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MODELING THE IMPACT OF VACCINATION AND VECTOR REDUCTION ON THE TRANSMISSION DYNAMICS OF MALARIA

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Abstract

In this paper, we formulated an host-vector malaria model by adding an entirely new compartment for immuned human population, a partially immune human population to account for waning immunity and also incorporate a vector reduction parameterin the vector population. We set to zero the newly incorporated vaccination and vector reduction parameters of the modified model to ensure consistency in performance compared with the existing model. We investigated the stability or otherwise of the disease- free equilibrium, endemic equilibrium states of the modified model, estimated the basic reproduction number using the next generation matrix operator. The modified model result shows that the disease free equilibrium state is asymptotically stable when $R_o < 1$ ***and unstable if otherwise. The Centre Manifold theorem were used to show that the endemic equilibrium point is locally asymptotically stable when*** $R_o > 1$**.** ***Some numerical simulations were carried out to confirm the analytic results, explore the impact of vaccination and vector reduction as well as other possible behavior of the modified model.***

***Keywords*:** Reproduction Number, Stability, Next Generation Matrix, Disease-free equilibrium points

1. Introduction

Malaria is one of the most important parasitic and infectious diseases commonly in tropical and subtropical areas caused by single-celled protozoan parasites of the *genus Plasmodium*. Among the parasites of the *genus plasmodium*, five species have been identified as causes of the disease in human. These include: Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and Plasmodium knowlesi. Of these, Plasmodium falciparum is of greatest risk to non-immune human with high predominance in Africa region [1]. This variety of parasite accounts for 80% of malaria cases and 90% of deaths [2]. Malaria, affecting mainly children and pregnant women is one of the greatest challenges of our society in terms of morbidity and mortality. It ranks alongside acute respiratory infections, measles and diarrhea diseases as a major cause of mortality worldwide and the prevalence of malaria in tropical and subtropical part of the world correlates with poverty and ignorance in the community [3]. Unfortunately, the disease kills an African child every 30 seconds and over 2,000 young lives are lost daily across the globe [4]. Globally, 3.3 billion people or half of the world's population in 104 countries are at the risk of getting infected by malaria disease [1,5]. It has been estimated that between 300 and 500 million individuals of all ages are infected annually and between 1.5 and 2.7 million people die of malaria every year [6]. The exact statistics are unknown because many cases occur in the rural areas where people lack access to hospital and/or the means to afford medical care. Consequently, many cases are treated at home and cannot be accounted for.

Malaria is spread by the bite of an infected female mosquito, of the genus anopheles each time the infected vector takes a blood meal. The symptoms in an infected human include headache, vomiting flu-like, bouts of fever and anemia (destroying red blood cell). Malaria kills by clogging the capillaries that carry blood to the brain (cerebral malaria) or other vital organs. On the average, the incubation period of Plasmodium falciparum is about 12 days in humans. Malaria is endemic in tropical areas where the climatic and weather conditions enhance continuous breeding of the mosquito. The factors that promote the resurgence and spread of malaria include:

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a. mosquito resistance to the usual insecticides.
b. resistance of some parasite strains to the commonly used anti malaria drugs
c. economic factors that inhibit the financing of malaria control operations.

Most malaria high-risk areas are also located in developing and underdeveloped countries where (a) the level of education is generally low and (b) drugs can be purchased without prescriptions. A combination of (a) and (b) generally results in maladministration of the drugs.

Mosquito control is a speciality in itself and includes the use of anti-malaria drugs, vaccines, insecticides, insecticide-treated bed nets (ITNs), treatment and control of breeding grounds as well as biological control. Each ecological region requires its own individual approach: savannah, primeval forest, agricultural areas with or without irrigation systems, the margins of uplands, desert margins and oases, city environments, coastal and marsh regions. Some of the many challeges encountered in controlling includes: mosquitoes quickly become resistant to insecticides, many people will not allow their houses to be sprayed, high costs, shortage of staff, ecological collateral damage due to insecticides and political instability which interferes with long-term planning. An exclusively technical approach will not be possible without simultaneous improvement in the social and economic conditions of the population at risk.

Mathematical models play a key role in the control of malaria. Koella and Boete [7] derive a model where humans move through multiple Susceptible Exposed-Infectious-Recovered (SEIR) stages, where history is kept of previous infections. They included a sub model for the mosquito population with subdivisions for juveniles and adults. They used the steady state value for the adult mosquito population, from this sub model, as the input into their model for malaria transmission. They introduced dependence of the parameters for the mosquito population sub model on an environmental parameter (eg. temperature or rainfall) and calculated the dependence of the reproductive number, for the full malaria model, on this environmental parameter.

Mathematical modeling has been an important tool in understanding the dynamics of disease transmission and also in decision making process regarding intervention mechanisms for disease control. The study of epidemiology of malaria was heralded by Ross [8] where he developed the first mathematical model for malaria transmission. His focus was on mosquito control and he showed that for the disease to be eliminated, the mosquito population should be brought below a certain threshold. Other studies include Koella and Anita [9] who included a latent class for mosquitoes. They considered different strategies to reduce the spread of the resistance and studied the sensitivity of their results to the parameters. Anderson and May [10] derived a malaria model with the assumption that acquired immunity in malaria is independent of exposure duration. Christopher and Jorge [11] derived a simple two-dimensional SIS (susceptible-infected-susceptible) model with vaccination and multiple endemic states. Guihua and Zhen [12] worked the global dynamics of an SEIR (susceptible-exposed-infected-recovered) epidemic model in which latent and immune states were infective. However, a few studies have been carried out with consideration to the impact of vaccination and waning immunity to malaria models

