International Journal of Mathematics Trends and Technology
ISSN: 2231 – 5373/doi:10.14445/22315373/IJMTT-V67I12P503
Volume 67 Issue 12, 21-40, December, 2021

Original Article

Sensitivity Analysis on Mathematical Modeling of Transmission Dynamics of Tuberculosis–Malaria Co-infections

M. A. Afolabi[1] and S. O. Adewale[2]

[1]*Department of Science and Social Sciences, Osun State Polytechnic, Iree. Nigeria.*
[2]*Department of Pure and Applied Mathematics, LAUTECH Ogbomoso, Oyo State, Nigeria.*

Abstract *- Tuberculosis (TB) and malaria are the most prevalent bacterial and parasitic infections in humans and continue to be major causes of morbidity and mortality in the population. A co-infection of TB and malaria epidemic model was formulated as a system of ordinary differential equation. Positivity and Invariant regions indicated that the model was mathematically well posed and epidemiologically feasible. Disease free equilibrium were locally and globally asymptotically stable whenever the basic reproduction number is less than unity and endemic when greater than one. The basic reproduction number* R_{0TM} *of 0.7359316 was obtained. Sensitivity results indicated that an effective contact rate was the most sensitive parameter with value of 1.000 which propels the basic reproduction. Significantly, the results obtained showed that the higher the value of effective contact rates the higher the basic reproduction number.*

Keywords - *Tuberculosis-malaria, basic reproduction number, sensitivity analysis, disease free equilibrium, numerical simulation*.**.**

I. INTRODUCTION

Infectious diseases are caused by micro-organisms such as bacteria, fungi, virus or parasites. TB and malaria are the most prevalent bacterial and parasitic infection in humans and continue to be major causes of morbidity and mortality in impoverished population in the tropics [25]. Tuberculosis or TB (short for tubercle bacillus) is a common infectious disease caused by Mycobacterium tuberculosis. Tuberculosis typically attacks the lungs, but can also affect other parts of the body. It is spread through the air when active TB infectious people cough, sneeze or otherwise transmit their saliva through the air. TB infections carrier can be active or latent. Symptoms of TB of are chronic cough which may result in blood-tinged sputum, fever, night sweats, loss of appetite, weight loss and fatigue [1, 4, 23]. TB remained the leading cause of death from a single infectious agent worldwide [8].

Malaria is a life-threatening disease caused by parasites transmitted to humans through the bites\blood meals of the infected female Anopheles mosquitoes [2, 14]. Plasmodium falciparum is the parasitic species that largely causes human malaria infections in Africa. The parasite requires two hosts to complete its life cycle – the infected female anopheles mosquito and human. Once an infected mosquito bites a human and transmits the parasite, the parasite first travels to a human's liver where it grows and multiplies and later to the bloodstream where it infects and destroys red blood cells. Malaria can be uncomplicated or severe depending on the symptoms which include fever, chills, nausea, vomiting and general weakness of the body. Its incubation periods span between seven and thirty days before symptoms start [5, 24]. Treatment of malaria depends of the type of plasmodium that causes it.

Human populations are rarely exposed to one pathogen particularly in high incidence regions such as sub-Saharan Africa where infections with more than one pathogen represent a public health problem [15, 16]. Tuberculosis (TB) and malaria were among major threats that undermine development in many resource-poor counties of the world. Despite significant advances in medical science, these diseases continue to impact human populations. In 2019, an estimated 229 million cases of malaria occurred worldwide while 409,000 people died in which the majority of victims are young children from sub-Saharan Africa [14, 24]. An estimated 10 million persons developed TB illness in 2019 while an estimated of 1.4 million TB-related deaths occurred [8].

Despite this treat, few studies of the effect of TB-malaria co-infection may be found in the literature [15, 17, 21]. [25] developed an experimental model to study Tuberculosis-malaria co-infection upon natural transmission of mycobacterium tuberculosis and plasmodium berghei. [12] worked on HIV/AIDS, malaria and tuberculosis. The model is analyzed to investigate the potential impact of counseling and treatment on disease progression by carrying out sensitivity analysis of the reproduction number with respect to counseling and treatment. [16] worked on Epidemiological features of the co-dynamics of malaria and tuberculosis (TB) is formulated and the effectiveness of current intervention strategies of these two diseases was analyzed. [18] studied the implications of HIV treatment on the HIV- malaria co-infection dynamics. Consequently, the objective of this work is to provide insights into TB and malaria transmission dynamics, especially by investigating the impact of each parameter in reproduction number that propel it to unsafe environment

II. MODEL FORMULATION

In modeling the dynamical spread, the total homogeneous population at time t, denoted by $N(t) = N_M(t) + N_V(t)$ where $(N_H(t))$ is human population and $(N_V(t))$ is vector (mosquitoes) population partitioned into fourteen compartments.

Human population $(N_H(t))$ is sub-divided into susceptible $(S_H(t))$ individuals, vaccinated $(V_T(t))$ individuals, Exposed $(E_T(t))$ individuals, infected undetected $(U_T(t))$ individuals, infected detected $(D_T(t))$ individuals, recovered $(R_T(t))$ individuals, individuals that are Exposed to TB-Malaria disease $(E_{TM}(t))$, active individuals infected with TB-malaria $(A_{TM}(t))$, recovered individuals from TB-malaria $(R_{TM}(t))$, individual exposed to malaria disease $(E_M(t))$, individuals infected with malaria disease $(I_M(t))$ and recovered malaria $(R_M(t))$ individual.

Vector population $(N_V(t))$ is also sub-divided into susceptible $(S_V(t))$ of mosquitoes and infected $I_V(t)$ mosquitoes as well. So that,

$$N_H(t) = S_H + V_T + E_T + U_T + D_T + R_T + E_M + I_M + R_M + E_{TM} + A_{TM} + R_{TM}$$

and (1)

$$N_V(t) = S_V + I_V$$

It is assumed that susceptible human population is increased by the recruitment of individuals (either by birth or immigration) into the population. All recruited individuals are assumed to be susceptible at rate π_H except those that have been vaccinated at the rate ρ. This population is decreased by both singly and dually infected individual acquired either TB or Malaria or co-infected following effective contact with infectious individuals. This population later decrease due to natural death of susceptible individuals at the rate μ and later increase by vaccine wanes off at the rate ω

Co-infected and singly infected individuals transmit either TB, Malaria or both infection as defined as follows:

Transmission rates

Susceptible individuals acquire infections with TB and malaria at rates λ_T and λ_M respectively for human and mosquito respectively.

Transmission rate of tuberculosis

The transmission rate for TB only is give as $$\lambda_T = \frac{\beta_T(U_T + \eta_D D_T)}{N} \quad (2)$$

In (2) β_T represents the effective contact rate (contact capable of leading to tuberculosis infection) while η_D is modification parameter which accounts for the risk of infectiousness of individuals in D_T class.

Transmission rate of malaria

The transmission rate of susceptible human is given as $$\lambda_M = \frac{a_M \beta_M(I_V)}{N_V} \quad (3)$$

Where β_M is per capital biting rate of infected mosquito and " a_M" is the probability that a bite by an infected mosquito on a susceptible human will transfer the infection to human.

Transmission rate of vector

The transmission rate of vector is given as $\lambda_V = \frac{a_M \beta_V (I_M + \eta_{TM} A_{TM})}{N_H}$ (4)

Where β_v is the biting rate of infected mosquito while η_{TM} is modification parameter which accounts for the risk of infectiousness of individuals in A_{TM} class.

Transmission rate of TB-malaria co-infection

The transmission rate of TB and malaria is given $\lambda_{TM} = \beta_{TM} \frac{A_{TM}}{N_H}$ (5)

Where β_{TM} is the effective contact rate for infection with TB-Malaria.

Thus, the rate of change of the susceptible population is given by:

$$\frac{dS_H}{dt} = (1-\rho)\pi_H - \lambda_T S_H - \lambda_M S_H - \lambda_{TM} S_H - \mu S_H + \omega V_T + \gamma_M R_M \quad (6)$$

The population of the vaccinated class increased by recruiting the vaccinated individuals into the vaccinated class at the rate $\rho\pi$. The population of vaccinated individual is decrease by the rate at which vaccine wanes off ω and also reduced by natural death of vaccinated individuals at the rate μ.

