SOCIETAL AND PUBLIC HEALTH MEASURES AGAINST THE EFFECTS OF SARS-COV-2 ON THE TRANSMISSION DYNAMICS OF MALARIA: A MATHEMATICAL MODELLING APPROACH

by

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DECLARATION

This project in its entirety or in part, has not been submitted to this or any other institution in support of an application for the award of a degree. It represents the author's own work and where the work of others has been used, proper reference has been made.

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CERTIFICATION

This is to certify that the content of this project entitled '**Societal and public health measures against the effects of SARS-COV-2 on the transmission dynamics of malaria: A mathematical modelling approach**' was prepared and submitted by **ADEDIRAN, Israel Adewale** in partial fulfillment of the requirements for the degree of **BACHELOR OF SCIENCE IN MATHEMATICS**. The original research work was carried out by him under by supervision and is hereby accepted.

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DEDICATION

This project is dedicated to the glory of Almighty God, THE FATHER, THE SON and THE HOLY SPIRIT, who has made this program a success.

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ABSTRACT

Malaria remains a major global health burden, causing hundreds of thousands deaths annually, especially in sub-Saharan Africa. However, in December 2019, a novel pneumonia-like condition termed coronavirus disease 2019 (COVID-19) with several clinical, epidemiological, and biological parallels to malaria, was reported in Wuhan, China. COVID-19 pandemic led to inaccessibility to healthcare services due to societal measures which subsequently could increase malaria morbidities, comorbidities with COVID-19 and mortalities. This study therefore aimed at investigating the effects of city lockdowns and chemotherapeutic impacts on the dynamical system of human and mosquito populations. The percentage increase in malaria mortalities as a result of inaccessibility to healthcare services was also quantified. Firstly, the basic reproduction number was computed. The stability of the system is analyzed for the existence of the disease-free and endemic equilibria points. We established that the disease-free equilibrium point is locally asymptotically stable when the reproduction number, $R_0 < 1$ and the disease always dies out. For $R_0 > 1$ the disease-free equilibrium becomes unstable and the disease continues to persist in the population. Furthermore, the parameters most responsible for the disease transmission in the populations with respect to R_0 by sensitivity analysis showed that deaths due to malaria increased by 10% in endemic malaria countries during lockdown (i.e year 2020 alone). This suggests that more concerted efforts are required to concurrently monitor the two diseases. Notably, malaria and COVID-19 screening and testing of suspected or confirmed COVID-19 patients could be done simultaneously to avoid misdiagnosis and enable easy management. Maintaining the most critical prevention activities, long-term suppression intervention and accessibility to healthcare services for malaria during lockdowns could substantially reduce the overall impact of the COVID-19 pandemic on malaria.

Keyword: mathematical model, Lockdown, Malaria, COVID-19, Stability

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Chapter 1

INTRODUCTION

Human beings are at constant risk of infectious diseases. No human can be exempted from the menace of epidemic disease (Ademola and Odeniran 2016) . The continuous reports from emerging and re-emerging infectious diseases remain a global concern. Transmission mechanisms of epidemic disease can only be properly understood by developing potent prophylactic tools for existing and emerging organisms (CDC 2019). Micro-organisms are usually the main causes of infectious diseases, depending on their virulence and pathogenic state. The major causal organisms causing infectious diseases are those of parasites, viruses and bacteria. The infectious attribute of pathogens connotes ”transmission of organism from an infected individual to a non-infected individual”. At this juncture, our discussion is limited to malaria, Lassa fever and malaria-Lassa fever co-infection diseases which are the main focus of this study.

Malaria, a common parasitic disease in some parts of sub-Saharan Africa, Asia and Latin America, is caused by the genus *Plasmodium*. There are several known species, however, humans are often affected through the bite of the female Anopheles mosquito vector. Global estimates of malaria show 80 percent cases from Africa, and malaria is responsible for more than a million annual death in affected developing countries(WHO, 2012; CDC, 2019). Among children under five years of age, malaria seems to be the leading cause of mortality, with similar incidence among pregnant women (WHO, 2012). In pregnant women, severe malaria cases have been reported to cause maternal death, still birth, severe anaemia, congenital malformations and low birth weights (WHO, 2012; Olaniyi et al 2018). The problem of chemotherapeutic drug resistance against the *Plasmodium* organism and insecticidal resistance on the mosquito

vector has been widely reported and also linked to the growing incidence rate of malaria disease in endemic communities (CDC, 2019). Therefore, the transmission dynamics can only be better understood by developing cogent parameters in the disease transmission coupled with strategically analysing the control measures to stem its spread.

The emergence of coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV 2) has caused an unprecedented global societal and public health crisis (Rothan et al. 2020). The World Health Organization (WHO) declared the outbreak a public health emergency of international concern on 30 January 2020 and a pandemic on 11 March 2020. This was due to the aftermath of basic reproduction number of the novel coronavirus significantly larger than 1 (ranges from 2.24 to 3.58) (Zhao et al. 2020). While malaria and COVID-19 can have similar presentation, common symptoms they share include but not limited to: fever, breathing difficulties, tiredness and acute onset headache, which may lead to misdiagnosis of malaria for COVID-19 and vice versa, particularly when clinician relies mainly on symptoms. Malaria testing and treatment are also disturbed due to the risks faced by health workers who provide health care services during the pandemic. Decision-makers will need to make difficult choices to ensure that COVID-19 and other urgent, ongoing public health problems- including malaria endemics—are addressed while minimizing

The current data showed a lower incidence of SARS-COV 2 in developing countries, although the number of positive cases kept increasing on daily basis in these areas. Incidentally, malaria disease is quite endemic in most of these developing countries especially Africa, of which the overburdened health systems and societal measures aimed at curbing the SARS-COV 2 pandemic could have necessitated a negative impact on the control of malaria and subsequently leading to more deaths. As of 19th August 2020, Africa COVID-19 statistics showed that there have been 874,036 cases; 18,498 deaths and 524,557 recoveries, while global reports showed 22 million cases, 777,000 deaths and 14 million recoveries. Meanwhile, WHO malaria cases showed that there are 228 million cases and 405,000 deaths globally in 2018, of which 94$\%$ are from Africa (WHO 2019).

The person-to-person transmission of COVID-19 infection led to the isolation of patients that were administered a variety of treatments at the onset of outbreak. At present, there are no specific antiviral drugs or vaccine against COVID-19 infection for potential therapy of humans. The commonly adopted option was strategically using broad-spectrum antiviral drugs like Nucleoside analogues and also HIV-protease inhibitors that could attenuate virus infection until the specific antiviral becomes available (Lu et al. 2020). The treatment that have so far been attempted showed that 75 patients were administrated existing antiviral drugs. Some of the treatment options include, twice a day oral administration of 75 mg oseltamivir, 500 mg lopinavir, 500 mg ritonavir and the intravenous administration of 0·25 g ganciclovir for 3–14 days (Chen et al.2020). Broad-spectrum antiviral remdesivir and chloroquine have been observed to be highly effective in the control of COVID-19 infection in vitro. These antiviral compounds have been used in human patients with a safety track record. Hence, these therapeutic agents can be considered to treat COVID-19 infection (Wang et al. 2020). However, the inclusion of chloroquine, a known malaria drug has drawn global debates on its effectiveness against the novel coronavirus, leading to scarcity of the drug in pharmacy especially in malaria-endemic countries.

COVID-19 intervention strategies such as city lockdown, restrictions of movements, supply chain interruptions, closure of shops and institutions, minimal contact between healthcare service providers and patients amongst others could have led to malaria prevention activities being disrupted (Sherrard-Smith, et al. 2020). Malaria prevention activities include seasonal malaria chemoprevention (SMC), mass distribution of long-lasting insecticidal nets (LLIN) and indoor residual spraying of insecticides (IRS), most of which are distributed in gatherings in form of local workshops, which could have been cancelled during COVID-19 lockdown rules. Restriction of vehicular movements could have negatively impacted the accessibility to antimalaria drugs in pharmacy for those who could afford it. Hoarding of medicines and preparations were common occurrence during the pandemic and the cost of antimalaria drugs in some countries were unaffordable due to shortages in supply.