Adding vaccination to the malaria disease control strategies could make a significant impact in our health challenges. Thus, the introduction of a vaccination compartment alongside the vector reduction parameter in existing malaria model of the authors in [13] are the major focus of this research work as these can help to gain more insight into the dynamics of malaria and also make our model more realistic. Although, malaria vaccines have not yet been licensed commercially for use, its prospect is quite encouraging. This new initiative could likely make a significant impact in our health challenges especially in a time like this where the piloting of the injectable vaccines had just been launched by the World Health Organization in three of African countries (Malawi, Ghana and Kenya), to hundreds of thousands of young children, who have been at high risk of death [14]. Among the potential malaria vaccines, the RTS,S also known as Mosquirix, is the furthest along. The vaccine, which for now has appreciable level of efficacy, has the potential to save tens of thousands of lives if used with existing measures [15]. The challenge however, is whether impoverished countries can deliver the required four doses of the vaccines, given through intramuscular injection, to each child. The vaccines will be tested on children between the ages of 5 - 17 months old to see whether its preventive effect shown so far in clinical trials can hold up under real-life conditions. At least 120,000 children in each of the three countries will receive the vaccine which has taken decades of work and hundreds of millions of dollars to develop [15]. Kenya, Ghana and Malawi were chosen for the vaccines pilot because all have strong prevention and vaccination programs but continue to have high number of malaria cases [15]. The countries will deliver the vaccines through their existing vaccination program. The malaria vaccine has been developed by pharmaceutical company GlaxoSmithKline, and the $49 million for the first phase of the first pilot is being funded by the global vaccine alliance GAVI, UNITAID and the Global fund to fight AIDS, Tuberculosis and Malaria.

Immunity to a disease can be acquired at birth through maternal antibodies (for children borne to immune mothers), vaccination or by infection. However, it wanes over time and needs to be boosted through exposure to infection (reinfection) or through vaccination [4]. Incorporating different stages of immunity in malaria models is important for two reasons. First, its neglect leads to such unrealistic predictions of a prevalence of close to 100% in endemic areas. Secondly, modeling the

impact of vaccines and immunity in particular can help to predict the outcome of vaccination programs. Such models can help to determine the proportion of the population that must be vaccinated for the eradication of the disease [16] and to determine the optimal age of vaccination [17]. Even among people exposed to continuous and intense malaria transmission, as in rural African communities, antimalarial immunity develops quite slowly. Therefore, immunity should be described as a continuum of different levels of protection rather than a yes/no response [18]. Full sterile immunity against asexual blood stages is rarely maintained, and gametocytes seem to be little affected by human immune responses and unless booster inoculations are received, the efficacy of such full and partial acquired immunity decreases with time [18]. The poor immunogenicity and the antigenic diversity of malaria antigens have been suggested as causes of the delayed development and short duration of protective immunity [19]. Where vaccination implies a risk to the individual of developing the disease due to the vaccine, models can help to find a balance between individual and public priorities [18]. Such predictions are difficult to make without the help of mathematical models because of the inherent nonlinearities in the transmission dynamics. Mass immunization changes endemicity and distribution of malaria through protection of vaccinated individuals, but also through indirect effects resulting from reduction in intensity of transmission. The discussion of antimalaria vaccines is further complicated by the loss of immunity when exposure is interrupted [4]. The incorporation of these nonlinearities into predictions of the effect of vaccines on endemicity can help to plan future vaccination.

2. Model formulation

We form a model of a system of ODE with nine compartments for the malaria model in focus. For convenience, we named the compartments for the human host the Susceptible, Exposed, Infected, Vaccinated/Preventive, Recovered/Immune and Partially Immune, while for the vector population: Susceptible, Exposed and Infected, as the case may be. As an analogical illustration to the interactions between the compartments named above, if we let: $X_1(t)$ = the number of susceptible human host at time *t*, $X_2(t)$ = the number of exposed human host at time *t*, $X_3(t)$ = the number infected human host at time *t*, $X_4(t)$ = the number of recovered human host at time *t*, $X_5(t)$ =the number of vaccinated human host at time *t*, $X_6(t)$ =the number of partially immune human host at time *t*, $Y_1(t)$ = the number of susceptible mosquito vector at time *t*, $Y_2(t)$ = the number of exposed mosquito vector at time *t* and $Y_3(t)$ = the number of infected mosquito vector at time *t*, then $N_h(t)$ = the total population of the human population considered at time *t* while $N_m(t)$ = the total population of the mosquito vector considered at time *t*, i.e. ($X_1 + X_2 + X_3 + X_4 + X_5 + X_6 = N_h(t)$ and $Y_1 + Y_2 + Y_3 = N_m(t)$). As an extension of the existing model, we shall consider the effect of the vector reduction parameter k_m on our malaria model. The model is given by the following system of differential equations:

$$\left.\begin{aligned}
\dot{x}_1(t) &= \lambda_h - \frac{b\beta_h x_1(t) y_3(t)}{1+v_h y_3(t)} - (\mu_h + \varphi_h)x_1(t) + \sigma x_6(t)\\
\dot{x}_2(t) &= \frac{b\beta_h x_1(t) y_3(t)}{1+v_h y_3(t)} - (\mu_h + \alpha_h)x_2(t)\\
\dot{x}_3(t) &= \alpha_h x_2(t) - (r + l + \delta_h + \mu_h)x_3(t)\\
\dot{x}_4(t) &= r x_3(t) - (\mu_h + \rho)x_4(t)\\
\dot{x}_5(t) &= \varphi_h x_1(t) - (\mu_h + e)x_5(t)\\
\dot{x}_6(t) &= l x_3(t) + \rho x_4(t) - (\mu_h + \sigma)x_6(t) + e x_5(t)\\
\dot{y}_1(t) &= \lambda_m - \frac{b\beta_m y_1(t) x_3(t)}{1+v_m x_3(t)} - (\mu_m + k_m)y_1(t)\\
\dot{y}_2(t) &= \frac{b\beta_m y_1(t) x_3(t)}{1+v_m x_3(t)} - (\alpha_m + \mu_m + k_m)y_2(t)\\
\dot{y}_3(t) &= \alpha_m y_2(t) - (\delta_m + \mu_m + k_m)y_3(t)
\end{aligned}\right\} \quad (1)$$

