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Mathematical Modelling of the Co-Infection Dynamics of Typhoid Fever with Plasmodium Vivax and Plasmodium Falciparum with Treatment

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Abstract: Malaria and typhoid fever are infectious and communicable diseases. Malaria remains one of the largest killer diseases in the world caused by one or more species of plasmodium parasites. Typhoid fever, also known as enteric fever, is a systemic bacterial infection disease caused by a highly virulent and invasive Salmonella enterica serovar Typhi (S. Typhi). Malaria and typhoid fever co-infection is the most endemic disease and a major public health problem in many tropical developing countries. Both diseases share similar transmission factor and often have the similar symptom. Because of the high prevalence of malaria and typhoid fever in these developing countries, co-infections are common. In addition to true co-infection of malaria and typhoid fever, the major challenges on managing controlling these diseases are false diagnoses due to similar signs and symptoms and false positive results in testing methods. In this study, we have formulated a mathematical model based on a system of non-linear first order ordinary differential equations to study the dynamics of the co-infection dynamics of plasmodium vivax- typhoid fever and plasmodium falciparum -typhoid fever. We have proved the existence of the disease free and endemic equilibrium points of the model and we used a non-linear stability analysis method to prove the local and global stabilities of these equilibrium points. Further, the positivity and boundedness of the solution of the model developed is verified to discover that the model equation is mathematically and epidemiologically well posed. We obtained the basic reproduction number R_0 for the co-infection dynamics of plasmodium vivax, plasmodium falciparum and typhoid fever diseases in terms of the three basic reproduction numbers of the separate diseases using the standard data obtained from different sources. The separate diseases disappear from the community whenever the reproduction number R_0 is very small and less than unity. On the other hand, the diseases co-exist whenever their reproduction numbers exceed unity (regardless which of the numbers is larger). The sensitivity analysis is discussed in detail to identify the most influential parameters that enhance the co-infection of malaria and typhoid fever disease in a given population. Numerical simulation is also done to illustrate the influence of different parameters on the basic reproduction number.

Keywords: Infectious Disease, Typhoid Fever, Malaria, Plasmodium Falciparum, Plasmodium Vivax, Co-infection

1. Introduction

An infectious disease is a clinically evident illness resulting from the presence of a pathogenic microbial agent. The microbial agent causing the disease can be bacterial, viral, fungal, parasitic, or it can be toxic proteins, called prions. Thus, an infectious disease is one that can be spread or transmitted from one host to another. The first significant epidemic described by historians was the plague of Athens, which struck the city of Athens in 430–426 B.C.E. The most precise description of that plague was provided by the scientific historian Thucydides (460–400 B.C.E.) in his History of the Peloponnesian War. This indicates that one of the most well documented epidemics that devastated Europe was the Black Death [16]. The burden of infectious diseases goes beyond the individual but extends to collectives including families, communities, countries and the whole world [14]. The emergence and re-emergence of infectious

diseases have become a significant worldwide problem. Infectious diseases can spread in various ways and pathogens cause infections by different modes of transmission. Some infections may take place through a direct contact while other may be caused through indirect contacts. Transmission can also be made through carriers or vectors [29].

Typhoid fever is an infectious disease. Typhoid fever, also known as enteric fever, is a systemic infection by Salmonella typhi or by the related but less virulent Salmonella paratyphi (S.paratyphi A, S.paratyphi B, S.paratyphi C and S.paratyphi D). Archeologists have found Salmonella typhi in Athenian mass graves from the era of the Peloponnesian Wars, implicating it as the cause of the Great Plague of Athens [31, 35]. Typhoid fever is endemic in many parts of the developing world and found only in human beings [7, 22, 24, 27]. Typhoid fever signs and symptoms vary widely and are very much similar to the symptoms of other microbial infections. Some of the common typhoid fever symptoms are variable degrees of high grade fever in about 75% of cases, muscle pains and body aches, chills, poor appetite, severe headaches, vomiting, nose bleeds, pain in the abdomen in 20 to 40% of cases, dizziness, rose spots (rashes) over the skin, weakness and fatigue, constipation or diarrhea, sore throat and a cough [9, 22, 27, 31]. An ongoing report on worldwide weight of typhoid fever announced 27 million diseases and 200,000 to 600,000 passing every year because of typhoid fever [23]. On the other hand, it is also estimated that the worldwide incidence of typhoid fever exceeds 50 million cases per year, with more than 600,000 deaths occurring annually [35].

Malaria is an infectious disease. The term “Malaria” originated from medieval Italian; “mal” and “aria” meaning “bad air”. The disease was formally called “ague” or “marsh fever” due to its association with swamps and marsh land [38]. Malaria is a protozoan disease and is one of the febrile illness and the most common fatal disease in the world caused by one or more species of plasmodium. These are plasmodium falciparum, plasmodium Vivax, plasmodium Ovale, plasmodium Malariae, and plasmodium Knowlesi. Most deaths are caused by P. falciparum because others generally cause a milder form of malaria. Recent evidence suggests that P. vivax malaria is also potentially life threatening disease. The biology of the five species of *Plasmodium* is generally similar and consists of two distinct phases: a sexual stage at the mosquito host and an asexual stage at the human host. The disease is transmitted by the biting of Female Anopheles Mosquitoes, and the symptoms usually begin ten to fifteen days after being bitten. A single bite by a malaria-carrying mosquito can lead to extreme sickness or death. Malaria starts with an extreme cold, followed by high fever and severe sweating. These symptoms can be accompanied by fever, joint pains, abdominal pains, headaches, vomiting, lassitude, occasional nausea, diarrhea and extreme fatigue. For severe and complicated malaria, symptoms such as yellow skin, seizures, splenomegaly, anemia, cerebral malaria, respiratory distress syndrome, acute renal failure, and in particular, convulsions, coma or death may arise [4, 10, 26, 33, 39].

Plasmodium falciparum and Plasmodium vivax are the major documented malaria parasite species, with approximately 1.2 million P. falciparum cases and 678,000 P. vivax cases reported in 2015 [3]. In Ethiopia, plasmodium falciparum and plasmodium vivax are the two predominant plasmodium species distributed all over the country accounting for 60% and 40% of malaria cases respectively [5, 32]. In sub-Saharan Africa, the pattern of malaria transmission varies markedly from region to region, depending on climate and biogeography and broad ecological categories [32]. Plasmodium falciparum, which is the most prevalent, deadliest and predominant in sub-Saharan Africa, is the major cause of malaria infections [4, 15, 32, 33, 38] and Anopheles gambiae is the primary vector for its transmission [38]. In 2016 there were 216 million cases of malaria worldwide resulting in an estimated 731 thousand deaths. Approximately 90% of both cases and deaths occurred in Africa [13].

An association between malaria and typhoid fever (malaria–typhoid co-infection) was first described in the Medical Literature in the middle of the 19^{th} century and was named typhoid-malarial fever by the United State Army Doctor Joseph J. Woodward (1833 – 1884) in 1862. Typhoid -malaria fever was found among young soldiers during the American Civil War who were suffering from febrile illness that seemed to be typhoid rather than a new species of disease. However, in the end of 19^{th} century the developed laboratory test rejects this theory, because they found that it was either one thing or other or in rare instance it is co-infection with both Salmonella typhi and the Plasmodium species. Although malaria and typhoid are caused by two different organisms in which one is protozoan and the other is gram negative bacilli, and which are transmitted by two different mechanisms, both diseases share similar symptomology. Also both diseases share social circumstances which are important for their transmission. The People living in the area which are endemic for both typhoid and malaria are at risk of getting disease either concurrently or acute infection superimpose the chronic one [24, 26, 28, 37]. The co-infection of malaria parasite and Salmonella species is common, especially in the tropics where malaria is endemic. Hence, some people treat malaria and typhoid concurrently once they have high antibody titre for Salmonella serotypes, even without adequate laboratory diagnoses for malaria and vice versa [19]. Co-infection of malaria and typhoid can result in serious complications and conditions such as maternal anemia, fever, fetal anemia, abortion, still-birth and even death of the child or mother before birth or soon after delivery. Co-infection of malaria and typhoid fever leads to chronic anemia and placental malaria infection, reducing the birth weight and increasing the risk of neonatal death [25]. It is known that anemia occurs in malaria infected individuals resulting in excessive deposition of iron in the liver, which supports the growth of salmonella bacteria that causes typhoid fever [21, 30].

In 2017 Stephen Edward and Nkuba Nyerere [6] studied

the transmission dynamics of typhoid fever with education, vaccination and treatment as control strategies in Tanzania. In their study results, they also emphasized that the education sector, sanitation sector, water supply organizations and health sector should work together to eradicate typhoid fever. Also, in 2017 [7] the researcher Stephen Edward studied the direct and indirect transmission dynamics of typhoid fever that incorporates person-to-person contact rate and person-environment. He concluded that typhoid fever is largely contracted from environmental bacteria and vaccination, therapeutic treatment and water sanitation play pivotal role in diminishing the outbreak. Limenih Habte et al [8], Aschalew Alelign et al [2], Ashenafi Assefa et al [3] and Hiwot S Taffese et al [34] studied the prevalence, burden, epidemiology, prevention, controlling techniques, spatial distribution and interventions of malaria in Ethiopia. Steady Mushayabasa et al [19] formulated and analyzed a deterministic dynamical model on the transmission dynamics of the co-infection of Typhoid Fever and Malaria in Zimbabwe and their study suggested that a typhoid fever outbreak in malaria endemic settings may lead to higher population of co-infected individuals displaying clinical symptoms of both infections than the singly-infected population displaying clinical symptoms of the disease. Okaka C. Akinyi et al [1] developed and analyzed a mathematical dynamics of malaria and typhoid fever co-infection to establish the effect of misdiagnosing typhoid fever as malaria and hence treating it with anti-malarial. They observed that misdiagnosis of typhoid fever as malaria increases the transmission of typhoid fever by increasing the rate of contact with salmonella typhi and the number of typhoid bacteria carrier and hence, it leads to high endemicity of typhoid fever. Finally, they concluded that accurate diagnosis in treatment of typhoid has positive impact in controlling typhoid in the community and reducing the rate of misdiagnosis through laboratory tests would have the largest effect on typhoid transmission.

Some deterministic mathematical models have been formulated on the co-infection dynamics of malaria and typhoid fever. Our paper work is based on the work done by Okaka C. Akinyi et al. In our paper we split the malaria disease into *p. vivax* and *p. falciparum* and we considered the co-infections of typhoid fever -*p. vivax* and typhoid fever -*p. falciparum* with single disease infection treatments. In this study we also assumed that co-infected individuals displaying clinical symptoms of one disease may be treated either both infections or single infection.

Our paper is organized as follows: In Section 2, a thirteen compartmental model for typhoid fever -*p. vivax* and typhoid fever-*p. falciparum* co-infection with treatment has been developed and also positivity and boundedness of the solutions is proved. In Sections 3, 4 and 5, typhoid fever only, *p. vivax* only and *p. falciparum* only sub-models are analyzed respectively. In Section 6, the full model is discussed with its reproduction number and stability of equilibria. In section 7, numerical simulations of the models are performed to explore the diseases dynamics. In section 8, we analyzed the sensitivity of parameters. In section 9, we discussed our results in detail. In section 10, we summarize our results with conclusion. Finally, in section 11, we indicated important recommendations.

2. Modified Model Formulation and Description

The total human population size $N_h(t)$ at time t is divided into thirteen epidemiological compartments such that $N_h = S_h + I_t + R + I_{hv} + I_{hf} + C_{vt} + C_{ft} + T_{vt} + T_{ft} + T_{vf}$ and the total mosquitoes (vectors) populations size $N_m(t)$ at time t is divided into three compartments so that $N_m = S_m + I_{mv} + I_{mf}$ and their descriptions are given in Table 1 below. Typhoid fever infected individuals in I_t class progress to the co-infected class C_{vt} at the rate $\alpha_1\lambda_{hv}$, where α_1 is the modification parameter accounting for increased rate of co-infection due to weakened individuals by typhoid fever, malaria infected individuals with plasmodium vivax in I_{hv} class progress to the co-infected class C_{vt} at the rate $\gamma\lambda_t$, where γ is the modification parameter since malaria infected individuals are more vulnerable or susceptible for typhoid fever in the endemic areas, malaria infected individuals with plasmodium falciparum in I_{hf} class progress to the co-infected class C_{ft} at the rate $\gamma\lambda_t$, where γ is the modification parameter, typhoid fever infected individuals in I_t class progress to the co-infected class C_{ft} at the rate $\alpha_2\lambda_{hf}$, where α_2 is the modification parameter accounting for increased rate of co- infection due to weakened individuals by typhoid fever; individuals in C_{vt} class suffer disease-induced death at the rate $\theta_1\delta_{vt}$, where θ_1 accounts for increased mortality due to the co-infection impact of the two diseases; individuals in C_{ft} class suffer disease-induced death at the rate $\theta_2\delta_{ft}$, where θ_2 accounts for increased mortality due to the co-infection impact of the two diseases, ω is the treatment rate of humans from typhoid fever, ϕ_1 and ϕ_2 are the treatment rates of the co-infected classes C_{vt} and C_{ft} respectively, malaria infected individuals with plasmodium vivax in I_{hv} and plasmodium falciparum in I_{hf} classes progress to the treatment class T_{vf} at the treatment rate ε. Susceptible humans acquire typhoid fever at the rate of $\lambda_t = \frac{\beta I_t}{N_h}$. The forces of infections of susceptible humans with plasmodium vivax and plasmodium falciparum are $\lambda_{hv} = \frac{a_1 b I_{mv}}{N_h}$ and $\lambda_{hf} = \frac{a_2 b I_{mf}}{N_h}$ respectively. The forces of infections of susceptible mosquitoes by plasmodium vivax and plasmodium falciparum infected humans are given by $\lambda_{mv} = \frac{a_3 b(I_{hv} + \eta_1 C_{vt})}{N_h}$ and $\lambda_{mf} = \frac{a_4 b(I_{hf} + \eta_2 C_{ft})}{N_h}$ respectively. In our work we assumed the following basic assumptions: The populations are homogenously mixing. There is no simultaneous infection of the diseases. Susceptible individuals get typhoid fever infection through contact with infected individuals of the disease. We assumed that birth rate and natural death rates are constant. We further assume that there is no natural recovery from typhoid infection.

Individuals in the co-infected classes are much weakened due to the impact of the two diseases. All the associated parameters in the system are non-negative for all time $t \geq 0$. All malaria infected individuals have equal typhoid fever force of infection and equal treatment rate. Even if the recovered class becomes susceptible again, our focus is typhoid infectious class that leads to co-infection with plasmodium parasites. Mosquitoes are not infected by typhoid fever and they do not transmit the disease.

The dynamical flow diagram of the model is given by:

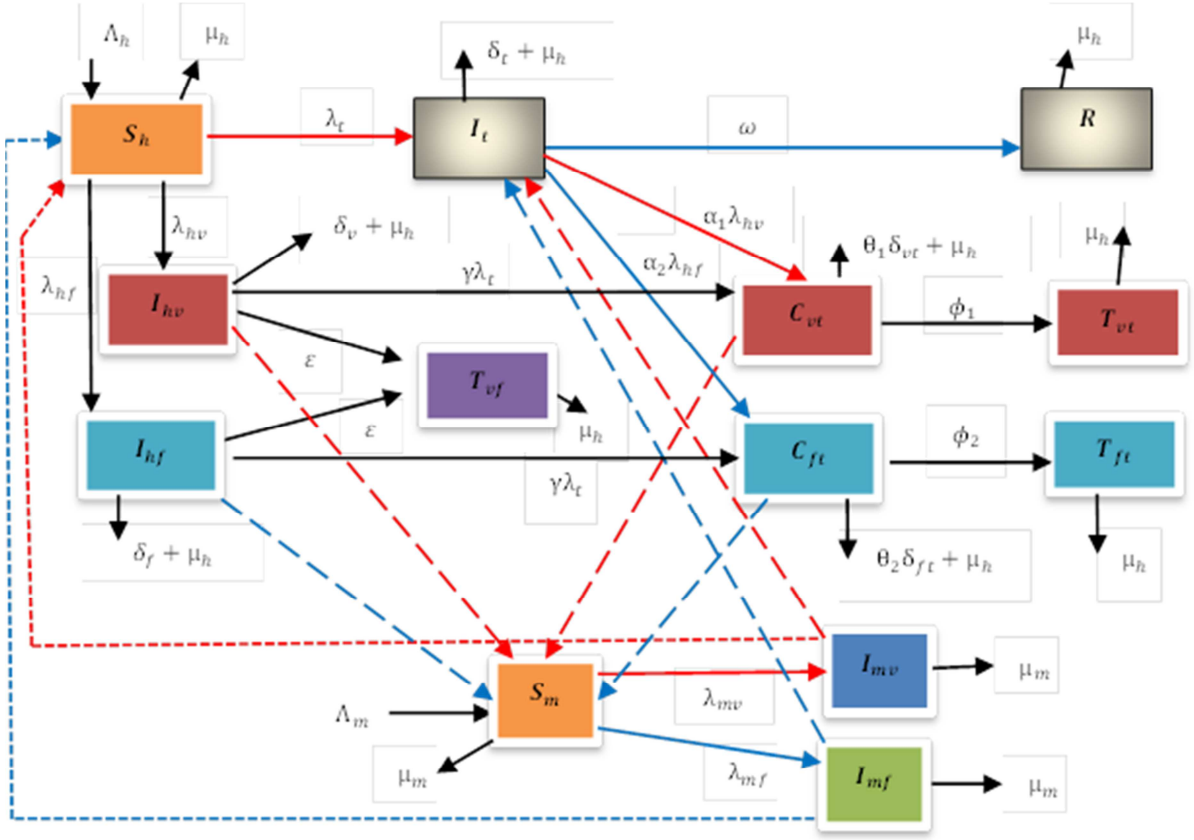

Figure 1. *The graph of the co-infection dynamics of malaria and typhoid fever diseases.*