Therefore, this study investigated the impact of societal measures such as city lockdown

against COVID-19 spread in malaria-endemic countries. It also estimates the proportionate increase or decrease of malaria due to insufficient access to antimalaria drugs during the pandemic and its global impact on the public health risk.

1.1 History of malaria

Here, we give a brief account of the origin, causes and transmission of malaria and Lassa fever diseases. However, a full account of the discovery of malaria and Lassa fever diseases can be seen in Nadezhda and David (2012) and Cox (2010) .

1.1.1 Malaria history

In 1880, a French physician, Charles Louis A. Laveran, while working in Algeria, made a landmark discovery of the main cause of the malaria disease that has been affecting human lives for a long period. He discovered the presence of a parasitic protozoan *Plasmodium* in the blood of humans infected with malaria and was as a result awarded the Nobel prize in 1907. In other discovery, an experiment was conducted in 1897 by a British Physician, Ronald Ross, who showed for the first time that mosquito is responsible for transmission of the *Plasmodium* parasite that causes malaria in human population.

Not less than half of the world's population, distributed across 104 countries are at risk of malaria disease (Olaniyi et al 2018; WHO, 2019). Meanwhile, an initial report of 300 - 500 million persons have been observed to be infected annually, of which 1.5 - 2.7 million annual deaths have been estimated (Magombedze et al, 2011; WHO, 2019). Malaria is widely spread in tropical and subtropical regions, including Africa, Asia, Latin America, the middle East and some parts of Europe. However the most cases and deaths occur in sub-Saharan countries of Africa which account for 80 percent of the world's malaria cases and 90 percent of the global malaria deaths (WHO, 2012; CDC, 2019).

Death of an African child occurs in every 30 seconds, while global report of deaths from malaria exceeds 2000 among the youth. (Tumwiine et al, 2007; Okosun and Makinde, 2011;

CDC 2019). For example, in Nigeria, malaria accounts for 60 percent of outpatient visits and 30 percent of hospitalization with children under five years of age most severely affected (USE, 2011).

1.1.2 Malaria parasites and cycle

Malaria is a disease characterized by fever, pain, paroxysms of chills, headache and vomitting. The disease is caused by protozoan parasite, known as *Plasmodium*. The commonest species that infect humans are; *Plasmodium vivax, P. ovale, P. falciparum, P. malariae* and *P. knowlesi*. The socioeconomic burden of malaria disease and its clinical signs include multi-organ failures such as lung, brain, liver and kidney (Tumwiine et al., 2007).

The life cycle of the *plasmodium* parasite can be divided into two phases: sexual and asexual phases, with the sexual phase taking place in the female *anopheles* mosquito and asexual phase in the human host (Ibezim). The infection subtly begins when an infectious mosquito pierces the human skin with its proboscis and injects parasite in the form of sporozoites into the human's bloodstream for blood circulation. In the process, the sporozoites enter the liver where each sporozoites undergoes asexual multiplication stage to produce cells called merozoites. This first asexual multiplication stage in human host is known as exoerythrocytic schizogony (Cox, 2010).

Following the rupture of the hepatocytes, merozites escape into circulatory system for asexual reproduction in the red cells, a stage called erythrocytic schizogony develops (Cox, 2010). At this stage, more merozoites are produced until the red blood cells burst and new merozoites are released to further infect other red blood cells while some merozoites developed into gametocytes (Cox, 2010). These geametocytes in the human's bloodstream can be taken up by a naive mosquito in the blood meal gametocytes and mature into male and female gametes in the mosquito's gut. Consequently, microgamete and macrogamete representing male and female gametes respectively, fuse salivary gland of the mosquito vector where they can be injected when the mosquito bites another human host to continue the cycle.

Chapter 2

LITERATURE REVIEW

Mathematical modelling of malaria began in 1911 with Ronald Ross who discovered the role of mosquito as an intermediate vector in the transmission of the pathogenic malaria parasite. He introduced the first deterministic model of the form:

$$\begin{aligned} \frac{dI_h}{dt} &= b\beta_h m(1-I_h)I_m - rI_h \\ \frac{dI_m}{dt} &= b\beta_m(1-I_m)I_h - \mu I_m \end{aligned}$$

with variable I_h representing the fraction of infectious humans and I_m representing the fraction of infectious mosquitoes; b is the mosquito biting rate; β_h represents the proportion of bites that produce infection in human; m denotes the fraction of number of mosquitoes to that of humans; r represents human recovery rate; β_m represents the proportion of bites that produce infection in mosquito; and μ denotes per capita rate of mosquito mortality. This model revealed that eradication of malaria could be made possible by decreasing vector (mosquitoes) biting rate and increasing the mosquito death rate resulting to reduction of threshold parameter given

$$R_0 = \frac{mb^2\beta_h\beta_m}{r\mu}$$

The Ross model was modified by Macdonald (1957), his model incorporates the latency period of parasite in mosquitoes in which the exposed class was introduced. His findings showed that the basic reproduction number of the disease decreases with an increase in the latency period. Macdonald's model was further extended by Anderson and May (1991) as they introduced

new exposed class into the human population. This improvement has further decreased the long-term prevalence of both infected humans and mosquitoes. The basic models discussed above are the building-ground for literature on malaria models. Since then, different factors have been incorporated in order to make the models epidemiologically more realistic. One such factor is the inclusion of recovered class into the human population on the idea that continuous exposure to reinfection could lead to acquired immunity in human. A deterministic model that incorporated human and mosquito populations with standard incidence function was developed by Nwga and shu (2000). Their model made an exploration of the structure in which an infectious human recovers with temporary immunity to become a recovered human before entering the susceptible compartment again. The result of their analysis revealed that there is persistence in the disease whenever the threshold parameter R_0 exceeds one and that the disease-free equilibrium is globally asymptotically stable when R_0 is below one.

Factors such as: environmental effects, mosquitoes resistance to insecticides, resistance of some parasite strains to anti-malaria drugs and the use of optimal control methods have been integrated into the models so as to gain more insight on the behaviour of the disease. Yang and Ferreira (2000) used bilinear incidence function to study malaria transmission model by incorporating socio-economic structure. Through the model analysis, they showed how the basic reproduction number changes with global warming and local social and economic conditions.

In addition, Iddi et al (2002) used deterministic model with standard incidence function to study the impact of infectious immigrants on vector-borne disease with direct transmission. The research work was analyzed qualitatively, the computation of the basic reproduction number using the next generation matrix method and the conditions for the stability of the equilibra were determined. It was revealed through numerical simulation that hike in the number of immigrants tends to result to an increment in the number of infected population which leads to the persistence of the disease in the population.

Koella and Anita (2003) developed a model in order to understand the epidemiology of anti-malaria resistance and to assess approaches to decrease resistance spread. Their analyses

showed that resistance to treatment does not spread if the fraction of infected individuals treated is less than a threshold value and if the drug treatment exceeds this value, then resistance to drug eventually becomes fixed in the population.

Chitnis et al (2006) presented a malaria model that incorporated human immigration and disease-induced death rates. This model was based on Nwga and Shu model. The basic reproduction number was obtained to investigate the stability of disease-free equilibrium point using the next generation operator approach. It was further depicted through numerical examples that backward bifurcation is possible for some positive values of disease-induced death rate.

In another development, Tumwiine et al (2007) developed a five dimensional model with standard incidence function for the dynamics of malaria in the human hosts and vectors. In this model, the reservoir of the susceptible human was refilled by immunity loss to the disease and newborns. The stability of the system was analysed for the existence of disease-free and endemic equilibra. However, it was shown that the basic reproduction number is independent of the rate of loss of immunity.

In addition, Chitnis et al (2008) carried out a sensitivity analysis of malaria model with human immigration factor and disease-induced death rate in order to determine the relative importance of model parameters to the disease transmission and prevalence. A computation of sensitivity indices of the basic reproduction number to parameters at the baseline values was done. It was found out that the basic reproduction number is most sensitive to the mosquito biting rate.

Labadin et al (2009) formulated and analysed a deterministic model with standard incidence function. In this model, a consideration of the recovered population with and without immunity and the impact of the different values of the average duration to build effective immunity on infectious humans were investigated numerically. The findings of their research showed that if the ability to build an effective immunity is fast for those who recovered from the disease, then the number of cases could be reduced.