with initial conditions

$$x_1(0) = x_{1(0)}, x_2(0) = x_{2(0)}, x_3(0) = x_{3(0)}, x_4(0) = x_{4(0)}, x_5(0) = x_{5(0)}, x_6(0) = x_{6(0)},$$
$$y_1(0) = y_{1(0)}, y_2(0) = y_{2(0)}, y_3(0) = y_{3(0)}$$

The term $\frac{b\beta_h x_1(t)y_3(t)}{1+v_h y_3(t)}$ represent the rate at which the susceptible humans x_1, becomes infected by infectious female anopheles mosquitoes y_3 and $\frac{b\beta_m y_1(t)x_3(t)}{1+v_m x_3(t)}$ represent the rate at which the susceptible mosquitoes y_1 are infected by infectious humans x_3. From the total population,

$$\left.\begin{aligned}\frac{dN_h}{dt} &= \frac{dx_1}{dt}+\frac{dx_2}{dt}+\frac{dx_3}{dt}+\frac{dx_4}{dt}+\frac{dx_5}{dt}+\frac{dx_6}{dt}\\ &= \lambda_h-\mu_h N_h-\delta_h x_3(t)\end{aligned}\right\} \quad (2)$$

$$\left.\begin{aligned}\frac{dN_m}{dt} &= \frac{dy_1}{dt}+\frac{dy_2}{dt}+\frac{dy_3}{dt}\\ &= \lambda_m-(\mu_m+k_m)N_m-\delta_m y_3(t)\end{aligned}\right\} \quad (3)$$

Our assumptions of the model are as follows

i. Every class of human population is decreased by natural death except for the infectious class which has an additional per capital disease-induced death.

ii. Mosquito leaves the population though natural death rate or through a disease induced death rate.

iii. Infected humans who are exposed to non-severe form of malaria and recover naturally acquire a lesser degree of immunity and are thus moved to the partially immune compartment.

iv. Recovered, vaccinated and partially immune human hosts all have temporary immunity that can be lost and later becomes susceptible for possible reinfection.

3. Analysis of the model

The malaria model (1) has a DFE, obtained by setting the right-hand sides of the equations in the model to zero, given by

$$\varepsilon_O=\left(\frac{\lambda_h}{\mu_h},0,0,0,0,0,\frac{\lambda_m}{\mu_m+k_m},0,0\right)$$

3.1 Stability of the disease-free equilibrium (DFE)

The linear stability of ε_O can be established using the next generation operator method in Driessche and Watmough [20] on the system (1). It follows that the reproduction number of the malaria model (1), denoted by $\Re_O$, is given by

$$\Re_O=\sqrt{\Re_h\Re_m}=\sqrt{\frac{b^2\alpha_h\beta_h\lambda_h\alpha_m\beta_m\lambda_m}{M_7(\mu_h)M_2M_9M_8M_3}} \quad (4)$$

where

$\Re_h=\frac{b\beta_h\alpha_h\lambda_h}{(\mu_h)M_2M_3}$, $\Re_m=\frac{b\beta_m\alpha_m\lambda_m}{M_7M_9M_8}$ and

$M_1=(\mu_h+\varphi_h), M_2=(\mu_h+\alpha_h), M_3=(r+l+\delta_h+\mu_h), M_4=(\mu_h+\rho), M_5=(\mu_h+e), M_6=(\mu_h+\sigma), M_7=(\mu_m+k_m),$

$M_8=(\alpha_m+\mu_m+k_m), M_9=(\delta_m+\mu_m+k_m),$

Further, using Theorem 2 in Driessche and Watmough [20], the following result is established. The DFE is locally asymptotically stable if $\Re_O<1$ and unstable if $\Re_O>1$

3.2 Existence of endemic equilibrium

Lemma 1. *The malaria model has a unique endemic equilibrium point if and only if* $\Re_O>1$

