Journal of the Nigerian Mathematical Society
Vol. 36, Issue 3, pp. 459-477, 2017

A MATHEMATICAL MODEL OF MALARIA TRANSMISSION DYNAMICS IN GENETICALLY RESISTANT AND SUSCEPTIBLE POPULATION

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ABSTRACT. The variation in host response to infection might have a genetic basis. Exposure to Plasmodium infection developed genetic mechanisms of protection against severe disease. Two genes affecting red cell confer relative host resistance to P. falciparum: the autosomal gene for haemoglobin S (Hb S) and the sex-linked gene for the glucose-6-phosphate dehydrogenase ($G6PD$) variant. A mathematical model was developed to understand the transmission and spread of malaria parasites. The existence of the region where the model is epidemiologically feasible and mathematically well-posed was established. The reproduction number R_0 was obtained from next generation matrix and the stability analysis of disease-free equilibrium was conducted. Numerical simulations of the model were presented by solving the system of differential equations to explore the behaviour of the model and confirm the analytical results. The results of this study shows a reduction in the number of death of genetically resistant human population which leads to increase in the number of death cases of susceptible human and increase in the number of infected mosquitoes. This study suggest that if genetically resistant person are encouraged to take prophylactic treatment the number of infected mosquitoes could reduce..

Keywords and phrases: Malaria, reproduction number, genetic factor, stability
2010 Mathematical Subject Classification: 92B05

1. INTRODUCTION

Malaria is an infectious disease caused by *Plasmodium* parasites and transmitted between humans through the bite of the female *Anopheles* mosquito. Malaria accounts for more than a million deaths each year, of which over 80% occur in tropical Africa, where malaria is the leading cause of mortality in children under five years

Received by the editors February 25, 2016; Revised: December 09, 2017; Accepted: December 13, 2017
www.nigerianmathematicalsociety.org; Journal available online at www.ojs.ictp.it
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of age. Aside from young children, pregnant women are among the most affected by the disease. Depending on malaria transmission intensity, the main complications of malaria during pregnancy include maternal death, severe anaemia, and adverse birth outcomes such as low birth weight. Constituting 10% of the overall disease burden, malaria places a substantial strain on health service An estimated 225 million malaria cases occur worldwide with 781000 death per year [19]. The incidence of malaria has been growing recently due to increasing parasite drug-resistance and mosquito insecticide-resistance. Therefore, it is important to understand the important parameters in the transmission of the disease and develop effective solution strategies for its prevention. Mathematical modeling of malaria began in 1911 with Ross and major extensions were described by MacDonald in 1957.

A model cannot encompass every feature of a problem. The hope is that the missing features (e.g., the genetic trait of human beings and their immune status are not crucial; however, these features affect the dynamics of transmission of the parasites. There is good evidence that when a population of animals is repeatedly exposed to an infectious disease resulting in significant mortality, the progeny of surviving animals show through several generations increasing resistance to the disease. This is a process of selection of genetically resistant animals. However, as a rule the genetic factors affecting resistance to disease are complex, depending upon many genes affecting antibody synthesis and other reactions. In the case of malaria in man, however, considerable host genetic resistance is known to be conferred by two major genes, the sickle-cell gene (α and β-globin) and the glucosed-phosphate dehydrogenase-deficiency gene; there is also strong circumstantial evidence that the same is true of other abnormal hemoglobin genes. The presence of Hb S in severe malaria patients is associated with less haemolysis and reduced levels of free haeme [2]. Many studies have described an association between the heterozygote HbAS and protection against malaria, with more than 90% protection against severe forms [7,11]. The gene for Hb S is distributed widely throughout sub-Sahara Africa, the Middle East and parts of the Indian sub-continent, where carrier frequencies range from 5 to 40% or more of the population. Hb C is restricted to parts of West and North Africa [18]. These population studies suggesting a protective effect of α thalassaemia

