A mathematical model of COVID-19 transmission dynamics with a case study in Ethiopia

Habtamu Teferi

A Thesis Submitted to the Department of Applied Mathematics

School of Applied Natural Science

Presented in Partial Fulfillment of the Requirement for the Degree of Master's in Applied Mathematics(Mathematical Modeling)

Office of Graduate Studies

Adama Science and Technology University

July 31, 2021

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Declaration

I hereby declare that this Master Thesis entitled “A mathematical model of COVID-19 transmission dynamics with a case study in Ethiopia ”is my original work. That is, it has not been submitted for the award of any academic degree, diploma or certificate in any other university. All sources of materials that are used for this thesis have been duly acknowledged through citation.

Name of student	Signature	Date

Recommendation

We, the advisors of this thesis, hereby certify that we have read the revised version of the thesis entitled “A mathematical model of COVID-19 transmission dynamics with a case study in Ethiopia ”prepared under our guidance by Habtamu Teferi submitted in partial fulfillment of the requirements for the degree of Master’s of Science in Applied Mathematics. Therefore, we recommend that the submission of revised version of the thesis to the department following the applicable procedures.

Major Advisor	Signature	Date
Co-advisor	Signature	Date

Approval Page

We, the advisors of the thesis entitled “A mathematical model of COVID-19 transmission dynamics with a case study in Ethiopia”and developed by Habtamu Teferi, hereby certify that the recommendation and suggestion made by the board of examiners are appropriately incorporated into the final version of the thesis.

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Co-advisor	Signature	Date

We, the undersigned, members of the Board of Examiners of the thesis by Habtamu Teferi have read and evaluated the thesis entitled “A mathematical model of COVID-19 transmission dynamics with a case study in Ethiopia”and examined the candidate during open defense. This is, therefore, to certify that the thesis is accepted for partial fulfillment of the requirement of the degree of Master of Science in Applied Mathematics.

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Acronyms

COVID-19	Corona Virus Diseases-2019
EE	Endemic Equilibrium
MERS-COV	Middle East Respiratory Syndrome Coronavirus
ODE	Ordinary Differential Equations
PMP	Pontryagin Minimum Principle
SARS-COV	Severe Acute Respiratory Syndrome Coronavirus
SARS-COV-2	Severe Acute Respiratory Syndrome Coronavirus-2
UNECA	United Nation Economic Commision Africa
WHO	World Health Organization

Abstract

COVID-19 is an infectious diseases caused by SARS-CoV-2, a betacoronavirus. Globally, it has been affecting many country including Ethiopia. This study aims to develop and analyze a mathematical model of COVID-19 transmission dynamics and apply it as case study in Ethiopia. For this, we formulated a deterministic mathematical model of seven compartments to describe the transmission dynamics of COVID-19 infection using a system of non-linear ordinary differential equations with optimal control. We investigated the dynamical behavior of this model and performed the qualitative analysis of the model. The system has two equilibrium points, namely the disease free equilibrium point and the endemic equilibrium point which exists conditionally. The basic reproduction number R_0 was calculated using the next-generation matrix and the stability of the equilibrium points were analyzed. From the qualitative analysis, the disease free equilibrium point is both locally and globally stable if $R_0 < 1$, and the endemic equilibrium point is also both locally and globally stable if $R_0 > 1$ under some conditions on the system parameters. Furthermore, sensitivity analysis of the model equation was performed on the key parameters to find out their relative significance and potential impact on the transmission dynamics of COVID-19 diseases. Also bifurcation analysis have been performed to reveal the transmission dynamics of corona virus diseases. Then we extended the proposed model to minimize the number of exposed and symptomatic individual with taking into account the cost of implementation. We proved the existence of optimal controls with the help of Pontryagin's Minimum Principle. Finally, numerical simulations of the model equations were carried out using MATLAB. The simulations result show that, it is more efficient when triple($u_1, u_2 \& u_3$) or all the four controls are considered in simulation at time to reduce the transmission dynamics COVID-19 infection.

Keywords: *Mathematical Modeling; COVID-19; Stability Analysis; Sensitivity Analysis; Optimal Control; Pontryagin's Minimum Principle.*

Chapter 1

Introduction

1.1 Background of the Study

The name "coronavirus," coined in 1968, is derived from the "corona"like or crown-like morphology observed for these viruses in the electron microscope as depicted in Figure1.1 . The families of this viruses are circulating among animals and sometimes can also be found in humans (Al-Jabir et al., 2020). It is renamed as COVID-19 by WHO in January 2020. COVID-19 is an infectious disease caused by SARS-CoV-2, a betacoronavirus.

As reported in Graham et al. (2020), COVID-19 are also a group of enveloped non-

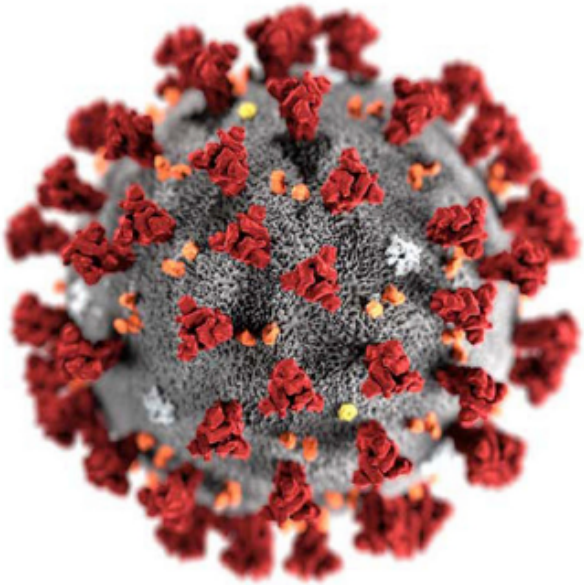


Figure 1.1: Illustration of the SARS-CoV-2 virion

(Verma et al., 2020)

segmented with a positive-sense, single-stranded RNA viruses that belongs to the order of Nidovirales, family of Coronaviridae, and subfamily of Ortho- coronavirinae and widely spread among the mammals and humans.

The disease was first identified in December 2019 in Wuhan city of China, and became the epicenter of COVID-19 (Wang et al., 2020). Most of the initial stages were usually incorporated to the wholesale Human seafood market, which also traded live animals. The continuing novel coronavirus or SARS-CoV-2 epidemic has been declared a pandemic by the World Health Organization (WHO) on March 11, 2020 (Turner-Musa et al., 2020). Novel coronavirus has already exceeded the earlier records of two life-threatening outbreaks, namely Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), posing the major warning to the global public health and economy after the 2nd world war (Samui et al., 2020). It is the third zoonotic human-to-human transmission COVID-19 that has arisen in the present century, after SARS- CoV, which spread around 37 countries and the MERS-CoV, which spread around 27 countries. The virus can be transmitted from an infected person to other people, through direct contact with handshakes and by touching surfaces contaminated with the disease, and then it affects parts of the body such as the eyes, nose and mouth (Verma et al., 2020). This communicable coronavirus disease has traits like fever, dry cough, sore throat, breathlessness and fatigue (Zou et al., 2020). Due to heavy mobility of human from continent to continent through air transportation, the disease has extremely spread throughout the world (Zheng et al., 2020).

Globally, coronavirus COVID-19 is affecting 223 countries. According to WHO data, the total confirmed cases are 129, 215, 179 and the reported deaths due the disease is 2, 820, 098 up to April 2, 2021 (WHO et al., 2020).

In Africa, COVID-19 case was first reported in Egypt on 14 February 2020. Then it addressed all the African countries. Initially, the disease was confined to capital cities, and gradually a significant number of countries in Africa are now reporting the cases in multiple provinces. Also, WHO report shows 3,106,171 total confirmed cases and 78,301 confirmed deaths are reported in Africa up to April 2, 2021.

In Ethiopia the first confirmed case of COVID-19 was on 13 March 2020, in capital city

of Ethiopia, Addis Ababa. Up to April 2, 2021, the total reported confirmed cases and death reported due to COVID-19 in Ethiopia respectively are 208,961, and 2,887.

Ethiopia shares a major proportion of the global burden of infectious diseases, while the patterns of COVID-19 are still at an earlier stage of the epidemiology curve. The Ethiopian government exerted tremendous efforts to curb the disease. It limited public gatherings, ordered school closures, directed high-risk civil servants to work from home, and closed borders. The government also suspended flights to 120 countries and restricted mass transports and declared a five-month national state of emergency and granted a pardon for 20402 prisoners. Due to the pandemic, the government officially postponed election. Despite all these important public health commitment measures, the outbreak still has the potential threat for greater loss of life in Ethiopia. This mainly due to the community is unable to reshape their regular behavioral and socio cultural norms that would facilitate the spread of the disease. Many Ethiopians live in crowded conditions (Mussie et al., 2020) and this would facilitate the spread of the disease.

As identified by the World Health Organization (WHO), the mathematical models, mainly those formulated in a timely manner, can play a crucial role in allowing public health decision and policy makers with evidence based statistics (Egger et al., 2017; Khajanchi et al., 2018).
Mathematical modeling can aid in understanding:

(i.) how transmissible the disease is,

(ii.) when does the infectivity become high during the course of epidemic,

(iii.) how acute the disease is, and

(iv.) how effectual interventions has been and ought to be.

The progression of any outbreak depends on the infectivity of pathogens as well as the available uninfected individuals.

For a novel infection, when the transmission dynamics of an epidemiological disease is unknown, mathematical models play a crucial role to estimate the worst and best scenarios.

It can also aid in estimating the effect of precautionary measures adopted against disease. With preventive techniques, the main object is to preserve the basic reproduction number R_0 below 1, to control further development of infection, whereas in a mitigation policy, the main object is to indelicate the effect of outbreak (Ferguson et al., 2020) .

Optimal control theory is an area of mathematics that is used extensively in controlling the spread of infection diseases. It is a powerful mathematical tool that can be used to make decisions involving complex biological situation (Fleming & Rishel, 2012). Mathematical models with optimal control have played a major role in increasing our understanding of the dynamics of infectious diseases and also to investigate the optimal use of intervention strategies to mitigate the spreads of infectious diseases. It has become a valuable tool in the analysis of infectious disease dynamics and to support the development of control strategies. Optimal control can be used to investigate the optimal use of intervention strategies to reduce the spread of infectious diseases (Lenhart & Workman, 2007).

Moore and Okyere (2020) used an optimal control theory model to assess the COVID-19 transmission dynamics and its control measures that can reduce the exposed and infectious individuals in a population. Chernet et al. (2020) considered public health education, personal protective measure, and treating COVID-19 patients as control strategies to analysis the pandemic. The study revealed that the optimal practice of combining all three intervention strategies or combination of any two of them leads to the required mitigation of transmission of the pandemic. The optimal control strategies for transmission risk of COVID-19 is also studied by (Legesse & Shiferaw, 2020). Samui et al. (2020), presented SAIU model on transmission dynamics of COVID-19 . They proposed a compartmental mathematical model to predict and control the transmission dynamics of COVID-19 pandemic in India with epidemic data up to April 30, 2020 without mentioning optimal intervention techniques.

Since, the outbreak of the disease various mathematical modeling have been proposed and analyzed to explore the consequence of transmission dynamics of COVID-19 among population. In the present study we planned to investigate the transmission dynamics COVID-19 using mathematical model with real data from Ethiopia classifying the populations into susceptible, exposed, asymptomatic infected, symptomatic infected, hospitalized, quarantined and recovered with appropriate assumptions. Then we extend the model to optimal

control and present optimal intervention techniques.

1.2 Statement of the problem

A pandemic corona virus which outbreak began in Wuhan, China, in December 2019 and nomenclatured by WHO as COVID-19 has become global problem. This virus affect all age group especially those whose ages are between 25 and 65 most vulnerable to Coronavirus infection compared to the rest of the age groups due to mobility (Kada et al., 2020). The WHO data showed that the total confirmed cases are 129, 215, 179 and the reported deaths due to the disease is 2, 820, 098 up to April 2, 2021. In the same report it reveals that the total reported confirmed cases and death reported due to COVID-19 in Ethiopia respectively are 208,961, and 2,887 (WHO et al., 2020).

As United Nations Economic Commission for Africa has estimated anywhere between 300,000 and 3.3 million African people could lose their lives as a direct result of COVID-19, depending on the intervention measures taken to stop the spread. According to this report, Africans are susceptible because 56 per cent of the urban population is concentrated in over-crowded and poorly serviced slum dwellings (excluding North Africa) and only 34 per cent of the households have access to basic hand washing facilities. In the report, the economic impact due to COVID-19 estimated that African economies could be the slowing of growth to 1.8 per cent in the best case scenario or a contraction of 2.6 per cent in the worst case. This has the potential to push 27 million people into extreme poverty (United Nations, 2020).

As cited and explained in UNICEF et al. (2020) , UNECA has estimated that due to the COVID- 19 crisis 48 percent fewer people could be lifted out of poverty in the continent and the projection of this estimate on Ethiopia situation with the same rate shows that (based on the progress made by the country during the period 2010/11-2015/16) additional 600,000 people per year will fall in absolute poverty measured according to national definition. From these recent reports, it is evident that the consequence of COVID-19 is very dangerous both in terms of health crisis and socio-economic impact unless appropriate mitigation strategies are studied and designed in Ethiopian context.

Many mathematical models have been developed to study the pandemic of COVID-19. For instance, modeling the spread of COVID-19 with new fractal-fractional differential equation blockdown save mankind before vaccination (Atangana, 2020), estimation of the transmission risk of the 2019-nCoV and its implication for public health interventions (Tang et al., 2020), modeling the COVID-19 epidemic and implementation of population wide interventions (Giordano et al., 2020a), modeling and forecasting the daily and cumulative number of cases for the COVID-19 pandemic (Khajanchi & Sarkar, 2020), a COVID-19 epidemic model with latency period (Moore & Okyere, 2020), effects of emergency containment measures on spread and dynamics of the COVID-19 epidemic (Gatto et al., 2020) are few to mention. Samui et al. (2020) also proposed a mathematical modeling on transmission dynamics of COVID-19 up to April 30, 2020. They verified their, model with real data. However, they do not included the exposed , quarantined, hospitalized and recovered individuals in connection with optimal control strategies in their model. Hence, in this research work we intend to develop new mathematical models based on the proposed model (Samui et al., 2020), by introducing exposed , quarantined, hospitalized and recovered compartment with optimal control strategies and studied both analytically and numerically with the help of Pontryagin's Minimum Principle. Then we apply our model to study the epidemic of COVID-19 and fit by real data from Ethiopia.

1.3 Objective of the study

1.3.1 General objective

The general objective of this study is to develop and analyze a mathematical model of COVID-19 transmission dynamics and apply it as case study in Ethiopia.

1.3.2 Specific objectives

- Formulate a deterministic mathematical model of COVID-19 transmission dynamics;
- Perform analysis of the proposed mathematical model;
- Extend the developed mathematical model into optimal control analysis;

- Fit the proposed mathematical model with real data on COVID-19 extracted from Ethiopia and forecast the trends of the disease.

1.4 Significant of the study

A well studied and organized research report on COVID-19 will provide strong information on how to design appropriate control and preventive measures in order to bring a long term solution. Thus, the outcome of this study are helpful to:

- predict the epidemic of coronavirus infectious and to take precautionary measures,
- guide policy makers in making appropriate intervention on how to control and minimize the repercussion effect of (COVID-19) infection,
- the findings of this study also helps to improve decision making at strategical level and adds advantage of interpret the situation of the coronavirus disease,
- motivate other researchers for further study and mathematical analysis.

1.5 Operational definition of technical terms

The following epidemiological terms are defined for later use.

Epidemic is the rapid spread of disease to a large number of people in a given population within a short period of time.

In epidemiology, an infection is said to be **endemic** in a population when that infection is constantly maintained at a baseline level in a geographic area without external inputs.

A **pandemic** is an epidemic of an infectious disease that has spread across a large region, for instance multiple continents or worldwide, affecting a substantial number of people.

In the context of COVID-19, a **contact** can be defined as a person who has experienced any one of the following exposures during the two days before and the 14 days after the onset of symptoms of a probable or confirmed case (WHO et al., 2020):

(a) face-to-face contact with a probable or confirmed case within 1 metre and for at least 15 minutes;

(b) direct physical contact with a probable or confirmed case;

(c) direct care for a patient with probable or confirmed COVID-19 disease without using recommended personal protective equipment;

(d) other situations as indicated by local risk assessments.

1.6 Mathematical Preliminary

In this section, we state some theorems and give the definitions of terminologies that provide the basic mathematical definitions and results, which are crucial for a better understanding for the thesis as an input. The following basic results and terminologies are taken from the known book of Coddingiton (Coddington & Levinson, 1955; Perko, 2013).

1.6.1 System of Ordinary Differential Equations

Consider a system of ordinary differential equation

$$\begin{cases} \dot{x_1} = f_1(x_1, x_2, \cdots, x_n, t), \\ \dot{x_2} = f_2(x_1, x_2, \cdots, x_n, t), \\ \vdots \\ \dot{x_n} = f_n(x_1, x_2, \cdots, x_n, t), \end{cases} \tag{1.1}$$

with $f_i = (x_1, x_2, \cdots, x_n, t)$, $i = 1, 2, 3, \cdots, n$ is a general function of $x_i, i = 1, 2, \cdots, n$ and time t.

If the system (1.1) can be further simplified into a system that do not depend on time, then the system is called autonomous and can be written as

$$\begin{cases} \dot{x_1} = f_1(x_1, x_2, \cdots, x_n), \\ \dot{x_2} = f_2(x_1, x_2, \cdots, x_n), \\ \vdots \\ \dot{x_n} = f_n(x_1, x_2, \cdots, x_n), \end{cases} \tag{1.2}$$

where $f_i = (x_1, x_2, \cdots, x_n, t)$, $i = 1, 2, 3, \cdots, n$ is a function that do not depend explicitly on the time t .

The compact form of system (1.2) can be written as

$$\dot{x} = f(x), x(0) = x_0. \tag{1.3}$$

Let $E \subset \mathbb{R}^n$ and $f : E \to \mathbb{R}^n$ be continuous function on E, then the system (1.2) is said to be linear if $f_1, f_2, \cdots, f_n$ each linear with respect to $x_1, x_2, \cdots x_n$. So the system (1.2) can be written in the form

$$\begin{cases} \dot{x_1} = a_{11}x_1 + a_{12}x_2 + \cdots + a_{1n}x_n, \\ \dot{x_2} = a_{21}x_1 + a_{22}x_2 + \cdots + a_{2n}x_n, \\ \vdots \\ \dot{x_n} = a_{n1}x_1 + a_{n2}x_2 + \cdots + a_{nn}x_n. \end{cases} \tag{1.4}$$

The system (1.2) can be expressed in the form

$$\dot{x} = Ax, \tag{1.5}$$

where $x \in E$, $\dot{x} = (\dot{x_1}, \dot{x_2}, \cdots, \dot{x_n})$ and A is an $n \times n$.
The system (1.2) is said to be nonlinear if there is i such that f_i is nonlinear. The long term behaviour of the solution around the equilibrium point of nonlinear systems (1.2) can be determined through linearization around the equilibrium point of the system (Anggreini, 2016).

Theorem 1.6.1 (Fundamental Existence and Uniqueness Theorem)**.** *Suppose the function $f(x) : \mathbb{R}^n \to \mathbb{R}^n$ is continuously differentiable. Then $x(t)$ is a solution of the differential equation $\frac{dx}{dt} = f(x)$ on an interval I if $x(t)$ is differentiable on I and if $\forall t \in I$,$x(t) \in \mathbb{R}^n$ and $\frac{dx}{dt} = f(x(t))$ and given $x_0 \in \mathbb{R}^n$, $x(t)$ is a solution of the initial value problem*

$$\frac{dx}{dt} = f(x), \quad x(t_0) = x_0$$

on an interval I if $t_0 \in I$, $x(t_0) = x_0$ and $x(t)$ is a solution of the differential (1.3) *on the interval I.*

Detailed analysis and the proof of this result can be found in (Perko, 2013). The following Lemma also taken from the same reference.

Lemma 1.6.1. *Let E be an open subset $\mathbb{R}^n$ and let $f : E \to \mathbb{R}^n$. Then, if $f \in C^1(E)$, f is locally Lipschitz on E.*

Definition 1.6.1. *(Layek, 2015). A point $\tilde{x} \in \mathbb{R}^n$ is said to be an equilibrium point (steady state) of the system* (1.3) *if $f(\tilde{x}) = 0$.*

The system (1.3) can be linearized about the equilibrium point $\tilde{x}$ by using Taylor's Theorem, $f(x) = f(\tilde{x}) + Df(\tilde{x})(x - \tilde{x}) + R(\tilde{x}) = Df(\tilde{x})(x - \tilde{x}) + R(\tilde{x})$ where $Df(\tilde{x})$ is the matrix of first-order partial derivatives of $f(x)$ evaluated at $\tilde{x}$ and $R(\tilde{x})$ is remainder that includes the second and higher order terms of the original function. Since $f(\tilde{x}) = 0$ and $R(\tilde{x})$ is very small and lastly neglected . If $f = (f_1, f_2, \cdots, f_n)$ and $x = (x_1, x_2, \cdots, x_n)$, then the first order partial derivative matrix

$$Df(x) = J = \begin{pmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \cdots & \frac{\partial f_1}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \cdots & \frac{\partial f_2}{\partial x_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \cdots & \frac{\partial f_n}{\partial x_n} \end{pmatrix}$$

is called a Jacobian matrix of f in point $\tilde{x}$.

By using the Jacobian matrix $J(\tilde{x})$ we study the local stability properties of hyperbolic equilibrium point $\tilde{x}$.

Definition 1.6.2. *(Layek, 2015). A point $\tilde{x}$ is said to be stable if for a given $\epsilon > 0$, there exist $\delta = \delta(\epsilon) > 0$ such that, for any other solution, $y(t)$ of* (1.3) *satisfying $|\tilde{x}(t_0) - y(t_0)| < \delta \Rightarrow |\tilde{x}(t) - y(t)| < \epsilon$, $\forall t > t_0$, $t_0 \in \mathbb{R}$.*

Definition 1.6.3. *(Anggreini, 2016). The system* (1.3) *at equilibrium point $\tilde{x} \in \mathbb{R}^n$ is said to be:*

(i) Stable if for every $\epsilon > 0$ there exist $\delta = \delta(\epsilon) >$ such that $x(t)$ satisfies $||x(t_0) - \tilde{x}|| < \delta \Rightarrow ||x(t) - \tilde{x}|| < \epsilon$ for each $t \geq t_0$.

(ii) Local asymptotically stable if the equilibrium point $\tilde{x} \in \mathbb{R}^n$ stable and there exist $\delta > 0$ such that for every solution $x(t)$ that satisfies $||x(t_0) - \tilde{x}|| < \delta$ apply $\lim_{t\to\infty} x(t) = \tilde{x}$.

(iii) Do not be stable if the equilibrium point $\tilde{x} \in \mathbb{R}^n$ doesn't meet i.

Theorem 1.6.2. *(Layek, 2015). Let A be a constant matrix in the system $\frac{dx}{dt} = Ax$ with eigenvalues λ_i, for $i = 1, 2, \cdots, n$*

(a) If the system is stable, then $Re(\lambda_i) \leq 0$ for $i = 1, 2, \cdots, n$.

(b) If either $Re(\lambda_i) < 0$; or if $Re(\lambda_i) \leq 0$ for $i = 1, 2, \cdots, n$ and there is no zero repeated eigenvalue; then the system is uniformly stable.

(c) The system is asymptotically stable if and only if $Re(\lambda_i) < 0$ *for* $i = 1, 2, \cdots, n$ *;note that it is also uniformly stable by* (b).

(e) If $Re(\lambda_i) > 0$ *for any* $i = 1, 2, \cdots, n$ *then, the solution is unstable .*

Theorem 1.6.3. *(Layek, 2015). Let* $\tilde{x} = 0$ *be a hyperbolic equilibrium point of the nonlinear system* (1.3) *with* $f \in C^1$ *(continuously differentiable of order one). Then the stability type of the equilibrium point origin for the nonlinear system is same as that of the linear system* $\dot{x} = Ax$.

For the study of global stability we employ Lyapunov functions given as follows.

Definition 1.6.4 ((Layek, 2015)). *A function* $L : \mathcal{D} \subset \mathbb{R}^n \to \mathbb{R}$ *is said to be positive definite if,*

- $L(x) > 0$ *, for all* $x \neq 0$,
- $L(x) = 0$ *, for all* $x = 0$,
- $L(x) \to \infty$ *, as* $x \to \infty$.

Any function L *is called a Lyapunov function, if it satisfies the conditions of positive definiteness and* $\frac{dL}{dt} \leq 0$ *for all* $x \in \mathcal{D} \backslash \{x_0\}$.

Theorem 1.6.4 (see in(Layek, 2015)). *Let* x_0 *be an equilibrium point of the system* (1.3) *and consider* $L : \mathcal{D} \subset \mathbb{R}^n \to \mathbb{R}$ *be continuously differentiable function such that*

- $L(x_0) = 0$
- $L(x) > 0$ *, for all* $x \in \mathcal{D} \subset \mathbb{R}^n$
- $\frac{dL}{dt} \leq 0 \; \forall x \in \mathcal{D} \backslash \{x_0\}$, $||x|| \to \infty \Rightarrow L(x) \to \infty$

Then the point x_0 *is globally asymptotically stable.*

Definition 1.6.5 (Invariant set). *A set* E *is an invariant set with respect to* (1.3) *if* $x(0) \in E$ *implies* $x(t) \in E$, $\forall t \in \mathbb{R}$ *and a set* E *is positively invariant set with respect to* (1.3) *if* $x(0) \in E$ *implies* $x(t) \in E, \forall t \geq 0$.

1.6.2 Routh-Hurwitz criteria

Routh-Hurwitz criteria is a method used to show the system stability by taking into consideration the coefficients of characteristic equation without counting the roots (Mahardika et al., 2019). The linear stability of a system of differential equations:

$$\frac{dx}{dt} = Ax$$

where $x = (x_1, x_2, \cdots, x_n)$ is eigenvector and its corresponding eigenvalues are determined by the roots of the characteristic polynomial of matrix A. The solution of the system is obtained by setting $x = x_0 e^{\lambda t}$. The equilibrium point is called Hurwitz or asymptotically stable if all the roots of the characteristic polynomial:

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + a_2\lambda^{n-2} + \cdots + a_{n-1}\lambda + a_n \tag{1.6}$$

lie in the left hand complex plane that is if $Re(\lambda) < 0$ for all roots of characteristic polynomial (La Salle, 1976).