Proof: Calculating the endemic equilibrium, we obtain,

$$
\left.\begin{aligned}
x_3^{e_1} &= \frac{\left[\lambda_h M_7 M_4 \left(M_1 M_5 M_6 - \mu_h M_5 M_6 \Re_o^2 - e\sigma\varphi_h\right)\right]}{\left(\begin{aligned}&-b\beta_h\lambda_h R_m M_7 M_5 M_4 M_6 - \lambda_h \nu_h \Re_m M_7 M_6 M_5 M_4 M_1\\&-b\lambda_h\beta_m M_6 M_5 M_4 M_1 - \lambda_h \nu_m M_7 M_6 M_5 M_4 M_1\\&+\sigma e\varphi_h\lambda_h\nu_h\Re_m M_7 M_4 + \sigma b e\varphi_h\lambda_h\beta_m M_4 + \sigma e\varphi_h\lambda_h\nu_m M_7 M_4\\&+\sigma l\mu_h R_o^2 M_7 M_5 M_4 + \sigma\rho r\mu_h\Re_o^2 M_7 M_5\end{aligned}\right)} = \Phi\\
x_1^{e_1}(t) &= \frac{\lambda_h\left(M_7\Re_m\nu_h + b\beta_m + M_7\nu_m\right)\Phi}{\Re_o^2\mu_h M_7} + \frac{\lambda_h}{\Re_o^2\mu_h}\\
x_2^{e_1}(t) &= \frac{M_3\Phi}{\alpha_h}\\
x_4^{e_1} &= \frac{r\Phi}{M_4}\\
x_5^{e_1} &= \frac{\lambda_h\left(M_7\Re_m\nu_h + b\beta_{,m} + M_7\nu_m\right)\varphi_h\Phi}{\mu_h\Re_o^2 M_7 M_5} + \frac{\lambda_h\varphi_h}{\mu_h\Re_o^2 M_5}\\
x_6^{e_1} &= \left(\frac{\begin{aligned}&eM_4M_7\Re_m\lambda_h\nu_h\varphi_h + be\varphi_h\lambda_h\beta_{,m}M_4 + e\varphi_h\lambda_h\nu_m M_7 M_4\\&+l\mu_h R_o^2 M_7 M_5 M_4 + \rho r\mu_h\Re_o^2 M_7 M_5\end{aligned}}{\mu_h\Re_o^2 M_7 M_5 M_4 M_6}\right)\Phi + \frac{e\varphi_h\lambda_h}{\mu_h\Re_o^2 M_5 M_6}\\
y_1^{e_1}(t) &= \frac{\lambda_m\left[\nu_m\Phi + 1\right]}{\Phi\left[b\beta_m + M_7\nu_m\right] + M_7}\\
y_2^{e_1}(t) &= \frac{b\beta_m\lambda_m\Phi}{\left[\Phi\left(b\beta_m + M_7\nu_m\right) + M_7\right]M_8}\\
y_3^{e_1}(t) &= \frac{\Re_m M_7\Phi}{\Phi\left(b\beta_m + M_7\nu_m\right) + M_7}
\end{aligned}\right\} \quad (5)
$$

3.2.1 Existence of backward bifurcation

Using the center manifold theory, the phenomenon of backward bifurcation can be proved on system (1). Applying the Centre Manifold theorem [21], we carry out bifurcation analysis. First, we consider the transmission rate Ψ^* as the bifurcation parameter, Thus Ψ^* can be solved from (4) when $\Re_O = 1$ as

$$
\Re_O = \sqrt{\frac{b^2\alpha_h\beta_h\lambda_h\alpha_m\beta_m\lambda_m}{\left(\mu_m + k_m\right)\left(\mu_h\right)\left(\alpha_h + \mu_h\right)\left(\delta_m + \mu_m + k_m\right)\left(\alpha_m + \mu_m + k_m\right)\left(r + l + \delta_h + \mu_h\right)}}
$$

i.e.

$$
1^2 = \frac{b^2\alpha_h\Psi * \lambda_h\alpha_m\beta_m\lambda_m}{\left(\mu_m + k_m\right)\left(\mu_h\right)\left(\alpha_h + \mu_h\right)\left(\delta_m + \mu_m + k_m\right)\left(\alpha_m + \mu_m + k_m\right)\left(r + l + \delta_h + \mu_h\right)}
$$

$$
\Psi^* = \frac{\left(\mu_m + k_m\right)\left(\mu_h\right)\left(\alpha_h + \mu_h\right)\left(\delta_m + \mu_m + k_m\right)\left(\alpha_m + \mu_m + k_m\right)\left(r + l + \delta_h + \mu_h\right)}{b^2\alpha_h\lambda_h\alpha_m\beta_m\lambda_m}
$$

We make the following change of variables and system of equations (1) becomes

$$
\left.\begin{aligned}
\dot{X}_1(t) &= \lambda_h - \frac{b\Psi * X_1(t)X_9(t)}{1 + \nu_h X_9(t)} - \left(\mu_h + \varphi_h\right)X_1(t) + \sigma X_6(t) = h_1\\
\dot{X}_2(t) &= \frac{b\Psi * X_1(t)X_9(t)}{1 + \nu_h X_9(t)} - \left(\mu_h + \alpha_h\right)X_2(t) = h_2\\
\dot{X}_3(t) &= \alpha_h X_2(t) - \left(r + l + \delta_h + \mu_h\right)X_3(t) = h_3\\
\dot{X}_4(t) &= rX_3(t) - \left(\mu_h + \rho\right)X_4(t) = h_4\\
\dot{X}_5(t) &= \varphi_h X_1(t) - \left(\mu_h + e\right)X_5(t) = h_5\\
\dot{X}_6(t) &= lX_3(t) + \rho X_4(t) - \left(\mu_h + \sigma\right)X_6(t) + eX_5(t) = h_5\\
\dot{X}_7(t) &= \lambda_m - \frac{b\beta_m X_7(t)X_3(t)}{1 + \nu_m X_3(t)} - \left(\mu_m + k_m\right)X_7(t) = h_7\\
\dot{X}_8(t) &= \frac{b\beta_m X_7(t)X_3(t)}{1 + \nu_m X_3(t)} - \left(\alpha_m + \mu_m + k_m\right)X_8(t) = h_8\\
\dot{X}_9(t) &= \alpha_m X_8(t) - \left(\delta_m + \mu_m + k_m\right)X_9(t) = h_9
\end{aligned}\right\} \quad (6)
$$

Where $N_h = X_1 + X_2 + X_3 + X_4 + X_5 + X_6$ and $N_m = X_7 + X_8 + X_9$ with $\Psi^* = \beta_h$