Thus: $\frac{dV_T}{dt} = \rho\pi_H - \mu V_T - \omega V_T$ (7)

A fraction θ_1 of the newly infected individuals is assumed to immediately display disease symptoms. These category of individuals known as "Fast progressor " are moved to the infected undetected class U_T (t) while the remaining fraction $(1-\theta_1)$ of the newly infected individuals are assumed to show no disease symptoms initially. These category of individuals known as "Slow progressor" are moved to exposed class $E_T(t)$. The population of the exposed individuals is decreased by the progression of exposed individuals to active TB at the rate κ_T, natural death at rate μ and by exogenous re-infection at the rate $\psi_e \gamma_T$ Thus:

$$\frac{dE_T}{dt} = (1-\theta_1)\lambda_T S_H - \mu E_T - \kappa_T E_T - \psi_e \lambda_T E_T \quad (8)$$

The population of infected undetected individuals is increased by infection of fast progressor $\theta_1 \lambda_T$. It is further increased by the progression of exposed individuals that have the probability of developing infectious TB at the rate $(1-\upsilon)$ (where υ is the fraction of progression of exposed individual that have the probability of developing infectious TB). It is further increase by exogenous re-infection of exposed individual at the rate $(1-P_2)\psi_e \gamma_T$ (where P_2 is the fraction of re-infected exposed individual who are detected) and recovered individuals at the rate $(1-P_3)\psi_a \gamma_T$ (where P_3 is the fraction of the re-infected recovered individuals who are detected). This population is decreased by natural death of TB patient at rate μ, disease-induced death rate δ, and by detection rate ϕ. Hence,

$$\frac{dU_T}{dt} = \theta_1 \lambda_T S_H + (1-P_2)\psi_e \lambda_T E_T - \mu U_T - \delta U_T - \phi U_T + (1-\upsilon)\kappa_T E_T + (1-P_3)\psi_a \lambda_T R_T \quad (9)$$

The population of infected detected individuals increased by progression of fraction of the exposed individuals that have the probability of developing infectious TB at the rate υ. It is further increased by detection rate ϕ of undetected individual, exogenous re-infection of exposed and recovered individuals at $P_2\psi_e\gamma_T$ and $P_3\psi_a\gamma_T$ respectively. The population is decreased by natural death of TB patient at rate μ and later by TB induced death rate δ. This is further reduced by treatment rate τ_T of infected detected individuals and natural immunity at the rate σ. Hence,

$$\frac{dD_T}{dt} = \upsilon\kappa_T E_T + P_2\psi_e\lambda_T E_T - \mu D_T - \delta D_T + \phi U_T - \tau_T D_T - \sigma D_T + P_3\psi_a\lambda_T R_T \quad (10)$$

The population of recovered individuals is increased by treatment rate τ_T of infected detected individuals and also by natural immunity at the rate σ and by exogenous re-infection at $\psi_a \gamma_T$. This population is reduced by natural death rate μ of recovered individual. Thus,

$$\frac{dR_T}{dt} = \tau_T D_T + \sigma D_T - \mu R_T - \psi_a \lambda_T R_T \quad (11)$$

The population of exposed malaria individuals is increased by infection of slow progressor of susceptible at the rate $(1-\theta_2)\lambda_M$. It reduces due to progression of human from exposed to infectious at rate κ_M and natural death at rate μ. It then increase by recovered human at the rate γ_M. Thus,

$$\frac{dE_M}{dt} = (1-\theta_2)\lambda_M S_H - \mu E_M - \kappa_M E_M + \gamma_M R_M \quad (12)$$

The population of infected malaria individuals is increased by infection of fast progressor of susceptible at the rate $\theta_2 \lambda_M$ and by progression of humans exposed to vector at a rate κ_M. It then reduce by natural death at rate μ, vector induced death rate δ and treatment of infection human at rate τ_M. Thus

$$\frac{dI_M}{dt} = \theta_2 \lambda_M S_H + \kappa_M E_M - \mu I_M - \delta I_M - \tau_M I_M \quad (13)$$

The recovered human population is increased by the treatment rate τ_M. It decreased by natural death rate μ and recovered individual at rate γ_M. This gives:

$$\frac{dR_M}{dt} = \tau_M I_M - \mu R_M - \gamma_M R_M \quad (14)$$

The population of exposed individuals with TB dually infected with malaria is increased by the newly infected individuals that slowly display the symptoms at rate $(1-\theta_3)$. It latter reduced by the natural death at the rate μ and progression rate of individuals with both diseases at rate κ_{TM}. It latter increase by recovered individuals at the rate γ_{TM}. Thus

$$\frac{dE_{TM}}{dt} = (1-\theta_3)\lambda_{TM} S_H - \mu E_{TM} - \kappa_{TM} E_{TM} + \gamma_{TM} R_{TM} \quad (15)$$

The population of active TB co-infected with malaria is increased by newly infected individuals that quickly display the symptoms at the rate θ_3 and the progression from exposed stage to active stage at the rate κ_{TM}. Also, the population of this class reduced by natural death rate μ and disease-induced mortality rate δ. It further reduced by treatment rate τ_{TM} as a result of TB-malaria infection. Hence

$$\frac{dA_{TM}}{dt} = \theta_3 \lambda_{TM} S_H + \kappa_{TM} E_{TM} - \mu A_{TM} - \delta A_{TM} - \tau_{TM} A_{TM} \quad (16)$$

The population of recovered TB dually infected with malaria increased by treatment received at the rate τ_{TM} .This population is reduced by natural death rate μ and recovered individual at rate γ_{TM} of individuals in this class. Then

$$\frac{dR_{TM}}{dt} = \tau_{TM} A_{TM} - \mu R_{TM} - \gamma_{TM} R_{TM} \quad (17)$$

The susceptible vector class was increased by the recruitment of vectors (anopheles mosquitoes) into the population at the rate π_v. This class was decreased by transmitted rate of susceptible vector. It further reduced by the natural death of vector at the rate μ_v and artificial death rate δ_V.

Then $$\frac{dS_V}{dt} = \pi_V - \lambda_V S_H - (\mu_V + \delta_V) S_V \quad (18)$$

The infected vector population is increased by transmission rate of infected vector. It then reduced by natural death at the rate μ_v and artificial death rate δ_V. Thus,

$$\frac{dI_V}{dt} = \lambda_V S_V - (\mu_V + \delta_V) I_V \tag{19}$$

Thus, the new Tuberculosis-Malaria co-infection transmission model is given by the following system of non-linear differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= (1-\rho)\pi_H - \lambda_T S_H - \lambda_M S_H - \lambda_{TM} S_H - \mu S_H + \omega V + \gamma_M R_M \\
\frac{dV_T}{dt} &= \rho\pi_H - (\mu+\omega)V_T \\
\frac{dE_T}{dt} &= (1-\theta_1)\lambda_T S_H - (\mu+\kappa_T)E_T - \psi_e \lambda_T E_T \\
\frac{dU_T}{dt} &= \theta\lambda_T S_H + (1-P_2)\psi_e \lambda_T E_T - (\mu+\delta+\phi)U_T + (1-\upsilon)\kappa_T E_T + (1-P_3)\psi_a \lambda_T R_T \\
\frac{dD_T}{dt} &= \upsilon\kappa_T E_T + P_2\psi_e \lambda_T E_T - (\mu+\delta+\tau+\sigma_T)D_T + \phi U_T + P_3\psi_a \lambda_T R_T \\
\frac{dR_T}{dt} &= (\tau_T + \sigma_T)D_T - \mu R_T - \psi_a \lambda_T R_T \\
\frac{dE_M}{dt} &= (1-\theta_2)\lambda_M S_H - (\mu+\kappa_M)E_M \\
\frac{dI_M}{dt} &= \theta_2 \lambda_M S_H + \kappa_M E_M - (\mu+\delta+\tau)I_M \\
\frac{dR_M}{dt} &= \tau_M I_M - (\mu+\gamma_M)R_M \\
\frac{dE_{TM}}{dt} &= (1-\theta_3)\lambda_{TM} S_H - (\mu+\kappa_{TM})E_{TM} + \gamma_{TM} R_{TM} \\
\frac{dA_{TM}}{dt} &= \theta_3 \lambda_{TM} S_H + \kappa_{TM} E_{TM} - (\mu+\delta+\tau_{TM})A_{TM} \\
\frac{dR_{TM}}{dt} &= \tau_{TM} A_{TM} - (\mu+\gamma_{TM})R_{TM} \\
\frac{dS_V}{dt} &= \pi_V - \lambda_V S_V - (\mu_V + \delta_V)S_V \\
\frac{dI_V}{dt} &= \lambda_V S_V - (\mu_V + \delta_V)I_V
\end{aligned} \tag{20}$$

