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MATHEMATICAL MODEL ON MIDDLE EAST RESPIRATORY SYNDROME AND CONTROL

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MATHEMATICAL MODEL ON MIDDLE EAST RESPIRATORY SYNDROME AND CONTROL

CERTIFICATION

This is to certify that this project on the **Mathematical Model on Middle East Respiratory Syndrme and Control** was done by Ezema,Godwin Izuchukwu with registration number: PG/MSC/17/03588, of the Department of Mathematics, Faculty of Physical Sciences, University of Nigeria, Nsukka.

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DEDICATION

To God and to all Men of Good Will.

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May the Almighty bless you all.

ABSTRACT

In this work,we considered the general overview of Middle East Respiratory Syndrome(MERS-CoV). A model for the transmission dynamics of the disease infection with control was formulated using a set of ordinary differential equations. The solution to the model equations were obtained using Homotopy Perturbation method, and ways for controlling or preventing the disease presented. The effective reproduction number ,R_0 of the system was obtained and it was shown that the disease will spread only if $R_0 > 1$ and would die off with time, if $R_0 < 1$. Numerical simulations carried out on the model showed that with the judicious use of Modified Virus Ankara(MVA) in combination with MERS-CoV inoculation, the disease will phase out rapidly in the population.

Contents

Chapter 1

INTRODUCTION

1.1 HISTORICAL BACKGROUND

INTRODUCTION

Middle East Respiratory Syndrome coronavirus (MERS-CoV) is a novel human coronavirus that was previously called "novel Human Corona Virus Erasmus Medical Center"(HCoV-EMC). The virus was discovered for the first time in Saudi Arabia in 2012 by Zaki et al. Subsequently, the virus was named Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in accordance with the geographical area of its first description and main occurrence. Until today, MERS-CoV represents an existential threat to global health

The World Health Organization (WHO) has confirmed 2279 cases of human infections with MERS-CoV in 27 countries since 2012; 806 (35%) infected patients have died as Feb. 13, 2019. Saudi Arabia still has the highest reported MERS-CoV mortality rate. Approximately 80% of the cases have been reported to occur there. MERS-CoV belongs to the family of coronaviridae, order Nidovirales. The family Coronaviridae is classified into four genera (α, β, γ *and* δ). Each genus is divided into linage sub-groups. MERS-CoV belongs to lineage-C of the β coronaviruses. Although bats are the main reservoir

for most coronaviruses, dromedary camels are considered the only known reservoir for MERS-CoV to date according to Ayman et al. Additionally, MERS-CoV isolated from dromedary camels is relatively closely related to some bat coronaviruses. According to the WHO, MERS-CoV transmission between humans is possible and occurs mostly in Middle East and the Republic of Korea. Viral spread has been observed among health-care workers and among individuals visiting MERS-CoV patients. The control of these outbreaks has been achieved by the local center of disease control and prevention (CDC). The interaction of MERS-CoV protein with the DPP4 receptor not only facilitates viral access into the host cell but also triggers signals that induce the immunosuppression of infected patients, enabling viral replication and spread Ayman et al.

Recently, Middle East Respiratory Syndrome Coronavirus has concerned the Arabian Peninsula. As a first virus that related to lineage C betacoronavirus (βCoV), and the sixth Coronavirus(CoV), MERS CoV is a virus transmitted to humans by contact with infected animals or humans. Symptoms are those of respiratory infections like: Pneumonia, asthma, common cold, shortness of breath, cough, and expectoration. All known cases so far have been linked to travel or residence in and around the Arabian Peninsula according to Sami et al (2015). The virus circulated in the Arabian Peninsula, particularly in Saudi Arabia. In May 2015, the Republic of Korea reported the largest outbreak outside the Middle East region. Many external factors could possibly impact the transmission of MERS-CoV among camels and human according to Qianying et al (2018).

In particular, Hajj and Umrah are two annual religious festivals that attract more than 10 million pilgrims from 184 countries to Saudi Arabia. Hajj is considered a major pilgrimage and involves mass gathering that lasts for six days during the 12th month of the Islamic calendar each year, whereas Umrah, a minor pilgrimage which could be highly individualized, is made mostly during Ramadan, a period of 29 to 30 days during the 9th month of the Islamic calendar. Several studies have demonstrated that these mass gatherings, which attracted pilgrims worldwide, were potential for transmission

of infectious diseases . Besides population movement and human mixing during religious events, camel racing, closing and reopening of camel markets, as well as climatic factors could impact on the transmission of MERS-CoV among camels, spill-over from camels to human and among human by Mahmoud et al (2018). Before MERS – CoV had emerged, the outbreak of the zoonotic coronavirus known as Sever Acute Respiratory Syndrome (SARS) spread in 26 countries, which exceeded 8000 cases in 2003. Then, SARS was the first known coronavirus infection. Before this time, coronavirus infection caused no more than a moderate upper respiratory track infection which was not considered as a major public health issue.

MERS – CoV related viruses have been discovered in bats that have direct contact with humans. Considerable indications assumed that the major source of MERS- CoV transmission is dromedary camel while the reservoir host is bats. It is then suggested that there may be a viral connection between bats, camels and humans. The result of the zoonotic transmission event that have generated MERS – CoV with clusters of human to human transmission of the virus is that animal is a preceding source of MERS – CoV. This viral connection between bats, camels and humans will be fully discussed as we proceed.

In early 1992, the antibodies of MERS existed in dromedaries, whereas the first case of MERS – CoV reported in human was in 2012. Even though some evidences suggested that camels are one of the major sources of MERS – CoV transmission, the precise source of its outbreak are still unknown. Even though MERS – CoV spread first in the Arabian Peninsula, the outbreak spread around the world in many countries. An Italian adult man who traveled to Jordan was reported as a first case of MER – CoV in Italy in May, 2013. In 2014, many cases of MERS – CoV were reported, in Soudi Arabia and in United Arab Emirates. At that time, the cases of MERS – CoV that were reported outside the Middle East had a history of visiting either United Arab Emirate (UAE) or the Kingdom of Saudi Arabia (KSA). MERS-CoV outbreaks are increasing since 2012 according to Ahmad et al (2014). Presently,in human, there is no antivirus or vaccine for MERS-CoV infection to prevent its spread. The only precaution

taken to limit the spread of the disease is isolation and hospitalization of infected patients. The visitors coming back from the Middle East must be investigated and isolated if they are suspected of having any contact with MERS-CoV cases or having the disease symptoms.

The main aim of this study is to develop an overview and concise understanding of MERS and its transmission dynamics as a result of MERS-CoV infection using a mathematical model. We will also give a detailed research on how this disease (MERS) can be controlled or possibly eradicated.

1.2 SCOPE OF THE STUDY

This work covers MERS, its transmission vector (camel),and MERS possible control technique. A mathematical model was developed using a system of ordinary differential equations.

1.3 AIM AND OBJECTIVES OF THE STUDY

The main aim of the study is to develop an understanding of MERS-CoV transmission dynamics as a result of infection between human and animal and how it can be controlled to prevent secondary cases. The specific objectives are to:

1. Carryout a detailed study of MERS-CoV disease.

2. Develop a mathematical model of the transmission and control of the disease.

3. Determine the effect of the control measures on the population.

4. Perform equilibrium and stability analysis of the model.

5. Interpret the results of the analysis.

1.4 LIMITATIONS OF THE STUDY

The mathematical model equations are presented as a system of first order ordinary differential equations. The research centered on analyzing the control of the disease by the method of animal vaccination. Hence, this work is open to further studies using any other approach of interest.

1.5 SIGNIFICANCE OF THE STUDY

A unique and most striking feature of this research work is the role that camels have in the control of MERS-CoV infection. Following the demonstration of the key role of hospitals in secondary spread, efforts were made to introduce careful infection control measures into affected hospitals. These appear to have been effective in reducing virus transmission and greatly decreasing the number of MERS, which likely occur either directly or indirectly from camels. These primary cases are the source for subsequent hospital outbreaks. So, preventing transmission from camel or within the community stands the best approach way to preventing subsequent secondary cases and hospital spread. While vaccine development usually target human population, MERS-CoV infects a much greater number and higher percentage of camels than humans in the Arabian Peninsula and in Africa. Thus, camel vaccination is an approach required to decrease the amount of circulating virus and also diminish the amount of virus secreted by infected animals. Our research showed that this approach is most viable and feasible and stands the optimal suggestion towards eradicating MERS-CoV infection.

Chapter 2

LITERATURE REVIEW

2.1 LITERATURE REVIEW

We begin this chapter by reviewing the works done by other researchers on Mathematical modeling and then review those on MERS-CoV. The study by Hethcote (2000) showed that modeling started in 1760 by Daniel Bernoulli. At this time, there were some controversies about inoculation. This is because this is one of the practices that could protect people but could still be harmful or deadly. Convincingly, using Halley's life table and analysis from smallpox, Bernoulli showed that inoculation was safe and healthy to apply if the risk factor of dying was less than 11 percent.

Ali Mohamed Zaki(2012) was the first to identify the coronavirus that causes MERS. Zaki had diagnosed "Patient A" of MERS virus at a Saudi Arabian diagnostic laboratory built in 1993. This patient commonly referred to as Patient A was inlet into the hospital and was diagnosed of respiratory related infection which quickly resulted to acute pneumonia, renal failure and eventually died 11 days later. Since the patient was reportedly dead, no one was interested to continue the investigation on the unprecedented disease. Not being comfortable of the development, Zaki's scientific inquisitiveness was immediately ignited and he concluded to personally unravel the mystery behind the death. Zaki, before

the patient's death, had collected sputum and blood sample called #38. This sample was immediately sent to his collaborators to be tested. Unfortunately, the laboratory staff has all gone on vacation. On this ground, he conducted the test himself. It was on this process that Zaki discovered the existence of a different type of coronavirus that had never been known in the human history.

Adney et al (2019), published online in May 23, studied the contribution of Dromedary camels in increasing the spread of MERS-CoV. The research showed that this animal contributes highly in the transmission of MERS-CoV. The research showed that camels are also vulnerable to MERS-CoV infection and transfer the virus to other potential carriers through nasal secretions. The short coming of the research was the use of two animals of which a seroconversion investigation was tested. In spite of the insufficient field facts, the study showed that camels can readily pass the virus through their nasal gland.

Al- Abdely et al (2019) carried out a research on the infectious dynamics of MER-CoV and the antibody reactions among different patients in Saudi Arabia. A good number of MERS-CoV patients were admitted in Saudi Arabian hospital. The intermittently specimens obtained through serological testing showed that the antibody reaction within the second and third week of treatment was not enough for patient recovery. The research also showed that cough and fever identified among patients aligned with RNA discovered in the upper respiratory organ.

Elkholy et al (2019) investigated the transmission of MERS-CoV within health professionals and potential factors for death. Using the past analysis of all laboratory verified cases as obtained from WHO from 2012 to June 2018, half of the reported cases of MERS-CoV infections have taken place among health workers. This study centered on describing the secondary stages of MERS-CoV infections in health facilities and established the risk factors for death.

Khudhair et al (2019) carried out experiment on danger of MERS-CoV seropositivity within animal market and abattoirs from 2014 to 2017. According to the study carried out, about 100 to 235 workers were seropositive for the disease. The research identified that handling camels, camel waste, the activities of camel salesmen, and having diabetes were linked with seropositivity among all workers. This analysis suggested that introduction of preventive measures among camel handlers is essential in widespread control of the disease.

In this study, our effort has been on developing a more efficient control of MERS-CoV. Our research has shown that animal vaccination is a better approach than any other techniques. This study however, is not disputing or condemning the effort of researchers in searching for human vaccine,however, our research has shown that the disease control is more efficient from its primary outbreak(animal) than from secondary outbreak(human). Hence,vaccination of animals using Modified Virus Ankara in combination with MERS-CoV inoculation produces antibody against MERS-CoV.

Chapter 3

MODE OF TRANSMISSION OF MERS

MERS is a respiratory disease caused by (MERS-CoV) that was first discovered in Saudi Arabia in 2012. The disease has cause about 600 deaths since its first occurrence and over 1600 individuals infected.No antiviral therapies or vaccines are available for its treatment.

3.1 Symptoms

[8]

The diagnosis of MERS-CoV infection ranges from no symptoms (asymptomatic) or mild respiratory symptoms to severe acute respiratory disease and death. Common symptom of MERS-CoV disease ranges from fever, cough, asthma,shortness of breath to pneumonia. Gastrointestinal symptoms,such as diarrhea, have also been reported. These symptoms if not discovered early could cause respiratory failure that requires mechanical ventilation and support in an intensive care unit. People with:weak immune system, cancer, diabetes, renal disease, and chronic diseases and the old are more vulnerable to the infection.

3.2 Source of the virus

MERS-CoV is a zoonotic virus. This means it is a virus that is transmitted between humans and animals. Research have confirmed that humans are infected through direct or indirect contact with infected dromedary camels. MERS-CoV has been found in dromedaries in several countries, including Egypt, Oman, Qatar, and Saudi Arabia. MERS-CoV specific antibodies (a finding that indicates an animal has previously been infected with MERS-CoV) have been identified in dromedaries in the Middle East, Africa and South Asia. Though the origin of the virus is not clear, analysis of the virus genomes show that it may have originated in bats and got to camels sometime in the past.