One of the contributory factors to the spread of malaria is proven to be the movement of

human from one environment to another. In the light of this, Arino et al (2011) came up with a metapopulation model for malaria where interaction between humans in rural and urban area was investigated. They brought to the light that the basic reproduction number governed the stability of the disease-free steady state. Also, the unrestricted movement of infected humans could lead to the persistence of the disease in the population. Again, the class of infectious individuals with drug resistance symptoms was incorporated in the standard incidence function deterministic model that was formulated and analysed by Okosun and Makinde (2011). The model was shown to exhibit backward bifurcation and by the basic reproduction number, the existence and stability of equilibria were established. Pontryagin maximum principle was used to obtain conditions for optimal control of the disease and their numerical results showed that effective control of the proportion of individuals with drug resistance has a positive impact in reducing the spread of the disease.

Magombedze et al (2011) developed an intra-host mathematical model of malaria that described the interaction of immune system with the blood stage malaria merozoites. Optimal control strategy was used to analysis their model. This led to a suggestion in their result that a malarial therapy that seeks to minimize merozoites population was beneficial to patients as this will lead to the reduction of infected red blood cells. Also, a seven-dimensional compartmental model of malaria that incorporated three control functions such as: the prevention of host-vector contacts, treatment of hosts and reduction of mosquito population was studied by Lashari et al (2012). In the analyses by the model, necessary conditions for optimal control of malaria were obtained. The numerical simulation of the model revealed that the combination of the control efforts has a very desirable effect on the population in reducing the number of infected individuals.

Furthermore, Olaniyi and Obabiyi (2013) formulated a mathematical model that incorporated antibodies to curtail transmission of parasite that causes malaria in both human and mosquito; and stability analyzed through threshold parameter. The results of their analyses showed that the disease will not persist in the population whenever R_0 is below unity. However, the system

become unstable whenever R_0 is above unity.

In a related work, a non- autonomous model that incorporated multiple control measures was developed by Olaniyi et al (2018) to investigate the dynamics of malaria transmission in both human and mosquito populations. With the aid of suitable Lyapunov functions, the stability of both disease-free and endemic equilibra was established. A suggestion was made in the result of their analysis that combination of multiple control at a time by human traveler will help to eliminate the spread of malaria in the population.

In another development, Okosun and Makinde (2014) proposed a mathematical model for malaria-cholera co-infection in order to investigate their synergistic relationship in the presence of treatments. The results of their analyses revealed that malaria infection may be associated with an increased risk of cholera. However, cholera infection is not associated with an increased risk for malaria. A suggestion was made in the result of their analysis that to effectively control malaria, the malaria intervention strategies by policy makers must at the same time also include cholera control.

Chapter 3

MODEL DEVELOPMENT AND ANALYSIS

3.1 Model development

We use the SEIRS-SEI malaria model developed by Chitnis et al. (2006, 2008).and shown in Figure 3.1. The human population undergoes the SEIRS dynamics. Humans are born as susceptible (S_H) at rate Λ_H. They are bitten by infected mosquitoes (I_M) at rate β and with probability p_H become exposed (E_H). The incubation period lasts σ_H^{-1} after which the exposed human becomes infectious (I_H). The infectious individuals receive treatment and become recovered (R_H) at rate γ_H. The recovered individuals lose their immunity and become susceptible at rate ω. All individuals have a natural mortality rate μ_H; infectious individuals have an additional malaria induced mortality δ_H. Note that R_H is assumed non-infectious to mosquitoes. This is unlike chitnis 2006 and chitnis 2008. There are more deviation from chitnis 2008 - they assumed logistic growth, immigration etc, we do not.

The mosquito population undergoes SEI dynamics. Mosquitoes are born susceptible (S_M) at rate Λ_M. After biting an infectious human, they become exposed (E_M) with probability p_M. The exposed mosquitoes become infectious (I_M) at the incubation rate σ_M. All mosquitoes die at rate μ_M; the infectious mosquitoes die at an additional malaria induced rate δ_M.

3.1.1 Ordinary Differential Equation system

In summary, the model consists of the following system of nonlinear deterministic differential equations

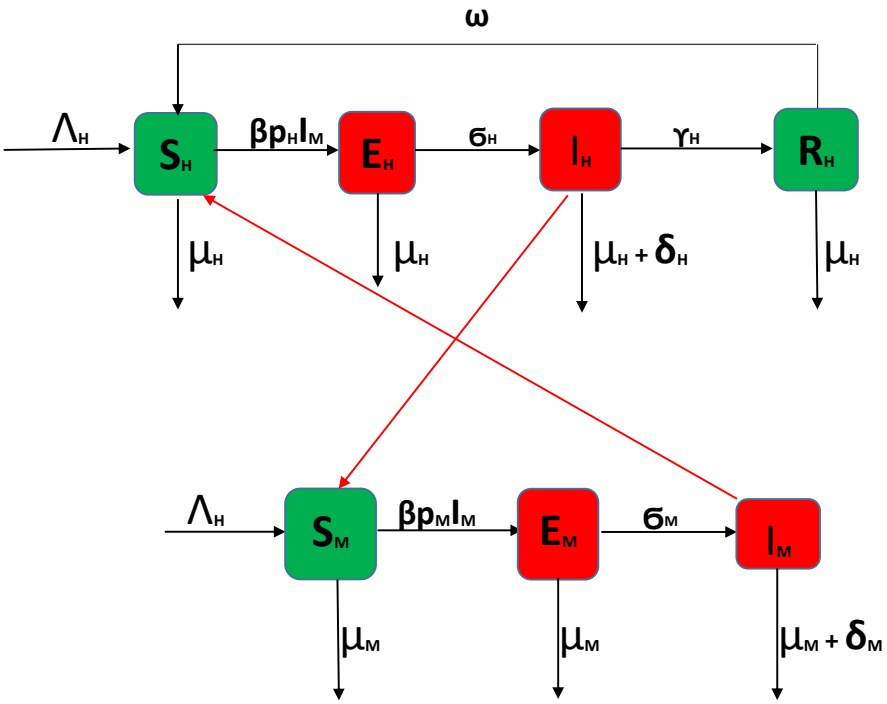

Figure 3.1: Compartmental diagram of the constructed model involving the interaction of susceptible human, exposed human infected human, recovered human, susceptible mosquito, exposed mosquito and infected mosquito.

$$\frac{dS_H}{dt} = \Lambda_H - p_H\beta S_H I_M + \omega R_H - \mu_H S_H \tag{3.1.1}$$

$$\frac{dE_H}{dt} = p_H\beta S_H I_M - (\sigma_H + \mu_H)E_H \tag{3.1.2}$$

$$\frac{dI_H}{dt} = \sigma_H E_H - \gamma_H I_H - (\delta_H + \mu_H)I_H \tag{3.1.3}$$

$$\frac{dR_H}{dt} = \gamma_H I_H - (\omega + \mu_H)R_H \tag{3.1.4}$$

$$\frac{dS_M}{dt} = \Lambda_M - p_M\beta S_M I_H - \mu_M S_M \tag{3.1.5}$$

$$\frac{dE_M}{dt} = p_M\beta S_M I_H - (\sigma_M + \mu_M)E_M \tag{3.1.6}$$

$$\frac{dI_M}{dt} = \sigma_M E_M - (\delta_M + \mu_M)I_M \tag{3.1.7}$$

3.1.2 Modelling the effect of lockdown

We will explicitly incorporate the following effects of lockdown on the malaria transmission.

- The biting rate, β, increases in lockdown because ITNs are less available.
- The probability of malaria infection, p_H, increases in lockdown because people do not take or do not have access to antimalaria drugs.
- The recovery rate, γ_H, decreases because people are afraid of treatment, there are not enough tests to properly diagnose malaria, there are not enough drugs for treatment, not enough beds in the hospital.