against *P. falciparum* malaria have been augmented by a prospective case-control study of nearly 250 children with severe malaria admitted to Madang Hospital on the north coast of Papua New Guinea, a region where there is a very high rate of malaria transmission [18]. Compared with normal children, the risk of contracting severe malaria, as defined by the strictest WHO guidelines, was 0.4 for α+-thalassaemia homozygotes, and 0.66 for α +-heterozygotes. These studies provide direct evidence for a very strong protective effect α+-thalassaemia against malaria, both in the heterozygous and homozygous state, [1]. It has also been believed for a long time that the high prevalence of individuals in Africa who do not carry the Duffy blood group antigen reflects the protective effect of this genotype against infection with *P. vivax*. This variant disrupts the Duffy antigen/chemokine receptor (DARC) promoter and alters a GATA-1-binding site, which inhibits DARC expression on red cells and therefore prevents DARC-mediated entry of *P. vivax*, [14,16].

The human major histocompatibility complex is the most polymorphic region of the human genome which has been analysed in detail. In the case of malaria there is strong evidence for associations between both HLA Class I and II alleles and susceptibility to *P. falciparum* malaria. Thus, at least in parts of Africa the Class I B53 allele and Class II DRB1* 1352 provide considerable host resistance against the severe manifestations of malaria, that is profound anaemia and cerebral malaria [12]. Further more, studies have identified a peptide from the parasite liver-stage antigen-1 (LAS-1) which is an epitope for specific CD8+ cytotoxic T lymphocytes (CTL) that lyse target cells expressing this antigen [6]. These observations suggest that parasite-specific CTL are present after natural infection and that this may be at least one mechanism for the HLA-B53 association.

After the early successes in identifying polymorphic systems that modify host responses to malaria, a number of other unrelated polygenes that have a similar effect were found. Tumour necrosis factor-α), a cytokine which is secreted by white blood cells and has widespread effects on immune activation, has been analysed in a number of studies. Several different polymorphisms in the promoter regions of the gene for TNF-α have been identified and have been associated with particularly severe forms of malaria [13]. One of these,

TNF-α-308, may cause increased expression of TNF-α [20]. Another influences transcription-factor binding and is associated with an increased risk of cerebral malaria [9]. This model considered genetic factor in addition to other factors previously used, which are critical for predictions and the need for extensions to enhance their predictive power for decision support.

2. MODEL FORMULATION

We present a new mathematical model to study the transmission and spread of malaria in two interacting population of humans (the host) and mosquitoes (the vector). In our model we put into account persons with any of the following genes: α-globin, β-globin, glycophorin, glycophorin B, No Duffy chemokine receptor, GCPD deficiency, blood group O, erythrocytes band 3, HLA-B, HLA-DR, CD36 or spectrin are resistant to malaria. Furthermore, neonates who acquired immunity from parents are also resistant to malaria. On the other hand, person with any of the following genes: TNF-α associated with severe malaria, ICAM-1 associated with severe malaria or pregnant women are highly susceptible to malaria.

Based on these facts, the total human population size at time t denoted by $N_h(t)$ was classified into two groups, genetically resistant and susceptible humans. Genetically resistant human was divided in two classes:1. genetically resistant human G_{hr} and 2. genetically resistant human infected by malaria parasite G_{hi} while genetically susceptible human was subdivided into three classes: susceptible humans S_h, infected humans I_h and recovered humans R_h. Hence we have

$$N_h(t) = G_{hr}(t) + G_{hi}(t) + S_h(t) + I_h(t) + R_h(t),$$

However, mosquito population was subdivided into subclasses: susceptible mosquito S_m and infected mosquito I_m. Thus, the total population size of the mosquito denoted by $N_m(t) = S_m(t) + I_m(t)$. Genetically resistant and susceptible population increased by recruitment of individuals into the human population at Λ_{hr} and Λ_{hs} respectively. Human population decline due to natural death at rate μ_h or through disease induced death rate δ_h. The term $b\beta_h G_{hr}(t)I_m(t)$ and $\beta_h S_h(r)I_m(t)$ are bilinear incident, refered to the rate at which genetically resistant and susceptible human $G_{hr}(t)$ and $S_h(t)$ are bitten by infected mosquitoes $I_m(t)$. In this