3.3 TRANSMISSION

Transmission of MERS-CoV is divided into two categories:non-human to human transmission and human to human transmission. The studies available to date shows that MERS-CoV has existed in bats before it spread to camels by the mid 1990s. And for the non-human to human transmission, the virus had been identified to have spread from camels to humans in early 2010.

3.4 EPIDEMIOLOGICAL CHARACTERISTICS

The incubation period, that is, the duration from the midpoint of the exposure to the symptom onset, was 6.5 days (median; range, 2 to 16 days). The median time from symptom onset to confirmation was 5 days (0 to 17 days), that from symptom onset to death was 13 days (1 to 41 days), and that from symptom onset to discharge from the hospital was 20 days (8 to 41 days)[3, 11] . Unlike influenza or the common cold, MERS-CoV doesn't seem to spread readily among people in communities. Instead, MERS-CoV has spread mostly among people who are in close contact, such as people living with or providing direct care for an infected person.

3.5 The Receptor for MERS-CoV and The Cells It Infect

MERS-CoV has been shown to infect a range of human primate, porcine, and bat cell lines. Ex-viro infections of human and human airway epithelial cell culture identified Type 11 alveolae cells and non-ciliated cells (Clara cells) as the targets of infection, rather than the ACE2 expressing ciliated epithelial cells that SARS-CoV targets. Interestingly, in at least one caseendothelial cells were infected as well, showing a distinct difference between the biology of SARS-CoV and MERS-CoV, as SARS-CoV specifically infects ciliated epithelial cells in the lung. The receptor for MERS-CoV was recently identified as dipeptidyl peptidase 4 (DDP4) by mass spectrometry analysis of Huh7 cell protein bound to the MERS- CoV spike protein in vitro. Transfection and localization experiments demonstrated that DPP4 is indeed the receptor for MERS-CoV and is necessary for infection of a non-permissive cell line. DPP4 has many diverse functions in glucose homeostasis, T-cell activation, neurotransmitter function, and modulation of cardiac signaling.

3.6 The Host Response to MERS-CoV

Transcriptional analysis of MERS-CoV infected cells has identified several pathways specifically modulated during infection. MERS-CoV is shown to modulate the innate immune response, antigen presentation, mitogen-activated protein kinase(MAPK), and apoptosis pathways. Importantly, several studies show that MERS-CoV, similar to SARS-CoV, does not induce an early Type 1 IFN response, suggesting that MERS-CoV may encode proteins that inhibit sensing of the viral RNA during infection. The modulation of these pathways may explain the increases lethality of MERS-CoV.

3.7 Diagnosis

A doctor will examine the patient and ask about symptoms and about recent activities, including travel. Samples will be taken from a patient's respiratory track (RT) for assessment. Polymerase chain reaction testing (RT-PCR testing) can confirm the presence of MERS-Cov. Tests can detect the relevant antibodies 10 days after the illness starts. If the test is negative 28 days after the onset of symptoms, the person is considered not to have MERS. Blood tests can determine if an individual has previously been infected, by testing for antibodies to MERS-CoV.

3.8 PREVENTION AND TREATMENT

There is no specific drug (i.e., antiviral) treatment for MERS and no vaccine available to protect against the disease. Medical management of patients with confirmed MERS focuses on symptom relief. As a general precaution for anyone visiting farms,they should practice regular hand washing before and after

contact with animals.

Camels play an important role in the transmission of the disease. Hence, camel vaccination is considered an important approach towards controlling human infection. though hospitals have intensified efforts in controlling the secondary spread of the disease, these efforts do not stop the acquisition of primary cases which is the source of secondary outbreak. Thus preventing the transmission within the camel community stands a better chance in eradicating the disease. Some of the people who have fallen ill with MERS contracted the virus, MERS-CoV(it is a coronavirus, as it belongs to the coronaviridae family), from camels they worked with. Dromedaries, or one-humped camels of the kind familiar in the Gulf, are a "reservoir" for MERS-CoV: they carry the virus but do not fall ill." you wouldn't call it a disease in camel; they don't get sick- they are infected, they are carriers of the virus," said Dr Ulrich Wernery, the CVRL's scientific director. Very young camels are protected from the virus by antibodies in the milk from their mothers, but by the time a calf is four to six months old, it will have lost this immunity. After that, there is a "window" of three to five months during which the animal may become infected – and pass the virus to people. "Maybe 95 per cent of all camel calves [that get infected] are infected during this time of three to five months. At this time, we can isolate the virus from the [calf's] nose; not from the lung," said Dr Wernery."Then after that they become immune again because they produce antibodies against the virus. The dangerous time for camel keepers is during this window." Fortunately, young camels tend to be lively and so direct contact with people, even those who work with camels, is rare. But it does happen, and there have been cases in Saudi Arabia of people being infected this way. "There's no need to vaccinate adult camels, but you vaccinate camels when they're four, five, six months old, then they cannot transmit to humans," said Dr Wernery. Researchers in Germany, the Netherlands and Spain have genetically engineered a vaccine called the modified vaccinia virus Ankara (MVA). This vaccine is used to stimulate immunity against pox, a type of disease caused by members of the poxviridae virus family, but can be used in combination with MERS-CoV virus. Part of the

MERS-CoV virus is inserted in the pox vaccine. In a study published in early 2016 in the journal Science, one of the world's top scientific publications, the researchers said that this recombinant vaccine appeared to confer immunity to MERS in camels on which it had been tested. Vaccinated animals produced antibodies against MERS-CoV and had much lower levels of the virus in their system.

Chapter 4

Mathematical model of Middle East Respiratory Syndrome and control

In this chapter, we apply Mathematical formula, using the variable tools of Differential Equations to build Mathematical equations and also perform Numerical or computer simulations of the disease transmission to gain a better knowledge of the diseases dynamics.

4.1 ASSUMPTION OF THE MODEL

1. There is no human to animal transmission of the disease.

2. The disease has no vaccine in human population.

3. The recovered human exhibits a temporal immunity through out the course of this study.

4. This study focuses on the control of the disease transmission from the primary source. Thus, our Numerical Simulation and Reproduction number is a function of the animal compartment.

5. Modified Virus Ankara(MVA) is the animal vaccine.

4.2 MODEL DIAGRAM

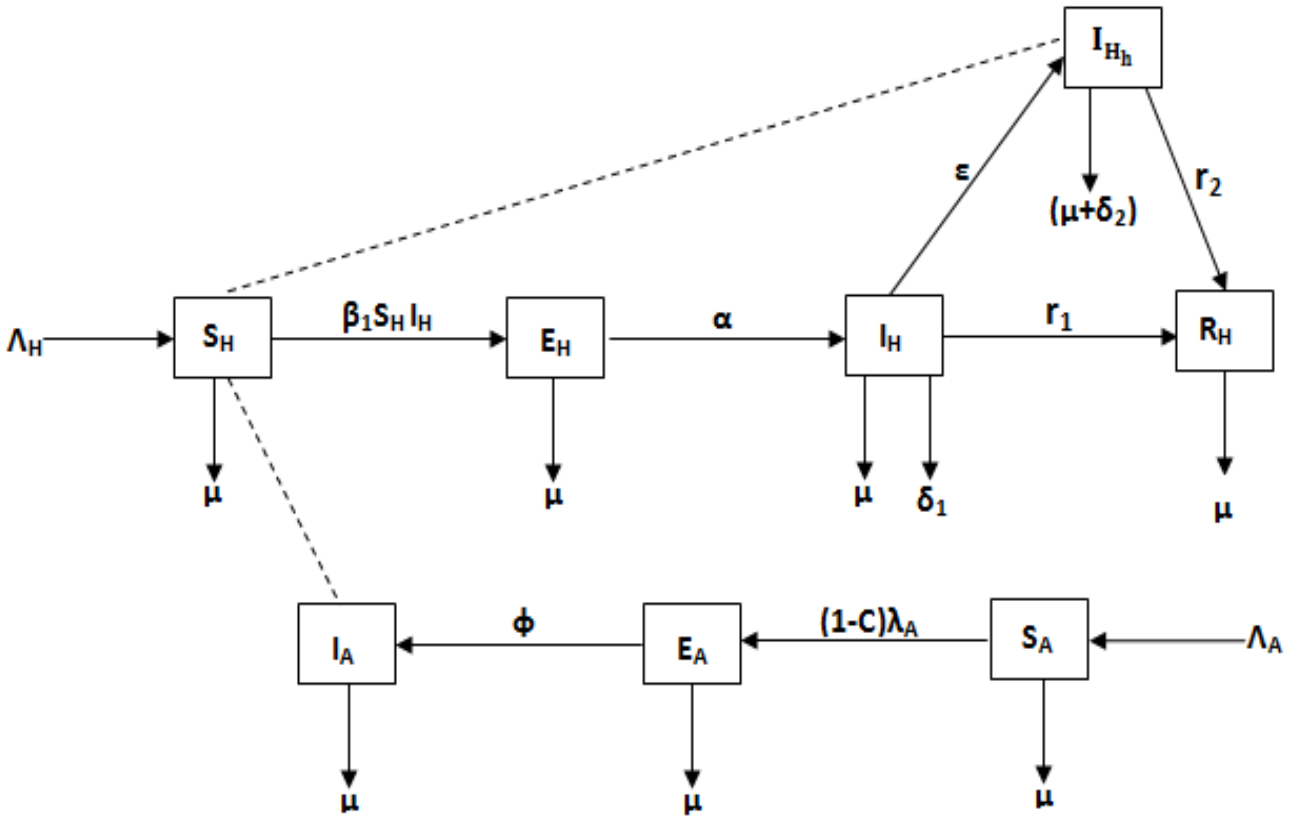

Figure 4.1: Flow Diagram of MERS-CoV

4.2.1 Model Equations

$$
\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - \mu S = f_1 \\
\frac{dE_H}{dt} &= (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - (\alpha + \mu) E_H = f_2 \\
\frac{dI_H}{dt} &= \alpha E_H - (\mu + \delta_1 + \epsilon + r_1) I_H = f_3 \\
\frac{dIH_h}{dt} &= \epsilon I_H - (\mu + \delta_2 + r_2) I_{H_h} = f_4 \\
\frac{dR_H}{dt} &= r_1 I_H + r_2 I_{H_h} - \mu R_H = f_5 \\
\frac{dS_A}{dt} &= \Lambda_A - (1 - c)\lambda_A - \mu S_A = f_6 \\
\frac{dE_A}{dt} &= (1 - c)\lambda_A - (\phi + \mu) E_A = f_7 \\
\frac{dI_A}{dt} &= \phi E_A - \mu I_A = f_8
\end{aligned}
\tag{4.1}
$$

Where $\lambda_A = \beta_4 S_A I_A$

Table 4.1: Variable Declaration

Variable	Description
S_H	Susceptible Human at time t
E_H	Exposed Human at time t
I_H	Infected Human at time t
I_{H_h}	Infected Human hospitalized at time t
R_H	Recovered Human at time t
S_A	Susceptible Animal at time t
E_A	Exposed Animal at time t
I_A	Infected Animal at time t

Table 4.2: Parameter Declaration

Parameter	Description
Λ_H	Recruitment rate of Humans
β_1	Rate of interaction between Susceptible and Exposed Human
β_2	Rate of interaction between Susceptible Human and Infected Human hospitalized
β_3	Rate of interaction between Susceptible Human and Infected Animal
μ	Natural death
δ_1, δ_2	Death due to the disease
α	Rate of interaction between Exposed Human and Infected Human
r_1	Rate of interaction between Infected Human and Recovered Human.
r_2	Rate of interaction between Infected Human hospitalized and Recovered human
Λ_A	Recruitment rate of Animal
Φ	Rate of interaction between Exposed and Infected Animal
ϵ	Rate of interaction between Infected Human and Infected Human Hospitalized
β_4	Interaction between Susceptible animal and Infected animal
c	control parameter(Modified Vaccine Ankara).