We will assume that

$$\beta = \beta_0(1 - \Delta_{ITN}) \tag{3.1.8}$$

$$\rho_H = \rho_{H,0}\,(1 - \Delta_{Drugs}) \tag{3.1.9}$$

$$\gamma_H = \gamma_{H,0}\,(1 - \Delta_{Drugs}) \tag{3.1.10}$$

where $\Delta_{ITN}, \Delta_{Drugs}, \in [0, 1]$ is the indicator lockdown restrictions, β_0, $p_{H,0}$, and $\gamma_{H,0}$ are pre-lockdown levels of biting rates, probability of transmission and recovery rate, and Δ_P is the effect of the lockdown on the parameter P.

3.2 Model analysis

In this section, mathematical model of malaria that incorporate inaccessibility to healthcare service due to city lockdown and treatment time delay was analysed to obtain the equilibria of the model and their stability. Since the model monitors changes in the human, and mosquito populations, the variables and the parameters are assumed to be non-negative for all $t \geq 0$. Therefore, equations (3.1.1)-(3.1.7) is analysed in a suitable feasible region $\mathcal{D}$ of biological interest. The biologically feasible region Ω of the malaria model (3.1.1 - 3.1.7) is positively invariant.

Proof. Adding the mode equations (3.1.1)-(3.1.4) together we obtain

$$\begin{aligned}\frac{dN_H}{dt} &= \Lambda_H - \mu_H N_H - \delta_H I_H \\ \frac{dN_H}{dt} &\leq \Lambda_H - \mu_H N_H \\ \frac{dN_H}{dt} + \mu_H N_H &\leq \Lambda_H \end{aligned} \tag{3.2.1}$$

Similarly, adding the model equations (3.1.5)-(3.1.7) together

$$\begin{aligned}\frac{dN_M}{dt} &= \Lambda_M - \mu_M N_M - \delta_M I_M \\ \frac{dN_M}{dt} &\leq \Lambda_M - \mu_M N_M \\ \frac{dN_M}{dt} + \mu_M N_M &\leq \Lambda_M \end{aligned} \tag{3.2.2}$$

Solving the differential equations (3.2.1) and (3.2.2) one after the other we have: Take the integrating factor

$$e^{\int \mu_H dt} = e^{\mu_H t}$$

$$e^{\mu_H t}\left[\frac{dN_H}{dt} + \mu_H N_H\right] \leq \Lambda_H e^{\mu_H t}$$

$$\frac{d}{dt}\left(N_H(t)e^{\mu_H t}\right) = \Lambda_H e^{\mu_H t}$$

$$\int_0^t \frac{d}{dt}\left((N_H(s)e^{\mu_H(s)}\right) = \int_0^t \Lambda_H e^{\mu_H s}$$

$$N_H(t)e^{\mu_H t} \leq N_H(0) + \frac{\Lambda_H}{\mu_H}e^{\mu_H t} - \frac{\Lambda_H}{\mu_H}$$

so that

$$N_H(t) \leq N_H(0)e^{-\mu_H t} + \frac{\Lambda_H}{\mu_H} - \frac{\Lambda_H}{\mu_H}e^{-\mu_H t}$$

this implies that

$$N_H(t) \leq \frac{\Lambda_H}{\mu_H}\left(1 - e^{-\mu_H t}\right) + N_H(0)e^{-\mu_H t} \tag{3.2.2}$$

Similarly from equation (3.2.2)

$$e^{\int \mu_M dt} = e^{\mu_M t}$$
$$e^{\mu_M t}\left[\frac{dN_M}{dt} + \mu_M N_M\right] \leq \Lambda_M e^{\mu_M t}$$
$$\frac{d}{dt}\left(N_M(t)e^{\mu_M t}\right) = \Lambda_M e^{\mu_M t}$$
$$\int_0^t \frac{d}{dt}\left((N_M(s)e^{\mu_M(s)}\right) = \int_0^t \Lambda_M e^{\mu_H s}$$
$$N_M(t)e^{\mu_M t} \leq N_M(0) + \frac{\Lambda_M}{\mu_M}e^{\mu_M t} - \frac{\Lambda_M}{\mu_M}$$

so that

$$N_M(t) \leq N_M(0)e^{-\mu_M t} + \frac{\Lambda_M}{\mu_M} - \frac{\Lambda_M}{\mu_M}e^{-\mu_M t}$$

this implies that

$$N_M(t) \leq \frac{\Lambda_M}{\mu_M}\left(1 - e^{-\mu_M t}\right) + N_M(0)e^{-\mu_M t} \tag{3.2.3}$$

Taking the limit of equations (3.2.3) and (3.2.4) as $t \to \infty$ gives

$$N_H(t) \leq \frac{\Lambda_H}{\mu_H}\ ;\ N_M(t) \leq \frac{\Lambda_M}{\mu_M}$$

Thus the following feasible region

$$\Omega = \{S_H, E_H, I_H, R_H, S_M, E_M, I_M, \in \mathcal{R}_+^7 : N_H(t) \leq \frac{\Lambda_H}{\mu_H},\ N_M(t) \leq \frac{\Lambda_M}{\mu_M}\}$$

□

Next, the existence of steady-state solutions (equilibrium points) of the autonomous model is determined is investigated.

3.2.1 Malaria-free equilibrium

The malaria-free equilibrium of the model (3.1.1)-(3.1.7), denoted by $\mathcal{M}_0$ is given by

$$\mathcal{M}_0 = (S_H^*, E_H^*, I_H^*, R_H^*, S_M^*, E_M^*, I_M^*) = \left(\frac{\Lambda_H}{\mu_H}, 0, 0, 0, \frac{\Lambda_m}{\mu_M}, 0, 0\right) \tag{3.2.4}$$

The local stability of $\mathcal{M}_0$ will be shown using the approach and notations in (Van den Driessche and J.Watmough, 2002). It can be deduced from model (3.1.1)- (3.1.7) that

$$\frac{d}{dt}\begin{pmatrix} E_H(t) \\ I_H(t) \\ E_M(t) \\ I_M(t) \end{pmatrix} = \begin{pmatrix} p_H\beta S_H I_H \\ 0 \\ p_M\beta S_M I_M \\ 0 \end{pmatrix} - \begin{pmatrix} (\sigma_H+\mu_H)E_H \\ -\sigma_H E_H + (\gamma_H+\delta_H+\mu_H)I_H \\ (\sigma_M+\mu_M)E_M \\ -\sigma_M E_M + (\delta_M+\mu_M)I_M \end{pmatrix}$$

from which the matrix F of new infection terms and matrix V of the transition terms are given, respectively, by

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{P_H\beta\lambda_H}{\mu_H} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{P_M\beta\lambda_M}{\mu_M} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \sigma_H+\mu_H & 0 & 0 & 0 \\ -\sigma_H & (\gamma_H+\delta_H+\mu_H) & 0 & 0 \\ 0 & 0 & \sigma_M+\mu_M & 0 \\ 0 & 0 & -\sigma_M & \delta_M+\mu_M \end{pmatrix} \tag{3.2.5}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{\sigma_H+\mu_H} & 0 & 0 & 0 \\ \frac{\sigma_H}{(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)} & \frac{1}{(\gamma_H+\delta_H+\mu_H)} & 0 & 0 \\ 0 & 0 & \frac{1}{\sigma_M+\mu_M} & 0 \\ 0 & 0 & \frac{\sigma_M}{(\sigma_M+\mu_M)(\delta_M+\mu_M)} & \frac{1}{\delta_M+\mu_M} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} 0 & 0 & \frac{\rho_H\beta\sigma_M\lambda_H}{\mu_H(\delta_M+\mu_M)(\sigma_m+\mu_M)} & \frac{\rho_H\beta\lambda_H}{\mu_H(\delta_M+\mu_M)} \\ 0 & 0 & 0 & 0 \\ \frac{\rho_M\beta\sigma_H\lambda_M}{\mu_M(\gamma_H+\delta_H+\mu_H)(\sigma_H+\mu_H)} & \frac{\rho_M\beta\lambda_H}{\mu_M(\gamma_H+\delta_H+\mu_H)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

Therefore, the basic reproduction number of the model (3.1.1)-(3.1.7), denoted by $R_0 = \rho(FV^{-1})$, where ρ is the spectral radius of the product FV^{-1} , is obtained by

$$R_0 = \sqrt{\frac{\rho_H \rho_M \beta^2 \sigma_H \sigma_M \lambda_M \lambda_H}{\mu_H(\sigma_H + \mu_H)(\gamma_H + \delta_H + \mu_H)(\sigma_M + \mu_M)(\delta_M + \mu_M)\mu_M}} \tag{3.2.6}$$

The following result is established by standard technique (see Theorem 2 of Van den Driessche and Watmough, 2002).