study, we use a saturated incidence of the form $\frac{b\beta_h G_{hr}(t)I_m(t)}{1+\rho w I_m(t)}$ and $\frac{b\beta_n S_h(t)I_m(t)}{1+\tau\sigma I_m(t)}$, where $\frac{1}{1+\rho w I_m(t)}$ denote a saturated feature inhibits the force of infection from infected mosquitoes to genetically resistant human and $\frac{1}{1+\tau\sigma I_m(t)}$ denote a saturated feature stimulate the force of infection from infected mosquitoes to genetically susceptible human.

Mosquitoes are recruited into susceptible class $S_m(t)$ at rate Λ_m. Susceptible mosquito becomes infected after ingestion of blood meal from malaria infected humans at rate $b\beta_h(G_{hi}(t)+I_h(t))$. Mosquito population decline due to natural death at rate μ_m and δ_m. It was assumed that the recruitment rate of mosquito is greater than mosquito's death rate at initial time i.e., $\Lambda_m \geq \mu_m N_m(0)$. Based on the above assumptions the following system of ordinary differential equations for the transmission dynamics of the disease was deduced.

$$\frac{dG_{hr}}{dt} = \Lambda_{hr} - \frac{b\beta_h G_{hr}(t)I_m(t)}{1+\rho w I_m(t)} - \mu_h G_{hr}(t) \tag{2.1}$$

$$\frac{dG_{hi}}{dt} = \frac{b\beta_h G_{hr}(t)I_m(t)}{1+\rho w I_m(t)} - \mu_h G_{hi}(t) \tag{2.2}$$

$$\frac{dS_h}{dt} = \Lambda_{hs} - \frac{b\beta_h S_h(t)I_m(t)}{1+\tau\sigma I_m(t)} + \varepsilon R_h(t) - \mu_h S_h(t) \tag{2.3}$$

$$\frac{dI_h}{dt} = \frac{b\beta_h S_h(t)I_m(t)}{1+\tau\sigma I_m(t)} - \gamma_h I_h(t) - \delta_h I_h(t) - \mu_h I_h(t) \tag{2.4}$$

$$\frac{dR_h}{dt} = \gamma I_h(t) - \varepsilon R_h(t) - \mu_h R_h(t) \tag{2.5}$$

$$\frac{dS_m}{dt} = \Lambda_m - \beta_m S_m(t)\frac{b}{N_h}[G_{hi}(t)+I_h(t)] - \mu_m S_m(t) \tag{2.6}$$

$$\frac{dI_m}{dt} = \beta_m S_m(t)\frac{b}{N_h}[G_{hi}(t)+I_h(t)] - (\mu_m+\delta_m)I_m(t) \tag{2.7}$$

together with the initial condition

$$\left.\begin{array}{l} G_{hr}(0)=G_{0hr}, \quad G_{hi}(0)=G_{0hi} \quad S_h(0)=S_{0h}, \quad I_h(0)=I_{0h}, \\ R_h(0)=R_{0h}, \quad S_m(0)=S_{0m}, \quad I_m(0)=I_{0m} \end{array}\right\} \tag{2.8}$$

