 + \phi K_2 + K_4$

$$a_2 = \psi\phi K_1 K_2 + \phi k_2 K_4 + \phi K_2\delta + K_5\delta + \phi K_3\epsilon_2 + \psi K_3\epsilon_1 - \psi\phi K_1 K_2$$

$$a_3 = \psi\phi K_1 K_2\delta + \psi K_1 K_5\delta + \psi\phi k_1 K_3\epsilon_2 + \phi k_2 K_4\delta + K_4 K_5\delta + \phi K_3 K_4\epsilon_2$$
$$+\psi\phi K_2 K_3\epsilon_1 - \psi\phi K_1 K_2\delta - \psi\phi K_2 K_3\epsilon_1 - \psi\phi K_1 K_3\epsilon_2$$

Using the characteristics polynomial representation the matrix is given by

$$H_1 = [a_1], \quad \det(H_1) = a_1 > 0$$

$$H_2 = \begin{bmatrix} a_1 & 1 \\ 0 & a_2 \end{bmatrix}, \quad \det(H_2) = a_1 a_2 > 0 \quad \text{if } a_1 > 0 \text{ and } a_2 > 0$$

$$H_3 = \begin{bmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & 0 & a_3 \end{bmatrix}, \quad \det(H_3) = (a_1 a_2 - a_3) > 0 \quad \text{if } a_i > 0,\ i = 1, 2, 3 \text{ and } a_1 a_2 > a_3$$

By Routh –Hurtwize criteria the determinant of Hurtwith matrix (H_3) becomes positive if the following conditions hold true

$$a_1 > 0, \quad a_2 > 0, \quad a_3 > 0, \quad a_1 a_2 > a_3$$

$$a_1 > 0, \quad \psi k_1 + \phi k_2 + k_4 > 0$$

$$a_2 > 0, \quad \psi\phi k_1 k_2 + \phi k_2 k_4 + \phi k_2 \delta + k_5 \delta + \phi k_3 \epsilon_2 + \psi k_3 \epsilon_1 - \psi\phi k_1 k_2 > 0$$

$$a_3 > 0, \quad \psi\phi k_1 k_2 \delta + \psi k_1 k_5 \delta + \psi\phi k_1 k_3 \epsilon_2 + \phi k_2 k_4 \delta + k_4 k_5 \delta + \phi k_3 k_4 \epsilon_2$$

$$+\psi\phi k_2 k_3 \epsilon_1 - \psi\phi k_1 k_2 \delta - \psi\phi k_2 k_3 \epsilon_1 - \psi\phi k_1 k_3 \epsilon_2 > 0$$

All the roots of polynomial equation are negative or have negative real part for a_1 , a_2 and a_3 holds and similar using the same procedure $a_1 a_2 > a_3$. We can deduced from this if $R_0 < 1$ the disease free equilibrium stability of the model is stable ,where as if $R_0 > 1$ it is unstable and then from the parameters of our model $R_0 < 1$. when all condition for a_1 , a_2 and a_3 holds and similar using the same procedure $a_1 a_2 > a_3$. Thus , the disease free equilibrium point $E^0 = \left(\frac{\Lambda N}{\mu}, 0, 0, 0, 0\right)$ is locally asymptotically stable.

4.8.2 Global Stability of the Disease free Equilibrium Point(DFE)

To investigate the global stability of the disease free equilibrium point E0, local stability is concerned with the behavior of the model solution near an equilibrium point , while the global stability can describe solution behavior in the whole domain that is in the region from the system . We will use castilo- chavez theorem to prove the global stability of the disease free equilibrium point (DFE).

Theorem 4.8.2. *The DFE of the model equation (4.1) is globally asymptotically stable if $R_0 < 1$ but unstable if $R_0 > 1$.*

Proof: To establish the global stability of the DFE, the two condition for the global

stability of DFE as in [2], for $R_0 < 1$ is used for the equations of model system 4.1 in the following way .

.If $R_0 < 1$,then the following conditions (1) and (2) below must be satisfied to guarantee globally asymptotically stable.

1. For $\frac{dh_1}{dt} = F(h_1, 0)$, globally asymptotically stable.
2. For $\frac{dh_2}{dt} = G(h_1, h_2)$ $G(h_1, h_2) = Ah_2 - \hat{G}(h_1, h_2) \geq 0 \in \Omega$.

Where $h_1 = (S, R) \in \mathbb{R}^{+2}$ represents the class of non-infected individuals and $h_2 = (I_s, I_a, B) \in \mathbb{R}^{+3}$ represents the class of infected individuals.

The equilibrium state is :

$$E0 = \left(\frac{\Lambda N}{\mu}, 0, 0, 0, 0\right)$$

From the model system 4.1

$$\frac{dh_1}{dt} = F(h_1, h_2) = \begin{pmatrix} \Lambda N - \Pi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu S \\ \tau_1 I_s + \tau_2 I_a - \mu R \end{pmatrix}$$

$$\frac{dh_2}{dt} = G(h_1, h_2) = \begin{pmatrix} \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s \\ \\ \phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_2 I_a \\ \\ \epsilon_1 I_s + \epsilon_2 I_a - \delta B \end{pmatrix}$$

1. To show E_0 is globally asymptotically stable for the system $\frac{dh_1}{dt} = F(h_1, 0)$.

   $\frac{dS}{dt} = F(h_1, 0)$

   $\frac{dS}{dt} = \Lambda N - \mu S$ by using separation method we can get

   $S(t) = \frac{\Lambda N}{\mu} - \frac{S(0)e^{\frac{-t}{\mu}}}{\mu}$, as t approaches to ∞

   S(t) $= \frac{\Lambda N}{\mu} \geq 0$

   $\frac{dR}{dt} = -\mu R$ by using separation method we can obtain

   $R(t) = e^{-\mu t}$, as t approaches to ∞

   R(t) approaches to 0

   Hence

   $$\{S(t), R(0), 0\} = \{\frac{\Lambda N}{\mu}, 0, 0\} = E_0$$

   Therefore E_0 is globally asymptotically stable.

2. We want to show that $G(h_1, h_2) = Ah_2 - \hat{G}(h_1, h_2) \geq 0 \in \Omega$. ,where A is a metzler matrix (whose off diagonal elements are non negatives) , Ω is a region where the model makes biological sense .

$$A = \frac{\partial G}{\partial h_2}(E_0, 0) = \begin{bmatrix} \frac{\partial I_s}{\partial I_s} & \frac{\partial I_s}{\partial I_a} & \frac{\partial I_s}{\partial B} \\ \frac{\partial I_a}{\partial I_s} & \frac{\partial I_a}{\partial I_a} & \frac{\partial I_a}{\partial B} \\ \frac{\partial B}{\partial I_s} & \frac{\partial B}{\partial I_a} & \frac{\partial B}{\partial B} \end{bmatrix} = \begin{bmatrix} \psi\beta_1 S^* - \mu - \tau_1 & \psi\beta_2 S* & \frac{\psi\lambda_e S*}{(K+B)^2} \\ \phi\beta_1 S* & \phi\beta_2 S^* - \mu - \tau_2 & \frac{\phi\lambda_e S*}{(K+B)^2} \\ \epsilon_1 & \epsilon_2 & -\delta \end{bmatrix}$$

$G(h_1, h_2) = Ah_2 - \hat{G}(h_1, h_2)$ which is

$$\begin{aligned} \hat{G}(h_1, h_2) &= Ah_2 - G(h_1, h_2) \\ &= \begin{bmatrix} \psi\beta_1 S^* - \mu - \tau_1 & \psi\beta_2 S* & \frac{\psi\lambda_e S*}{(K+B)^2} \\ \phi\beta_1 S* & \phi\beta_2 S^* - \mu - \tau_2 & \frac{\phi\lambda_e S*}{(K+B)^2} \\ \epsilon_1 & \epsilon_2 & -\delta \end{bmatrix} \begin{bmatrix} I_s \\ I_a \\ B \end{bmatrix} \\ &- \begin{bmatrix} \psi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_s - \tau_1 I_s \\ \\ \phi\left(\lambda_e S\frac{B}{K+B} + \beta_1 I_s S + \beta_2 I_a S\right) - \mu I_a - \tau_2 I_a \\ \\ \epsilon_1 I_s + \epsilon_2 I_a - \delta B \end{bmatrix} \\ &= \begin{bmatrix} \frac{\psi K\lambda_e S^0}{(K+B)^2} - \frac{\psi\lambda_e S^0}{(K+B)} \\ \frac{\phi K\lambda_e S^0}{(K+B)^2} - \frac{\phi\lambda_e S^0}{(K+B)} \end{bmatrix} \\ \hat{G}(h_1, h_2) &= \begin{bmatrix} \frac{\psi\lambda_e S^0}{(K+B)}\left(\frac{K}{(K+B)} - 1\right) \\ \\ \frac{\phi\lambda_e S^0}{(K+B)}\left(\frac{K}{(K+B)} - 1\right) \end{bmatrix} \\ &= \left(\frac{K}{(K+B)} - 1\right) \begin{bmatrix} \frac{\psi\lambda_e S^0}{(K+B)} \\ \\ \frac{\phi\lambda_e S^0}{(K+B)} \end{bmatrix} \end{aligned}$$

If $\left(\frac{K}{(K+B)} - 1\right) \geq 0$, implies that $B \leq 0$

Then $\hat{G}(h_1, h_2) = \left(\frac{K}{(K+B)} - 1\right) \begin{bmatrix} \frac{\psi\lambda_e S^0}{(K+B)} \\ \\ \frac{\phi\lambda_e S^0}{(K+B)} \end{bmatrix} \geq 0$ which implies that condition 2 holds true .