Let

Then zero is a simple eigenvalue, with other eigenvalues having negative real parts of the following Jacobian matrix, J_{bif} with the application of the bifurcation parameters

$$\begin{pmatrix} -(\mu_h+\varphi_h) & 0 & 0 & 0 & 0 & \sigma & 0 & 0 & -\dfrac{b\Psi^*\lambda_h}{(\mu_h)} \\ 0 & F & 0 & 0 & 0 & 0 & 0 & 0 & \dfrac{b\Psi^*\lambda_h}{(\mu_h)} \\ 0 & \alpha_h & C & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & r & -\begin{pmatrix}\mu_h \\ +\rho\end{pmatrix} & 0 & 0 & 0 & 0 & 0 \\ \varphi_h & 0 & 0 & 0 & -\begin{pmatrix}\mu_h \\ +e\end{pmatrix} & 0 & 0 & 0 & 0 \\ 0 & 0 & l & \rho & e & -\begin{pmatrix}\mu_h \\ +\sigma\end{pmatrix} & 0 & 0 & 0 \\ 0 & 0 & D & 0 & 0 & 0 & -\begin{pmatrix}\mu_h \\ +k_m\end{pmatrix} & 0 & 0 \\ 0 & 0 & E & 0 & 0 & 0 & 0 & G & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_m & -\begin{pmatrix}\delta_m \\ +\mu_m \\ +k_m\end{pmatrix} \end{pmatrix} \tag{7}$$

where $C = -\begin{pmatrix} r+l+ \\ \delta_h+\mu_h \end{pmatrix}, D = -\dfrac{b\beta_m\lambda_m}{(\mu_m+k_m)}, E = \dfrac{b\beta_m\lambda_m}{(\mu_m+k_m)}, F = -(\mu_h+\alpha), G = -\begin{pmatrix}\alpha_m \\ +\mu_m \\ +k_m\end{pmatrix}$

A right eigenvector associated with the eigenvalue zero is $w = (w_1 + w_2 + w_3 + w_4 + w_5 + w_6 + w_7 + w_8 + w_9)$. We get

$$\left.\begin{aligned} &-(\mu_h+\varphi_h)w_1 + \sigma w_6 - \frac{b\beta_h\lambda_h}{(\mu_h)}w_9 = 0 \\ &-(\mu_h+\alpha_h)w_2 + \frac{b\beta_h\lambda_h}{(\mu_h)}w_9 = 0 \\ &\alpha_h w_2 - (r+l+\delta_h+\mu_h)w_3 = 0 \\ &rw_3 - (\mu_h+\rho)w_4 = 0 \\ &\varphi_h w_1 - (\mu_h+e)w_5 = 0 \\ &lw_3 + \rho w_4 + ew_5 - (\mu_h+\sigma)w_6 = 0 \\ &-\frac{b\beta_m\lambda_m}{(\mu_m+k_m)}w_3 - (\mu_m+k_m)w_7 = 0 \\ &\frac{b\beta_h\lambda_h}{(\mu_m+k_m)}w_3 - (\alpha_m+\mu_m+k_m)w_8 = 0 \\ &\alpha_m w_8 - (\delta_m+\mu_m+k_m)w_9 = 0 \end{aligned}\right\} \tag{8}$$

Solving (8), we have the following right eigenvector

$$\left.\begin{aligned}
w_1 &= \frac{\left[\sigma w_6 - \frac{b\beta_h\lambda_h}{(\mu_h)} w_9\right]}{(\mu_h+\varphi_h)} \\
w_2 &= \frac{\left(\frac{b\beta_h\lambda_h}{(\mu_h)} w_9\right)}{(\mu_h+\alpha_h)} = \frac{b\beta_h\lambda_h}{(\mu_h)(\mu_h+\alpha_h)} w_9 \\
w_3 &= \frac{\alpha_h w_2}{(r+l+\delta_h+\mu_h)} \\
w_4 &= \frac{rw_3}{(\mu_h+\rho)} \\
w_5 &= \frac{\varphi_h w_1}{(\mu_h+e)} \\
w_6 &= \frac{lw_3+\rho w_4+ew_5}{(\mu_h+\sigma)} \\
w_7 &= \frac{-\frac{b\beta_m\lambda_m}{(\mu_m+k_m)} w_3}{(\mu_m+k_m)} \\
w_8 &= \frac{\frac{b\beta_m\lambda_m}{(\mu_m+k_m)} w_3}{(\alpha_m+\mu_m+k_m)} = \frac{b\beta_m\lambda_m}{(\mu_m+k_m)(\alpha_m+\mu_m+k_m)} w_3 \\
w_9 &= w_9 > 0 \; free
\end{aligned}\right\} \quad (9)$$

and the left eigenvector satisfying $v.w = 1$ is $v = (v_1+v_2+v_3+v_4+v_5+v_6+v_7+v_8+v_9)$. To find these left eigenvector associated with the eigenvalue 0, the matrix (9) should be transposed and this gives matrix, J_{left}