The co-infection dynamics of the system is given by

$$\frac{dS_h}{dt} = \Lambda_h - (\lambda_{hv} + \lambda_{hf} + \lambda_t + \mu_h)S_h \tag{1}$$

$$\frac{dI_t}{dt} = \lambda_t S_h - (\alpha_1\lambda_{hv} + \alpha_2\lambda_{hf} + \omega + \delta_t + \mu_h)I_t \tag{2}$$

$$\frac{dR}{dt} = \omega I_t - \mu_h R \tag{3}$$

$$\frac{dI_{hv}}{dt} = \lambda_{hv} S_h - (\gamma\lambda_t + \varepsilon + \delta_v + \mu_h)I_{hv} \tag{4}$$

$$\frac{dI_{hf}}{dt} = \lambda_{hf} S_h - (\gamma\lambda_t + \varepsilon + \delta_f + \mu_h)I_{hf} \tag{5}$$

$$\frac{dC_{vt}}{dt} = \alpha_1\lambda_{hv} I_t + \gamma\lambda_t I_{hv} - (\phi_1 + \theta_1\delta_{vt} + \mu_h)C_{vt} \tag{6}$$

$$\frac{dC_{ft}}{dt} = \alpha_2\lambda_{hf} I_t + \gamma\lambda_t I_{hf} - (\phi_2 + \theta_2\delta_{ft} + \mu_h)C_{ft} \tag{7}$$

$$\frac{dT_{vt}}{dt} = \phi_1 C_{vt} - \mu_h T_{vt} \tag{8}$$

$$\frac{dT_{ft}}{dt} = \phi_2 C_{ft} - \mu_h T_{ft} \tag{9}$$

$$\frac{dT_{vf}}{dt} = \varepsilon(I_{hv} + I_{hf}) - \mu_h T_{vf} \tag{10}$$

$$\frac{dS_m}{dt} = \Lambda_m - (\lambda_{mv} + \lambda_{mf} + \mu_m)S_m \tag{11}$$

$$\frac{dI_{mv}}{dt} = \lambda_{mv}S_m - \mu_m I_{mv} \tag{12}$$

$$\frac{dI_{mf}}{dt} = \lambda_{mf}S_m - \mu_m I_{mf} \tag{13}$$

with initial conditions $S_h(0) > 0, I_t(0) \geq 0, R(0) \geq 0, I_{hv}(0) \geq 0, I_{hf}(0) \geq 0, C_{vt}(0) \geq 0,\ C_{ft}(0) \geq 0, T_{vt}(0) \geq 0, T_{ft}(0) \geq 0, T_{vf}(0) \geq 0, S_m(0) > 0, I_{mv}(0) \geq 0, I_{mf}(0) \geq 0.$

Table 1. *Malaria and Typhoid Fever Model State Variables, Parameters and Their Definitions.*

State Variables/Parameters	Definitions and Descriptions
S_h	Susceptible human population size at time t
I_t	Infectious human infected with typhoid fever only at time t
R	individuals that have recovered from typhoid fever disease at time t
I_{hv}	Infectious human with plasmodium vivax only at time t
I_{hf}	Infectious human with plasmodium falciparum only at time t
C_{vt}	Co-infected individuals with p. vivax and typhoid fever at time t
C_{ft}	Co-infected individuals with p. falciparum and typhoid fever at time t
T_{vt}	Treated individuals both from plasmodium vivax and typhoid fever
T_{ft}	Treated individuals both from p. falciparum and typhoid fever at time t
T_{vf}	Treated individuals both from p. vivax and p. falciparum at time t
S_m	Susceptible mosquito population size at time t
I_{mv}	Infectious mosquitoes with plasmodium vivax only at time t
I_{mf}	Infectious mosquitoes with plasmodium falciparum only at time t
N_h	Total human population size at time t
N_m	Total mosquito population size at time t
Λ_h	New recruitment rate into the susceptible human population
Λ_m	New recruitment rate into the susceptible mosquito population
μ_h	Natural death rate for human population
μ_m	Natural death rate for mosquito population
δ_t	Typhoid fever disease- induced death rate for human population
δ_v	Plasmodium vivax disease- induced death rate for human population
δ_f	Plasmodium falciparum disease- induced death rate for human population
α_1, α_2	The modification parameters from infected typhoid fever to co- infection classes
γ	The modification parameter for typhoid fever to co-infection
θ_1, θ_2	The modification parameters accounts for increased mortality due to the co-infection impact of the two diseases
ω	The treatment rate of humans from typhoid fever.
ϕ_1, ϕ_2	The treatment rates of the co-infected classes C_{vt} and C_{ft} respectively.
β	The effective transmission rate of typhoid fever on contact with infected individuals
a_1	The transmission probability of human infection due to per bite of an infected mosquito with plasmodium vivax
a_2	The transmission probability of human infection due to per bite of an infected mosquito with plasmodium falciparum
a_3	The transmission probability that a mosquito will become infected by biting an infected human with plasmodium vivax
a_4	The transmission probability that a mosquito will become infected by biting an infected human with plasmodium falciparum
b	Per capita biting rate of mosquito.
η_1, η_2	The modification parameters for mosquitoes to be infected from the co-infected individuals
ε	The rate of treatment for malaria

2.1. Invariant Aregion and Boundedness of Solutions

In this section, we will find a region in which the solution of (1-13) is bounded. The total number of human population at any time t is given by $N_h = S_h + I_t + R + I_{hv} + I_{hf} + C_{vt} + C_{ft} + T_{vt} + T_{ft} + T_{vf}$. Then, after differentiating the human population N_h with respect to time t and substituting the corresponding values of the rates, we obtain:

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_t}{dt} + \frac{dR}{dt} + \frac{dI_{hv}}{dt} + \frac{dI_{hf}}{dt} + \frac{dC_{vt}}{dt} + \frac{dC_{ft}}{dt} + \frac{dT_{vt}}{dt} + \frac{dT_{ft}}{dt} + \frac{dT_{vf}}{dt}.$$

$$\Longrightarrow \frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \left[\delta_t I_t + \delta_v I_{hv} + \delta_f I_{hf} + \theta_1 \delta_{vt} C_{vt} + \theta_2 \delta_{ft} C_{ft}\right]$$

If there is no infection and mortality of typhoid fever and malaria diseases, we get $\frac{dN_h}{dt} \leq \Lambda_h - \mu_h N_h$. Thus, $\frac{dN_h}{dt} + \mu_h N_h \leq \Lambda_h$. After integrating and simplifying both sides, we obtain $N_h(t) \leq \frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}$. Therefore, $\lim_{t\to\infty} sup N_h(t) \leq \lim_{t\to\infty} sup\left(\frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}\right) = \frac{\Lambda_h}{\mu_h}$. Hence, the total human population N_h is bounded in the region:

$$\Omega_h = \left\{\left(S_h, I_t, R, I_{hv}, I_{hf}, C_{vt}, C_{ft}, T_{vt}, T_{ft}, T_{vf}\right) \in \mathbb{R}_+^{10}: 0 \le N_h \le \frac{\Lambda_h}{\mu_h}\right\} \quad (14)$$

Similarly, the total number of mosquito population at any time t is given by $N_m = S_m + I_{mv} + I_{mf}$. Differentiating, substituting the corresponding values and simplifying both sides of this equation gives $\frac{dN_m}{dt} = \frac{dS_m}{dt} + \frac{dI_{mv}}{dt} + \frac{dI_{mf}}{dt}$. This implies that $\frac{dN_m}{dt} \le \Lambda_m - \mu_m N_m$. After integrating and simplifying both sides, we obtain

$N_m(t) \le \frac{\Lambda_m}{\mu_m} + \left(N_m(0) - \frac{\Lambda_m}{\mu_m}\right) e^{-\mu_m t}$. Therefore,

$\lim_{t\to\infty} sup N_m(t) \le \lim_{t\to\infty} sup \left(\frac{\Lambda_m}{\mu_m} + (N_m(0) - \frac{\Lambda_m}{\mu_m}) e^{-\mu_h t}\right) = \frac{\Lambda_m}{\mu_m}$. Hence, the total mosquito population N_m is bounded in the region:

$$\Omega_m = \left\{\left(S_m, I_{mv}, I_{mf}\right) \in \mathbb{R}_+^3: 0 \le N_m \le \frac{\Lambda_m}{\mu_m}\right\} \quad (15)$$

From (14) and (15), we can see that the model is well posed epidemiologically and mathematically in the region:

$$\Omega = \Omega_h \, \mathrm{X} \, \Omega_m \subset \mathbb{R}_+^{10} \mathrm{X} \mathbb{R}_+^3$$

$$= \left\{\left(S_h, I_t, R, I_{hv}, I_{hf}, C_{vt}, C_{ft}, T_{vt}, T_{ft}, T_{vf}, S_m, I_{mv}, I_{mf}\right) \in \mathbb{R}_+^{13}: 0 \le N_h \le \frac{\Lambda_h}{\mu_h}; 0 \le N_m \le \frac{\Lambda_m}{\mu_m}\right\}$$

2.2. Positivity of the Solutions

The positivity of the solution of a dynamical system can be shown by considering each differential equation separately and proving its solution is positive.

Theorem -1: If $\left\{\left(S_h, I_t, R, I_{hv}, I_{hf}, C_{vt}, C_{ft}, T_{vt}, T_{ft}, T_{vf}, S_m, I_{mv}, I_{mf}\right) \in \mathbb{R}_+^{13}: S_h > 0, I_t \ge 0, R \ge 0, I_{hv} \ge 0, I_{hf} \ge 0, C_{vt} \ge 0, C_{ft} \ge 0, T_{vt} \ge 0, T_{ft} \ge 0, T_{vf} \ge 0, S_m > 0, I_{mv} \ge 0, I_{mf} \ge 0\right\}$, then the set of solutions $\left\{S_h, I_t, R, I_{hv}, I_{hf}, C_{vt}, C_{ft}, T_{vt}, T_{ft}, T_{vf}, S_m, I_{mv}, I_{mf}\right\}$ are non-negative for $t \ge 0$ in the feasible region Ω.

Proof: All the forces of infections are positives and we apply this concept in the next subsequent proofs.

In equation (1), we have: $\frac{dS_h}{dt} = \Lambda_h - \left(\lambda_{hv} + \lambda_{hf} + \lambda_t + \mu_h\right)S_h$ and its solution is

$$S_h(t) = S_h(0)e^{-p\tau} + \Lambda_h e^{-p\tau} \int_0^t e^{p\tau}\, d\tau > 0, \text{ since } \Lambda_h > 0, S_h(0) > 0, e^{-p\tau} > 0 \; and \; e^{p\tau} > 0.$$

Let us take equation (2): $\frac{dI_t}{dt} = \lambda_t S_h - \left(\alpha_1\lambda_{hv} + \alpha_2\lambda_{hf} + \omega + \delta_t + \mu_h\right)I_t$ and the solution is

$$I_t(t) = I_t(0)e^{-pt} + e^{-pt} \int_0^t e^{p\tau}\lambda_t S_h(\tau) d\tau > 0, \text{ since } \lambda_t > 0, S_h > 0, I_t(0) > 0, e^{-pt} > 0 \; and \; e^{p\tau} > 0.$$

In equation (3), we have: $\frac{dR}{dt} = \omega I_t - \mu_h R$ with its solution $R(t) = R(0)e^{-\mu_h t} + e^{-\mu_h pt} \int_0^t e^{\mu_h \tau}\omega I_t(\tau) d\tau > 0$, since $I_t > 0, \omega > 0, R(0) > 0, e^{-\mu_h t} > 0 \; and \; e^{\mu_h \tau} > 0$.

In equation (4), we have: $\frac{dI_{hv}}{dt} = \lambda_{hv} S_h - (\gamma\lambda_t + \delta_v + \varepsilon + \mu_h) I_{hv}$ and the solution is

$$I_{hv}(t) = I_{hv}(0)e^{-pt} + e^{-pt} \int_0^t e^{p\tau}\lambda_{hv} S_h(\tau) d\tau > 0, \text{ since } \lambda_{hv} > 0, S_h > 0, I_{hv}(0) > 0, e^{-pt} > 0 \; \& \; e^{p\tau} > 0$$

From equation (5), we have:

$\frac{dI_{hf}}{dt} = \lambda_{hf} S_h - \left(\gamma\lambda_t + \delta_f + \varepsilon + \mu_h\right)I_{hf}$ with solution

$$I_{hf}(t) = I_{hf}(0)e^{-pt} + e^{-pt} \int_0^t e^{p\tau}\lambda_{hf} S_h(\tau) d\tau > 0, \text{ since } \lambda_{hf} > 0, S_h > 0, I_{hf}(0) > 0, e^{-pt} > 0 \; \& \; e^{p\tau} > 0$$

In equation (6), we have: $\frac{dC_{vt}}{dt} = \gamma\lambda_t I_{hv} + \alpha_1\lambda_{hv} I_t - (\phi_1 + \theta_1\delta_{vt} + \mu_h) C_{vt}$ and the solution is

$$C_{vt}(t) = C_{vt}(0)e^{-pt} + e^{-pt} \int_0^t e^{p\tau}(\gamma\lambda_t I_{hv} + \alpha_1\lambda_{hv} I_t)(\tau)\, d\tau > 0, \text{ since } (\gamma\lambda_t I_{hv} + \alpha_1\lambda_{hv} I_t) > 0, S_h > 0, C_{vt}(0) > 0, e^{-pt} > 0 \; and \; e^{p\tau} > 0.$$

In equation (7), we have: $\frac{dC_{ft}}{dt} = \alpha_2\lambda_{hf} I_t + \gamma\lambda_t I_{hf} - \left(\phi_2 + \theta_2\delta_{ft} + \mu_h\right)C_{ft}$ and the solution is

$$C_{ft}(t) = C_{ft}(0)e^{-pt} + e^{-pt} \int_0^t e^{p\tau}(\gamma\lambda_t I_{hf} + \alpha_2\lambda_{hf} I_t)(\tau)\, d\tau > 0, \text{ since } (\gamma\lambda_t I_{hf} + \alpha_2\lambda_{hf} I_t) > 0, S_h > 0, C_{ft}(0) > 0, e^{-pt} > 0 \; and \; e^{p\tau} > 0.$$

In equation (8), we have: $\frac{dT_{vt}}{dt} = \phi_1 C_{vt} - \mu_h T_{vt}$ and the solution is $T_{vt}(t) = T_{vt}(0)e^{-\mu_h t} + e^{-\mu_h t} \int_0^t e^{\mu_h \tau}\phi_1 C_{vt}(\tau)\, d\tau > 0$, since $C_{vt} > 0, \phi_1 > 0, T_{vt}(0) > 0, e^{-\mu_h t} > 0 \; \& \; e^{\mu_h \tau} > 0$

In equation (9), we have: $\frac{dT_{ft}}{dt} = \phi_2 C_{ft} - \mu_h T_{ft}$ and the solution is

$$T_{ft}(t) = T_{ft}(0)e^{-\mu_h t} + e^{-\mu_h t}\int_0^t e^{\mu_h \tau}\phi_2 C_{ft}(\tau)\, d\tau > 0, \text{ since } C_{ft} > 0, \phi_2 > 0, T_{ft}(0) > 0, e^{-\mu_h t} > 0 \text{ and } e^{\mu_h \tau} > 0$$

In equation (10), we have: $\frac{dT_{vf}}{dt} = \varepsilon I_{hv} + \varepsilon I_{hf} - \mu_h T_{vf}$ and the solution is

$$T_{vf}(t) = T_{vf}(0)e^{-\mu_h t} + e^{-\mu_h t}\int_0^t e^{\mu_h \tau}(\varepsilon I_{hv} + \varepsilon I_{hf})(\tau)\, d\tau > 0, \text{ since } (\varepsilon I_{hv} + \varepsilon I_{hf}) > 0, \phi_2 > 0, T_{vf}(0) > 0, e^{-\mu_h t} > 0 \text{ and } e^{\mu_h \tau} > 0.$$

In equation (11), we have: $\frac{dS_m}{dt} = \Lambda_m - (\lambda_{mv} + \lambda_{mf} + \mu_m)S_m$ and the solution is

$$S_m(t) = S_m(0)e^{-pt} + e^{-pt}\int_0^t e^{p\tau}\Lambda_m\, d\tau > 0, \text{ since } \Lambda_m > 0, S_m(0) > 0, e^{-pt} > 0 \text{ and } e^{p\tau} > 0.$$

In equation (12), we have: $\frac{dI_{mv}}{dt} = \lambda_{mv} S_m - \mu_m I_{mv}$ and the solution is

$$I_{mv}(t) = I_{mv}(0)e^{-\mu_m t} + e^{-\mu_m t}\int_0^t e^{\mu_m \tau}\lambda_{mv} S_m(\tau)\, d\tau > 0, \text{ since } S_m > 0, \lambda_{mv} > 0, I_{mv}(0) > 0, e^{-\mu_m t} > 0 \text{ and } e^{\mu_m \tau} > 0.$$

From equation (13), we have: $\frac{dI_{mf}}{dt} = \lambda_{mf} S_m - \mu_m I_{mf}$ and the solution is

$$I_{mf}(t) = I_{mf}(0)e^{-\mu_m t} + e^{-\mu_m t}\int_0^t e^{\mu_m \tau}\lambda_{mf} S_m(\tau)\, d\tau > 0, \text{ since } S_m > 0, \lambda_{mf} > 0, I_{mf}(0) > 0, e^{-\mu_m t} > 0 \text{ and } e^{\mu_m \tau} > 0.$$

Next we consider the dynamics of the three sub-models, namely; Typhoid Fever only, Plasmodium vivax and Plasmodium Falciparum only models separately. This helps us to analyze the dynamics of the full model.

3. The Dynamics of Typhoid Fever Sub-Model Only

Using the full model (1-13), the dynamics of the typhoid fever sub-model only is obtained by setting $I_{hv} = I_{hf} = C_{vt} = C_{ft} = T_{vt} = T_{ft} = T_f = S_m = T_{vt} = I_{mf} = 0$ and given by

$$\frac{dS_h}{dt} = \Lambda_h - (\lambda_t + \mu_h)S_h \tag{16}$$

$$\frac{dI_t}{dt} = \lambda_t S_h - (\omega + \delta_t + \mu_h)I_t \tag{17}$$

$$\frac{dR}{dt} = \omega I_t - \mu_h R \tag{18}$$

with initial conditions $S_h(0) > 0, I_t(0) \geq 0, R(0) \geq 0$, $\lambda_t = \frac{\beta I_t}{N_h}$ and $N_h = S_h + I_t + R$.