Where $\lambda_T = \frac{\beta_T (U_T + \eta_d D_T)}{N_H}$, $\lambda_V = \frac{a_V \beta_V (I_M + \eta_{TM} A_{TM})}{N_H}$, $\lambda_M = \frac{a_M \beta_H (I_V)}{N_V}$

and $\lambda_{TM} = \frac{\beta_{TM} A_{TM}}{N_H}$

Table 1: Definition of variables

Variables	Definition
S_H	Population of susceptible Human at time t.
S_V	Population of susceptible vector at time t.
V_T	Vaccination Class for TB
E_T	Exposed TB individuals at time t
U_T	Undetected TB individuals at time t
D_T	Detected TB individuals at time t
R_T	Recovered TB individuals at time t
E_M	Exposed Malaria individual at time t
I_M	Infected Malaria individual at time t
R_M	Recovered malaria individual at time t
E_V	Exposed vector at time t
E_{TM}	Exposed TB induced Malaria at time t
A_{TM}	Active TB induced Malaria at time t
R_{TM}	TB induced Malaria recovered individual at time t
N	Total Population

Table 2 Definition of Parameters used in the model

Parameters	Definition
π_H, π_V	Recruitment rate for human and vector respectively
$\beta_T, \beta_M, \beta_V$	Effective contact rate for TB , Malaria and Infected vector
μ, μ_{tm}, μ_V	Natural death rate for human and vector respectively
σ	Natural immunity rate for TB
$\tau_T, \tau_m, \tau_{tm}$	Treatment rate for TB, Malaria and TB-malaria co-infection respectively
$\delta, \delta v\ \delta_{tm}$	Disease induced mortality rate for human in TB, vector and TB-malaria Co-infection respectively
η_{tm} , η_D	Modification parameters for λ_{TM} , *and* λ_T respectively
γ_M, γ_{TM}	Human Recovery rate for malaria and TB-malaria co-infection respectively
ϕ	Detection rate for undetected TB
ρ	Vaccination rate for TB only
ω	Vaccine wanes off for TB in V_T
υ	Probability of developing infectious TB rate
$\kappa_T, \kappa_M\ \kappa_{TM}$	Progression rate from E_T to U_T, E_M to I_M and E_{TM} to A_{TM} respectively
$\theta_1, \theta_2, \theta_3$	Fast progressor rate for TB, Malaria and TB-Malaria co-infection
$\lambda_T, \lambda_M, \lambda_V$	Force of infection for TB, Malaria and infected vectors (mosquitoes)
λ_{TM}	Force of infection for TB co-infection with Malaria
σ	Natural immunity for TB
a_m	Number of human bitten by mosquito per unit time
a_V	Number of mosquito bites per unit time
ψ_e	Exogenous re-infection of TB in exposed class
ψ_a	Exogenous re-infection of TB in recovered class

III. QUALITATIVE PROPERTIES OF SOLUTIONS

Positivity of solutions

Theorem 1: The closed set $D = \{(S_H, V_T, E_T, U_T, D_T, R_T, E_{TM}, A_{TM}, R_{TM}, E_M, I_M, R_M, S_V, I_V)\}$ is positive for all $t > 0$ with respect to the model equation (20) above.

Let the initial data be

$\{(S_H(0) \geq 0,\ V_T(0) \geq 0,\ E_T(0) \geq 0,\ U_T(0) \geq 0,\ D_T(0) \geq 0\ \ R_T(0) \geq 0\ \ E_{TM}(0) \geq 0\ \ A_{Tm}(0) \geq 0$

$R_{TM}(0) \geq 0\ \ E_M(0) \geq 0\ \ I_M(0) \geq 0\ \ R_M(0) \geq 0\ \ S_V(0) \geq 0\ \ I_V(0) \geq 0\} \in \xi$

Then the solution set

$D = \{(S_H, V_T, E_T, U_T, D_T, R_T, E_{TM}, A_{TM}, R_{TM}, E_M, I_M, R_M, S_V, I_V)\}$ of the model is positive for every $t \geq 0$

Proof:

To prove, the equations of the system (20) was considered. Thus from the first equation of the model

$$\frac{dS_H}{dt} = (1-\rho)\pi - \lambda_T S_H - \lambda_M S_H - \lambda_{TM} S_H - \mu S_H + \omega V \tag{21}$$

It follows that

$$\frac{dS_H}{dt} \geq -(\mu + \lambda_T + \lambda_H + \lambda_{TM}) S_H \tag{22}$$

Consequently,

$$\frac{dS_H}{dt} + (\mu + \lambda_T + \lambda_H + \lambda_{TM}) S_H \geq 0 \tag{23}$$

which is the first order homogeneous differential equation.

using the integrating factor $I.F = e^{\int (\mu+\lambda_T+\lambda_H + \lambda_{TM})dt}$

$$I.F = e^{\int (\mu+\lambda_T+\lambda_H + \lambda_{TM})dt} = e^{(\mu+\lambda_T+\lambda_H + \lambda_{TM})t} \tag{24}$$

By multiplying both sides of equation (23) by equation (24) implies:

$$d(S_H e^{(\mu+\lambda_T+\lambda_H + \lambda_{TM})t}) \geq 0\, dt \tag{25}$$

Integrate both sides with respect to t

$$S_H e^{-(\mu+\lambda_T+\lambda_H + \lambda_{TM})t} \geq K \quad (\text{where k is a constant}) \tag{26}$$

Multiply both sides of equation (26) by $e^{-d(S_H e^{(\mu+\lambda_T+\lambda_H + \lambda_{TM})t}}$

It becomes:

$$S_H(t) \geq K e^{-(\mu+\lambda_T+\lambda_H + \lambda_{TM})t} \tag{27}$$

Applying the initial condition that when t = 0 , $S_H(t) = S_H(0)$

$$S_H(0) \geq K$$

Hence, $S_H(t) \geq S_H(0) e^{-(\mu+\lambda_T+\lambda_H + \lambda_{TM})t}$

Since $\mu + \lambda_T + \lambda_H + \lambda_{TM} \geq 0$ and $S_H(0) \geq 0$ then

$S_H(t) \geq 0$ if $t = 0$ *and* $t \to \infty$

Therefore, $S_H(t) \geq 0 \quad \forall\ t \geq 0$.

It can be shown, using similar method , that the remaining state variables, $V_T(t)$; $E_T(t)$; $U_T(t)$; $D_T(t)$; $R_T(t)$; $E_M(t)$; $I_M(t)$; $R_M(t)$; $E_{TM}(t)$; $A_{TM}(t)$; $R_{TM}(t)$; $S_V(t)$; $I_V(t)$, are non-negative for all the time t>0

Invariant Region

Theorem 2 The biologically feasible region Ω of TB-malaria model (20) is positively invariant.

The solutions of the model (20) are feasible for all $t > 0$ if they enter the invariant region $\Omega = \Omega_h \times \Omega_v \subset R_+^{12} \times R_+^2$

Where $\Omega_h = (S_H, V_T, E_T, U_T, D_T, R_T, E_{TM}, A_{TM}, R_{TM}, E_M, I_M, R_M \in R_+^{12}$ and $\Omega_v . = S_V, I_V \in R_+^2$

Proof:

Let $\Omega = \{(S_H, V_T, E_T, U_T, D_T, R_T, E_{TM}, A_{TM}, R_{TM}, E_M, I_M, R_M, S_V, I_V)\} \in R_+^{14}$ be any solution of the system (20) with non-negative initial conditions.

It is clear from the first twelve equations of the model) that in absence of the TB-malaria,

that is when $I_h = 0$, equation (20) becomes

$$\frac{dN_h(t)}{dt} \leq \pi_h - \mu_h N_h$$

$$\frac{dN_h}{dt} + \mu_h N_h \leq \pi_h \tag{28}$$

After solving the equation (28) and evaluating it as time t tends to infinity, then

$$N_h \leq \frac{\pi_h}{\mu_h} + \left(N_{h0} - \frac{\pi_h}{\mu_h} \right) e^{-\mu_h t} \tag{29}$$

Applying the theorem of differential inequality [26], gives

$0 \leq N_h \leq \frac{\pi_h}{\mu_h}$ as $t \to \infty$.