Lemma 1: The malaria-free equilibrium,M_0, of the model (3.1.1)-(3.1.7) is locally asymptotically stable in Ω if $R_0 < 1$ and unstable if $R_0 > 1$.

The basic reproduction number,R_0, is a measure of the spread potential of malaria in a population governed by the model (3.1.1)-(3.1.7). The implication of Lemma 1, from epidemiological viewpoint, is that the spread of malaria can be effectively controlled in the population when $R_0 < 1$, if the initial sizes of the sub-populations of the model (3.1.1)-(3.1.7) are in the basin of attraction of the malaria-free equilibrium $\mathcal{M}_0$. It can be noted, following (Egonmwan and Okuonghae, 2019), that the partial derivative of the basic reproduction number,R_0, given by (3.2.7) with respect to the treatment rate, γ_H when there is no lockdown and no diversion of the resources that would otherwise be used to fight malaria towards COVID-19. Then we have

$$\frac{\partial R_0}{\partial \gamma_H} = -\left(\frac{\left(\rho_H \rho_M \beta^2 \sigma_H \sigma_M \lambda_M (\mu_H(\sigma_H + \mu_H)\mu_M(\sigma_M + \mu_M)(\delta_M + \mu_M)(\delta_H + \mu_H)\right)}{2\mu_H(\sigma_H + \mu_H)\mu_M(\sigma_M + \mu_M(\delta_M + \mu_M)(\gamma_H + \delta_H + \mu_H)(\gamma_H + \delta_H + \mu_H)}\right)^{-\frac{1}{2}} < 0 \tag{3.2.7}$$

It follows from(3.2.8) that increase in the human treatment rate γ_H when there is no lockdown and no diversion of the resources that would otherwise be used to fight malaria towards COVID-19 can lead to the reduction of the basic reproduction number R_0 below unity, which in turn reduces the burden of malaria transmission in the population.

3.2.2 Malaria-present equilibrium

Here, we set the first derivative to zero and then solve the resulting solutions we have:

$$\sigma_M E_M - (\delta_M + \mu_M) I_M = 0$$
$$I_M^* = \frac{\sigma_M E_M^*}{\delta_M + \mu_M}$$
$$\rho_M \beta S_M I_H - (\sigma_M + \mu_M) E_M = 0$$
$$E_M^* = \frac{\rho_M \beta S_M^* I_H^*}{\sigma_M + \mu_M}$$
$$\Lambda_M - \rho_M \beta S_M I_H - \mu_M S_M = 0$$

$$\Lambda_M = S_M(\rho_M \beta I_H + \mu_M)$$
$$S_M^* = \frac{\Lambda_M}{\rho_M \beta_M I_H^* + \mu_M}$$
$$I_M^* = \frac{\sigma_M}{\delta_M + \mu_M} \times \frac{\rho_M \beta S_M^* I_H^*}{\sigma_M + \mu_M}$$
$$= \frac{\sigma_M \rho_M \beta S_M I_H^*}{(\delta_M + \mu_M)(\sigma_M + \mu_M)}$$
$$I_M^* = \frac{\sigma_M \rho_M \beta I_H^*}{(\delta_M + \mu_M)(\sigma_M + \mu_M)} \times \frac{\Lambda_M}{\rho_M \beta_M I_H^* + \mu_M}$$

$$I_M^* = \frac{\Lambda_M \sigma_M \rho_M \beta I_H^*}{(\delta_M + \mu_M)(\sigma_M + \mu_M)(\rho_M \beta_M I_H^* + \mu_M)}$$

$$\gamma_H I_H - (\omega + \mu_H) R_H$$

$$R_H^* = \frac{\gamma_H I_H^*}{\omega + \mu_H}$$

$$\sigma_H E_H - (\gamma_H + \delta_H + \mu_H) I_H = 0$$

$$\sigma_H E_H^* = (\gamma_H + \delta_H + \mu_H) I_H$$

$$E_H^* = \frac{(\gamma_H + \delta_H + \mu_H) I_H^*}{\sigma_H}$$

$$\rho_H \beta S_H I_M - (\sigma_H + \mu_H) E_H = 0$$

$$\rho_H \beta S_H I_M = (\sigma_H + \mu_H) E_H^*$$

$$S_H^* = \frac{(\sigma_H + \mu_H) E_H^*}{\rho_H \beta I_M^*}$$

$$S_H^* = \frac{(\sigma_H + \mu_H)}{\rho_H \beta_H} \times \frac{E_H^*}{I_M}$$

$$S_H^* = \frac{\sigma_H + \mu_H}{\rho_H \beta_H} \times \frac{(\gamma_H + \delta_H + \mu_H) I_H^*}{\sigma_H} \times \frac{1}{\Lambda_M \sigma_M \rho_M \beta I_H^*} \times \frac{1}{(\delta_M + \mu_M)(\sigma_M + \mu_M)(\rho_H \beta I_H^* + \mu_H)}$$

$$S_H^* = \frac{\sigma_H + \mu_H}{\rho_H \beta_H} \times \frac{(\gamma_H + \delta_H + \mu_H) I_H^* (\delta_M + \mu_M)(\sigma_M + \mu_M)(\rho_H \beta I_H^* + \mu_M)}{\sigma_H (\Lambda_M \sigma_M \rho_M \beta I_H^*)}$$

$$S_H^* = \frac{\Lambda_H(\rho_H \beta I_H^* + \mu_M)}{\mu_M \mu_H R_0^2}$$

$$\Lambda_H - \rho_H \beta S_H I_M + \omega R_H - \mu_H S_H = 0$$

$$\Lambda_H - (\rho_H \beta S_H I_M + \mu_M) S_H + \omega R_H = 0$$

$$\Lambda_H - \frac{\Lambda_H(\beta \rho_M I_H + \mu_M)}{\mu_H \mu_M R_0^2} \left[\rho_H \beta \left(\frac{\Lambda_M \sigma_M \rho_M I_H}{(\delta_M + \mu_M)(\sigma_M + \mu_M)(\rho_M \beta_M I_H + \mu_M)} \right) + \mu_M \right] + \frac{\omega \gamma_H I_H}{\omega + \mu_H} = 0 \tag{3.2.8}$$

$$\Lambda_H - \frac{\Lambda_H(\beta \rho_M I_H + \mu_M)}{\mu_H \mu_M R_0^2} \left[\frac{\rho_H \beta^2 \rho_M \Lambda_M \sigma_M I_H}{(\sigma_M + \mu_M)(\sigma_M + \mu_M)} + \mu_H(\beta \rho_M I_H + \mu_M) \right] + \frac{\omega \gamma_H I_H}{\omega + \mu_H} = 0 \tag{3.2.9}$$

$$\Lambda_H \times \frac{\mu_H \mu_M R_0^2}{\Lambda_H} - \frac{\Lambda_H}{\mu_H \mu_M R_0^2} \times \frac{\mu_H \mu_M R_0^2}{\Lambda_H} \left[\frac{\rho_H \beta^2 \rho_M \Lambda_M \sigma_M I_M}{(\delta_M + \mu_M)(\sigma_M + \mu_M) + \mu_H \beta_M \rho_M I_H + \mu_H \mu_M} \right] \tag{3.2.10}$$

$$+ \frac{\mu_M \mu_H R_0^2 \omega \gamma_H I_H}{\Lambda_H(\omega + \mu_H)} = 0 \tag{3.2.11}$$

$$\mu_H \mu_M R_0^2 - \frac{\rho_H \rho_M \beta^2 \Lambda_M \sigma_M I_H}{(\delta_M + \mu_M)(\sigma_M + \mu_M)} - \mu_H \beta_M \rho_M I_H - \mu_H \mu_M + \frac{\mu_M \mu_H R_0^2 \omega \gamma_H I_H}{\Lambda_H(\omega + \mu_H)} = 0 \tag{3.2.12}$$

$$\mu_H \mu_M (R_0^2 - 1) = I_H \left[\frac{\rho_H \rho_M \lambda_M \sigma_M \beta^2 \Lambda_H(\omega + \mu_H) + \mu_H \beta \rho_M \lambda_H (\delta_M + \mu_M)(\sigma_M + \mu_M)(\omega + \mu_H)}{(\delta_M + \mu_M)(\sigma_M + \mu_M)\Lambda_H(\omega + \mu_H)} \right] \tag{3.2.13}$$

$$- \frac{\mu_M \mu_H R_0^2 \gamma_H (\delta_M + \mu_M)(\sigma_M + \mu_M)}{\sigma_M + \mu_M} (\sigma_M + \mu_M)\Lambda_H(\omega + \mu_H)$$

$$I_H^* = \frac{\mu_M \mu_H \Lambda_H(\omega + \mu_H)(R_0^2 - 1)}{G + \mu_H \beta \rho_M \Lambda_H(\delta_M + \mu_M)(\sigma_M + \mu_M)(\omega + \mu_H) - \mu_H \mu_M R_0^2 \omega \gamma_H (\delta_M + \mu_M)(\sigma_M + \mu_M)} \tag{3.2.14}$$