3.1. Invariant Region, Boundedness and Positivity of Solutions of Typhoid Fever Sub-Model Only

The total human population is given by $N_h = S_h + I_t + R$. Then, differentiating both sides of this equation gives $\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_t}{dt} + \frac{dR}{dt}$. After substituting the corresponding values of the rates and simplifying the terms we obtain: $\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \delta_t I_t$. It gives $\frac{dN_h}{dt} + \mu_h N_h \leq \Lambda_h$. Thus, $N_h(t) \leq \frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}$. Therefore, $\limsup_{t\to\infty} N_h(t) \leq \lim_{t\to\infty} sup\left(\frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}\right) = \frac{\Lambda_h}{\mu_h}$. Hence, the system of the sub-model is bounded for the total human population N_h in the region: $\Omega_h = \left\{(S_h, I_t, R) \in \mathbb{R}_+^3 : 0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$ and hence, all solutions of the dynamical system are bounded in Ω_h.

3.2. Disease-Free Equilibrium Point of Typhoid Fever Sub-model Only

The disease-free equilibrium (DFE) point is obtained when we assume that the susceptible populations do not consist of infected individuals. i.e. $I_t = R = 0$. To find this DFE point; we set the right hand side of the non-linear system of differential equations given by the sub-model (16-18) to zero. Thus, the DFE point of the sub-model is $E_0 = (\frac{\Lambda_h}{\mu_h}, 0, 0)$.

3.3. Basic Reproduction Number, $\mathbf{R_{0t}}$ for Typhoid Fever Sub-model Only

The basic reproduction number, R_{0t}, is defined as the average number of secondary infections caused by a single infectious individual introduced into the entire susceptible populations during his or her infectious period. We use the next generation matrix method to calculate R_{0t} for the system (16-18). When $R_{0t} < 1$, the disease will decline and eventually dies out. When $R_{0t} > 1$, the disease will spread in the population [12]. In the dynamical system (16-18) the rate of appearance of new infections $\mathcal{F}$ and the transfer rate of individuals V at the disease free equilibrium point $E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0\right)$ are given by the following functions as:

$$\mathrm{F} = [\beta],\ \mathrm{V} = [\omega + \delta_t + \mu_h] \text{ and } \mathrm{V}^{-1} = \left[\frac{1}{\omega + \delta_t + \mu_h}\right].$$

The basic reproduction number R_{0t} of the typhoid fever sub-model only is the largest eigenvalue of the next generation matrix $\mathcal{F}V^{-1}$ and given by $\rho(\mathcal{F}V^{-1}) = R_{0t} = \frac{\beta}{(\omega + \delta_t + \mu_h)} > 0$.

3.4. Local Stability of the Disease Free Equilibrium Point for Typhoid Fever Sub-model Only

Theorem-2: The disease free equilibrium point E_0 of the typhoid fever sub-model is locally asymptotically stable (LAS) if $R_{0t} < 1$ and unstable if $R_{0t} > 1$.

Proof: The Jacobian matrix of (14-16) at E_0 is given by:

$$J(E_0) = \begin{bmatrix} -\mu_h & -\beta & 0 \\ 0 & \beta - (\omega + \delta_t + \mu_h) & 0 \\ 0 & \omega & -\mu_h \end{bmatrix}$$

The characteristic equation of the Jacobian matrix is $\begin{vmatrix} -\mu_h - \lambda & -\beta & 0 \\ 0 & \beta - (\omega + \delta_t + \mu_h) - \lambda & 0 \\ 0 & \omega & -\mu_h - \lambda \end{vmatrix} = 0$

Simplifying this determinant, we get:

$(-\mu_h - \lambda)^2(\beta - (\omega + \delta_t + \mu_h) - \lambda) = 0$. Thus, the roots of this polynomial are given by $\lambda_1 = \lambda_2 = -\mu_h < 0$ *or* $\lambda_3 = \beta - (\omega + \delta_t + \mu_h) = (\omega + \delta_t + \mu_h)(R_{0t} - 1)$.

Hence, the DFE E_0 is locally asymptotically stable (LAS) if $R_{0t} < 1$. Otherwise, it is unstable if $R_{0t} > 1$.

3.5. Global Stability of the Disease Free Equilibrium Point for Typhoid Fever Sub-model Only

Theorem-3: The disease free equilibrium point E_0 of the typhoid fever sub-model is globally asymptotically stable (GAS) if $R_{0t} < 1$.

Proof: We define a Lyapunov function $L: R_+^3 \longrightarrow R_+$ by $L(S_h, I_t, R) = \frac{1}{\omega + \delta_t + \mu_h} I_t$. The function L and its partial derivatives with respect to the corresponding state variables are all continues. L has a minimum value at the DFE point $E_0 = (\frac{\Lambda_h}{\mu_h}, 0, 0)$ which is $L(E_0) = 0$. Also, $\frac{dL}{dt} = \frac{dL}{dS_h}\frac{dS_h}{dt} + \frac{dL}{dI_t}\frac{dI_t}{dt} + \frac{dL}{dR}\frac{dR}{dt} = 0 + \frac{1}{\omega + \delta_t + \mu_h}\frac{dI_t}{dt} + 0 = \frac{1}{\omega + \delta_t + \mu_h}\frac{dI_t}{dt}$. After substituting for $\frac{dI_t}{dt}$ and simplifying it we obtain the value of $\frac{dL}{dt}$ at $E_0 = (\frac{\Lambda_h}{\mu_h}, 0, 0)$ as: $\frac{dL}{dt} = (R_{0t} - 1)I_t$.

Thus, $\frac{dL}{dt} < 0$ if $R_{0t} < 1$. Furthermore, $\frac{dL}{dt} = 0$ *if* $R_{0t} = 1$ *or* $I_t = 0$. Hence, L is a Lyapunov function. From this we conclude that the DFE E_0 is the only singleton in the region. That is, the largest invariant set contained in $\Omega_h = \left\{(S_h, I_t, R) \in \mathbb{R}_+^3 : \frac{dL}{dt} = 0\right\}$ is reduced to the DFE E_0. Therefore, the DFE E_0 is globally asymptotically stable (GAS) on Ω_h if $R_{0t} < 1$.

3.6. Existence of Endemic Equilibrium (EE) Point for Typhoid Fever Sub-model Only

Endemic equilibrium points are steady state solutions where the disease persists in the population. To find this EE point, we set the right hand side of the non-linear system of differential equations given by (16-18) to zero. Therefore, the unique endemic equilibrium point of the typhoid fever sub-model is given by $E^* = (S_h^*, I_t^*, R^*)$. Thus,

$$E^* = \left(\frac{N_h}{R_{0t}}, \frac{R_{0t}\Lambda_h - \mu_h N_h}{\beta}, \frac{\omega(R_{0t}\Lambda_h - \mu_h N_h)}{\mu_h \beta}\right).$$

3.7. Local Stability of the Endemic Equilibrium (EE) Point

Theorem-4: The endemic equilibrium point E^* of the typhoid fever sub-model is locally asymptotically stable if $R_{0t} > 1$

Proof: The Jacobian matrix of (16-18) at E^* is

$$J(E^*) = \begin{bmatrix} \frac{-\Lambda_h R_{0t}}{N_h} & \frac{-\beta}{R_{0t}} & 0 \\ (\frac{\Lambda_h R_{0t}}{N_h} - \mu_h) & \frac{\beta}{R_{0t}} - e_1 & 0 \\ 0 & \omega & -\mu_h \end{bmatrix},$$

where $e_1 = (\omega + \delta_t + \mu_h)$

The characteristic equation of the Jacobian matrix at E^* is

$$\begin{vmatrix} \frac{-\Lambda_h R_{0t}}{N_h} - \lambda & \frac{-\beta}{R_{0t}} & 0 \\ (\frac{\Lambda_h R_{0t}}{N_h} - \mu_h) & \frac{\beta}{R_{0t}} - e_1 - \lambda & 0 \\ 0 & \omega & -\mu_h - \lambda \end{vmatrix} = 0$$

After simplifying this determinant, we get: $(-\mu_h - \lambda)(\lambda^2 + \left(\frac{\Lambda_h R_{0t}}{N_h} - \frac{\beta}{R_{0t}} + e_1\right)\lambda + \frac{\Lambda_h R_{0t} e_1}{N_h} - \frac{\mu_h \beta}{R_{0t}}) = 0$

The first root (eigenvalue) of this polynomial is $\lambda_1 = -\mu_h < 0$ and the remaining two eigenvalues can be obtained from the quadratic equation part. We have proved that all coefficients of this quadratic equation are positive and by Routh-Hurwitz criteria all roots of this quadratic equation have negative real parts. Therefore, the EE E^* is locally asymptotically stable (LAS) if $R_{0t} > 1$.

3.8. Global Stability of the Endemic Equilibrium Point for Typhoid Fever Sub-model Only

Theorem-5: The endemic equilibrium E^* of the typhoid fever sub-model is globally asymptotically stable if $R_{0t} > 1$.

Proof: We define a Lyapunov function $L: R_+^3 \longrightarrow R_+$ by $L(S_h, I_t, R) = A\left(S_h - S_h^* + S_h^* ln\frac{S_h^*}{S_h}\right) + B\left(I_t - I_t^* + I_t^* ln\frac{I_t^*}{I_t}\right) + C\left(R - R^* + R^* ln\frac{R^*}{R}\right)$, where A, B *and* C are positive constants. Then, the function L and its partial derivatives with respect to the corresponding state variables are all continues. L has a minimum value at E^* which is $L(E^*) = 0$.

Also, $\frac{dL}{dt} = \frac{\partial L}{\partial S_h}\frac{dS_h}{dt} + \frac{\partial L}{\partial I_t}\frac{dI_t}{dt} + \frac{\partial L}{\partial R}\frac{dR}{dt} = A(1 - \frac{S_h^*}{S_h})\frac{dS_h}{dt} + B(1 - \frac{I_t^*}{I_t})\frac{dI_t}{dt} + C(1 - \frac{R^*}{R})\frac{dR}{dt}$. After substituting the values of $\frac{dS_h}{dt}, \frac{dI_t}{dt}$ *and* $\frac{dR}{dt}$ and simplifying expressions we obtain the value of $\frac{dL}{dt}$ at the EE E^* as:

$$\frac{dL}{dt} = -[A(\lambda_t + \mu_h)\left(1 - \frac{S_h^*}{S_h}\right)^2 S_h$$

$$+B(\omega + \delta_t + \mu_h)\left(1 - \frac{I_t^*}{I_t}\right)^2 I_t + C\mu_h\left(1 - \frac{R^*}{R}\right)^2 R] < 0$$

$\Longrightarrow \frac{dL}{dt} \leq 0$, for any positive values of A, B *and* C.

Moreover, $\frac{dL}{dt} = 0$ at the EE E^*. Thus, L is a Lyapunov function. From this we conclude that E^* is the largest compact invariant singleton set in the region. Therefore, the endemic equilibrium point E^* is globally asymptotically stable (GAS) in the invariant region if $R_{0t} > 1$.

4. The Dynamics of Plasmodium Vivax Sub-model Only

Using the full model (1-13), the plasmodium vivax sub-model dynamics is obtained by setting $I_t = R = I_{hf} = C_{vt} = C_{ft} = T_{vt} = T_{ft} = T_{vf} = I_{mf} = 0$ and is given by

$$\frac{dS_h}{dt} = \Lambda_h - (\lambda_{hv} + \mu_h)S_h \tag{19}$$

$$\frac{dI_{hv}}{dt} = \lambda_{hv}S_h - (\varepsilon + \delta_v + \mu_h)I_{hv} \tag{20}$$

$$\frac{dT_v}{dt} = \varepsilon I_{hv} - \mu_h T_v \tag{21}$$

$$\frac{dS_m}{dt} = \Lambda_m - (\lambda_{mv} + \mu_m)S_m \tag{22}$$

$$\frac{dI_{mv}}{dt} = \lambda_{mv}S_m - \mu_m I_{mv} \tag{23}$$

with initial conditions $S_h > 0, I_{hv} \geq 0, T_v \geq 0, S_m > 0, I_{mv} \geq 0$, $\lambda_{hv} = \frac{a_1 b I_{mv}}{N_h}, \lambda_{mv} = \frac{a_3 b I_{hv}}{N_h}$ and $N_h = S_h + I_{hv} + T_v$ and $N_m = S_m + I_{mv}$.

4.1. Invariant Region, Boundedness and Positivity of Solutions for Plasmodium Vivax Sub-model Only

The total human population is $N_h = S_h + I_{hv} + T_v$. Then, $\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_{hv}}{dt} + \frac{dT_v}{dt}$. After substituting and simplifying different terms we get: $\frac{dN_h}{dt} + \mu_h N_h \leq \Lambda_h$. Thus, $N_h(t) \leq \frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}$. Therefore, $\lim_{t\to\infty} sup\, N_h(t) \leq \lim_{t\to\infty} sup\left(\frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}\right) = \frac{\Lambda_h}{\mu_h}$. Hence, the system of the sub-model is bounded for the total human population N_h in the region: $\Omega_h = \left\{(S_h, I_{hv}, T_v) \in \mathbb{R}_+^3 : 0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$.

Similarly, the total mosquito population is $N_m = S_m + I_{mv}$. Then, $\frac{dN_m}{dt} = \frac{dS_m}{dt} + \frac{dI_{mv}}{dt}$. After substituting and simplifying different terms we get: $\frac{dN_m}{dt} + \mu_m N_m \leq \Lambda_m$. This implies that $N_m(t) \leq \frac{\Lambda_m}{\mu_m} + (N_m(0) - \frac{\Lambda_m}{\mu_m})e^{-\mu_m t}$. Therefore, $\lim_{t\to\infty} sup N_m(t) \leq \lim_{t\to\infty} sup\left(\frac{\Lambda_m}{\mu_m} + (N_m(0) - \frac{\Lambda_m}{\mu_m})e^{-\mu_h t}\right) = \frac{\Lambda_m}{\mu_m}$. Hence, the system of the sub-model is bounded for the total mosquito population N_m in the region: $\Omega_m = \left\{(S_m, I_{mv}) \in \mathbb{R}_+^2 : 0 \leq N_m \leq \frac{\Lambda_m}{\mu_m}\right\}$.

From Ω_h and Ω_m we can see that the sub-model is well posed epidemiologically and mathematically in the region: $\Omega = \Omega_h \, X \, \Omega_m \subset \mathbb{R}_+^3 X \mathbb{R}_+^2 = \left\{(S_h, I_{hv}, T_v, S_m, I_{mv}) \in \mathbb{R}_+^5 : 0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}; 0 \leq N_m \leq \frac{\Lambda_m}{\mu_m}\right\}$

4.2. Disease-Free Equilibrium Point for Plasmodium Vivax Sub-model Only

The disease-free equilibrium (DFE) point of the sub-model (19-23) is obtained by setting $I_{hv} = T_v = I_{mv} = 0$ and is given by $E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_m}{\mu_m}, 0\right)$.

4.3. Basic Reproduction Number, R_{0v} for Plasmodium Vivax Sub-model Only

Using the next generation matrix we will obtain the reproduction number R_{0v} of the sub-model. In the dynamical system (19-23) the rate of appearance of new infections $\mathcal{F}$ and the transfer rate of individuals V at the disease free equilibrium point $E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_m}{\mu_m}, 0\right)$ are given by the following functions as:

$$F = \begin{bmatrix} 0 & a_1 b \\ \frac{a_3 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 \end{bmatrix}, \mathrm{V} = \begin{bmatrix} (\varepsilon + \delta_v + \mu_h) & 0 \\ 0 & \mu_m \end{bmatrix} \text{ and}$$

$$\mathrm{V}^{-1} = \begin{bmatrix} \frac{1}{(\varepsilon + \delta_v + \mu_h)} & 0 \\ 0 & \frac{1}{\mu_m} \end{bmatrix}$$

The basic reproduction number R_{0v} of the plasmodium vivax sub-model only is the largest eigenvalue of the next generation matrix $\mathcal{F}V^{-1}$ and given by $\rho(\mathcal{F}V^{-1}) = R_{0v} = \sqrt{\frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m^2 \Lambda_h (\varepsilon + \delta_v + \mu_h)}} > 0$.

4.4. Local Stability of the Disease Free Equilibrium Point

Theorem-6: The disease free equilibrium point E_0 is locally asymptotically stable if $R_{0v} < 1$ and unstable if $R_{0v} > 1$.