2.1 EXISTENCE AND POSITIVITY OF SOLUTIONS

The following results which guarantee that the malaria model governed by the system (2) is epidemiologically and mathematically well posed in a feasible region $\mathcal{D}$ is given by:

$$\mathcal{D} = \mathcal{D}_h \times \mathcal{D}_m \subset \mathbb{R}_+^5 \times \mathbb{R}_+^2$$

where

$$\begin{aligned} \mathcal{D}_h &= \left\{ (G_{hr}, G_{hi}, S_h, I_h, R_h) \in \mathbb{R}_+^5 : \frac{\Lambda_{hr} + \Lambda_{hs}}{\mu_h} \right\} \\ \mathcal{D}_m &= \left\{ (S_m, I_m) \in \mathbb{R}_+^2 : N_m \leq \frac{\Lambda_m}{\mu_m} \right\} \end{aligned}$$

Theorem 2.1: There exist a domain $\mathcal{D}$ in which the solution set $\{G_{hr}, G_{hi}, S_h, I_h, R_h, S_m, I_m\}$ is contained and bounded.

Proof. Adding equation (2.1) to (2.5) equations (2.9) was obtained

$$\frac{dN_h}{dt} = \Lambda_{hr} + \Lambda_{hs} + \mu_h N_h(t)$$

$$\frac{d}{dt}(\ell^{\mu_h t} N_h(t)) = \exp(\mu_h t)(\Lambda_{hr} + \Lambda_{hs})$$

$$\int_0^t d(\exp(\mu_h s) N_h(s)) = \int_0^t \exp(\mu_h s)(\Lambda_{hr} + \Lambda_{hs}) ds$$

$$\exp(\mu_h t) N_h(t) - N_h(0) = \frac{\Lambda_{hr} + \Lambda_{hs}}{\mu_h} \exp(\mu_h t) - \frac{\Lambda_{hr} + \Lambda_{hs}}{\mu_h}$$

$$N_h(t) = \frac{\Lambda_{hr} + \Lambda_{hs}}{\mu_h} - (\Lambda_{hr} + \Lambda_{hs} - N_h(0)) \exp(-\mu_h t) \tag{2.9}$$

Similarly, adding (2.6) and (2.7) equation 2.10 was obtained

$$\frac{dN_m}{dt} = \Lambda_m - \mu_m N_h(t)$$

$$\frac{d}{dt}(\exp(\mu_m t) N_m(t)) = \Lambda_m \exp(\mu_m t)$$

$$\int_0^t d(\exp(\mu_m s) N_m(s)) = \int_0^t \Lambda_m \exp(\mu_m s) ds$$

$$\exp(\mu_m t) N_m(t) - N_m(0) = \frac{\Lambda_m}{\mu_m} \exp(\mu_m t) - \frac{\Lambda_m}{\mu_m}$$

$$N_m(t) = \frac{\Lambda_m}{\mu_m} - \left(\frac{\Lambda_m}{\mu_m} - N_m(0) \right) \exp(-\mu_m t) \tag{2.10}$$

Consequently, taking the limits of (2.9) and (2.10) as $t \longrightarrow \infty$ gives $N_h \leq \dfrac{\Lambda_{hr} + \Lambda_{hs}}{\mu_h}$ and $N_m \leq \dfrac{\Lambda_m}{\mu_m}$.
Thus, all solutions of the human population are confined only in the feasible region $\mathcal{D}_h$ and all solution of the mosquitoes (vector) are confined in $\mathcal{D}_m$. Which shows that the feasible region for the formulated model (2) exist and is given by

$$\mathcal{D} = \left\{(G_{hr}, G_{hi}, S_h.I_h, R_h, S_m.I_m) \in \mathbb{R}^7_+ : N_h \leq \frac{\Lambda_{hr} + \Lambda_{hs}}{\mu_h}; N_m \leq \frac{\Lambda_m}{\mu_m}\right\} \quad \square$$

Therefore, it is important to prove that the solution of system (2) are nonnegative in $\mathcal{D}$ for any time $t > 0$ since the model monitors humans and mosquitoes populations.

Theorem 2.2. The solution $G_{hr}, G_{hi}, S_h, I_h, R_h, S_m, I_m$ of the malaria model (2) with nonnegative initial data (2.8) in the feasible domain $\mathcal{D}$, remain nonnegative in $\mathcal{D}$ for all $t > 0$.