We assume the initial condition such that

$S_H(0) = S_{H_0}, E_H(0) = E_{H_0}, I_H(0) = I_{H_0}, I_H(0) = I_{H_0}, R_H(0) = R_{H_0}, S_A(0) = S_{A_0}, E_A(0) = E_{A_0}, I_A(0) = I_{A_0}$

The total population size for the human model is;

$N_H = S_H + E_H + I_H + I_{H_h} + R_H$

This means that;

$$\frac{dN_H}{dt} = \frac{dS_H}{dt} + \frac{dE_H}{dt} + \frac{dI_H}{dt} + \frac{dI_{H_h}}{dt} + \frac{dR_H}{dt} \tag{4.2}$$

Therefore,

$$\begin{aligned}
\frac{dN_H}{dt} &= (\Lambda_H - k_1 S_H - \mu S_H) + (k_1 S_H - \alpha E_H - \mu E_H) + (\alpha E_H - \mu I_H - \delta_1 I_H - \epsilon I_H - r_1 I_H) \\
&+ (\epsilon I_H - \mu I_{H_h} - \delta_2 I_{H_h} - r_2 I_{H_h}) + (r_1 I_H + r_2 I_{H_h} - \mu R_H) \\
&= \Lambda_H - \mu S_H - \mu E_H - \mu I_H - \delta_1 I_H - \mu I_{H_h} - \delta_2 I_{H_h} - \mu R_H \\
&= \Lambda_H - (S_H + E_H + I_H + I_{H_h} + R_H)\mu - (\delta_1 I_H + \delta_2 I_{H_h}) \\
&= \Lambda_H - \mu N - (\delta_1 I_H + \delta_2 I_{H_h}) \qquad (4.3)
\end{aligned}$$

The total population size for animal;

$N_A = S_A + E_A + I_A$

So that;

$$\begin{aligned}
\frac{dN_A}{dt} &= \frac{dS_A}{dt} + \frac{dE_A}{dt} + \frac{dI_A}{dt} \\
&= (\Lambda_A - (1-c)\lambda_A - \mu S_A) + ((1-c)\lambda_A - \phi E_A - \mu E_A) + (\phi E_A - \mu I_A) \\
&= \Lambda_A - \mu(S_A + E_A + I_A) \\
&= \Lambda_A - \mu N_A \qquad (4.4)
\end{aligned}$$

4.3 INVARIANT REGION

This region can be obtained by this theorem;

Theorem: The solutions of the system(4.1) are feasible for all $t > 0$ if they enter the invariant region

$'\Omega =' \Omega_H \times' \Omega_A$

Proof

Let $\Omega_H = (S_H, E_H, I_H, I_{H_h}, R_H)$ *and* $\Omega_A = (S_A, E_A, I_A)$

Then, let $'\Omega = (S_H, E_H, I_H I_{H_h}, R_H, S_A, E_A, I_A) \in \Re^8_+$,

be any solution of system (4.1)with non negative initial conditions (i.e at $t > 0, S_H \geq 0, E_H \geq 0,$

$I_H \geq 0, I_{H_h} \geq 0, R_H \geq 0, S_A \geq 0, E_A \geq 0, I_A \geq 0$).

In the absence of the disease(MERS), equation(4.3) becomes

$$\begin{aligned} \frac{dN_H}{dt} &\leq \Lambda_H - \mu N \\ \frac{dN_H}{dt} + \mu N &\leq \Lambda_H \end{aligned} \tag{4.5}$$

The integrating factor $I = \exp(\int(\mu dt) = \exp(\mu t)$

$$\begin{aligned} \exp(\mu t)\left(\frac{dN_H}{dt} + \mu N\right) &\leq \Lambda_H \ell^{(\mu t)} \\ \frac{d}{dt}(N_H \ell^{\mu t}) &\leq \Lambda_H \ell^{\mu t} \end{aligned} \tag{4.6}$$

integrating both sides we have:

$$\begin{aligned} N_H \exp(\mu t) &\leq \frac{\Lambda_H}{\mu}\ell^{\mu t} + C \\ N_H(t) &\leq \frac{\Lambda_H}{\mu} + C\exp(-\mu t) \end{aligned} \tag{4.7}$$

Introducing our initial condition; $t = 0$ *and* $N_H(0) = N_{H_0}$, we have that:

$$\begin{aligned} N_{H_0} &\leq \frac{\Lambda_H}{\mu} + C \\ &or \\ N_{H_0} - \frac{\Lambda_H}{\mu} &\leq C \end{aligned} \tag{4.8}$$

This implies that;

$$\begin{aligned} N_H(t) &\leq \frac{\Lambda_H}{\mu} + (N_{H_0} - \frac{\Lambda_H}{\mu})\ell^{-\mu t} \\ &\leq \frac{\Lambda_H}{\mu} + N_{H_0}\ell^{-\mu t} - \frac{\Lambda_H}{\mu}\ell^{-\mu t} \\ N_H(t) &\leq \frac{\Lambda_H}{\mu}(1 - \ell^{-\mu t}) + N_{H_0}\ell^{-\mu t} \end{aligned} \tag{4.9}$$

Applying the theorem of differential inequality by Birkoff and Rota(1982), we have that:

at $t = 0$, $\quad N_H(t) \leq N_{H_0}$ and as $t \longrightarrow \infty$, $\quad N_H(t) \leq \frac{\Lambda_H}{\mu}$.

Thus, $\quad 0 \leq N_H(t) \leq N_{H_0}$.

This shows that as $t \longrightarrow \infty$, the human population $N_H(t) \to K = \frac{\Lambda_H}{\mu}$, where K is the carrying capacity [1].

This means that all the feasible solution sets of the human population of model (4.1) enter the invariant region:

$'\Omega_H = \ (S_H, E_H I_H I_{H_h}, R_H) \in \Re^5_+ : S_H > 0, E_H \geq 0, I_H \geq 0, I_{H_h} \geq 0, R_H \geq 0, N_H \leq \frac{\Lambda_H}{\mu}$.

INVARIANT REGION FOR ANIMAL. From equation (4.4), we observe that disease-induced death is insignificant or negligible. Thus,

$$\begin{aligned} \frac{dN_A}{dt} &= \Lambda_A - \mu N_A \\ \frac{dN_A}{dt} + \mu N_A &= \Lambda_A \end{aligned}$$

The integrating factor is; $\ell^{\int \mu dt} = \ell^{\mu t}$

$$\begin{aligned}
\frac{dN_A}{dt}\ell^{\mu t} + \mu N_A \ell^{\mu t} &= \Lambda_A \ell^{\mu t} \\
\frac{d}{dt}(N_A \ell^{\mu t}) &= \Lambda_A \ell^{\mu t} \\
N_A \ell^{\mu t} &= \frac{\Lambda_A}{\mu}\ell^{\mu t} + C \\
N_A(t) &= \frac{\Lambda_A}{\mu} + C\ell^{-\mu t}
\end{aligned}$$

at $t = 0, N_A(0) = N_{A_0}$; then,

$$\begin{aligned}
N_{A_0} &= \frac{\Lambda_A}{\mu} + C \\
N_{A_0} - \frac{\Lambda_A}{\mu} &= C, \quad thus; \\
N_A(t) &= \frac{\Lambda_A}{\mu} + (N_{A_0} - \frac{\Lambda_A}{\mu})\ell^{-\mu t} \\
&= \frac{\Lambda_A}{\mu}(1 - \ell^{-\mu t}) + N_{A_0}\ell^{-\mu t} \qquad (4.10)
\end{aligned}$$

By the theorem of differential inequality,

at $t = 0, \qquad N_{A_0} \leq N_{A_0}$

as t $\longrightarrow \infty, \quad N_A(t) \leq \frac{\Lambda_A}{\mu}$

This implies that; $0 \leq N_{A_{(t)}} \leq \frac{\Lambda_A}{\mu}$. Hence all the feasible solution sets of the animal population of model (4.1) enter the invariant region; $'\Omega_A = (S_A, E_A, I_A) \in \Re^3_+ : S_A > 0, E_A \geq 0, I_A \geq 0, N_A \leq \frac{\Lambda_A}{\mu}$. This shows that the region $'\Omega =' \Omega_H \times' \Omega_A$ is positively invariant such that the solutions remain positive for all times,t and the model (4.1) is biologically meaningful and mathematically well posed in the domain $'\Omega$.

4.4 POSITIVITY OF SOLUTION

Lemma 4.5. let $\{(S_H(0), S_A(0)) > 0, (E_H(0), I_H(0), I_{H_h}(0), R_H(0), E_A(0), I_A(0)) \geq 0\} \in \Omega$ be the initial data. then the solution set, $\{S_H, E_H, I_H, I_{H_h}, R_H, S_A, E_A, I_A\}(t)$ of the system(4.1) is positive for all $t > 0$.

Proof:

from the first equation in the model (4.1), we have:

$$\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - \mu S_H \\
\frac{dS_H}{dt} &= \Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H \geq -\mu S_H \\
\frac{dS_H}{dt} &\geq -\mu S_H \\
\frac{dS_H}{S_H} &\geq -\mu dt \\
\Rightarrow \quad ln(S_H) &\geq -\mu t + c \\
ln(\frac{S_H}{c}) &\geq -\mu t, \qquad S_H(t) \geq C\ell^{-\mu t}
\end{aligned}$$

But at $t = 0, S_H(0) \geq C$. Hence, $S_H(t) \geq S_H(0)\ell^{-\mu t}$

Observe that as $t \to \infty$, $S_H(t) \geq 0$, $(since \ \ \mu > 0)$

from the second equation in model (4.1),

$$\begin{aligned}
\frac{dE_H}{dt} &= (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - (\alpha + \mu) E_H \\
\frac{dE_H}{dt} &= (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H \geq -(\alpha + \mu) E_H \\
\frac{dE_H}{E_H} &\geq -(\alpha + \mu) dt \\
\frac{dE_H}{dt} &\geq -(\alpha + \mu) E_H \\
lnE_H &\geq -(\alpha + \mu) t + C \\
E_H(t) &\geq C\ell^{-(\alpha+\mu)t}
\end{aligned}$$

But at $t = 0, E_H(0) \geq$ C. Hence, $\quad E_H(t) \geq E_H(0)\ell^{-(\alpha+\mu)t}$

Observe that as $t \to \infty, \quad E_H(t) \geq 0, \qquad (since \quad (\alpha + \mu) > 0)$

from the third equation in model(4.1),

$$\begin{aligned}
\frac{dI_H}{dt} &= \alpha E_H - (\mu + \delta_1 + \epsilon + r_1) I_H \geq -(\mu + \delta_1 + \epsilon + r_1) I_H \\
\frac{dI_H}{dt} &\geq -(\mu + \delta_1 + \epsilon + r_1) I_H \\
\frac{dI_H}{I_H} &\geq (\mu + \delta_1 + \epsilon + r_1) dt \\
lnI_H &\geq (\mu + \delta_1 + \epsilon + r_1) t + C \\
I_H(t) &\geq C\ell^{-(\mu+\delta_1+\epsilon+r_1)t}
\end{aligned}$$

But at $t = 0, I_H(0) \geq$ C. Hence, $\quad I_H(t) \geq I_H(0)\ell^{-(\mu+\delta_1+\epsilon+r_1)t}$

Observe that as $t \to \infty, \quad I_H(t) \geq 0, \quad (since \quad (\mu + \delta_1 + \epsilon + r_1) > 0)$

With out lose of genarality, it is now trivial that the same argument holds for the remaining compartments.

4.6 DISEASE FREE EQUILIBRIUM

The Disease Free Equilibrium determines the equilibrium point of the model in the absence of the disease. When analysis shows that the DFE is stable, it implies that the infection could die out of the population giving it a clean health bill.If DFE is unstable, the disease could be prevalent in the system. Using the system(4.1), the right hand side is set to zero at equilibrium or steady state.

$$\begin{aligned}
\Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - \mu S &= 0 \\
(\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - (\alpha + \mu) E_H &= 0 \\
\alpha E_H - (\mu + \delta_1 + \epsilon + r_1) I_H &= 0 \\
\epsilon I_H - (\mu + \delta_2 + r_2) I_{H_h} &= 0 \\
r_1 I_H + r_2 I_{H_h} - \mu R_H &= 0 \\
\Lambda_A - (1 - C)\lambda_A - \mu S_A &= 0 \\
(1 - C)\lambda_A - (\phi + \mu) E_A &= 0 \\
\phi E_A - \mu I_A &= 0
\end{aligned}$$

In the disease free equilibrium, there is no more infections. Consequently, there will be no more exposed, hospitalized, and recovered human and animal population. Hence;($E_H = I_H = I_{H_h} = R_H = E_A = I_A = 0$)

from the first equation above,

$$\begin{aligned}
\Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) S_H - \mu S_H &= 0 \\
\Lambda_H - \mu S_H &= 0 \\
S_H^{t_o} &= \frac{\Lambda_H}{\mu}
\end{aligned}$$

from the sixth equation above,

$$\begin{aligned} \Lambda_A - (1-C)\lambda_A - \mu S_A &= 0 \\ \Lambda_A - \mu S_A &= 0 \\ S_A^{t_o} &= \frac{\Lambda_A}{\mu} \end{aligned}$$

$DFE:\ E_0 = (S_H^{t_0}, E_H^{t_0}, I_H^{t_0}, I_{H_h}^{t_0}, R_H^{t_0}, S_A^{t_0}, E_A^{t_0}, I_A^{t_0})$

$= (\frac{\Lambda_H}{\mu}, 0, 0, 0, 0, \frac{\Lambda_A}{\mu}, 0, 0)$

This represents the state inwhich there is no MERS-CoV in the society.