Consider the polynomial (1.6) where all the coefficients $a_1, a_2, \cdots, a_n$ are real and $a_n \neq 0$, then the necessary and sufficient condition for all the roots of the characteristic polynomial to have $Re(\lambda) < 0$ is given by Routh-Hurwitz conditions (Merkin, 2012; Mahardika et al., 2019).

Define the n Hurwitz matrices using the coefficients a_i of the characteristic polynomial as:

$$H = \begin{bmatrix} a_1 & 1 & 0 & 0 & \cdots & 0 \\ a_3 & a_2 & a_1 & 1 & \cdots & 0 \\ a_5 & a_4 & a_3 & a_2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & a_n \end{bmatrix}$$

then Routh-Hurwitz condition with $a_n > 0$ are described as follows,

$H_1 = a_1 > 0, \quad \det(H_2) = \begin{vmatrix} a_1 & 1 \\ a_3 & a_2 \end{vmatrix} = a_1a_2 - a_3 > 0$ for polynomial degree 2.

$$\det(H_3) = \begin{vmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & 0 & a_3 \end{vmatrix} = a_1a_2a_3 - a_3^2 > 0 \text{ for polynomial degree 3.}$$

$$\vdots$$

$$\det(H_n) = \begin{vmatrix} a_1 & a_3 & a_5 & \cdots & \\ 1 & a_2 & a_4 & \cdots & \\ 0 & a_1 & a_3 & \cdots & \\ \vdots & & & & \\ 0 & 0 & 0 & \cdots & a_k \end{vmatrix} > 0 \text{ for } k = 1, 2, \cdots, n$$

Chapter 2

Literature Review

In this chapter, we review some related literature on mathematical model of COVID-19 and its transmission that are directly related to the objectives of this study. Currently, COVID-19 is of great concern to researchers, governments, and all people because of the high rate of the infection spread and the significant number of deaths that occurred (Zeb et al., 2020). The group of modelers throughout the global has accepted the challenge in delineating mathematical models of the transmission dynamics of COVID-19 or SARS-CoV-2 and has rapidly reacted to the ongoing novel coronavirus epidemic (Samui et al., 2020).

Atangana (2020) proposed and analyzed an SCIRD type mathematical model to study the transmission dynamics of COVID-19 pandemic by using a system of fractal- fractional differential equations. In this study, the author considered the possibility of transmission of COVID-19 from dead bodies to humans and the effect of lock-down. Three cases were considered. The first case suggested that there is the possibility of transmission from dead to the living (medical staffs as they perform postmortem procedures on corpses, and direct contacts with during burial ceremonies). This case has no equilibrium points except for disease free equilibrium, a clear indication that care must be taken when dealing with corpses due to corona-19. In the second case the transmission rate from dead bodies removed. This case showed an equilibrium point, the number of deaths, carriers and infected grew exponentially up to a certain stability level. In the last case, the author incorporated a lock-down and social distancing effect, using the next generation matrix and achieved a zero reproduction number, with number of deaths, infected and carriers decaying very rapidly. Finally , from the result the author concluded that the integral lock-down is effective in saving human lives.

Tang et al. (2020) investigated a general SEIR-type epidemiological model of COVID-19, which incorporates appropriate compartments relevant to interventions such as quarantine, isolation and treatment. The authors used deterministic compartmental model based on the clinical progression of the disease, epidemiological status of the individuals, and intervention measures. They used the next generation matrix and derived a formula for the control reproduction number. Further, they used data of laboratory confirmed 2019-nCOV cases of mainland china and fitted the model using Markov Chain Monte Carlo (MCMC) method with an adaptive Metropolis-Hastings (M-H) algorithm to carry out the MCMC procedure. Further more, they have been estimated the basic reproduction numbers using different methods (likelihood-based and model-based approaches). The estimations based on likelihood and model analysis showed that the control reproduction number may be as high as 6.47 (95% CI 5.71-7.23) which is very high for the infectious diseases. The sensitivity analyses show that interventions, such as intensive contact tracing followed by quarantine and isolation, can effectively reduce the control reproduction number and transmission risk, with the effect of travel restriction adopted by Wuhan on 2019-nCoV infection in Beijing being almost equivalent to increasing quarantine by a 100 thousand baseline value. Finally, the authors concluded that when travel restriction(no imported exposed individuals) holds in Beijing, then the number of infected individuals in seven days will decrease by 91.14% in Beijing, compared with the scenario of no travel restriction.

Giordano et al. (2020b) developed a new SIDARTHE model for COVID-19 pandemic. They investigated the sensitivity of the model to parameter variations, focusing in particular on the parameters that can be influenced by policymakers such as transmission parameters, related to lockdown measures , testing parameters and related to testing and contact tracing policies. Their model discriminates between infected individuals depending on whether they have been diagnosed and on the severity of their symptoms. They understood the distinction between diagnosed and non-diagnosed individuals is important because the former are typically isolated and hence less likely to spread the infection . This delineation also helps to explain misperceptions of the case fatality rate and of the epidemic spread. Finally, they concluded that Diagnosis campaigns and restrictive social distancing can reduce the widespread of coronavirus among the human.

Khajanchi and Sarkar (2020) proposed a mathematical model SAIUQR to forecast the daily and cumulative number of cases for the COVID-19 pandemic in India. They performed the model validation with real data from four India provinces. They also studied the qualitative properties of the model, including feasible equilibria and their stability with respect to the basic reproduction number R_0. The disease-free equilibrium becomes stable and the endemic equilibrium becomes unstable when the recovery rate of infected individuals increases, but if the disease transmission rate remains higher, then the endemic equilibrium always remains stable. For the estimated model parameters, $R_0 > 1$ for all four states of India, which indicate the significant outbreak of COVID-19. They also performed the short-term prediction as well as long-term prediction. The short-time prediction shows the increasing trend of daily and cumulative cases of COVID-19 for the four states of India. Finally, from the model simulation the authors suggested that quarantine, reported, and unreported symptomatic individuals as well as government intervention polices like media effect, lockdown, and social distancing can play a key role in mitigating the transmission of COVID-19.

Liu et al. (2020) developed SEIRU and SEIRUδ mathematical model by considering reported and unreported cases to study the transmission dynamics of novel coronavirus. The first model incorporates infected persons in the exposed class and the second model incorporates a time delay in infected persons, before transmission is possible. In order to compare the two models, they used the Median of Absolute Deviation (MAD) as an indicator. Later, they applied both models to the COVID-19 epidemic in china and estimated the epidemiological parameters in the models such as the transmission rate and the basic reproductive number. Finally they evaluated the role of the exposed or latency period in the dynamics of a COVID-19 epidemic.

Gatto et al. (2020) proposed a mathematical model to studies the Spread and dynamics of the COVID-19 epidemic in Italy. They studied the effects of drastic measures for transmission containment, based on modeling of the unfolding epidemic. They tested modeling options of the spatially explicit type, suggested by the wave of infections spreading from the initial foci to the rest of Italy. Also, they estimated parameters of a Susceptible-Exposed-Infected-Recovered (SEIR) like transmission model that includes a network of 107 provinces

connected by mobility at high resolution, and the critical contribution of pre-symptomatic and asymptomatic transmission. They estimated a generalized reproduction number (R_0 = 3.60 [3.49 to 3.84]), the spectral radius of a suitable next-generation matrix that measures the potential spread in the absence of containment interventions. The numerical simulation Result indicated the sequence of restrictions posed to mobility and human-to-human interactions have reduced transmission by 45% (42 to 49%). Finally, they conclude asymptomatic and pre-asymptomatic infected individuals are believed to play a key role in the transmission dynamics of COVID-19 outbreak.

Benrhmach et al. (2020) proposed a mathematical model SELIAHRD (Susceptible, Exposed, Latent, Symptomatic, Asymptomatic, Hospitalized, Recovered, and Death), with two kinds of infected people, that is, symptomatic and asymptomatic. The authors assumed that asymptomatic people will not be hospitalized and had the probability to go either recovered or dead. They computed the basic reproduction number R_0 using next generation matrix and investigated the stability analysis of free diseases and endemic equilibrium points of the model. They also presented the numerical simulation of SELIAHRD model in two different scenarios . In first simulation, they assumed when there is no social distancing and in second simulation they assumed that 90% of population obey the rule of social distancing. From the simulation they concluded that the importance of the social distancing in making the number of infected and deaths decrease significantly even with the presence of asymptomatic infection and not overload the health care system.

Djaoue et al. (2020) formulated a mathematical model of COVID-19 transmission using biological features of the disease and control strategies based on the isolation of exposed people, confinement (lock-downs) of the human population, testing people living risks area, wearing of masks and respect of hygienic rules. In the proposed model they classified total human population into susceptible, quarantined, partially confined, totally confined , latency phase , asymptomatic, infected with benign (moderated), infected with serious , quarantined infected and recovered individuals. They provided a theoretical study of the model and derived the basic reproduction number R_0 which determines the extinction and the persistence of the infection. Also they shown that the model exhibits a backward bifurcation at $R_0 = 1$. The authors also performed sensitivity analysis of the model to determine the impact of

related parameters on outbreak severity. They observed that the asymptomatic infectious group of individuals may play a major role in the spreading of transmission. Moreover, various mitigation strategies are investigated and numerical evaluation of control strategies has been performed based on the proposed model. They founded that isolation has a real impact on COVID-19 transmission. As they elaborated when effective efforts are made through the tracing to isolate 80% of exposed people the disease disappears about 100 days. Although they observed that partial confinement does not eradicate the disease due to during partial confinement, when at least 10% of the partially confined population is totally confined, COVID-19 spread stops after 150 days. From massif testing strategy they observed, when more than 95% of moderate and symptomatic infected people are identified and isolated, the disease is also really controlled after 90 days. Finally they concluded that wearing of masks and respecting hygiene rules are fundamental conditions to control the COVID-19 .

Din et al. (2020) constructed a mathematical model for novel coronavirus-19 infectious disease which consists of three different compartments: susceptible, infected, and recovered under convex incident rate involving immigration rate. They derived the formulation of model and some qualitative aspects for the model including existence of equilibriums and its stability results by using various tools of nonlinear analysis. The authors used nonstandard finite difference scheme (NSFD) and simulated the results by using the real data of Wuhan city during the last sixty days from 10 February 2020 to 10 April 2020 against two different sets of values of immigration parameter. The model has been simulated for the fixed values of the parameters except immigration rate. They observed from the simulation how protection, exposure, death, and cure rates affect the susceptible, infected, and recovered population with the passage of time involving immigration. Finally they concluded that Minimizing the immigration during outbreak can cause the increase in protection rate or in other words avoiding unnecessary immigration of people will greatly help in reducing or controlling this disease.

Bugalia et al. (2020) proposed a compartmental mathematical model "S Q_1AQ_2IMR" on epidemiology of COVID-19 transmission dynamics with intervention strategies such as lockdown, quarantine, and hospitalization. They computed the basic reproduction number (R_0), which plays a vital role in mathematical epidemiology. Based on R_0, it is revealed that

the system has two equilibrium, namely disease-free and endemic. They also demonstrated the non-negativity and boundedness of the solutions, local and global stability of equilibria and transcritical bifurcation to analyze its epidemiological relevance. They estimated the model parameters and predict the near future scenario of the disease. The global sensitivity analysis has also been performed to observe the impact of different parameters on R_0. They also investigated the dynamics of disease in respect of different situations of lockdown such as complete lockdown, partial lockdown, and no lockdown. The analysis show that if there is partial or no lockdown case, then endemic level would be high. Along with this, the high transmission rate ensures higher level of endemicity. From the short time prediction, they predicted that India may face a crucial phase (approx 6000000 infected individuals within 140 days) in near future due to COVID-19. Finally, they suggested that COVID-19 may be controllable by reducing the contacts and increasing the efficacy of lockdown.

Khoshnaw et al. (2020) proposed a mathematical modeling for corona virus (COVID-19) in predicting future behavior and sensitivity analysis. They formulated their model by stratifying the total population in to susceptible, exposed, pre-symptomatic, symptomatic, quarantined susceptible , quarantined exposed, hospitalize and recovered individuals. They used SimBiology Toolbox for MATLAB to calculate the local sensitivity of each model state with respect to model constants. They also applied the idea of local sensitivity to calculate the sensitivity of each model state with respect to model parameters. furthermore, they used three different techniques those are non normalizations, half normalizations and full normalizations to calculate the model sensitivities. Finally, they suggested identifying a critical model parameters based on computational simulations is an effective way to further study the model practically and theoretically and give some suggestions for future improvements of the novel coronavirus vaccination programs, interventions and controlling the spread of disease.

Kassahun et al. (2021) proposed a mathematical model for the transmission dynamics of Coronavirus diseases (COVID-19) using a system of nonlinear ordinary differential equations by incorporating self protection behavior changes in the population. They subdivides the human population into five disjoint compartments; susceptible, exposed, infected, recovered, death and one compartment, which is the contaminated material or surface. They

computed the basic reproduction number using next generatin matrix and performed the local and global stability analysis of the model. Based on the available data, they estimated the unknown model parameters using a combination of least square and Bayesian estimation methods for different countries. They also determined and identified the key model parameters for the spread of disease dynamics using forward sensitivity index and they observed the sensitive parameters for the spread of the virus vary from country to country. Moreover, the numerical simulations of the model were performed to supplement and verify the effectiveness of the analytical findings. From the result they found out that the reproduction number depends mostly on the infection rates, the threshold value of the force of infection for a population, the recovery rates, and the virus decay rate in the environment. Finally they illustrated that control of the effective transmission rate (recommended human behavioral change towards self-protective measures) is essential to stop the spreading of the virus.

Eshetu et al. (2020) formulated a dynamical model of COVID-19 to describe the transmission dynamics of the disease. They stratified the total population into sub-classes consisting of protected, susceptible, asymptomatic, symptomatic, quarantine,recovered and coronavirus (COVID-19) individuals. They proved the well possedness of the formulated model equations and established both local and global stability of the disease free equilibrium and endemic equilibrium point of the model equations. The sensitivity analysis of the model equation was performed on the key parameters to find out their relative significance and potential impact on the transmission dynamics of COVID-19. They also performed the numerical simulation using the software $MATLAB\ R2015b$ with $ODE45$ solver and sketched the graph. Finally, from the simulation carried out on the model they concluded that an increase in level of contact rate among individuals has an effect on reducing the prevalence of COVID-19 and COVID-19 disease.

Zeb et al. (2020) developed a mathematical model to present the dynamical behavior of COVID-19 infection by incorporating isolation class. The authors stratified the total population in to susceptible, exposed, infected, isolated and recovered individuals. They discussed about non negativity of the model solutions and computed the reproduction number of the model using next generation matrix. Also they presented the local and global stability of the proposed model by using the approach of the basic reproductive . For the numerical simula-

tion of the proposed model, nonstandard finite difference (NSFD) scheme and Runge-Kutta fourth order method are used. The result of simulation show that human to human contact has a great potential to cause the outbreaks of COVID-19. Therefore, they conclude isolation of the infected human overall can reduce the risk of future COVID-19 spread.

Samui et al. (2020) proposed SAIU compartmental mathematical model to predict and control the transmission dynamics of COVID-19 pandemic in India with epidemic data up to April 30, 2020. They computed the basic reproduction number R_0 for the given period and mathematical analysis of the model in terms of stability analysis. The sensitivity analysis of the model parameters are performed and their corresponding graphical result are presented. Finally, the numerical results for the sensitive parameters are plotted and their effects are shown graphically. Based on the numerical simulation, they predicted that about 60 days the peak will be higher for COVID-19 in India and after that the curve will plateau but the coronavirus diseases will persist for a long time.

All of the above authors were developed a mathematical model of COVID-19 transmission dynamics by viewing in different aspects. They formulated their model by considering different compartments based on their assumptions and investigated the dynamical behavior, qualitative analysis of their model. However, they do not considered compartments(susceptible, exposed, asymptomatic, symptomatic, quarantined, hospitalized and recovered) with optimal control strategies simultaneously in their model. In addition some of the model which included asymptomatic infectious class do not concern induced death rate in asymptomatic class in model. Thus, in order to fill the entire gap of the study in this research work we develop the mathematical model for COVID-19 transmission dynamics based on proposed model by (Samui et al., 2020), we introduced exposed, quarantined, hospitalized and recovered class with optimal control strategies to study the epidemic of COVID-19. The propose model will be validated by real data from Ethiopia.

Chapter 3

Research Methodology

In this section we present: study area, source of information, approach of the study and mathematical procedures.

3.1 Study area

Ethiopia is in the northeast African region known as the Horn of Africa. It is the second-most populous nation with 114961850 populations (2020 est.) in Africa (after Nigeria) and the 12th in the world with 1.47% of the total world population (WHO, 2020b). It is bounded by Eritrea to the north, Djibouti to the northeast, Somalia to the east, Kenya to the south, and Sudan and South Sudan to the west. Ethiopia is slightly less than twice the size of Texas, USA (or as large as France and Spain combined) . The country occupies an area of total 1,104,300 square km. The total land area is 1,096,570 square km and the area occupied by water bodies is 7,444 sq.km. According to 2020 estimates, there are 31.6 births per 1,000

Figure 3.1: Map of Ethiopia:source Wikipidia

people and the death rate is 5.9 deaths per 1,000 people. The average fertility rate is around 4 children born per woman. Around 40% of the population is below the age of 15. As the pacific prime website provided Ethiopia currently has about 1 doctor per 100,000 people, 119 hospitals, and 412 health facilities. These public centers are usually in urban areas.

3.2 Source of information

The applicable source of information for this research study are:

• Data of COVID-19 compromised from the Ethiopian Public Health Institute.

• Other source of information are taken from WHO COVID-19, books, published journals, and related studies from Internet are used.

3.3 Method of data analysis

The study involved both qualitative and quantitative analysis. Thus, the data is analyzed using MATLAB software and the results are displayed in the form of tables and figures.

3.4 Descriptions of Mathematical Procedure

To achieve the objective of this research, we employ analytical and numerical method.
First we formulate a **SEAIQHR** mathematical model which describes the transmission dynamics of coronavirus(COVID-19) using a system of non-linear ordinary differential equations. Then well possedness of the formulated model is determined both in the mathematical and epidemiological sense and presented. We also performed the qualitative analysis of the model as well as basic reproduction number and sensitivity analysis of the model. Local and global stability analysis of the equilibrium points of the model are investigated by using Jacobian matrix and Lyapunov function respectively. Then we extended the proposed model into control problem. The existence and characterization of optimal control was performed using Pontryagin Minimum Principle (PMP). To supplement the analytical solution of the model, we performed numerical simulation using MATLAB software.

Chapter 4

Model Formulation and Analysis

In this chapter, we formulate a deterministic mathematical model governed by a system of nonlinear ordinary differential to investigate the transmission dynamics of coronavirus disease. Detailed model description and analysis are also discussed.

4.1 Description of model variables and assumptions

In this section, we present the description of model variables with varying population size in homogeneously mixing population.

Stopping the spread of COVID-19 requires finding and testing all suspected cases so that confirmed cases are promptly and effectively isolated and receive appropriate care, and the close contacts of all confirmed cases are rapidly identified so that they can be quarantined and medically monitored for the 14-day incubation period of the virus (COVID, 19). These WHO recommendations are not partial feasible in developing counties like Ethiopia due to economic issue and community understanding. Moreover, the health systems are ill-equipped to cope with COVID-19 and the work-forces are heavily reliant on the support of donors, UN and NGO partners. With these in mind the following assumptions are considered.

- Tracing and testing all the exposed population are impossible,
- Some portion of the exposed populations are infectious without symptoms of the disease and remain in the community,
- Portion of the exposed populations are all confirmed cases and effectively isolated

(in hospitals and/or designated housing for mild and moderate cases, or at home with sufficient support if designated housing is not available) immediately and until they are no longer infectious,

- The severe and critical COVID-19 patients are treated separately with special care in hospital by health-care professionals;
- Some portion of the exposed populations having close contacts are traced, quarantined and monitored for 14 days, whether in specialized accommodation or self-quarantine. Monitoring and support are also rendered through a combination of visits by community volunteers(relatives), phone calls, or messaging,
- Some part of the quarantined populations develop symptoms and isolated to infectious class,

Under these assumptions, the population is stratified into seven epidemiological compartments defined as:

- $S(t)$ denotes susceptible individuals who are vulnerable to the disease at time t,
- $E(t)$ represents individuals who are exposed to the diseases but not yet infectious,
- $A(t)$ an infectious individuals who do not show symptoms of the disease and do not quarantined at time t,
- $I(t)$ an infectious individuals who show symptoms of the disease at time t and isolated,
- $Q(t)$ an individuals those who are quarantined at time t,
- $H(t)$ represents severe and critical COVID-19 patients treated under special care in hospital at time t,
- $R(t)$ recovered individuals at any time t,
- $N((t)$ total population at time t , such that

$$N(t) = S(t) + E(t) + A(t) + I(t) + Q(t) + H(t) + R(t)$$

.

4.2 Model Formulation

The population is stratified into the proportions of: susceptible $S(t)$, exposed $E(t)$, asymptomatic infectious $A(t)$, symptomatic infectious $I(t)$, quarantined $Q(t)$, hospitalized $H(t)$ and recovered individuals $R(t)$. We assumed that a susceptible population is recruited (by birth or immigration) into population at a constant rate Λ. A proportion of the susceptible individuals become exposed to the COVID-19 infection at a rate $\lambda = \frac{\beta(bA+I)}{N}$ which is called force of infection(or rate of infection) as given in (Eshetu et al., 2020). Here, β denotes the effective contact rate with an infectious individuals and b represents the transmission coefficient of asymptomatic infectious individuals to susceptible individuals. In this context, $b > 1$, means the asymptomatic infected individuals infect the susceptible individuals more likely than the symptomatic infected individuals. In the contrary, $b < 1$, implies that the symptomatic infected individuals have more chance to infect the susceptible individuals than asymptomatic infected individuals. The case $b = 1$, tell us that both asymptomatic and symptomatic infected individuals have equal chance to infect the susceptible populations. Besides, we assumed that an individuals in the compartment $E(t)$ may develop a symptoms of the COVID-19 infection and move to the symptomatic infected compartment $I(t)$ at a constant rate r.

Individuals who do not show symptoms enter in to asymptomatic class $A(t)$ at a rate p. The alleged individuals in exposed class enter in to the quarantined class at a rate θ. Further, individuals in the asymptomatic $A(t)$ compartment are assumed to be recovered due to natural immunity and move to recovered class $R(t)$ at a rate k_1. Furthermore, infected individuals in compartment $I(t)$ may recovered at a rate α and those at critical risk are assumed hospitalized at a constant rate q. The portion of individuals in class $Q(t)$ are recovered at a constant rate η while the remaining individuals isolated in to $I(t)$ compartment at a rate n. In addition, all treated individuals from compartment $H(t)$ directly move to class $R(t)$ at a constant rate K_2. Natural death rate in each categories of the population is denoted by μ. COVID-19 induced death rate in the compartment $A(t)$, $I(t)$, and $H(t)$ are respectively denoted as δ_1, δ_2 and δ_3 . All parameters and state variables in the model are assumed to be non-negative. Summarizing the above assumption, the flow diagram is depicted in Figure 4.1. Compared to the mathematical model introduced by (Samui et al., 2020), the present model differ due to incorporation of exposed, quarantined, hospitalized and recovered class .

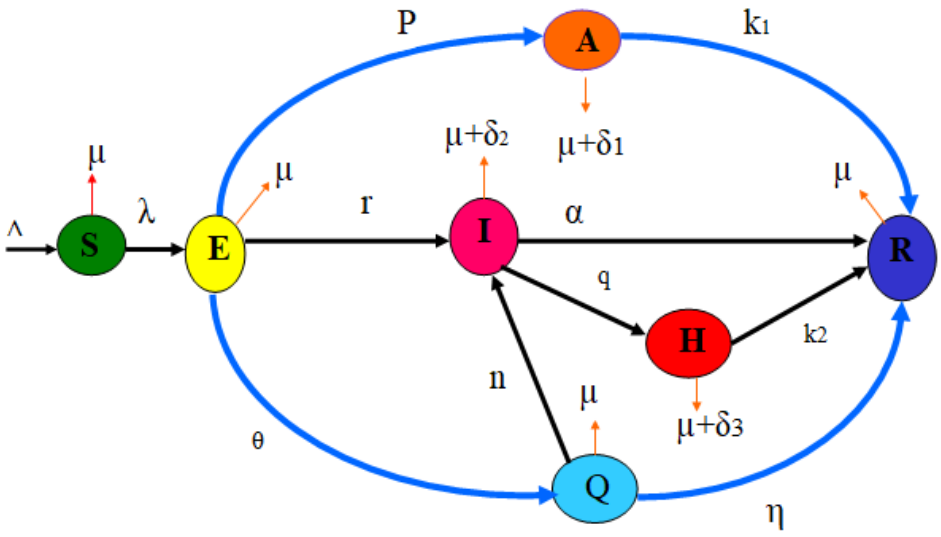


Figure 4.1: Schematic flow diagram for the proposed model.

Thus, the resulting mathematical model is given by a system of nonlinear ordinary differential equations:

$$\begin{cases} \frac{dS}{dt} = \Lambda - (\lambda + \mu)S, \\ \frac{dE}{dt} = \lambda S - (\mu + p + r + \theta)E, \\ \frac{dA}{dt} = pE - (k_1 + \mu + \delta_1)A, \\ \frac{dI}{dt} = rE + nQ - (\mu + \delta_2 + q + \alpha)I, \\ \frac{dQ}{dt} = \theta E - (\mu + n + \eta)Q, \\ \frac{dH}{dt} = qI - (\mu + \delta_3 + k_2)H, \\ \frac{dR}{dt} = k_1 A + \alpha I + \eta Q + k_2 H - \mu R, \end{cases} \tag{4.1}$$

where $\lambda = \frac{\beta(bA+I)}{N}$ with initial condition : $S(0) = S_0 > 0$, $E(0) = E_0 \geq 0$, $A(0) = A_0 \geq 0$, $I(0) = I_0 \geq 0$, $Q(0) = Q_0 \geq 0$, $H(0) = H_0 \geq 0$ and $R(0) = R_0 \geq 0$.

The initial data are assumed non-negative due to the present study deals with human population. Notations and description of model parameters are given in Table 4.1.