Therefore , by Castillo – chavez theorem the disease free equilibrium point of the system is globally asymptotically stable for $R_0 < 1$.

4.8.3 Local Stability Analysis of Endemic Equilibrium Eoints(EEP)

We analyze the stability of the disease present —Endemic equilibrium point by linearizing the system of differential equations to get the Jacobian matrix . The Jacobian matrix is computing each equation of system 4.1 with respect to the state variables with respect to the state variables . The local stability of is determined by considering the sign of the eignvalues of the Jacobian matrix system 4.1 and finally , we will use routh- Hurwith stability criteria , which is used to determined asymptotic stability of equilibrium point for a non – linear system of ordinary differential equations .

Theorem 4.8.3. *The positive Endemic equilibrium point of system 4.1 is locally asymptotically stable if R_0 ¿ 1 , otherwise unstable .*

Proof stability of E^* of the model system is determined based on the signs of the eigenvalue of the Jacobian matrix . The Jacobian matrix of system 4.1 around the endemic equilibrium is given by

$$\mathbf{J}(\mathbf{E}^*) = \begin{bmatrix} \frac{\partial F_1}{\partial S} & \frac{\partial F_1}{\partial I_s} & \frac{\partial F_1}{\partial I_a} & \frac{\partial F_1}{\partial B} & \frac{\partial F_1}{\partial R} \\ \frac{\partial F_2}{\partial S} & \frac{\partial F_2}{\partial I_s} & \frac{\partial F_2}{\partial I_a} & \frac{\partial F_2}{\partial B} & \frac{\partial F_2}{\partial R} \\ \frac{\partial F_3}{\partial S} & \frac{\partial F_3}{\partial I_s} & \frac{\partial F_3}{\partial I_a} & \frac{\partial F_3}{\partial B} & \frac{\partial F_3}{\partial R} \\ \frac{\partial F_4}{\partial S} & \frac{\partial F_4}{\partial I_s} & \frac{\partial F_4}{\partial I_a} & \frac{\partial F_4}{\partial B} & \frac{\partial F_4}{\partial R} \\ \frac{\partial F_5}{\partial S} & \frac{\partial F_5}{\partial I_s} & \frac{\partial F_5}{\partial I_a} & \frac{\partial F_5}{\partial B} & \frac{\partial F_5}{\partial R} \end{bmatrix}$$

$$J(E^*) = \begin{pmatrix} -\pi(\lambda_e \frac{B}{K+B^*} + \beta_1 I^* + \beta_2 I^*) - \mu & -n\pi S^* & -n\pi S^* & 0 \\ \psi(\lambda_e \frac{B}{K+B^*} + \beta_1 I^* + \beta_2 I^*) & \psi B S^* - \tau_1 - \mu & \psi B S^* & 0 \\ \phi(\lambda_e \frac{B}{K+B^*} + \beta_1 I^* + \beta_2 I^*) & \phi B S^* & \phi B S^* - \tau_2 - \mu & 0 \\ 0 & 0 & 0 & -\mu \end{pmatrix}$$

Where $a = \pi(\lambda_e \frac{B}{K+B^*} + \beta_1 I^* + \beta_2 I^*) - \mu$, $b = n\pi B S^*$, $c = n\pi B S^*$, $d = -n\frac{\delta K S^*}{(K+B^*)^2}$. After some computation, the characteristic polynomial of the Jacobian matrix at $J(E^*)$ is given by

$$J(E^*) = \begin{vmatrix} -a & -b & -c & -d & 0 \\ e & f & g & h & 0 \\ I & J & K & L0 & \\ 0 & \epsilon_1 & \epsilon_2 & -\delta & 0 \\ 0 & \tau_1 & \tau_2 & 0 & -\mu \end{vmatrix}$$

Where $e = \psi(\lambda_e \frac{B}{K+B^*} + \beta_1 I^* + \beta_2 I^*)$, $f = \psi B S^* - \tau_1 - \mu$, $g = \psi B S^*$, $h = -\frac{\delta K S^*}{(K+B^*)^2}$.

$$\lambda = \phi(\lambda_e \frac{B}{K+B^*} + \beta_1 I^* + \beta_2 I^*), J = \phi B S^*, K = \phi \frac{B S^*}{K+B^*} - \tau_2 - \mu, L = \frac{\phi \delta K S^*}{(K+B^*)^2}$$

The characteristic polynomial of the Jacobian matrix at E^* is given by $|J(E^*) - \lambda I| = 0$, where I is the Identity matrix and λ is the eigenvalue of the Jacobian matrix.

$$J(E^*) = \begin{vmatrix} -a-\lambda & -b & -c & -d & 0 \\ e & f-\lambda & g & h & 0 \\ I & J & K-\lambda & L0 & \\ 0 & \epsilon_1 & \epsilon_2 & -\delta-\lambda & 0 \\ 0 & \tau_1 & \tau_2 & 0 & -\mu-\lambda \end{vmatrix} = 0$$

Therefore , we have to show all the eigenvalues of the Jacobean matrix at E^* are negative . The fifth column contain only the diagonal term , which form the one eigenvalue . i.e $-(\mu + \lambda) = 0$, $\lambda = -\mu$. The other four eigenvalues can be obtained form the sub – matrix of $J(E*)$ by excluding the fifth column and row the new sub- matrix becomes:

$$\begin{vmatrix} -a-\lambda & -b & -c & -d \\ e & f-\lambda & g & h \\ I & J & K-\lambda & L \\ 0 & \epsilon_1 & \epsilon_2 & -\delta-\lambda \end{vmatrix} = 0$$

$$(-a-\lambda)\begin{vmatrix} f-\lambda & g & h \\ J & K-\lambda & L \\ \epsilon_1 & \epsilon_2 & -\delta-\lambda \end{vmatrix} + b\begin{vmatrix} e & g & h \\ I & K-\lambda & L \\ 0 & \epsilon_2 & -\delta-\lambda \end{vmatrix} - c\begin{vmatrix} e & f-\lambda & h \\ I & J & L \\ 0 & \epsilon_1 & -\delta-\lambda \end{vmatrix}$$

$$+d\begin{vmatrix} e & f-\lambda & g \\ I & J & K-\lambda \\ 0 & \epsilon_1 & \epsilon_2 \end{vmatrix} = 0$$

$$(-a-\lambda)\left((f-\lambda)\begin{vmatrix} K-\lambda & L \\ \epsilon_2 & -\delta-\lambda \end{vmatrix}\right) + b\left((e)\begin{vmatrix} K-\lambda & L \\ \epsilon_2 & -\delta-\lambda \end{vmatrix}\right) - c\left((e)\begin{vmatrix} J & L \\ \epsilon_1 & -\delta-\lambda \end{vmatrix}\right)$$

$$+d\left((e)\begin{vmatrix} J & K-\lambda \\ \epsilon_1 & \epsilon_2 \end{vmatrix}\right) = 0$$

$$(-a-\lambda)\left((f-\lambda)(k-\lambda)(-\delta-\lambda) - L\epsilon_2\right) + b\left((e)(k-\lambda)(-\delta-\lambda) - L\epsilon_2\right) - c\left((e)(J(-\delta-\lambda) - L\epsilon_1\right)$$

$$+d\left((e)(J\epsilon_2 - \epsilon_1(K-\lambda))\right) = 0$$

After some simplification, we have the following characteristics equation :

$$P(\lambda) = \lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4$$

$$\begin{aligned}
\text{Where} \quad a &= \pi\left(\frac{\lambda e B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right) - \mu, \\
b &= \pi\beta_1 S^*, \\
c &= \pi\beta_2 S^*, \\
d &= \frac{-\pi\lambda_e K S^*}{(K+B^*)^2}, \\
e &= \Psi\left(\frac{\lambda_e B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right), \\
f &= \Psi\beta_1 S^* - \tau_1 - \mu, \\
g &= \psi\beta_2 S^*, \\
h &= \frac{\psi\lambda_e K S^*}{(K+B^*)^2}, \\
I &= \frac{\lambda_e B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*, \\
J &= \phi\beta_1 S^*, \\
K &= \phi\beta_1 S^* - \tau_2 - \mu, \\
L &= \frac{\phi\lambda e K S^*}{(K+B^*)^2}.
\end{aligned}$$