4.7 ENDEMIC EQUILIBRIUM POINT(EEP)

The Disease Endemic Equilibrium Point determines the equilibrium point of the model in the presence of the disease. If the Endemic Equilibrium point is stable, then the disease is prevalent, if unstable, the

disease could either be endemic or die out.

$$\Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - \mu S = 0 \quad (4.11)$$

$$(\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - (\alpha + \mu)E_H = 0 \quad (4.12)$$

$$\alpha E_H - (\mu + \delta_1 + \epsilon + r_1)I_H = 0 \quad (4.13)$$

$$\epsilon I_H - (\mu + \delta_2 + r_2)I_{H_h} = 0 \quad (4.14)$$

$$r_1 I_H + r_2 I_{H_h} - \mu R_H = 0 \quad (4.15)$$

$$\Lambda_A - (1 - C)\lambda_A - \mu S_A = 0 \quad (4.16)$$

$$(1 - C)\lambda_A - (\phi + \mu)E_A = 0 \quad (4.17)$$

$$\phi E_A - \mu I_A = 0 \quad (4.18)$$

from equation(4.16),

$$\Lambda_A - (1 - C)\lambda_A - \mu S_A = 0$$

$$but \quad \lambda_A = \beta_4 S_A I_A$$

$$\Rightarrow \Lambda_A - [(1 - C)\beta_4 I_A + \mu]S_A = 0$$

$$S_A^* = \frac{\Lambda_A}{(1 - C)\beta_4 I_A + \mu}$$

from equation(4.17),

$$\begin{aligned}(1-C)\lambda_A-(\phi+\mu)E_A &= 0\\ \Rightarrow E_A &= \frac{(1-C)\beta_4 S_A I_A}{(\phi+\mu)}\\ &= \frac{(1-C)\beta_4\Lambda_A I_A}{(\phi+\mu)[(1-C)\beta_4 I_A+\mu}\end{aligned}$$

from equation(4.18),

$$\begin{aligned}\phi E_A-\mu I_A &= 0\\ E_A &= \frac{\mu I_A}{\phi}\end{aligned}$$

This means that,

$$\begin{aligned}\frac{(1-C)\beta_4\Lambda_A I_A}{(\phi+\mu)[(1-C)\beta_4 I_A+\mu} &= \frac{\mu I_A}{\phi}\\ \mu[(\phi+\mu)[(1-C)\beta_4 I_A+\mu] &= \phi(1-C)\beta_4\Lambda_A\\ I_A^* &= \frac{\phi(1-C)\beta_4\Lambda_A-\mu^2(\phi+\mu)}{\mu(\phi+\mu)(1-C)\beta_4}\\ &= \frac{\phi\Lambda_A}{\mu(\phi+\mu)}-\frac{\mu}{(1-C)\beta_4}\end{aligned}$$

from

$$E_A^* = \frac{\mu I_A}{\phi}$$

We have:

$$\begin{aligned} E_A &= \frac{\mu}{\phi}\left(\frac{\phi\Lambda_A}{\mu(\phi+\mu)} - \frac{\mu}{(1-C)\beta_4}\right) \\ &= \frac{\Lambda_A}{(\phi+\mu)} - \frac{\mu^2}{(1-C)\phi\beta_4} \end{aligned}$$

from

$$S_A = \frac{\Lambda_A}{(1-C)\beta_4 I_A + \mu}$$

We have:

$$S_A = \frac{\Lambda_A}{(1-C)\beta_4\left[\frac{\phi(1-C)\beta_4\Lambda_A - \mu^2(\phi+\mu)}{\mu(\phi+\mu)(1-C)\beta_4}\right] + \mu}$$

$$\begin{aligned} &= \frac{\Lambda_A}{\frac{\phi(1-C)\beta_4\Lambda_A - \mu^2(\phi+\mu)}{\mu(\phi+\mu)} + \mu} \\ &= \frac{\mu(\phi+\mu)\Lambda_A}{\phi(1-C)\beta_4\Lambda_A} \quad \Rightarrow \quad S_A^* = \frac{\mu(\phi+\mu)}{\phi(1-C)\beta_4} \end{aligned}$$

from equation(4.14),

$$\begin{aligned} \epsilon I_H - (\mu+\delta_2+r_2)I_{H_h} &= 0 \\ I_{H_h}^* &= \frac{\epsilon I_H}{\mu+\delta_2+r_2} \\ I_H^* &= \frac{(\mu+\delta_2+r_2)I_{H_h}}{\epsilon} \end{aligned}$$

from equation(4.15),

$$\begin{aligned} r_1 I_H + r_2 I_{H_h} - \mu R_H &= 0 \\ R_H &= \frac{r_1 I_H + r_2 I_{H_h}}{\mu} \end{aligned}$$

substituting in I_{H_h} we have;

$$\begin{aligned} R_H^* &= \frac{r_1 I_H + r_2(\frac{\epsilon I_H}{\mu+\delta_2+r_2})}{\mu} \\ &= \frac{(\mu+\delta_2+r_2)r_1 I_H + r_2\epsilon I_H}{\mu(\mu+\delta_2+r_2)} \\ &= \frac{[(\mu+\delta_2+r_2)r_1 + r_2\epsilon]I_H}{\mu(\mu+\delta_2+r_2)} \end{aligned}$$

from equation(4.13),

$$\begin{aligned} \alpha E_H - (\mu+\delta_1+\epsilon+r_1)I_H &= 0 \\ E_H^* &= \frac{(\mu+\delta_1+\epsilon+r_1)I_H}{\alpha} \end{aligned}$$

from eq(4.12),

$$\begin{aligned} (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - (\alpha+\mu)E_H &= 0 \\ (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H &= (\alpha+\mu)E_H \\ &= (\alpha+\mu)\frac{(\mu+\delta_1+\epsilon+r_1)I_H}{\alpha} \end{aligned}$$

We set $I_A = \frac{\phi\Lambda_A}{\mu(\phi+\mu)} - \frac{\mu}{(1-C)\beta_4}$ *to be* K_1. Substituting this with the value of I_{H_h} into the above equation

we have;

$$(\beta_1 I_H + \beta_2 \frac{\epsilon I_H}{\mu + \delta_2 + r_2} + \beta_3 K_1) S_H = \frac{(\alpha + \mu)(\mu + \delta_1 + \epsilon + r_1) I_H}{\alpha}$$

Dividing through by I_A, we have:

$$\begin{aligned} (\beta_1 + \beta_2 \frac{\epsilon}{\mu + \delta_2 + r_2} + \frac{\beta_3 K_1}{I_H}) S_H &= \frac{(\alpha + \mu)(\mu + \delta_1 + \epsilon + r_1)}{\alpha} \\ S_H^* &= \frac{(\alpha + \mu)(\mu + \delta_1 + \epsilon + r_1)}{\alpha(\beta_1 + \beta_2 \frac{\epsilon}{\mu + \delta_2 + r_2} + \frac{\beta_3 K_1}{I_H})} \end{aligned} \tag{4.19}$$

The Endemic Equilibrium for MERS-CoV is :

$$\begin{aligned} (S_H^*, E_H^*, I_H^*, I_{H_h}^*, R_H^*, S_A^*, E_A^*, I_A^*) = \Bigg[& \frac{(\alpha + \mu)(\mu + \delta_1 + \epsilon + r_1)}{\alpha \left(\beta_1 + \frac{\beta_2 \epsilon}{\mu + \delta_2 + r_2} + \frac{\beta_3 K_1}{I_H} \right)}, \frac{(\mu + \delta_1 + \epsilon + r_1) I_H}{\alpha}, \frac{(\mu + \delta_2 + r_2) I_{H_h}}{\epsilon}, \\ & \frac{\epsilon I_H}{\mu + \delta_2 + r_2}, \frac{r_1 I_H + r_2 (\frac{\epsilon I_H}{\mu + \delta_2 + r_2})}{\mu}, \frac{\mu(\phi + \mu)}{\phi(1 - C)\beta_4}, \frac{\Lambda_A}{(\phi + \mu)} - \frac{\mu^2}{(1 - C)\phi\beta_4}, \\ & \frac{\phi \Lambda_A}{\mu(\phi + \mu)} - \frac{\mu}{(1 - C)\beta_4} \Bigg] \end{aligned} \tag{4.20}$$

This shows the size of each disease compartment of the model in the presence of the disease.

4.8 BASIC REPRODUCTION NUMBER

The basic reproduction number (R_o) measures the transmission potential of a disease. It is the average number of infections produced by a typical case of an infectious person in a population of susceptible class.The basic reproduction number is affected by several factors:

1. The rate of contacts in the host population

2. The probability of infection being transmitted during contact

3. The duration of infectiousness.

In general, for an epidemic to occur in a susceptible population, R_o must be greater than one, indicating that the number of cases is increasing. The basic reproduction number is calculated using Next Generation Matrix. Rewriting the system(4.1) by starting with the infected compartments in both human and animal population ($i.e\ E_H, I_H, I_{H_h}, E_A, I_A$), and followed by the uninfected classes ($i.e\ S_H, R_H, S_A$), the model equation becomes;

$$\begin{aligned}
\frac{dE_H}{dt} &= (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - (\alpha + \mu)E_H \\
\frac{dI_H}{dt} &= \alpha E_H - (\mu + \delta_1 + \epsilon + r_1)I_H \\
\frac{dIH_h}{dt} &= \epsilon I_H - (\mu + \delta_2 + r_2)I_{H_h} \\
\frac{dE_A}{dt} &= (1-c)\lambda_A - (\phi + \mu)E_A \\
\frac{dI_A}{dt} &= \phi E_A - \mu I_A \\
\frac{dS_H}{dt} &= \Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - \mu S \\
\frac{dR_H}{dt} &= r_1 I_H + r_2 I_{H_h} - \mu R_H \\
\frac{dS_A}{dt} &= \Lambda_A - (1 - c\lambda_A - \mu S_A
\end{aligned} \tag{4.21}$$

From the system(4.12) F_i and V_i are defined as:

$$F_i = \begin{bmatrix} (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H \\ 0 \\ 0 \\ (1-c)\beta_4 I_A S_A \\ 0 \end{bmatrix}$$

$$V_i = \begin{bmatrix} (\alpha+\mu)E_H \\ (\mu+\delta_1+\epsilon+r_1)I_H - \alpha E_H \\ (\mu+\delta_2+r_2)I_{H_h} - \epsilon I_H \\ (\phi+\mu)E_A \\ \mu I_A - \phi E_A \end{bmatrix}$$

The partial derivative of F_i with respect to $(E_H, I_H, I_{H_h}, E_A, I_A)$and the Jacobian matrix at disease free equilibrium are:

$$F = \begin{bmatrix} \frac{\partial f_1}{\partial E_H} & \frac{\partial f_1}{\partial I_H} & \frac{\partial f_1}{\partial I_{H_h}} & \frac{\partial f_1}{\partial E_A} & \frac{\partial f_1}{\partial I_A} \\ \frac{\partial f_2}{\partial E_H} & \frac{\partial f_2}{\partial I_H} & \frac{\partial f_2}{\partial I_{H_h}} & \frac{\partial f_2}{\partial E_A} & \frac{\partial f_2}{\partial I_A} \\ \frac{\partial f_3}{\partial E_H} & \frac{\partial f_3}{\partial I_H} & \frac{\partial f_3}{\partial I_{H_h}} & \frac{\partial f_3}{\partial E_A} & \frac{\partial f_3}{\partial I_A} \\ \frac{\partial f_4}{\partial E_H} & \frac{\partial f_4}{\partial I_H} & \frac{\partial f_4}{\partial I_{H_h}} & \frac{\partial f_4}{\partial E_A} & \frac{\partial f_4}{\partial I_A} \\ \frac{\partial f_5}{\partial E_H} & \frac{\partial f_5}{\partial I_H} & \frac{\partial f_5}{\partial I_{H_h}} & \frac{\partial f_5}{\partial E_A} & \frac{\partial f_5}{\partial I_A} \end{bmatrix} = \begin{bmatrix} 0 & \beta_1 S_H & \beta_2 S_H & 0 & \beta_3 S_H \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (1-c)\beta_4 S_A \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Similarly, the partial derivative of (4.2) with respect to $(E_H, I_H, I_{H_h}, E_A, I_A)$, and the Jacobian matrix of V_i at the disease-free equilibrium is;

$$V = \begin{bmatrix} \frac{\partial v_1}{\partial E_H} & \frac{\partial v_1}{\partial I_H} & \frac{\partial v_1}{\partial I_{H_h}} & \frac{\partial v_1}{\partial E_A} & \frac{\partial v_1}{\partial I_A} \\ \frac{\partial v_2}{\partial E_H} & \frac{\partial v_2}{\partial I_H} & \frac{\partial v_2}{\partial I_{H_h}} & \frac{\partial v_2}{\partial E_A} & \frac{\partial v_2}{\partial I_A} \\ \frac{\partial v_3}{\partial E_H} & \frac{\partial v_3}{\partial I_H} & \frac{\partial v_3}{\partial I_{H_h}} & \frac{\partial v_3}{\partial E_A} & \frac{\partial v_3}{\partial I_A} \\ \frac{\partial v_4}{\partial E_H} & \frac{\partial v_4}{\partial I_H} & \frac{\partial v_4}{\partial I_{H_h}} & \frac{\partial v_4}{\partial E_A} & \frac{\partial v_4}{\partial I_A} \\ \frac{\partial v_5}{\partial E_H} & \frac{\partial v_5}{\partial I_H} & \frac{\partial v_5}{\partial I_{H_h}} & \frac{\partial v_5}{\partial E_A} & \frac{\partial v_5}{\partial I_A} \end{bmatrix} = \begin{bmatrix} (\alpha+\mu) & 0 & 0 & 0 & 0 \\ -\alpha & \mu+\delta_1+\epsilon+r_1 & 0 & 0 & 0 \\ 0 & -\epsilon & \mu+\delta_2+r_2 & 0 & 0 \\ 0 & 0 & 0 & (\phi+\mu) & 0 \\ 0 & 0 & 0 & -\phi & \mu \end{bmatrix}$$

$$V^-1 = \begin{bmatrix} \frac{1}{(\alpha+\mu)} & 0 & 0 & 0 & 0 \\ \frac{\alpha}{K_1(\alpha+\mu)} & \frac{1}{K_1} & 0 & 0 & 0 \\ \frac{\alpha\epsilon}{K_1K_2(\alpha+\mu)} & \frac{\epsilon}{K_1K_2} & \frac{1}{K_2} & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{(\phi+\mu)} & 0 \\ 0 & 0 & 0 & \frac{\phi}{\mu(\phi+\mu)} & \frac{1}{\mu} \end{bmatrix}$$