Where

$$G = p_H p_M \Lambda_M \sigma_M \beta^2 \Lambda_H (\omega + \mu_H)$$
$$I_H^* = \frac{\mu_M \mu_H \Lambda_H (\omega + \mu_H)(R_0^2 - 1)}{K} \tag{3.2.15}$$

Where

$$K = \rho_H \rho_M \Lambda_M \sigma_M \beta^2 \Lambda_H (\omega + \mu_H) + \mu_H \beta \rho_M \lambda_H (\delta_M + \mu_M)(\sigma_M + \mu_M)(\omega + \mu_H)$$
$$- \mu_H \mu_M R_0^2 \omega \gamma_H (\delta_M + \mu_M)(\sigma_M + \mu_M)$$

In summary, we have the following results

Let $\pi_p = (S_h^*, E_h^*, I_h^*, R_h^*, S_m^*, E_m^*, I_m^*)$ represents the malaria-present equilibrium of the model (3.1.1)-(3.1.7). At steady states, let $\lambda_H^* = p_H \beta I_M^*$ be the force of infection for humans and $\lambda_M^* = p_M \beta I_H^*$ be the force of infection for mosquitoes. Then, solving the system (1.1)-(1.7) at the steady states yields

$$I_M^* = \frac{\Lambda_M \sigma_M \lambda_M^*}{(\delta_M + \mu_M)(\sigma_M + \mu_M)(\lambda_M^* + \mu_M)} \tag{3.2.16}$$
$$E_M^* = \frac{\lambda_M^* \Lambda_M}{(\sigma_M + \mu_M)(\lambda_M^* + \mu_M)} \tag{3.2.17}$$
$$S_M^* = \frac{\Lambda_M}{\lambda_M^* + \mu_M} \tag{3.2.18}$$
$$E_H^* = \frac{(\gamma_H + \delta_H + \mu_H) I_H^*}{\sigma_H} \tag{3.2.19}$$
$$R_H^* = \frac{\gamma_H I_H^*}{\omega + \mu_H} \tag{3.2.20}$$
$$S_H^* = \frac{\Lambda_H (\lambda_M^* + \mu_M)}{\mu_M \mu_H R_0^2} \tag{3.2.21}$$
$$I_H^* = \frac{\mu_H \mu_M \Lambda_H (\omega + \mu_H)(\delta_M + \mu_M)(\sigma_M + \mu_M)(R_0^2 - 1)}{K} \tag{3.2.22}$$

where K is given by

$$p_H p_M \Lambda_M \Lambda_H \sigma_M \beta^2 (\omega + \mu_H) + \mu_H \beta p_M \Lambda_H (\delta_M + \mu_M)(\sigma_M + \mu_M)(\omega + \mu_H)$$
$$- \mu_H \mu_M \omega \gamma_H R_0^2 (\delta_M + \mu_M)(\sigma_M + \mu_M)$$

we need to show that $K > 0$

$$R_0^2 = \frac{\rho_H \rho_M \beta^2 \sigma_H \lambda_H \sigma_M \lambda_M}{\mu_H (\sigma_H + \mu_H)(\gamma_H + \delta_H + \mu_H) \mu_M (\sigma_M + \mu_M)(\delta_M + \mu_M)}$$

From K,

$$\Rightarrow \rho_H\rho_M\lambda_M\lambda_H\sigma_M\beta^2(\omega+\mu_M)$$
$$-\mu_H\mu_M\omega\gamma_H(\delta_M+\mu_M)(\delta_M+\mu_M)\times\left[\frac{\rho_H\rho_M\beta^2\sigma_H\lambda_H\sigma_M\lambda_M}{\mu_H(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)\mu_M(\delta_M+\mu_M)}\right]$$

$$\Rightarrow \rho_H\rho_M\lambda_H\lambda_M\beta^2\left[\sigma_M\left((\omega+\mu_H)-\frac{\mu_H\mu_M\omega\gamma_H(\delta_M+\mu_M)(\delta_M+\mu_M)\sigma_H}{\mu_M\mu_H(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)(\sigma_M+\mu_M)(\delta_M+\mu_M)}\right)\right]$$

$$\Rightarrow \rho_H\rho_M\lambda_H\lambda_M\beta^2\sigma_M\left[(\omega+\mu_M)-\frac{\omega\gamma_H\sigma_H}{(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)}\right]$$

$$(\omega+\mu_M)-\frac{\omega\gamma_H\sigma_H}{\sigma_H+\mu_H}(\gamma_H+\delta_H+\mu_H)=\frac{(\omega+\mu_M)(\sigma_H+\mu_H)(\gamma_H+\sigma_H+\mu_H)-\omega\gamma_H\sigma_H}{(\sigma_H+\mu_H)(\gamma_H+\sigma_H+\mu_H)} \tag{3.2.23}$$

$$=\omega(\sigma_H+\mu_H)(\gamma_H+\sigma_H+\mu_H)+\mu_M(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)-\omega\gamma_H\sigma_H \tag{3.2.24}$$
$$=(\omega\sigma_H+\omega\mu_H)(\gamma_H+\delta_H+\mu_H)+\mu_M(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)-\omega\gamma_H\sigma_H \tag{3.2.25}$$
$$=\omega\sigma_H\gamma_H(\gamma_H+\delta_H+\mu_H)+\omega\mu_H(\gamma_H+\delta_H+\mu_H)+\mu_M(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)-\omega\gamma_H\sigma_H \tag{3.2.26}$$

$$=\omega\sigma_H\gamma_H+\omega\sigma_H(\delta_H+\mu_H)+\omega\mu_H(\gamma_H+\delta_H+\mu_H)+\mu_M(\sigma_H+\mu_H)(\gamma_H+\delta_H+\mu_H)-\omega\gamma_H\sigma_H \tag{3.2.27}$$

hence

$$K>0$$

i.e K is positive

Remark 1: From this, one sees that model (3.1.1)-(3.1.7) has no positive solution when $R_0<1$.

Table 3.1: Parameters description and values.

Symbol	Meaning	Value	Source
Λ_H	Human birth rate	$31/1000$ people/year	Chitnis et al. 2008
μ_H	Natural human death rate	$1/65$ years^{-1}	Olaniyi et al. 2018
σ_H	Malaria incubation rate in humans	$\frac{1}{13}$	Okosun et al. 2014
δ_H	Malaria related death	0.05 day^{-1}	Chitnis et al. 2008
γ_H	Recovery rate of malaria infected individual	0.048	Estimated
ω	Malaria immunity waning rate	$\frac{1}{(60\times356)}day^{-1}$	Chitnis et al. 2008
Λ_M	Mosquitoes birth rate*	0.091	Estimated
μ_M	Natural death rate of mosquitoes	0.143	Chitnis et al. 2008
σ_M	Malaria incubation rate in mosquitoes	0.056	Chitnis et al. 2008
δ_M	Disease-induced death rate of mosquitoes	0.01	Chitnis et al. 2008
Δ_{ITN}	Shortfall of ITNs due to lockdown effects	variable	WHO 2020
Δ_{drugs}	Shortfall of malaria drugsdue to lockdown effects	variable	WHO 2020
β_0	Baseline biting rate (pre-COVID19)	0.3 per day	Estimated
β	Actual biting rate	$\beta_0(1-\Delta_{ITN}$	Assumed
p_H	Probability of human getting infected	0.33 day^{-1}	Estimated
p_M	Probability of mosquitoes getting infected	0.092	Estimated

However, a unique endemic equilibrium exists when $R_0 > 1$. This complete the proof.