Proof: The Jacobian matrix of (17-21) at E_0 is given by

$$J(E_0) = \begin{bmatrix} -\mu_h & 0 & 0 & 0 & -a_1 b \\ 0 & -(\varepsilon + \delta_v + \mu_h) & 0 & 0 & a_1 b \\ 0 & \varepsilon & -\mu_h & 0 & 0 \\ 0 & -\frac{a_3 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & -\mu_m & 0 \\ 0 & \frac{a_3 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & 0 & -\mu_m \end{bmatrix}$$

The corresponding characteristic equation of the Jacobian matrix is obtained by:

$$\begin{vmatrix} -\mu_h - \lambda & 0 & 0 & 0 & -a_1 b \\ 0 & -(\varepsilon + \delta_v + \mu_h) - \lambda & 0 & 0 & a_1 b \\ 0 & \varepsilon & -\mu_h - \lambda & 0 & 0 \\ 0 & -\frac{a_3 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & -\mu_m - \lambda & 0 \\ 0 & \frac{a_3 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & 0 & -\mu_m - \lambda \end{vmatrix} = 0$$

Simplifying this determinant gives:

$$(-\mu_h-\lambda)(-\mu_m-\lambda)(-\mu_m-\lambda)[\lambda^2+(\varepsilon+\delta_v+\mu_h+\mu_m)\lambda+(\varepsilon+\delta_v+\mu_h)\mu_m-\frac{a_1a_3b^2\mu_h\Lambda_m}{\mu_m\Lambda_h}]=0$$

$$\Longrightarrow \lambda_1=-\mu_h, \lambda_2=-\mu_m, \lambda_3=-\mu_m \text{ or } \lambda^2+(\varepsilon+\delta_v+\mu_h+\mu_m)\lambda+(\varepsilon+\delta_v+\mu_h)\mu_m-\frac{a_1a_3b^2\mu_h\Lambda_m}{\mu_m\Lambda_h}=0$$

$$\Longrightarrow \lambda_4=\frac{-(\varepsilon+\delta_v+\mu_h+\mu_m)-\sqrt{(\varepsilon+\delta_v+\mu_h+\mu_m)^2-4((\varepsilon+\delta_v+\mu_h)\mu_m-\frac{a_1a_3b^2\mu_h\Lambda_m}{\mu_m\Lambda_h})}}{2} \text{ or}$$

$$\lambda_5=\frac{-(\varepsilon+\delta_v+\mu_h+\mu_m)+\sqrt{(\varepsilon+\delta_v+\mu_h+\mu_m)^2-4((\varepsilon+\delta_v+\mu_h)\mu_m-\frac{a_1a_3b^2\mu_h\Lambda_m}{\mu_m\Lambda_h})}}{2}$$

From these eigenvalues we can see that $\lambda_1, \lambda_2, \lambda_3$ *and* λ_4 are all less than zero. So, the DFE will be stable if $\lambda_5<0$. Then,

$$\frac{-(\varepsilon+\delta_v+\mu_h+\mu_m)+\sqrt{(\varepsilon+\delta_v+\mu_h+\mu_m)^2-4((\varepsilon+\delta_v+\mu_h)\mu_m-\frac{a_1a_3b^2\mu_h\Lambda_m}{\mu_m\Lambda_h})}}{2}<0$$

Simplifying this inequality gives: $\sqrt{\frac{a_1a_3b^2\mu_h\Lambda_m}{(\varepsilon+\delta_v+\mu_h)\mu_m^2\Lambda_h}}<1$. It implies that $R_{0v}<1$. Therefore, the DFE E_0 is locally asymptotically stable if $R_{0v}<1$ and unstable if $R_{0v}>1$.

4.5. Global Stability of the Disease Free Equilibrium Point for Plasmodium Vivax Sub-model Only

Theorem-7: The disease free equilibrium point E_0 is globally asymptotically stable if $R_{0v}<1$.

Proof: We define a Lyapunov function $L: R_+^5 \longrightarrow R_+$ by $L(S_h, I_{hv}, T_v, S_m, I_{mv}) = A\left(S_h - S_h^* + S_h^* ln\frac{S_h^*}{S_h}\right) + I_{hv} + T_v + B\left(S_m - S_m^* + S_m^* ln\frac{S_m^*}{S_m}\right) + I_{mv}$, where C *and* D are positive constants. After some calculations, we obtain the value of $\frac{dL}{dt}$ at the DFE point E_0 as: $\frac{dL}{dt}(E_0) = -[A\left(1-\frac{S_h^*}{S_h}\right)^2(\lambda_{hv}+\mu_h)S_h + B\left(1-\frac{S_m^*}{S_m}\right)^2(\lambda_{mv}+\mu_m)S_m]$

Thus, $\frac{dL}{dt}\leq 0$, for any positive constants C *and* D. Furthermore, $\frac{dL}{dt}=0$ at the DFE point E_0. Hence, L is a Lyapunov function. From this we conclude that the DFE E_0 is the only singleton in the region. That is, the largest invariant set contained in the region $\Omega_h = \left\{(S_h, I_{hv}, T_v, S_m, I_{mv}) \in \mathbb{R}_+^5 : \frac{dL}{dt}=0\right\}$ is reduced to the DFE E_0. Therefore, the DFE E_0 is globally asymptotically stable (GAS) on Ω_h if $R_{0v}<1$.

4.6. Existence of Endemic Equilibrium (EE) Point for Plasmodium Vivax Sub-model Only

To find the EE point, we set the right hand side of the non-linear system of differential equations given by (19-23) to zero. Then, an arbitrary endemic equilibrium point E^* is given by $E^* = (S_h^*, I_{hv}^*, T_v^*, S_m^*, I_{mv}^*)$, where

$$S_h^*=\frac{N_{0h}N_h(a_3b\Lambda_h+N_h\mu_me)}{\mu_meN_{0h}^2R_{0v}^2+N_ha_3b\Lambda_h},\ I_{hv}^*=\frac{N_{0h}\mu_h\mu_m(N_{0h}^2R_{0v}^2-N_h^2)}{\mu_meN_{0h}^2R_{0v}^2+N_ha_3b\Lambda_h},\ T_v^*=\frac{\varepsilon N_{0h}\mu_m(N_{0h}^2R_{0v}^2-N_h^2)}{\mu_meN_{0h}^2R_{0v}^2+N_ha_3b\Lambda_h}$$

$$S_m^*=\frac{\Lambda_mN_h(\mu_meN_{0h}^2R_{0v}^2+N_ha_3b\Lambda_h)}{a_3b\,N_{0h}\mu_h\mu_m(N_{0h}^2R_{0v}^2-N_h^2)+\mu_mN_h(\mu_meN_{0h}^2R_{0v}^2+N_ha_3b\Lambda_h)}\ \&\ I_{mv}^*=\frac{\Lambda_ma_3b\,N_{0h}\mu_h(N_{0h}^2R_{0v}^2-N_h^2)}{a_3b\,N_{0h}\mu_h\mu_m(N_{0h}^2R_{0v}^2-N_h^2)+\mu_mN_h(\mu_meN_{0h}^2R_{0v}^2+N_ha_3b\Lambda_h)}$$

4.7. Local Stability of the Endemic Equilibrium Point for Plasmodium Vivax Sub-model Only

Theorem-8: The endemic equilibrium $E^*$of the P. Vivax sub-model (19-23) is locally asymptotically stable if $R_{0v}>1$.

Proof: The Jacobian matrix of the dynamical system (19-23) at the EE point E^* is given by:

$$J(E^*)=\begin{bmatrix} -(\frac{a_1bI_{mv}^*}{N_h}+\mu_h) & 0 & 0 & 0 & -\frac{a_1bS_h^*}{N_h} \\ \frac{a_1bI_{mv}^*}{N_h} & -e & 0 & 0 & \frac{a_1bS_h^*}{N_h} \\ 0 & \varepsilon & -\mu_h & 0 & 0 \\ 0 & -\frac{a_3bS_m^*}{N_h} & 0 & -(\frac{a_3bI_{hv}^*}{N_h}+\mu_m) & 0 \\ 0 & \frac{a_3bS_m^*}{N_h} & 0 & \frac{a_3bI_{hv}^*}{N_h} & -\mu_m \end{bmatrix},$$

where $e = \varepsilon + \delta_v + \mu_h$

The characteristic equation of the Jacobian matrix at the EE point E^* is

$$\begin{vmatrix} -(\frac{a_1 b I_{mv}^*}{N_h} + \mu_h) - \lambda & 0 & 0 & 0 & -\frac{a_1 b S_h^*}{N_h} \\ \frac{a_1 b I_{mv}^*}{N_h} & -e - \lambda & 0 & 0 & \frac{a_1 b S_h^*}{N_h} \\ 0 & \varepsilon & -\mu_h - \lambda & 0 & 0 \\ 0 & -\frac{a_3 b S_m^*}{N_h} & 0 & -(\frac{a_3 b I_{hv}^*}{N_h} + \mu_m) - \lambda & 0 \\ 0 & \frac{a_3 b S_m^*}{N_h} & 0 & \frac{a_3 b I_{hv}^*}{N_h} & -\mu_m - \lambda \end{vmatrix} = 0$$

Simplifying this determinant gives:

$$(-\mu_h - \lambda)(\mu_m + \lambda)(\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0) = 0,$$

where $A_0 = \frac{a_1 b I_{mv}^*}{N_h}(\frac{a_3 b I_{hv}^*}{N_h} + \mu_m)e + \frac{a_3 b I_{hv}^*}{N_h}\mu_h e + \mu_m\mu_h e - \mu_h \frac{a_1 a_3 b^2 S_h^* S_m^*}{N_h^2}$, $A_1 = (\frac{a_1 b I_{mv}^*}{N_h} + \mu_h)(\frac{a_3 b I_{hv}^*}{N_h} + \mu_m + e) + \frac{a_3 b I_{hv}^*}{N_h} e + \mu_m e - \frac{a_1 a_3 b^2 S_h^* S_m^*}{N_h^2}$ and $A_2 = \frac{a_1 b I_{mv}^*}{N_h} + \mu_h + \frac{a_3 b I_{hv}^*}{N_h} + \mu_m + e$.

The first two roots (eigenvalues) of this polynomial are $\lambda_1 = -\mu_h < 0 \; and \; \lambda_2 = -\mu_m < 0$ and the remaining three eigenvalues can be obtained from the cubic polynomial part. We have proved that all coefficients of this cubic polynomial are positive and by Routh-Hurwitz criteria all roots of this cubic polynomial have negative real parts. Therefore, the EE E^* is locally asymptotically stable (LAS) if $R_{0v} > 1$.

4.8. Global Stability of the Endemic Equilibrium Point for Plasmodium Vivax Sub-model Only

Theorem-9: The endemic equilibrium point E^* of the p. vivax sub- model is globally asymptotically stable if $R_{0v} > 1$.

Proof: We define a Lyapunov function $L: R_+^5 \longrightarrow R_+$ by

$$L(S_h, I_{hv}, T_v, S_m, I_{mv}) = A\left(S_h - S_h^* + S_h^* ln\frac{S_h^*}{S_h}\right) + B\left(I_{hv} - I_{hv}^* + I_{hv}^* ln\frac{I_{hv}^*}{I_{hv}}\right) + C\left(T_v - T_v^* + T_v^* ln\frac{T_v^*}{T_v}\right) + D\left(S_m - {S_m}^* + {S_m}^* ln\frac{{S_m}^*}{S_m}\right) + E\left(I_{mv} - I_{mv}^* + I_{mv}^* ln\frac{I_{mv}^*}{I_{mv}}\right)$$

where $A, B, C, Dand\ E$ are positive constants. After some computations, the value of $\frac{dL}{dt}$ at the EE point E^* will be:

$$\frac{dL}{dt} = -[A\left(1 - \frac{S_h^*}{S_h}\right)^2(\lambda_{hv} + \mu_h)S_h + B\left(1 - \frac{I_{hv}^*}{I_{hv}}\right)^2(\varepsilon + \delta_v + \mu_h)I_{hv}$$

$$+C\left(1 - \frac{T_v^*}{T_v}\right)^2\mu_h T_v + D\left(1 - \frac{S_m^*}{S_m}\right)^2(\lambda_{mv} + \mu_m)S_m$$

$$+E\left(1 - \frac{I_{mv}^*}{I_{mv}}\right)^2\mu_m I_{mv}].$$

Thus, $\frac{dL}{dt} \leq 0$ for any positive values of $A, B, C, D \; and \; E$. Furthermore, $\frac{dL}{dt} = 0$ at the EE point E^*. Hence, L is a Lyapunov function. From this we conclude that E^* is the largest compact invariant singleton set in the region.

Therefore, the endemic equilibrium point E^* is globally asymptotically stable (GAS) in the invariant region if $R_{0v} > 1$.

5. The Dynamics of Plasmodium Falciparum Sub-model Only

Using the full model (1-13), the plasmodium falciparum sub-model dynamics is obtained by setting $I_t = R = I_{hv} = C_{vt} = C_{ft} = T_{vt} = T_{ft} = T_{vf} = I_{mv} = 0$ and is given by

$$\frac{dS_h}{dt} = \Lambda_h - (\lambda_{hf} + \mu_h)S_h \quad (24)$$

$$\frac{dI_{hf}}{dt} = \lambda_{hf}S_h - (\varepsilon + \delta_f + \mu_h)I_{hf} \quad (25)$$

$$\frac{dT_f}{dt} = \varepsilon I_{hf} - \mu_h T_f \quad (26)$$

$$\frac{dS_m}{dt} = \Lambda_m - (\lambda_{mf} + \mu_m)S_m \quad (27)$$

$$\frac{dI_{mf}}{dt} = \lambda_{mf}S_m - \mu_m I_{mf} \quad (28)$$

with initial conditions $S_h > 0, I_{hf} \geq 0, T_f \geq 0, S_m >$

$0, I_{mf} \geq 0$, $\lambda_{hf} = \frac{a_2 b I_{mf}}{N_h}$, $\lambda_{mf} = \frac{a_4 b I_{hf}}{N_h}$ and $N_h = S_h + I_{hf} + T_f$ and $N_m = S_m + I_{mf}$.

5.1. Invariant Region, Boundedness and Positivity of Solutions

The total human population is $N_h = S_h + I_{hf} + T_f$. Then, $\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_{hf}}{dt} + \frac{dT_f}{dt}$. After substituting and simplifying different terms we get: $\frac{dN_h}{dt} + \mu_h N_h \leq \Lambda_h$. Thus, $N_h(t) \leq \frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}$. Therefore, $\lim_{t\to\infty} sup\, N_h(t) \leq \lim_{t\to\infty} sup\left(\frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu_h t}\right) = \frac{\Lambda_h}{\mu_h}$. Hence, the system of the sub-model is bounded for the total human population N_h in the region:

$\Omega_h = \left\{\left(S_h, I_{hf}, T_f\right) \in \mathbb{R}^3_+ : 0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$.

Similarly, the total mosquito population is $N_m = S_m + I_{mf}$. Then, $\frac{dN_m}{dt} = \frac{dS_m}{dt} + \frac{dI_{mf}}{dt}$. After substituting and simplifying different terms we get: $\frac{dN_m}{dt} + \mu_m N_m \leq \Lambda_m$. This implies that $N_m(t) \leq \frac{\Lambda_m}{\mu_m} + (N_m(0) - \frac{\Lambda_m}{\mu_m})e^{-\mu_m t}$. Therefore, $\lim_{t\to\infty} sup N_m(t) \leq \lim_{t\to\infty} sup\left(\frac{\Lambda_m}{\mu_m} + (N_m(0) - \frac{\Lambda_m}{\mu_m})e^{-\mu_h t}\right) = \frac{\Lambda_m}{\mu_m}$. Hence, the system of the sub-model is bounded for the total mosquito population N_m in the region:

$$\Omega_m = \left\{\left(S_m, I_{mf}\right) \in \mathbb{R}^2_+ : 0 \leq N_m \leq \frac{\Lambda_m}{\mu_m}\right\}.$$

From Ω_h and Ω_m we can see that the sub-model is well posed epidemiologically and mathematically in the region: $\Omega = \Omega_h \,\mathrm{X}\, \Omega_m \subset \mathbb{R}^3_+ \mathrm{X} \mathbb{R}^2_+ = \left\{\left(S_h, I_{hf}, T_f, S_m, I_{mf}\right) \in \mathbb{R}^5_+ : 0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}; 0 \leq N_m \leq \frac{\Lambda_m}{\mu_m}\right\}$.

5.2. Disease-Free Equilibrium Point for Plasmodium Falciparum Sub-model Only

The disease-free equilibrium (DFE) point of the sub-model (24-28) is obtained by setting $I_{hf} = T_f = I_{mf} = 0$ and is given by $E_0 = (\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_m}{\mu_m}, 0)$.

5.3. Basic Reproduction Number, R_{0f}

Using the next generation matrix we will obtain the reproduction number R_{0f} of the sub-model. In the dynamical system (24-28) the rate of appearance of new infections $\mathcal{F}$ and the transfer rate of individuals V at the disease free equilibrium point $E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_m}{\mu_m}, 0\right)$ are given by the following functions as:

$$F = \begin{bmatrix} 0 & a_2 b \\ \frac{a_4 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 \end{bmatrix}, \mathrm{V} = \begin{bmatrix} (\varepsilon + \delta_f + \mu_h) & 0 \\ 0 & \mu_m \end{bmatrix} \text{ and } \mathrm{V}^{-1} = \begin{bmatrix} \frac{1}{(\varepsilon+\delta_f+\mu_h)} & 0 \\ 0 & \frac{1}{\mu_m} \end{bmatrix}$$

The basic reproduction number R_{0f} of the plasmodium falciparum sub-model only is the largest eigenvalue of the next generation matrix $\mathcal{F}V^{-1}$ and given by $\rho(\mathcal{F}V^{-1}) = R_{0f} = \sqrt{\frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m^2 \Lambda_h (\varepsilon+\delta_f+\mu_h)}} > 0$.

5.4. Local Stability of the Disease Free Equilibrium Point

Theorem-10: The disease free equilibrium point is locally asymptotically stable if $R_{0f} < 1$ and unstable if $R_{0f} > 1$.