Proof. Theorem 2.2 was then proven according to the method used by [4,10]. The result therefore shows that $G_{hr}(t) > 0$ and $S_h(t) > 0$ for all $t \geq 0$. If not, let there exist $t^* > 0$ such that $G_{hr}(t^*) = 0$ and $S_h(t^*) = 0$, $G'_{hr}(t^*) \leq 0$, $S'_h(t^*) \leq 0$ and $G_{hr}, G_{hi}, S_h, I_h, R_h, S_m, I_m > 0$ for $0 < t < t^*$. Then from (2.4) and (2.1) of system (2) the equations below are derived

$$\begin{aligned} S'_h(t^*) &= \Lambda_{hs} - \frac{b\beta_h S_h(t^*) I_m(t^*)}{1 + \tau\sigma I_m(t^*)} + \varepsilon R_h(t^*) - \mu_h S_h(t^*) \\ &= \Lambda_{hs} + \varepsilon R_h(t^*) > 0 \end{aligned}$$

and

$$\begin{aligned} G'_{hr}(t^*) &= \Lambda_{hr} - \frac{b\beta_h G_{hr}(t^*) I_m(t^*)}{1 + \tau w I_m(t^*)} - \mu_h G_h r(t^*) \\ &= \Lambda_{hr} > 0 \end{aligned}$$

which contradicts the expected result. Hence $S_h(t) > 0$ and $G_{hr}(t) > 0$.

Suppose there exist $t^* = \sup\{t > 0 : G_{hr}, G_{hs}, S_h, I_h, R_h, S_m, I_m > 0\}$. Then system (2.2) gives

$$\frac{d}{dt}(\exp(\mu_h t) G_{hi}(t)) = \frac{b\beta_h G_{hr}(t) I_m(t)}{1 + \rho w I_m(t)} \exp(\mu_h t) \tag{2.11}$$

Integrating (2.11) from 0 to t^*, gives

$$\int_0^{t^*} \frac{d}{dt}(\exp(\mu_h t^*) G_{hi}(t^*) = \int_0^{t^*} \frac{b\beta_h G_{hr}(\theta) I_m(\theta)}{1 + \rho w I_m(\theta)} \exp(\mu_h \theta) d\theta$$

$$G_{hi}(t^*) = \exp(-\mu_h t^*)G_{hi}(0) + \exp(-\mu_h t^*) \times \int_0^{t^*} \exp(\mu_h \theta)\frac{b\beta_h G_{hr}(\theta)I_m(\theta)}{1+\rho w I_m(\theta)}d\theta > 0$$

Hence $G_{hi}(t^*) > 0$.

For $I_h(t)$, suppose $t^* > 0 \ni I_h(t^*) = 0$ and $I_h(t) > 0$ where $t \in [0, t^*)$. Then from (2.4)

$$\frac{d}{dt}(\exp(\gamma+\delta_h+\mu_h)t\ I_h(t)) = \exp(\gamma+\delta_h+\mu_h)t\frac{b\beta_h S_h(t)I_m(t)}{1+\tau\sigma I_m(t)} \quad (2.12)$$

Integrating (2.12) from 0 to t^*

$$\int_0^{t^*} \frac{d}{dt}(\exp(\gamma+\delta_h+\mu_h)t^*\ I_h(t^*)) = \int_0^{t^*} \frac{b\beta_h S_h(\theta)I_m(\theta)}{1+\tau\sigma I_m(\theta)}\exp(\gamma+\delta_h+\mu_h)\theta d\theta$$

$$\begin{aligned} I_h(t^*) &= I_h(0)\exp\{-(\gamma+\delta_h+\mu_h)t^*\} + \exp\{-(\gamma+\delta_h+\mu_h)t^*\} \\ &\quad \times \int_0^{t^*} \frac{b\beta_h S_h(\theta)I_m(\theta)}{1+\tau\sigma I_m(\theta)}\exp(\gamma+\delta_h+\mu_h)\theta\ d\theta > 0 \end{aligned}$$