Table 4.1: Notations and description of the model parameters

parameters	Description of the model parameter
Λ	Recruitment rate
β	Effective contact rate of infection.
λ	Force of infection or infection rate
θ	Rate at which exposed individuals moves to the quarintined class
μ	The natural death rate.
p	Rate of exposed individuals enter into asymptomatic infectious class
r	Rate at which exposed individuals moves to the symptomatic infectious class
b	Transmission coefficient of asymptomatic individuals
q	Rate of transmission from $I(t)$ to $H(t)$
n	Rate of transmission from $Q(t)$ to $I(t)$
η	Rate of transmission from $Q(t)$ to $R(t)$
α	Rate of $I(t)$ individual recovered and move into $R(t)$
k_2	rate of hospitalized individual recovered and moved to $R(t)$
k_1	Treatment rate from compartment $A(t)$ to $R(t)$
δ_1	Diseases induced mortality rate for asymptomatic individuals in $A(t)$
δ_2	Diseases induced mortality rate for symptomatic individuals in $I(t)$
δ_3	Diseases induced mortality rate for hospitalized individuals in $H(t)$

4.3 Model Analysis

This section presents, the invariant region, non-negativity of model solution, equilibria, reproduction number, stability of equilibria and sensitivity analysis.

4.3.1 Invariant Region

In this subsection, we study the properties of model solution in certain feasible region. To obtain the set of feasible region, we add the model equations (4.1) so that,

$$\frac{d}{dt}(S+E+A+I+Q+H+R)(t) = \Lambda-\mu(S+E+A+I+Q+H+R)(t)-(\delta_1 A+\delta_2 I+\delta_3 H)(t)$$

$= \Lambda - \mu N(t) - (\delta_1 A + \delta_2 I + \delta_3 H)(t)$. Since $\delta_1, \delta_2, \delta_3$ is non-negative, we have, $\frac{dN}{dt} = \Lambda - \mu N(t) - (\delta_1 A + \delta_2 I + \delta_3 H)(t) \leq \Lambda - \mu N(t)$. From this one can easily conclude that

$$\frac{dN}{dt} + \mu N(t) \leq \Lambda. \tag{4.2}$$

Solving equation (4.2) and rearranging we have

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} + (N(0) - \frac{\Lambda}{\mu})e^{-\mu t} \tag{4.3}$$

where $N(0)$ denotes the initial population. As $t \longrightarrow \infty$ in equation (4.3), the population size $N(t) \longrightarrow \frac{\Lambda}{\mu}$. From this we can conclude that $0 \leq N(t) \leq \frac{\Lambda}{\mu}$. Thus, the feasible region for the model system (4.1) can be expressed as:

$$\Omega = \left\{(S(t), E(t), A(t), I(t), Q(t), H(t), R(t)) \in \mathbb{R}^7_+ : 0 \leq N(t) \leq \frac{\Lambda}{\mu}\right\} \tag{4.4}$$

Here, all the state variables with the initial values as given in (4.1) are remain bounded in the octant $\mathbb{R}^7_+$. What follow is that, all solutions of the model equations with nonnegative initial data remain positive for all time $t \geq 0$. That is, for the COVID-19 transmission dynamics model (4.1) to be epidemiological meaningful and mathematical well-posed, we shall prove that all state variables are non-negative for all time $t \geq 0$. Thus, the following consecutive result presents that the system (4.1) is meaningful in the given domain Ω.

Theorem 4.3.1 (Existence and Uniqueness of Solution)**.** *Let $t_0 > 0$ and the initial conditions satisfies $S(0) > 0$, $E(0) \geq 0$, $A(0) \geq 0$, $I(0) \geq 0$, $Q(0) \geq 0$, $H(0) \geq 0$ and $R(0) \geq 0$ in the prescribed region Ω. Then the solutions of the model system* (4.1) *exists and unique in $\mathbb{R}^7_+$.*

Proof. The right hand side of (4.1) can be compactly written as

$$f(X) = \begin{pmatrix} \Lambda - (\lambda + \mu)S \\ \lambda S - (\mu + p + r + \theta)E \\ pE - (k_1 + \mu + \delta_1)A \\ rE + nQ - (\mu + \delta_2 + q + \alpha)I \\ \theta E - (\mu + n + \eta)Q \\ qI - (\mu + \delta_3 + k_2)H \\ k_1 A + \alpha I + \eta Q + k_2 H - \mu R \end{pmatrix}$$

where $X = [S, E, A, I, Q, H, R]^T$. Here, f has a continuous partial derivative with respect to each state variables in $\mathbb{R}^7_+$ and all are bounded. Thus, f is locally Lipschitz in $\mathbb{R}^7_+$. Hence, the result is the direct consequence of the Fundamental Existence and Uniqueness Theorem (Perko, 2013). □

Theorem 4.3.1 infers that the proposed mathematical model is meaningful in the feasible region.

Theorem 4.3.2. *[Non-negativity of solutions] If $S(0)$, $E(0)$, $A(0)$, $I(0)$, $Q(0)$, $H(0)$ and $R(0)$ are all non-negative, then the solutions $S(t)$, $E(t)$, $A(t)$, $I(t)$, $Q(t)$, $H(t)$ and $R(t)$ are all non-negative for $t \geq 0$.*

Proof. We shall prove this theorem by the method of contradiction. For this, assume that the total population $N(t) \neq 0$ for all $t \geq 0$. For the first equation in the model system (4.1), there exists time t_1 such that the susceptible population becomes $S(t_1) = 0,$ and $\frac{dS(t_1)}{dt} < 0$ provided that

$$E(0) \geq 0, A(0) \geq 0, I(0) \geq 0, Q(0) \geq 0, H(0) \geq 0, R(0) \geq 0, 0 \leq t \leq t_1.$$

This implies that $\frac{dS(t)}{dt}|_{t=t_1} = \Lambda - (\lambda + \mu)S(t_1) = \Lambda < 0$, which is a contradiction. Thus, we conclude that $S(t) > 0, \forall t \geq 0$.

Next, corresponding to the second equation in (4.1), assume that there exists time t_2 such that the exposed population satisfies $E(t_2) = 0,$ and $\frac{dE(t_2)}{dt} < 0$ whenever

$$S(0) > 0, A(0) \geq 0, I(0) \geq 0, Q(0) \geq 0, H(0) \geq 0, R(0) \geq 0, 0 \leq t \leq t_2.$$

Again, from this we obtain that

$$\frac{dE(t)}{dt}|_{t=t_2} = \lambda S(t_2) - (\mu + p + r + \theta)E(t_2) = \lambda S(t_2) < 0.$$

This is also a contradiction. That means, $E(t) \geq 0, \forall t \geq 0$. By similar approach it can be shown that $A(t) \geq 0,\ I(t) \geq 0\ , Q(t) \geq 0\ , H(t) \geq 0,\ R(t) \geq 0,\ \forall t \geq 0$.

Hence, we conclude that all the state variables $S(t) > 0$, $E(t) \geq 0$, $A(t) \geq 0$, $I(t) \geq 0$, $Q(t) \geq 0$, $H(t)$, $R(t) \geq 0$, $\forall t \geq 0$. This complete the proof. □

Remark 4.3.1. *Note that all the state variables are bounded in the feasible region. Besides, the solutions are remain non-negative by Theorem 4.3.2. Thus, the domain of attraction*

defined by the set Ω *is an invariant region. That is, all solutions of the model equations* (4.1) *with initial data in inside the interior of the prescribed region remains in the* $\mathbb{R}^7_+$ *and no solution path moves beyond the boundary of* Ω.

4.3.2 Disease free Equilibrium Point

Disease free equilibrium points are steady-state solutions where there is no corona virus(COVID-19) infection. That is, all the infected classes are zero and the entire population comprise of only susceptible individuals. To find the disease free equilibrium, we set the left hand side of model (4.1) equal to zero. That means

$$\begin{cases} \Lambda - (\lambda + \mu)S = 0, \\ \lambda S - (\mu + p + r + \theta)E = 0, \\ pE - (k_1 + \mu + \delta_1)A = 0, \\ rE + nQ - (\mu + \delta_2 + q + \alpha)I = 0, \\ \theta E - (\mu + n + \eta)Q = 0, \\ qI - (\mu + \delta_3 + k_2)H = 0, \\ k_1 A + \alpha I + \eta Q + k_2 H - \mu R = 0, R = 0. \end{cases} \tag{4.5}$$

Evaluating it at $E = A = I = Q = H = 0$ and solving for the non-infected state variable, we obtain the disease free equilibrium point $E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0)$.

4.3.3 Basic Reproduction number

The basic reproduction number is denoted by R_0 and it is defined as the expected number of new cases (infections), that one infected case will generate during its entire infectious lifetime (Diekmann et al., 1990). It is very important in determining whether the global dynamics of the disease can be spread or not. When the value of the basic reproduction number falls less than unity, then the disease will not be spread in the community, whereas, when its values cross the unity, then the disease can be spread in the community i.e., the disease becomes endemic and will produce deaths and sometimes outbreak which is called epidemics. In epidemiology, the epidemic is expected to be eliminated if $R_0 < 1$, and persists if $R_0 > 1$. Therefore, the basic reproduction number is a threshold parameter for a disease and its biological significance is obvious.

We use the next generation method given in (Diekmann et al., 2010) to compute R_0.
Let $x = (E, A, I, Q, H)^T$ corresponds an infected compartments among the seven compartments. In order to compute R_0, it is important to distinguish new infections from all other changes in population as follows:

- $\mathcal{F}_i(x)$ denotes the rate of appearance of new infections in compartment i ,
- $\mathcal{V}_i^+(x)$ represents the rate of transfer of individuals into compartment i by all others means,
- $\mathcal{V}_i^-(x)$ denotes the rate of transfer of individuals out of compartment i.

It is assumed that each function is continuously differentiable at least twice in each variable. The disease transmission model consists of nonnegative initial conditions together with the following system of equations:

$$\frac{dx_i}{dt} = \mathcal{F}_i(x) - \mathcal{V}_i(x), i = 1, 2, 3, 4, 5 \tag{4.6}$$

where $\mathcal{V}_i = \mathcal{V}_i^- - \mathcal{V}_i^+$.
The next step is the computation of the square matrices F and V of order 5×5 ,where 5 is the number of infected class, then it can be defined by:
F=$\left[\frac{\partial \mathcal{F}_i(x_0)}{\partial x_j}\right]$ and V=$\left[\frac{\partial \mathcal{V}_i(x_0)}{\partial x_j}\right]$, where

$$\mathcal{F}(x) = \begin{bmatrix} \frac{\beta S(bA+I)}{N} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \text{ and } \mathcal{V}(x) = \begin{bmatrix} (\mu + p + r + \theta)E \\ -pE + (k_1 + \mu + \delta_1)A \\ -rE - nQ + (\mu + \delta_2 + q + \alpha)I \\ -\theta E + (\mu + n + \eta)Q \\ -qI + (\mu + \delta_3 + k_2)H \end{bmatrix}$$

with $1 \leq i, j \leq 5$ such that F is non negative, V is non singular matrix and E_0 is the disease free equilibrium point . Now, the jacobian matrices of $\mathcal{F}(x)$ and $\mathcal{V}(x)$ at the diseases-free equilibrium point E_0 are:

$$D\mathcal{F}(E_0) = \begin{pmatrix} 0 & \frac{\beta b S_0}{N} & \frac{\beta S_0}{N} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } D\mathcal{V}(E_0) = \begin{pmatrix} c_1 & 0 & 0 & 0 & 0 \\ -p & c_2 & 0 & 0 & 0 \\ -r & 0 & c_3 & -n & 0 \\ -\theta & 0 & 0 & c_4 & 0 \\ 0 & 0 & -q & 0 & c_5 \end{pmatrix}$$

respectively, where $c_1 = \mu+p+r+\theta$, $c_2 = k_1+\mu+\delta_1$, $c_3 = \mu+\delta_2+q+\alpha$, $c_4 = \mu+n+\eta$ and $c_5 = \mu+\delta_3+k_2$.

The linearization of the system (4.1) associated with matrix F and V at DFE point E_0 is given by

$$F = \begin{pmatrix} 0 & \beta b & \beta & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} c_1 & 0 & 0 & 0 & 0 \\ -p & c_2 & 0 & 0 & 0 \\ -r & 0 & c_3 & -n & 0 \\ -\theta & 0 & 0 & c_4 & 0 \\ 0 & 0 & -q & 0 & c_5 \end{pmatrix} \text{ respectively.}$$

Now the determinant of V denoted as $\det(V)$ becomes $\det(V) = c_1c_2c_3c_4c_5 \neq 0$ and this verify that V is non-singular matrix. After some algebraic computations the inverse matrix of V is constructed as

$$V^{-1} = \begin{pmatrix} \frac{1}{c_1} & 0 & 0 & 0 & 0 \\ \frac{p}{c_1c_2} & \frac{1}{c_2} & 0 & 0 & 0 \\ \frac{n\theta+rc_4}{c_1c_3c_4} & 0 & \frac{1}{c_3} & \frac{n}{c_3c_4} & 0 \\ \frac{\theta}{c_1c_4} & 0 & 0 & \frac{1}{c_4} & 0 \\ \frac{q(n\theta+c_4r)}{c_1c_3c_4c_5} & 0 & \frac{q}{c_3c_5} & \frac{qn}{c_3c_4c_5} & \frac{1}{c_5} \end{pmatrix} \text{ and } M = FV^{-1} = \begin{pmatrix} \frac{\beta[pbc_3c_4+c_2(n\theta+rc_4)]}{c_1c_2c_3c_4} & \frac{\beta b}{c_2} & \frac{\beta}{c_3} & \frac{\beta n}{c_3c_4} & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

Since F is non-negative and V is non-singular, then V^{-1} is non-negative and FV^{-1} is non-negative. Hence, the matrix M is called next generation matrix for the model. From this matrix, we determine the dominant eigenvalues given as $\det(M-\lambda I) = |M-\lambda I| = 0$. This implies that

$$\begin{vmatrix} \frac{\beta[pbc_3c_4+c_2(n\theta+rc_4)]}{c_1c_2c_3c_4} - \lambda & \frac{\beta b}{c_2} & \frac{\beta}{c_3} & \frac{\beta n}{c_3c_4} & 0 \\ 0 & -\lambda & 0 & 0 & 0 \\ 0 & 0 & -\lambda & 0 & 0 \\ 0 & 0 & 0 & -\lambda & 0 \\ 0 & 0 & 0 & 0 & -\lambda \end{vmatrix} = 0.$$

It reduces to the fifth power equation for λ as $\lambda^4(\frac{\beta[pbc_3c_4+c_2(n\theta+rc_4)]}{c_1c_2c_3c_4} - \lambda) = 0$ giving five eigenvalues as $\lambda_1 = 0$, $\lambda_2 = 0$, $\lambda_3 = 0$, $\lambda_4 = 0$ and $\lambda_5 = \frac{\beta[pbc_3c_4+c_2(n\theta+rc_4)]}{c_1c_2c_3c_4}$. However, the largest eigenvalue here is $\lambda_5 = \frac{\beta[pbc_3c_4+c_2(n\theta+rc_4)]}{c_1c_2c_3c_4}$ and is the spectral radius $\rho(M)$ as the threshold value or the basic reproductive number. Thus, it can be concluded that the

reproduction number of the model is given by

$$R_0 = \frac{\beta[pbc_3c_4 + c_2(n\theta + rc_4)]}{c_1c_2c_3c_4}$$

where $c_1 = \mu + p + r + \theta$, $c_2 = k_1 + \mu + \delta_1$, $c_3 = \mu + \delta_2 + q + \alpha$ and $c_4 = \mu + n + \eta$.

4.4 Stability analysis of disease free equilibrium

In absence of the infectious disease, the system (4.1) have a unique disease free steady state E_0 which is given by

$$E_0 = \left\{S^0, E^0, A^0, I^0, Q^0, H^0, R^0\right\} = \left\{\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0\right\}.$$

Now, the stability analysis of E_0 is conducted and the results are presented in the form of theorem as follows.

4.4.1 Local stability of disease free equilibrium

Theorem 4.4.1. *The DFE, E_0 of the system* (4.1) *is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. Consider the right hand side expressions of the equations (4.1) as functions so as to find the Jacobian matrix at the DFE as follows:

$$\begin{cases} \Lambda - (\lambda + \mu)S = f_1(S, E, A, I, Q, H, R), \\ \lambda S - (\mu + p + r + \theta)E = f_2(S, E, A, I, Q, H, R), \\ pE - (k_1 + \mu + \delta_1)A = f_3(S, E, A, I, Q, H, R), \\ rE + nQ - (\mu + \delta_2 + q + \alpha)I = f_4(S, E, A, I, Q, H, R), \\ \theta E - (\mu + n + \eta)Q = f_5(S, E, A, I, Q, H, R), \\ qI - (\mu + \delta_3 + k_2)H = f_6(S, E, A, I, Q, H, R), \\ k_1A + \alpha I + \eta Q + k_2H - \mu R = f_7(S, E, A, I, Q, H, R). \end{cases} \tag{4.7}$$

The Jacobian matrix of the f_1, f_2, f_3, f_4, f_5, f_6, f_7 with respect to x=(S, E, A, I, Q, H, R) is

given by

$$J(x) = \begin{pmatrix} \frac{-\beta(bA+I)}{N} - \mu & 0 & \frac{-\beta bS}{N} & \frac{-\beta S}{N} & 0 & 0 & 0 \\ \frac{\beta(bA+I)}{N} & -c_1 & \frac{\beta bS}{N} & \frac{\beta S}{N} & 0 & 0 & 0 \\ 0 & p & -c_2 & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -c_3 & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -c_4 & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -c_5 & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -\mu \end{pmatrix} \tag{4.8}$$

Therefore, the Jacobian matrix J of model at the disease free equilibrium E_0 reduces to

$$J(E_0) = \begin{pmatrix} -\mu & 0 & -\beta b & -\beta & 0 & 0 & 0 \\ 0 & -c_1 & \beta b & \beta & 0 & 0 & 0 \\ 0 & p & -c_2 & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -c_3 & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -c_4 & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -c_5 & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -\mu \end{pmatrix}$$

where $c_1 = \mu + p + r + \theta$, $c_2 = k_1 + \mu + \delta_1$, $c_3 = \mu + \delta_2 + q + \alpha$, $c_4 = \mu + n + \eta$ and $c_5 = \mu + \delta_3 + k_2$. The eigenvalues of $J(E_0)$ are the solutions of the characteristics equation $\det[J(E_0) - \lambda I_7] = 0$,where I_7 is an identity matrix of order 7. Then we have

$$|J(E_0) - \lambda I_7| = \begin{vmatrix} -\mu - \lambda & 0 & -\beta b & -\beta & 0 & 0 & 0 \\ 0 & -c_1 - \lambda & \beta b & \beta & 0 & 0 & 0 \\ 0 & p & -c_2 - \lambda & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -c_3 - \lambda & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -c_4 - \lambda & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -c_5 - \lambda & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -\mu - \lambda \end{vmatrix} = 0.$$

This implies that

$$|J(E_0)-\lambda I_7| = -(\mu+\lambda)\begin{vmatrix} -c_1-\lambda & \beta b & \beta & 0 & 0 & 0 \\ p & -c_2-\lambda & 0 & 0 & 0 & 0 \\ r & 0 & -c_3-\lambda & n & 0 & 0 \\ \theta & 0 & 0 & -c_4-\lambda & 0 & 0 \\ 0 & 0 & q & 0 & -c_5-\lambda & 0 \\ 0 & k_1 & 0 & \eta & k_2 & -\mu-\lambda \end{vmatrix} = 0$$

$$= -(\mu+\lambda)^2(c_5+\lambda)\begin{vmatrix} -c_1-\lambda & \beta b & \beta & 0 \\ p & -c_2-\lambda & 0 & 0 \\ r & 0 & -c_3-\lambda & n \\ \theta & 0 & 0 & -c_4-\lambda \end{vmatrix} = 0. \quad (4.9)$$

Thus, from equation (4.9) the characteristic equation becomes

$-(\mu+\lambda)^2(c_5+\lambda)[\lambda^4+(c_1+c_2+c_3+c_4)\lambda^3+[c_3c_4+c_1c_4+c_2c_4+c_1c_3+c_2c_3+c_1c_2-(\beta r+\beta bp)]\lambda^2+[c_1c_3c_4+c_2c_3c_4+c_1c_2c_4+c_1c_2c_3-\beta[n\theta+pb(c_3+c_4)+r(c_2+c_4)]]\lambda+c_1c_2c_3c_4-\beta[(n\theta+rc_4)c_2+pbc_3c_4]]=0$

which is equivalent to

$(\mu+\lambda)^2(c_5+\lambda)=0$ and $\lambda^4+(c_1+c_2+c_3+c_4)\lambda^3+[c_3c_4+c_1c_4+c_2c_4+c_1c_3+c_2c_3+c_1c_2-(\beta r+\beta bp)]\lambda^2+[c_1c_3c_4+c_2c_3c_4+c_1c_2c_4+c_1c_2c_3-\beta[n\theta+pb(c_3+c_4)+r(c_2+c_4)]]\lambda+c_1c_2c_3c_4-\beta[(n\theta+rc_4)c_2+pbc_3c_4]=0.$

We can write the characteristic equation as $\lambda_1=\lambda_2=-\mu, \lambda_3=-c_5$ and $\lambda^4+(c_1+c_2+c_3+c_4)\lambda^3+[c_3c_4+c_1c_4+c_2c_4+c_1c_3+c_2c_3+c_1c_2-(\beta r+\beta bp)]\lambda^2+[c_1c_3c_4+c_2c_3c_4+c_1c_2c_4+c_1c_2c_3-\beta[n\theta+pb(c_3+c_4)+r(c_2+c_4)]]\lambda+c_1c_2c_3c_4-\beta[(n\theta+rc_4)c_2+pbc_3c_4]=0,$ where $a_1=c_1+c_2+c_3+c_4$, $a_2=c_3c_4+c_1c_4+c_2c_4+c_1c_3+c_2c_3+c_1c_2-\beta(r+bp)$, $a_3=c_1c_3c_4+c_2c_3c_4+c_1c_2c_4+c_1c_2c_3-\beta[n\theta+pb(c_3+c_4)+r(c_2+c_4)]$, $a_4=c_1c_2c_3c_4-\beta[pbc_3c_4+(n\theta+rc_4)c_2]$

It can be observed that the first three eigenvalues λ_1, λ_2 and λ_3 are negative as all the model parameters are positive.

To determine the sign of the remaining four eigenvalues we use the Routh-Hurwitz criteria (Merkin, 2012) for the fourth order equation; $\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4=0$.

According to the Routh-Hurwitz criteria the four roots of a polynomial of order four of the type $\rho(\lambda)=\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4$, are real distinct and negative if the coefficients satisfy the conditions $a_1>0, a_2>0, a_3>0, a_4>0$ and $a_1a_2a_3>a_3^2+a_1^2a_4$.

Let us check the conditions as follows:

- $a_1 > 0 \Rightarrow c_1 + c_2 + c_3 + c_4 > 0$ because all parameters are positive and their sum is also positive.

- $a_2 > 0 \Rightarrow a_2 = c_3c_4 + c_1c_4 + c_2c_4 + c_1c_3 + c_2c_3 + c_1c_2 - \beta(r + bp) > 0 \Rightarrow a_2 > 0$ holds if $c_3c_4 + c_1c_4 + c_2c_4 + c_1c_3 + c_2c_3 + c_1c_2 > \beta(bp + r)$.

- $a_3 > 0 \Rightarrow a_3 = c_1c_3c_4 + c_2c_3c_4 + c_1c_2c_4 + c_1c_2c_3 - \beta[n\theta + pb(c_3 + c_4) + r(c_2 + c_4)] > 0 \Rightarrow a_3 > 0$ holds if $c_1c_3c_4 + c_2c_3c_4 + c_1c_2c_4 + c_1c_2c_3 > \beta[n\theta + pb(c_3 + c_4) + r(c_2 + c_4)]$.

- $a_4 > 0 \Rightarrow a_4 = c_1c_2c_3c_4 - \beta[pbc_3c_4 + (n\theta + rc_4)c_2] > 0 \Rightarrow c_1c_2c_3c_4 > \beta[pbc_3c_4 + (n\theta + rc_4)c_2] \Rightarrow 1 > \frac{\beta[pbc_3c_4 + (n\theta + rc_4)c_2]}{c_1c_2c_3c_4} = R_0 \Rightarrow 1 > R_0$, hence $a_4 > 0$ if $R_0 < 1$ holds.

- Lastly, $a_1a_2a_3 > a_3^2 + a_1^2a_4 \Rightarrow a_1a_2a_3 - a_3^2 + a_1^2a_4 > 0$.

This implies those remained four eigenvalues are also real distinct and negative for $R_0 < 1$. Therefore, the disease free equilibrium point E_0 of the system of ordinary differential equation (4.1) is locally asymptotically stable if $R_0 < 1$. □

4.4.2 Global stability of disease free equilibrium

Theorem 4.4.2. *The disease free equilibrium of system* (4.1) *is globally asymptotically stable if* $R_0 < 1$.

Proof. To establish the global stability of the disease-free equilibrium point, we construct a Lyapunov function
$L(S, E, A, I, Q, H, R) : \Omega \subset \mathbb{R}^7_+ \longrightarrow \mathbb{R}^+$ defined by

$$L(S, E, A, I, Q, H, R) = \frac{D_1(E(t))^2}{2} + \frac{D_2(A(t))^2}{2} + \frac{D_3(I(t))^2}{2} + \frac{D_4(Q(t))^2}{2}$$

where Di, for $i = 1, 2, 3, 4$ are arbitrary positive constant to be chosen and Ω is an open neighborhood of the disease free equilibrium point E_0.
Then the function $L(S, E, A, I, Q, H, R)$ should satisfies the following three condition to be a Lyapunov function

- L is continuously differentiable.

- $L > 0, \forall (S, E, A, I, Q, H, R) \in \Omega \backslash \{E_0\}$ and $L(E_0) = 0$ as $(E(t))^2 \geq 0, (A(t))^2 \geq 0, (I(t))^2 \geq 0, (Q(t))^2 \geq 0$.

- $\frac{dL}{dt} \leq 0$ in Ω, then E_0 is stable.