$$\begin{aligned}
\text{Therefore} \quad a_1 &= a + \delta - k - f, \\
a_2 &= a\delta + fk + \varepsilon_1 h + be + CI - ak - af - k\delta - L\varepsilon_2 - f\delta - gJ, \\
a_3 &= afk + fL\varepsilon_2 + J\varepsilon_2 h + be\delta + bgI + ceJ + cI\delta + c^2 I\varepsilon_1 h \\
&\quad + de\varepsilon_1 + dI\varepsilon_2 + fk\delta - ak\delta - aL\varepsilon_2 - af\delta - agJ \\
&\quad - gJ\delta - gL\varepsilon_1 - a\varepsilon_1 h - \varepsilon_1 kh - bek - bI\varepsilon_2 Jh - cfI, \\
a_4 &= afk\delta + afL\varepsilon_2 + akh\varepsilon_1 + bgI\delta + ceJ\delta + ceL\varepsilon_1 \\
&\quad + deJ\varepsilon_2 + dgI\varepsilon_2 - agJ\delta - agL\varepsilon_1 - aJh\varepsilon_2 \\
&\quad - bek\delta - beL\varepsilon_2 - bJ\delta Ih\varepsilon_2 - bILh\varepsilon_1\varepsilon_2 - cfI\delta \\
&\quad - c^2 fIh\varepsilon_1 - dek\varepsilon_1 - dfI\varepsilon_2.
\end{aligned}$$

All the roots of the polynomial $p(\lambda = 0)$ are negative or have negative real parts if and only if the determinants of all Hurwitz matrices are positive . i.e.$det(H_j)$ for all j= 1,2,3,4 . for the above characteristics polynomial , the Hurwitz matrices can be con-

structed using the coefficients a_i , i=1,2,3,4 and its determinant is computed as follow:-

$$H_2 = \begin{vmatrix} a_1 & 0 \\ \\ 1 & a_2 \end{vmatrix}, \quad \det(H_2) = a_1 a_2 > 0 \quad \text{if } a_1 > 0 \text{ and } a_2 > 0.$$

$$H_3 = \begin{vmatrix} a_1 & 0 & 0 \\ 1 & a_2 & 0 \\ 0 & 1 & a_3 \end{vmatrix}, \quad \det(H_3) = a_1 a_2 a_3 > a_3^2.$$

$$H_4 = \begin{vmatrix} a_1 & 0 & 0 & 0 \\ 1 & a_2 & 0 & 0 \\ 0 & 1 & a_3 & 0 \\ 0 & 0 & 1 & a_4 \end{vmatrix}, \quad \det(H_4) = (a_1 a_2 a_3 a_4 - a_3^2) > 0.$$

If $a_i > 0, \quad i = 1, 2, 3, 4, \text{ and } (a_1 a_2 a_3) > a_1^2 a_4 + a_3^2.$

$$\begin{aligned}
a_1 &= a + \delta - (k + f), \\
a_1 &= \pi \left(\frac{\lambda e B^*}{K + B^*} + \beta_1 I_s^* + \beta_2 I_a^* \right) - \mu + \delta - \left(\phi \beta_1 S^* - \tau_2 - \mu + \psi \beta_1 S^* - \tau_1 - \mu \right), \\
a_1 &= \pi \left(\frac{\lambda e B^*}{K + B^*} + \beta_1 I_s^* + \beta_2 I_a^* \right) + \delta - (\phi \beta_1 S^* - \tau_2 + \psi \beta_1 S^* - \tau_1 - \mu) > 0, \\
&\text{if and only if} \quad \pi \left(\frac{\lambda e B^*}{K + B^*} + \beta_1 I_s^* + \beta_2 I_a^* \right) + \delta > \phi \beta_1 S^* - \tau_2 + \psi \beta_1 S^* - \tau_1 - \mu.
\end{aligned}$$

Therefore $a_1 > 0$.

$$\begin{aligned}
a_2 &= a\delta + fk + \epsilon_1 h + be + CI - ak - af - k\delta - L\epsilon_2 - f\delta - gJ, \\
a_2 &= a\delta + fk + \epsilon_1 h + be + CI - (ak + af + k\delta + L\epsilon_2 + f\delta + gJ) \\
a_2 &= \left(\pi \left(\frac{\lambda e B^*}{K + B^*} + \beta_1 I_s^* + \beta_2 I_a^* \right) - \mu \right) \delta + \left(\psi \beta_1 S^* - \tau_1 - \mu \right) \left(\phi \beta_1 S^* - \tau_2 - \mu \right) + \\
&\quad + \frac{(\psi \lambda e K S^*)}{(K + B^*)^2} \epsilon_1 + \\
&\quad + (\pi \beta_1 S^*) \left(\psi \left(\frac{\lambda_e B^*}{K + B^*} + \beta_1 I_s^* + \beta_2 I_a^* \right) \right) + \\
&\quad + (\pi \beta_2 S^*) \left(\phi \left(\frac{\lambda_e B^*}{K + B^*} + \beta_1 I_s^* + \beta_2 I_a^* \right) - \right.
\end{aligned}$$

$$\left[\left(\pi\left(\frac{\lambda eB^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)-\mu\right)\left(\phi\beta_1 S^*-\tau_2-\mu\right)\right]+$$
$$\left[\left(\pi\left(\frac{\lambda eB^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)-\mu\right)\left(\Psi\beta_1 S^*-\tau_1-\mu\right)\right]+$$
$$\left(\phi\beta_1 S^*-\tau_2-\mu\right)\delta+\frac{\left(\phi\lambda eKS^*\right)}{\left(K+B^*\right)^2}\epsilon_2+$$
$$\left(\psi\beta_1 S^*-\tau_1-\mu\right)\delta+\left(\psi\beta_2 S^*\right)\left(\phi\beta_1 S^*\right)>0.$$

If and only if

$$\begin{aligned}
a_2=&\left(\pi\left(\frac{\lambda eB^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)-\mu\right)\delta+\\
&+\left(\Psi\beta_1 S^*-\tau_1-\mu\right)\left(\phi\beta_1 S^*-\tau_2-\mu\right)+\\
&+\frac{\left(\Psi\lambda eKS^*\right)}{\left(K+B^*\right)^2}\epsilon_1+\\
&+\left(\pi\beta_1 S^*\right)\left(\Psi\left(\frac{\lambda eB^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)\right)+\\
&+\left(\pi\beta_2 S^*\right)\left(\phi\left(\frac{\lambda eB^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)\right)\\
&>-2\pi\left(\frac{\lambda_e B^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*+2\mu+\pi\left(\frac{\lambda_e B^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)-\mu\right)\\
&\left(\phi\beta_2 S^*-\tau_2+\psi\beta_1 S^*-\tau_1\right)+\\
&+\left(\phi\beta_2 S^*-\tau_2\right)\delta+\frac{\left(\phi\lambda eKS^*\right)}{\left(K+B^*\right)^2}\epsilon_2+\left(\psi\beta_1 S^*-\tau_1\right)-2\mu\delta+\\
&+\left(\psi\beta_2 S^*\right)\left(\phi\beta_1 S^*\right).
\end{aligned}$$