$$\begin{pmatrix}
-(\mu_h+\varphi_h) & 0 & 0 & 0 & \varphi_h & 0 & 0 & 0 & 0 \\
0 & F & \alpha_h & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & C & r & 0 & l & D & E & 0 \\
0 & 0 & 0 & -\left(\begin{matrix}\mu_h \\ +\rho\end{matrix}\right) & 0 & \rho & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & -\left(\begin{matrix}\mu_h \\ +e\end{matrix}\right) & e & 0 & 0 & 0 \\
\sigma & 0 & 0 & 0 & 0 & -\left(\begin{matrix}\mu_h \\ +\sigma\end{matrix}\right) & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & -\left(\begin{matrix}\mu_h \\ +k_m\end{matrix}\right) & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & G & \alpha_m \\
-\frac{b\beta_h\lambda_h}{(\mu_h)} & \frac{b\beta_h\lambda_h}{(\mu_h)} & 0 & 0 & 0 & 0 & 0 & 0 & -\left(\begin{matrix}\delta_m \\ +\mu_m \\ +k_m\end{matrix}\right)
\end{pmatrix} \quad (10)$$

where $C = -\left(\begin{matrix}r+l+ \\ \delta_h+\mu_h\end{matrix}\right), D = -\frac{b\beta_m\lambda_m}{(\mu_m+k_m)}, E = \frac{b\beta_m\lambda_m}{(\mu_m+k_m)}, F = -(\mu_h+\alpha), G = -\left(\begin{matrix}\alpha_m \\ +\mu_m \\ +k_m\end{matrix}\right)$

We now have the following system

$$\left.\begin{aligned}
&-(\mu_h+\varphi_h)v_1 + \varphi_h v_5 = 0 \\
&-(\mu_h+\alpha_h)v_2 + \alpha_h v_3 = 0 \\
&-(r+l+\delta_h+\mu_h)v_3 + rv_4 + lv_6 - \frac{b\beta_m\lambda_m}{(\mu_m+k_m)} v_7 + \frac{b\beta_m\lambda_m}{(\mu_m+k_m)} v_8 = 0 \\
&-(\mu_h+\rho)v_4 + \rho v_6 = 0 \\
&-(\mu_h+e)v_5 + ev_6 = 0 \\
&\sigma v_1 - (\mu_h+\sigma)v_6 = 0 \\
&-(\mu_h+k_m)v_7 = 0 \\
&-(\alpha_m+\mu_m+k_m)v_8 + \alpha_m v_9 = 0 \\
&-\frac{b\beta_h\lambda_h}{(\mu_h)} v_1 + \frac{b\beta_h\lambda_h}{(\mu_h)} v_2 - (\delta_m+\mu_m+k_m)v_9 = 0
\end{aligned}\right\} \quad (11)$$

From the left eigenvector, we have the following results

$$\left.\begin{aligned} v_1 &= \frac{\varphi_h v_5}{(\mu_h+\varphi_h)} \\ v_2 &= v_2 > 0 \; free \\ v_3 &= \frac{(\mu_h+\alpha_h)v_2}{\alpha_h} \\ v_4 &= \frac{\rho v_6}{(\mu_h+\rho)} \\ v_5 &= \frac{e v_6}{(\mu_h+e)} \\ v_6 &= \frac{\sigma v_1}{(\mu_h+\sigma)} \\ v_7 &= 0 \\ v_8 &= \frac{\alpha_m v_9}{(\alpha_m+\mu_m+k_m)} \\ v_9 &= \frac{\frac{b\beta_h\lambda_h}{(\mu_h)}v_2}{(\delta_m+\mu_m+k_m)} \end{aligned}\right\} \quad (12)$$

After rigorous computation, it can be shown that

$$a = v_2 w_2 w_9 \frac{\partial^2 h_2}{\partial x_2 \partial x_9} + v_2 w_3 w_9 \frac{\partial^2 h_2}{\partial x_3 \partial x_9} + v_8 w_8 w_3 \frac{\partial^2 h_8}{\partial x_8 \partial x_3} + v_8 w_9 w_3 \frac{\partial^2 h_8}{\partial x_9 \partial x_3}$$

$$= v_2 w_2 w_9(-b\Psi) + v_2 w_3 w_9(-b\Psi) + v_8 w_8 w_3(-b\beta_m) + v_8 w_9 w_3(-b\beta_m)$$

$$= -b\left[v_2 w_9 \Psi(w_2+w_3) + v_8 w_3 \beta_m (w_8+w_9)\right]$$

$$= -b\left[\begin{array}{l} \frac{v_2 w_9^2 \Psi^2 b\lambda_h}{(\mu_h)}\left(\frac{r+l+\delta_h+\mu_h+\alpha_h}{(\mu_h+\alpha_h)(r+l+\delta_h+\mu_h)}\right) + \\ v_8 w_3 \beta_m \left(\frac{b^2\beta_m \Psi \lambda_h \lambda_m \alpha_h}{(\mu_m+k_m)(\alpha_m+\mu_m+k_m)(r+l+\delta_h+\mu_h)(\mu_h+\alpha_h)(\mu_h)}+1\right) \end{array}\right] < 0$$

$$b = v_2 w_9 \frac{\partial^2 h_2}{\partial \Psi \partial x_9} = v_2 w_9 \frac{b\lambda_h}{(\mu_h)} > 0.$$

Hence $a < 0$ and $b > 0$. Therefore the following theorem holds

Theorem 1

The model (1) has a unique endemic equilibrium which is locally asymptotically stable when $R_o < 1$ and unstable when $R_o > 1$.

4. Numerical Simulation, Results and Discussion

Here, we study numerically the behavior of the system (1) using some of the parameter values compatible with malariaas given in Table 1 and by considering initial conditions,

$x_1(0)=15, x_2(0)=15, x_3(0)=10, x_4(0)=0, x_5(0)=10, x_6(0)=12,$

$y_1(0)=50, y_2(0)=20, y_3(0)=13$

The numerical simulations are conducted using Maple software and the results are given in Figures 1-5 to illustrate the system's behavior for different values of model's parameters.