Clearly, the first two condition holds since L is nonnegative in Ω except at E_0 and $L(E_0) = 0$. Now let us check the third condition $\frac{dL}{dt} \leq 0$ in Ω. By differentiating $L(S, E, A, I, Q, H, R)$ with respecting to time t yields

$\frac{dL}{dt} = D_1 \frac{dE}{dt} + D_2 \frac{dA}{dt} + D_3 \frac{dI}{dt} + D_4 \frac{dQ}{dt}$

$= D_1[\lambda S - (\mu + p + r + \theta)E] + D_2[pE - (k_1 + \mu + \delta_1)A] + D_3[rE + nQ - (\mu + \delta_2 + q + \alpha)I] + D_4[\theta E - (\mu + n + \eta)Q]$

$= D_1[\frac{\beta(bA+I)S}{N} - \underbrace{(\mu + p + r + \theta)}_{c_1} E] + D_2[pE - \underbrace{(k_1 + \mu + \delta_1)}_{c_2} A] + D_3[rE + nQ - \underbrace{(\mu + \delta_2 + q + \alpha)}_{c_3} I] + D_4[\theta E - \underbrace{(\mu + n + \eta)}_{c_4} Q]$

$\leq D_1(\beta bA + \beta I - c_1 E) + D_2(pE - c_2 A) + D_3(rE + nQ - c_3 I) + D_4(\theta E - c_4 Q)$, since $S \leq N$ at E_0

$= (D_2 p + r D_3 + D_4 \theta - C_1 D_1)E + (\beta b D_1 - D_2 c_2)A + (\beta D_1 - D_3 c_3)I + (D_3 n - D_4 c_4)Q$

$= c_1 D_1(\frac{D_2 p + r D_3 + D_4 \theta}{c_1 D_1} - 1)E + (\beta b D_1 - D_2 c_2)A + (\beta D_1 - D_3 c_3)I + (D_3 n - D_4 c_4)\theta.$

Now choosing $D_1 = c_2 c_3 c_4$, $D_2 = \beta b c_3 c_4$, $D_3 = \beta c_2 c_4$ and $D_4 = \beta c_2 n$, then we get

$\frac{dL}{dt} \leq c_1 D_1(\frac{\beta[b c_3 c_4 p + r c_2 c_4 + c_2 n \theta]}{c_1 c_2 c_3 c_4} - 1)E + (\beta b c_2 c_3 - \beta b c_2 c_3)A + (\beta c_2 c_3 - \beta c_2 c_3)I + (\beta c_2 c_4 n - \beta c_2 n c_4)\theta$

$= c_1 D_1(\underbrace{\frac{\beta[b c_3 c_4 p + r c_2 c_4 + c_2 n \theta]}{c_1 c_2 c_3 c_4}}_{R_0} - 1)E = c_1 D_1(R_0 - 1)E.$

This implies that $\frac{dL}{dt} \leq c_1 D_1(R_0 - 1)E$. Therefore, $\frac{dL}{dt} \leq c_1 D_1(R_0 - 1)E < 0$ if $R_0 - 1 < 0$. Hence, the largest compact invariant set in Ω is the singleton set $E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0)$. Hence by LaSalle's invariant principle (La Salle, 1976), every solution trajectory of the model equations (4.1) with initial conditions in the set Ω approaches to E_0 as time t tends to infinity $(t \longrightarrow \infty)$ whenever $R_0 < 1$. This implies that the disease-free equilibrium is globally asymptotically stable in Ω. □

4.5 Stability of Endemic Equilibrium

The endemic equilibrium point denoted by $E_1 = (S^*, E^*, A^*, I^*, Q^*, H^*, R^*)$ is a steady state solution where the disease persists in the population. It is obtained by setting rates of

changes of variables with respect to time in the model equation (4.1) to zero. That is, setting

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dA}{dt} = \frac{dI}{dt} = \frac{dQ}{dt} = \frac{dH}{dt} = \frac{dR}{dt} = 0.$$

Solving we obtain

$$S^* = \frac{N^*}{R_0},$$
$$E^* = \frac{\Lambda(R_0-1)}{c_1 R_0},$$
$$A^* = \frac{\Lambda p(R_0-1)}{c_1 c_2 R_0}$$
$$, I^* = \frac{\Lambda(rc_4+n\theta)(R_0-1)}{c_1 c_3 c_4 R_0},$$
$$Q^* = \frac{\Lambda\theta(R_0-1)}{c_1 c_4 R_0},$$
$$H^* = \frac{\Lambda q(rc_4+n\theta)(R_0-1)}{c_1 c_3 c_4 c_5 R_0},$$
$$R^* = \frac{\Lambda[c_2(\alpha c_5+k_2 q)(rc_4+n\theta)+c_3 c_5(k_1 pc_4+\eta\theta c_2)](R_0-1)}{c_1 c_2 c_3 c_4 c_5 \mu R_0},$$

where, $c_1 = \mu + p + r + \theta$, $c_2 = k_1 + \mu + \delta_1$, $c_3 = \mu + \delta_2 + q + \alpha$, $c_4 = \mu + n + \eta$ and $c_5 = \mu + \delta_3 + k_2$.

Clearly, from the above we conclude that a positive unique endemic equilibrium point exists whenever $R_0 > 1$.

4.5.1 Local stability of the Endemic equilibrium (EE)

Theorem 4.5.1. *The Endemic Equilibrium point E_1 of the system* (4.1) *is locally asymptotically stable if $R_0 > 1$.*

Proof. To obtain the local stability of E_1, the Jacobian matrix (4.8) of the model equations computed under local stability of DFE is used at E_1. Thus, the jacobian matrix at E_1 becomes

$$J(E_1) = \begin{pmatrix} \frac{-\beta(bA^*+I^*)}{N} - \mu & 0 & \frac{-\beta bS^*}{N} & \frac{-\beta S^*}{N} & 0 & 0 & 0 \\ \frac{\beta(bA^*+I^*)}{N} & -c_1 & \frac{\beta bS^*}{N} & \frac{\beta S^*}{N} & 0 & 0 & 0 \\ 0 & p & -c_2 & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -c_3 & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -c_4 & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -c_5 & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -\mu \end{pmatrix}$$

$$= \begin{pmatrix} -\mu R_0 & 0 & \frac{-\beta b}{R_0} & \frac{-\beta}{R_0} & 0 & 0 & 0 \\ (R_0-1)\mu & -c_1 & \frac{\beta b}{R_0} & \frac{\beta}{R_0} & 0 & 0 & 0 \\ 0 & p & -c_2 & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -c_3 & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -c_4 & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -c_5 & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -\mu \end{pmatrix} \tag{4.10}$$

where $E_1 = (S^*, E^*, A^*, I^*, Q^*, H^*, R^*)$ is the endemic equilibrium of the system (4.1).

The eigenvalues of (4.10) are the solution of the characteristic equation $\det(J(E_1) - \lambda I_7) = 0$. This means that

$$|J(E_1)-\lambda I_7| = \begin{vmatrix} -(\mu R_0+\lambda) & 0 & \frac{-\beta b}{R_0} & \frac{-\beta}{R_0} & 0 & 0 & 0 \\ (R_0-1)\mu & -(c_1+\lambda) & \frac{\beta b}{R_0} & \frac{\beta}{R_0} & 0 & 0 & 0 \\ 0 & p & -(c_2+\lambda) & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -(c_3+\lambda) & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -(c_4+\lambda) & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -(c_5+\lambda) & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -(\mu+\lambda) \end{vmatrix} = 0.$$

This is the same as

$$|J(E_1)-\lambda I_7| = [(\mu+\lambda)(c_5+\lambda)] \begin{vmatrix} -(\mu R_0+\lambda) & 0 & \frac{-\beta b}{R_0} & \frac{-\beta}{R_0} & 0 \\ (R_0-1)\mu & -(c_1+\lambda) & \frac{\beta b}{R_0} & \frac{\beta}{R_0} & 0 \\ 0 & p & -(c_2+\lambda) & 0 & 0 \\ 0 & r & 0 & -(c_3+\lambda) & n \\ 0 & \theta & 0 & 0 & -(c_4+\lambda) \end{vmatrix} = 0.$$

After computing determinant of the 5×5 matrix above, lastly we get the following characteristic equation

$$[(\mu+\lambda)(c_5+\lambda)][\lambda^5 + B_1\lambda^4 + B_2\lambda^3 + B_3\lambda^2 + B_4\lambda + B_5] = 0 \tag{4.11}$$

where $B_1 = c_1 + c_2 + c_3 + c_4 + \mu R_0$, $B_2 = c_2c_4 + c_3(c_1 + c_2 + c_4) + c_1(c_2 + c_4) + (c_1 + c_2 + c_3 + c_4)\mu R_0 - \frac{\beta(bp+r)}{R_0}$,

$B_3 = c_1c_2c_3 + c_4(c_1c_3 + c_2c_3 + c_1c_2) + (c_3(c_1 + c_2 + c_4) + c_1(c_2 + c_4) + c_2c_4)\mu R_0 - \frac{\beta}{R_0}(r(c_2 + \mu) + n\theta + pb(c_3 + \mu + c_4 + rc_4))$, $B_4 = (c_4(c_1c_3 + c_2c_3 + c_1c_2) + c_1c_2c_3)\mu R_0 - \frac{\beta\mu}{R_0}(2pbc_3 +$

$r(c_2 + c_4) + \theta n)$ and $B_5 = \mu(R_0 - 1)$.

Clearly, from the equation (4.11) we have $\lambda_1 = -\mu$, $\lambda_2 = -c_5$, and $\lambda^5 + B_1\lambda^4 + B_2\lambda^3 + B_3\lambda^2 + B_4\lambda + B_5 = 0$.

Thus, the first two eigenvalues λ_1 and λ_2 are negative due to all the parameter are positive. To determine the sign of the remaining five eigenvalues we apply the Routh-Hurwitz criteria (Merkin, 2012) for the polynomial equation

$$\lambda^5 + B_1\lambda^4 + B_2\lambda^3 + B_3\lambda^2 + B_4\lambda + B_5 = 0$$

The Routh-Hurwitz criteria implies that the roots of the eigen polynomial

$$\rho(\lambda) = \lambda^5 + B_1\lambda^4 + B_2\lambda^3 + B_3\lambda^2 + B_4\lambda + B_5$$

are real distinct and negative if the coefficients satisfy the conditions $B_i > 0$ for $i = 1, 2, 3, 4, 5$ and the determinant of $\rho(\lambda) > 0$.

It is straight forward to verify that this conditions are satisfied and hence the last five eigenvalues are real distinct and negative. That is

- $B_1 > 0 \Rightarrow c_1 + c_2 + c_3 + c_4 + \mu R_0 > 0$ because all parameters are positive and their sum is also positive.
- $B_2 > 0 \Rightarrow c_2c_4 + c_3(c_1 + c_2 + c_4) + c_1(c_2 + c_4) + (c_1 + c_2 + c_3 + c_4)\mu R_0 - \frac{\beta(bp+r)}{R_0} > 0$. That is true if $c_2c_4 + c_3(c_1 + c_2 + c_4) + c_1(c_2 + c_4) + (c_1 + c_2 + c_3 + c_4)\mu R_0 > \frac{\beta(bp+r)}{R_0}$
- $B_3 > 0 \Rightarrow c_1c_2c_3 + c_4(c_1c_3 + c_2c_3 + c_1c_2) + (c_3(c_1 + c_2 + c_4) + c_1(c_2 + c_4) + c_2c_4)\mu R_0 - \frac{\beta}{R_0}(r(c_2 + \mu) + n\theta + pb(c_3 + \mu + c_4 + rc_4)) > 0$. Equivalently, $c_1c_2c_3 + c_4(c_1c_3 + c_2c_3 + c_1c_2) + (c_3(c_1 + c_2 + c_4) + c_1(c_2 + c_4) + c_2c_4)\mu R_0 > \frac{\beta}{R_0}(r(c_2 + \mu) + n\theta + pb(c_3 + \mu + c_4 + rc_4))$.
- $B_4 > 0 \Rightarrow (c_4(c_1c_3 + c_2c_3 + c_1c_2) + c_1c_2c_3)\mu R_0 - \frac{\beta\mu}{R_0}(2pbc_3 + r(c_2 + c_4) + \theta n) > 0$.
- $B_5 > 0 \Rightarrow \mu(R_0 - 1) > 0$. This holds if $R_0 > 1$.

and the determinant,

$D_1 = B_1 > 0$

$D_2 = B_1B_2 > 0$

$D_3 = B_1B_2 - B_3 > 0$

$D_4 = B_1B_2B_3 - B_3^2 - B_1^2B_4 > 0$

$D_5 = B_1B_2B_3B_4 + 2B_1B_4B_5 + B_2B_3B_5 - B_1B_2^2B_5 - B_1^2B_4^2 - B_3^2B_4 - B_5^2 > 0.$

Therefore the system (4.1) become local asymptotically stable at endemic equilibrium E_1 if $R_0 > 1$. □

4.5.2 Global stability of the endemic equilibrium Point(EE)

Theorem 4.5.2. *The endemic equilibrium point of the model equation* (4.1) *is globally asymptotically stable if* $R_0 > 1$.

Proof. To establish this result define the Lyapunov function L by:

$L(S^*, E^*, A^*, I^*, Q^*, H^*, R^*) = [S - S^* - S^* \ln(\frac{S}{S^*})] + [E - E^* - E^* \ln(\frac{E}{E^*})] + [A - A^* - A^* \ln(\frac{A}{A^*})] + [I - I^* - I^* \ln(\frac{I}{I^*})] + [Q - Q^* - Q^* \ln(\frac{Q}{Q^*})] + [H - H^* - H^* \ln(\frac{H}{H^*})] + [R - R^* - R^* \ln(\frac{R}{R^*})]$.

Differentiating L with respect to time t we obtain

$\frac{dL}{dt} = (\dot{S} - \frac{S^*}{S}\dot{S}) + (\dot{E} - \frac{E^*}{E}\dot{E}) + (\dot{A} - \frac{A^*}{A}\dot{A}) + (\dot{I} - \frac{I^*}{I}\dot{I}) + (\dot{Q} - \frac{Q^*}{Q}\dot{Q}) + (\dot{H} - \frac{H^*}{H}\dot{H}) + (\dot{R} - \frac{R^*}{R}\dot{R})$.

$= (1 - \frac{S^*}{S})\dot{S} + (1 - \frac{E^*}{E})\dot{E} + (1 - \frac{A^*}{A})\dot{A} + (1 - \frac{I^*}{I})\dot{I} + (1 - \frac{Q^*}{Q})\dot{Q} + (1 - \frac{H^*}{H})\dot{H} + (1 - \frac{R^*}{R})\dot{R}$

Substituting $\dot{S}, \dot{E}, \dot{A}, \dot{I}, \dot{Q}, \dot{H}$ and $\dot{R}$ from model equation (4.1) leads to

$\frac{dL}{dt} = (1 - \frac{S^*}{S})[\Lambda - (\lambda + \mu)S] + (1 - \frac{E^*}{E})[\lambda S - (\mu + p + r + \theta)E] + (1 - \frac{A^*}{A})[pE - (k_1 + \mu + \delta_1)A] + (1 - \frac{I^*}{I})[rE + nQ - (\mu + \delta_2 + q + \alpha)I] + (1 - \frac{Q^*}{Q})[\theta E - (\mu + n + \eta)Q] + (1 - \frac{H^*}{H})[qI - (\mu + \delta_3 + k_2)H] + (1 - \frac{R^*}{R})[k_1A + \alpha I + \eta Q + k_2H - \mu R]$

$= [\Lambda - \lambda S - \mu S - \frac{\Lambda S^*}{S} + \lambda S^* + \mu S^*] + [\lambda S - \mu E - pE - rE - \theta E - \lambda S\frac{E^*}{E} + \mu E^* + pE^* + rE^* + \theta E^*] + [pE - k_1A - \mu A - \delta_1 A - pE\frac{A^*}{A} + \mu A^* + \delta_1 A^* + k_1 A^*] + [rE + nQ - \alpha I - qI - \mu I - \delta_2 - rE\frac{I^*}{I} - nQ\frac{I^*}{I} + \alpha I^* + qI^* + \mu I^* + \delta_2 I^*] + [\theta E - \mu Q - nQ - \eta Q - \theta E\frac{Q^*}{Q} + \eta Q^* + nQ^* + \eta Q^*] + [qI - k_2H - \mu H - \delta_3 H - qI\frac{H^*}{H} + k_2H^* + \mu H^* + \delta_3 H^*] + [\alpha I + k_2H + k_1A + \eta Q - \mu R - \alpha I\frac{R^*}{R} - k_2H\frac{R^*}{R} - k_1A\frac{R^*}{R} - \eta\theta\frac{R^*}{R} + \mu R^*]$.

After mathematical manipulation and collecting like terms it becomes

$\frac{dL}{dt} = [\Lambda + (\lambda + \mu)S^* + \underbrace{(\mu + p + r + \theta)}_{c_1}E^* + \underbrace{(k_1 + \mu + \delta_1)}_{c_2}A^* + \underbrace{(\alpha + q + \mu + \delta_2)}_{c_3}I^* + \underbrace{(\mu + n + \eta)}_{c_4}Q^* + \underbrace{(k_2 + \mu + \delta_3)}_{c_5}H^* + \mu R^*] - [\Lambda\frac{S^*}{S} + \lambda S\frac{E^*}{E} + \delta_1 A + pE\frac{A^*}{A} + \delta_2 I + rE\frac{I^*}{I} + nQ\frac{I^*}{I} + \theta E\frac{Q^*}{Q} + \delta_3 H + qI\frac{H^*}{H} + \alpha I\frac{R^*}{R} + k_2H\frac{R^*}{R} + k_1A\frac{R^*}{R} + \eta\theta\frac{R^*}{R} + \underbrace{(S + E + A + I + Q + H + R)}_{N}\mu]$

$= [\Lambda + (\lambda + \mu)S^* + c_1E^* + c_2A^* + c_3I^* + c_4Q^* + c_5H^* + \mu R^*] - [\Lambda\frac{S^*}{S} + \lambda S\frac{E^*}{E} + pE\frac{A^*}{A} + (rE + nQ)\frac{I^*}{I} + \theta E\frac{Q^*}{Q} + qI\frac{H^*}{H} + (\alpha I + k_2H + K_1A + \eta\theta)\frac{R^*}{R} + \delta_1 A + \delta_2 I + \delta_3 H + N\mu]$

$= [\Lambda + (\lambda + \mu)S^* + c_1E^* + c_2A^* + c_3I^* + c_4Q^* + c_5H^* + \mu R^*] - [\Lambda\frac{S^*}{S} + \lambda S\frac{E^*}{E} + pE\frac{A^*}{A} + (rE + nQ)\frac{I^*}{I} + \theta E\frac{Q^*}{Q} + qI\frac{H^*}{H} + (\alpha I + k_2H + K_1A + \eta\theta)\frac{R^*}{R} + \delta_1 A + \delta_2 I + \delta_3 H + \Lambda]$, since

$N \leq \frac{\Lambda}{\mu}$

$= [(\lambda+\mu)S^* + c_1E^* + c_2A^* + c_3I^* + c_4Q^* + c_5H^* + \mu R^*] - [\Lambda\frac{S^*}{S} + \lambda S\frac{E^*}{E} + pE\frac{A^*}{A} + (rE+nQ)\frac{I^*}{I} + \theta E\frac{Q^*}{Q} + qI\frac{H^*}{H} + (\alpha I + k_2H + K_1A + \eta\theta)\frac{R^*}{R} + \delta_1A + \delta_2I + \delta_3H]$

Setting

$M_1 = (\lambda+\mu)S^* + c_1E^* + c_2A^* + c_3I^* + c_4Q^* + c_5H^* + \mu R^*$ and

$M_2 = \Lambda\frac{S^*}{S} + \lambda S\frac{E^*}{E} + pE\frac{A^*}{A} + (rE+nQ)\frac{I^*}{I} + \theta E\frac{Q^*}{Q} + qI\frac{H^*}{H} + (\alpha I + k_2H + K_1A + \eta\theta)\frac{R^*}{R} + \delta_1A + \delta_2I + \delta_3H.$

Compactly this becomes

$$\frac{dL}{dt} = M_1 - M_2.$$

Thus, we get $\frac{dL}{dt} < 0$ if $M_1 < M_2$ and $\frac{dL}{dt} = 0$ if $M_1 = M_2$, this holds if $S = S^*, E = E^*, A = A^*, I = I^*, Q = Q^*, H = H^*$ and $R = R^*$.

Therefore, the largest compact invariant set $\left\{(S^*, E^*, A^*, I^*, Q^*, H^*, R^*) \in \Omega; \frac{dL}{dt} = 0\right\}$ is a singleton E_1 which is the endemic equilibrium of (4.1). Thus by the LaSalle's Invariance Principle (La Salle, 1976), E_1 is globally asymptotically stable in the set Ω for $M_1 < M_2$ and $R_0 > 1$. □

4.6 Sensitivity analysis

Sensitivity analysis is a statistical technique that can be applied to mathematical or computational model to provide insight on how uncertainty in the input variables affect the model outputs and which input variables tends to drive variation in the outputs to achieve the desired goals (Powell et al., 2005). We compute the sensitivity indices of the basic reproductive number R_0 to the parameters in the model. These indices allow us how important each parameter is to disease transmission. Sensitivity analysis is mainly utilized to describe the robustness of model forecasting to the parameter values (since there are usually errors in the collection of data and presumed model parameter values) (Chitnis et al., 2008). Here, we perform a sensitivity analysis of the basic reproductive number R_0 to quantify the fluctuations in the SEAIQHR model parameters. Now from this, we can identify the parameters that have a high impact on the basic reproduction number as well as on the disease transmission. Sensitivity indices permit us to quantify the relative change in a state variable when a parameter alters.

To perform sensitivity of R_0 we use the normalized forward sensitivity index of a variable to

a parameter which is the ratio of the relative change in the variable to the relative change in the parameter. The explicit expression of R_0 is given by

$$R_0 = \frac{\beta[pb(\mu+\delta_2+q+\alpha)(\mu+n+\eta)+(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))]}{(\mu+p+r+\theta)(k_1+\mu+\delta_1)(\mu+\delta_2+q+\alpha)(\mu+n+\eta)}$$

The reproduction number above contains thirteen parameters and we compute the normalized forward sensitivity index for each parameters of R_0.

Definition 4.6.1 ((Rodrigues et al., 2013))**.** *The normalized forward sensitivity index of R_0, which is differentiable with respect to a given parameter, w, is defined as:*

$$\phi_w^{R_0} = \frac{\partial R_0}{\partial w} \times \frac{w}{R_0}. \tag{4.12}$$

By using equation (4.12) we compute the normalized forward sensitivity indices of the model parameters as follows:

$\phi_\beta^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1,$

$\phi_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0} = \frac{p[b(\alpha+q+\mu+\delta_2)(\mu+n+\eta)[c_1-p]-(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))]}{c_1[pb(\alpha+q+\mu+\delta_2)(\mu+n+\eta)+(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))]},$

$\phi_b^{R_0} = \frac{\partial R_0}{\partial b} \times \frac{b}{R_0} = \frac{bp(\alpha+q+\mu+\delta_2)(\mu+n+\eta)}{bp(\alpha+q+\mu+\delta_2)(\mu+n+\eta)+(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))},$

$\phi_\alpha^{R_0} = \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0} = \frac{-\alpha(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))}{(\alpha+q+\mu+\delta_2)[bp(\alpha+q+\mu+\delta_2)(\mu+n+\eta)+(n\theta+r(\mu+n+\eta))]},$

Similarly, we compute for the rest parameters and over all the sensitivity indices of the model parameters are summarized in table 4.2 below.

Table 4.2: Sensitivity indices for model parameters

parameters	**Description**	**Sensitivity indices**
β	Effective contact rate of infection	+1
θ	Rate at which E(t) moves to Q(t) class	0.1753
μ	The natural death rate	-0.0160
p	Rate of E(t) enter into A(t) class	-0.3214
r	Rate at which E(t) moves to I(t) class	0.1467
b	Rate of transmission from $I(t)$ to $S(t)$	0.02584
q	Rate of transmission from $I(t)$ to $H(t)$	-0.0051
n	Rate of I(t) moved to $Q(t)$	0.0914
k_1	Treatment rate $A(t)$ to $R(t)$	-0.02576
δ_1	Diseases induced mortality rate for $A(t)$	-0.000017876
δ_2	Diseases induced mortality rate for $I(t)$	-0.00018206
α	Treatment rate for $I(t)$	-0.7291
η	Treatment rate for $Q(t)$	-0.0854

From the above table 4.2 based on sign of the values of the parameters those with positive indices, β, b, r, and n show that they have great impact on expanding the disease in the population. Due to if their values are increasing(decreasing) by some percentage then, the basic reproduction number R_0 increase(decrease) by the same percentage. In contrary, parameters θ, μ, q, α, k_1, p, δ_1, η and δ_2 those whose their sensitivity indices are negative have an influence of minimizing the spread of the disease in the community. Due to as their values increase by some percentage then, the basic reproduction number R_0 decreases. The bar diagram of sensitivity indices in table 4.2 is depicted in figure 4.2 below.

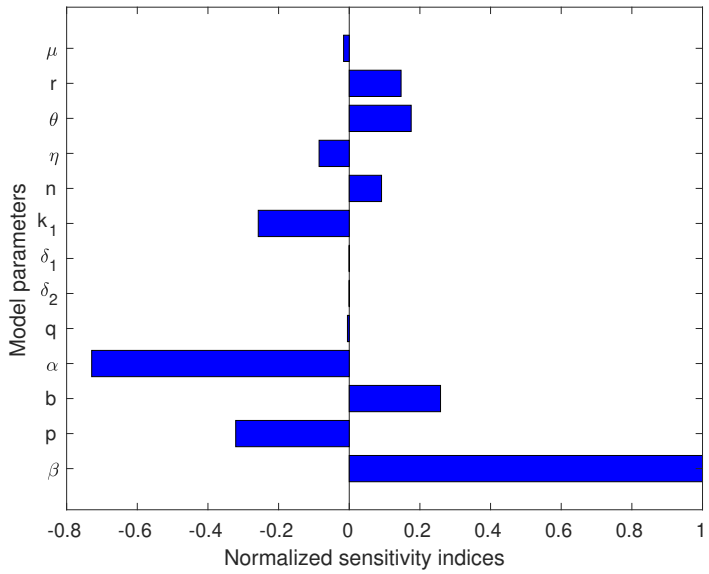


Figure 4.2: Normalized sensitivity indices of R_0 with respect to parameters of the model (4.1). Parameter values are taken from Table 4.2.

4.7 Bifurcation analysis of the model

Bifurcation of a system first reported by French mathematician Henri Poincaré and it means structural change in the orbit of a system (Layek, 2015). In dynamical systems, bifurcation occurs when a small smooth change made to the parameter values of a system causes a sudden "qualitative" or topological change in its behaviour. Generally, at a bifurcation, the local stability properties of equilibria, periodic orbits or other invariant sets changes (Faye, 2011) .