Proof: The Jacobian matrix of (24-28) at E_0 is given by:

$$J(E_0) = \begin{bmatrix} -\mu_h & 0 & 0 & 0 & -a_2 b \\ 0 & -(\varepsilon + \delta_f + \mu_h) & 0 & 0 & a_2 b \\ 0 & \varepsilon & -\mu_h & 0 & 0 \\ 0 & -\frac{a_4 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & -\mu_m & 0 \\ 0 & \frac{a_4 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & 0 & -\mu_m \end{bmatrix}$$

The corresponding characteristic equation of the Jacobian matrix is obtained by:

$$\begin{vmatrix} -\mu_h - \lambda & 0 & 0 & 0 & -a_2 b \\ 0 & -(\varepsilon + \delta_f + \mu_h) - \lambda & 0 & 0 & a_2 b \\ 0 & \varepsilon & -\mu_h - \lambda & 0 & 0 \\ 0 & -\frac{a_4 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & -\mu_m - \lambda & 0 \\ 0 & \frac{a_4 b \mu_h \Lambda_m}{\mu_m \Lambda_h} & 0 & 0 & -\mu_m - \lambda \end{vmatrix} = 0$$

Simplifying this determinant gives:

$$(-\mu_h - \lambda)(-\mu_m - \lambda)(-\mu_m - \lambda)[\lambda^2 + (\varepsilon + \delta_f + \mu_h + \mu_m)\lambda + (\varepsilon + \delta_f + \mu_h)\mu_m - \frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h}] = 0$$

$$\Longrightarrow \lambda_1 = -\mu_h, \lambda_2 = \lambda_3 = -\mu_m \text{ or } \lambda_4 = \frac{-(\varepsilon+\delta_f+\mu_h+\mu_m) - \sqrt{(\varepsilon+\delta_f+\mu_h+\mu_m)^2 - 4((\varepsilon+\delta_f+\mu_h)\mu_m - \frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h})}}{2} \text{ or}$$

$$\lambda_5 = \frac{-(\varepsilon+\delta_f+\mu_h+\mu_m)+\sqrt{(\varepsilon+\delta_f+\mu_h+\mu_m)^2-4((\varepsilon+\delta_f+\mu_h)\mu_m-\frac{a_2a_4b^2\mu_h\Lambda_m}{\mu_m\Lambda_h})}}{2}$$

From these eigenvalues we can see that $\lambda_1, \lambda_2, \lambda_3$ *and* λ_4 are all less than zero. So, the DFE will be stable if $\lambda_5 < 0$. Then, $\frac{-(\varepsilon+\delta_f+\mu_h+\mu_m)+\sqrt{(\varepsilon+\delta_f+\mu_h+\mu_m)^2-4((\varepsilon+\delta_f+\mu_h)\mu_m-\frac{a_2a_4b^2\mu_h\Lambda_m}{\mu_m\Lambda_h})}}{2} < 0$. Simplifying this inequality gives: $\sqrt{\frac{a_2a_4b^2\mu_h\Lambda_m}{(\varepsilon+\delta_f+\mu_h)\mu_m^2\Lambda_h}} < 1$. It implies that $R_{0f} < 1$. Therefore, the DFE E_0 is locally asymptotically stable if $R_{0f} < 1$ and unstable if $R_{0f} > 1$.

5.5. Global Stability of the Disease Free Equilibrium Point for Plasmodium Falciparum Sub-Model Only

Theorem-11: The disease free equilibrium point is globally asymptotically stable if $R_{0f} < 1$.

Proof: We define a Lyapunov function $L: R_+^5 \longrightarrow R_+$ by $L(S_h, I_{hf}, T_f, S_m, I_{mf}) = C\left(S_h - S_h^* + S_h^* ln\frac{S_h^*}{S_h}\right) + I_{hf} + T_f + D\left(S_m - S_m^* + S_m^* ln\frac{S_m^*}{S_m}\right) + I_{mf}$, where C *and* D are positive constants. After some calculations, we obtain the value of $\frac{dL}{dt}$ at the DFE point E_0 as: $\frac{dL}{dt}(E_0) = -[C\left(1-\frac{S_h^*}{S_h}\right)^2(\lambda_{hf}+\mu_h)S_h + D\left(1-\frac{S_m^*}{S_m}\right)^2(\lambda_{mf}+\mu_m)S_m]$

Thus, $\frac{dL}{dt} \leq 0$, for any positive constants C *and* D. Furthermore, $\frac{dL}{dt} = 0$ at the DFE point E_0. Hence, L is a Lyapunov function. From this we conclude that the DFE E_0 is the only singleton in the region. That is, the largest invariant set contained in the region $\Omega_h = \left\{(S_h, I_{hf}, T_f, S_m, I_{mf}) \in \mathbb{R}_+^5 : \frac{dL}{dt} = 0\right\}$ is reduced to the DFE E_0. Therefore, the DFE E_0 is globally asymptotically stable (GAS) on Ω_h if $R_{0f} < 1$.

5.6. Existence of Endemic Equilibrium Point

To find the EE point, we set the right hand side of the non-linear system of differential equations given by (24-28) to zero. Then, an arbitrary endemic equilibrium point E^* is given by $E^* = (S_h^*, I_{hf}^*, T_f^*, S_m^*, I_{mf}^*)$, where

$$S_h^* = \frac{N_{0h}N_h(a_4b\Lambda_h+N_h\mu_me)}{\mu_meN_{0h}^2R_{0f}^2+N_ha_4b\Lambda_h},\ I_{hf}^* = \frac{N_{0h}\mu_h\mu_m(N_{0h}^2R_{0f}^2-N_h^2)}{\mu_meN_{0h}^2R_{0f}^2+N_ha_4b\Lambda_h},\ T_f^* = \frac{\varepsilon N_{0h}\mu_m(N_{0h}^2R_{0f}^2-N_h^2)}{\mu_meN_{0h}^2R_{0f}^2+N_ha_4b\Lambda_h},$$

$$S_m^* = \frac{\Lambda_mN_h(\mu_meN_{0h}^2R_{0f}^2+N_ha_4b\Lambda_h)}{a_4b\,N_{0h}\mu_h\mu_m(N_{0h}^2R_{0f}^2-N_h^2)+\mu_mN_h(\mu_meN_{0h}^2R_{0f}^2+N_ha_4b\Lambda_h)}\ \&\ I_{mf}^* = \frac{\Lambda_ma_4b\,N_{0h}\mu_h(N_{0h}^2R_{0f}^2-N_h^2)}{a_4b\,N_{0h}\mu_h\mu_m(N_{0h}^2R_{0f}^2-N_h^2)+\mu_mN_h(\mu_meN_{0h}^2R_{0f}^2+N_ha_4b\Lambda_h)}$$

5.7. Local Stability of the Endemic Equilibrium (EE) Point for Plasmodium Falciparum Sub-model Only

Theorem-12: The endemic equilibrium point E^* of the plasmodium falciparum sub-model (24-28) is locally asymptotically stable if $R_{0f} > 1$.

Proof: The Jacobian matrix of the dynamical system (24-28) at the EE point E^* is given by:

$$J(E^*) = \begin{bmatrix} -(\frac{a_2bI_{mf}^*}{N_h}+\mu_h) & 0 & 0 & 0 & -\frac{a_2bS_h^*}{N_h} \\ \frac{a_2bI_{mf}^*}{N_h} & -e & 0 & 0 & \frac{a_2bS_h^*}{N_h} \\ 0 & \varepsilon & -\mu_h & 0 & 0 \\ 0 & -\frac{a_4bS_m^*}{N_h} & 0 & -(\frac{a_4bI_{hf}^*}{N_h}+\mu_m) & 0 \\ 0 & \frac{a_4bS_m^*}{N_h} & 0 & \frac{a_4bI_{hf}^*}{N_h} & -\mu_m \end{bmatrix},$$

where $e = \varepsilon + \delta_f + \mu_h$

The characteristic equation of the Jacobian matrix at the point E^* is

$$\begin{vmatrix} -(\frac{a_2bI_{mf}^*}{N_h}+\mu_h)-\lambda & 0 & 0 & 0 & -\frac{a_2bS_h^*}{N_h} \\ \frac{a_2bI_{mf}^*}{N_h} & -e-\lambda & 0 & 0 & \frac{a_2bS_h^*}{N_h} \\ 0 & \varepsilon & -\mu_h-\lambda & 0 & 0 \\ 0 & -\frac{a_4bS_m^*}{N_h} & 0 & -(\frac{a_4bI_{hf}^*}{N_h}+\mu_m)-\lambda & 0 \\ 0 & \frac{a_4bS_m^*}{N_h} & 0 & \frac{a_4bI_{hf}^*}{N_h} & -\mu_m-\lambda \end{vmatrix} = 0$$

Simplifying this determinant gives:
$(-\mu_h-\lambda)(\mu_m+\lambda)(\lambda^3+A_2\lambda^2+A_1\lambda+A_0)=0$, where

$$A_0=\frac{a_2bI^*_{mf}}{N_h}\left(\frac{a_4bI^*_{hf}}{N_h}+\mu_m\right)e+\frac{a_4bI^*_{hf}}{N_h}\mu_he+\mu_m\mu_he-\mu_h\frac{a_2a_4b^2S^*_hS^*_m}{N_h^2},\ A_1=\left(\frac{a_2bI^*_{mf}}{N_h}+\mu_h\right)\left(\frac{a_4bI^*_{hf}}{N_h}+\mu_m+e\right)+\frac{a_4bI^*_{hf}}{N_h}e+\mu_me-\frac{a_2a_4b^2S^*_hS^*_m}{N_h^2}\text{ and }A_2=\frac{a_2bI^*_{mf}}{N_h}+\mu_h+\frac{a_4bI^*_{hf}}{N_h}+\mu_m+e.$$

The first two roots (eigenvalues) of this polynomial are $\lambda_1=-\mu_h<0\ and\ \lambda_2=-\mu_m<0$ and the remaining three eigenvalues can be obtained from the cubic polynomial part. We have proved that all coefficients of this cubic polynomial are positive and by Routh-Hurwitz criteria all roots of this cubic polynomial have negative real parts. Therefore, the EE E^* is locally asymptotically stable (LAS) if $R_{0f}>1$.

5.8. Global Stability of the Endemic Equilibrium Point for Plasmodium Falciparum Sub-model Only

Theorem-13: The endemic equilibrium E^* of the plasmodium falciparum sub- model (24-28) is globally asymptotically stable if $R_{0f}>1$.

Proof: We define a Lyapunov function $L:R_+^5\longrightarrow R_+$ by $L(S_h,I_{hf},T_f,S_m,I_{mf})=A\left(S_h-S_h^*+S_h^*ln\frac{S_h^*}{S_h}\right)+B\left(I_{hf}-I_{hf}^*+I_{hf}^*ln\frac{I_{hf}^*}{I_{hf}}\right)+C\left(T_f-T_f^*+T_f^*ln\frac{T_f^*}{T_f}\right)+D\left(S_m-S_m^*+S_m^*ln\frac{S_m^*}{S_m}\right)+E\left(I_{mf}-I_{mf}^*+I_{mf}^*ln\frac{I_{mf}^*}{I_{mf}}\right)$, where $A,B,C,D\ and\ E$ are positive constants. After some calculations, the value of $\frac{dL}{dt}$ at the EE point E^* will be: $\frac{dL}{dt}=-[A\left(1-\frac{S_h^*}{S_h}\right)^2(\lambda_{hf}+\mu_h)S_h+B\left(1-\frac{I_{hf}^*}{I_{hf}}\right)^2(\varepsilon+\delta_f+\mu_h)I_{hf}+C\left(1-\frac{T_f^*}{T_f}\right)^2\mu_hT_f+D\left(1-\frac{S_m^*}{S_m}\right)^2(\lambda_{mf}+\mu_m)S_m+E\left(1-\frac{I_{mf}^*}{I_{mf}}\right)^2\mu_mI_{mf}]$

Thus, $\frac{dL}{dt}\le 0$ for any positive values of $A,B,C,D\ and\ E$. Furthermore, $\frac{dL}{dt}=0$ at the EE point E^*. Hence, L is a Lyapunov function. From this we conclude that E^* is the largest compact invariant singleton set in the region. Therefore, the endemic equilibrium point E^* is globally asymptotically stable (GAS) in the invariant region if $R_{0f}>1$.

6. The Full Dynamics of the Co-Infection of *P. vivax*, *P. Falciparum* Malaria and Typhoid Fever Model

After we analyzed the dynamics of the three sub-models, that is, Typhoid Fever-only, Plasmodium Vivax and Plasmodium Falciparum-only models, the full typhoid fever and malaria co-infection model (1-13) will be considered and analyzed in the positively invariant region Ω.

6.1. Disease-Free Equilibrium Point for the Full Model

The disease-free equilibrium point E_0 of the non-linear system of differential equations given by (1-13) is obtained by setting $I_t=R=I_{hv}=I_{hf}=C_{vt}=C_{ft}=T_{vt}=T_{ft}=T_{vf}=I_{mv}=I_{mf}=0$. Thus,

$$E_0=\left(\frac{\Lambda_h}{\mu_h},0,0,0,0,0,0,0,0,0,\frac{\Lambda_m}{\mu_m},0,0\right).$$

6.2. The Basic Reproduction Number, R_0 for the Full Model

Using the next generation matrix we will obtain the co-infection reproduction number R_0 of the model (1-13). In the dynamical system (1-13) the rate of appearance of new infections $\mathcal{F}$ and the transfer rate of individuals V at the disease free equilibrium point E_0 are given by the following functions as:

$$\mathrm{F}=\begin{bmatrix}\beta&0&0&0&0\\0&0&0&a_1b&0\\0&0&0&0&a_2b\\0&\frac{a_3b\mu_h\Lambda_m}{\mu_m\Lambda_h}&0&0&0\\0&0&\frac{a_4b\mu_h\Lambda_m}{\mu_m\Lambda_h}&0&0\end{bmatrix},\ \mathrm{V}=\begin{bmatrix}e_1&0&0&0&0\\0&e_2&0&0&0\\0&0&e_3&0&0\\0&0&0&\mu_m&0\\0&0&0&0&\mu_m\end{bmatrix}\text{ and }\mathrm{V}^{-1}=\begin{bmatrix}\frac{1}{e_1}&0&0&0&0\\0&\frac{1}{e_2}&0&0&0\\0&0&\frac{1}{e_3}&0&0\\0&0&0&\frac{1}{\mu_m}&0\\0&0&0&0&\frac{1}{\mu_m}\end{bmatrix}$$

Hence, the basic reproduction number R_0 of the full dynamics of the co-infection of Plasmodium vivax, Plasmodium falciparum and typhoid fever is the largest eigenvalue of the next generation matrix $\mathcal{F}V^{-1}$ or the spectral radius of $\mathcal{F}V^{-1}$ and given by $R_0=Max\{R_{0t},R_{0v},R_{0f}\}$, where $R_{0t}=\frac{\beta}{(\omega+\delta_t+\mu_h)}$, $R_{0v}=\sqrt{\frac{a_1a_3b^2\mu_h\Lambda_m}{\mu_m^2\Lambda_h(\varepsilon+\delta_v+\mu_h)}}$ and $R_{0f}=\sqrt{\frac{a_2a_4b^2\mu_h\Lambda_m}{\mu_m^2\Lambda_h(\varepsilon+\delta_f+\mu_h)}}$.

6.3. Local Stability of the Disease Free Equilibrium Point for the Full Model

Theorem-14: The disease free equilibrium point E_0 of the co-infection of Plasmodium vivax, Plasmodium falciparum

malaria and typhoid fever is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: The Jacobian Matrix of the model at the disease free equilibrium E_0 is given by

$$J(E_0) = \begin{bmatrix} -\mu_h & -\beta & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -a_1 b & -a_2 b \\ 0 & \beta - e_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \omega & -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -e_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_1 b & 0 \\ 0 & 0 & 0 & 0 & -e_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_2 b \\ 0 & 0 & 0 & 0 & 0 & -e_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -e_5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \phi_1 & 0 & -\mu_h & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi_2 & 0 & -\mu_h & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \varepsilon & \varepsilon & 0 & 0 & 0 & 0 & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{-a_3 b\mu_h\Lambda_m}{\mu_m\Lambda_h} & \frac{-a_4 b\Lambda_m}{\mu_m\Lambda_h} & \frac{-a_3 b\eta_1\mu_h\Lambda_m}{\mu_m\Lambda_h} & \frac{-a_4 b\eta_2\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & 0 & 0 & -\mu_m & 0 & 0 \\ 0 & 0 & 0 & \frac{a_3 b\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & \frac{a_3 b\eta_1\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & 0 & 0 & 0 & 0 & -\mu_m & 0 \\ 0 & 0 & 0 & 0 & \frac{a_4 b\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & \frac{a_4 b\eta_2\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & 0 & 0 & 0 & 0 & -\mu_m \end{bmatrix}$$

The corresponding characteristic equation of the Jacobian matrix is

$$\begin{vmatrix} -\mu_h - \lambda & -\beta & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -a_1 b & -a_2 b \\ 0 & \beta - e_1 - \lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \omega & -\mu_h - \lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -e_2 - \lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_1 b & 0 \\ 0 & 0 & 0 & 0 & -e_3 - \lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_2 b \\ 0 & 0 & 0 & 0 & 0 & -e_4 - \lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -e_5 - \lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \phi_1 & 0 & -\mu_h - \lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi_2 & 0 & -\mu_h - \lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \varepsilon & \varepsilon & 0 & 0 & 0 & 0 & -\mu_h - \lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{-a_3 b\mu_h\Lambda_m}{\mu_m\Lambda_h} & \frac{-a_4 b\Lambda_m}{\mu_m\Lambda_h} & \frac{-a_3 b\eta_1\mu_h\Lambda_m}{\mu_m\Lambda_h} & \frac{-a_4 b\eta_2\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & 0 & 0 & -\mu_m - \lambda & 0 & 0 \\ 0 & 0 & 0 & \frac{a_3 b\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & \frac{a_3 b\eta_1\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & 0 & 0 & 0 & 0 & -\mu_m - \lambda & 0 \\ 0 & 0 & 0 & 0 & \frac{a_4 b\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & \frac{a_4 b\eta_2\mu_h\Lambda_m}{\mu_m\Lambda_h} & 0 & 0 & 0 & 0 & 0 & -\mu_m - \lambda \end{vmatrix} = 0$$

Simplifying this determinant gives

$$(-\mu_h - \lambda)^5(\beta - e_1 - \lambda)(-e_4 - \lambda)(-e_5 - \lambda)(-\mu_m - \lambda)\left[(e_2 + \lambda)(\mu_m + \lambda) - \frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h}\right]$$

$$[(e_3 + \lambda)(\mu_m + \lambda) - \frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h}] = 0$$

$$\Longrightarrow \lambda_1 = \lambda_2 = \lambda_3 = \lambda_4 = \lambda_5 = -\mu_h, \lambda_6 = \beta - e_1, \lambda_7 = -e_4, \lambda_8 = -e_5, \lambda_9 = -\mu_m,$$

$$\lambda_{10} = \frac{-(e_2+\mu_m) - \sqrt{(e_2+\mu_m)^2 - 4(e_2\mu_m - \frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h})}}{2}, \lambda_{11} = \frac{-(e_2+\mu_m) + \sqrt{(e_2+\mu_m)^2 - 4(e_2\mu_m - \frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h})}}{2},$$

$$\lambda_{12} = \frac{-(e_3+\mu_m) - \sqrt{(e_3+\mu_m)^2 - 4(e_3\mu_m - \frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h})}}{2} \text{ and } \lambda_{13} = \frac{-(e_3+\mu_m) + \sqrt{(e_3+\mu_m)^2 - 4(e_3\mu_m - \frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h})}}{2}$$

where, $e_1 = \omega + \delta_t + \mu_h, e_2 = \varepsilon + \delta_v + \mu_h, e_3 = \varepsilon + \delta_f + \mu_h$

From these eigenvalues we can see that $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_7, \lambda_8, \lambda_9, \lambda_{10}$ *and* λ_{12} are all less than zero. So, the DFE will be stable if $\lambda_6 < 0, \lambda_{11} < 0$ *and* $\lambda_{13} < 0$. Then, $\lambda_6 = \beta - e_1 = e_1(R_{0t} - 1) < 0$ if $R_{0t} < 1$.