which contradicts $I_h(t^*) = 0$. Similarly, $R_h(t)$, assumming there is some $t^* > 0$ such that $I_h(t) > 0$. Then integrating (2.5) of system (2) from 0 to t^* gives

$$\int_0^{t^*} \frac{d}{dt}\exp(\varepsilon+\mu_h)t\ R_h(t) = \int_0^{t^*} \gamma I_h(\theta)\exp(\varepsilon+\mu_h)\theta\ d\theta$$

$$\exp(\varepsilon+\mu_h)t^*\ R_h(t^*) - R_h(0) = \int_0^{t^*} \gamma I_h(\theta)\exp(\varepsilon+\mu_h)\theta\ d\theta$$

$$\begin{aligned} R_h(t^*) &= R_h(0)\exp\{-(\varepsilon+\mu_h)t^*\} + \exp\{-(\varepsilon+\mu_h)t^*\} \\ &\quad \times \int_0^{t^*} \gamma I_h(\theta)\exp(\varepsilon+\mu_h)\theta\ d\theta > 0 \end{aligned}$$

which contradicts $R_h(t^*) = 0$.

Assuming further that $S_m(t)$ is a non-increasing and other variables are positive with $S_m(t) > 0$ for $t \in [0, t^*)$. It follows from (2.5) that

$$S_m'(t^*) = \Lambda_m - \beta_m S_m(t^*)\frac{b}{N_h(t^*)}(G_{hi}(t^*) + I_h(t^*)) - \mu_m S_m(t^*) > 0$$

which is a contradicts the result of theorem 2.2. Hence, there is no such t^* for which $S_m(t^*) = 0$.

Finally, it shows that equation (2.7) of system (2) gives

$$\begin{aligned} \frac{dI_m}{dt} &\geq -(\mu_m + \delta_m)I_m(t) \\ I_m(t) &\geq I_m(0)\exp\{-(\mu_m + \delta_m)t\} \geq 0 \end{aligned}$$

This completes the proof. □

3. EXISTENCE AND STABILITY OF EQUILIBRIUM POINT.

In this section, the model was analysed and the condition that guarantee the stability of the disease-free equilibrium was stated. When modelling infectious diseases, the most important issue that arises is whether the disease could attain pandemic level or it could be eradicated.

3.1 DISEASE-FREE EQUILIBRIUM POINT

Setting the disease states and left side of (2.1) - (2.7) to zero, the resulting system is solved. The following points was therefore obtained.

$$\begin{aligned} G_{hr} &= \frac{\Lambda_{hr}}{\mu_h}, \quad S_h = \frac{\Lambda_{hs}}{\mu_h}, \quad S_m = \frac{\Lambda_m}{\mu_m} \\ E_0 &= \left(\frac{\Lambda_{hr}}{\mu_h},\ 0,\ \frac{\Lambda_{hs}}{\mu_h},\ 0,\ 0,\ \frac{\Lambda_m}{\mu_m},\ 0\right) \end{aligned}$$

3.2 REPRODUCTION NUMBER R_0

For epidemiology models, a quantity R_0 is derived to asses the stability of the disease-free equilibrium. R_0 represents the number of secondary cases that are caused by a single infectious case introduced into a complete susceptible population. It is an important parameter that indicate whether an infection will spread through the population or not.
To obtain R_0 for model (2),the next generation matrix technique described by [5,17] was used. Let $x = (G_{hr}, I_h, I_m, G_{hr}, S_h, R_h, S_m)^T$. Then the model (2) can be written as