There fore $a_2>0$

$$\begin{aligned}
a_3=&afkfLe_2+bek+bgl+ceI+cJ\delta+c^2l_2h+dee_1+dle_2+fk\delta\\
&-ak\delta-aLe_2afg-agJ-gLe_1-a\varepsilon_1 h-\varepsilon_1 kh-bek-ble_2h-cfl\\
a_3=&afkfLe_2+bek+bgl+cel\delta+c^2l_2h+dee_1+dle_2fk\delta\\
&-(ak\delta+Le_2afgagJ+gLe_1+\varepsilon_1 h\delta h+bekble_2hcfl).\\
a_3=&\,\pi\left(\lambda e\frac{B^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)-\mu\times\left(\psi\beta_1 S^*-\tau_1-\mu\right)\left(\phi\beta_1 S^*-\tau_2-\mu\right)\\
&+\left(\psi\beta_1 S^*-\tau_1-\mu\right)\left(\frac{\phi\lambda eKS^*}{(K+B^*)^2}\right)\varepsilon_2+\left(\phi\beta_1 S^*\right)\left(\frac{\psi\lambda_e KS^*}{(K+B^*)^2}\right)\varepsilon_2\\
&+\left(\pi\beta_1 S^*\right)\left(\psi\left(\lambda e\frac{B^*}{K+B^*}+\beta_1 I_s^*+\beta_2 I_a^*\right)\delta\right)
\end{aligned}$$

$$
\begin{aligned}
&+ (\pi\beta_1 S^*)(\psi\beta_2 S^*)\left(\phi\left(\lambda e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)\right)\\
&+ (\pi\beta_2 S^*)\left(\psi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)(\phi\beta_1 S^*)\right)\\
&+ (\pi\beta_2 S^*)(\phi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)\delta)\\
&+ (\pi\beta_2 S^*)^2\left(\phi\left(\lambda e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)\left(\frac{\psi\lambda_e K S^*}{(K+B^*)^2}\right)\varepsilon_1\right)\\
&+ \left(-\frac{\pi\lambda_e K S^*}{(K+B^*)^2}\right)\left(\psi\left(\lambda e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)\epsilon_1\right)\\
&+ \left(-\frac{\pi\lambda_e K S^*}{(K+B^*)^2}\right)(\phi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)\epsilon_2)\\
&+ (\psi\beta_1 S^* - \tau_1 - \mu)(\phi\beta_1 S^* - \tau_2 - \mu)\delta > \pi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right) - \mu
\end{aligned}
$$

$$
\begin{aligned}
&\times (\phi\beta_1 S^* - \tau_2 - \mu)\delta\\
&+ \pi\left(\lambda e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right) - \mu\\
&\times \left(\frac{\phi\lambda_e K S^*}{(K+B^*)^2}\right)\varepsilon_2\\
&+ \pi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right) - \mu\\
&\times (\psi\beta_1 S^* - \tau_1 - \mu)\delta\\
&+ \pi\left(\lambda e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right) - \mu\\
&\times (\psi\beta_2 S^*)(\phi\beta_1 S^*)\\
&+ (\psi\beta_2 S^*)(\phi\beta_1 S^*)\delta\\
&+ (\psi\beta_2 S^*)\left(\frac{\phi\lambda_e K S^*}{(K+B^*)^2}\right)\varepsilon_1\\
&+ \pi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right) - \mu\\
&\times \left(\frac{\psi\lambda_e K S^*}{(K+B^*)^2}\right)\varepsilon_1
\end{aligned}
$$

$$+ (\phi\beta_1 S^* - \tau_2 - \mu)\left(\frac{\psi\lambda eKS^*}{(K+B^*)^2}\right)\varepsilon_1$$
$$+ (\pi\beta_1 S^*)\left(\psi\left(\lambda e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)(\phi\beta_1 S^* - \tau_2 - \mu)\right)$$
$$+ (\pi\beta_1 S^*)\left(\phi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right)(\phi\beta_1 S^*)\left(\frac{\psi\lambda_e KS^*}{(K+B^*)^2}\right)\varepsilon_2\right)$$
$$+ (\pi\beta_2 S^*)(\psi\beta_1 S^* - \tau_1 - \mu)(\phi\left(\lambda_e\frac{B^*}{K+B^*} + \beta_1 I_s^* + \beta_2 I_a^*\right))$$

Therefore$a_3 > 0$

$$a_4 = afk\delta + afL\epsilon_2 + akh\epsilon_1 + bgI\delta + ceJ\delta + ceL\epsilon_1 + deJ\epsilon_2 + dgI\epsilon_2 - agJ\delta - agL\epsilon_1 - aJh\epsilon_2 - bek\delta - beL\epsilon_2 - bJ\delta Ih\epsilon_2 - bILh\epsilon_1\epsilon_2 - cfI\delta - c^2fIh\epsilon_1 - dek\epsilon_1 - dfI\epsilon_2$$

$$a_4 = afk\delta + afL\epsilon_2 + akh\epsilon_1 + bgI\delta + ceJ\delta + ceL\epsilon_1 + deJ\epsilon_2 + dgI\epsilon_2 > agL\epsilon_1 + aJh\epsilon_2 + bek\delta + beL\epsilon_2 + bJ\delta Ih\epsilon_2 + bILh\epsilon_1\epsilon_2 + cfI\delta + c^2fIh\epsilon_1 + dek\epsilon_1 + dfI\epsilon_2$$

Therefore, $a_4 > 0$

Thus,

$$a_1 > 0,\ a_2 > 0,\ a_3 > 0,\ a_4 > 0,\ a_1a_2 > 0, \text{ and } a_1a_2 > a_3 \qquad (*)$$

Similarly,

$$a_1a_2a_3 - a_3^2 - a_1^2a_4 \text{ if and only if } a_1a_2a_3 > a_3^2 + a_1^2a_4 \qquad (**)$$

Hence, by the Routh–Hurwitz criteria, all roots are real, distinct, and negative. Therefore, the endemic equilibrium point E^* of the model 4.1 is locally asymptotically stable if (* and **) are satisfied other wise unstable .

4.8.4 Sensitivity analysis of R_0 with respect to model parameters

We compute numerical sensitivity indices to enable us to single out parameters that have a high impact on reproduction number and which should to target by intervention strategies. That means it is used to determine the sensitivity parameters of model that take different values and to change in the structure of the model. Sensitivity analysis studies the variation of the out puts of a model caused by variations in the input. Sensitivity analysis tells the researcher which parameters deserve the most numerical attention .The

sensitivity of these parameters is determined by computing the partial derivatives of R_0 with respect to each parameter any time. Given the explicit formula for R_0 we can easily derive an analytical expression for the sensitivity of R_0 with respect to each parameter that comprises R_0 . In order to study the effect of these parameters on R_0 us performed a sensitivity analysis on R_0 with respect to these parameters. The normalized sensitivity index S_x is defined as:

$$S_x = \frac{\partial R_0}{\partial x} \times \frac{x}{R_0}$$

Where x is the parameter of interest, the large the magnitude of the sensitivity index leads to more sensitivity R_0 with respect to those parameters . [9]. First, we start with the analysis of the absolute change. We recall that the basic reproduction number R_0 is given by

$$R_0 = \frac{k\delta\beta_1\Lambda\psi + \epsilon_1\lambda_e\lambda\psi}{\mu k\delta(\mu+\tau_1)} + \frac{k\delta\beta_2\Lambda\phi + \epsilon_2\lambda_e\Lambda\phi}{\mu k\delta(\mu+\tau_2)}$$

If $x = \beta_1$

$$S_{\beta_1} = \frac{\partial R_0}{\partial \beta_1} \times \frac{\beta_1}{R_0} = \left(\frac{\Lambda\psi k\delta}{\mu k\delta(\mu+\tau_1)}\right) \times \frac{\beta_1}{R_0} > 0$$

$$S_{\beta_1} = \left(\frac{\Lambda\psi k\delta}{\mu k\delta(\mu+\tau_1)}\right) \times \frac{\beta_1\mu\delta k(\mu+\tau_1)}{k\delta\beta_1\Lambda\psi} = 1 > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter β_1.(since the basic reproduction number R_0 decreases as β_1 decreases).

If x=β_2

$$S_{\beta_2} = \frac{\partial R_0}{\partial \beta_2} \times \frac{\beta_2}{R_0} = \left(\frac{\Lambda\phi k\delta}{\mu k\delta(\mu+\tau_2)}\right) \times \frac{\beta_2}{R_0} > 0$$

$$S_{\beta_2} = \left(\frac{\Lambda\phi k\delta}{\mu k\delta(\mu+\tau_2)}\right) \times \frac{\beta_2\mu\delta k(\mu+\tau_2)}{k\delta\beta_2\Lambda\phi} = 1 > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter β_2.(since the basic reproduction number R_0 decreases as β_2 decreases).Moreover

$$\lim_{\beta_2 \to 0} R_0 = 0$$

This implies that we can reach the state of no secondary infection if the contact rate between the susceptible populations with asymptomatic infected β_2 significantly decreases up to zero .

If x=Λ

$$S_\lambda = \frac{\partial R_0}{\partial \Lambda} \times \frac{\Lambda}{R_0} = \left(\frac{\beta_1 \psi k\delta + \beta_2 \phi k\delta}{\mu k\delta(\mu + \tau_1)} + \frac{\epsilon_2 \lambda_e}{\mu k\delta(\mu + \tau_2)} \right) \times \frac{\Lambda}{R_0} > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter Λ.(since the basic reproduction number R_0 decreases as Λ decreases).Moreover

$$\lim_{\Lambda \to 0} R_0 = 0.$$

If x=τ_2

$$S_{\tau_2} = \frac{\partial R_0}{\partial \tau_2} \times \frac{\tau_2}{R_0} = -\left(\frac{\beta_2 \Lambda \phi k\delta + \epsilon_2 \Lambda \lambda_e}{\mu k\delta(\mu + \tau_2)^2} \right) \times \frac{\tau_2}{R_0} < 0$$

Thus τ_2 is inversely proportional to R_0 .Hence to decrease the number of secondary infection R_0 one can increase the rate of therapeutic treatment .