Table 1: ***Description of variables and parameters of the modified models***

Parameters	Description	Values	Sources
λ_h	recruitment term of the susceptible humans	0.000215	[13]
λ_m	recruitment term of the susceptible mosquitoes	0.07	[13]
b	biting rate of the mosquito	0.12	[13]
β_h	probability that a bite by an infectious mosquito results in transmission of disease to human	0.01	[13]
β_m	probability that a bite by an infectious human results in transmission of disease to mosquito	0.09	[13]
μ_h	per capita natural death rate of humans	0.07	[22]
μ_m	per capita natural death rate of the mosquitoes	$\frac{1}{15}$	[13]
δ_h	disease-induced death rate of infected human	0.089	[22]
δ_m	disease-induced death rate of infected mosquito	0.01	[22]
α_h	per capital rate of progression of humans from the exposed state to the infectious state	$\frac{1}{17}$	[22]
α_m	per capital rate of progression of mosquitoes from the exposed state to the infectious state	$\frac{1}{18}$	[22]
r	per capital recovery rate of humans from the infectious state to the recovered state	0.25	[23]
l	per capital rate at which human host acquire partial immunity due to natural recovery	0.17	[24]
υ_h	proportion of antibody produced by human in response to the incidence of infection caused by mosquito	0.0, 0.5, 1.0	[13]
υ_m	proportion of antibody produced by mosquito in response to the incidence of infection caused by human	0.0, 0.5, 1.0	[13]
φ_h	the 'vaccination rate' on human	0.0, 0.25, 0.5, 0.75	Assumed
k_m	the per capital death induced rate of mosquitoes	0.3, 0.6, 0.9	Assumed
e	the per capita rate of loss of immunity from vaccinated human to partially immune human host to susceptible human	0.008333	Assumed
σ	the per capita rate of loss of immunity from partially immune human to susceptible human host to susceptible human	0.057	Assumed
ρ	the per capita rate of loss of immunity from recovered/immune human to partially immune human	0.015	Assumed

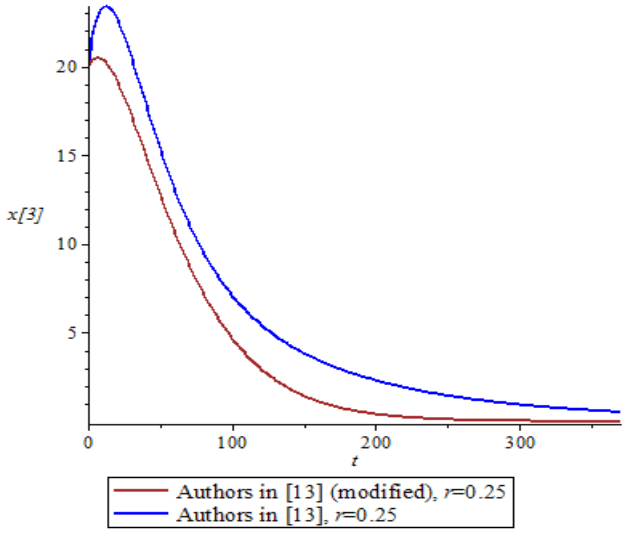

Fig 1
The effect of varied vaccination rate on susceptible human population

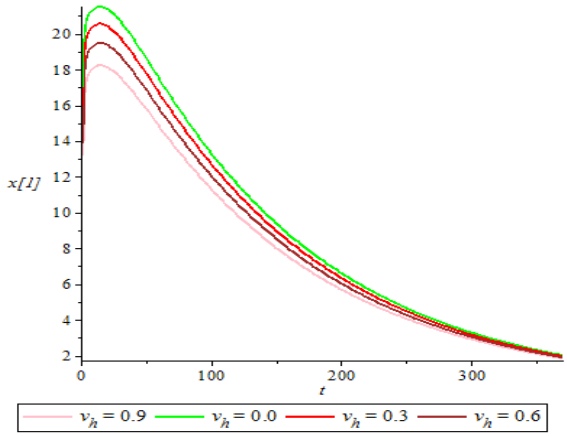

Fig 2
The effect of v_h *on susceptible human population* $R_o < 1,\ b = 0.12$

The graph in Fig 1 above shows clearly the comparison between the existing model of authors in [13] malaria model (without the vaccination parameter, φ) and the modified model (with φ set to zero). We observed closely same model behavior in this compartment. However, the effect of increasing φ (vaccination) through the rates 0.0 - 0.9 on the susceptible human population shows a steady drop in the population with time. This hamper on the interaction between susceptible human population and infected mosquitoes thereby making it difficult for infectious mosquitoes to cause infections on the human population. The graph in Fig 2 above shows the behavior of the susceptible human population as the antibody v_h, increases in proportion on the new model. We observe that the susceptible human population drops as a result of infection by infectious mosquito and later stabilizes when the human develops an antibody against the parasite-causing malaria. A steady increase in the proportion of the antibody reduces the sharp decrease in the susceptible human population.