Similarly, , the ate of change of the total population of vector Nv(t) is:

$$\frac{dN_V}{dt} + \mu_V N_V \leq \pi_V \tag{30}$$

After solving the equation (30) and evaluating it as time t tends to infinity, then

$$N_h \leq \frac{\pi_h}{\mu_h} + \left(N_{h0} - \frac{\pi_h}{\mu_h} \right) e^{-\mu_h t} \tag{31}$$

Hence, all feasible solution set of the human population of the malaria model enters the region

$$\Omega_h = \left\{ \begin{array}{l} \left(\{S_H, V_T, E_T, U_T, D_T, R_T, E_{TM}, A_{TM}, R_{TM}, E_M, I_M, R_M\}\right) \in R_+^{12} : \\ S_h \geq 0, V_T \geq 0 \;\; E_T \geq 0, D_T \geq 0, R_T \geq 0, E_{TM} \geq 0, A_{TM} \geq 0, \\ R_{TM} \geq 0, E_M \geq 0, I_M \geq 0, R_M \geq 0, N_h \leq \dfrac{\pi_h}{\mu_h} \end{array} \right\}.$$

Similarly, the feasible solution set of the vector population enter the region

$$\Omega_v = \left\{ \left(S_v, I_v,\right) \in R_+^2 : S_v \geq 0, I_v \geq 0, N_v \leq \frac{\pi_v}{\mu_v} \right\}.$$

Therefore, the region Ω is positively invariant i.e. solution remains positive for all temporal values. Thus, the model (20) is biologically meaningful and mathematical well-posed in the domain Ω.

TB-malaria co-infection free equilibrium

At critical point,

$$\frac{dS_H}{dt} = \frac{dV_T}{dt} = \frac{dE_T}{dt} = \frac{dU_T}{dt} = \frac{dD_T}{dt} = \frac{dR_T}{dt} = \frac{dE_{TM}}{dt} = \frac{dA_{TM}}{dt} = \frac{dR_{TM}}{dt} = \frac{dE_M}{dt} = \frac{dI_M}{dt} = \frac{dR_M}{dt} = \frac{dS_V}{dt} = \frac{dI_V}{dt} = 0$$

Let DFE be denoted by ε_2, then, at DFE,

$$E_T = U_T = D_T = R_T = E_{TM} = A_{TM} = R_{TM}, = E_M, = I_M =, R_M, =, I_V = 0 \tag{32}$$

Then, the set of the uninfected classes of the model presented as:

$$\varepsilon_2 = \left\{ \frac{\pi_H(\mu + \omega - \rho\mu)}{\mu(\mu + \omega)}, \frac{\rho\pi_H}{\mu + \omega}, 0,0,0,0,0,0,0,0,0,0, \frac{\pi_V}{\mu_V}, 0 \right\} \tag{33}$$

Derivation of basic reproduction number (R_{0TM}) for TB-malaria

The basic reproduction number of the whole model shall be calculated using the next generation matrix method [7]. The associated matrices F and V, are derived from the model equation (20) where

New infection terms F= $\begin{pmatrix} F_1 & F_2 \\ F_3 & F_4 \end{pmatrix}$ (34)

Can be partitioned as follows:

Are $F_1 = \begin{pmatrix} 0 & (1-\theta)\beta_T & \eta_D(1-\theta)\beta_T & 0 & 0 \\ 0 & \theta\beta_T & \eta_D\theta\beta_T & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$, $F_2 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (1-\theta_2)\dfrac{a_M\beta_M\mu_V\pi_H}{\mu\pi_V} \end{pmatrix}$

$$F_3=\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},\quad F_4=\begin{pmatrix} 0 & 0 & 0 & 0 & \dfrac{\theta_2 a_M \beta_M \mu_V \pi_H}{\mu \pi_V} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & (1-\theta_3)\beta_{TM}\eta_{TM} & 0 \\ 0 & 0 & 0 & \theta_3 \beta_{TM}\eta_{TM} & 0 \\ \dfrac{a_V \beta_V \pi_V \mu}{\mu_V \pi_H} & 0 & 0 & \dfrac{a_V \beta_V \eta_{TM} \pi_V \mu}{\mu_V \pi_H} & 0 \end{pmatrix}$$

And non singular matrix $V=\begin{bmatrix} V_1 & V_2 \\ V_3 & V_4 \end{bmatrix}$ (35)

are

$$V_1=\begin{pmatrix} K_2 & 0 & 0 & 0 & 0 \\ -(1-\upsilon)\kappa_T & K_3 & 0 & 0 & 0 \\ -\upsilon\kappa_T & -\phi & K_4 & 0 & 0 \\ 0 & 0 & -(\tau+\sigma) & K_5 & 0 \\ 0 & 0 & 0 & 0 & K_9 \end{pmatrix},\quad V_2=\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & -\gamma_M & 0 & 0 & 0 \end{pmatrix}$$

$$V_3=\begin{pmatrix} 0 & 0 & 0 & 0 & -\kappa_M \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},\quad V_4=\begin{pmatrix} K_{10} & 0 & 0 & 0 & 0 \\ -\tau_M & K_{11} & 0 & 0 & 0 \\ 0 & 0 & K_6 & 0 & 0 \\ 0 & 0 & -\kappa_{TM} & K_7 & 0 \\ 0 & 0 & 0 & 0 & K_{12} \end{pmatrix}$$

Where $K_1=(\mu+\omega)$ $K_2=(\mu+\kappa_T)$ $K_3=(\mu+\delta+\phi)$ $K_4=(\mu+\delta+\tau+\sigma_T)$
$K_5=\mu$ $K_6=(\mu+\kappa_{TM})$ $K_7=(\mu+\delta_{TM}+\tau_{TM})$ $K_8=(\mu+\gamma_{TM})$
$K_9=(\mu+\kappa_M)$ $K_{10}=(\mu+\delta+\tau_M)$ $K_{11}=(\mu+\gamma_M)$ $K_{12}=(\mu_V+\delta_V)$

From the above matrix (34) and (35), V_2 and V_3 are singular matrices, then $F_1V_1^{-1}$ and $F_4V_4^{-1}$ will be considered for the calculation of the reproduction number "R_{0TM}"

The Reproduction number R_1 of the matrix $F_1.V_1^{-1}$ is:

$$R_1=\frac{\beta_T}{K_4K_3K_2}\begin{pmatrix}\phi\upsilon\eta_D\kappa_T\theta_1-\upsilon K_3\eta_D\kappa_T\theta_1-\phi\upsilon\eta_D\kappa_T+\phi K_2\eta_D\theta_1-\phi\eta_D\kappa_T\theta_1+\upsilon K_3\eta_D\kappa_T \\ +\upsilon K_4\kappa_T\theta_1+\phi\eta_D\kappa_T-\upsilon K_4\kappa_T+K_2K_4\theta_1-K_4\kappa_T\theta_1+K_4\kappa_T)\end{pmatrix} \quad (36)$$

While $F_4.V_4^{-1}$ is $R_4=\dfrac{\beta_{TM}(K_6\theta_3-\kappa_{TM}\theta_3+\kappa_{TM}}{K_6K_7}$ (37)

$$F_2.V_2^{-1} = F_3.V_3^{-1} = 0$$

Hence ,the associated reproduction number for the TB-malaria co-infection is known as

$$R_{0TM} = Max\{R_1.R_4\} \tag{38}$$

It follows that the basic reproduction number of TB- malaria co-infection model denoted by R_{0TM} measures the average number of secondary TB-malaria co-infection caused by single TB-Malaria infected human introduced into an entirely susceptible population.

Local stability of disease free equilibrium (DFE) for TB-malaria co-infection

Theorem 3

The disease free equilibrium of the equation (20) is locally asymptotically stable (LAS) if $R_{0TM} < 1$ and unstable when $R_{0TM} > 1.$

This theorem implies that the disease can be eliminated in the society if the basic reproduction number R_{0TM} is less than unity ie $R_{0TM} < 1$

Proof:

To determine the local stability of disease free equilibrium, the Jacobian matrix of equation (20) is computed at point ε_0 = (0.0,0,0,0,0,0,0,0,0,0,0,0,0,0).