If $x = \lambda_e$

$$S_{\lambda_e} = \frac{\partial R_0}{\partial \lambda_e} \times \frac{\lambda_e}{R_0} = \left(\frac{\epsilon_1 \psi}{\mu k\delta(\mu + \tau_1)} + \frac{\epsilon_2 \Lambda}{\mu k\delta(\mu + \tau_2)} \right) \times \frac{\lambda_e}{R_0} > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter λ_e.(since the basic reproduction number R_0 decreases as λ_e decreases).Moreover

$$\lim_{\lambda_e \to 0} R_0 = 0$$

This implies that we can reach the state of no secondary infection if the contact rate between the susceptible populations with asymptomatic infected λ_e significantly decreases up to zero .

If $x = \phi$

$$S_\phi = \frac{\partial R_0}{\partial \phi} \times \frac{\phi}{R_0} = \left(\frac{\beta_2 \Lambda k\delta}{\mu k\delta(\mu + \tau_2)} \right) \times \frac{\phi}{R_0} > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter ϕ.(since the basic reproduction number R_0 decreases as ϕ decreases).Moreover

$$\lim_{\phi \to 0} R_0 = 0$$

This implies that we can reach the state of no secondary infection if the contact rate between the susceptible populations with asymptomatic infected ϕ significantly decreases up to zero .

If $x = \psi$

$$S_\psi = \frac{\partial R_0}{\partial \psi} \times \frac{\psi}{R_0} = \left(\frac{\beta_1 \Lambda k\delta + \epsilon_1 \lambda_e}{\mu k\delta(\mu + \tau_1)} \right) \times \frac{\psi}{R_0} > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter ψ.(since the basic reproduction number R_0 decreases as ψ decreases).Moreover

$$\lim_{\psi \to 0} R_0 = 0$$

This implies that we can reach the state of no secondary infection if the contact rate between the susceptible populations with asymptomatic infected ψ significantly decreases up to zero .

If $x = k$

$$S_k = \frac{\partial R_0}{\partial k} \times \frac{k}{R_0} = -\left(\frac{\beta_1 \Lambda \psi \delta + \epsilon_1 \lambda_e \psi}{\mu \delta (\mu + \tau_1)} + \frac{\beta_2 \Lambda \phi \delta + \epsilon_2 \Lambda \lambda_e}{\mu \delta (\mu + \tau_2)} \right) \times \frac{k}{R_0} < 0$$

Thus K is inversely proportional to R_0 .Hence to decrease the number of secondary infection R_0 one can increase the rate of K .

If $x = \delta$

$$S_\delta = \frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = -\left(\frac{\beta_1 \Lambda \psi k + \epsilon_1 \lambda_e \psi k}{\mu k (\mu + \tau_1)} + \frac{\beta_2 \Lambda \phi k + \epsilon_2 \Lambda \lambda_e k}{\mu k (\mu + \tau_2)} \right) \times \frac{\delta}{R_0} < 0$$

Thus δ is inversely proportional to R_0 .Hence to decrease the number of secondary infection R_0 one can increase the rate of the decay rate of vibrio cholera δ .

If $x = \epsilon_1$

$$S_{\epsilon_1} = \frac{\partial R_0}{\partial \epsilon_1} \times \frac{\epsilon_1}{R_0} = \left(\frac{\lambda_e \psi}{\mu k \delta (\mu + \tau_1)} \right) \times \frac{\epsilon_1}{R_0} > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter ϵ_1.(since the basic reproduction number R_0 decreases as ϵ_1 decreases).

If $x = \epsilon_2$

$$S_{\epsilon_2} = \frac{\partial R_0}{\partial \epsilon_2} \times \frac{\epsilon_2}{R_0} = \left(\frac{\Lambda \lambda_e}{\mu k \delta (\mu + \tau_2)} \right) \times \frac{\epsilon_2}{R_0} > 0$$

Thus to decrease the number of secondary infection R_0 one can decrease the parameter ϵ_2.(since the basic reproduction number R_0 decreases as ϵ_2 decreases).

If τ_1

$$S_{\tau_1} = \frac{\partial R_0}{\partial \tau_1} \times \frac{\tau_1}{R_0} = -\left(\frac{\beta_1 \Lambda \psi k \delta + \epsilon_1 \lambda_e \psi}{\mu k \delta (\mu + \tau_1)^2} \right) \times \frac{\tau_1}{R_0} < 0$$

$$S_{\tau_1} = -\left(\frac{\beta_1 \Lambda \psi k \delta + \epsilon_1 \lambda_e \psi}{\mu k \delta (\mu + \tau_1)^2} \right) \times \frac{\tau_1}{R_0} < 0$$

Thus τ_1 is inversely proportional to R_0 .Hence to decrease the number of secondary infection R_0 one can increase the rate of therapeutic treatment .

The following table 4.3 presents the sensitivity indeces of the basic reproduction number R_0 ,in relation to various parameters used in the epidemological model .

Table 4.3: The sensitivity indices of R_0 with respect to the parameters.

Parameter	**Sensitivity index**
k	-0.39
δ	-0.39
β_1	0.34
λ	1
ψ	0.57
ϵ_1	0.23
λ_e	0.37
μ	-1.03
τ_1	-0.55
β_2	0.27
ϕ	0.43
ϵ_2	0.16
τ_2	-0.42

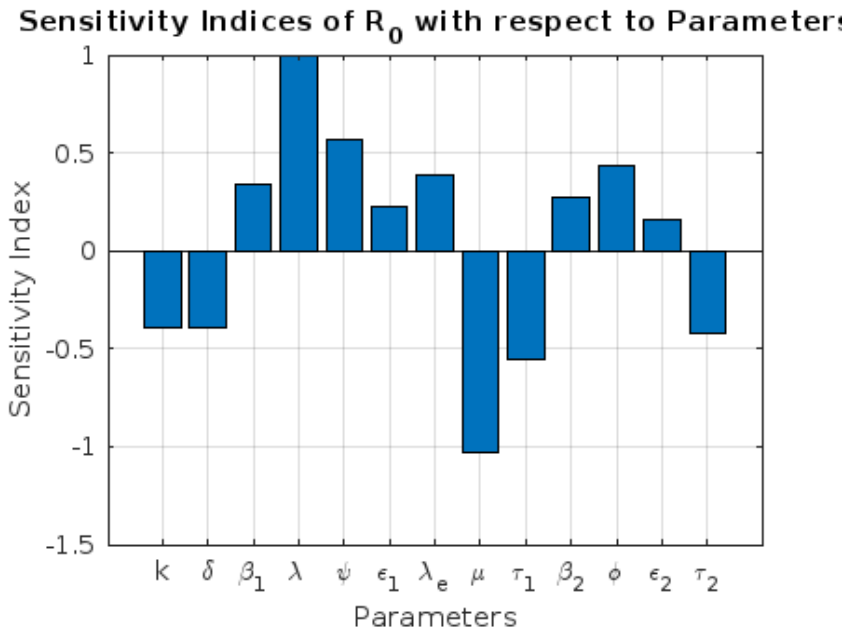

Figure 4.3: The sensitivity indices of R_0 with respect to the parameters.

The bar graph in the figure 4.3, illustrates sensitivity indices of the reproduction number R_0 , in relation to various parameters within our epidemiological model .

Parameters with positive sensitivity indices contribute positively to R_0, meaning that an increase in these parameters leads to an increase in R_0. Notably, λ_e, ϕ and ψ has the highest positive sensitivity index, indicating it has the strongest impact on increasing R_0. Other parameters, such as β_1, ϵ_1,β_2 and ϵ_2, also have positive sensitivity but to a lesser

extent.
Parameters with negative sensitivity indices contribute negatively to R_0, meaning an increase in these parameters leads to a decrease in R_0. The parameter τ_1 shows a strong negative sensitivity, suggesting it has the most substantial impact on decreasing R_0. Other parameters, such as δ , τ_2 and k also have negative sensitivity values, but their impact is less pronounced. Parameters with strong positive or negative sensitivity indices could be targeted for controlling R_0.

In general , this figure highlights which parameters are most influential on R_0 and thus provides insights for prioritizing control measures based on their sensitivity indices.

Chapter 5
NUMERICAL SIMULATION AND RESULTS

5.1 Numerical simulations of the system

In this section, we use the numerical simulation to show the dynamic behavior of our model. The numerical simulations of the model system 4.1 were carried out to graphically illustrate with help of the ODE45 MATLAB tool. The sources of these parameters are mainly from parameter estimation using assumptions and literature.

5.2 Parameter Estimations

The sources of these parameters are mainly from parameter estimation using assumptions and literature.