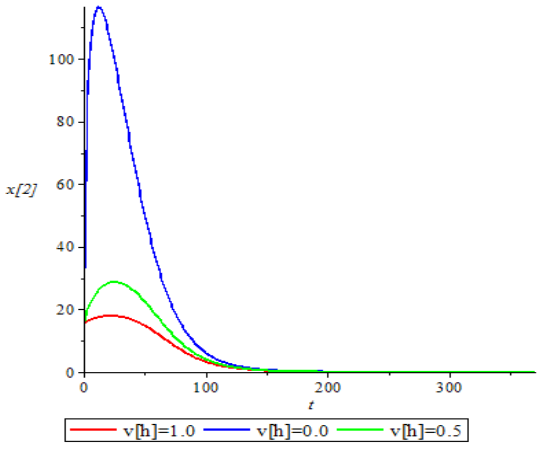

Fig 3a

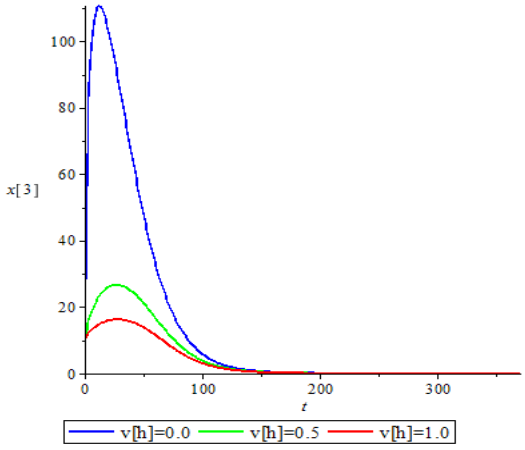

Fig 3b

Effect of v_h *on exposed and infected human population* $R_o < 1,\ b = 0.12$

On the new model, we observed that the magnitudes of the exposed and infectious human populations in Figures 3a & b under the stability condition, respectively decreases with a steady increase in the presence of antibody. Thus, the decreased number of exposed and infectious human population contributes to the initial increase in the number of recovered human population

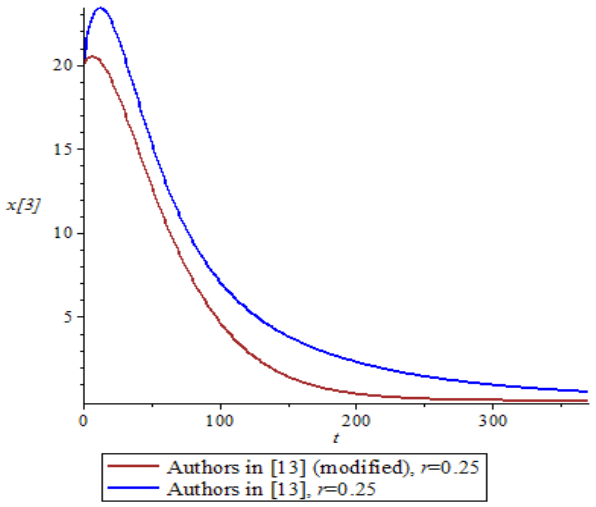

Fig. 4: The comparative graph of infected class of the authors in [3] and the new model at same treatment rate r of 0.25

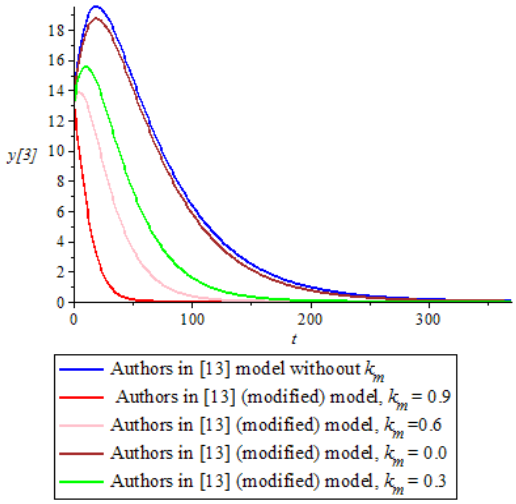

Fig. 5: The effect of K_m (vector reduction) on Susceptible exposed and infected mosquito population

The graph in Fig 4 shows the effect of treatment kept at a constant rate of *0.25* on both models. It's quite clear that the new model averts more disease than the existing model of the authors in [13]. We observed in Fig 5, a similar trend as the graph of the modified model with k_m set to zero(i.e. k_m = 0) corresponds and tracks with the existing model of authors in [13] malaria model (without k_m) Figures 5 depict the varying effects of the mass reduction of susceptible, exposed and infected mosquito population possibly through indoor residual spraying. Increasing the vector reduction rates through 0.0-0.9 clearly shows a sharp and sudden reduction in the mosquito population translating to a lower chances of infection due to the minimized interaction between the mosquitoes and the human population, thus signifying the importance of the control strategy.

5. Conclusion

In this paper, we gleaned on existing model of authors in [13] malaria model, formulated and analyzed a system of nine non-linear differential equations which described the dynamics of malaria within the human host and mosquito vector population. The next generation matrix method were used to determine the basic reproduction number R_o (a threshold quantity that determines whether a disease can be eradicated or not). We investigated and showed that the disease-free equilibrium is stable if $R_o < 1$, signifying the possibility of eradication of the disease from the population, and unstable if $R_o > 1$. The Centre Manifold theorem were used to show that the endemic equilibrium point is locally asymptotically stable when $R_o > 1$. Numerical simulations were performed to see the effects of proportion of antibodies, vaccination as well as vector reduction on the spread of the disease and the following results were obtained:

i. Increasing the proportion of antibodies have tremendous effect in curbing the spread of malaria disease and vice-versa with increased mosquito bites
ii. Introducing and promoting vaccination programs in the malaria disease-fighting mix will make a significant impact in preventing the spread of malaria. Our result reveals that vaccination reduces the susceptible human population tremendously thereby hampering on the interaction between the susceptible human host and the mosquito vector population.
iii. We can attain a malaria free society by intensifying the vector reduction approach through the use of insecticides, regular indoor residual spray, clearing of stagnant waters, clean environment and all other forms of vector control measures as these has significant effect in reducing the transmission of malaria

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