Theorem 4.7.1 ((Castillo-Chavez & Song, 2004))**.** *Suppose , a general system of ODEs with a parameter ϕ is given by:*

$$\frac{dx}{dt} = f(x, \phi), f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n, f \in C^2(\mathbb{R}^n \times \mathbb{R}). \tag{4.13}$$

Without loss of generality, it is assumed that 0 is an equilibrium for system (4.13) *for all values of the parameter ϕ , i.e $f(0, \phi) = 0$ for all ϕ. Then the following assumption raised :*
$A_1 : A = \mathcal{D}_x f(0, 0) = \frac{\partial f_i}{\partial x_i}(0, 0)$ *is the linearization matrix of system* (4.13) *around the equilibrium 0 with ϕ evaluated at 0. Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;*
A_2 : *Matrix A has a non-negative right eigenvector w and a left eigenvector v corresponding*

to the zero eigenvalue .

Let f_k *be the* k^{th} *component of* f *and*

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \left[\frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)\right]$$

and

$$b = \sum_{k,i,=1}^{n} v_k w_i \left[\frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0)\right].$$

The local dynamics of (4.13) *around 0 are totally determined by* a *and* b*.*

(i) $a > 0$, $b > 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is locally asymptotically stable, and there exists a positive unstable equilibrium; when* $0 < \phi \ll 1$, 0 *is unstable and there exists a negative and locally asymptotically stable equilibrium;*

(ii) $a < 0$, $b < 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is unstable; when* $0 < \phi \ll 1$, 0 *is locally asymptotically stable, and there exists a positive unstable equilibrium;*

(iii) $a > 0$, $b < 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is unstable, and there exists a locally asymptotically stable negative equilibrium; when* $0 < \phi \ll 1$, 0 *is stable, and a positive unstable equilibrium appears;*

(iv) $a < 0$, $b > 0$. *When* ϕ *changes from negative to positive,* 0 *changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable .*

Particularly, if $a < 0$ and $b > 0$, then a forward bifurcation occurs at ϕ=0; if $a > 0$ and $b > 0$, then a backward bifurcation occurs at ϕ=0.

Using this approach , we can identify the possibility of bifurcation occur for our system (4.1) at $R_0 = 1$ by choosing parameter from R_0.

Let $S = x_1$, $E = x_2$, $A = x_3$, $I = x_4$, $Q = x_5$, $H = x_6$, $R = x_7$ and $N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7$. Moreover, by using vector notation $x = (x_1, x_2, x_3, x_4, x_5, x_6, x_7)^T$. Then the system (4.1) can be re-written in the form $\frac{dx}{dt} = (f_1, f_2, f_3, f_4, f_5, f_6, f_7)^T$ as follow

$$\begin{cases} \frac{dx_1}{dt} = \Lambda - (\lambda + \mu)x_1 = f_1 \\ \frac{dx_2}{dt} = \lambda x_1 - (\mu + p + r + \theta)x_2 = f_2 \\ \frac{dx_3}{dt} = px_2 - (k_1 + \mu + \delta_1)x_3 = f_3 \\ \frac{dx_4}{dt} = rx_2 + nx_5 - (\mu + \delta_2 + q + \alpha)x_4 = f_4 \\ \frac{dx_5}{dt} = \theta x_2 - (\mu + n + \eta)x_5 = f_5 \\ \frac{dx_6}{dt} = qx_4 - (\mu + \delta_3 + k_2)x_6 = f_6 \\ \frac{dx_7}{dt} = k_1x_3 + \alpha x_4 + \eta x_5 + k_2x_6 - \mu x_7 = f_7 \end{cases} \tag{4.14}$$

If we choose β= β^* as bifurcation parameter, then at $R_0 = 1$ we get $\beta = \beta^* = \frac{c_1c_2c_3c_4}{pbc_3c_4+c_2(n\theta+rc_4)}$. The disease free equilibrium is given by $E_0 = (x_1^* = \frac{\Lambda}{\mu}, x_2^* = 0, x_3^* = 0, x_4^* = 0, x_5^* = 0, x_6^* = 0, x_7^* = 0)$.

Then the linearization matrix of system (4.14) at disease free equilibrium point when β= β^* is given by:

$$J(E_0, \beta^*) = \begin{pmatrix} -\mu & 0 & -\frac{c_1c_2c_3c_4}{pbc_3c_4+c_2(n\theta+rc_4)}b & -\frac{c_1c_2c_3c_4}{pbc_3c_4+c_2(n\theta+rc_4)} & 0 & 0 & 0 \\ 0 & -c_1 & \frac{c_1c_2c_3c_4}{pbc_3c_4+c_2(n\theta+rc_4)}b & \frac{c_1c_2c_3c_4}{pbc_3c_4+c_2(n\theta+rc_4)} & 0 & 0 & 0 \\ 0 & p & -c_2 & 0 & 0 & 0 & 0 \\ 0 & r & 0 & -c_3 & n & 0 & 0 \\ 0 & \theta & 0 & 0 & -c_4 & 0 & 0 \\ 0 & 0 & 0 & q & 0 & -c_5 & 0 \\ 0 & 0 & k_1 & \alpha & \eta & k_2 & -\mu \end{pmatrix}$$

where $c_1 = \mu+p+r+\theta$, $c_2 = k_1+\mu+\delta_1$, $c_3 = \mu+\delta_2+q+\alpha$, $c_4 = \mu+n+\eta$, $c_5 = \mu+\delta_3+k_2$ and $J(E_0, \beta^*)$ is Jacobian matrix at (E_0, β).

Clearly, 0 is a simple eigenvalue of $J(E_0, \beta^*)$ obtained at β^* after some computation or by substituting in characteristic equation (4.9).

To compute the right eigenvector, $w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7)^T$, we consider the system $J(E_0, \beta^*).w = 0$. Then the system becomes

$$
\begin{aligned}
-\mu w_1 - \frac{c_1c_2c_3c_4}{pbc_3c_4 + c_2(n\theta + rc_4)}bw_3 - \frac{c_1c_2c_3c_4}{pbc_3c_4 + c_2(n\theta + rc_4)}w_4 &= 0\\
-c_1w_2 + \frac{c_1c_2c_3c_4}{pbc_3c_4 + c_2(n\theta + rc_4)}bw_3 + \frac{c_1c_2c_3c_4}{pbc_3c_4 + c_2(n\theta + rc_4)}w_4 &= 0\\
pw_2 - c_2w_3 &= 0\\
rw_2 - c_3w_4 + nw_5 &= 0\\
\theta w_2 - c_4w_5 &= 0\\
qw_4 - c_5w_6 &= 0\\
k_1w_3 + \alpha w_4 + \eta w_5 + k_2w_6 - \mu w_7 &= 0
\end{aligned}
\tag{4.15}
$$

From system (4.15) we obtain

$w_1 = \frac{-c_1w_2}{\mu}$, $w_2 = w_2 > 0$, $w_3 = \frac{pw_2}{c_2}$, $w_4 = \frac{(rc_4+n\theta)w_2}{c_3c_4}$, $w_5 = \frac{\theta w_2}{c_4}$, $w_6 = \frac{[q(rc_4+n\theta)]w_2}{c_3c_4c_5}$ and $w_7 = \frac{[c_3c_5(c_4k_1p+c_2\eta\theta)+(\alpha c_5+k_2q(rc_4+n\theta))c_2(rc_4+n\theta)]w_2}{c_2c_3c_4c_5\mu}$.

Next we compute the left eigenvector, $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7)$ from $v.J(E_0, \beta^*)$ and the system becomes

$$
\begin{aligned}
-\mu v_1 &= 0\\
-c_1v_2 + pv_3 + rv_4 + \theta v_5 &= 0\\
\frac{-c_1c_2c_3c_4b}{pbc_3c_4 + c_2(n\theta + rc_4)}v_1 + \frac{c_1c_2c_3c_4b}{pbc_3c_4 + c_2(n\theta + rc_4)}v_2 - c_2v_3 + k_1v_7 &= 0\\
\frac{-c_1c_2c_3c_4}{pbc_3c_4 + c_2(n\theta + rc_4)}v_1 + \frac{c_1c_2c_3c_4}{pbc_3c_4 + c_2(n\theta + rc_4)}v_2 - c_3v_4 + qv_6 + \alpha v_7 &= 0\\
nv_4 - c_4v_5 + \eta v_7 &= 0\\
-c_5v_6 + k_2v_7 &= 0\\
-\mu v_7 &= 0
\end{aligned}
\tag{4.16}
$$

From system (4.16) we obtain

$v_1 = v_6 = v_7 = 0$, $v_3 = \frac{c_1c_3c_4b}{pbc_3c_4+c_2(n\theta+rc_4)}v_2$, $v_5 = \frac{nc_1c_2}{pbc_3c_4+c_2(n\theta+rc_4)}v_2$.

where v_2 is calculated to ensure that the eigenvectors satisfy the condition $v.w = 1$.

Since $v_1 = v_6 = v_7 = 0$ from the component of v and all partial derivative of f_3, f_4 and f_5 are zero for $i, j = 1, 2, 3, 4, 5, 6, 7$ we don't need to compute derivatives of f_1, f_3, f_4, f_5, f_6 and f_7 . Thus, we evaluate a and b by substituting non zero partial derivative of f_2 only in to the formula.

From the partial derivatives of f_2, the only ones that are nonzero are the following:

$\frac{\partial^2 f_2}{\partial x_1 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_1} = \frac{\beta^*\mu b}{\Lambda}$ and $\frac{\partial^2 f_2}{\partial x_1 \partial x_4} = \frac{\partial^2 f_2}{\partial x_4 \partial x_1} = \frac{\beta^*\mu}{\Lambda}$

with

$\frac{\partial^2 f_2}{\partial x_1 \partial \beta^*} = \frac{\mu}{\Lambda}(bx_3^* + x_4^*)$, $\frac{\partial^2 f_2}{\partial x_3 \partial \beta^*} = \frac{\mu b x_1^*}{\Lambda}$, $\frac{\partial^2 f_2}{\partial x_4 \partial \beta^*} = \frac{\mu x_1^*}{\Lambda}$ and all the other partial derivatives of f_2 are zero. The direction of the bifurcation at $R_0 = 1$ is determined by the signs of the bifurcation coefficients a and b, obtained from the above partial derivatives as follows:

$a = v_2 \sum_{i,j=1}^{7} w_i w_j \frac{\partial^2 f_2}{\partial x_i \partial x_j}(0,0)$

$=2v_2 w_1 w_4(\frac{\beta^* \mu}{\Lambda}) + 2v_2 w_1 w_3(\frac{\beta^* \mu b}{\Lambda})$

$=2v_2(\frac{-c_1 w_2}{\mu})(\frac{r w_2}{c_3})(\frac{\beta^* \mu}{\Lambda}) + 2v_2(\frac{-c_1 w_2}{\mu})(\frac{p w_2}{c_2})(\frac{\beta^* \mu b}{\Lambda})$

$=-2\beta^* c_1(\frac{c_2 r + bpc_3}{\Lambda c_2 c_3}) v_2 w_2^2 < 0.$

and

$b = \sum_{i=1}^{7} v_2 w_i \frac{\partial^2 f_2}{\partial x_i \partial \beta^*}(0,0)$

$=v_2 w_1 \frac{\partial^2 f_2}{\partial x_1 \partial \beta^*}(0,0) + v_2 w_3 \frac{\partial^2 f_2}{\partial x_3 \partial \beta^*}(0,0) + v_2 w_4 \frac{\partial^2 f_2}{\partial x_4 \partial \beta^*}(0,0)$

$=v_2(\frac{-c_1 w_2}{\mu})\frac{\mu}{\Lambda}(bx_3^* + x_4^*) + v_2 \frac{p w_2}{c_2}(\frac{\mu b x_1^*}{\Lambda}) + v_2 \frac{r w_2}{c_3}(\frac{\mu x_1^*}{\Lambda})$

$=\frac{c_3 p + c_2 r}{c_2 c_3} v_2 w_2 > 0.$

Since $a < 0$ and $b > 0$, so the system (4.1) exhibits forward bifurcation at $R_0 = 1$.

Chapter 5

Optimal Control Analysis

In chapter four, we discussed from the formulation of the model to sensitivity analysis in detail without considering the intervention of optimal control measures. In this chapter, the intervention mechanism is addressed using the theory of optimal control and Pontryagin's minimum principle which govern the necessary conditions for the optimal control of the spread of COVID-19 infection.

Targeted and time-limited implementation of these measures will potentially reduce mortality by flattening the trajectory of the epidemic and relieving some pressure on clinical care services. However, these measures are blunt tools with considerable social and economic costs, and should be implemented with the understanding, consent, and participation of communities, and based on the principle of doing no harm. The risks of implementing these measures must be effectively communicated to the affected populations and communities engaged to own and participate in them.

The precise nature and feasibility of implementing these measures will be heavily dependent on the context of affected communities. In low-income and crisis settings, physical distancing and movement restrictions are structurally more difficult to implement, and should only be implemented where justified by an analysis of the trade-offs between public health measures against COVID-19 and the necessity for people to meet their basic food and protection needs.

Control sporadic cases and clusters and prevent community transmission by rapidly finding and isolating all cases, providing them with appropriate care, and tracing, quarantining,

and supporting all contacts.

5.1 Extension into optimal control

In this section, we extended a SEAIQHR compartmental model presented in chapter 4 to study the transmission dynamics of COVID-19 epidemic. In the model, we introduce four control functions those are: the control function u_1 which represent preventive measures such as physical distance, wearing mask, washing hand with soap frequently or using sanitizer, avoiding touching contaminated surface and applying rule and regulation daily announced from world health organization(WHO) to reduce contact rate of susceptible individuals with infected people, the second control u_2 which represents the effort of the screening exposed individuals and quarantine the alleged individuals to reduce transmission of COVID-19, u_3 represent intensive medical care for all the confirmed cases to increase recover rate of the isolated individuals and u_4 represent special treatment(care) and check up for severe and critical COVID -19 patients to increase recover rate of the hospitalized individuals. The controls are bounded between 0 and 1. When the controls vanish, it means no extra measures are implemented for the reduction of the disease. When the controls take the maximum value 1, it means that the intervention is 100% perfectly implemented which is not true in reality and thus we assumed $u_i \leq 1-\epsilon, i = 1,2,3,4$, where $\epsilon \ll 1$ denotes a positive real number. The resulting dynamical control system of (4.1) is given by the following system of nonlinear ordinary differential equations:

$$\begin{cases} \frac{dS}{dt} = \Lambda - (\lambda(1-u_1)+\mu)S, \\ \frac{dE}{dt} = (1-u_1)\lambda S - (\mu+p+r)E - (\theta+u_2)E, \\ \frac{dA}{dt} = pE - (k_1+\mu+\delta_1)A, \\ \frac{dI}{dt} = rE + nQ - (\mu+\delta_2+q)I - (\alpha+u_3)I, \\ \frac{dQ}{dt} = (\theta+u_2)E - (\mu+n+\eta)Q, \\ \frac{dH}{dt} = qI - (\mu+\delta_3)H - (u_4+k_2)H, \\ \frac{dR}{dt} = k_1A + (u_3+\alpha)I + \eta Q + (k_2+u_4)H - \mu R, \end{cases} \tag{5.1}$$

where $\lambda = \frac{\beta(bA+I)}{N}$ with initial condition : $S(0) = S_0 > 0$, $E(0) = E_0 \geq 0$, $A(0) = A_0 \geq 0$, $I(0) = I_0 \geq 0$, $Q(0) = Q_0 \geq 0$, $H(0) = H_0 \geq 0$ and $R(0) = R_0 \geq 0$.

The objective of this extension is to find the optimal values $\bar{u} = (\bar{u}_1, \bar{u}_2, \bar{u}_3, \bar{u}_4)$ of the controls $u = (u_1, u_2, u_3, u_4)$ such that the associated state trajectories $\bar{S}, \bar{E}, \bar{A}, \bar{I}, \bar{Q}, \bar{H}$ and $\bar{R}$ are solution of the system (5.1) in the intervention time interval $[0, T]$ with initial conditions to minimize the objective functional.

The optimal control problem is to minimize the objective (cost) functional (J) considering the costs of preventive measure of susceptible individuals, cost of screening and quarantine of exposed individuals, cost of intensive medical care of symptomatic infected individuals and cost of spatial treatment for hospitalized individuals. The goal of the implemented strategy is to reduce exposed, symptomatic infected individuals with optimal cost.

we define the cost functional for the minimization problem as

$$J[u_1, u_2, u_3, u_4] = \int_0^T \left(C_1 E(t) + C_2 I(t) + \frac{1}{2} \sum_{i=1}^{4} B_i u_i^2 \right) dt \to min \tag{5.2}$$

subject to (5.1) with its initial condition and where C_1 and C_2 are relative constant that measures the relative importance of reducing the associated classes on the spread of the disease and the relative weight constants B_i is a measure of the relative cost of the interventions associated with the control u_i for $i = 1, 2, 3, 4$ and balances the units of integrand to reduce the dominance of any of the term in the integral. In the cost functional, the term $C_1 E(t)$ describe the cost related to exposed class while $C_2 I(t)$ denotes the cost related to symptomatic compartment. Additionally, the functional J corresponds the total cost due to coronavirus infection and its control strategies. Further, the integrand function

$$F(t, S, E, A, I, Q, H, R, u) = C_1 E(t) + C_2 I(t) + \frac{1}{2} \sum_{i=1}^{4} B_i u_i^2.$$

Lastly, the fixed constant T denotes the terminal intervention time. The set of admissible control functions is defined by

$$\Omega_\epsilon = \left\{ (u_1(.), u_2(.), u_3(.), u_4(.)) \in (Ł^\infty(0, T))^4 : 0 \leq u_1(t), u_2(t), u_3(t), u_4(t) \leq 1 - \epsilon, \forall t \in [0, T] \right\} \tag{5.3}$$

Then we consider the optimal control problem of obtaining $\bar{S}, \bar{E}, \bar{A}, \bar{I}, \bar{Q}, \bar{H}$ and $\bar{R}$ associated with an admissible control $(u_1(.), u_2(.), u_3(.), u_4(.)) \in \Omega_\epsilon$ on the intervention time interval [0, T], subjected to the state control system (5.1) in $\mathbb{R}_+^7$ with its initial condition and minimizing the cost functional (5.2). More precisely, the optimal control problem can be defined as

$$J[\bar{u}_1, \bar{u}_2, \bar{u}_3, \bar{u}_4] = \min_{\Omega_\epsilon} J[u_1(.), u_2(.), u_3(.), u_4(.)] \tag{5.4}$$

satisfying (5.1) and its initial conditions.

5.2 Existence of the optimal control problem

In this section, we prove the existence of an optimal control of our model (5.1). The boundedness of solutions to system (5.1) for finite time interval is needed to establish the existence of an optimal control and the uniqueness of the optimality system.

Theorem 5.2.1. *There exist an optimal control* $u = (u_1, u_2, u_3, u_4)$ *and a corresponding solution vector* $(\bar{S}, \bar{E}, \bar{A}, \bar{I}, \bar{Q}, \bar{H}, \bar{R})$ *to the state initial value problem* (5.1) *that minimizes the cost functional* $J(u)$ *of* (5.2) *over the set of admissible control* Ω_ϵ.

Proof. The non trivial requirement on the set of admissible controls and the set of end conditions are followed by (Fleming & Rishel, 2012).

(i) The set of all solution to system (5.1) with corresponding control functions in Ω_ϵ is non empty.

(ii) The control set is convex and closed.

(iii) The integral of the objective function is convex.

(iv) The integrand $F(t, S, E, A, I, Q, H, R, u)$ in equation (5.2) is convex with respect to control variables and additionally fulfills that $F(t, S, L, I, T, R, u) \geq g(u)$, where g is continuous and $||u||^{-1} g(u) \longrightarrow +\infty$ as $||u|| \longrightarrow \infty$.

In order to established condition (i), we consider the Picard-Lindelo'f existence theorem (Coddington & Levinson, 1955). If $g(t, x, u)$ is bounded, continuous, and Lipschitz in the state variables, then there exists a unique solution corresponding to every admissible control Ω_ϵ. Hence, for any $u \in \Omega_\epsilon$ and the state variables, we have

$$0 \leq N \leq \frac{\Lambda}{\mu} \tag{5.5}$$

and non empty by model assumption. Furthermore, with the bounded established (5.5) it implies that the state system is continuous and bounded. It is possible to show the boundedness of the partial derivative with respect to the state variable i.e $\frac{\partial g}{\partial x}$ exist and finite, which

established the system is Lipschitz with respect to the state variables. This established the proof of condition (i) is complete.

To prove (ii), consider

$\Omega_\epsilon = \{u \in \mathbb{R}^4 : ||u|| \leq 1 - \epsilon\}$.

Let $u_1, u_2 \in \Omega_\epsilon$ such that $u_1 \leq 1 - \epsilon$ and $u_2 \leq 1 - \epsilon$. Then for any $k \in [0, 1]$, $||ku_1 + (1 - k)u_2|| \leq k||u_1|| + (1 - k)||u_2|| \leq 1 - \epsilon$. This implies that Ω_ϵ is convex and closed.

Next we verify condition (iii) as follows; the integral of the cost function is given by

$F(t, S, L, I, T, R, u) = C_1E(t) + C_2I(t) + \frac{1}{2}\sum_{i=1}^{4} B_iu_i^2$

Recall that any affine function is a convex and the sum of a convex function is a convex (Chong & Zak, 2004). Thus, F is convex on Ω_ϵ and (iii) is satisfied.

Finally, to verify condition (iv), we note that the integrand $F(t, S, E, A, I, Q, H, R, u)$ of the objective functional is clearly convex in control. To prove the bound on the $F(t, S, E, A, I, Q, H, R, u)$ we note that the state system (5.1) is linear in control variable u with coefficients depending on state variables. The integrand of the cost functional $F(t, S, E, A, I, Q, H, R, u) = C_1E(t) + C_2I(t) + \frac{1}{2}\sum_{i=1}^{4} B_iu_i^2$ is the sum of convex function and hence convex with respect to control variables. Furthermore,

$$F(t, S, E, A, I, Q, H, R, u) = C_1E(t) + C_2I(t) + \frac{1}{2}\sum_{i=1}^{4} B_iu_i^2 \geq \frac{1}{2}\sum_{i=1}^{4} B_iu_i^2. \tag{5.6}$$

Let $\delta = min(\frac{B_1}{2}, \frac{B_2}{2}, \frac{B_3}{2}, \frac{B_4}{2}) > 0$ and define a continuous function $g(u) = \delta||u||^2$. Then from equation (5.6) we have $F(t, S, E, A, I, Q, H, R, u) \geq g(u)$. Clearly $||u||^{-1}g(u) \longrightarrow +\infty$ as $||u|| \longrightarrow \infty$. Thus, condition (iv) is achieved. With this we conclude that the existence of an optimal control $(\bar{S}, \bar{E}, \bar{A}, \bar{I}, \bar{Q}, \bar{H}, \bar{R}, \bar{u})$ that minimizes the cost functional of (5.2) over the set of admissible control Ω_ϵ. The proof is completed. □

5.3 Characterization of Optimal Control Solutions

In order to derive the necessary conditions for the optimal control pair the Pontryagin's Minimum Principle (Pontryagin, 2018) is used. According to the Pontryagin's Minimum Principle, if $\bar{u} \in \Omega_\epsilon$ (5.4) with fixed final time T, then there exists a non-trivial absolutely continuous mapping

$\lambda : [0, T] \longrightarrow \mathbb{R}^7, \lambda = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t), \lambda_6(t), \lambda_7(t))$ called the adjoint vector, such that

$$J[u_1,u_2,u_3,u_4]=\int_0^T\left(C_1E(t)+C_2I(t)+\frac{1}{2}\sum_{i=1}^{4}B_iu_i^2\right)dt\rightarrow min \tag{5.7}$$

subject to

$\sum_{i=1}^{7}\lambda_i(t)g_i(t,S,E,A,I,Q,H,R,u_1,u_2,u_3,u_4)$

where $g_i(t,S,E,A,I,Q,H,R,u_1,u_2,u_3,u_4)$ stands for the right hand side of the constraints (5.1) for $i=1,2,3,4,5,6,7$.

Then

1. The Hamiltonian of the given system is defined as follows:

$$\mathcal{H}=C_1E(t)+C_2I(t)+\frac{1}{2}\sum_{i=1}^{4}B_iu_i^2+\sum_{i=1}^{7}\lambda_i(t)g_i(t,S,E,A,I,Q,H,R,u_1,u_2,u_3,u_4) \tag{5.8}$$

where g_i stands for the right hands of the constraints (5.1) for $i=1,2,3,4,5,6,7$.

2. The control system,

$S'=\frac{\partial\mathcal{H}}{\partial\lambda_1},E'=\frac{\partial\mathcal{H}}{\partial\lambda_2},A'=\frac{\partial\mathcal{H}}{\partial\lambda_3},I'=\frac{\partial\mathcal{H}}{\partial\lambda_4},Q'=\frac{\partial\mathcal{H}}{\partial\lambda_5},H'=\frac{\partial\mathcal{H}}{\partial\lambda_6},R'=\frac{\partial\mathcal{H}}{\partial\lambda_7};$

3. The adjoint system

$\lambda_1'=-\frac{\partial\mathcal{H}}{\partial S},\lambda_2'=-\frac{\partial\mathcal{H}}{\partial E},\lambda_3'=-\frac{\partial\mathcal{H}}{\partial A},\lambda_4'=-\frac{\partial\mathcal{H}}{\partial I},\lambda_5'=-\frac{\partial\mathcal{H}}{\partial Q},\lambda_6'=-\frac{\partial\mathcal{H}}{\partial H},\lambda_7'=-\frac{\partial\mathcal{H}}{\partial\lambda_7};$

4. The optimality condition

$\mathcal{H}(\bar{S},\bar{E},\bar{A},\bar{I},\bar{Q},\bar{H},\bar{R},\bar{u},\bar{\lambda})=\min_{\Omega_\epsilon}\mathcal{H}(\bar{S},\bar{E},\bar{A},\bar{I},\bar{Q},\bar{H},\bar{R},\bar{u},\bar{\lambda})$ holds for almost all $t\in[0,T]$.

5. Moreover, the transversality condition

$\lambda_i(T)=0$, for all $i=1,2,3,4,5,6,7$ also holds true.

In the following result, we give the characterization of optimal control.