Table 3.2: Sensitivity indices for the number of malaria deaths.

Parameter	Sensitivity index
Λ_H	1.062
δ_H	0.721
l	0.348
Δ_{γ_H}	0.275
β_0	0.083
p_M	0.062
Λ_M	0.058
Δ_β	0.042
Δ_{p_H}	0.031
$p_{H,0}$	0.031
σ_M	0.028
σ_H	0.009
ω	0.008
δ_M	-0.008
μ_H	-0.234
μ_M	-0.322
$\gamma_{H,0}$	-1.098

3.2.3 Numerical simulations

In order to understand the overall picture of the disease behaviour, next we provide numerical simulations of each of the formulated models using a MATLAB software package and parameter values in Table 1

3.2.4 Sensitivity analysis

The sensitivity of the outcomes (incidence rates and malaria caused death rates) on different parameter values is displayed in Figure 3.3 and Tables 3.2-3.4. We followed Arriola and Hyman (2009) and calculated υ_p^v, the normalized forward sensitivity index of a variable v to a parameter p, by

$$\Upsilon_p^v = \frac{\partial v}{\partial p} \times \frac{p}{v}.$$

The sensitivity index $\upsilon_p^v = -0.5$ p means that a 1% increase of a parameter value p will result in the 0.5% decrease of the variable v.

Table 3.3: Sensitivity indices for the incidence rates.

Parameter	Sensitivity index
μ_M	2.245
Λ_H	1.062
μ_H	0.966
σ_H	0.877
$\gamma_{H,0}$	0.859
σ_M	0.307
δ_H	0.212
β_0	0.083
p_M	0.062
Λ_M	0.058
δ_M	0.057
Δ_β	0.042
Δ_{p_H}	0.031
$p_{H,0}$	0.031
ω	0.008
l	-0.142
Δ_{γ_H}	-0.215

Table 3.4: Sensitivity indices for the reproduction number.

Parameter	Sensitivity index
l	0.828
β_0	0.666
Λ_H	0.499
p_M	0.499
Λ_M	0.465
Δ_β	0.333
Δ_{p_H}	0.250
$p_{H,0}$	0.250
Δ_{γ_H}	0.245
σ_M	0.220
ω	0.000
δ_M	-0.065
δ_H	-0.245
σ_H	-0.433
$\gamma_{H,0}$	-0.978
μ_H	-1.114
μ_M	-2.564

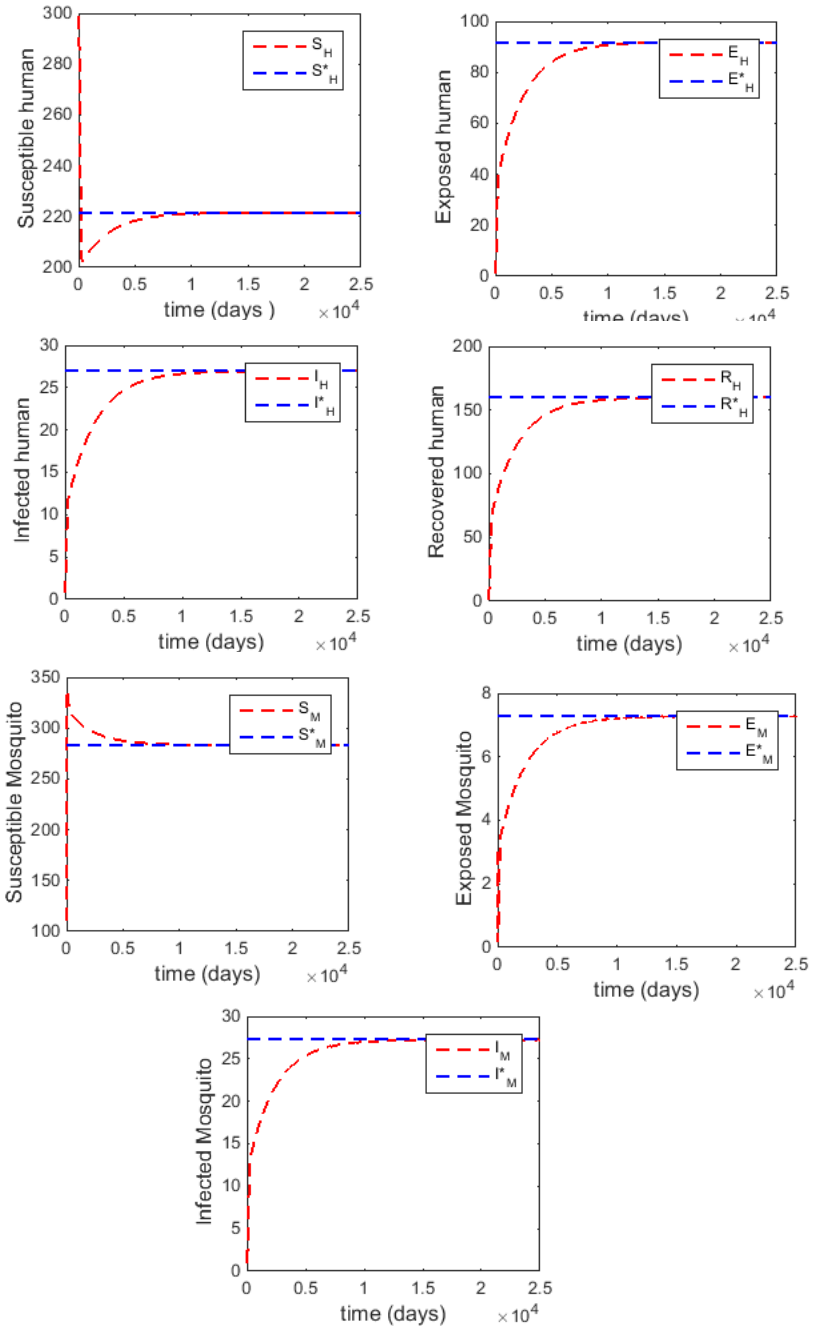

Figure 3.2: Behaviour of the malaria model when $R_0 < 1$

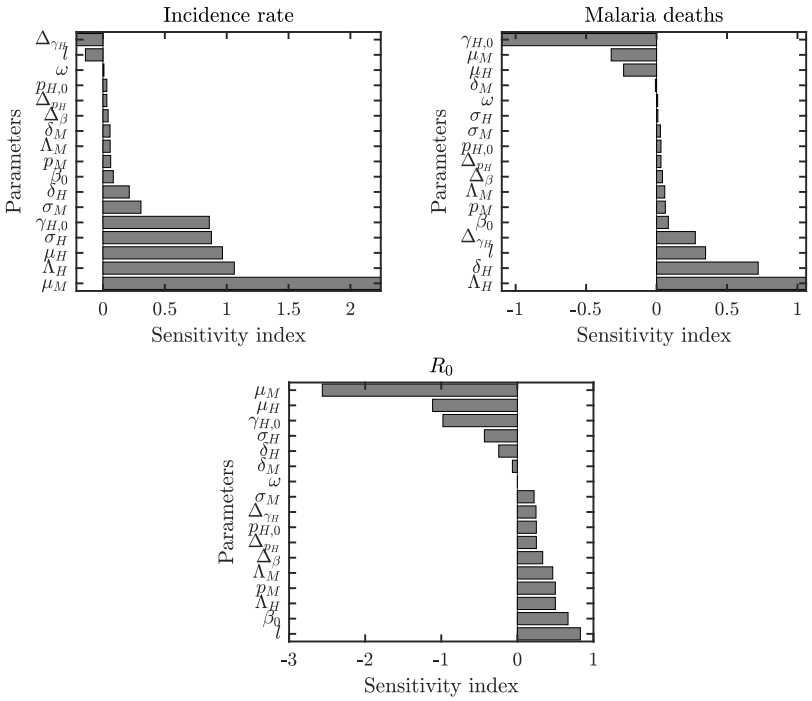

Figure 3.3: Graphical representation of the sensitivity indices for the incidence rate (left), malaria deaths (center) and R_0 (right). The numerical values are shown in Tables 2-4