Solving, $|FV^{-1} - \lambda I| = 0$

Implies that;

$$\begin{vmatrix} (\frac{\alpha\beta_1 S_H}{K_1(\alpha+\mu)} + \frac{\alpha\beta_2 S_H}{K_1K_2(\alpha+\mu)}) - \lambda & \frac{\beta_1 S_H}{K_1} + \frac{\epsilon\beta_2 S_H}{K_1K_2} & \frac{\beta_2 S_H}{K_2} & \frac{\phi\beta_3 S_H}{\mu(\phi+\mu)} & \frac{\beta_3 S_H}{\mu} \\ 0 & -\lambda & 0 & 0 & 0 \\ 0 & 0 & -\lambda & 0 & 0 \\ 0 & 0 & 0 & \frac{(1-C)\phi\beta_4 S_A}{\mu(\phi+\mu)} - \lambda & (1-C)\beta_4 S_A \\ 0 & 0 & 0 & 0 & -\lambda \end{vmatrix} = 0$$

Set $M = (\frac{\alpha\beta_1 S_H}{K_1(\alpha+\mu)} + \frac{\alpha\beta_2 S_H}{K_1K_2(\alpha+\mu)})$ *and* $N = \frac{(1-C)\phi\beta_4 S_A}{\mu(\phi+\mu)}, then$

$(M - \lambda)(N - \lambda)(-\lambda^3) = 0$

So that

$\lambda_1 = M$

$\lambda_2 = N$

4.9 STABILITY AT DISEASE FREE EQUILIBRIUM (DFE)

To analyze stability at DFE, we find the Jacobian matrix, J, of the system as follows:

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial f_1} & \frac{\partial f_1}{\partial E_H} & \frac{\partial f_1}{\partial I_H} & \frac{\partial f_1}{\partial I_{H_h}} & \frac{\partial f_1}{\partial R_H} & \frac{\partial f_1}{\partial S_A} & \frac{\partial f_1}{\partial E_A} & \frac{\partial f_1}{\partial I_A} \\ \frac{\partial f_2}{\partial S_H} & \frac{\partial f_2}{\partial E_H} & \frac{\partial f_2}{\partial I_H} & \frac{\partial f_2}{\partial I_{H_h}} & \frac{\partial f_2}{\partial R_H} & \frac{\partial f_2}{\partial S_A} & \frac{\partial f_2}{\partial E_A} & \frac{\partial f_2}{\partial I_A} \\ \frac{\partial f_3}{\partial S_H} & \frac{\partial f_3}{\partial E_H} & \frac{\partial f_3}{\partial I_H} & \frac{\partial f_3}{\partial I_{H_h}} & \frac{\partial f_3}{\partial R_H} & \frac{\partial f_3}{\partial S_A} & \frac{\partial f_3}{\partial E_A} & \frac{\partial f_3}{\partial I_A} \\ \frac{\partial f_4}{\partial S_H} & \frac{\partial f_4}{\partial E_H} & \frac{\partial f_4}{\partial I_H} & \frac{\partial f_4}{\partial I_{H_h}} & \frac{\partial f_4}{\partial R_H} & \frac{\partial f_4}{\partial S_A} & \frac{\partial f_4}{\partial E_A} & \frac{\partial f_4}{\partial I_A} \\ \frac{\partial f_5}{\partial S_H} & \frac{\partial f_5}{\partial E_H} & \frac{\partial f_5}{\partial I_H} & \frac{\partial f_5}{\partial I_{H_h}} & \frac{\partial f_5}{\partial R_H} & \frac{\partial f_5}{\partial S_A} & \frac{\partial f_5}{\partial E_A} & \frac{\partial f_5}{\partial I_A} \\ \frac{\partial f_6}{\partial S_H} & \frac{\partial f_6}{\partial E_H} & \frac{\partial f_6}{\partial I_H} & \frac{\partial f_6}{\partial I_{H_h}} & \frac{\partial f_6}{\partial R_H} & \frac{\partial f_6}{\partial S_A} & \frac{\partial f_6}{\partial E_A} & \frac{\partial f_6}{\partial I_A} \\ \frac{\partial f_7}{\partial S_H} & \frac{\partial f_7}{\partial E_H} & \frac{\partial f_7}{\partial I_H} & \frac{\partial f_7}{\partial I_{H_h}} & \frac{\partial f_7}{\partial R_H} & \frac{\partial f_7}{\partial E_A} & \frac{\partial f_7}{\partial E_A} & \frac{\partial f_7}{\partial I_A} \\ \frac{\partial f_8}{\partial S_H} & \frac{\partial f_8}{\partial E_H} & \frac{\partial f_8}{\partial I_H} & \frac{\partial f_8}{\partial I_{H_h}} & \frac{\partial f_8}{\partial R_H} & \frac{\partial f_8}{\partial S_A} & \frac{\partial f_8}{\partial E_A} & \frac{\partial f_8}{\partial I_A} \end{bmatrix}$$

$$J = \begin{bmatrix} -(\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) - \mu & 0 & -\beta_1 S_H & \beta_2 S_H & 0 & 0 & 0 & -\beta_3 S_H \\ (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A) & -(\alpha + \mu) & \beta_1 S_H & \beta_2 S_H & 0 & 0 & 0\beta_3 S_H & \\ 0 & \alpha & -(\mu + \delta_1 + \epsilon + r_1) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \epsilon & -(\mu + \delta_2 + r_2) & 0 & 0 & 0 & 0 \\ 0 & 0 & r_1 & r_2 & -\mu_H & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(1-C)\beta_4 I_A - \mu & 0 & -(1-C)\beta_4 S_A \\ 0 & 0 & 0 & 0 & 0 & (1-C)\beta_4 I_A & -(\phi + \mu) + (1-C)\beta S_A & \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi & -\mu \end{bmatrix}$$

At DFE we have

$$J(E^0) = \begin{bmatrix} -\mu & 0 & -\beta_1 S_H^0 & \beta_2 S_H^0 & 0 & 0 & 0 & -\beta_3 S_H^0 \\ 0 & -(\alpha+\mu) & \beta_1 S_H^0 & \beta_2 S_H^0 & 0 & 0 & 0 & \beta_3 S_H^0 \\ 0 & \alpha & -(\mu+\delta_1+\epsilon+r_1) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \epsilon & -(\mu+\delta_2+r_2) & 0 & 0 & 0 & 0 \\ 0 & 0 & r_1 & r_2 & -\mu & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu & 0 & -(1-C)\beta_4 S_H^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -(\phi+\mu) & (1-C)\beta S_H^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi & -\mu \end{bmatrix}$$

$|J(E^0) - \lambda I| = 0$

$$\begin{vmatrix} -\mu-\lambda & 0 & -\beta_1 S_H^0 & \beta_2 S_H^0 & 0 & 0 & 0 & -\beta_3 S_H^0 \\ 0 & -(\alpha+\mu)-\lambda & \beta_1 S_H^0 & \beta_2 S_H^0 & 0 & 0 & 0 & \beta_3 S_H^0 \\ 0 & \alpha & -(\mu+\delta_1+\epsilon+r_1)-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \epsilon & -(\mu+\delta_2+r_2)-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & r_1 & r_2 & -\mu_H-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu-\lambda & 0 & -(1-C)\beta_4 S_H^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -(\phi+\mu)-\lambda & (1-C)\beta S_H^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi & -\mu-\lambda \end{vmatrix} = 0$$

Thus,

$\lambda_1 = -\mu$ $(three\ times)$,

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

$\lambda_3 = -(\mu+\delta_1+\epsilon+r_1)$,

$\lambda_4 = -(\mu+\delta_2+r_2)$

and

$$\begin{bmatrix} -(\phi+\mu)-\lambda & (1-C)\beta_4 S_H^0 \\ \phi & -\mu-\lambda \end{bmatrix} = 0. \quad Set\ \ b_1 = (\phi+\mu)\ \ and\ \ b_2 = (1-C)\beta_4 S_H^0,$$

so that,

$$\begin{bmatrix} -b_1-\lambda & b_2 \\ \phi & -\mu-\lambda \end{bmatrix} = 0$$

or

$(b_1 + \lambda)(\mu + \lambda) - \phi b_2 = 0$

$then \lambda^2 + (b_1 + \mu)\lambda + (\mu b_1 - \phi b_2) = 0$

sothat

$\lambda_7 = \frac{-(b_1+\mu)+\sqrt{b_1^2+\mu^2+4\phi b_2-2\mu b_1}}{2}$

$\lambda_8 = \frac{-(b_1+\mu)-\sqrt{b_1^2+\mu^2+4\phi b_2-2\mu b_1}}{2}$

At $4\phi b_2 - 2\mu b_1 < 0$,

Then, $\frac{4\phi(1-C)\beta_4\Lambda_A}{\mu} - 2\mu(\phi + \mu) < 0$

$2\mu(\phi + \mu)\left[\frac{2\phi(1-C)\beta_4\Lambda_A}{\mu^2(\phi+\mu)} - 1\right] < 0$

$2\mu(\phi + \mu)\left[2R_A - 1\right] < 0$ iff $R_A << 1$ Hence, DFE is stable (all the λs are negative)

The stability at this point of disease free implies that there is no presence of disease in the system.

4.10 STABILITY OF ENDEMIC EQUILIBRIUM

Let

$A_1 = \beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A + \mu$

$A_2 = \beta_1 I_H$

$A_3 = \beta_2 I_H$

$A_4 = \beta_3 I_H$

$A_5 = \beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A$

$A_6 = \alpha + \mu$

$A_7 = \mu + \delta_1 + r_1 + \epsilon$

$A_8 = \mu + \delta_2 + r_2$

$A_9 = (1 - c)\beta_4 I_A + \mu$

$A_{10} = (1-c)\beta_4 S_A$

$A_{11} = (1-c)\beta_4 I_A$

$A_{12} = \phi + \mu$

$|J(E^e) - \lambda I| = 0$

$$\begin{vmatrix} -A_1-\lambda & 0 & -A_2 & -A_3 & 0 & 0 & 0 & -A_4 \\ A_5 & -A_6-\lambda & A_2 & A_3 & 0 & 0 & 0 & A_4 \\ 0 & \alpha & -A_7-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \epsilon & -A_8-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & r_1 & r_2 & -\mu-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -A_9-\lambda & 0 & -A_{10} \\ 0 & 0 & 0 & 0 & 0 & -A_{11} & -A_{12}-\lambda & A_{10} \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi & -\mu-\lambda \end{vmatrix} = 0$$

The characteristic equation:

$(-\mu-\lambda)(-\lambda^7 - D_6\lambda^6 - D_5\lambda^5 - D_4\lambda^4 - D_3\lambda^3 - D_2\lambda^2 - D\lambda - D_0) = 0$

$Where$

$D_6 = -\mu - A_1 - A_6 - A_7 - A_8 - A_9 - A_{12}$

$D_5 = -\mu A_9 - \mu A_8 - \mu A_1 - \mu A_6 - \mu A_7 - \mu A_{12} - A_8A_9 - A_1A_9 - A_6A_9 - A_7A_9 - A_{12}A_9 - A_8A_{12} - A_{12}(A_1 + A_6 + A_7) - A_8(A_1 + A_6 + A_7) - A_1(A_6 + A_7) - A_6A_7 + \phi A_1 0 + \alpha A_2$