Table 5.1: Parameter values and sources.

Parameter	**Value**	**Source**
μ	0.01	Assumed
τ_1	0.7	Assumed
τ_2	0.15	Assumed
ϵ_1	0.0001	[31]
ϵ_2	0.02	[31]
δ	0.107	Assumed
ϕ	0.04	Assumed
ψ	0.033	Assumed
λ	0.4	Assumed
λ_e	0.06	Assumed
β_1	0.06	Assumed
β_2	0.02	Assumed

5.3 Numerical simulation Results and Discussion

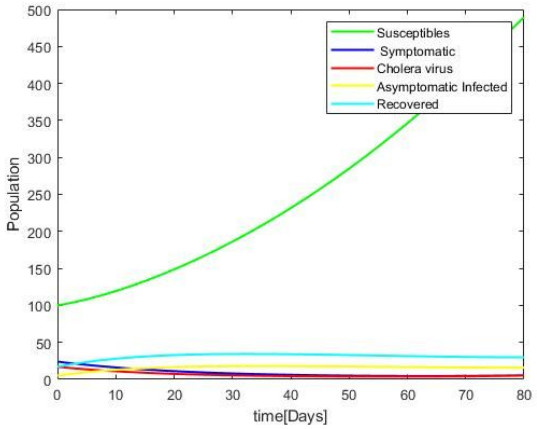

Figure 5.1: Trajectories of state variables for R_0=0.11

From figure (5.1) with $R_0 = 0.11$ we observe that for the basic reproduction number R_0 <1 , all solutions curve goes to the disease free equilibrium point. As a result, the disease dies out. In Figure 5.1 with R_0 <1 and different initial conditions for the state variables, all trajectories of state variables goes to their components of the disease free equilibrium point. This indicate that the disease-free equilibrium point is locally and globally asymptotically stable for the values of $R_0 < 1$.

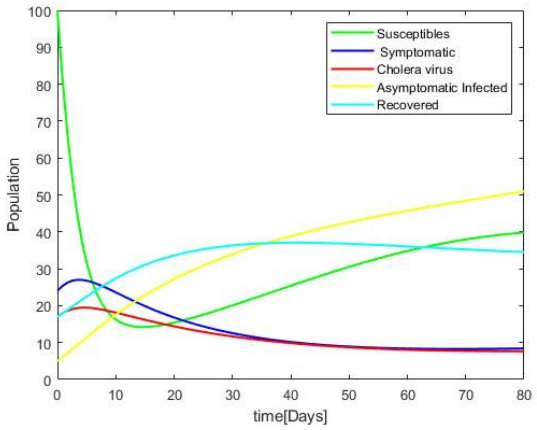

Figure 5.2: Trajectories of state variables for R_0=1.34

In Figure (5.2) we tried to show the possible dynamics of cholera disease and we can see from the graph that at $R_0 > 1$,the infected classes of the populations are at increase. This means that there is need for reduction of the value of the basic reproduction number to a value less than unity.

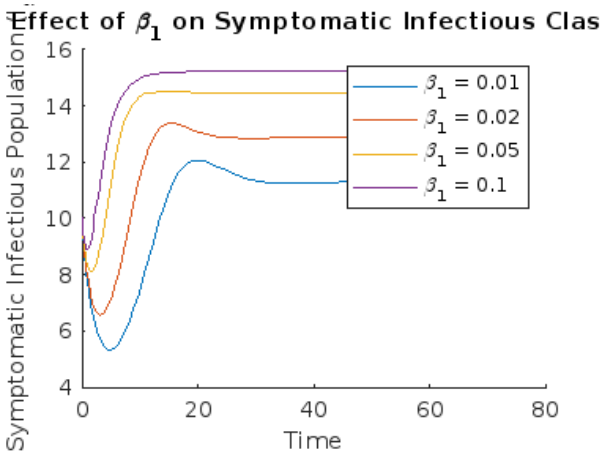

Figure 5.3: The effect of β_1 on I_s

From figure 5.3 , as β_1 increases, the transmission rate from symptomatic individuals increases, which leads to a higher number of symptomatic infectious individuals over time. This results in faster spread of the disease and a larger outbreak. By simulating different values of β_1 , we can observe the direct relationship between the rate of transmission from symptomatic individuals and the progression of an outbreak, allowing for better-informed control strategies.

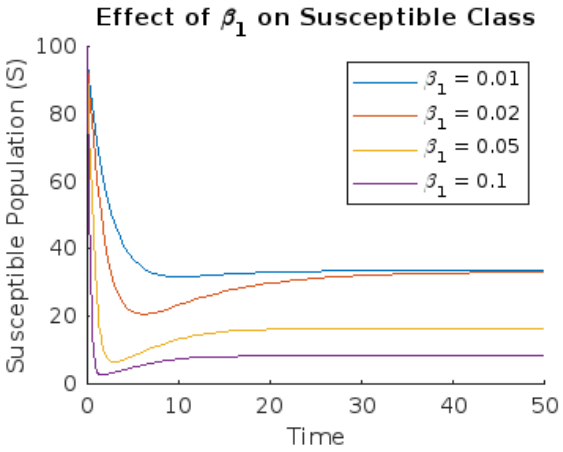

Figure 5.4: The effect of β_1 on S

Figure 5.4 shows that β_1 , the contact rate from symptomatic individuals, has a significant impact on the size and speed of reduction of the susceptible population. As β_1 increases, the number of susceptible individuals decreases more rapidly, leading to faster transmission and a larger potential outbreak. In contrast, when β_1 is small, the disease spreads more slowly, and a larger portion of the population remains susceptible over time.

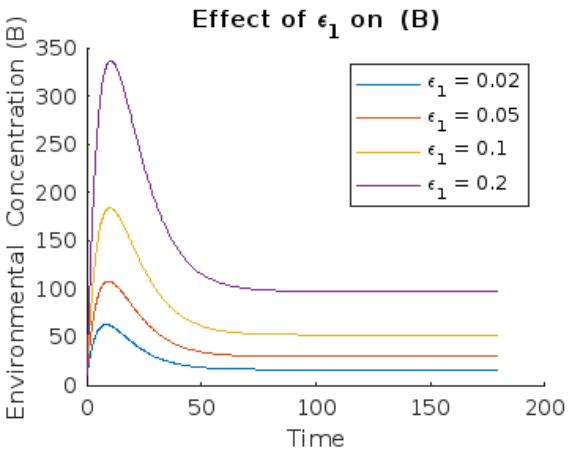

Figure 5.5: The effect of ϵ_1 on B

The simulation shows that ϵ_1 has a significant effect on the pathogen concentration in the environment. As ϵ_1 increases, the environmental contamination becomes more severe, which amplifies the risk of infection for the susceptible population. These findings highlight the importance of controlling environmental contamination from symptomatic individuals to reduce the spread of cholera .

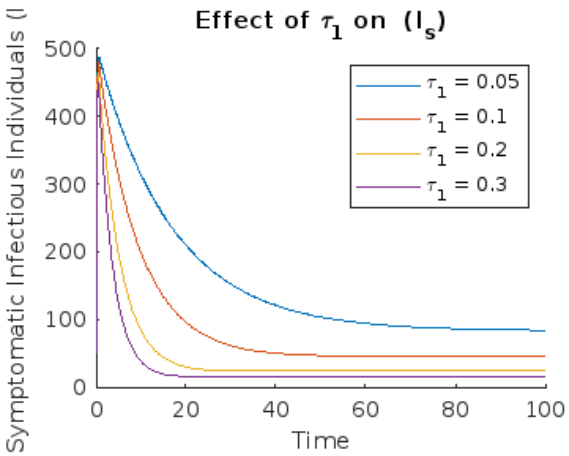

Figure 5.6: The effect of τ_1 on I_s

The simulation of different values of τ_1 on the population of symptomatic infectious individuals (τ_1) provides insight into how treatment and recovery rates influence the dynamics of cholera outbreaks. Faster recovery (higher τ_1) leads to a quicker reduction in the symptomatic population, potentially controlling the outbreak more effectively. On the other hand, slower recovery (lower τ_1) prolongs the presence of symptomatic individuals, increasing the chances of further disease spread. This underscores the importance of rapid treatment in mitigating cholera outbreaks.