Let J_{TM} denotes the Jacobian matrix, then,

$$J_{TM} = \begin{pmatrix} -\mu & \omega & 0 & 0 & 0 & 0 & 0 & 0 & \gamma_m & 0 & 0 & 0 & 0 & 0 \\ 0 & -K_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -K_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-\upsilon)\kappa_T & -K_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \upsilon\kappa_T & \phi & -K_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (\tau+\sigma) & -\mu & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -K_9 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \kappa_M & -K_{10} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_M & -K_{11} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -K_6 & 0 & \gamma_{TM} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \kappa_{TM} & -K_7 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_{TM} & -K_8 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_V & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -K_{12} \end{pmatrix} \tag{39}$$

$$where \quad k_1 = \mu + \omega, \quad K_2 = \mu + \kappa_T \ , \quad K_3 = \mu + \delta + \phi, \ K_4 = \mu + \delta + \tau + \sigma_T \ ,$$
$$K_6 = \mu + \kappa_{TM} \ , \ K_7 = \mu + \delta_{TM} + \tau_{TM} \ , \ K_8 = \mu + \gamma_{TM} \ , K_9 = \mu + \kappa_M \ ,$$
$$K_{10} = \mu + \delta + \tau_M \ , \ K_{11} = \mu + \tau_M \ , K_{12} = \mu_V + \delta_V$$

Then, the characteristic equation of the matrix above is given as $\left| J_{TM}{}^* - \lambda^* I \right| = 0$

$$\begin{pmatrix} -\mu-\lambda & \omega & 0 & 0 & 0 & 0 & 0 & 0 & \gamma_m & 0 & 0 & 0 & 0 & 0 \\ 0 & -K_1-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -K_2-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-\upsilon)\kappa_T & -K_3-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \upsilon\kappa_T & \phi & -K_4-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (\tau+\sigma) & -\mu-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -K_9-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \kappa_M & -K_{10}-\lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_M & -K_{11}-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -K_6-\lambda & 0 & \gamma_{TM} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \kappa_{TM} & -K_7-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_{TM} & -K_8-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_V-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -K_{12}-\lambda \end{pmatrix} \quad (40)$$

From the equation (40), the first column has only non zero term in the diagonal. Thus, the first eigenvalue is $\lambda_1 = -\mu$ and subsequent sub-matrix gave:

$\lambda_2 = -K_1,$ $\lambda_3 = -K_2$ $\lambda_4 = -K_3$ $\lambda_5 = -K_4$ $\lambda_6 = -\mu$

$\lambda_7 = -K_9$ $\lambda_8 = -K_{10}$ $\lambda_9 - K_{11}$ $\lambda_{13} = -\mu_V$ $\lambda_{14} = -K_{12}$

$$\begin{pmatrix} -K_6-\lambda_{10} & 0 & \gamma_{TM} \\ \kappa_{TM} & -K_7-\lambda_{11} & 0 \\ 0 & \tau_{TM} & -K_8-\lambda_{12} \end{pmatrix} = 0 \quad \textbf{(41)}$$

The characteristics polynomial of the above equation (41) is given by:

$$A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 = 0 \quad (42)$$

Where $A_3=1$

$$A_2 = K_8 + K_7 + K_6$$

$$A_1 = K_8K_6 + K_7K_8 + K_6K_7$$

$$A_0 = K_8K_6K_7 - \tau_{TM}\kappa_{TM}\lambda_{TM}$$

The determination of the nature of the roots of the polynomial is being explored by making use of Routh Hurwitz criterion [14]. The matrices are all positive, then all the eigen-values of the Jacobian matrix have negative real roots when $R_{0TM} < 1$, therefore, the disease free equilibrium is locally asymptotically stable.

Global stability of disease free equilibrium of TB-malaria co-infection

Theorem 4

The disease free equilibrium of the system of equation (20) is globally asymptotically stable (GAS) whenever $R_{0TM} < 1$ and unstable if $R_{0TM} > 1$.

Proof:

It follows that $S_H = N_T - V_T - E_T - U_T - D_T - R_T - E_M - I_M - R_M - E_{TM} - A_{TM} - R_{TM} - I_V$ at steady state.

The proof is based on using the comparison theorem [10] to prove the global stability for the model (20). Using the comparison method

Where:

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (1-\theta_1)\beta_T & (1-\theta_1)\beta_T\eta_D & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \theta_1\beta_T & \theta_1\beta_T\beta_D & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{(1-\theta_2)a_M\beta_M\mu_V\pi_H}{\mu\pi_V} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\theta_2 a_M\beta_M\mu_V\pi_H}{\mu\pi_V} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & (1-\theta_3)\beta_{TM} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \theta_3\beta_{TM} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{a_V\beta_V\pi_V\mu}{\mu_V\pi_H} & 0 & 0 & \frac{a_V\beta_V\eta_{TM}\pi_V\mu}{\mu_V\pi_H} & 0 & 0 \end{bmatrix} \quad (43)$$

$$V = \begin{bmatrix} K_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & K_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -(1-\upsilon)\kappa_T & K_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\upsilon\kappa_T & -\phi & K_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\tau+\sigma) & K_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & K_9 & 0 & -\gamma_M & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\kappa_M & K_{10} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\tau_M & K_{11} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & K_6 & 0 & -\gamma_{TM} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\kappa_{TM} & K_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\tau_{TM} & K_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & K_{12} \end{bmatrix} \quad (44)$$

Then (F-V) goes thus

$$(F-V) = \begin{bmatrix} -K_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -K_2 & L_1 & L_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & L_{11} & L_{12} & L_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \upsilon\kappa_T & \phi & -K_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & L_{13} & -K_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -K_9 & 0 & \gamma_M & 0 & 0 & 0 & L_5 \\ 0 & 0 & 0 & 0 & 0 & \kappa_M & -K_{10} & 0 & 0 & 0 & 0 & L_6 \\ 0 & 0 & 0 & 0 & 0 & 0 & \tau_M & -K_{11} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -K_6 & L_7 & \gamma_{TM} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \kappa_{TM} & L_{14} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_{TM} & -K_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & L9 & 0 & 0 & L_{10} & 0 & -K_{12} \end{bmatrix} \quad (45)$$

Where $L_1=(1-\theta_1)\beta_T$, $L_2=(1-\theta_1)\eta_D\beta_T$, $L_3=\theta_1\beta_T$, $L_4=(1-\theta_1)\beta_T$, $L_5=\frac{(1-\theta_2)a_M\beta_M\mu_V\pi_H}{\mu\pi_V}$, $L_6=\frac{\theta_2 a_M\beta_M\mu_V\pi_H}{\mu\pi_V}$, $L_7=(1-\theta_3)\beta_{TM}$, $L_8=\theta_3\beta_{TM}$ $L_9=\frac{a_V\beta_V\pi_V\mu}{\mu_V\pi_H}$, $L_{10}=\frac{a_V\beta_V\eta_{TM}\pi_V\mu}{\mu_V\pi_H}$, $L_{11}=(1-\upsilon)\kappa_T$, $L_{12}=(1-\theta_1)\beta_T-K_3$, $L_{13}=(\tau+\sigma)$, $L_{14}=\theta_3\beta_{TM}-K_7$, $K_1=(\mu+\omega)$ $K_2=(\mu+\kappa_T)$ $K_3=(\mu+\delta+\phi)$, $K_4=(\mu+\delta+\tau+\sigma)$, $K_5=(\mu+\gamma_T)$, $K_6=(\mu+\kappa_{TM})$, $K_7=(\mu+\delta+\tau_{TM})$, $K_8=(\mu+\gamma_{TM})$, $K_9=(\mu+\kappa_M)$, $K_{10}=(\mu+\delta+\tau_M)$, $K_{11}=(\mu+\gamma_M)$, $K_{12}=(\mu_V+\delta_V)$,

Then, by computing $\frac{dZ}{dt}\leq(F-V)[Z]$ (46)

Where $Z = V_T, E_T, U_T, D_T, R_T, E_M, I_M, R_M, E_{TM}, A_{TM}, R_{TM}, I_V$.

Thus, according to [3] and [7], all eigen values of the matrix (F-V) have negative real parts. It follows that the linearized differential inequality above is stable when $R_{0TM}<1$. Hence, it shows that disease free equilibrium is globally asymptotically stable whenever $R_{0TM}<1$ and unstable when $R_{0TM}>1$.

IV. SENSITIVITY ANALYSIS OF THE MODEL

In determining the best way to control and reduce human morbidity and mortality due to TB-Malaria co-infection, it is necessary to know the relative importance of the different factors responsible for its transmission. According to [6, 28], the normalized forward sensitivity index "ξ" of a variable "u" that depends differentiably on a parameter "p" is defined as:

$$\xi_p^u=\frac{\partial u}{\partial p}\times\frac{p}{u} \quad (47)$$

Upon substituting the values of parameters in Table 4 for the basic reproduction number R_{0TM} in equation (37), the result R_{0TM} = 0.7359316 was obtained.