$D_4 = -\mu A_9(A_8 + A_{12}) - \mu A_9(A_1 + A_6 + A_7) - \mu(A_1 + A_6 + A_7) - \mu A_8(A_1 + A_6 + A_7) - A_{12}A_9(A_1 + A_6 + A_7) - A_8A_9(A_1 + A_6 + A_7) - A_8A_{12}(A_1 + A_6 + A_7) - \mu(A_1A_6 + A_1A_7 + A_6A_7) - A_9(A_1A_6 + A_1A_7 + A_6A_7) - A_{12}(A_1A_6 + A_1A_7 + A_6A_7) - A_8(A_1A_6 + A_1A_7 + A_6A_7) - \mu A_8A_{12} - A_8A_9A_{12} - A_1A_6A_7 + \phi A_{10}(A_1 + A_6 + A_7 + \mu) + \alpha\left[A_2(A_{12} + A_9 + A_8 + 2\mu) + \epsilon A_3\right]$

$$D_3 = -\mu A_{12}A_9(A_1+A_6+A_7+A_8)-\mu A_8A_9(A_1+A_6+A_7)-\mu A_9(A_1A_6+A_1A_7+A_6A_7)-\mu A_8A_{12}(A_1+A_6+A_7)-\mu A_{12}(A_1A_6+A_1A_7+A_6A_7)-\mu A_8(A_1A_6+A_1A_7+A_6A_7)-A_9A_{12}(A_1A_6+A_1A_7+A_6A_7)-A_8A_9(A_1A_6+A_1A_7+A_6A_7)-A_8A_{12}(A_1A_6+A_1A_7+A_6A_7)-A_1A_6A_7(A_8+A_9+A_{12})-\alpha\phi A_2A_{10}+\alpha A_1A_{10}(A_6+A_7+\mu)+\phi A_{10}(A_6A_7+\mu A_6+A_7A_8+\mu A_7+\mu A_8)+\alpha A_2A_{12}(A_9+A_8+2\mu)+\alpha A_2A_9(2\mu+A_8)+\alpha\epsilon A_3(A_{12}+A_9+2\mu)+\alpha A_2(\mu^2+2A_8\mu)$$

$$D_2 = A_{12}A_8A_9(A_1A_6+A_1A_7+A_6A_7)-A_9A_{12}A_1A_6A_7-A_9A_8A_1A_6A_7-A_8A_{12}A_1A_6A_7-\mu A_9A_8A_{12}(A_1+A_6+A_7)-\mu A_9A_{12}(A_1A_6+A_1A_7+A_6A_7)-\mu A_8A_9(A_1A_6+A_1A_7+A_6A_7)-\mu A_9A_1A_6A_7-\mu A_8A_{12}(A_1A_6+A_1A_7+A_6A_7)-\mu A_{12}A_1A_6A_7-\mu A_8A_1A_6A_7-\alpha\phi\epsilon A_3A_{10}-\alpha\phi A_2A_9A_{10}-\alpha\phi\epsilon A_2A_{10}-\alpha\phi A_2A_8A_{10}+\phi A_1A_7A_{10}(A_1+A_8+\mu)+\mu\phi A_6A_{1o}(A_1+A_7+A_8)+\phi A_7A_8A_{10}(\mu+A_6)+\alpha\mu A_2A_{12}(2A_8+2A_9+\mu)+\alpha A_9A_{12}(A_2A_8+\epsilon A_3)+\alpha\mu A_9(2A_2A_8+\mu A_2+2\epsilon A_3)+\alpha\mu A_9(2\epsilon A_3+\mu A_2A_8+\mu\epsilon A_3)$$

$$D_1 = -\mu A_9A_8A_{12}(A_1A_6+A_1A_7+A_6A_7)-\mu A_9A_1A_6A_7A_{12}-\mu A_8A_9A_1A_6A_7-\mu A_8A12A_1A_6A_7-A_8A_9A_{12}A_1A_6A_7-\alpha\phi\epsilon A_3A_9A_{10}-\alpha\phi\epsilon\mu A_3A_{10}-\alpha\phi A_2A_8A_9A_{10}-\alpha\phi\mu A_2A_9A_{10}-\alpha\phi\mu A_2A_8A_{10}+\alpha\phi A_{10}A_{11}(\mu A_2+A_2A_8+\epsilon A_3)+\phi A_7A_8A_{10}(A_1A_6+\mu A_1+\mu A_6)+\alpha\mu^2A_2(A_9A_{12}+A_8A_{12}+\epsilon A_3+A_8A_9)+\alpha\mu^2\epsilon A_3A_9+2\mu A_9A_{12}(\phi A_2A_8+\alpha\epsilon A_3)$$

$$D_0 = -\mu A_8A_9A_{12}A_1A_6A_7-\alpha\mu\phi\epsilon A_3A_9A_{10}-\alpha\mu\phi A_2A_8A_9A_{10}+\mu\alpha\phi(A_2A_8+\epsilon A_3)+\mu\phi A_8A_1A_6A_8A_{10}+\alpha\mu^2A_9A_{12}(A_8A_2+A_9A_3)$$

Theorem(4.1): Descartes' Rule of Signs

Let $P(x) = a_nx^n + a_{n-1}x^{n-1} + \cdots + a_2x^2 + a_1x + a_0$ be the polynomial with real coefficients.

1. The number of positive zeros of P is either equal to the number of variation in sign of $P(x)$ or less than this by an even number.

2. The number of negative zeros of P is either equal to the number of variations in sign of $P(-x)$ or less than this by an even number.

Considering the characteristic equation,

$(-\mu - \lambda)(-\lambda^7 - D_6\lambda^6 - D_5\lambda^5 - D_4\lambda^4 - D_3\lambda^3 - D_2\lambda^2 - D\lambda - D_0) = 0$

$Let P(\lambda) = -\lambda^7 - D_6\lambda^6 - D_5\lambda^5 - D_4\lambda^4 - D_3\lambda^3 - D_2\lambda^2 - D\lambda - D_0$

And

$P(-\lambda) = \lambda^7 - D_6\lambda^6 + D_5\lambda^5 - D_4\lambda^4 + D_3\lambda^3 - D_2\lambda^2 + D\lambda - D_0$

For $P(\lambda)$, the signs of the coefficients are

$- \ - \ - \ - \ - \ - \ -$

Since there is no change in sign, the characteristic equation has no positive eigenvalue by Descartes' Rule of Signs

For $P(-\lambda)$, the signs of the coefficients are,

$+ - + - + - +$ Clearly, there are seven (7) changes in signs.

By Descartes' Rule of Signs we have 7, 5, 3, or 1 negative eigenvalues.

Since our characteristics equation has no positive eigenvalue and none of them is zero, then our eigenvalues are all negative.

Thus, the model is stable at Endemic Equilibrium.

The system being stable at Endemic Equilibrium point indicates that the disease will persist in the system despite the use of hospitalization as a control measure.

4.11 SOLUTION OF THE MODEL

4.12 APPLICATION OF HOMOTOPY PERTURBATION

Let P be an embedding parameter in [0,1] so that the model equations can be written as:

$$
\begin{aligned}
(1-P)\frac{dS_H}{dt} + P\left[\frac{dS_H}{dt} - \Lambda_H + (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H + \mu S_H\right] &= 0 \\
(1-P)\frac{dE_H}{dt} + P\left[\frac{dE_H}{dt} - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H + (\alpha+\mu)E\right] &= 0 \\
(1-P)\frac{dI_H}{dt} + P\left[\frac{dI_H}{dt} - \alpha E_H + (\mu + \delta_1 + \epsilon + r_1)I_H\right] &= 0 \\
(1-P)\frac{dI_{H_h}}{dt} + P\left[\frac{dI_{H_h}}{dt} - \epsilon E_H + (\mu + \delta_2 + r_2)I_{H_h}\right] &= 0 \\
(1-P)\frac{dR_H}{dt} + P\left[\frac{dR_H}{dt} - r_1 I_H - r_2 I_{H_h} - \mu R_H\right] &= 0 \\
(1-P)\frac{dS_A}{dt} + P\left[\frac{dS_A}{dt} - \Lambda_A + (1-C)\beta_4 I_A S_A + \mu S_H\right] &= 0 \\
(1-P)\frac{dE_A}{dt} + P\left[\frac{dE_A}{dt} - (1-C)\beta_4 I_A S_A + (\phi+\mu)E_A\right] &= 0 \\
(1-P)\frac{dI_A}{dt} + P\left[\frac{dI_A}{dt} - \phi E_A + \mu I_A\right] &= 0
\end{aligned}
$$

This implies that:

$$
\begin{aligned}
\frac{dS_H}{dt} &= P\left[\frac{dS_H}{dt} - \frac{dS_H}{dt} + \Lambda_H - (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - \mu S_H\right] \\
\frac{dE_H}{dt} &= P\left[\frac{dE_H}{dt} - \frac{dE_H}{dt} + (\beta_1 I_H + \beta_2 I_{H_h} + \beta_3 I_A)S_H - (\alpha + \mu)E\right] \\
\frac{dI_H}{dt} &= P\left[\frac{dI_H}{dt} - \frac{dI_H}{dt} + \alpha E_H - (\mu + \delta_1 + \epsilon + r_1)I_H\right] \\
\frac{dI_{H_h}}{dt} &= P\left[\frac{dI_{H_h}}{dt} - \frac{dI_{H_h}}{dt} + \epsilon I_H - (\mu + \delta_2 + r_2)I_{H_h}\right] \\
\frac{dR_H}{dt} &= P\left[\frac{dR_H}{dt} - \frac{dR_H}{dt} + r_1 I_H - r_2 I_{H_h} + \mu R_H\right] \\
\frac{dS_A}{dt} &= P\left[\frac{dS_A}{dt} - \frac{dS_A}{dt} + \Lambda_A - (1 - C)\beta_4 I_A S_A - \mu S_A\right] \\
\frac{dE_A}{dt} &= P\left[\frac{dE_A}{dt} - \frac{dE_A}{dt} + (1 - C)\beta_4 I_A S_A - (\phi + \mu)E_A\right] \\
\frac{dI_A}{dt} &= P\left[\frac{dI_A}{dt} - \frac{dI_A}{dt} + \phi E_A - \mu I_A\right]
\end{aligned}
\tag{4.22}
$$

The basic assumption is that the solution of the equation 4.2 can be written as a series in powers of P:

$$
\begin{aligned}
S_H &= S_{H_0} + PS_{H_1} + P^2 S_{H_2} + \cdots \\
E_H &= E_{H_0} + PE_{H_1} + P^2 E_{H_2} + \cdots \\
I_H &= I_{H_0} + PI_{H_1} + P^2 I_{H_2} + \cdots \\
I_{H_h} &= I_{H_{h_o}} + PI_{H_{h_1}} + P^2 I_{H_{h_2}} + \cdots \\
R_H &= R_{H_0} + PR_{H_1} + P^2 R_{H_2} + \cdots \\
S_A &= SA_0 + PS_{A_1} + P^2 S_{A_2} + \cdots \\
E_A &= E_{A_0} + PE_{A_1} + P^2 E_{A_2} + \cdots \\
I_A &= I_{A_0} + PI_{A_1} + P^2 I_{A_2} + \cdots
\end{aligned}
\tag{4.23}
$$

The initial conditions are as follow:

$S_{H_0} = K_1, E_{H_0} = K_2, I_{H_0} = K_3, I_{H_{h_0}} = K_4, R_{H_0} = K_5, S_{A_0} = K_6, E_{A_0} = K_7, I_{A_0} = K_8$

Substituting appropriately in system (4.13) we have:

Comparing the co-efficient of P we have:

P^0 :

$\frac{dS_{H_0}}{dt} = 0, \quad \frac{dE_{H_0}}{dt} = 0, \quad \frac{dI_{H_0}}{dt} = 0, \quad \frac{dI_{H_{h_0}}}{dt} = 0,$

$\frac{dR_{H_0}}{dt} = 0, \quad \frac{dS_{A_0}}{dt} = 0, \quad \frac{dE_{A_0}}{dt} = 0, \quad \frac{dI_{A_0}}{dt} = 0$

P^1 :

$$\begin{aligned}
\frac{dS_{H_1}}{dt} &= \Lambda_H - \beta_1 I_{H_0} S_{H_0} - \beta_2 I_{H_{h_0}} S_{H_0} - \beta_3 I A_0 S_{H_0} - \mu S_{H_0} \\
\frac{dE_{H_1}}{dt} &= \beta_1 I_{H_0} S_{H_0} + \beta_2 I_{H_{h_0}} S_{H_0} + \beta_3 I_{A_0} S_{H_0} - (\alpha + \mu) E_{H_0} \\
\frac{dI_{H_1}}{dt} &= \alpha E_{H_0} - (\mu + \delta_1 + \epsilon + r_1) I_{H_0} \\
\frac{dI_{H_{h_1}}}{dt} &= \epsilon I_{H_0} - (\mu + \delta_2 + r_2) I_{H_{h_0}} \\
\frac{dR_{H_1}}{dt} &= r_1 I_{H_0} + r_2 I_{H_{h_0}} + \mu R_{H_0} \\
\frac{dS_{A_1}}{dt} &= \Lambda_A - (1 - C) \beta_4 I_{A_0} S_{A_0} - \mu S_{A_0} \\
\frac{dE_{A_1}}{dt} &= (1 - C) \beta_4 I_{A_0} S_{A_0} - (\phi + \mu) E_{A_0} \\
\frac{dI_{A_1}}{dt} &= \phi_E A_0 - \mu I_{A_0}
\end{aligned}$$

P^2 :

$$
\begin{aligned}
\frac{dS_{H_2}}{dt} &= -\beta_1 I_{H_1} S_{H_0} - \beta_2 I_{H_0} S_{H_1} - \beta_2 I_{H_{h_1}} S_{H_0} - \beta_2 I_{H_{h_0}} S_{H_1} - \beta_3 I A_0 S_{H_1} - \beta_3 I A_1 S_{H_0} - \mu S_{H_1} \\
\frac{dE_{H_2}}{dt} &= \beta_1 I_{H_1} S_{H_0} + \beta_2 I_{H_0} S_{H_1} + \beta_2 I_{H_{h_1}} S_{H_0} + \beta_2 I_{H_{h_0}} S_{H_1} + \beta_3 I A_0 S_{H_1} + \beta_3 I A_1 S_{H_0} - (\alpha + \mu) E_{H_1} \\
\frac{dI_{H_2}}{dt} &= \alpha E_{H_1} - (\mu + \delta_1 + \epsilon + r_1) I_{H_1} \\
\frac{dI_{H_{h_2}}}{dt} &= \epsilon I_{H_1} - (\mu + \delta_2 + r_2) I_{H_{h_1}} \\
\frac{dR_{H_2}}{dt} &= r_1 I_{H_1} + r_2 I_{H_{h_1}} + \mu R_{H_1} \\
\frac{dS_{A_2}}{dt} &= -(1-c)\beta_4 I_{A_1} S_{A_0} - (1-c)\beta_4 I_{A_0} S_{A_1} - \mu S_{A_1} \\
\frac{dE_{A_2}}{dt} &= (1-c)\beta_4 I_{A_1} S_{A_0} + (1-c)\beta_4 I_{A_0} S_{A_1} - (\phi + \mu) E_{A_1} \\
\frac{dI_{A_2}}{dt} &= \phi E_{A_1} - \mu I_{A_1}
\end{aligned}
$$