Next, we have $\frac{-(e_2+\mu_m)}{2} + \sqrt{\frac{(e_2-\mu_m)^2}{4} + \frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m \Lambda_h}} < 0$. Simplifying this gives $\sqrt{\frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m^2 \Lambda_h (\varepsilon + \delta_v + \mu_h)}} < 1$.

Hence, $R_{0v} < 1$. Similarly, $\sqrt{\frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m^2 \Lambda_h (\varepsilon + \delta_f + \mu_h)}} < 1$ and $R_{0f} < 1$. So, $R_0 < 1$ if $R_{0t} < 1, R_{0v} < 1$ *and* $R_{0f} < 1$.

Finally, the DFE E_0 of the co-infection of Plasmodium vivax, Plasmodium falciparum malaria and typhoid fever is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

6.4. Global Stability of the Disease Free Equilibrium Point for the Full Model

Theorem-15: The disease free equilibrium point E_0 of the co-infection of malaria and typhoid fever is globally asymptotically stable (GAS) if $R_0 < 1$.

Proof: We define a Lyapunov function $L: R_+^{13} \longrightarrow R_+$ by $L(S_h, I_t, R, I_{hv}, I_{hf}, C_{vt}, C_{ft}, T_{vt}, T_{ft}, T_{vf}, S_m, I_{mv}, I_{mf}) = A\left(S_h - S_h^* + S_h^* ln\frac{S_h^*}{S_h}\right) + I_t + R + I_{hv} + I_{hf} + C_{vt} + C_{ft} + T_{vt} + T_{ft} + T_{vf} + B\left(S_m - S_m^* + S_m^* ln\frac{S_m^*}{S_m}\right) + I_{mv} + I_{mf}$.

After some calculations, we get the value of $\frac{dL}{dt}$ at E_0 as:

$$\frac{dL}{dt} = -[A\left(1 - \frac{S_h^*}{S_h}\right)^2 e_1 S_h + B\left(1 - \frac{S_m^*}{S_m}\right)^2 e_6 S_m]$$

Thus, $\frac{dL}{dt} \leq 0$, for any positive constants A and B. Furthermore, $\frac{dL}{dt} = 0$ at the DFE point E_0. Hence, L is a Lyapunov function. From this we conclude that the DFE E_0 is the only singleton in the region. That is, the largest invariant set contained in $\Omega = \left\{(S_h, I_t, R, \dots, I_{mf}) \in \mathbb{R}_+^{13} : \frac{dL}{dt} = 0\right\}$ is reduced to the DFE E_0. Therefore, the DFE E_0 is globally asymptotically stable on Ω if $R_0 < 1$.

6.5. Existence of Endemic Equilibrium Point for the Full Model

To determine the endemic equilibrium point of the dynamical system (1-13) we make the right hand side of the dynamical system equal to zero and we solve for the state variables in termof positive force of infections and other parameters. Then, we obtained the endemic equilibrium point $E^* = (S_h^*, I_t^*, R^*, I_{hv}^*, I_{hf}^*, C_{vt}^*, C_{ft}^*, T_{vt}^*, T_{ft}^*, T_{vf}^*, S_m^*, I_{mv}^*, I_{mf}^*)$ where,

$$S_h^* = \frac{\Lambda_h}{\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h}, I_t^* = \frac{\Lambda_h \lambda_t^*}{(\alpha_1 \lambda_{hv}^* + \alpha_2 \lambda_{hf}^* + e_1)(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}, R^* = \frac{\omega \Lambda_h \lambda_t^*}{\mu_h(\alpha_1 \lambda_{hv}^* + \alpha_2 \lambda_{hf}^* + e_1)(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)},$$

$$I_{hv}^* = \frac{\Lambda_h \lambda_{hv}^*}{(\gamma \lambda_t^* + e_2)(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}, I_{hf}^* = \frac{\Lambda_h \lambda_{hf}^*}{(\gamma \lambda_t^* + e_3)(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}, C_{vt}^* = \frac{\Lambda_h \lambda_{hv}^* \lambda_t^*}{e_4(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}\left(\frac{\gamma}{(\gamma \lambda_t^* + e_2)} + \frac{\alpha_1}{(\alpha_1 \lambda_{hv}^* + \alpha_2 \lambda_{hf}^* + e_1)}\right),$$

$$C_{ft}^* = \frac{\Lambda_h \lambda_{hf}^* \lambda_t^*}{e_5(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}\left(\frac{\gamma}{(\gamma \lambda_t^* + e_3)} + \frac{\alpha_2}{(\alpha_1 \lambda_{hv}^* + \alpha_2 \lambda_{hf}^* + e_1)}\right), T_{vt}^* = \frac{\phi_1 \Lambda_h \lambda_{hv}^* \lambda_t^*}{\mu_h e_4(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}\left(\frac{\gamma}{(\gamma \lambda_t^* + e_2)} + \frac{\alpha_1}{(\alpha_1 \lambda_{hv}^* + \alpha_2 \lambda_{hf}^* + e_1)}\right),$$

$$T_{ft}^* = \frac{\phi_2 \Lambda_h \lambda_{hf}^* \lambda_t^*}{\mu_h e_5(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}\left(\frac{\gamma}{(\gamma \lambda_t^* + e_3)} + \frac{\alpha_2}{(\alpha_1 \lambda_{hv}^* + \alpha_2 \lambda_{hf}^* + e_1)}\right), T_{vf}^* = \frac{\varepsilon \Lambda_h}{\mu_h(\lambda_{hv}^* + \lambda_{hf}^* + \lambda_t^* + \mu_h)}\left(\frac{\lambda_{hv}^*}{(\gamma \lambda_t^* + e_2)} + \frac{\lambda_{hf}^*}{(\gamma \lambda_t^* + e_3)}\right),$$

$$S_m^* = \frac{\Lambda_m}{\lambda_{mv}^* + \lambda_{mf}^* + \mu_m}, I_{mv}^* = \frac{\Lambda_m \lambda_{mv}^*}{\mu_m(\lambda_{mv}^* + \lambda_{mf}^* + \mu_m)}, I_{mf}^* = \frac{\Lambda_m \lambda_{mf}^*}{\mu_m(\lambda_{mv}^* + \lambda_{mf}^* + \mu_m)} \text{ with } e_1 = \omega + \delta_t + \mu_h, e_2 = \varepsilon + \delta_v + \mu_h,$$

$$e_3 = \varepsilon + \delta_f + \mu_h, e_4 = \phi_1 + \theta_1 \delta_{vt} + \mu_h \text{ and } e_5 = \phi_2 + \theta_2 \delta_{ft} + \mu_h.$$

After substituting appropriate values of one into the other and simplifying expressions we get

$$\lambda_{hv}^*[A_1(\lambda_{hv}^*)^2 + A_2 \lambda_{hv}^* + A_3] = 0,$$

where A_1, A_2 and A_3 are constants. Since $\lambda_{hv}^* = 0$ corresponds to the DFE of the system, we consider the second quadratic equation to determine the EE point of the model given by

$$A_1(\lambda_{hv}^*)^2 + A_2 \lambda_{hv}^* + A_3 \quad (29)$$

Thus, positive endemic equilibrium points E^* are obtained by solving for λ_{hv}^* from the quadratic equation (29). Then, the number of possible real roots of this quadratic polynomial depends on the signs of A_1, A_2 and A_3. Therefore, the co-infection dynamical system will have an endemic equilibrium point E^* when:

Case-1: $A_1 > 0, A_2 < 0$, and $A_2^2 - 4A_1A_3 = 0$

Case-2: $A_1 < 0, A_2 > 0$, and $A_2^2 - 4A_1A_3 = 0$

Case-3: $A_1 > 0, A_2 < 0$, and $A_3 = 0$

Case-4: $A_1 > 0, A_2 > 0, A_2^2 - 4A_1A_3 > 0$ and $\sqrt{A_2^2 - 4A_1A_3} > A_2$

Case-5: $A_1 < 0, A_2 > 0, A_2^2 - 4A_1A_3 > 0$ and $\sqrt{A_2^2 - 4A_1A_3} > A_2$

Finally, from the above cases we conclude that we can get an endemic equilibrium point E^* in the first quadrant for the full co-infection dynamics of typhoid fever and malaria diseases.

6.6. Local Stability of Endemic Equilibrium Point

Theorem-16: The endemic equilibrium E^* of the co-infection of malaria and typhoid fever model (1-13) is locally asymptotically stable (LAS) if $R_0 > 1$.

Proof: The Jacobian matrix of the dynamical system (1-13) at the EE point E^* is given by:

$$J(E^*)=\begin{bmatrix}
-D_1 & -D_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -D_3 & -D_4\\
\lambda_t^* & D_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -D_6 & -D_7\\
0 & \omega & -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
\lambda_{hv}^* & -D_8 & 0 & -D_9 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & D_3 & 0\\
\lambda_{hf}^* & -D_{10} & 0 & 0 & -D_{11} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & D_4\\
0 & D_{12} & 0 & \gamma\,\lambda_t^* & 0 & -e_4 & 0 & 0 & 0 & 0 & 0 & D_6 & 0\\
0 & D_{13} & 0 & 0 & \gamma\,\lambda_t^* & 0 & -e_5 & 0 & 0 & 0 & 0 & 0 & D_7\\
0 & 0 & 0 & 0 & 0 & \phi_1 & 0 & -\mu_h & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & \phi_2 & 0 & -\mu_h & 0 & 0 & 0 & 0\\
0 & 0 & 0 & \varepsilon & \varepsilon & 0 & 0 & 0 & 0 & -\mu_h & 0 & 0 & 0\\
0 & 0 & 0 & -D_{14} & -D_{15} & -D_{16} & -D_{17} & 0 & 0 & 0 & -D_{18} & 0 & 0\\
0 & 0 & 0 & D_{14} & 0 & D_{16} & 0 & 0 & 0 & 0 & \lambda_{mv}^* & -\mu_m & 0\\
0 & 0 & 0 & 0 & D_{15} & 0 & D_{17} & 0 & 0 & 0 & \lambda_{mf}^* & 0 & -\mu_m
\end{bmatrix}$$

where, $D_1=(\lambda_{hv}^*+\lambda_{hf}^*+\lambda_t^*+\mu_h)$, $D_2=\frac{\beta}{N_h}S_h^*$, $D_3=\frac{a_1 b}{N_h}S_h^*$, $D_4=\frac{a_2 b}{N_h}S_h^*$ $D_5=D_2-(\alpha_1\lambda_{hv}^*+\alpha_2\lambda_{hf}^*+e_1)$, $D_6=\frac{\alpha_1 a_1 b}{N_h}I_t^*$, $D_7=\frac{\alpha_2 a_2 b}{N_h}I_t^*$, $D_8=\frac{\gamma\beta}{N_h}I_{hv}^*$, $D_9=\gamma\,\lambda_t^*+e_2$, $D_{10}=\frac{\gamma\beta}{N_h}I_{hf}^*$, $D_{11}=(\gamma\,\lambda_t^*+e_3)$, $D_{12}=D_8+\alpha_1\lambda_{hv}^*$, $D_{13}=D_{10}+\alpha_2\lambda_{hf}^*$, $D_{14}=\frac{a_3 b}{N_h}S_m^*$, $D_{15}=\frac{a_4 b}{N_h}S_m^*$, $D_{16}=\frac{a_3 b\eta_1 S_m}{N_h}$, $D_{17}=\frac{a_4 b\eta_2 S_m}{N_h}$, $D_{18}=(\lambda_{mv}^*+\lambda_{mf}^*+\mu_m)$

The characteristic equation of the Jacobian matrix at the EE point E^* is

$$\begin{vmatrix}
-D_1-\lambda & -D_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -D_3 & -D_4\\
\lambda_t^* & D_5-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -D_6 & -D_7\\
0 & \omega & -\mu_h-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
\lambda_{hv}^* & -D_8 & 0 & -D_9-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & D_3 & 0\\
\lambda_{hf}^* & -D_{10} & 0 & 0 & -D_{11}-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & D_4\\
0 & D_{12} & 0 & \gamma\,\lambda_t^* & 0 & -e_4-\lambda & 0 & 0 & 0 & 0 & 0 & D_6 & 0\\
0 & D_{13} & 0 & 0 & \gamma\,\lambda_t^* & 0 & -e_5-\lambda & 0 & 0 & 0 & 0 & 0 & D_7\\
0 & 0 & 0 & 0 & 0 & \phi_1 & 0 & -\mu_h-\lambda & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & \phi_2 & 0 & -\mu_h-\lambda & 0 & 0 & 0 & 0\\
0 & 0 & 0 & \varepsilon & \varepsilon & 0 & 0 & 0 & 0 & -\mu_h-\lambda & 0 & 0 & 0\\
0 & 0 & 0 & -D_{14} & -D_{15} & -D_{16} & -D_{17} & 0 & 0 & 0 & -D_{18}-\lambda & 0 & 0\\
0 & 0 & 0 & D_{14} & 0 & D_{16} & 0 & 0 & 0 & 0 & \lambda_{mv}^* & -\mu_m-\lambda & 0\\
0 & 0 & 0 & 0 & D_{15} & 0 & D_{17} & 0 & 0 & 0 & \lambda_{mf}^* & 0 & -\mu_m-\lambda
\end{vmatrix}=0$$

After simplifying this determinant, we get:

$$(\lambda+\mu_h)^4[\lambda^9+P_1\lambda^8-P_2\lambda^7+P_3\lambda^6+P_4\lambda^5+P_5\lambda^4+P_6\lambda^3+P_7\lambda^2+P_8\lambda-P_9]=0$$

where $P_i, i=1,\dots 9$ are constants. Thus, the roots of this polynomial are given by: $\lambda_1=\lambda_2=\lambda_3=\lambda_4=-\mu_h<0$ or

$$\lambda^9+P_1\lambda^8-P_2\lambda^7+P_3\lambda^6+P_4\lambda^5+P_5\lambda^4+P_6\lambda^3+P_7\lambda^2+P_8\lambda-P_9=0 \quad (30)$$

Here in applying Routh-Hurwitz stability criterion for the polynomial (30) of degree nine we proved that when $R_0>1$ all roots of the polynomial equation has negative real parts. Therefore, the endemic equilibrium point E^* is locally asymptotically stable (LAS) if $R_0>1$.

6.7. Global Stability of Endemic Equilibrium Point

Theorem-17: The endemic equilibrium E^* of the co-infection of malaria and typhoid fever model (1-13) is globally asymptotically stable (GAS) if $R_0>1$

Proof: We define a Lyapunov function $L: R_+^{13}\longrightarrow R_+$ by $L\left(S_h,I_t,R,I_{hv},I_{hf},C_{vt},C_{ft},T_{vt},T_{ft},T_{vf},S_m,I_{mv},I_{mf}\right)=$
$J_1\left(S_h-S_h^*+S_h^* ln\frac{S_h^*}{S_h}\right)+J_2\left(I_t-I_t^*+I_t^* ln\frac{I_t^*}{I_t}\right)+$
$J_3\left(R-R^*+R^* ln\frac{R^*}{R}\right)+J_4\left(I_{hv}-I_{hv}^*+I_{hv}^* ln\frac{I_{hv}^*}{I_{hv}}\right)+$
$J_5\left(I_{hf}-I_{hf}^*+I_{hf}^* ln\frac{I_{hf}^*}{I_{hf}}\right)+J_6\left(C_{vt}-C_{vt}^*+C_{vt}^* ln\frac{C_{vt}^*}{C_{vt}}\right)+$
$J_7\left(C_{ft}-C_{ft}^*+C_{ft}^* ln\frac{C_{ft}^*}{C_{ft}}\right)+J_8\left(T_{vt}-T_{vt}^*+T_{vt}^* ln\frac{T_{vt}^*}{T_{vt}}\right)+$
$J_9\left(T_{ft}-T_{ft}^*+T_{ft}^* ln\frac{T_{ft}^*}{T_{ft}}\right)+J_{10}\left(T_{vf}-T_{vf}^*+T_{vf}^* ln\frac{T_{vf}^*}{T_{vf}}\right)+$
$J_{11}\left(S_m-S_m^*+S_m^* ln\frac{S_m^*}{S_m}\right)+J_{12}\left(I_{mv}-I_{mv}^*+I_{mv}^* ln\frac{I_{mv}^*}{I_{mv}}\right)+$
$J_{13}\left(I_{mf}-I_{mf}^*+I_{mf}^* ln\frac{I_{mf}^*}{I_{mf}}\right)$, where $J_1,J_2,J_3,\dots,J_{13}$ are positive constants. Again after some calculations, we obtain the value of $\frac{dL}{dt}$ at the EE E^* as:

$$\frac{dL}{dt}=-[J_1\left(1-\frac{S_h^*}{S_h}\right)^2(\lambda_{hv}+\lambda_{hf}+\lambda_t+\mu_h)S_h+J_2\left(1-\frac{I_t^*}{I_t}\right)^2(\alpha_1\lambda_{hv}+\alpha_2\lambda_{hf}+\omega+\delta_t+\mu_h)I_t+J_3\left(1-\frac{R^*}{R}\right)^2\mu_h R$$

$$+J_4\left(1-\frac{I_{hv}^*}{I_{hv}}\right)^2(\gamma\lambda_t+\varepsilon+\delta_v+\mu_h)I_{hv}+J_5\left(1-\frac{I_{hf}^*}{I_{hf}}\right)^2(\gamma\lambda_t+\varepsilon+\delta_f+\mu_h)I_{hf}+J_6\left(1-\frac{C_{vt}^*}{C_{vt}}\right)^2(\phi_1+\theta_1\delta_{vt}+\mu_h)C_{vt}$$
$$+J_7\left(1-\frac{C_{ft}^*}{C_{ft}}\right)^2(\phi_2+\theta_2\delta_{ft}+\mu_h)C_{ft}+J_8\left(1-\frac{T_{vt}^*}{T_{vt}}\right)^2\mu_hT_{vt}+J_9\left(1-\frac{T_{ft}^*}{T_{ft}}\right)^2\mu_hT_{ft}+J_{10}\left(1-\frac{T_{vf}^*}{T_{vf}}\right)^2\mu_hT_{vf}$$
$$+J_{11}\left(1-\frac{S_m^*}{S_m}\right)^2(\lambda_{mv}+\lambda_{mf}+\mu_m)S_m+J_{12}\left(1-\frac{I_{mv}^*}{I_{mv}}\right)^2\mu_mI_{mv}+J_{13}\left(1-\frac{I_{mf}^*}{I_{mf}}\right)^2\mu_mI_{mf}]$$

Thus, $\frac{dL}{dt}\leq 0$ for any positive values of $J_1, J_2, J_3, \dots, J_{12}\ and\ J_{13}$. Furthermore, $\frac{dL}{dt}=0$ at the EE point. Hence, L is a Lyapunov function. From this we conclude that E^* is the largest compact invariant singleton set in the region. Therefore, the endemic equilibrium point E^* is globally asymptotically stable (GAS) in the invariant region if $R_0>1$.