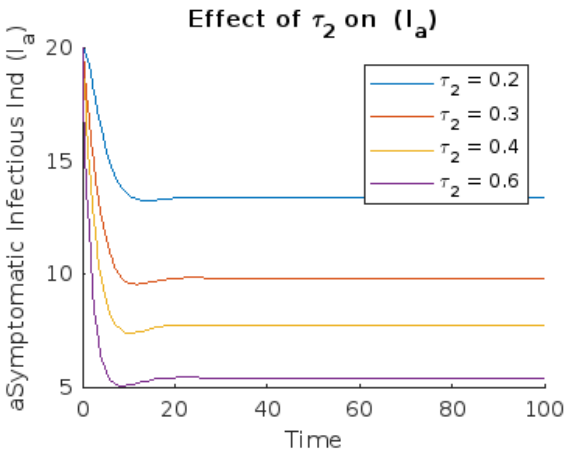

Figure 5.7: The effect of τ_2 on I_a

The simulation of different values of τ_2 on the population of asymptomatic infectious individuals (τ_2) provides insight into how the recovery rate of asymptomatic individuals influences the dynamics of cholera transmission. Faster recovery (higher τ_2) leads to a quicker reduction in the asymptomatic population, limiting the duration of the outbreak and the contribution to environmental contamination. Slower recovery (lower τ_2) prolongs the presence of asymptomatic individuals, increasing the potential for further disease spread. This underscores the importance of addressing asymptomatic carriers in public health interventions aimed at controlling cholera.

Chapter 6
CONCLUSION AND RECOMMENDATION

6.1 Conclusion

This study has developed a mathematical model to describe the transmission dynamics of cholera, providing a valuable tool for understanding the disease's behavior and potential control mechanisms. Through the analysis of the model's equilibrium points and stability, we have identified the key factors that influence the spread of cholera within a population. The model successfully captures the nonlinear interactions between susceptible, infected, and recovered individuals, as well as the environmental reservoir of the cholera pathogen.

By employing sensitivity analysis, we have pinpointed critical parameters—such as the rate that a therapeutic treatment of symptomatic infected class ,rate that a therapeutic treatment of asymptomatic infected class(recovery rates) and environmental contamination decay rate—that have the most significant impact on cholera transmission. These findings contribute to a better understanding of cholera outbreaks and offer a framework for predicting the disease's spread under different conditions.

6.2 Recommendations

1. **Targeted Public Health Interventions:** Public health authorities should prioritize interventions in regions where cholera transmission rates are highest. This includes improving water sanitation systems, ensuring access to clean drinking water, and promoting hygiene practices.

2. **Environmental Control Measures:** Reducing the environmental contamination rate is crucial to controlling cholera. Investment in infrastructure that improves waste disposal and prevents contamination of water sources should be a key focus for governments and public health organizations.

3. **Resource Allocation Based on Sensitivity Analysis:** The model highlights specific parameters that significantly affect the spread of cholera. Resource allocation should be focused on addressing these parameters, ensuring that public health interventions target the most critical areas.

4. **Further Research:** The current model can be expanded to include additional factors such as climate variations, population mobility, and genetic variations in pathogens. Future research should aim to refine the model and incorporate real-world data to improve its predictive power and applicability in diverse settings.

By following these recommendations, public health authorities can better manage cholera outbreaks, reduce transmission, and improve health outcomes in vulnerable populations.

6.3 Limitations of the study

1. **Parameter Estimation and Sensitivity:** The model contains several parameters $(\lambda, \Pi, \lambda_e, \beta_1, \beta_2, \psi, \phi, \mu, \tau_1, \tau_2, \epsilon_1, \epsilon_2, \delta)$, which may be challenging to estimate accurately. High sensitivity to these parameters can lead to significant variations in model predictions, affecting reliability.

2. **Inclusion of Only One Pathogen**: The model appears to focus on a single pathogen or bacterial agent. In real-world conditions, multiple pathogens may interact, influencing the transmission dynamics and outcomes of infections.

3. **No Consideration of Immune Memory or Waning Immunity:** The model does not include immune memory or the potential for immunity to wane over time, which can impact the dynamics of recovery and reinfection.

6.4 Future Work

This research effort holds promising potential to pave new pathways for addressing real-world challenges and supporting decision-making processes. The thesis encompasses a wide range of possible future applications, some of which are outlined below:

1. **Parametrization and Data Integration:** Future work could involve collecting empirical data for robust parametrization and validation.

2. **Multi-Pathogen Interactions:** Extending the model to incorporate multiple pathogens and interactions between them (such as co-infections) may reflect more realistic scenarios, particularly in settings with high infection rates from multiple sources.

3. **Immunity Dynamics:** Extending the model to include waning immunity, immune boosting upon exposure, or vaccination effects would improve its applicability in real-world settings where immunity is dynamic.