Theorem 5.3.1. *The optimal control problem* (5.4) *with fixed final time T admits a unique optimal solution $(\bar{S},\bar{E},\bar{A},\bar{I},\bar{Q},\bar{H},\bar{R})$ associated with an optimal control $u=(u_1,u_2,u_3,u_4)$*

for all $t \in [0, T]$. *Moreover, there exist adjoint function* λ_i, *for* $i = 1, 2, 3, 4, 5, 6, 7$ *such that*

$$\begin{cases} \frac{d\lambda_1}{dt} = (\lambda_1 - \lambda_2)\lambda(1 - u_1) + \lambda_1\mu \\ \frac{d\lambda_2}{dt} = -C_1 + \lambda_2(\mu + p + r) + (\lambda_2 - \lambda_5)(\theta + u_2) - \lambda_3 p - \lambda_4 r \\ \frac{d\lambda_3}{dt} = \frac{\beta b S}{N}(1 - u_1)(\lambda_1 - \lambda_2) + (k_1 + \mu + \delta_1)\lambda_3 - \lambda_7 k_1 \\ \frac{d\lambda_4}{dt} = -C_2 + \frac{\beta S}{N}(1 - u_1)(\lambda_1 - \lambda_2) + \lambda_4(\mu + \delta_2 + q) + (\lambda_4 - \lambda_7)(\alpha + u_3) - \lambda_6 q \\ \frac{d\lambda_5}{dt} = -n\lambda_4 + (\mu + n + \eta)\lambda_5 - \eta\lambda_7 \\ \frac{d\lambda_6}{dt} = (\mu + \delta_3)\lambda_6 + (\lambda_6 - \lambda_7)(k_2 + u_4) \\ \frac{d\lambda_7}{dt} = \mu\lambda_7 \end{cases} \tag{5.9}$$

with transiversality conditions $\lambda_i(T) = 0$ *for all* $i = 1, 2, 3, 4, 5, 6, 7$.

Moreover, the corresponding optimal controls $\bar{u}_1(t), \bar{u}_2(t)$, $\bar{u}_3(t)$ *and* $\bar{u}_4(t)$ *are given by*

$$\bar{u}_1 = min\left\{max\left\{0, \frac{\bar{\lambda}\bar{S}(\lambda_2 - \lambda_1)}{B_1}\right\}, 1 - \epsilon\right\},$$
$$\bar{u}_2 = min\left\{max\left\{0, \frac{(\lambda_2 - \lambda_5)\bar{E}}{B_2}\right\}, 1 - \epsilon\right\},$$
$$\bar{u}_3 = min\left\{max\left\{0, \frac{(\lambda_4 - \lambda_7)\bar{I}}{B_3}\right\}, 1 - \epsilon\right\}.$$
$$\bar{u}_4 = min\left\{max\left\{0, \frac{(\lambda_6 - \lambda_7)\bar{H}}{B_4}\right\}, 1 - \epsilon\right\}.$$

Proof. The Hamiltonian function associated with the system is defined as follows:

$\mathcal{H}(t, S, E, A, I, Q, H, R, u_1, u_2, u_3, u_4) = C_1E(t) + C_2I(t) + \frac{1}{2}\sum_{i=1}^{4} B_i u_i^2 + \sum_{i=1}^{7} \lambda_i(t) g_i(t)$
$= C_1E(t) + C_2I(t) + \frac{1}{2}(B_1u_1^2 + B_2u_2^2 + B_3u_3^2 + B_4u_4^2) + \lambda_1[\Lambda - (\lambda(1 - u_1) + \mu)S] + \lambda_2[(1 - u_1)\lambda S - (\mu + p + r)E - (u_2 + \theta)E] + \lambda_3[pE - (k_1 + \mu + \delta_1)A] + \lambda_4[rE + nQ - (\mu + \delta_2 + q)I - (\alpha + u_3)I] + \lambda_5[(u_2 + \theta)E - (\mu + n + \eta)Q] + \lambda_6[qI - (\mu + \delta_3)H - (u_4 + k_2)H] + \lambda_7[k_1A + (u_3 + \alpha)I + \eta Q + (u_4 + k_2)H - \mu R]$

where $\lambda_i(t)$, for $i = 1, 2, 3, 4, 5, 6, 7$ are the adjoint functions to be determined suitably. The form of the adjoint equations and transversality conditions are standard results from PMP.

The adjoint system can be obtained as follows:

$$\begin{cases} \frac{d\lambda_1}{dt} = -\frac{\partial \mathcal{H}}{\partial S} = (\lambda_1 - \lambda_2)\lambda(1-u_1) + \lambda_1\mu \\ \frac{d\lambda_2}{dt} = -\frac{\partial \mathcal{H}}{\partial E} = -C_1 + \lambda_2(\mu + p + r) + (\lambda_2 - \lambda_5)(\theta + u_2) - \lambda_3 p - \lambda_4 r \\ \frac{d\lambda_3}{dt} = -\frac{\partial \mathcal{H}}{\partial A} = \frac{\beta b S}{N}(1-u_1)(\lambda_1 - \lambda_2) + (k_1 + \mu + \delta_1)\lambda_3 - \lambda_7 k_1 \\ \frac{d\lambda_4}{dt} = -\frac{\partial \mathcal{H}}{\partial I} = -C_2 + \frac{\beta S}{N}(1-u_1)(\lambda_1 - \lambda_2) + \lambda_4(\mu + \delta_2 + q) + (\lambda_4 - \lambda_7)(\alpha + u_3) - \lambda_6 q \\ \frac{d\lambda_5}{dt} = -\frac{\partial \mathcal{H}}{\partial Q} = -n\lambda_4 + (\mu + n + \eta)\lambda_5 - \eta\lambda_7 \\ \frac{d\lambda_6}{dt} = -\frac{\partial \mathcal{H}}{\partial H} = (\mu + \delta_3)\lambda_6 + (\lambda_6 - \lambda_7)(k_2 + u_4) \\ \frac{d\lambda_7}{dt} = -\frac{\partial \mathcal{H}}{\partial R} = \mu\lambda_7 \end{cases}$$

The state variables are not assigned at the final time T. Hence, following Lenhart, S.(Lenhart & Workman, 2007) the transversality conditions (or boundary conditions) becomes $\lambda_i(T) = 0$, for $i = 1, 2, 3, 4, 5, 6, 7$.

By the optimality condition, we obtain $\bar{u}_i$ from $\frac{\partial \mathcal{H}}{\partial u_i} = 0$, for $i = 1, 2, 3, 4$. This implies

(i) $\frac{\partial \mathcal{H}}{\partial u_1} = B_1 u_1 + \lambda S(\lambda_1 - \lambda_2) = 0$ from this $\bar{u}_1 = \frac{\bar{\lambda}\bar{S}(\lambda_2 - \lambda_1)}{B_1}$, where $\bar{\lambda} = \frac{\beta(b\bar{A} + \bar{I})}{N}$.

(ii) $\frac{\partial \mathcal{H}}{\partial u_2} = B_2 u_2 - (\lambda_2 - \lambda_5)E = 0 \Rightarrow \bar{u}_2 = \frac{(\lambda_2 - \lambda_5)\bar{E}}{B_2}$.

(iii) $\frac{\partial \mathcal{H}}{\partial u_3} = B_3 u_3 - (\lambda_4 - \lambda_7)\bar{I} = 0 \Rightarrow \bar{u}_3 = \frac{(\lambda_4 - \lambda_7)\bar{I}}{B_3}$.

(iv) $\frac{\partial \mathcal{H}}{\partial u_4} = B_4 u_4 - (\lambda_6 - \lambda_7)H = 0 \Rightarrow u_4 = \frac{(\lambda_6 - \lambda_7)\bar{H}}{B_4}$.

From boundedness on $\bar{u} = (\bar{u}_1, \bar{u}_2, \bar{u}_3, \bar{u}_4)$ and minimality condition we obtain;

$$\bar{u}_1 = \begin{cases} 0, & \text{if } \frac{\partial \mathcal{H}}{\partial u_1} > 0; \\ \frac{\bar{\lambda}\bar{S}(\lambda_2 - \lambda_1)}{B_1}, & \text{if } \frac{\partial \mathcal{H}}{\partial u_1} = 0; \\ 1 - \epsilon, & \text{if } \frac{\partial \mathcal{H}}{\partial u_1} < 0 \end{cases}$$

$$\bar{u}_2 = \begin{cases} 0, & \text{if } \frac{\partial \mathcal{H}}{\partial u_2} > 0; \\ \frac{(\lambda_2 - \lambda_5)\bar{E}}{B_2}, & \text{if } \frac{\partial \mathcal{H}}{\partial u_2} = 0; \\ 1 - \epsilon, & \text{if } \frac{\partial \mathcal{H}}{\partial u_2} < 0 \end{cases}$$

$$\bar{u}_3 = \begin{cases} 0, & \text{if } \frac{\partial \mathcal{H}}{\partial u_3} > 0; \\ \frac{(\lambda_4 - \lambda_7)\bar{I}}{B_3}, & \text{if } \frac{\partial \mathcal{H}}{\partial u_3} = 0; \\ 1 - \epsilon, & \text{if } \frac{\partial \mathcal{H}}{\partial u_3} < 0 \end{cases}$$

$$\bar{u}_4 = \begin{cases} 0, & \text{if } \frac{\partial \mathcal{H}}{\partial u_4} > 0; \\ \frac{(\lambda_6 - \lambda_7)\bar{H}}{B_4}, & \text{if } \frac{\partial \mathcal{H}}{\partial u_4} = 0; \\ 1 - \epsilon, & \text{if } \frac{\partial \mathcal{H}}{\partial u_4} < 0 \end{cases}$$

In compact form, the optimal control $\bar{u} = (\bar{u}_1, \bar{u}_2, \bar{u}_3, \bar{u}_4)$ can be summarized as

$\bar{u}_1 = min\left\{max\left\{0, \frac{\bar{\lambda}\bar{S}(\lambda_2 - \lambda_1)}{B_1}\right\}, 1 - \epsilon\right\},$

$\bar{u}_2 = min\left\{max\left\{0, \frac{(\lambda_2 - \lambda_5)\bar{E}}{B_2}\right\}, 1 - \epsilon\right\},$

$\bar{u}_3 = min\left\{max\left\{0, \frac{(\lambda_4 - \lambda_7)\bar{I}}{B_3}\right\}, 1 - \epsilon\right\}.$

$\bar{u}_4 = min\left\{max\left\{0, \frac{(\lambda_6 - \lambda_7)\bar{H}}{B_4}\right\}, 1 - \epsilon\right\}.$

This completes the proof. □

Chapter 6

Numerical Simulations

In this chapter, we present and discusses numerically the behaviour of the solutions of the system (4.1) and (5.1) for different values of parameters given in the model. The simulation process is carried out using MATLAB software. We start by estimating the values of parameter used in the model. Then we illustrate the simulation results graphically.

6.1 Parameter Estimations

In this section, we fit the proposed model using monthly cumulative data of total confirmed COVID-19 infection cases in Ethiopia and we estimate the unknown model parameters. Table 6.1 depicts monthly data of total confirmed cases of COVID-19 infection in Ethiopia from March 2020 to April 2021 extracted from WHO situation reports (WHO, 2021).
To solve the dynamic parameter estimation problem, we formulate system (4.1) in the following form

$$I' = f(t, I, \theta), I(t_0) = I_0, \tag{6.1}$$

where I is the vector of dependent variables and θ is the vector of unknown parameters.

The squared sum of errors (SSE) between model solution and the data can be computed as

$$SSE(\theta) = argmin \sum_{i=1}^{n} ||I_i(t) - \bar{I}_i(t)||^2 \tag{6.2}$$

where $||.||$ denotes the Euclidean norm in R^n and n is the number of available real data points. The expression $\bar{I}_i(t)$ represents the actual total confirmed cases of COVID-19 and $I_i(t)$ are the corresponding model solutions at time t_i. In the process of least-squares fitting,

Table 6.1: Monthly Cumulative cases of COVID-19 infection in Ethiopia from March 2020 to April 2021.

N_0	Month	COVID-19 Confirmed cases	N_0	Month	COVID-19 confirmed cases
1	March	26	8	October	96169
2	April	131	9	November	110074
3	May	1172	10	December	124264
4	June	5846	11	January	137650
5	July	17530	12	February	159072
6	August	22253	13	March	206589
7	September	74584	14	April	25742

we are looking for a value $\bar{\theta}$ of model parameter θ such that the squared sum of errors is the minimum. Clearly, such a problem is nonlinear least squares problem, since the dependence of a solution $I(t, \theta)$ on the parameter θ is through a highly nonlinear system of differential equations.

The parameter estimation algorithm is summarized below:

Algorithm

Result: Optimal estimated parameter values θ.

- Step1: Guess initial parameter values θ_0. Set $\theta = \theta_0$.
- Step2: Using MATLAB ode23 solver, solve equation (6.1) using θ to find the solution ϕ_i.
- Step3: Evaluate error using (6.2) until the error between real data and the corresponding model solutions are minimum.
- Step4: Update the values θ=$\hat{\theta}$.
- Step5: Chech convergence criteria. If not converged, go to step 2.
- Step6: On convergence, set θ=$\hat{\theta}$ to current parameter values.

The model parameters of system (4.1) are estimated using least-square fitting methods

which provides a better fit for the model solution to the real data as shown in figure 6.1 and the corresponding parameters value are depicted in Table 6.2 below for the numerical simulation.

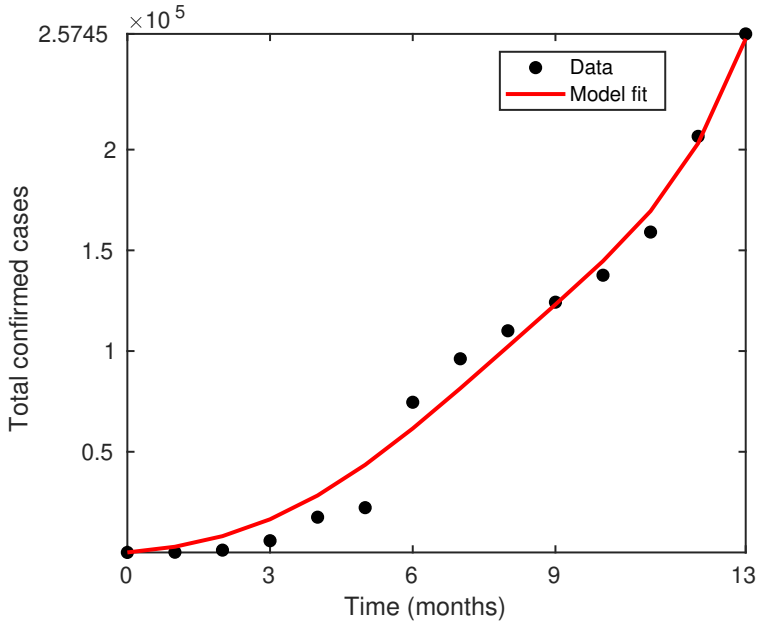


Figure 6.1: SEAIQHR model fit with real data on the number of COVID-19 cases in Ethiopia

In the next section, we study the dynamics of COVID-19 through numerical simulations by using the estimated values of parameters in the proposed model with appropriate initial conditions with the help of least square technique.

6.2 Simulation procedure and graphical results discussion

In this section, we illustrate numerically the solution of the optimal control problem proposed in system (5.1) and explain the impact of control strategy on the spread of corona virus diseases. For this purpose, we use the forward-backward sweep method presented in the book of Lenhart and Workman (Lenhart & Workman, 2007).

To briefly summarize the numerical simulation procedure, first we perform forward fourth order Runge-Kutta scheme to solve system (5.1) over the interval $[0, T]$ with its initial condition and the transversality conditions $\lambda_i(T) = 0$; $i = 1, 2, 3, 4, 5, 6, 7$, where $T = 25$ is simulation time. In contrary we use backward fourth order Runge-Kutta scheme to solve system (5.9) using the current iteration solution of (5.1). The control is updated by using a

convex combination of the previous control and the values computed in the characterizations process. The iteration continuous until the values of the unknowns at the previous iteration are very close to the values of present iteration.

To perform the numerical simulation, we assumed the initial population of $E(0) = 65000$, $A(0) = 23000$, $Q(0) = 60600$, $H(0) = 0$, $R(0) = 50000$ and the remaining $I(0) = 26$ from the collected real data. Also the initial susceptible population is obtained from $S(0) = N(0) - (E(0) + A(0) + I(0) + Q(0) + H(0) + R(0)) = 114763224$ and the total population of Ethiopia is $N(0) = 114961850$ populations (2020 est.) (WHO, 2020b). The natural death rate is computed as $\mu = 1/(66.71 \times 12)$ per year, where 66.71 years is the average life expectancy in Ethiopia (WHO, 2020a). The recruitment rate, is then calculated as $\Lambda = \mu \times N(0) = 143608$ per month.

Table 6.2: The values of parameters used in the simulations.

parameters	Value	Reference
Λ	143608	Estimated
β	0.71961	Estimated
θ	0.47448	Estimated
μ	0.0012	Estimated
p	0.98745	Estimated
r	0.24021	Estimated
b	0.77484	Estimated
q	0.00084	Estimated
n	0.07166	Estimated
η	0.01688	Estimated
α	0.12014	Estimated
k_2	0.04881	Estimated
k_1	0.43234	Estimated
δ_1	0.00003	Estimated
δ_2	0.00003	Estimated
δ_3	0.00125	Estimated

The estimation of basic reproduction number for the model is given by

$$R_0 = \frac{\beta[pb(\mu+\delta_2+q+\alpha)(\mu+n+\eta)+(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))]}{(\mu+p+r+\theta)(k_1+\mu+\delta_1)(\mu+\delta_2+q+\alpha)(\mu+n+\eta)} = 2.8857 > 1.$$

Since $R_0 > 1$, the prevalence of COVID-19 will result in an epidemic.

To make sense to our controls u_i; $i = 1, 2, 3, 4$ with the existing reality we set $\epsilon = 0.05$. The cost coefficients corresponding to control variables are estimated to be $B_1 = 20$, $B_2 = 15$, $B_3 = 13$, $B_4 = 10$ and the relative importance of reducing the associated classes on the spread of the disease are $C_1 = 5$ and $C_2 = 4$. Using all necessary information above as input , we analysis and compare the numerical results of the effect of controls on the spread of COVID-19 in populations.

Implementing one intervention only is not enough to reduce the disease totally from the community. Thus we considered the following listed strategies which incorporate pairwise control, triple-wise control and all control intervention at a time.

- **Strategy A:** Applying preventive measures (u_1) and the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) without considering intensive medical care for all the confirmed cases of the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals.
- **Strategy B:** Applying preventive measures (u_1) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) without considering the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and special treatment and check up (u_4) for hospitalized individuals.
- **Strategy C:** Applying preventive measures (u_1) and special treatment and check up (u_4) for hospitalized individuals without the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and intensive medical care for all the confirmed cases of the isolated individuals (u_3).
- **Strategy D:** Applying the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) without considering preventive measures (u_1) and special treatment and check up (u_4) for hospitalized individuals .

- **Strategy E:** Applying the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and special treatment and check up (u_4) for hospitalized individuals without preventive measures (u_1) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) .

- **Strategy F:** Applying intensive medical care for all the confirmed cases of the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals without preventive measures (u_1) and the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) .

- **Strategy G:** Applying preventive measures (u_1) , the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) without special treatment and check up (u_4) for hospitalized individuals.

- **Strategy H:** Applying preventive measures (u_1) , intensive medical care for all the confirmed cases for the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals without the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) .

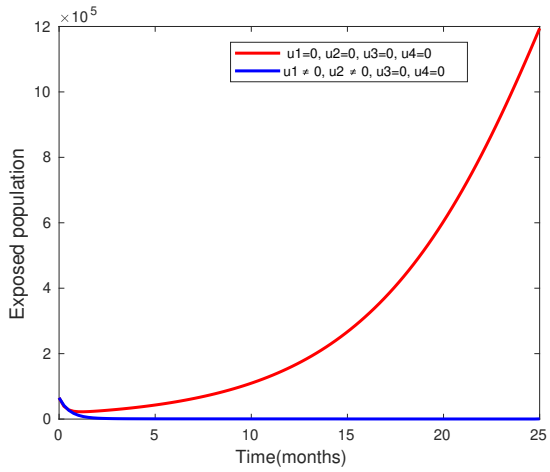
- **Strategy I:** Applying preventive measures (u_1) , the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and special treatment and check up (u_4) for hospitalized individuals without intensive medical care for all the confirmed cases of the isolated individuals (u_3).

- **Strategy J:** Applying the effort of the screening exposed individuals and quarantine the alleged individuals (u_2), intensive medical care for all the confirmed cases of the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals without preventive measures (u_1).

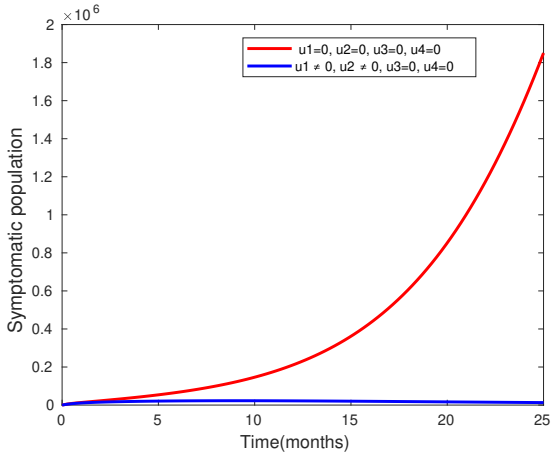
- **Strategy K:** Using all the four control intervention on susceptible, exposed, asymptomatic, symptomatic and isolated, quarantined and hospitalized populations.

6.2.1 Strategy A: Control with preventive measures and the effort of screening exposed individuals and quarantine the alleged individuals

Under this strategies, we simulated the model using preventive measures (u_1) and the effort of screening exposed individuals and quarantine the alleged individuals (u_2) to optimize the objective functional $J(u)$ while intensive medical care for all the confirmed cases of the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals were set to zero. From the numerical result depicted in Figure 6.2 below (a), we observed that in the absence of control strategies the number of exposed populations of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_1 and u_2 controls the number of exposed populations of COVID-19 are decreasing and about 637.2 at final time. From the second numerical result depicted in Figure 6.2 below (b) experimented, we observed that the number of symptomatic individuals of COVID-19 are increasing rapidly in the absence of control strategies and it will be 1.85×10^6 and in the presence of u_1 and u_2 controls the number of symptomatic populations are decreasing and 1.309×10^4 at final time. Hence, this strategy is effective to reduce the number of exposed individuals and less effective to reduce the number of symptomatic individuals.



(a) Exposed population without and with control.

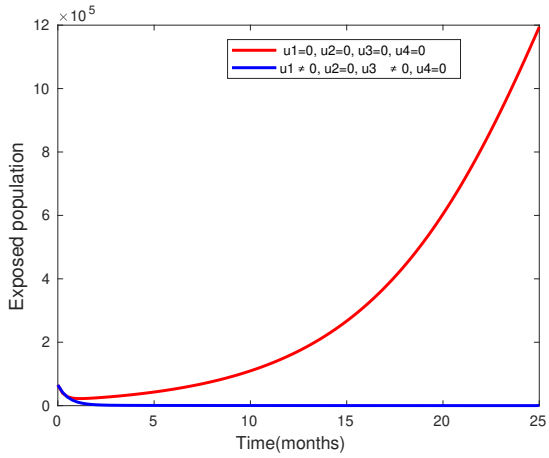


(b) Symptomatic population without and with control.

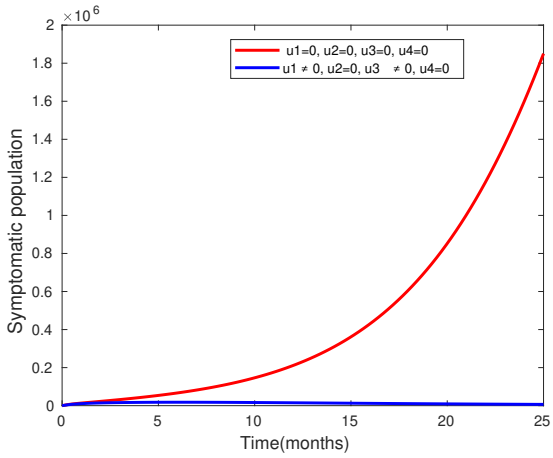
Figure 6.2: A simulation result of exposed and symptomatic population without control and in the presence of preventive measure and screening alleged to quarantine.

6.2.2 Strategy B: Control with preventive measure and intensive medical care

Here we have applied preventive measures (u_1) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) to optimize the objective functional $J(u)$ without considering the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and special treatment and check up (u_4) for hospitalized individuals. From the numerical result depicted in Figure 6.3 below (a), we observed that in the absence of control strategies the number of exposed populations of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_1 and u_3 controls the number of exposed populations of COVID-19 are decreasing and about 417.6 at final time. From numerical result depicted in Figure 6.3 below (b) experimented, we observed that the number of symptomatic individuals of COVID-19 are increasing rapidly in the absence of control and decreasing in the presence of u_1 and u_3 controls and it will be 1.85×10^6 and 6796 respectively at final time. Hence, this strategy is effective to reduce both the number of exposed and symptomatic individuals.



(a) Exposed population without and with control.

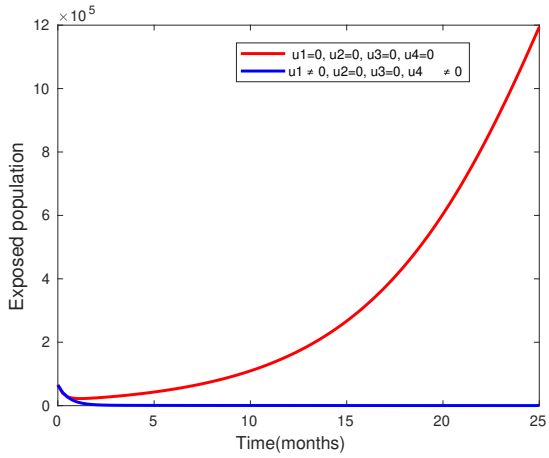


(b) Symptomatic population without and with control.

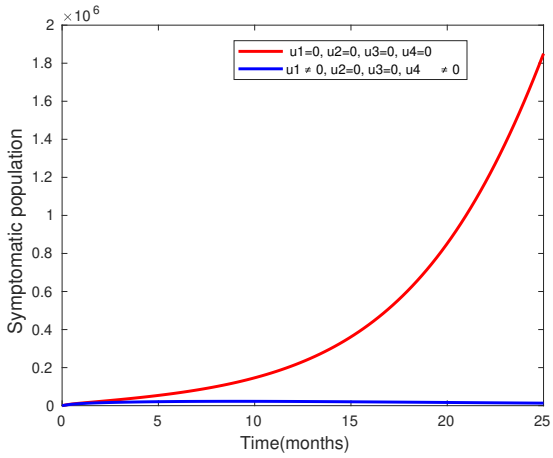
Figure 6.3: A simulation result of exposed and symptomatic population without control and in the presence of preventive measure and intensive medical care.