$$\frac{dx}{dt} = \mathcal{F}(x) - \mathcal{V}(x),$$

where

$$\mathcal{F} = \begin{pmatrix} \dfrac{b\beta_h G_{hr} I_m}{1+\rho w I_m} \\ \dfrac{b\beta_h S_h I_m}{1+\tau\sigma I_m} \\ \beta_m S_m \dfrac{b}{N_h}(G_{hi} + I_h) \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

and

$$\mathcal{V} = \begin{pmatrix} \mu_h G_{hi} \\ (\gamma + \mu_h + \delta_h) I_h \\ (\mu_m + \delta_m) I_m \\ \mu_h G_r - \Lambda_{hr} \\ \mu_h S_h - \Lambda_{hs} - \varepsilon R_h \\ (\varepsilon + \mu_h) R_h - \gamma I_h \\ \mu_m S_m - \Lambda_m \end{pmatrix}$$

Finding the derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the disease-free equilibrium point E_0 gives F and V respectively where

$$F = \begin{pmatrix} 0 & 0 & \frac{b\beta_h\Lambda_{hr}}{\mu_h} \\ 0 & 0 & b\beta_h\frac{\Lambda_{hs}}{\mu_h} \\ \frac{b\beta_m\Lambda_m\mu_h}{\mu_m(\Lambda_{hr}+\Lambda_{hs})} & \frac{b\beta_m\Lambda_m\mu_h}{\mu_m(\Lambda_{hr}+\Lambda_{hs})} & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \mu_h & 0 & 0 \\ 0 & \gamma+\mu_h+\delta_h & 0 \\ 0 & 0 & \mu_m+\delta_m \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} 0 & 0 & b\beta_h\Lambda_{hr} \\ 0 & 0 & \frac{b\beta_h\Lambda_{hs}}{\mu_h} \\ \frac{b\beta_m\Lambda_m\mu_h^2}{\mu_m(\mu_m+\delta_m)(\Lambda_{hr}+\Lambda_{hs})} & \frac{b\beta_m\Lambda_m\mu_h^2}{\mu_m(\mu_m+\delta_m)(\Lambda_{hr}+\Lambda_{hs})} & 0 \end{pmatrix}$$

R_0 is the maximum eigenvalue of FV^{-1} given by

$$R_0 = \sqrt{\frac{b^2\mu_h^2\beta_h\Lambda_m\beta_m[\Lambda_{hs}+\Lambda_{hr}(\gamma+\mu_h+\delta_h)]}{\mu_m(\mu_m+\delta_m)(\Lambda_{hr}+\Lambda_{hs})(\gamma+\mu_h+\delta_h)}}$$

3.3 STABILITY OF THE DISEASE-FREE EQUILIBRIUM POINT

Theorem 3.3. The disease-free equilibrium for system (2.1) - (2.7) is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof. The Jacobian of the system (2.1) - (2.7) evaluated at the disease-free equilibrium point is

$$J(E_0) = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & 0 & 0 & J_{17} \\ 0 & -\mu_h & 0 & 0 & 0 & 0 & J_{27} \\ 0 & 0 & -\mu_h & 0 & \varepsilon & 0 & J_{37} \\ 0 & 0 & 0 & -(\gamma+\mu_h+\delta_h) & 0 & 0 & J_{47} \\ 0 & 0 & 0 & \gamma & -(\varepsilon+\mu_h) & 0 & 0 \\ 0 & J_{62} & 0 & J_{64} & 0 & -\mu_m & 0 \\ 0 & J_{72} & 0 & J_{74} & 0 & 0 & -(\mu_m+\delta_m) \end{pmatrix}$$