P^3 :

$$\begin{aligned}
\frac{dS_{H_3}}{dt} &= -\beta_1 I_{H_1} S_{H_1} - \beta_1 I_{H_0} S_{H_2} - \beta_1 I_{H_2} S_{H_0} - \beta_2 I_{H_{h_0}} S_{H_2} - \beta_2 I_{H_{h_1}} S_{H_1} - \beta_2 I_{H_{h_2}} S_{H_0} - \beta_3 I A_0 S_{H_2} \\
&\quad -\beta_3 I A_1 S_{H_1} - \beta_3 I A_2 S_{H_0} - \mu S_{H_2} \\
\frac{dE_{H_3}}{dt} &= \beta_1 I_{H_1} S_{H_1} + \beta_1 I_{H_0} S_{H_2} + \beta_1 I_{H_2} S_{H_0} + \beta_2 I_{H_{h_0}} S_{H_2} + \beta_2 I_{H_{h_1}} S_{H_1} + \beta_2 I_{H_{h_2}} S_{H_0} + \beta_3 I A_0 S_{H_2} \\
&\quad +\beta_3 I A_1 S_{H_1} + \beta_3 I A_2 S_{H_0} - (\alpha + \mu) E_{H_2} \\
\frac{dI_{H_2}}{dt} &= \alpha E_{H_2} - (\mu + \delta_1 + \epsilon + r_1) I_{H_2} \\
\frac{dI_{H_{h_3}}}{dt} &= \epsilon I_{H_2} - (\mu + \delta_2 + r_2) I_{H_{h_2}} \\
\frac{dR_{H_3}}{dt} &= r_1 I_{H_2} + r_2 I_{H_{h_2}} + \mu R_{H_2} \\
\frac{dS_{A_2}}{dt} &= -(1-c)\beta_4 I_{A_0} S_{A_2} - (1-c)\beta_4 I_{A_1} S_{A_1} - (1-c)\beta_4 I_{A_2} S_{A_0} - \mu S_{A_2} \\
\frac{dE_{A_2}}{dt} &= (1-c)\beta_4 I_{A_0} S_{A_2} + (1-c)\beta_4 I_{A_1} S_{A_1} - (1-c)\beta_4 I_{A_2} S_{A_0} - (\phi + \mu) E_{A_2} \\
\frac{dI_{A_2}}{dt} &= \phi E_{A_2} - \mu I_{A_2}
\end{aligned}$$

The homotopy perturbation solutions for the system (4.1) are derived from the following:

From P^0, integrating each of the equation we have that:

$S_{H_0} = K_1, \quad E_{H_0} = K_1, \quad I_{H_0} = K_3, \quad I_{H_{h_0}} = K_4,$

$R_{H_0} = K_5, \quad S_{A_0} = K_6, \quad E_{A_0} = K_7, \quad I_{A_0} = K_8$

From P^1, integrating we have:

$S_{H_1} = \Lambda_H t - \beta_1 K_1 K_3 t - \beta_2 K_1 K_4 - \beta_3 K_1 K_8 t - \mu K_1 t$

$S_{H_1} = Q_1 t \qquad\qquad where \;\; Q_1 = (\Lambda_H - \beta_1 K_1 K_3 - \beta_2 K_1 K_4 - \beta_3 K_1 K_8 - \mu K_1)$

$E_{H_1} = \beta_1 K_1 K_3 t + \beta_2 K_1 K_4 t + \beta_3 K_1 K_8 t - (\alpha + \mu) K_2 t$

$E_{H_1} = Q_2 t \qquad\qquad where \;\; Q_2 = (\beta_1 K_1 K_3 + \beta_2 K_1 K_4 + \beta_3 K_1 K_8 - (\alpha + \mu) K_2)$

$$I_{H_1} = \alpha K_2 t - (\mu + \delta_1 + \epsilon + r_1) K_3 t$$

$$I_{H_1} = Q_3 t \qquad where \;\; Q_3 = (\alpha K_2 - (\mu + \delta_1 + \epsilon + r_1) K_3)$$

$$I_{H_{h_1}} = \epsilon K_2 t - (\mu + \delta_2 + r_2) K_4 t$$

$$I_{H_{h_1}} = Q_4 t \qquad where \;\; Q_4 = (\epsilon K_2 - (\mu + \delta_2 + r_2) K_4)$$

$$R_{H_1} = r_1 K_3 t + r_2 K_4 t + \mu K_5 t$$

$$R_{H_1} = Q_5 t \qquad where \;\; Q_5 = (r_1 K_3 + r_2 K_4 + \mu K_5)$$

$$S_{A_1} = \Lambda_A t - (1 - C) \beta_4 K_6 K_8 t - \mu K_6 t$$

$$S_{A_1} = Q_6 t \qquad where \;\; Q_6 = (\Lambda_A - (1 - C) \beta_4 K_6 K_8 - \mu K_6)$$

$$E_{A_1} = (1 - C) \beta_4 K_6 K_8 t - (\phi + \mu) K_7 t$$

$$E_{A_1} = Q_7 t \qquad where \;\; Q_7 = ((1 - C) \beta_4 K_6 K_8 - (\phi + \mu) K_7)$$

$$I_{A_1} = \phi K_7 t - \mu K_8 t$$

$$I_{A_1} = Q_8 t \qquad where \;\; Q_8 = (\phi K_7 - \mu K_8)$$

From P^2 : integrating we have;

$$S_{H_2} = (-K_1 \beta_1 Q_3 - K_3 \beta_1 Q_1 - K_1 \beta_2 Q_4 - K_4 \beta_2 Q_1 - K_8 \beta_3 Q_1 - K_1 \beta_3 Q_7 - \mu Q_1) t^2$$

$$E_{H_2} = \left[(K_1 \beta_1 Q_3 + K_3 \beta_1 Q_1 + K_1 \beta_2 Q_4 + K_4 \beta_2 Q_1 + K_8 \beta_3 Q_1 + K_1 \beta_3 Q_7 - (\alpha + \mu) K_2 \right] t^2$$

$$I_{H_2} = \left[\alpha Q_2 - (\mu + \delta_1 + \epsilon + r_1) Q_3 \right] t^2$$

$$I_{H_{h_2}} = \left[\epsilon Q_3 - (\mu + \delta_2 + r_2) Q_4 \right] t^2$$

$$R_{H_2} = (r_1 Q_3 + r_2 Q_4 + \mu Q_5) t^2$$

$$S_{A_2} = [-(1-C)K_6\beta_4 Q_7 - (1-C)K_8\beta_4 Q_5 - \mu Q_5]\, t^2$$

$$E_{A_2} = [(1-C)K_6\beta_4 Q_7 + (1-C)K_8\beta_4 Q_5 - (\phi+\mu)Q_6]\, t^2$$

$$I_{A_2} = (\phi Q_6 - \mu Q_7)t^2$$

Substituting into our basic assumption solution (4.14) we have:

Let the $o(P^3)$ be very small such that by asymptotic series approximation:

$$S_H = K_1 + PQ_1 t + P^2(-K_1\beta_1 Q_3 - K_3\beta_1 Q_1 - K_1\beta_2 Q_4 - K_4\beta_2 Q_1 - K_8\beta_3 Q_1 - K_1\beta_3 Q_7 - \mu Q_1)t^2 + o(P^3$$

$$E_H = K_2 + PQ_2 t + P^2\,[(K_1\beta_1 Q_3 + K_3\beta_1 Q_1 + K_1\beta_2 Q_4 + K_4\beta_2 Q_1 + K_8\beta_3 Q_1 + K_1\beta_3 Q_7 - (\alpha+\mu)K_2]\, t^2 + o(P^3$$

$$I_H = K_3 + PQ_3 t + P^2\,[\epsilon Q_3 - (\mu + \delta_2 + r_2)Q_4]\, t^2 + o(P^3$$

$$I_{H_h} = K_4 + PQ_4 t + P^2\,[\epsilon Q_3 - (\mu + \delta_2 + r_2)Q_4]\, t^2 + o(P^3$$

$$R_H = K_5 + PQ_5 t + P^2(r_1 Q_3 + r_2 Q_4 + \mu Q_5)t^2 + o(P^3$$

$$S_A = K_6 + PQ_6 t + P^2\,[-(1-C)K_6\beta_4 Q_7 - (1-C)K_8\beta_4 Q_5 - \mu Q_5]\, t^2 + o(P^3$$

$$E_A = K_7 + PQ_7 t + P^2\,[(1-C)K_6\beta_4 Q_7 + (1-C)K_8\beta_4 Q_5 - (\phi+\mu)Q_6]\, t^2 + o(P^3$$

$$I_A = K_8 + PQ_8 t + P^2(\phi Q_6 - \mu Q_7)t^2 + o(P^3$$

We then have that,

$$S_H - K_1 - PQ_1t - P^2(-K_1\beta_1Q_3 - K_3\beta_1Q_1 - K_1\beta_2Q_4 - K_4\beta_2Q_1 - K_8\beta_3Q_1 - K_1\beta_3Q_7 - \mu Q_1)t^2 < o(P^3$$

$$E_H - K_2 - PQ_2t - P^2\left[(K_1\beta_1Q_3 + K_3\beta_1Q_1 + K_1\beta_2Q_4 + K_4\beta_2Q_1 + K_8\beta_3Q_1 + K_1\beta_3Q_7 - (\alpha+\mu)K_2\right]t^2 < o(P^3$$

$$I_H - K_3 - PQ_3t - P^2\left[\epsilon Q_3 - (\mu+\delta_2+r_2)Q_4\right]t^2 < o(P^3$$

$$I_{H_h} - K_4 - PQ_4t - P^2\left[\epsilon Q_3 - (\mu+\delta_2+r_2)Q_4\right]t^2 < o(P^3$$

$$R_H - K_5 - PQ_5t - P^2(r_1Q_3 + r_2Q_4 + \mu Q_5)t^2 < o(P^3$$

$$S_A - K_6 - PQ_6t - P^2\left[-(1-C)K_6\beta_4Q_7 - (1-C)K_8\beta_4Q_5 - \mu Q_5\right]t^2 < o(P^3$$

$$E_A - K_7 - PQ_7t - P^2\left[(1-C)K_6\beta_4Q_7 + (1-C)K_8\beta_4Q_5 - (\phi+\mu)Q_6\right]t^2 < o(P^3$$

$$I_A - K_8 - PQ_8t - P^2(\phi Q_6 - \mu Q_7)t^2 < o(P^3$$

Thus

$$S_H \approx K_1 + PQ_1t + P^2(-K_1\beta_1Q_3 - K_3\beta_1Q_1 - K_1\beta_2Q_4 - K_4\beta_2Q_1 - K_8\beta_3Q_1 - K_1\beta_3Q_7 - \mu Q_1)t^2$$

$$E_H \approx K_2 + PQ_2t + P^2\left[(K_1\beta_1Q_3 + K_3\beta_1Q_1 + K_1\beta_2Q_4 + K_4\beta_2Q_1 + K_8\beta_3Q_1 + K_1\beta_3Q_7 - (\alpha+\mu)K_2\right]t^2$$

$$I_H \approx K_3 + PQ_3t + P^2\left[\epsilon Q_3 - (\mu+\delta_2+r_2)Q_4\right]t^2$$

$$I_{H_h} \approx K_4 + PQ_4t + P^2\left[\epsilon Q_3 - (\mu+\delta_2+r_2)Q_4\right]t^2$$

$$R_H \approx K_5 + PQ_5t + P^2(r_1Q_3 + r_2Q_4 + \mu Q_5)t^2$$

$$S_A \approx K_6 + PQ_6t + P^2\left[-(1-C)K_6\beta_4Q_7 - (1-C)K_8\beta_4Q_5 - \mu Q_5\right]t^2$$

$$E_A \approx K_7 + PQ_7t + P^2\left[(1-C)K_6\beta_4Q_7 + (1-C)K_8\beta_4Q_5 - (\phi+\mu)Q_6\right]t^2$$

$$I_A \approx K_8 + PQ_8t + P^2(\phi Q_6 - \mu Q_7)t^2$$

4.13 NUMERICAL SIMULATION

Having seen that the use of hospitalization as a control measure is not a sufficient approach in controlling the spread of MERS-CoV, the numerical simulation here aim at testing the efficacy or effectiveness of Modified Virus Ankara vaccine which is the new approach adopted in this research work.