6.2.3 Strategy C: Control with preventive measure and special treatment and check up

Under this strategies, we simulated the model using preventive measures (u_1) and special treatment and check up (u_4) for hospitalized individuals to optimize the objective functional $J(u)$ without considering the effort of screening exposed individuals and quarantine the alleged individuals (u_2) and intensive medical care for all the confirmed cases of the isolated individuals (u_3). The numerical result depicted in Figure 6.4 below (a) show as in the absence of control strategies the number of exposed populations of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_1 and u_4 controls the number of exposed populations of COVID-19 are decreasing and about 792.8 at final time. Also, the numerical result depicted in Figure 6.4 below (b) show that in the absence of control measure the number of symptomatic populations of COVID-19 are increasing and it will be 1.85×10^6 and in the presence of u_1 and u_4 controls the number of symptomatic populations of COVID-19 are decreasing and 1.327×10^4 at final time. Therefore, this strategy is effective to reduce the number of exposed individuals and less effective to reduce the number of symptomatic individuals.



(a) Exposed population without and with control.

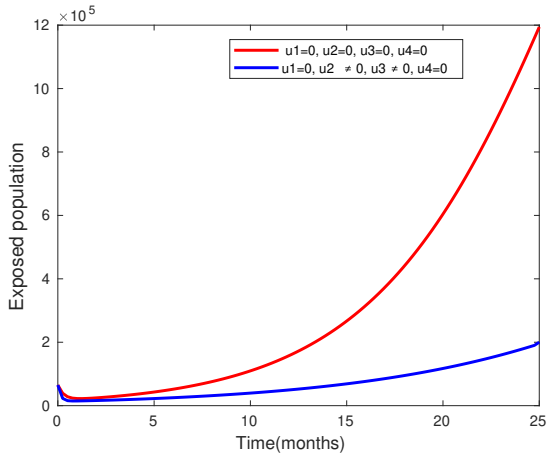


(b) Symptomatic population without and with control.

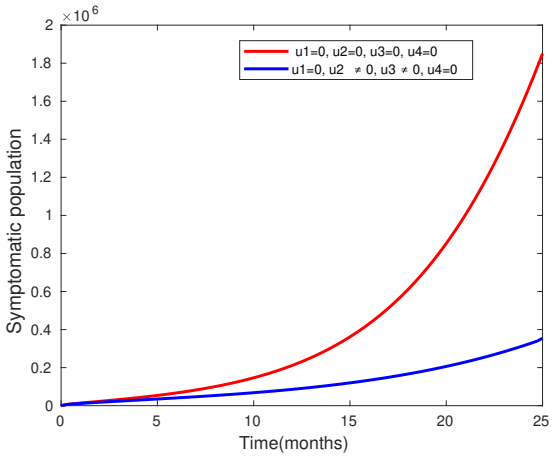
Figure 6.4: A simulation result of exposed and symptomatic population without control and in the presence of preventive measure and special treatment and check up.

6.2.4 Strategy D: Control with effort of screening to quarantine and intensive medical care

Here we have applied the effort of screening exposed individuals and quarantine the alleged individuals (u_2) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) to optimize the objective functional $J(u)$ while preventive measures (u_1) and special treatment and check up (u_4) for hospitalized individuals were set to zero. From the numerical result depicted in Figure 6.5 below (a), we observed that in the absence of control measure the number of exposed populations of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_2 and u_3 controls the number of exposed populations of COVID-19 are decreasing and about 2.002×10^5 at final time. Also, the numerical result depicted in Figure 6.5 below (b) show that the number of symptomatic population by COVID-19 in the absence of control measures are increasing and it will be 1.85×10^6 and in the presence of u_2 and u_3 controls the number of symptomatic population of COVID-19 are decreasing and 3.549×10^5 at final time. Hence, this strategy is less effective to reduce the number of exposed and symptomatic individuals.



(a) Exposed population without and with control.

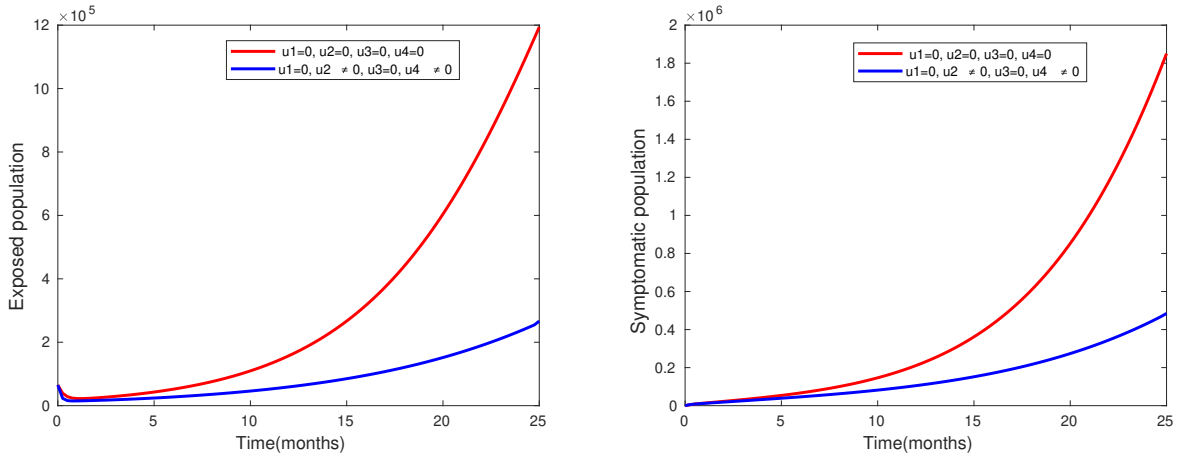


(b) Symptomatic population without and with control.

Figure 6.5: A simulation result of exposed and symptomatic population without control and in the presence of effort of screening to quarantine and intensive medical care.

6.2.5 Strategy E: Control with the effort of screening to quarantine and special treatment and check up

Under this strategies, we simulated the model using effort of screening exposed individuals and quarantine the alleged individuals (u_2) and special treatment and check up (u_4) for hospitalized individuals to optimize the objective functional $J(u)$ while preventive measures (u_1) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) were set to zero. From the numerical result depicted in Figure (6.6) below (a), we observed that in the absence of control measure the number of exposed population of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_2 and u_4 controls the number of exposed population of COVID-19 are 2.667×10^5 at final time. From the second numerical result depicted in Figure (6.6) below (b), we observed that in the absence of control measure the number of symptomatic populations of COVID-19 are increasing rapidly and it will be 1.85×10^6 and in the presence of (u_2) and (u_4) controls the number of symptomatic populations of COVID-19 are decreasing and 4.849×10^5 at final time. Therefore, this strategy is less effective to control exposed and symptomatic individuals.



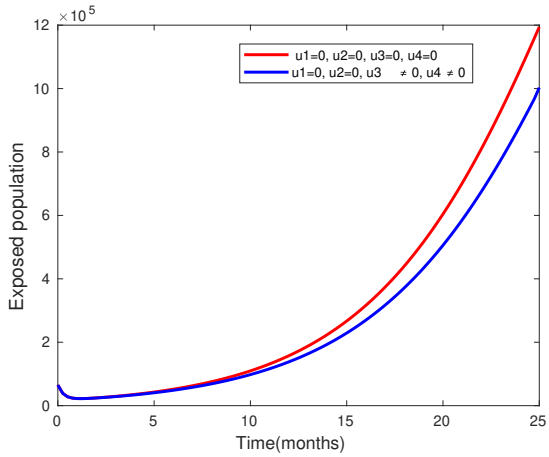
(a) Exposed population without and with control.

(b) Symptomatic population without and with control.

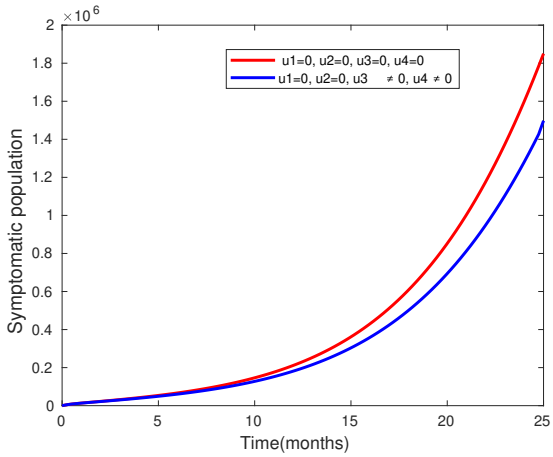
Figure 6.6: A simulation result of exposed and symptomatic population without control and in the presence of the effort of screening to quarintine and special treatment and check up.

6.2.6 Strategy F: Control with intensive medical care and spatial treatment and check up

Here we have applied intensive medical care for all the confirmed cases of the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals to optimize the objective functional $J(u)$ without implementing preventive measures (u_1) and the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) . The numerical result depicted in Figure 6.7 below (a) show as in the absence of control measure the number of exposed population of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_3 and u_4 controls the number of exposed population of COVID-19 are decreasing and 1.003×10^6 at final time. Also from numerical result depicted in Figure 6.7 below (b), we observed that in the absence of controlling intervention the number of symptomatic population by COVID-19 are increasing and it will be 1.85×10^6 and in the presence of u_3 and u_4 controls the number of symptomatic population by COVID-19 are decreasing and 1.498×10^6 at final time. Thus, this strategy is less effective to control exposed and symptomatic individuals.



(a) Exposed population without and with control.

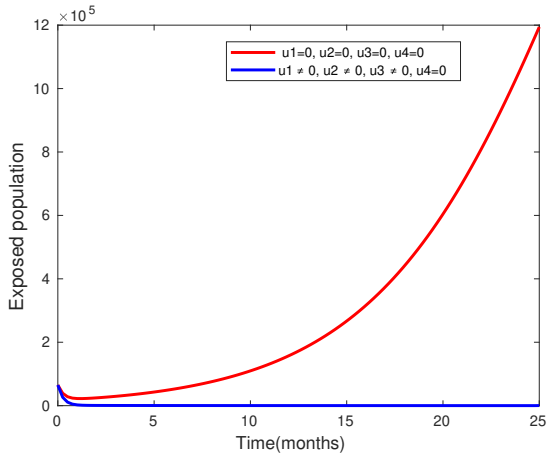


(b) Symptomatic population without and with control.

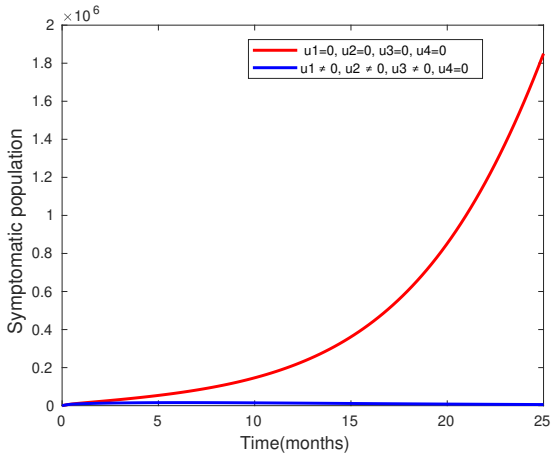
Figure 6.7: A simulation result of exposed and symptomatic population without control and in the presence of intensive medical care and spatial treatment and check up

6.2.7 Strategy G: Control with preventive measure, the effort of screening to quarantine and intensive medical care

Under this strategies, we simulated the model using preventive measures (u_1) , the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) and intensive medical care for all the confirmed cases of the isolated individuals (u_3) to optimize the objective functional $J(u)$ while special treatment and check up (u_4) for hospitalized individuals was set to zero. The numerical result depicted in Figure 6.8 below (a) show as in the absence of control strategies the number of exposed population of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_1, u_2 and u_3 controls the number of exposed population of COVID-19 are decreasing and 301.3 at final time. Also, from numerical result depicted in Figure 6.8 below (b), we observed that in the absence of control intervention the number of symptomatic population of COVID-19 are increasing and it will be 1.85×10^6 and in the the presence of u_1, u_2 and u_3 controls the number of symptomatic population of COVID-19 are decreasing and 5975 at final time. Therefore, this strategy is more effective to control exposed and symptomatic individuals.



(a) Exposed population without and with control.

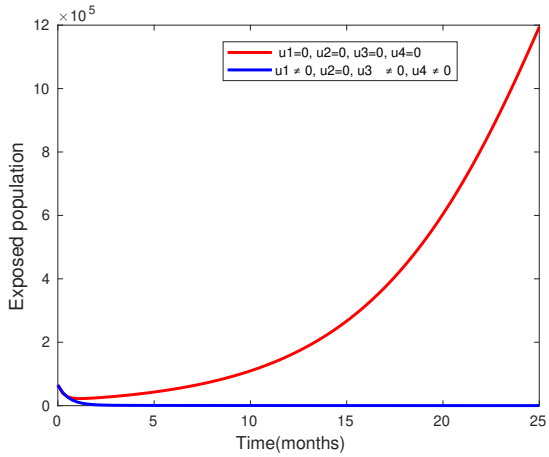


(b) Symptomatic population without and with control.

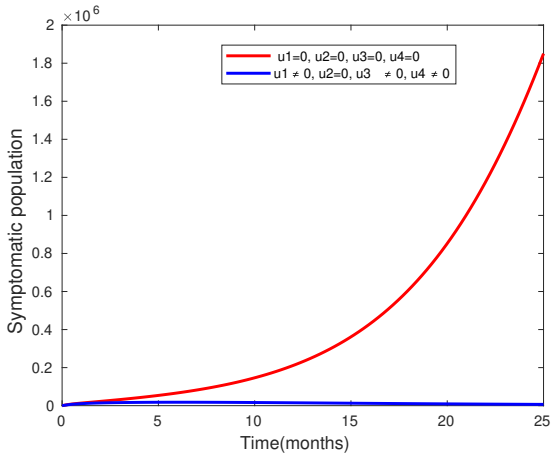
Figure 6.8: A simulation result of exposed and symptomatic population without control and in the presence of preventive measure, the effort of screening to quarantine and intensive medical care

6.2.8 Strategy H: Control with preventive measure, intensive medical care and special treatment and check up

Here we have applied preventive measures (u_1) , intensive medical care for all the confirmed cases for the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals to optimize the objective functional $J(u)$ while the effort of the screening exposed individuals and quarantine the alleged individuals (u_2) was set to zero. From the numerical result depicted in Figure 6.9 below (a), we observed that in the absence of control strategies the number of exposed population of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_1, u_3 and u_4 controls the number of exposed population of COVID-19 are 4176 at final time. Also, we observed from the second numerical result depicted in Figure 6.9 below (b) in the absence of control measures the number of symptomatic populations of COVID-19 are increasing and it will be 1.85×10^6 and in the presence of u_1, u_3 and u_4 controls the number of symptomatic populations of COVID-19 are decreasing and 6796 at final time. Hence, this strategy is effective to control exposed and symptomatic individuals.



(a) Exposed population without and with control.

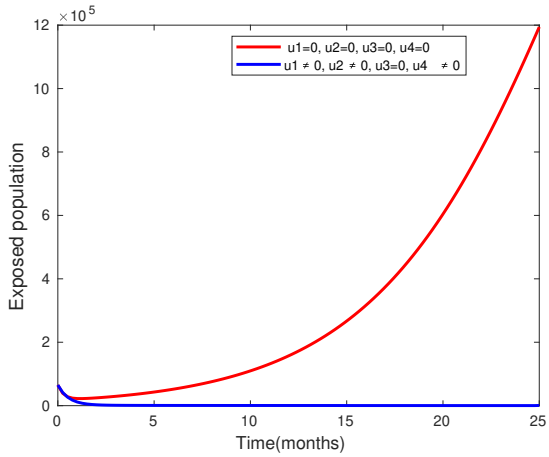


(b) Symptomatic population without and with control.

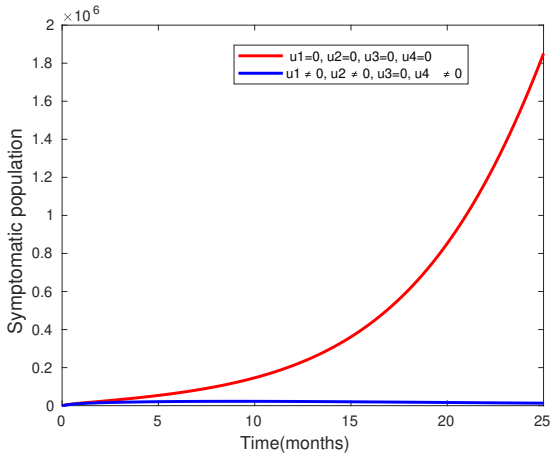
Figure 6.9: A simulation result of exposed and symptomatic population without control and in the presence of preventive measure, intensive medical care and special treatment and check up

6.2.9 Strategy I: Control with preventive measure, the effort of screening to quarantine and special treatment and check up

Under this strategies, we simulated the model using preventive measures (u_1) , the effort of screening exposed individuals and quarantine the alleged individuals (u_2) and special treatment and check up (u_4) for hospitalized individuals to optimize the objective functional $J(u)$ while intensive medical care for all the confirmed cases of the isolated individuals (u_3) was set to zero. The numerical result depicted in Figure 6.10 below (a) show as in the absence of control strategies the number of exposed populations of COVID-19 are increasing rapidly and it will be 1.194×10^6 and in the presence of u_1, u_2 and u_4 controls the number of exposed populations of COVID-19 are decreasing and about 637.2 at final time. Also from numerical result depicted in Figure 6.10 below (b), we observed that in the absence of control intervention the number of symptomatic populations of COVID-19 are increasing and it will be 1.85×10^6 and when u_1, u_2 and u_4 controls applied the number of symptomatic populations of COVID-19 are decreasing and 1.309×10^4 at final time. Therefore, this strategy is effective to reduce the number of exposed individuals and less effective to reduce the number of symptomatic individuals.



(a) Exposed population without and with control.

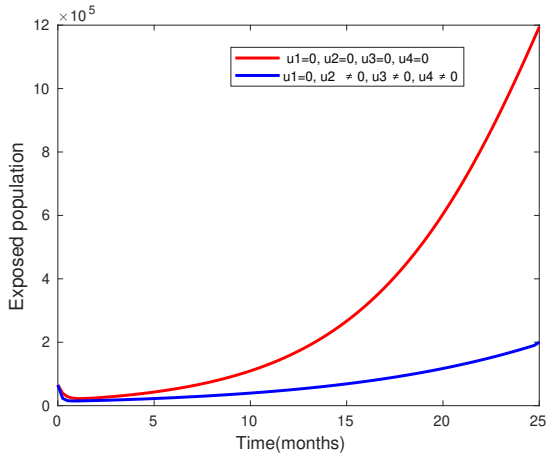


(b) Symptomatic population without and with control.

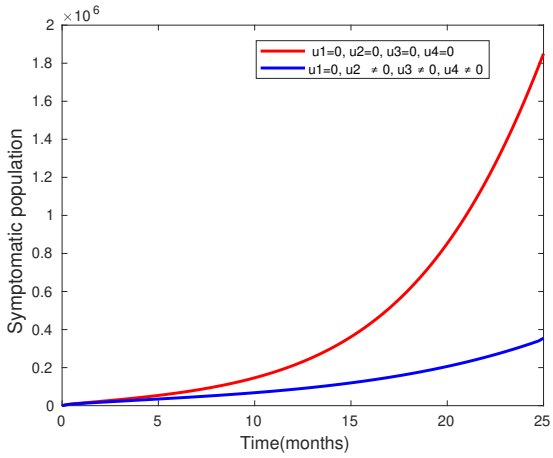
Figure 6.10: A simulation result of exposed and symptomatic population without control and in the presence of preventive measure, the effort of screening to quarantine and special treatment and check up

6.2.10 Strategy J: Control with the effort of screening to quarantine, intensive medical care and special treatment and check up

Here we have applied the effort of the screening exposed individuals and quarantine the alleged individuals (u_2), intensive medical care for all the confirmed cases of the isolated individuals (u_3) and special treatment and check up (u_4) for hospitalized individuals to optimize the objective functional $J(u)$ without considering preventive measures (u_1). From the numerical result depicted in Figure 6.11 below (a), we observed that in the absence of control strategies the number of exposed populations of COVID-19 are increasing rapidly and it will be 1.194×10^6 and when u_2, u_3 and u_4 controls applied, the number of exposed populations of COVID-19 are decreasing and 2.002×10^5 at final time. From the second numerical result depicted in Figure 6.11 below (b), we observed that in the absence of control the number of symptomatic populations of COVID-19 are increasing and it will be 1.85×10^6 and in the presence of u_2, u_3 and u_4 controls the number of symptomatic populations of COVID-19 are decreasing and 3.549×10^5 at final time. Hence, this strategy is less effective to reduce the number of exposed and symptomatic individuals.



(a) Exposed population without and with control.

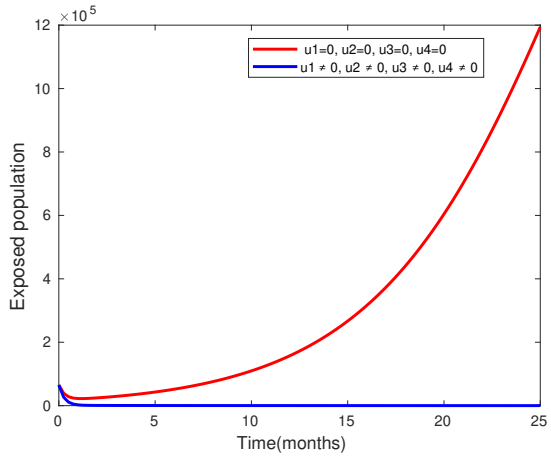


(b) Symptomatic population without and with control.

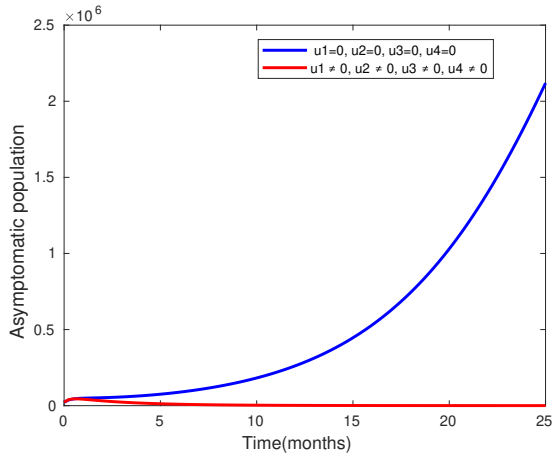
Figure 6.11: A simulation result of exposed and symptomatic population without control and in the presence of effort of screening to quarantine, intensive medical care and special treatment and check up

6.2.11 Strategy K: Applying all control strategies

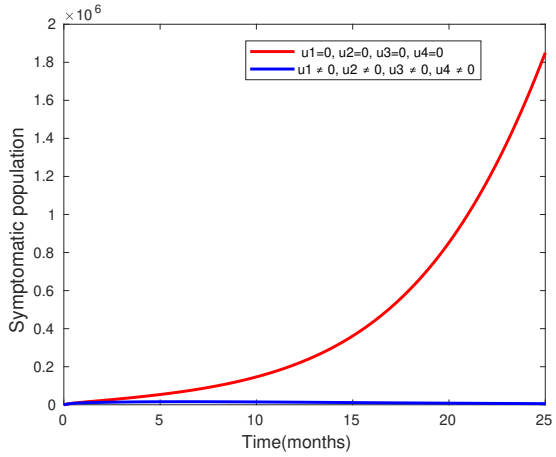
Here we have applied all the four control intervention on each compartment and from the numerical result depicted in Figure 6.12 below, we observed that in the absence of control intervention the number of exposed , asymptomatic, symptomatic(isolated), quarantined and hospitalized populations are increasing rapidly. In contrary, we observed that when all the four controls implemented, the number of exposed , asymptomatic, symptomatic(isolated), quarantined and hospitalized populations are decreasing. Further more the control profile depicted in figure 6.12 (f) show that the control u_1, u_2 and u_3 are at maximum level (95%) in all months and the control u_4 is at minimum level. This control profile has the same interpretation in all above strategies.



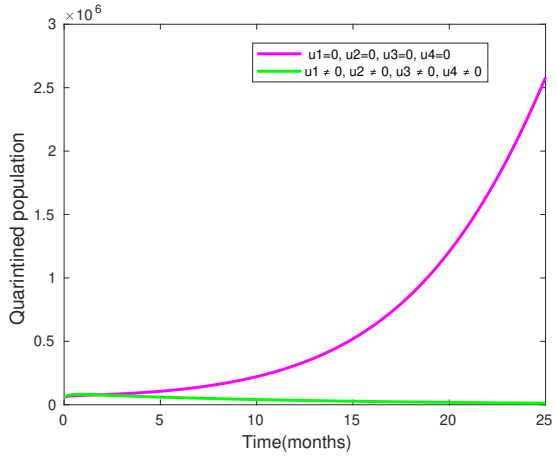
(a) Exposed population without and with control.



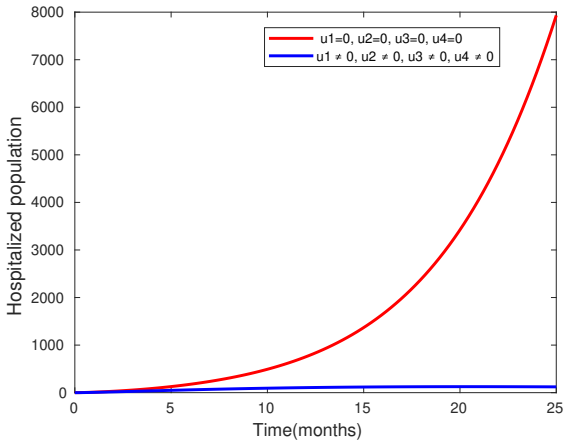
(b) Asymptomatic population without and with control.



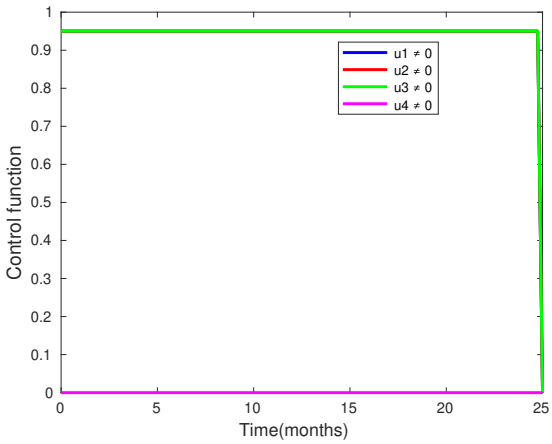
(c) Symptomatic population without and with control.