7. Numerical Simulations

In this section we will present numerical simulations of our models in order to illustrate our theoretical and mathematical results which were previously established. The simulations describe the dynamics of typhoid fever only, p. vivax only and p. falciparum only separately based on parameter values obtained from different sources.

Table 2. *Typhoid fever and malaria model parameter values and their descriptions.*

Parameters Descriptions	Parameters	Values	Source
New recruitment rate into the susceptible human population	Λ_h	0.05/day	[18]
New recruitment rate into the susceptible mosquito population	Λ_m	1000/day	[19]
Natural death rate for human population	μ_h	0.00004/day	[21]
Natural death rate for mosquito population	μ_m	0.1429/day	[18]
Typhoid fever disease- induced death rate	δ_t	0.002/day	[21]
The treatment rate of humans from typhoid fever.	ω	0.002485/day	[11]
The effective transmission rate of typhoid fever on contact	β	0.01/day	[19]
Plasmodium vivax disease- induced death rate	δ_v	0.068/day	[17]
Plasmodium falciparum disease- induced death rate	δ_f	0.0019/day	[21]
The transmission probability of human infection due to per bite of an infected mosquito with plasmodium vivax	a_1	0.8333/day	[18]
The transmission probability of human infection due to per bite of an infected mosquito with plasmodium falciparum	a_2	0.15096/day	[21]
The transmission probability that a mosquito will become infected by biting an infected human with plasmodium vivax	a_3	0.48/day	[36]
The transmission probability that a mosquito will become infected by biting an infected human with p. falciparum	a_4	0.24/day	[17]
Per capita biting rate of mosquito	b	0.29/day	[17]
The rate of treatment for malaria	ε	0.038 /day	[21]

Next, to get a clear idea about the numerical analysis of the co-infection of p. vivax, p. falciparum malaria and typhoid fever we consider the following cases one by one as follows.

Case-1: If the basic reproduction number $R_0<1$ i.e. $R_{0t}<1$, $R_{0v}<1$ and $R_{0f}<1$, then the co-infection of p. vivax, p. falciparum malaria and typhoid fever dies out with time and approaches the disease free equilibrium point E_0 when appropriate treatment is considered for the single disease infected or the co-infected population.

Case-2: If the basic reproduction number $R_0>1$ i.e. $R_{0t}>1$, $R_{0v}>1$ and $R_{0f}>1$, there is always a co-existence of p. vivax, p. falciparum malaria and typhoid fever no matter which of the reproduction numbers is greater. Hereafter, we consider the case when $R_0>1$ for the co-infection of the diseases.

Case-3: If $R_0=Max\{R_{0t},R_{0v},R_{0f}\}=R_{0t}$ and $R_{0t}<1$, then the co-infection of p. vivax, p. falciparum malaria and typhoid fever dies out with time and it can't be endemic disease in the community for long period of time. But, if $R_0=Max\{R_{0t},R_{0v},R_{0f}\}=R_{0t}$ and $R_{0t}>1$ and also the others are less than unity, then the typhoid fever disease persists in the population. That means if $R_{0t}>1$, $R_{0v}<1$ and $R_{0f}<1$, the malaria disease dies out with time and the typhoid fever disease continues to be endemic in the community. This implies that the co-infection of malaria and typhoid fever decreases in the community. On the other hand, if $R_{0t}>1$, $R_{0v}>1$ and $R_{0f}>1$, the typhoid fever disease enhances or aggravates the co-infection disease in the community and we need to control it using different treatment methods so as to reduce the co-infection dynamics of the disease. Thus, the numerical analysis of the typhoid fever disease under this situation will be discussed as follow.

7.1. Estimation of Basic Reproduction Number R_{0t}

We computed $R_{0t}=2.20994475138>1$ and the typhoid fever disease spreads in the community.

7.1.1. R_{0t} Versus β

From figure 2 we observe that if $\beta<0.004525$, then R_{0t}

increases but $R_{0t} < 1$ and the typhoid fever disease does not spread in the community and hence, it dies out through time. If $\beta > 0.004525$, then R_{0t} increases with $R_{0t} > 1$ and the typhoid fever disease persists in the community.

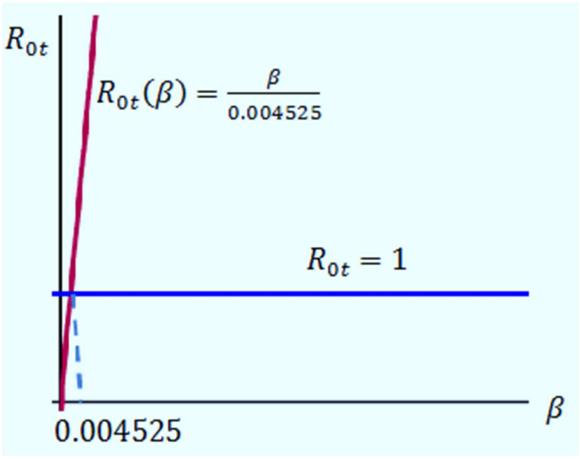

Figure 2. *The graph of the reproduction number R_{0t} versus the effective transmission rate β of typhoid fever on contact parameter keeping all other parameters constant.*

7.1.2. R_{0t} Versus ω

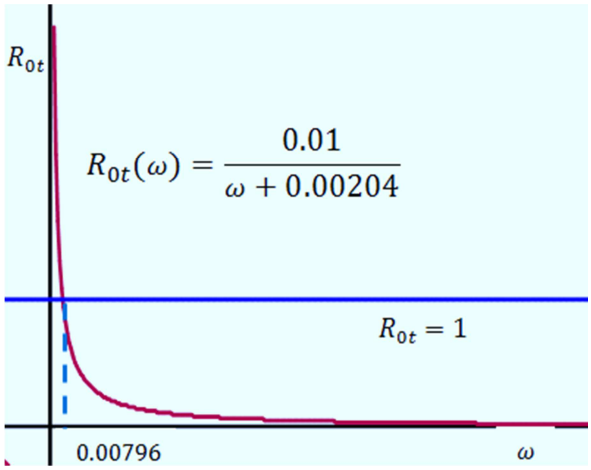

Figure 3. *The graph of the reproduction number R_{0t} versus the treatment rate from typhoid fever ω keeping all other parameters constant.*

From figure 3 we see that if $\omega < 0.00796$, then R_{0t} decreases but $R_{0t} > 1$ and the typhoid fever disease spreads and persists in the community. If $\omega > 0.00796$, then R_{0t} decreases with $R_{0t} < 1$ and the typhoid fever disease treatment rate from typhoid fever is effective and it dies out through time from the community.

Case-4: If $R_0 = Max\{R_{0t}, R_{0v}, R_{0f}\} = R_{0v}$ and $R_{0v} > 1$ and also the others are less than unity (i.e. $R_{0t} < 1$ and $R_{0f} < 1$), then the *p. vivax* disease persists in the population. That means if $R_{0v} > 1$, $R_{0f} < 1$ and $R_{0t} < 1$, the P. falciparum and the typhoid fever diseases die out with time and the *p. vivax* disease continues to be endemic in the community. This implies that the co-infection of *p. vivax* and typhoid fever decreases in the community. Thus, the numerical analysis of the *p. vivax* disease under this situation will be discussed as follow.

7.2. Estimation of Basic Reproduction Number R_{0v}

We computed $R_{0v} = 3.52530918626 > 1$ and the *p. vivax* disease spreads in the community.

7.2.1. R_{0v} Versus a_1

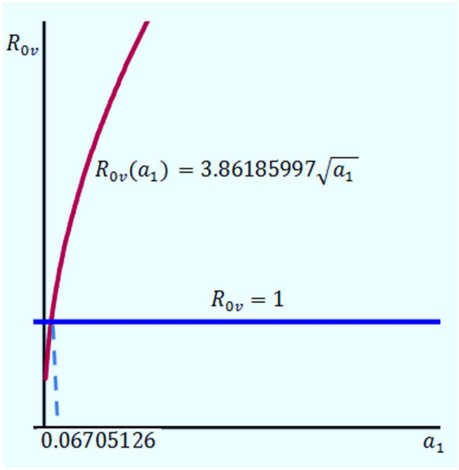

Figure 4. *The graph of the reproduction number R_{0v} versus the transmission probability a_1 of human infection by infected mosquito with plasmodium vivax keeping all other parameters constant.*

From figure 4 we see that if $a_1 < 0.06705126$, then R_{0v} increases but $R_{0v} < 1$ and the transmission probability of human infection by infected mosquito with plasmodium vivax decreases and finally, it dies out from the community. If $a_1 > 0.06705126$, then R_{0v} increases with $R_{0v} > 1$. That means the transmission probability of human infection by infected mosquito with plasmodium vivax increases and the disease persists in the community.

7.2.2. R_{0v} Versus a_3

From figure 5 we see that if $a_3 < 0.03862307$, then R_{0v} increases but $R_{0v} < 1$. This implies that the transmission probability that a mosquito will become infected by biting an infected human with plasmodium vivax decreases and finally, it dies out from the community. If $a_3 > 0.03862307$, then R_{0v} increases with $R_{0v} > 1$. That means the transmission probability that a mosquito will become infected by biting an infected human with plasmodium vivax increases and the disease persists in the community.

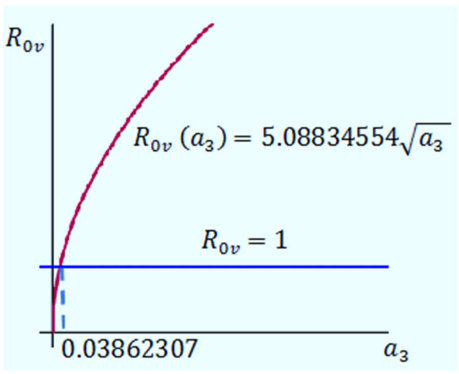

Figure 5. *The graph of the reproduction number R_{0v} versus the transmission probability a_3 that a mosquito will become infected by biting an infected human with plasmodium vivax keeping all other parameters constant.*

7.2.3. R_{0v} Versus b

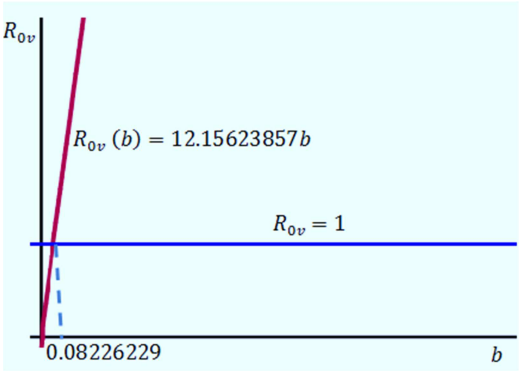

Figure 6. *The graph of the reproduction number R_{0v} versus per capita biting rate of mosquito b keeping all other parameters constant.*

From figure 6 we see that if $b < 0.08226229$, then R_{0v} increases but $R_{0v} < 1$ and the per capita biting rate of mosquito decreases and the disease dies out through time from the community. If $b > 0.08226229$, then R_{0v} increases with $R_{0v} > 1$. That means the per capita biting rate of mosquito increases and the disease persists in the community.

7.2.4. R_{0v} Versus ε

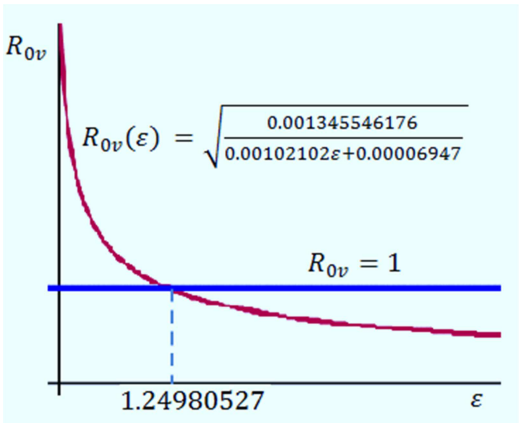

Figure 7. *The graph of the reproduction number R_{0v} versus the rate of treatment for malaria ε keeping all other parameters constant.*

From figure 7 we see that if $\varepsilon < 1.24980527$, then R_{0v} decreases but $R_{0v} > 1$. This implies that the malaria disease caused by p. vivax spreads and persists in the community. If $\varepsilon > 1.24980527$, then the reproduction number R_{0v} decreases with $R_{0v} < 1$. That means the treatment rate from malaria disease caused by p. vivax is effective and it dies out through time from the community.

Case-5: If $R_0 = Max\{R_{0t}, R_{0v}, R_{0f}\} = R_{0f}$ and $R_{0f} > 1$ and also the others are less than unity (i.e. $R_{0t} < 1$ and $R_{0v} < 1$), then the *p. falciparum* disease persists in the population. That means if $R_{0f} > 1$, $R_{0v} < 1$ and $R_{0t} < 1$, the P. vivax and the typhoid fever diseases die out with time and the *p. falciparum* disease continues to be endemic in the community. This implies that the co-infection of *p. falciparum* and typhoid fever decreases in the community. Thus, the numerical analysis of the p. falciparum disease under this situation will be discussed as follow.

7.3. Estimation of Basic Reproduction Number R_{0f}

We computed $R_{0f} = 1.7287941991 > 1$ and the plasmodium falciparum disease spreads in the community.

7.3.1. R_{0f} Versus a_2

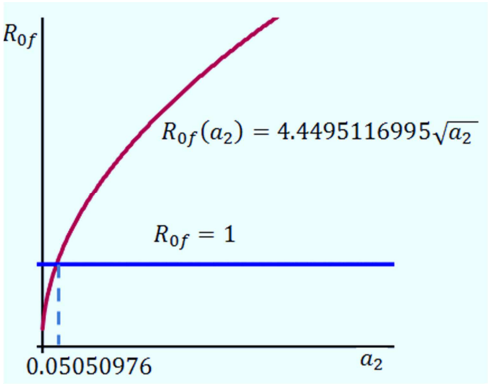

Figure 8. *The graph of the reproduction number R_{0f} versus the transmission probability a_2 of human infection by infected mosquito with plasmodium falciparum.*

From figure 8 we see that if $a_2 < 0.05050976$, then R_{0f} increases but $R_{0f} < 1$ and the transmission probability of human infection by infected mosquito with plasmodium falciparum decreases and finally, it dies out from the community. If $a_2 > 0.05050976$, then R_{0f} increases with $R_{0f} > 1$. That means the transmission probability of human infection by infected mosquito with plasmodium falciparum increases and the disease persists in the community.

7.3.2. R_{0f} Versus a_4

From figure 9 we see that if $a_4 < 0.08030168$, then R_{0f} increases but $R_{0f} < 1$ and the transmission probability that a mosquito will become infected by biting an infected human with plasmodium falciparum decreases and finally, it dies out from the community. If $a_4 > 0.08030168$, then R_{0f} increases with $R_{0f} > 1$. That means the transmission probability that a mosquito will become infected by biting an infected human with plasmodium falciparum increases and the disease persists in the community.

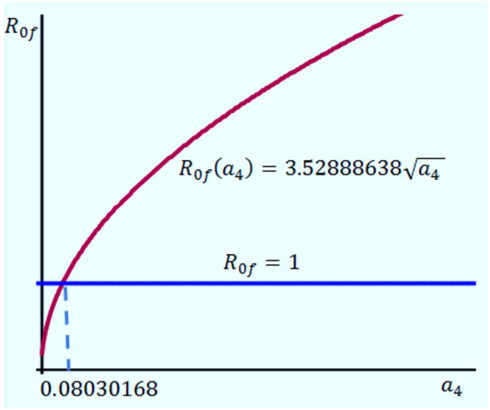

Figure 9. *The graph of the reproduction number R_{0f} versus the transmission probability a_4 that a mosquito will become infected by biting an infected human with p. falciparum keeping all other parameters constant.*

7.3.3. R_{0f} Versus b

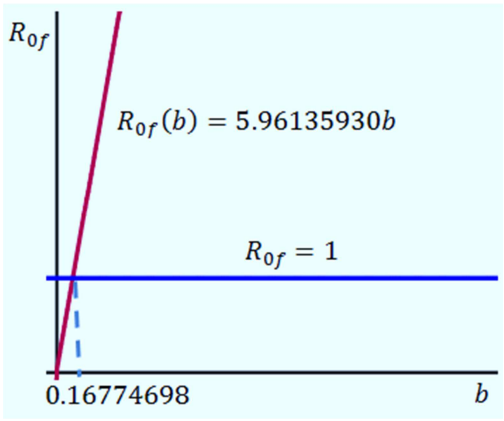

Figure 10. *The graph of the reproduction number R_{0f} versus per capita biting rate of mosquito b keeping all other parameters constant.*

From figure 10 we see that if $b < 0.16774698$, then R_{0f} increases but $R_{0f} < 1$. This implies that the per capita biting rate of mosquito decreases and the disease dies out through time from the community. If $b > 0.16774698$, then R_{0f} increases with $R_{0f} > 1$ and the per capita biting rate of mosquito increases and the disease persists in the community.