Parameters	**Values**	**Source**
Λ_H	0.002	[5]
Λ_A	0.0011	[9]
β_1	0.33	[1]
β_2	0.23	[1]
β_3	0.45	[1]
β_4	0.0031	[1]
μ	0.0000456	[8]
α	0.122	Estimated
δ_1	0.003	[9]
δ_2	0.004	[9]
ϵ	0.13	Estimated
ϕ	0.0113	[9]
r_1	0.54	[9]
r_2	0.31	[9]
C	0.152	[9]

Figure 4.2:

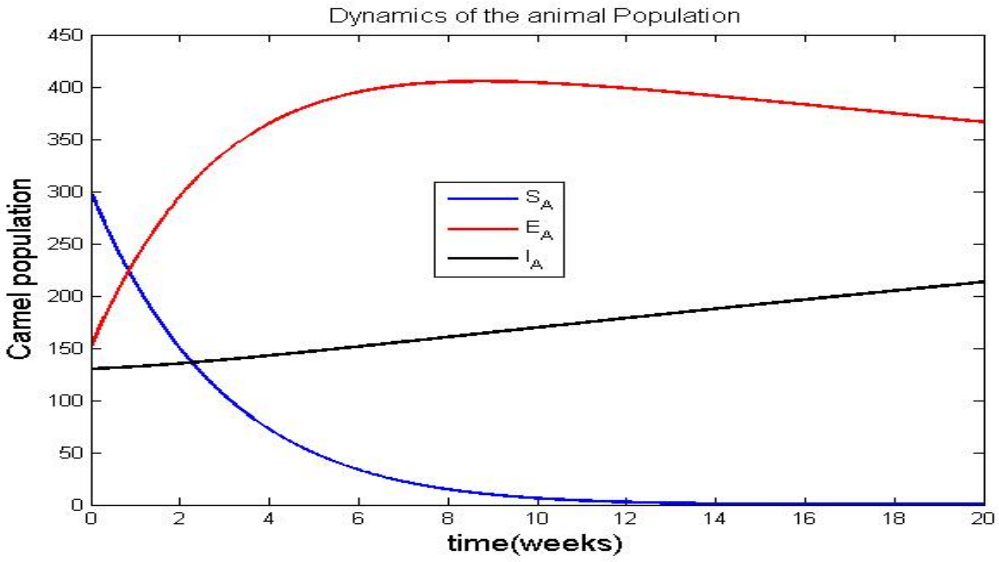

Figure 4.2 is a solution plot illustrating the changes in the dynamics of the animal population with time. It shows the susceptible animals, exposed animals and recovered animals.

Figure 4.3:

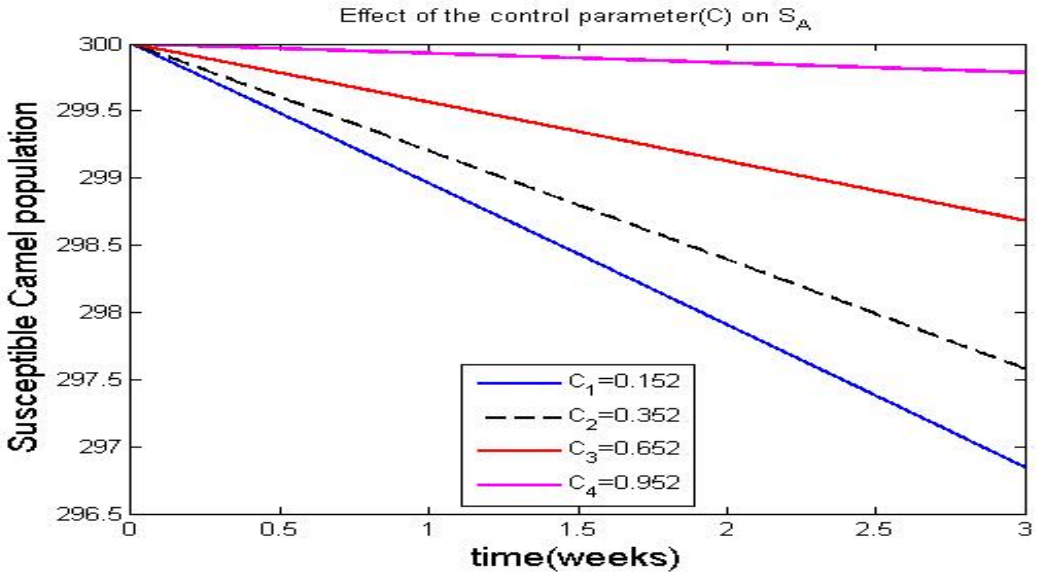

Figure 4.3 shows the dynamics of the susceptible animal population, but with increase in the control strategies in form of MVA vaccine.

Figure 4.4:

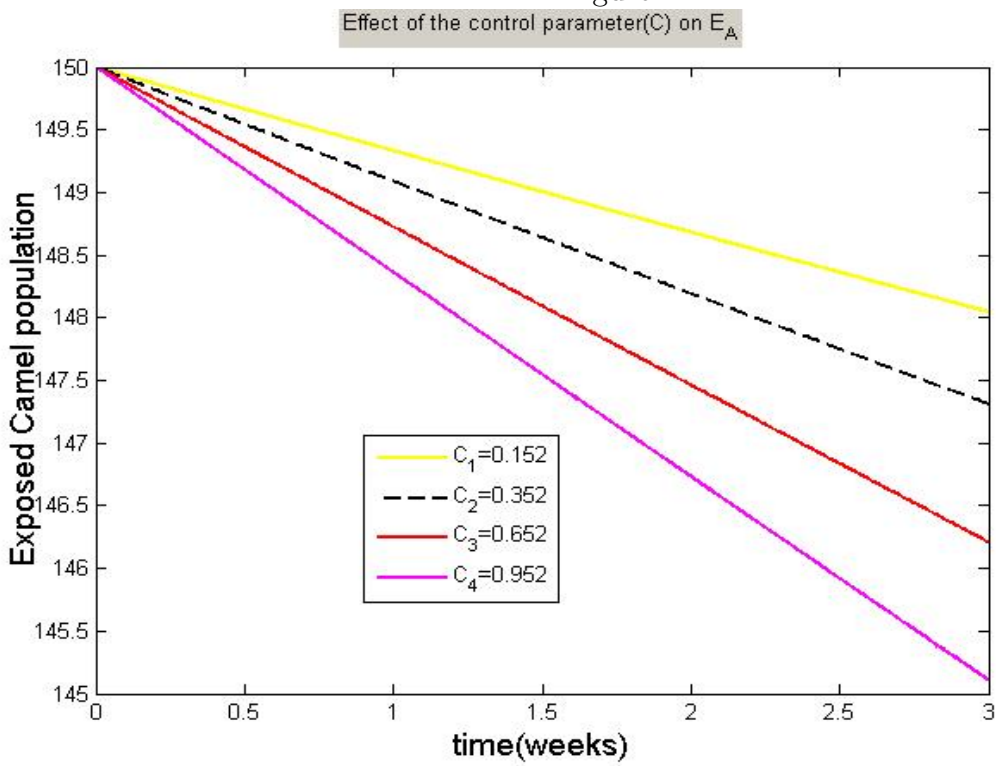

Figure 4.4 shows the dynamics of the exposed animal population, but with increase in the control strategies in form of MVA vaccine.

Chapter 5

DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 DISCUSSION

We have derived and analyzed a mathematical model for the transmission and control of MERS-CoV. A flow diagram of the transmission, control strategies and treatment was shown. The solution to the model equations was obtained and ways for controlling or preventing the disease were elaborated. The effective basic reproduction number, R_0 of the system was obtained and it was shown that the disease will spread only if $R_0 > 1$ and would die off with time ,if $R_0 < 1$. Numerical simulations carried out using MATLAB on the model showed that with judicious use of Modified Virus Ankara(MVA)in combination with MERS-CoV inoculation, the disease will phase out rapidly in the population.

Figure 4.2: Shows the dynamics of the animal population. We observed thet the infection rate of MERS-CoV increases in the absence of the control measure(Modified Virus Ankara). Hence the disease will persist in the population as time increases.

Figure 4.3: Shows the effect of the control measure on the susceptible animal population. The graph shows that the increase in the use of the animal vaccine leads to an increase in the susceptible population.

The implication means that the vaccine reduces the movement of animal population into the exposed class.

Figure 4.4: Shows the effect of the control parameter on the exposed class. we observed from the grap that the increase in the control measure leads to a reduction in the exposed animal population. Implying that the application of the animal vaccine reduces the rate of exposure to MERS-CoV.

5.2 CONCLUSION

We derived and analyzed a mathematical model to better understand the transmission dynamics of MERS-CoV in the population.The model considered a varying total human and animal population that incorporated and exit of new individuals into the susceptible class through birth and death respectively.In chapter four, the analysis of MERS-CoV showed that the disease-free and endemic equilibrium are stable. The numercal analysis of the model suggested that the most effective strategy for controlling or eradicating MERS-Cov is the use of (MVA)in combination with MERS-CoV inoculation.

5.3 RECOMMENDATION

The stability of the disease endemic equilibrium shows that the disease will persist in the system over time. Thus,hospitalization of infected individual is not a sufficient means of controlling the disease. This research has included, along hospitalization, the use of Modified Virus Ankara vaccine (MVA). This vaccine targets the primary source of transmission which is the animals. Our numerical simulation has shown the effectiveness of this vaccine in eradicating the spread of this disease. Therefore, as important as hospitalization of infected individual is, we must realize that that alone cannot stop the spread of the disease. Hence the need to adopt this new but sophisticated measure which is application of Modified Virus Ankara in combination with MERS-CoV inoculation.

References

[1] Ayman M., Wael A., Maged, G.H.(2019).Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Infection, Immunological Response, and Vaccine Development. *Journal of Immunology Research*, 2019(ID: 6491738), 1-11. https://doi.org/10.1155/2019/6491738

[2] Sami A. and Yaseen M.A.(2015). Infection with Middle East respiratory syndrome Coronavirus. *Journal of Respiratory Therapy*, 51(4),98-102

[3] Qianying L., Alice P.Y., and Daihai H. (2018).Modelling the spread of Middle East respiratorysyndrome coronavirus (MERS-CoV) in Saudi Arabia. *Journal Ststistical methods in Medical Research*,27, 1968-1978

[4] Mahmoud E.,Nedaa A., Bushra R.,Lama A. and Ejaz C.(2018). Evaluation of preparedness of healthcare student volunteers against Middle East respiratory syndrome coronavirus (MERS-CoV) in Makkah, Saudi Arabia: a cross-sectional study. 26(6), 607–612.

[5] Ahmad S.Y. and Souha S.K.(2014).Emergence of MERS-CoV in the Middle East: Origins, Transmission, Treatment, and Perspectives. *PLoS Pathogens journal*, 10(12)

[6] Danielle R.A, Michael L, Izabela K.R. and Vincent J.M.(2019).Bactrian camels shed large quantities of Middle East respiratory syndrome coronavirus (MERS-CoV) after experimental infection.*Emerg Microbes Infect*, 8(1), 717-723.

[7] Al-Abdely H.M., Midgley C.M.,and Alkhamis A.M.(2019). Middle East respiratory syndrome coronavirus infection dynamics and antibody responses among clinically diverse patients, Saudi Arabia.*Emerg Infect Dis* 25(4):753-66

[8] Elkholy A.A., Grant R., and Assiri A. (2019). MERS-CoV infection among healthcare workers and risk factors for death: retrospective analysis of all laboratory-confirmed cases reported to WHO from 2012 to 2 June 2018, *Journal of Infection and Public Health* Doi:10.10106/j.jiph.2019.04.011.

[9] Khudhair A, Killerby M.E., and Mulla A.M. (2019). Risk factors for MERS-CoV seropositivity among animal market and slaughterhouse workers, Abu Dhabi, United Arab Emirates, 2014-2017. *Infect Dis 2019*

[10] Te N., Vergara-Alert J.and Lehmbecker A. (2018). Co-localization of Middle East respiratory syndrome coronavirus (MERS-CoV) and dipeptidyl peptidase-4 in the respiratory tract and lymphoid tissues of pigs and llamas. Transbound Emerg Dis 201866(2):831-841

[11] Okba N., Raj V.S, and Widjaja I.(2019)Sensitive and specific detection of low-level antibody responses to mild Middle East respiratory syndrome coronavirus infections.*Emerg Infect Dis 2019* 25(10):1868-1879

[12] Modjarrad K., Roberts C.C, Mills K.T.(2019) Safety and immunogenicity of an anti-Middle East respiratory syndrome coronavirus DNA vaccine: a phase 1, open-label, single-arm, dose-escalation trial.*Lancet Infect Dis* 19(9): 1013-1022

[13] Farag E.A., Nour M., and El Idrissi A. (2019)Survey on implementation of One Health approach for MERS-CoV preparedness and control in Gulf Cooperation Council and Middle East countries. *Emerg Infect Dis* 25(3).

[14] Arabi Y., Shalhoub S.,and Mandourah Y.(2019) Ribavirin and interferon therapy for critically ill patients with the Middle East respiratory syndrome: a multicenter observational study. Infectious Disease Society of America. https://doi.org/10.1093/cid/ciz544

[15] Al-Tawfiq J.A. and Gautret P.(2018) Asymptomatic Middle East respiratory syndrome coronavirus (MERS-CoV) infection: extent and implications for infection control: a systematic review. *Travel Med Infect Dis*

[16] Ayman M.,Wael A and Maged G.H.(2019) Middle East Respiratory Syndrome Coronavirus (MERS-CoV):Infection, Immunological Response, and Vaccine Development.*Journal of Immunology Research* 1(1-11)

[17] A.M. Zaki, S.Van Boheemen, T.M. Bestebroer, A.D.M.E. Osterbause,and R.A.M Fouchier (2012),"Isolation of novel coronavirus from a man with pneumonia in Saudi Arabia," The New England Journal of Medicine, Vol.367,no.19,pp.1814-1820.

[18] Herbert W. Hethcote (2000), "The Mathematics of Infectious Disease," SIAM Review, https:——doi.org—10.1137—soo36144500371907.