Table 3: Values of Numerical Sensitivity for Model

Parameters	Sensitivity values
β_{TM}	0.99999999
μ	-0.04114534510
τ_{TM}	-0.9333333333
δ_{TM}	-0.040000000
θ_3	0.2031340685
κ_{TM}	0.03370634492

V. NUMERICAL SIMULATION

The analytical results of this study are illustrated by carrying out numerical simulations of the model using parameter values in Table 3 with the help of Maple 18 software with the following initial values $S_H(0)$ = 5000, $V_T(0)$ = 1800, $E_T(0)$ = 1200, $U_T(0)$ = 900, $D_T(0)$ = 500, $R_T(0)$ = 300, $E_M(0)$ = 2000, $I_M(0)$ = 1500, $R_M(0)$ = 1200, $E_{TM}(0)$ = 700, $A_{TM}(0)$ = 300, $R_{TM}(0)$ = 100, $S_V(0)$ = 700, $I_V(0)$ = 300.

Table 4: Parameters values used for the numerical simulation

Parameters	Values	Sources
π_H	2000	[13]
π_V	1000	[26]
μ , μ_V	0.02, 0,04	[1], Estimated
δ_{TM}	0.03	[17]
$\theta_2, \theta_3, \theta_1$	0.7, 0.7, 0.7	Estimated, [20]
β_{TM}, β_T	0.6, 0.3	Estimated
κ_{TM} , κ_M	0.05492, 0.238	[16]
τ_{TM}	0.7	Estimated
τ_M , τ_T	0.7 0.8	Estimated, [11]
δ , δ_V	0.05, 0.01	[11, 16]
γ_M , γ_{TM}	0.2 , 0.2	Estimated
ρ	0.2	[11]
β_M , β_V	0.833, 0.48	[6]
υ	0.16	Estimated
a_M , a_V	0.12, 0,12	[27]
σ	0.2	[9]
ϕ	0.2	Estimated
κ_T	0.2522	[1]
ω	0.1	Estimated
P_2, P_3	0.7 , 0.7	[1]
ψ_e, ψ_a	0.35, 0.35	[1]
η_D , η_{TM}	0.001, 0.001	[20], Estimated

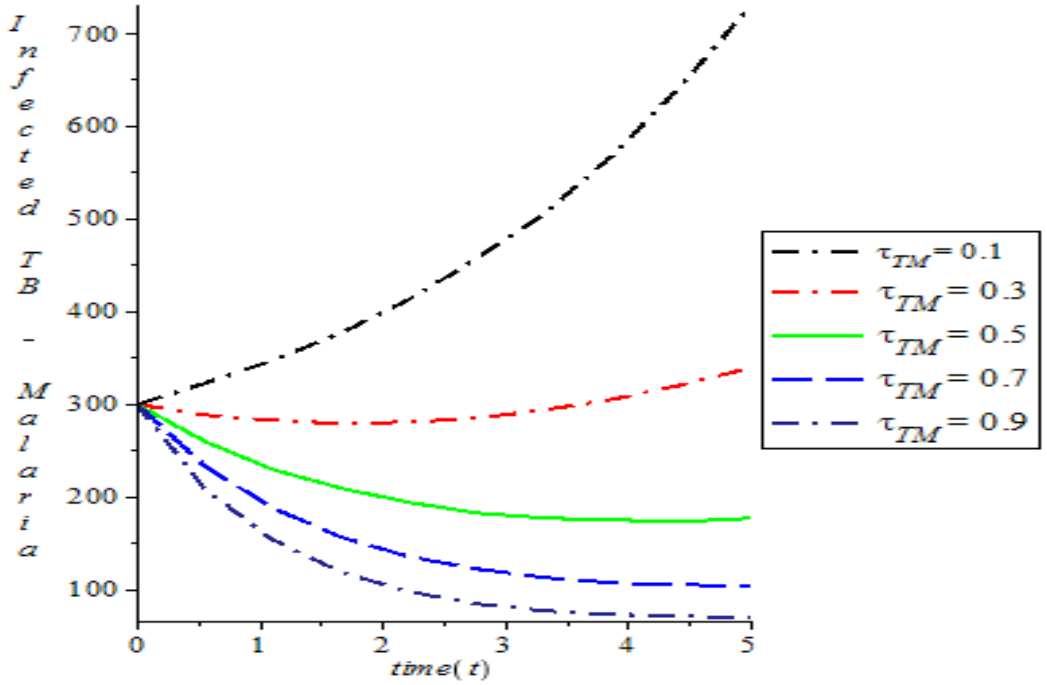

Figure 1: Graph of infected population against time (t) at different treatment rates

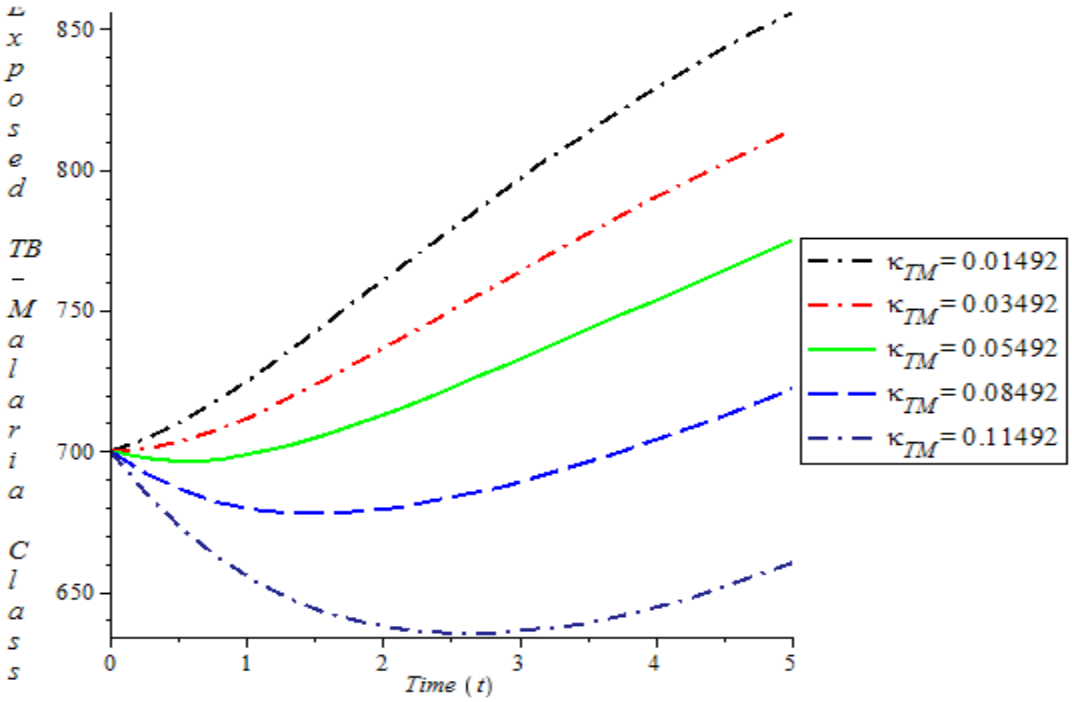

Figure 2: Graph of exposed population against time (t) at different progression rate