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Appendix

MATLAB CODES

```
    % Definition of the system of ODEs
function dydt = Alex16(~, y, lambda,
lambda_e, Pi, beta_1, beta_2, mu, psi,
phi, tau_1, tau_2, epsilon_1, epsilon_2, delta, K, N)
    S = y(1);   % Susceptible individuals
    I_s = y(2); % Symptomatic infected individuals
    I_a = y(3); % Asymptomatic infected individuals
    B = y(4);   % Bacteria concentration
    R = y(5);   % Recovered individuals

    % Definition of the equations
    dS_dt = lambda * N - Pi * (lambda_e * S * B / (K + B) + ...
    beta_1 * I_s * S + beta_2 * I_a * S) - mu * S;
    dI_s_dt = psi * (lambda_e * S * B / (K + B) + ...
    beta_1 * I_s * S + beta_2 * I_a * S) - mu * I_s - tau_1 * I_s;
    dI_a_dt = phi * (lambda_e * S * B / (K + B) +...
    beta_1 * I_s * S + beta_2 * I_a * S) - mu * I_a - tau_2 * I_a;
    dB_dt = epsilon_1 * I_s + epsilon_2 * I_a - delta * B;
    dR_dt = tau_1 * I_s + tau_2 * I_a - mu * R;

    dydt = [dS_dt; dI_s_dt; dI_a_dt; dB_dt; dR_dt];
end



%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%

%Save it as Alex16DFEP
% Parameters
```

```
lambda = 0.99;
lambda_e = 0.75;
Pi = 0.0001;
beta_1 = 0.00001;
beta_2 = 0.00005;
mu = 0.2;
psi = 0.6;
phi = 0.05;
tau_1 = 0.5;
tau_2 = 0.3;
epsilon_1 = 0.1;
epsilon_2 = 0.05;
delta = 0.2;
K = 50;
N = 2000;
P=1;


% Calculate numerator of R_0
numerator = lambda * (mu * beta_1 * psi * K * delta + beta_1 * psi * K
            lambda_e * psi * epsilon_1 * tau_2 + mu * lambda_e * psi *
            mu * phi * beta_2 * K * delta + mu * phi * beta_2 * tau_2 *
            lambda_e * phi * epsilon_2 * beta_2 + tau_1 * delta * epsil

% Calculate denominator of R_0
denominator = mu * K * delta * (mu^2 + mu * tau_2 + mu * tau_1 + tau_1



tsp=[0,150];
Y_0=[1000 200 200 200 400 ];
```

```
fprintf('Value of parameter R0 is %.5f', numerator / denominator)

[T,Y]=ode45(@(t,y)Alex16(t,y,lambda, lambda_e, Pi, beta_1, beta_2, mu,
plot(T,Y(:,1) ,T,Y(:,2),'c',T,Y(:,3),T,Y(:,4),T,Y(:,5),'g','LineWidth',
% plot(T,Y(:,1),T,Y(:,2),'c',T,Y(:,3),T,Y(:,4),'LineWidth',2.5)
legend('S','I_s','I_a','B','R')
xlabel('time in days')
ylabel('Population size')
title ('All Population with R_0 =0.02 ');



%%%%%%%%%%
%%%%%%%%%%%%%%
%%   EEP  %%
% Parameters
lambda = 0.99;
lambda_e = 0.05;
Pi = 0.0001;
beta_1 = 0.0001;
beta_2 = 0.05;
mu = 0.1;
psi = 0.6;
phi = 0.25;
tau_1 = 0.005;
tau_2 = 0.0003;
epsilon_1 = 0.001;
epsilon_2 = 0.05;
delta = 0.03;
K = 80;
N = 2000;
```

```
%P=1;

% Calculate numerator of R_0
numerator = lambda * (mu * beta_1 * psi * K * delta + beta_1 * psi * K
            lambda_e * psi * epsilon_1 * tau_2 + mu * lambda_e * psi *
            mu * phi * beta_2 * K * delta + mu * phi * beta_2 * tau_2 *
            lambda_e * phi * epsilon_2 * beta_2 + tau_1 * delta * epsil

% Calculate denominator of R_0
denominator = mu * K * delta * (mu^2 + mu * tau_2 + mu * tau_1 + tau_1



tsp=[0,100];
Y_0=[1000 200 200 200 400 ];
fprintf('Value of parameter R0 is %.5f', numerator / denominator)

[T,Y]=ode45(@(t,y)Alex16(t,y,lambda, lambda_e, Pi, beta_1, beta_2, mu,
plot(T,Y(:,1) ,T,Y(:,2),'c',T,Y(:,3),T,Y(:,4),T,Y(:,5),'g','LineWidth',
% plot(T,Y(:,1),T,Y(:,2),'c',T,Y(:,3),T,Y(:,4),'LineWidth',2.5)
legend('S','I_s','I_a','B','R')
xlabel('time in days')
ylabel('Population size')
title ('All Population with R_0 =1.19 ');



%%%%%%
function effect_of_beta1_on_Is
    % Define parameter values
    lambda = 0.01;
```

```
N = 1000;
lambda_e = 0.05;
beta_2 = 0.01;
mu = 0.1;
psi = 0.5;
tau_1 = 0.21;
tau_2 = 0.2;
epsilon_1 = 0.05;
epsilon_2 = 0.03;
delta = 0.1;     % Decay rate of environmental pathogen
K = 100;        ation constant

% Initial conditions
S0 = 0;  % Initial number of susceptible individuals
I_s0 = 10; % Initial number of symptomatic infectious individuals
I_a0 = 10; % Initial number of asymptomatic infectious individuals
B0 = 10;   % Initial pathogen concentration in environment
R0 = 10;   % Initial number of recovered individuals

% Time span for the simulation
tspan = [0 70];

% Initial state vector
y0 = [S0, I_s0, I_a0, B0, R0];

% Values of beta_1 to test
beta_1_values = [0.01, 0.02, 0.05, 0.1]; % Different beta_1 values

% Set up plot
figure;
hold on;
```

```
    % Loop over different beta_1 values
    for i = 1:length(beta_1_values)
        beta_1 = beta_1_values(i); % Current value of beta_1

        % Solve the system using ode45
        [t, y] = ode45(@(t, y) systemODE(t, y, lambda, N, lambda_e, bet

        % Plot I_s class over time
        plot(t, y(:,2), 'DisplayName', ['\beta_1 = ', num2str(beta_1)])
    end

    % Customize plot
    xlabel('Time');
    ylabel('Symptomatic Infectious Population (I_s)');
    title('Effect of \beta_1 on Symptomatic Infectious Class');
    legend show;
    hold off;
end

%%%%%%%%%%%%%
%%%%%%%%%%%%%
function effect_of_beta1_on_susceptible
    % Define parameter values
    lambda = 0.01;
    N = 1000;
    lambda_e = 0.0000005;
    beta_2 = 0.00001;
    mu = 0.3;
    psi = 0.5;
    phi = 1 - psi;
```

```
tau_1 = 0.1;
tau_2 = 0.2;
epsilon_1 = 0.05;
epsilon_2 = 0.03;
delta = 0.1;     % Decay rate of environmental pathogen
K = 100;

% Initial conditions
S0 = 100;  % Initial number of susceptible individuals
I_s0 = 10; % Initial number of symptomatic infectious individuals
I_a0 = 10; % Initial number of asymptomatic infectious individuals
B0 = 10;   % Initial pathogen concentration in environment
R0 = 10;   % Initial number of recovered individuals

% Time span for the simulation
tspan = [0 50];

% Initial state vector
y0 = [S0, I_s0, I_a0, B0, R0];

% Values of beta_1 to test
beta_1_values = [0.01, 0.02, 0.05, 0.1]; % Different beta_1 values

% Set up plot
figure;
hold on;

% Loop over different beta_1 values
for i = 1:length(beta_1_values)
    beta_1 = beta_1_values(i); % Current value of beta_1
```

```
        % Solve the system using ode45
        [t, y] = ode45(@(t, y) systemODE(t, y, lambda, N, lambda_e, bet

        % Plot susceptible class over time
        plot(t, y(:,1), 'DisplayName', ['\beta_1 = ', num2str(beta_1)])
    end

    % Customize plot
    xlabel('Time');
    ylabel('Susceptible Population (S)');
    title('Effect of \beta_1 on Susceptible Class');
    legend show;
    hold off;
end

%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%

function effect_of_beta2_on_Is
    % Define parameter values
    lambda = 0.01;
    N = 1000;
    lambda_e = 0.05;
    beta_1 = 0.02;
    mu = 0.1;
    psi = 0.5;
    phi = 1 - psi;
    tau_1 = 0.21;
    tau_2 = 0.2;
    epsilon_1 = 0.05;
    epsilon_2 = 0.03;
```

```
delta = 0.1;     % Decay rate of environmental pathogen
K = 100;

% Initial conditions
S0 = 20;  % Initial number of susceptible individuals
I_s0 = 20; % Initial number of symptomatic infectious individuals
I_a0 = 20; % Initial number of asymptomatic infectious individuals
B0 = 10;   % Initial pathogen concentration in environment
R0 = 20;   % Initial number of recovered individuals

% Time span for the simulation
tspan = [0 50];

% Initial state vector
y0 = [S0, I_s0, I_a0, B0, R0];

% Values of beta_2 to test
beta_2_values = [0.005, 0.01, 0.02, 0.04]; % Different beta_2 value

% Set up plot
figure;
hold on;

% Loop over different beta_2 values
for i = 1:length(beta_2_values)
    beta_2 = beta_2_values(i); % Current value of beta_2

    % Solve the system using ode45
    [t, y] = ode45(@(t, y) systemODE(t, y, lambda, N, lambda_e, bet

    % Plot I_s class over time
```

```
        plot(t, y(:,2), 'DisplayName', ['\beta_2 = ', num2str(beta_2)])
    end

    % Customize plot
    xlabel('Time');
    ylabel('Symptomatic Infectious Population (I_s)');
    title('Effect of \beta_2 on Symptomatic Infectious Class');
    legend show;
    hold off;
end

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
function effect_of_beta2_on_susceptible
    %  parameter values
    lambda = 0.01;
    N = 1000;
    lambda_e = 0.05;
    beta_1 = 0.02;
    mu = 0.01;
    psi = 0.5;
    phi = 1 - psi;
    tau_1 = 0.1;
    tau_2 = 0.2;
    epsilon_1 = 0.05;
    epsilon_2 = 0.03;
    delta = 0.1;
    K = 100;
    % Initial conditions
    S0 = 20;
    I_s0 = 10;
```

```
I_a0 = 10;
B0 = 10;
R0 = 10;

% Time span for the simulation
tspan = [0 40] ;

% Initial state vector
y0 = [S0, I_s0, I_a0, B0, R0];

% Values of beta_2 to test
beta_2_values = [0.005, 0.01, 0.02, 0.04];

% Set up plot
figure;
hold on;

% Loop over different beta_2 values
for i = 1:length(beta_2_values)
    beta_2 = beta_2_values(i); % Current value of beta_2

    % Solve the system using ode45
    [t, y] = ode45(@(t, y) systemODE(t, y, lambda, N, lambda_e, bet

    % Plot susceptible class over time
    plot(t, y(:,1), 'DisplayName', ['\beta_2 = ', num2str(beta_2)])
end

% Customize plot
xlabel('Time');
ylabel('Susceptible Population (S)');
```

```
    title('Effect of \beta_2 on Susceptible Class');
    legend show;
    hold off;
end



%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%
function effect_of_epsilon1_on_B
    % Define parameter values
    lambda = 0.01;     N = 1000;          lambda_e = 0.05;
    beta_1 = 0.02;
    beta_2 = 0.01;
    mu = 0.01;       % Natural death rate
    psi = 0.5;
    phi = 1 - psi;
    tau_1 = 0.1;
    tau_2 = 0.2;
    epsilon_2 = 0.03;
    delta = 0.1;     % Decay rate of environmental pathogen
    K = 100;

    % Initial conditions
    S0 = 700;  % Initial number of susceptible individuals
    I_s0 = 50; % Initial number of symptomatic infectious individuals
    I_a0 = 20; % Initial number of asymptomatic infectious individuals
    B0 = 10;   % Initial pathogen concentration in environment
    R0 = 20;   % Initial number of recovered individuals

    % Time span for the simulation
```

```
    tspan = [0 180];

    % Initial state vector
    y0 = [S0, I_s0, I_a0, B0, R0];

    % Values of epsilon_1 to test
    epsilon_1_values = [0.02, 0.05, 0.1, 0.2]; % Different epsilon_1 va

    % Set up plot
    figure;
    hold on;

    % Loop over different epsilon_1 values
    for i = 1:length(epsilon_1_values)
        epsilon_1 = epsilon_1_values(i); % Current value of epsilon_1

        % Solve the system using ode45
        [t, y] = ode45(@(t, y) systemODE(t, y, lambda, N, lambda_e, bet

        % Plot B class over time
        plot(t, y(:,4), 'DisplayName', ['\epsilon_1 = ', num2str(epsilo
    end

    % Customize plot
    xlabel('Time');
    ylabel('Environmental  Concentration (B)');
    title('Effect of \epsilon_1 on  (B)');
    legend show;
    hold off;
end
```