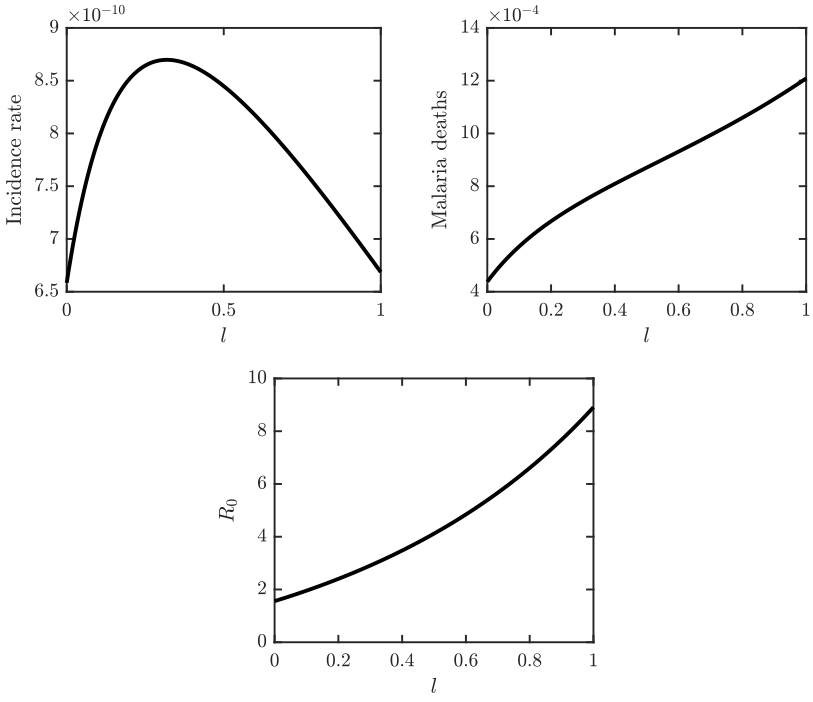

Figure 3.4: The effects of lockdown on malaria related deaths (left), malaria incidence rate (center) and R_0 (right).

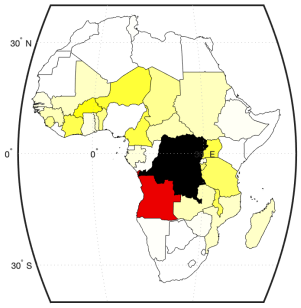

Figure 3.5: An Illustration for country specific results of mortalities. Pre covid mortalities downloaded from 2019 World Malaria Report are used

Chapter 4

DISCUSSION OF RESULTS AND CONCLUSION

4.1 Discussion of results

COVID-19 pandemic has led countries institutionalise several measures to contain the virus. Some of these measures have dire consequences on the socioeconomic, public health and political atmosphere. From sensitivity analysis, with high burdens of malaria, inaccessibility to healthcare services or scarcity of antimalarial medicines during COVID-19 pandemic could cause an increase in deaths due to malaria of up to 10% in 12 months compared with periods of no COVID-19 pandemic from our sensitivity analysis. Moreover, since both COVID-19 and malaria have similar symptomatic presentations, several persons have exhausted antimalaria drugs in their possession due to media confusion on whether or not to use antimalaria drugs to combat the virus without proper diagnosis as a result of lockdown. Self-isolation of suspected COVID-19 cases, a major preventive measure to curb the spread of the virus was adopted by several countries, might further reduce malaria diagnosis and lead to more deaths (Sherrard-Smith et al. 2020). In regions with *Plasmodium falciparum* malaria burden, COVID-19 societal measures could cause an additional number of life lost due to limitations to healthcare services. The logistical, financial and subnational timing of LLIN campaigns disruptions in Africa during COVID-19 pandemic could have substantial effects on malaria morbidities and mortalities. Hence, the local stability of the model revealed that $R_0 > 1$. Therefore, maintaining continuity of services is essential, while recovery programmes should be of high priority to reduce the broader health impact of the COVID-19 pandemic. This indirect impact of the pandemic might be largely avoided through maintenance of core programme elements and recovery campaigns.

For malaria, preventive measures must be prioritised, ensuring prophylactic treatments, such as mass drug distribution or seasonal malaria chemoprevention during lockdowns.

The results of this study underscore the extraordinarily difficult decisions facing policy makers. Well managed, long-term suppression interventions could avert the most deaths through avoiding a COVID-19 pandemic; however, if the interventions are not well-managed, they could lead to an increase in malaria deaths and other diseases over five years. An intense but short period of suppression intervention could generate a valuable delay in the pandemic that provides the opportunity to increase hospital capacity and engineer reductions in contacts. Yet, if such changes were not possible, then the impact of the pandemic would simply be compounded by the disruptions incurred during the initial period of intervention. Furthermore, Our analysis revealed that ignoring the risk of COVID19 deaths by easing lockdown for continuation of some services, such as long-lasting insecticidal net distribution, access to health care services would not exceed the benefit that might be gained in reducing malaria deaths and other diseases. However, malaria diagnosis needs to be coupled to the COVID-19 screening and testing of suspected or confirmed COVID-19 patients to reduce the burden of COVID-19 pandemic and also to avoid misdiagnosis and enable easy management. The disruptions (inaccessibility to healthcare services due to lockdowns) impact and the extent to which other disease apart from malaria (e.g. HIV/AIDS, tuberculosis) programmes would be disrupted on population health could have significant effect on the general population in developing countries.

Another factor that could diminish capability during the periods of highest demand is healthcare staff shortages due to COVID-19 illness. Disruptions to supply chains have not yet occurred on a large scale, although it is a threat given the reliance on international trade routes that could be affected by economic factors and travel restrictions. It is of note that this type of effect has been observed before (Plucinski et al. 2015)-for example, during the Ebola epidemic in Guinea in 2014, more additional people died from malaria that year due to fewer malaria treatments being administered than died from Ebola (Plucinski et al. 2015). Estimating the impact of some types of disruption on population health, especially over longer time periods, is restricted by the

paucity of data on relevant mechanisms because such disruptions have not previously occurred on the scale being considered here. Therefore, the longer term effects will be more uncertain than the short-term effects. We also do not consider how the increased stress of the health system could continue after the COVID-19 pandemic, when programmes must be reinstituted and demand increases due to new infections acquired during the pandemic. We also do not consider how long-term global changes will affect disease programmes, such as the effect of a global recession, permanent changes to the global medical supply chain, or drug development pipelines. These effects could be profound and dwarf the effects considered here, but it is not currently possible to gauge the full extent of these global changes.

The coordinated and measurable way in which inaccessibility to healthcare services due to societal measures (e.g. city lockdown) represented for malaria showed the importance of this model. In addition, data on disease and health system impact were culminated and enabled projections to be made and updated as the pandemic evolves. However, this analysis was limited to the impact of COVID-19 pandemic that led to inaccessibility to healthcare service due to lockdowns on malaria.

4.2 Conclusion

In this study, we considered autonomous SEIRS-SEI malaria models transmission that incorporates inaccessibility to healthcare services due to city lockdown and scarcity of antimalarial medicines during COVID-19 pandemic. The basic reproduction number of the autonomous model was computed to investigate the existence of the disease-free and endemic equilibra when $R_0 < 1$ and $R_0 > 1$. The parameters most responsible for the disease transmission in the populations were examined with respect to R_0 by sensitivity analysis.The effects of inaccessibility to healthcare services due to lockdown, long-lasting insecticidal net and spraying on different groups of human and mosquito populations showed its negative effect on the control plans and associated public health risk with an increasing number of deaths. It was concluded that maintaining the most critical prophylactic activities, such as long-term suppression intervention and

accessibility to healthcare services for malaria during lockdown could substantially reduce the overall impact of the COVID-19 pandemic on malaria.

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