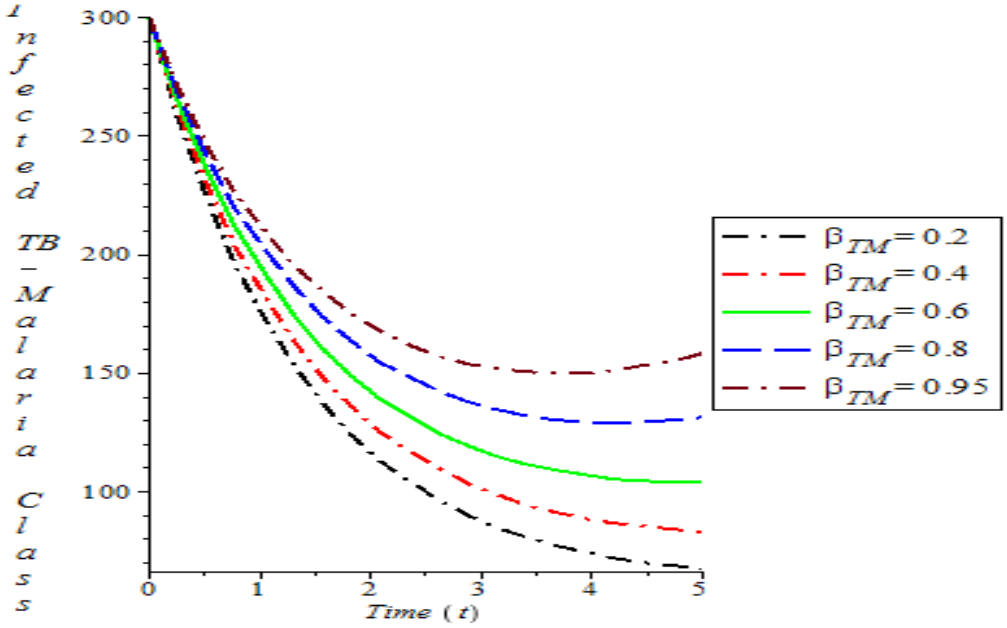

Figure 3: Behavior of contact rate on infected population against time (t)

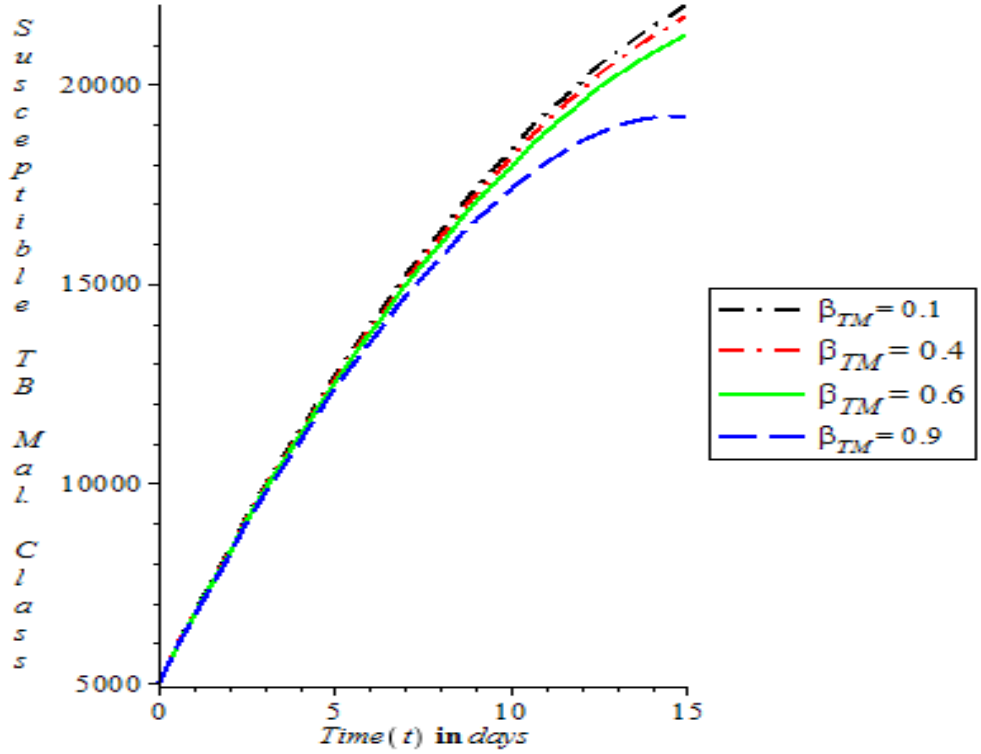

Figure 4: Behavior of contact rate on susceptible population against time (t)

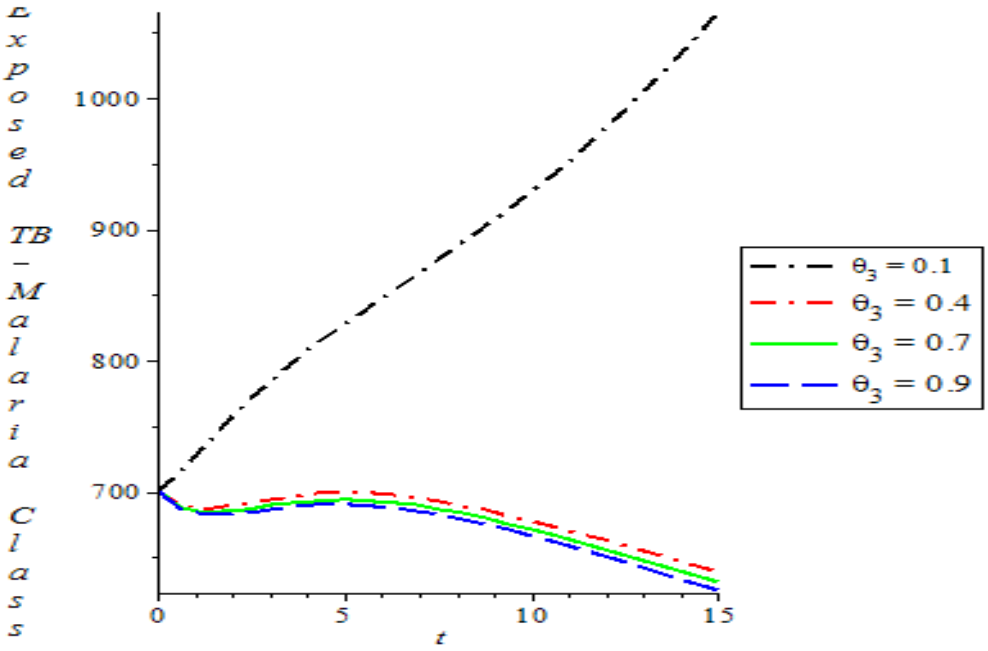

Figure 5: Graph of exposed population against time (t) at different fast progressor rates

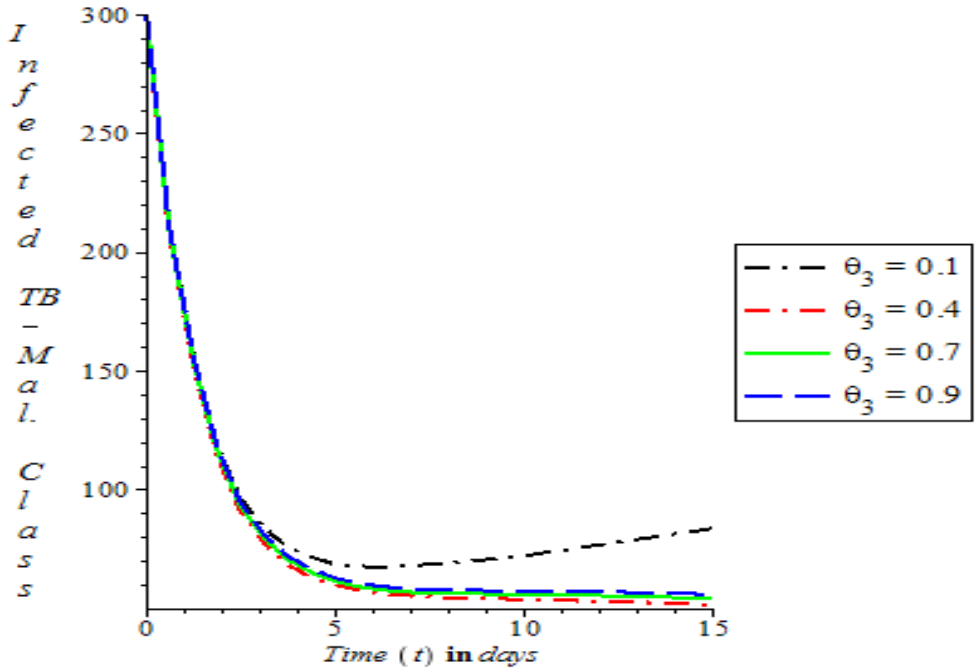

Figure 6: Graph of infected population against time (t) at different fast progressor rates

VI. DISCUSSION OF RESULTS

As shown in figure 1, the magnitude of infected population reduces more rapidly when the treatment rate is high as 0.9. Conversely, the population increases when the treatment rate is low as it appeared at 0.1. Figure 2 shows the impact of

progression rate from exposed population to infected class. The reduction rate of exposed population when the progression rate is high as 0.11492 with population about 630 as compared to when the progression rate is low as 0.01492 which resulted into population around 820 at time (t) = 4. In figure 3, the magnitude of infected population reduces more rapidly when the contact rate is low as 0.2 and 0.4 than when it is 0.6, 0.8 and 0.95. Implication of this is that when the contact rate is low, the infected population will be reduced. As shown in figure 4, the magnitude of susceptible population increases more when the contact rate is low as 0.1 than when they were 0.4, 0.6 and 0.9. Implication of this is that when the contact rate is low, the susceptible population will be increased. Figure 5 shows the impact of fast progressor rate on exposed population. The low-value fast progressor rate increases the exposed population while the high-value fast progressor rate reduces the same population. The impact of fast progressor rate on infected population was shown in figure 6. The magnitude of infected population reduces more rapidly when the fast progressor rate is high as 0.7 and 0.9 than when it is 0.1.