7.3.4. R_{0f} Versus ε

From figure 11 we see that if $\varepsilon < 0.11743159$, then R_{0f} decreases but $R_{0f} > 1$. This implies that the malaria disease caused by p. falciparum spreads and persists in the community. If $\varepsilon > 0.11743159$, then R_{0f} decreases with $R_{0f} < 1$. That means the treatment rate from malaria disease caused by p. falciparum is effective and it dies out through time from the community.

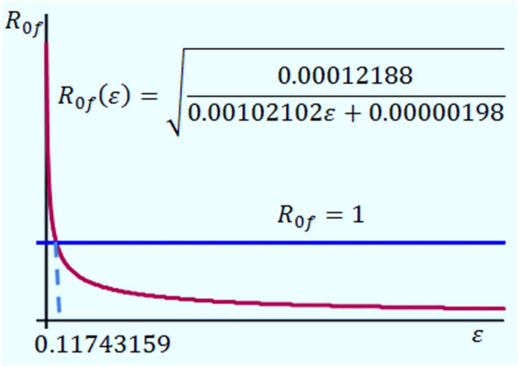

Figure 11. *The graph of the reproduction number R_{0f} versus the rate of treatment for malaria ε keeping all other parameters constant.*

8. Sensitivity Analysis

Next, we perform some sensitivity analysis to determine the parameters that have great influence on the basic reproduction number R_0 of our dynamics of disease transmissions. We use the sensitivity analysis technique given in [20] by the following definition.

Definition: The normalized forward sensitivity index of a variable R_0 that depends differentially on a parameter p is defined as: $SI(p) = \frac{\partial R_0}{\partial p} X \frac{p}{R_0}$.

Thus, the most sensitive parameter is the one with the highest magnitude as compared to the others. The larger the magnitude of the number, the greater impact that parameter has on R_0 and correspondingly, the smaller the magnitude, the weaker the impact on R_0. Since $R_0 = Max\{R_{0t}, R_{0v}, R_{0f}\}$, we obtain the sensitivity analysis of R_{0t}, R_{0v} and R_{0f} separately with respect to each parameter to decide the influential parameters on the co-infection of *p. vivax*, p. falciparum and typhoid fever disease as follow.

First let us consider the basic reproduction number R_{0t} of typhoid fever.

$$SI(\beta) = \frac{\partial R_{0t}}{\partial \beta}\frac{\beta}{R_{0t}} = 1 > 0, SI(\omega) = \frac{\partial R_{0t}}{\partial \omega}\frac{\omega}{R_{0t}} = \frac{-\omega}{(\omega+\delta_t+\mu_h)} < 0, SI(\delta_t) = \frac{\partial R_{0t}}{\partial \delta_t}\frac{\delta_t}{R_{0t}} = \frac{-\delta_t}{(\omega+\delta_t+\mu_h)} < 0, SI(\mu_h) = \frac{\partial R_{0t}}{\partial \mu_h}\frac{\mu_h}{R_{0t}} = \frac{-\mu_h}{(\omega+\delta_t+\mu_h)} < 0$$

Based on the data given on table 2 for typhoid fever disease the sensitivity indices of R_{0t} with respect to the four parameters are computed and listed in the following table.

Table 3. *The sensitivity index of R_{0t} with respect to the four parameters.*

Parameters	sensitivity index
β	1
ω	−0.54917127
δ_t	−0.38095238
μ_h	−0.00883978

From the sensitivity index table, it is observed that the effective transmission rate of typhoid fever on contact with infected individuals β is the most sensitive parameter. The second sensitive parameter for typhoid fever transmission is the treatment rate of humans from typhoid fever ω.

Next let us consider the basic reproduction number R_{0v} of plasmodium vivax.

$$SI(a_1) = \frac{\partial R_{0v}}{\partial a_1}\frac{a_1}{R_{0v}} = \frac{1}{2} > 0, SI(a_3) = \frac{\partial R_{0v}}{\partial a_3}\frac{a_3}{R_{0v}} = \frac{1}{2} > 0, SI(b) = \frac{\partial R_{0v}}{\partial b}\frac{b}{R_{0v}} = 1 > 0, SI(\mu_h) = \frac{\partial R_{0v}}{\partial \mu_h}\frac{\mu_h}{R_{0v}} = \frac{(\varepsilon+\delta_v)}{2(\varepsilon+\delta_v+\mu_h)} > 0, SI(\mu_m) = \frac{\partial R_{0v}}{\partial \mu_m}\frac{\mu_m}{R_{0v}} = -1 < 0, SI(\varepsilon) = \frac{\partial R_{0v}}{\partial \varepsilon}\frac{\varepsilon}{R_{0v}} = \frac{-\varepsilon}{2(\varepsilon+\delta_v+\mu_h)} < 0, SI(\delta_v) = \frac{\partial R_{0v}}{\partial \delta_v}\frac{\delta_v}{R_{0v}} = \frac{-\delta_v}{2(\varepsilon+\delta_v+\mu_h)} < 0$$

Based on the data given on table 2 for *p. vivax* disease the sensitivity indices of R_{0v} with respect to the seven parameters are computed and listed in the following table.

Table 4. *The sensitivity index of R_{0v} with respect to the seven parameters.*

Parameters	sensitivity index
a_1	0.5
a_3	0.5
b	1
μ_h	0.49981139
μ_m	−1
ε	−0.17917767
δ_v	−0.32063372

From the sensitivity index table, it is observed that the per capita biting rate of mosquito b is the most sensitive parameter. The transmission probability of human infection due to per bite of an infected mosquito with plasmodium vivax a_1 and the transmission probability that a mosquito will become infected by biting an infected human with plasmodium vivax a_3 are also the influential parameters in malaria transmission dynamics.

Finally, let us consider the basic reproduction number R_{0f} of plasmodium falciparum.

$$SI(a_2) = \frac{\partial R_{0f}}{\partial a_2}\frac{a_2}{R_{0f}} = \frac{1}{2} > 0, SI(a_4) = \frac{\partial R_{0f}}{\partial a_4}\frac{a_4}{R_{0f}} = \frac{1}{2} > 0,$$
$$SI(b) = \frac{\partial R_{0f}}{\partial b}\frac{b}{R_{0f}} = 1 > 0, SI(\mu_h) = \frac{\partial R_{0f}}{\partial \mu_h}\frac{\mu_h}{R_{0f}} =$$
$$\frac{(\varepsilon+\delta_f)}{2(\varepsilon+\delta_f+\mu_h)} > 0, SI(\mu_m) = \frac{\partial R_{0f}}{\partial \mu_m}\frac{\mu_m}{R_{0f}} = -1 < 0, SI(\varepsilon) =$$
$$\frac{\partial R_{0f}}{\partial \varepsilon}\frac{\varepsilon}{R_{0f}} = \frac{-\varepsilon}{2(\varepsilon+\delta_f+\mu_h)} < 0, SI(\delta_f) = \frac{\partial R_{0f}}{\partial \delta_f}\frac{\delta_f}{R_{0f}} =$$
$$\frac{-\delta_f}{2(\varepsilon+\delta_f+\mu_h)} < 0$$

Based on the data given on table 2 for p. falciparum disease the sensitivity indices of R_{0f} with respect to the seven parameters are computed and listed in the following table.

Table 5. *The sensitivity index of R_{0f} with respect to the seven parameters.*

Parameters	sensitivity index
a_2	0.5
a_4	0.5
b	1
μ_h	0.49949925
μ_m	-1
ε	-0.47571357
δ_f	-0.11266900

From the sensitivity index table, it is observed that the per capita biting rate of mosquito b is the most sensitive parameter. The transmission probability of human infection due to per bite of an infected mosquito with plasmodium falciparum a_2 and the transmission probability that a mosquito will become infected by biting an infected human with plasmodium falciparum a_4 are also the influential parameters in malaria transmission dynamics.

9. Results and Discussions

In this study, we considered non-linear system of ordinary differential equation to study the transmission dynamics of the co-infection of *p. vivax*, *p. falciparum* malaria and typhoid fever disease with treatment in a community. To get clear idea about the real transmission dynamics of the co-infection of *p. vivax*, *p. falciparum* malaria and typhoid fever disease, we have investigated the basic reproduction numbers of each disease in the numerical and sensitivity analysis of the co-infection of *p. vivax*, *p. falciparum* and typhoid fever disease separately. We used the Next Generation Matrix Method to calculate the reproduction number R_0 for the co-infection dynamics of *p. vivax*, *p. falciparum* and typhoid fever disease. In doing so, we obtained the basic reproduction number R_0 of the co-infection in terms of the dynamics of the three basic reproduction numbers of the separate diseases i.e. $R_{0t}, R_{0v}\ and\ R_{0f}$ that represent basic reproduction numbers for typhoid fever, *p. vivax*, and p. falciparum respectively. From this we conclude that the basic reproduction number for the co-infection of *p. vivax*, *p. falciparum* and typhoid fever disease is $R_0 = Max\{R_{0t}, R_{0v}, R_{0f}\}$. We know that the reproduction number R_0 of the system helps us to decide the number of secondary infections that one infectious individual generates. After computing the disease free equilibrium and the endemic equilibrium points of the co-infection dynamics of the system, we have checked the local and global stabilities of the co-infection model using the Jacobian matrix method for local stability and the Lyapunov function method for global stability. Also, the full *p. vivax* and *p. falciparum* - typhoid fever model has a locally asymptotically stable disease-free equilibrium point when its basic reproduction number is less than unity, and unstable if it exceeds unity. The separate diseases disappear from the community whenever the reproduction number R_0 is very small and less than unity. On the other hand, the diseases co-exist whenever their reproduction numbers exceed unity (regardless which of the numbers is larger). That means the disease persists in the community and we need to start treatment for the infected people. Before we discuss the sensitivity analysis of the co-infected dynamics of the model to determine the most influential parameters of the system, we investigated the sensitivity analysis on each parameters of the separate diseases based on the standard data taken from different journal sources. For this purpose we used the basic reproduction numbers of the separate diseases obtained from the basic reproduction number of the co-infection disease model. We discussed and presented in detail the numerical simulation results of the separate diseases based on the standard data taken from different journal sources in the form of graphics to support the dynamics of the co-infection disease. Thus, based on these ideas we discussed each basic reproduction numbers versus some of the corresponding influential parameters of the diseases one by one as follows.

We obtained the basic reproduction number R_{0t} of the typhoid fever infection from the co-infection model (sub-model) as $R_{0t} = \frac{\beta}{\omega+\delta_t+\mu_h}$ with four parameters. Also, we got the numerical value of the basic reproduction number based on the standard data taken from different journal sources as $R_{0t} = 2.20994475138 > 1$. This shows us that the disease spreads in the population. From graph 2 we see that when $\beta > 0.004525$, the reproduction number R_{0t} increases with $R_{0t} > 1$. That means the basic reproduction number R_{0t} increases when the effective transmission rate of typhoid fever on contact with infected individuals β increases and the disease persists in the community. On the other hand, in figure 3 the reproduction number R_{0t} decreases with $R_{0t} < 1$ if $\omega > 0.00796$. That means the typhoid fever disease treatment rate ω is effective and the disease dies out through time from the community.

Next, we computed the basic reproduction number R_{0v} of the plasmodium vivax disease from the co-infection model

(sub-model) as $R_{0v} = \sqrt{\frac{a_1 a_3 b^2 \mu_h \Lambda_m}{\mu_m^2 \Lambda_h (\varepsilon+\delta_v+\mu_h)}}$ with nine parameters. The graph in figure 4 shows us that if $a_1 > 0.06705126$, then the reproduction number R_{0v} increases with $R_{0v} > 1$. That means if the transmission probability of human infection by infected mosquito with plasmodium vivax a_1 increases, the basic reproduction number R_{0v} increases and the disease persists in the community. If $a_1 < 0.06705126$, then the reproduction number R_{0v} increases with $R_{0v} < 1$ and the disease dies out from the community through time. Thus, a_1 affects the reproduction number R_{0v}. In figure 5 we see that if $a_3 > 0.03862307$ then the reproduction number R_{0v} increases with $R_{0v} > 1$. That means the transmission probability that a mosquito will become infected by biting an infected human with plasmodium vivax a_3 increases, the basic reproduction number R_{0v} increases and the disease persists in the community. If $a_3 < 0.03862307$, then the reproduction number R_{0v} increases with $R_{0v} < 1$ and the disease dies out from the community through time. Thus, a_3 affects the reproduction number R_{0v}. From figure 6 we observe that when the per capita biting rate of mosquito b increases, the basic reproduction number R_{0v} also increases and the disease persists in the community.

In figure 7 we see that the mosquito treatment rate ε influences the basic reproduction number R_{0v}. If $\varepsilon < 1.24980527$, then the reproduction number R_{0v} decreases with $R_{0v} > 1$. This implies that the malaria disease caused by plasmodium vivax spreads and persists in the community. If $\varepsilon > 1.24980527$, then the reproduction number R_{0v} decreases with $R_{0v} < 1$. That means the treatment rate ε from malaria disease caused by plasmodium vivax is effective and it dies out through time from the community.

We also computed the basic reproduction number R_{0f} of the plasmodium falciparum disease from the co-infection model (sub-model) as $R_{0f} = \sqrt{\frac{a_2 a_4 b^2 \mu_h \Lambda_m}{\mu_m^2 \Lambda_h (\varepsilon+\delta_f+\mu_h)}}$ with nine parameters. The graph in figure 8 shows us that if $a_2 > 0.05050976$, then the reproduction number R_{0f} increases with $R_{0f} > 1$. That means if the transmission probability of human infection by infected mosquito with plasmodium falciparum a_2 increases, the basic reproduction number R_{0f} increases and the disease persists in the community. If $a_2 < 0.05050976$, then the reproduction number R_{0f} increases with $R_{0f} < 1$ and the disease dies out from the community through time. Thus, a_2 affects the reproduction number R_{0f}. In figure 9 we see that if $a_4 > 0.08030168$, then the reproduction number R_{0f} increases with $R_{0f} > 1$. That means the transmission probability that a mosquito will become infected by biting an infected human with plasmodium falciparum a_4 increases, the basic reproduction number R_{0f} increases and the disease persists in the community. If $a_4 < 0.08030168$, then the reproduction number R_{0f} increases with $R_{0f} < 1$ and the disease dies out from the community through time. Thus, a_4 affects the reproduction number R_{0f}. From figure 10 we observe that when the per capita biting rate of mosquito b increases, the basic reproduction number R_{0f} also increases and the disease persists in the community.

In figure 11 we see that the mosquito treatment rate ε influences the basic reproduction number R_{0f}. If $\varepsilon < 0.11743159$, then the reproduction number R_{0f} decreases with $R_{0f} > 1$. This implies that the malaria disease caused by plasmodium falciparum spreads and persists in the community. If $\varepsilon > 0.11743159$, then the reproduction number R_{0f} decreases with $R_{0f} < 1$. That means the treatment rate ε from malaria disease caused by plasmodium falciparum is effective and it dies out through time from the community.

From table 3 of sensitivity index of typhoid fever disease sub-model we see that the most sensitive parameters are the effective transmission rate of typhoid fever on contact parameter β and the treatment rate of humans from typhoid fever ω. Also, from tables 4 and 5 of sensitivity indices of plasmodium vivax and plasmodium falciparum diseases sub-models we observe that the most sensitive parameter is the per capita biting rate of mosquito b as well as the transmission probabilities of the malaria infection parameters a_1, a_2, a_3 and a_4. Thus, having analyzed the sensitivity of the parameters for the three separate diseases that are typhoid fever, plasmodium vivax and plasmodium falciparum, we discussed in detail the sensitive parameters for the full p. vivax, p. falciparum and typhoid fever co-infection disease dynamics.

10. Conclusion

In this study, we presented and analyzed a non-linear system of ordinary differential equation to study the transmission dynamics of the co-infection of *p. vivax*, p. falciparum and typhoid fever disease with treatment in a community. That means we developed a mathematical model in order to understand the *p. vivax*, p. falciparum malaria and typhoid fever diseases co-infections to improve the treatments and control of the diseases. We found the basic reproduction number of the full co-infection model of *p. vivax*, p. falciparum and typhoid fever diseases. When we analyze the co-infection model, the disease free equilibrium and the endemic equilibrium points are locally asymptotically stable and globally asymptotically stable.

From the sensitivity analysis of the typhoid fever we observed that the effective transmission rate of typhoid fever on contact with infected individual parameter β is the most sensitive (influential) parameter in changing the reproduction number of the system and the transmission dynamics of typhoid fever. Also, from the sensitivity analysis of the malaria disease we see that the most sensitive parameter is the per capita biting rate of mosquito b as well as the transmission probabilities of the malaria infection parameters.

Based on the values of the reproduction numbers i.e. $R_{0t} = 2.20994475138$, $R_{0v} = 3.52530918626$ and $R_{0f} = 1.7287941991$ that we computed using the standard data obtained from different sources, we concluded that *p. vivax* is more co-infected with typhoid fever than p. falciparum co-infected with typhoid fever.

Thus, the results in this study show us that controlling the

transmission means of the diseases and getting appropriate treatment are very important to eradicate the diseases from the community. Therefore, to reduce the reproduction number of the dynamical system we have to focus on the influential parameters. That means to eliminate the typhoid fever disease we must reduce the contact rate with typhoid fever infectious individuals in the community and also to reduce malaria diseases we must protect the population from mosquito biting using different methods.

11. Recommendation

In this study we have observed that the reproduction number of the co-infection of *p. vivax*, p. falciparum and typhoid fever disease is greater than unity. This implies that typhoid fever and malaria diseases as well as the co-infection of these diseases spread and persist in the community. Thus, to reduce the spread of the diseases we have to give attention for the sensitive parameters like the effective transmission rate of typhoid fever on contact parameter β, the per capita biting rate of mosquito b and the transmission probabilities of the malaria infection parameters a_1, a_2, a_3 and a_4.

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