(d) Quarantined population without and with control.



(e) Hospitalized population without and with control.



(f) Profiles of optimal control function u_1, u_2, u_3 and u_4.

Figure 6.12: A simulation result of susceptible, exposed, asymptomatic, symptomatic, quarantined and hospitalized and recovered population without control and in the presence of all control

Chapter 7

Result and Discussion

7.1 Result and Discussion

In this thesis work, we have considered a mathematical model of transmission dynamics of a pandemic disease, COVID-19 infection. We have developed a seven-compartmental deterministic mathematical model, namely susceptible, exposed, asymptomatic, symptomatic and isolated, quarantined, hospitalized and recovered populations and investigated the dynamical behavior of this model. The model analysis show that there exists a domain where the model is epidemiologically and mathematically well-posed. We have stated about the invariant region in which the model solution is bounded. The existence and uniqueness of the solution of the model equation is show by the direct consequence of the Fundamental Existence and Uniqueness Theorem (Perko, 2013) and positivity of the solution of the model is shown by a contradiction. Using the next generation matrix method, we have found a basic reproduction number of the model system (4.1) and it is given by

$$R_0 = \frac{\beta[pb(\mu+\delta_2+q+\alpha)(\mu+n+\eta)+(k_1+\mu+\delta_1)(n\theta+r(\mu+n+\eta))]}{(\mu+p+r+\theta)(k_1+\mu+\delta_1)(\mu+\delta_2+q+\alpha)(\mu+n+\eta)}$$

which helps us to determine the dynamical behavior of the system. Based on the values of R_0 we have two distinct equilibriums for the model systems with both local and global stability those are disease-free and endemic equilibrium points. The system (4.1) is locally asymptotically stable at the disease free equilibrium point E_0 when $R_0 < 1$. When $R_0 > 1$, the endemic equilibrium E_1 exists and the system becomes unstable at E_0 and locally asymptotically stable at E_1 under some conditions. Also sensitivity indices of R_0 with respect to the

model parameters and bifurcation analysis are performed to reveal the transmission dynamics of corona virus diseases.

We have addressed the main target of this thesis work which is an optimal control problem relative to the epidemic model so as to minimize the exposed and symptomatic populations as well as to minimize the cost of control using Pontryagin's minimum principle which govern the necessary conditions for the optimal control of the spread of COVID-19 infection. We have considered four kinds of controls to reduce/mitigate the transmission dynamic of corona virus diseases. Those control functions are u_1(preventive measures) , u_2 (effort of screening exposed individuals and quarantine the alleged individuals to reduce transmission of COVID-19), u_3 (intensive medical care for all the confirmed cases to increase recover rate of the isolated individuals) and u_4 (special treatment and check up for severe and critical COVID -19 patients to increase recover rate of the hospitalized individuals). We applied those control intervention in order to fit our goal to minimize the objective function by reducing the number of exposed and symptomatic and isolated infective individuals.

The numerical simulation of the model system (4.1) and (5.1) have been performed and the simulation process is carried out using MATLAB software. For the numerical simulation we take the real data of total confirmed cases of COVID-19 infection in Ethiopia from March 2020 to April 2021 extracted from WHO situation reports (WHO, 2021). Parameters of the model system have been estimated using least-square fitting methods with MATLAB software. Also we used the forward fourth order Runge-Kutta scheme and back ward fourth order Runge-Kutta scheme to solve system (5.1) and (5.9) respectively. The control function is updated by using a convex combination of the previous control and the values computed in the characterizations process. Further more, to reduce the spread of COVID-19 infection disease we have experimented by combining pair wise, triple and all the four controls. We focused on the exposed $E(t)$ and symptomatic and isolated $I(t)$ in order to minimize the objective function. As the numerical result show as, it is more efficient when triple control like $u_1, u_2 \& u_3$ or all the four control are considered in simulation at a time to reduce the spread of corona virus diseases.

Conclussion and Recommendation

Conclussion

In this thesis work, we develop a deterministic mathematical model which describes the transmission dynamics of COVID-19 with optimal control using a system of nonlinear ordinary differential equations. In chapter four, we have developed a seven-compartmental deterministic mathematical model, namely susceptible, exposed, asymptomatic, symptomatic and isolated, quarantined, hospitalized and recovered populations. We investigated the dynamical behavior of this model and performed the qualitative analysis of the model. Both local and global stability analysis of the equilibrium points of the model equations have been done using Jacobian matrix and Lyapunov functions respectively. Sensitivity analysis of the model have been studied and determined a parameter which plays greater role in the transmission dynamics of COVID-19 and bifurcation analysis are performed to reveal the transmission dynamics of corona virus diseases.

In chapter five, an optimal control problem relative to the epidemic model so as to minimize the exposed and symptomatic populations as well as to minimize the cost of control using Pontryagin's minimum principle (PMP) have been addressed. We have used four controls those are u_1(preventive measures) , u_2 (effort of screening exposed individuals and quarantine the alleged individuals to reduce transmission of COVID-19), u_3 (intensive medical care for all the confirmed cases to increase recover rate of the isolated individuals) and u_4 (special treatment and check up for severe and critical COVID -19 patients to increase recover rate of the hospitalized individuals) to reduce the spread of COVID-19 infection.

In chapter six, the numerical simulation of the model system have been carried out using MATLAB software. For the numerical simulation we take the real data of total confirmed cases of COVID-19 infection in Ethiopia from March 2020 to April 2021 extracted from WHO situation reports (WHO, 2021). The parameters of the model system have been estimated using least-square fitting methods with MATLAB software. In order to reduce the spread of COVID-19 infection disease we have used by combining pair wise, triple and all the four controls at a time on the exposed $E(t)$ and symptomatic and isolated $I(t)$ to minimize the objective function. The numerical result show as, it is more efficient when triple or all the four control are considered in simulation to reduce the spread of COVID-19 infection. Thus, all people ,health sectors and government have to take their role in fighting the spread of corona virus disease by applying especially preventive measure such as physical distance, wearing mask, washing hand with soap frequently or using sanitizer, avoiding touching contaminated surface and applying the rule and regulation daily announced from World Health Organization(WHO) then it is possible to reduce/mitigate the spread of the diseases.

Recommendation

The mathematical models on pandemic diseases are rather simple, but nevertheless they give insight into some of the consequences of public health policies. Controlling the spread of pandemic disease significantly COVID-19 infection is now a world wide challenging problem and important issue to study. So, to predict and identify the cost-effective strategies to control the spread of COVID-19 diseases and minimize the cost of the control programme are the primary goals of all concerned stake holders such as health sector, researchers and others. Since COVID-19 infection is pandemic diseases, eradicating of this infection remains a challenge to the whole world especially in developing countries like Ethiopia. From results of this study we recommend that, the whole peoples must protect themselves from this diseases by applying combination of control strategies to mitigate/reduce the spread of corona virus infection.

Future work

In the future work, we plan to extend the study of this model by incorporating time delays in the system to make it more realistic.

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Appendix A

The Matlab code for simulation of ode system (4.1)

Listing A.1: Matlab Program for model (4.1) both without & with optimal control.

```
function y =EI(t,y1,y2,y3,y4,y5,y6,y7)
test = -1;
delta=0.08373;
tf=25;
M = 99;
t = linspace(0,tf,M+1);
h = tf/M;
h2 = h/2;

Lambda=143608;      % recruitment rate of the susceptible
    population
N =114961850;                  % Tolatl population population
beta = 0.71961;
mu = 0.0012;
theta= 0.47448;
p=0.98745;
r=0.24021;
b=0.77484;
q= 0.00084;
n=0.07166;
eta=0.01688;
```

```
alpha=0.12014;
k1=0.43234;
k2=0.04881;
delta1 = 0.00003;
delta2 = 0.00003;
delta3 = 0.00125;
C1 =5;
C2=4;
B1 =20;
B2 =15;
B3 =13;
B4 =10;
x1=zeros(1,M+1);
x2=zeros(1,M+1);
x3=zeros(1,M+1);
x4=zeros(1,M+1);
x5=zeros(1,M+1);
x6=zeros(1,M+1);
x7=zeros(1,M+1);
u1 = zeros(1,M+1);
u2 = zeros(1,M+1);
u3 = zeros(1,M+1);
u4 = zeros(1,M+1);
lambda1 = zeros(1,M+1);
lambda2 = zeros(1,M+1);
lambda3 = zeros(1,M+1);
lambda4 = zeros(1,M+1);
lambda5 = zeros(1,M+1);
lambda6 = zeros(1,M+1);
lambda7 = zeros(1,M+1);

x1(1) = 114763224;
```

```
x2(1) = 65000;
x3(1) = 23000;
x4(1) = 26;
x5(1) = 60600;
x6(1) =    0;
x7(1) = 50000;
while(test < 0)
      oldx1 = x1;
     oldx2 = x2;
     oldx3 = x3;
     oldx4 = x4;
     oldx5 = x5;
     oldx6 = x6;
     oldx7 = x7;


     oldu1 = u1;
     oldu2 = u2;
     oldu3 = u3;
     oldu4 = u4;

     oldlambda1 = lambda1;
     oldlambda2 = lambda2;
     oldlambda3 = lambda3;
     oldlambda4 = lambda4;
     oldlambda5 = lambda5;
     oldlambda6 = lambda6;
     oldlambda7 = lambda7;

for i = 1:M % forward in state
         auxu1 = 1-u1(i);
         auxu2 = 1+u2(i);
```

```
auxu3 = 1+u3(i);
auxu4 = 1+u4(i);
m11 = Lambda - ((beta*(b*x3(i)+x4(i))/N)*auxu1+mu)*x1
    (i);
m12 = auxu1*(beta*(b*x3(i)+x4(i))/N)*x1(i)-(mu +p+
    theta*auxu2+r)*x2(i);
m13 = p*x2(i)-(delta1 +mu+k1)*x3(i);
m14 = r*x2(i)+n*x5(i)-(q+mu+delta2+alpha*auxu3)*x4(i
    );
m15 = auxu3*theta*x2(i)- (mu+n+eta)*x5(i);
m16 = q*x4(i)- (k2*auxu4+mu+delta3)*x6(i);
m17 = auxu3*alpha*x4(i)+auxu4*k2*x6(i)+k1*x3(i)+eta*
    x5(i)-mu*x7(i);


%-----------------------------------------------
% Second Runge-Kutta parameter in state
%-----------------------------------------------

aux1 =x1(i)+h2*m11; aux2 = x2(i)+h2*m12; aux3 = x3(i)
    +h2*m13; aux4 = x4(i)+h2*m14; aux5 = x5(i)+h2*m15;
    aux6 = x6(i)+h2*m16; aux7 = x7(i)+h2*m17;
auxu1 = 1-0.5 * (u1(i) + u1(i+1));
auxu2 = 1+0.5 * (u2(i) + u2(i+1));
auxu3 = 1+0.5 * (u3(i) + u3(i+1));
auxu4 = 1+0.5 * (u4(i) + u4(i+1));

m21 = Lambda - ((beta*(b*aux3+aux4)/N)*auxu1+mu)*
    aux1;
m22 = auxu1*(beta*(b*aux3+aux4)/N)*aux1-(mu +p+theta
    *auxu2+r)*aux2;
m23 = p*aux2-(delta1 +mu+k1)*aux3;
```

```
m24 =   r*aux2+n*aux5-(q+mu+delta2+alpha*auxu3)*aux4;
m25 = auxu3*theta*aux2- (mu+n+eta)*aux5;
 m26 = q*aux4- (k2*auxu4+mu+delta3)*aux6;
 m27 = auxu3*alpha*aux4+auxu4*k2*aux6+k1*aux3+eta*
     aux5-mu*aux7;



%-------------------------------------------------
% Third Runge-Kutta parameter in state
%-------------------------------------------------
aux1 =x1(i)+h2*m21; aux2 = x2(i)+h2*m22; aux3 = x3(i)
    +h2*m23; aux4 = x4(i)+h2*m24; aux5 = x5(i)+h2*m25;
    aux6 = x6(i)+h2*m26;aux7 = x7(i)+h2*m27;
auxu1 = 1-0.5 * (u1(i) + u1(i+1));
auxu2 = 1+0.5 * (u2(i) + u2(i+1));
 auxu3 = 1+0.5 * (u3(i) + u3(i+1));
  auxu4 = 1+0.5 * (u4(i) + u4(i+1));

m31 =  Lambda - ((beta*(b*aux3+aux4)/N)*auxu1+mu)*
    aux1;
m32 =  auxu1*(beta*(b*aux3+aux4)/N)*aux1-(mu +p+theta
    *auxu2+r)*aux2;
m33 = p*aux2-(delta1 +mu+k1)*aux3;
m34 =  r*aux2+n*aux5-(q+mu+delta2+alpha*auxu3)*aux4;
m35 = auxu3*theta*aux2- (mu+n+eta)*aux5;
 m36 = q*aux4- (k2*auxu4+mu+delta3)*aux6;
 m37 = auxu3*alpha*aux4+auxu4*k2*aux6+k1*aux3+eta*
     aux5-mu*aux7;



%-------------------------------------------------
```

```
% Fourth Runge-Kutta parameter in state
%-----------------------------------------------------

 aux1 =x1(i)+h*m31; aux2 = x2(i)+h*m32; aux3 = x3(i)+
    h*m33; aux4 = x4(i)+h*m34; aux5 = x5(i)+h*m35;
    aux6 = x6(i)+h*m36; aux7 = x7(i)+h*m37;
 auxu1 = 1-u1(i+1);
 auxu2 = 1+u2(i+1);
 auxu3 = 1+u3(i+1);
 auxu4 = 1+u4(i+1);
 m41 =  Lambda - ((beta*(b*aux3+aux4)/N)*auxu1+mu)*
    aux1;
m42 =  auxu1*(beta*(b*aux3+aux4)/N)*aux1-(mu +p+theta
   *auxu2+r)*aux2;
m43 = p*aux2-(delta1 +mu+k1)*aux3;
m44 =  r*aux2+n*aux5-(q+mu+delta2+alpha*auxu3)*aux4;
m45 = auxu3*theta*aux2- (mu+n+eta)*aux5;
 m46 = q*aux4- (k2*auxu4+mu+delta3)*aux6;
 m47 = auxu3*alpha*aux4+auxu4*k2*aux6+k1*aux3+eta*
    aux5-mu*aux7;



x1(i+1) = x1(i) + (h/6)*(m11 + 2*m21 + 2*m31 + m41);
x2(i+1) = x2(i) + (h/6)*(m12 + 2*m22 + 2*m32 + m42);
x3(i+1) = x3(i) + (h/6)*(m13 + 2*m23 + 2*m33 + m43);
x4(i+1) = x4(i) + (h/6)*(m14 + 2*m24 + 2*m34 + m44);
x5(i+1) = x5(i) + (h/6)*(m15 + 2*m25 + 2*m35 + m45);
 x6(i+1) = x6(i) + (h/6)*(m16 + 2*m26 + 2*m36 + m46);
  x7(i+1) = x7(i) + (h/6)*(m17 + 2*m27 + 2*m37 + m47)
     ;
```

```
end

    %-------------------------------------------------------------------
    % Backward Runge-Kutta iterations in co-state variables
    %-------------------------------------------------------------------

for i = 1:M
        j = M + 2 - i;

        %-----------------------------------------------
        % First Runge-Kutta parameter in co-state
        %-----------------------------------------------

        auxu1 = 1-u1(j);
        auxu2 = theta+u2(j);
        auxu3 = alpha+u3(j);
        auxu4 = k2+u4(j);
        h1=lambda1(j) - lambda2(j);
        h2 = mu+p+r;
        h3 = lambda2(j) - lambda5(j);
        h4 = k1+mu+delta1;
        h5 = mu+delta2+q;
        h6 = lambda4(j) - lambda7(j);
        h7=mu+n+eta;
        h8=mu+delta3;
        h9 = lambda6(j) - lambda7(j);

        n11 =  h1*auxu1*(beta*(b*x3(j)+x4(j))./N)+lambda1(j)
           *mu;
```

```
n12 = -C1+lambda2(j)*h2+h3*auxu2-lambda3(j)*p-
    lambda4(j)*r;
n13 = (beta*b*x1(j)./N)*auxu1*h1+lambda3(j)*h4-
    lambda7(j)*k1;
n14 = -C2+(beta*x1(j)./N)*auxu1*h1+lambda4(j)*h5+h6*
    auxu3-lambda6(j)*q;
n15 = -n*lambda4(j)+h7*lambda5(j)-eta*lambda7(j);
n16 = h8*lambda6(j)+h9*auxu4;
n17 = mu*lambda7(j);


%-------------------------------------------------
% Second Runge-Kutta parameter in co-state
%-------------------------------------------------

aux1 = 0.5*(x1(j)+x1(j-1)); aux3 = 0.5*(x3(j)+x3(j
    -1)); aux4 = 0.5*(x4(j)+x4(j-1));
auxL1 = lambda1(j)-h2*n11; auxL2 = lambda2(j)-h2*n12
    ; auxL3 = lambda3(j)-h2*n13;
auxL4 = lambda4(j)-h2*n14; auxL5 = lambda5(j)-h2*n15
    ; auxL6 = lambda6(j)-h2*n16; auxL7 = lambda7(j)-h2
    *n17;


  auxu1 = 1-u1(j);
 auxu2 = theta+u2(j);
 auxu3 = alpha+u3(j);
 auxu4 = k2+u4(j);
h1=lambda1(j) - lambda2(j);
 h2 = mu+p+r;
 h3 =lambda2(j) - lambda5(j);
 h4 = k1+mu+delta1;
```

```
h5 = mu+delta2+q;
h6 = lambda4(j) - lambda7(j);
h7=mu+n+eta;
h8=mu+delta3;
h9 = lambda6(j) - lambda7(j);

n21 =  h1*auxu1*(beta*(b*aux3+aux4)./N)+auxL1*mu;
n22 = -C1+auxL2*h2+h3*auxu2-auxL3*p-auxL4*r;
n23 = (beta*b*aux1./N)*auxu1*h1+auxL3*h4-auxL7*k1;
n24 = -C2+(beta*aux1./N)*auxu1*h1+auxL4*h5+h6*auxu3-
    auxL6*q;
n25 = -n*auxL4+h7*auxL5-eta*auxL7;
n26 = h8*auxL6+h9*auxu4;
n27 = mu*auxL7;



%-----------------------------------------------
% Third Runge-Kutta parameter in co-state
%-----------------------------------------------

aux1 = 0.5*(x1(j)+x1(j-1)); aux3 = 0.5*(x3(j)+x3(j
    -1)); aux4 = 0.5*(x4(j)+x4(j-1));
auxL1 = lambda1(j)-h2*n21; auxL2 = lambda2(j)-h2*n22
    ;
auxL3 = lambda3(j)-h2*n23; auxL4 = lambda4(j)-h2*n24
    ; auxL5 = lambda5(j)-h2*n25; auxL6 = lambda6(j)-
    h2*n26; auxL7 = lambda7(j)-h2*n27;

 auxu1 = 1-u1(j);
auxu2 = theta+u2(j);
auxu3 = alpha+u3(j);
```

```
 auxu4 = k2+u4(j);
h1=lambda1(j) - lambda2(j);
 h2 = mu+p+r;
 h3 =lambda2(j) - lambda5(j);
 h4 = k1+mu+delta1;
 h5 = mu+delta2+q;
 h6 = lambda4(j) - lambda7(j);
 h7=mu+n+eta;
 h8=mu+delta3;
 h9 = lambda6(j) - lambda7(j);

 n31 =  h1*auxu1*(beta*(b*aux3+aux4)./N)+auxL1*mu;
 n32 = -C1+auxL2*h2+h3*auxu2-auxL3*p-auxL4*r;
 n33 = (beta*b*aux1./N)*auxu1*h1+auxL3*h4-auxL7*k1;
 n34 = -C2+(beta*aux1./N)*auxu1*h1+auxL4*h5+h6*auxu3-
    auxL6*q;
 n35 = -n*auxL4+h7*auxL5-eta*auxL7;
 n36 = h8*auxL6+h9*auxu4;
 n37 = mu*auxL7;


 %-------------------------------------------
 % Fourth Runge-Kutta parameter in co-state
 %-------------------------------------------

aux1 = x1(j-1); aux3 = x3(j-1); aux4 = x4(j-1);
auxL1 = lambda1(j)-h.*n31;  auxL2 = lambda2(j)-h.*n32
   ;  auxL3 = lambda3(j)-h.*n33;
auxL4 = lambda4(j)-h.*n34;  auxL5 = lambda5(j)-h.*n35
   ; auxL6 = lambda6(j)-h.*n36; auxL7 = lambda7(j)-h
   .*n37;
```

```
auxu1 = 1-u1(j);
auxu2 = theta+u2(j);
auxu3 = alpha+u3(j);
auxu4 = k2+u4(j);
h1=lambda1(j) - lambda2(j);
h2 = mu+p+r;
h3 =lambda2(j) - lambda5(j);
h4 = k1+mu+delta1;
h5 = mu+delta2+q;
h6 = lambda4(j) - lambda7(j);
h7=mu+n+eta;
h8=mu+delta3;
h9 = lambda6(j) - lambda7(j);

n41 =  h1*auxu1*(beta*(b*aux3+aux4)./N)+auxL1*mu;
n42 = -C1+auxL2*h2+h3*auxu2-auxL3*p-auxL4*r;
n43 = (beta*b*aux1./N)*auxu1*h1+auxL3*h4-auxL7*k1;
n44 = -C2+(beta*aux1./N)*auxu1*h1+auxL4*h5+h6*auxu3-
   auxL6*q;
n45 = -n*auxL4+h7*auxL5-eta*auxL7;
n46 = h8*auxL6+h9*auxu4;
n47 = mu*auxL7;


%-------------------------------------------------
% Runge-Kutta new approximation in co-state
%-------------------------------------------------


lambda1(j-1) = lambda1(j) - h/6*(n11 + 2*n21 + 2*n31
  + n41);
```

```
        lambda2(j-1) = lambda2(j) - h/6*(n12 + 2*n22 + 2*n32
            + n42);
        lambda3(j-1) = lambda3(j) - h/6*(n13 + 2*n23 + 2*n33
            + n43);
        lambda4(j-1) = lambda4(j) - h/6*(n14 + 2*n24 + 2*n34
            + n44);
        lambda5(j-1) = lambda5(j) - h/6*(n15 + 2*n25 + 2*n35
            + n45);
        lambda6(j-1) = lambda6(j) - h/6*(n16 + 2*n26 + 2*n36
            + n46);
        lambda7(j-1) = lambda7(j) - h/6*(n17 + 2*n27 + 2*n37
            + n47);



    end

    D = (beta.*(b.*x3+x4).*(lambda2-lambda1)).*x1;
    F= (lambda2-lambda5).*x2;
    G=(lambda4-lambda7).*x4;
    S=(lambda6-lambda7).*x6;


      u1 =   min(0.95,max(0,D./N.*B1));
      u2 = min(0.95,max(0,F./B2));
      u3 = min(0.95,max(0,G./B3));
      u4 = min(0.95,max(0,S./B4));


    u1 = 0*(u1 + oldu1);
      u2 = 0*(u2 + oldu2);
      u3 = 0*(u3 + oldu3);
      u4 = 0*(u4 + oldu4);
       dt = t(i+1)-t(i);
```

```
J = sum(( C1*x2+C2*x4+ +1/2*B1*u1.^2+1/2*B2*u2.^2+1/2*B3*
    u3.^2+1/2*B4*u4.^2 )*dt);


%-----------------------------------------
% Absolute error for convergence
%-----------------------------------------


temp1 = delta1*sum(abs(x1)) - sum(abs(oldx1 - x1));
temp2 = delta1*sum(abs(x2)) - sum(abs(oldx2 - x2));
temp3 = delta1*sum(abs(x3)) - sum(abs(oldx3 - x3));
temp4 = delta1*sum(abs(x4)) - sum(abs(oldx4 - x4));
temp5 = delta1*sum(abs(x5)) - sum(abs(oldx5 - x5));
temp6 = delta1*sum(abs(x6)) - sum(abs(oldx6 - x6));
temp7 = delta1*sum(abs(x7)) - sum(abs(oldx7 - x7));
temp8 = delta1*sum(abs(u1)) - sum(abs(oldu1 - u1));
temp9 = delta1*sum(abs(u2)) - sum(abs(oldu2 - u2));
temp10 = delta1*sum(abs(u3)) - sum(abs(oldu3 - u3));
temp11 = delta1*sum(abs(u4)) - sum(abs(oldu4 - u4));

temp12 = delta1*sum(abs(lambda1)) - sum(abs(oldlambda1 -
    lambda1));
temp13 = delta1*sum(abs(lambda2)) - sum(abs(oldlambda2 -
    lambda2));
temp14 = delta1*sum(abs(lambda3)) - sum(abs(oldlambda3 -
    lambda3));
temp15 = delta1*sum(abs(lambda4)) - sum(abs(oldlambda4 -
    lambda4));
```

```
    temp16 = delta1*sum(abs(lambda5)) - sum(abs(oldlambda5 -
        lambda5));
    temp17 = delta1*sum(abs(lambda6)) - sum(abs(oldlambda6 -
        lambda6));
    temp18 = delta1*sum(abs(lambda7)) - sum(abs(oldlambda7 -
        lambda7));
    test = min(temp1, min(temp2, min(temp3, min(temp4, min(
        temp5,min(temp6,min(temp7, min(temp8, min(temp9, min(
        temp10,min(temp11,min(temp12,min(temp13,min(temp14,min
        (temp15,min(temp16,min(temp17,temp18)))))))))))))));
end

y(1,:) = t;
y(2,:) = x1;
y(3,:) = x2;
y(4,:) = x3;
y(5,:) = x4;
y(6,:) = x5;
y(7,:) = x6;
y(8,:) = x7;
y(9,:) = lambda1;
y(10,:) = lambda2;
y(11,:) = lambda3;
y(12,:) = lambda4;
y(13,:) = lambda5;
y(14,:) = lambda6;
y(15,:) = lambda7;
y(16,:) = u1;
y(17,:) = u2;
y(18,:) = u3;
y(19,:) = u4;
y(20,:) = J;
```

```
box on
hold on
plot(y(1,:),y(3,:),'r','LineWidth',2)
xlabel('Time(months)','fontsize',12)
ylabel('cases','fontsize',13)
legend('E(t) without control','I(t) without control')

end
```