VII. CONCLUSIONS

This works entails the formulation and analysis of a mathematical model for the transmission dynamics of TB-malaria co-infection. The mathematical model incorporates some epidemiological features for the dynamical spread and control of the disease. The analysis of the model revealed that that it *was* mathematically well-posed epidemiology feasible. Also, the basic reproduction numbers R_{0TM} was obtained using next generation matrix method. It was established that disease free equilibrium was locally and globally asymptotically stable whenever the basic reproduction number is less than unity for disease free equilibrium and greater than unity for endemic equilibrium. Sensitivity results revealed that contact rate (β_{TM}) for TB- malaria full model is the most sensitive parameter. Any increment in contact rate increases the basic reproduction which thereby leads to endemicity in the society.

REFERENCES

[1] Adewale, S.O., Podder, C.N. and Gummel A.B., Mathematical Analysis of a TB transmission model with DOTS, Canadian Applied Mathematical Quarterly, 17(1) (2009) Spring.

[2] Adewale, S.O., Ajao, S.O., Olopade, I.A. Adeniran, G.A. and Oyewumi, A.A., Effect of Chemoprophylaxis Treatment on Dynamical Spread of Malaria. International Journal of Scientific and Engineering Research, 7(1) (2016) January 2016. ISSN 2229-5518.

[3] Castillo-Chavez C and Song B. Dynamical Models of Tuberculosis and their Application. Mathematical Biosciences Eng 1(2) (2004) 361-404. https://doi.org/10.3934/mbe.2004.1,361.

[4] Centre for Disease Control and Prevention (CDC) (2000), On emergence of mycobacterium tuberculosis with extensive resistance to second line drugs-worldwide, http://www.ncbi.nln.nih.gov/pubmed/1655723

[5] Centre for Disease Control and Prevention (CDC) (2007): Malaria, Retrievedfromhttp://www.cdc.gov/malaria/fact.html.

[6] Chitnis, N., Hyman J. M. and Cushing J. M, Determining Important Parameters in the spread of malaria Through the Sensitivity Analysis of a Model, Bulletin of Mathematics Biology (2008) Dot 10 1007/s1538 008 9299 0.

[7] Driessche, P. V. and Watmought, J. Reproduction Numbers and Sub-Threshold Endemic Equlibria for Compartmental Models of Disease Transmission. Math. Biosciences, 180(2002)29-48. https://doi.org/1o.1016/S0025-5564(02)00108-6

[8] Fukunaga, R., Glaziou, P., Harris, J.B., Date, A., Floyd, K. and Kasaeva, T. (2021). Epidemilogy of Tuberculosis and Progress Towards Meeting Global Targets-Worldwide. Morbidity and Mortality Weekly Report (MMWR) v.70(12) p427-430, 2021 March 26. Doi-10.15585/mmwr.mm7012a4.

[9] Hethcole, H.W. (2000), The mathematics of infectious diseases. Society for industrial and applied mathematics (SIAM) 42(4): pp 599-653

[10] Lakshmikanthan V., Laela S. and Martynyuk, A.A. (1989), Stability Analysis of Nonlinear Systems. Marcel Dekker, Inc., New York and Basel

[11] Nainggolan, J., Sudradjat Supian, Supriatna A.K. and Anggrian N. (2013), Mathematical Model of Tuberculosis Transmission with Recurrent Infection and Vaccination, Journal of Physics: Conference Series 423 (2013) 012059.

[12] Ochieng Ombaka. Sensitivity of Treatment and Counseling in Co-infection Model of HIV/AIDS, Tuberculosis and Malaria. IJRRAS 26 (2) (2016) 78-89 (2016)

[13] Okuonghae, D and Korobeinikov A., Dynamics of tuberculosis: The effect of Direct Observation Therapy Strategy (DOTS) in Nigeria, Math. Modeling Natural Phenomena 2(1) (2007) 101-113
[14] Olaniyi, S., Okosun, K.O. and Adesanya, S.O. (2018). Global stability and Optimal Control Analysis of Malaria Dynamics in the Presence of Travelers. Open Infect. Dis. J. 10 (2018) 166-186 doi.2174/1874279308181001016 6
[15] Page, K.R., Jedlicka, A.E., Fakheri, B., Noland, G.S. Kesavan, A.K. Scott, A.L.,Kumar, N. and Manabe, Y.C. (2005). Mycobacterium Induced Potentiation of type 1 immune Response and Protection Against Malaria are host Specific. Infect Immun. 73(12) (2005) 8369-8380
[16] Mwamtobe, P. M., Simelane, S. M, Abelman, S. and Tchuenche, J. M. Optimal Control of Intervention Strategies in Malaria-Tuberculosis Co-infection with Relapse. International Journal of Biomathematics. 11(2) (2018) 1850017. Doi:10.1142/S1793524518500171.
[17] Mtisi, J.E., Rwezaura, H. and Tchuenche, J,M,. A mathematical analysis of Malaria-Tuberculosis Co-dynamics. Discrete Cintin. Dynam. Syst. Ser. B. 12(4) (2009) 827-864
[18] Nyabadza, F., Bekele, B. T., Rua, M. A., Malonza, D. M., Chiduk. N. and Kgosimore, M. (2015): The implications of HIV treatment on the HIV-malaria co-infection Dynamics: A modeling perspective. Biomed. Research International. Hindawi, Publishing corporation article ID 659651
[19] Rollback Malaria(2010):What is malaria?Available at http://www.rollbackmalaria.org/cmc__upload/0/0000/015/372/RBMinfosheet_1.pdf
[20] Sharomi, O., Podder, C. N., Gumel, A. B., and Song, B. Mathematical analysis of transmission dynamics of HIV/TB co-infection in the presence of treatment. Mathematical Biosciences and Engineering Journal 5(1) (2008) 145 – 174.
[21] Vroj Wiwanikit, Co-infection between tuberculosis and malaria: A consideration Interaction of Molecules and Pathogenesis. J Vect. Borne Dis. 43 (2006) 195-197
[22] World Health Organization Report. "malaria vaccine becomes first to achieve WHO-Specified 75% efficacy goal" https://www.eurekalert.org/news-releases/744976. furekAlert 23, April, 2021.
[23] World Health Organization (WHO) Global tuberculosis control: Surveillance, planning financing. Geneva 2006b, WHO/HTM/TB/2006.376
[24] WHO (2018): 10 facts on malaria. Available at http://www.who.int/features/factfiles/malaria/en/ Accessed on 09/11/19
[25] Mueller, A..k., Behrends, J., Blank, J., Schaible, U. E., and Schneider, B. E. An Experimental Model to Study Tuberculosis-Malaria Co-infection upon Natural Transmission of Mycobacterium tuberculosis and Plasmodium bergehi. Journal of Visualized Experiments. J. Vis.Exp (84), e50829, doi:10.3791/50829 (2014)
[26] Okosun, K. O. and Makinde, O. D. A co-infection model of malaria and cholera diseases with optimal control. Mathematical Biosciences. 258 (2014) 19-32
[27] Olaniyi, S. and Obabiyi, O.S. Qualitative Analysis of malaria Dynamics with nonlinear incidence Function. Appl. Math. Sci. 8(78) (2014)3889-3904. Doi:10.12988/ams.2014.45326.
[28] Afolabi, M.A., Adewoye, K.S., Folorunso, A.I. and Omoloye, M. A. A Mathematical Model on Transmission Dynamics of Meningococcal Meningitis. Iconic Research and Engineering Journal. APR 2021. IRE journals, 4(10) (2021) 59-66. ISSN:2456-8880.