where

$$\begin{aligned} J_{17} &= \frac{-b\beta_h\Lambda_{hr}}{\mu_h}, \quad J_{27} = \frac{b\beta_h\Lambda_{hr}}{\mu_h} \\ J_{37} &= \frac{-b\beta_h\Lambda_{hr}}{\mu_h}, \quad J_{47} = \frac{b\beta_h\Lambda_{hr}}{\mu_h}, \quad J_{62} = \frac{-b\beta_h\Lambda_m\mu_h}{\mu_m(\Lambda_{hr}+\Lambda_{hs})} \\ J_{64} &= \frac{-b\beta_m\Lambda_m}{\mu_m(\Lambda_{hr}+\Lambda_{hs})}, \quad J_{72} = \frac{b\beta_m\Lambda_m\mu_h}{\mu_h(\Lambda_{hr}+\Lambda_{hs})} \\ J_{74} &= \frac{b\beta_m\Lambda_m\mu_h}{\mu_m(\Lambda_{hr}+\Lambda_{hs})} \end{aligned}$$

The first, third and sixth columns have diagonal entries. Therefore the diagonal entries $-\mu_h$, $-\mu_h$ and $-\mu_m$ are three of the eigenvalues of the Jacobian. Thus, the remaining eigenvalues was obtained by excluding these columns and the corresponding rows. These eigenvalues are the solutions of the characteristics polynomial given by

$$\lambda^3 + B_2\lambda^2 + B_1\lambda + B_0 = 0 \tag{2.12}$$

where

$$\begin{aligned} B_0 &= (\mu_m+\delta_m)(\gamma+\mu_h+\delta_h) - \frac{b^2\mu_h^2\beta_h\Lambda_m\beta_m[\Lambda_{hs}+\Lambda_{hr}(\gamma+\mu_h+\delta_h)]}{\mu_m(\Lambda_{hs}+\Lambda_{hr})} \\ B_1 &= (\mu_m+\delta_m)(\gamma+\mu_h+\delta_h)\frac{-2b^2\mu_h^2\beta_h\Lambda_m\beta_m[\Lambda_{hs}+\Lambda_{hr}(\gamma+\mu_h+\delta_h)]}{\mu_m(\Lambda_{hs}+\Lambda_{hr})} \end{aligned}$$

Let $A_1 = (\mu_m+\delta_m)$, , $A_2 = (\gamma+\mu_h+\delta_h)$, then B_0 and B_1 becomes

$$\begin{aligned} B_0 &= A_1A_2 - \frac{b^2\mu_h^2\beta_h\Lambda_m\beta_m[\Lambda_{hs}+\Lambda_{hr}(\gamma+\mu_h+\delta_h)]}{\mu_m(\Lambda_{hs}+\Lambda_{hr})} \\ B_1 &= A_1A_2\frac{-b^2\mu_h^2\beta_h\Lambda_m\beta_m[\Lambda_{hs}+\Lambda_{hr}(\gamma+\mu_h+\delta_h)]}{\mu_m(\Lambda_{hs}+\Lambda_{hr})} \end{aligned}$$

Further algebraic manipulation of B_0 and B_1 in terms of the basic reproduction number, R_0, gives

$$B_0 = A_1A_2(1-R_0^2) \tag{2.13}$$

$$B_1 = A_1A_2(1-2R_0^2) \tag{2.14}$$

Routh-Hurwitz condition [8]. are necessary and sufficient to verify if all the roots of (2.12) have negative real parts. For (2.12) the condition are

$$H_2 = B_2 > 0, \quad H_2 = \begin{vmatrix} B_2 & 1 \\ B_0 & B_1 \end{vmatrix} > 0, \quad H_3 = \begin{vmatrix} B_2 & 1 & 0 \\ B_0 & B_1 & B_2 \\ 0 & 0 & B_0 \end{vmatrix} > 0$$

Clearly $B_2 > 0 \Longrightarrow H_2 = B_2 > 0$. Moreover, suppose $R_0 < 1$ then $B_0 > 0$ and $B_2 > 0$. Therefore all the eigenvalues of the Jacobian matrix (2.11) have negative real parts when $R_0 < 1$. Also the Hurwitz matrices for the polynomial (2.12) are found to be positive. Therefore the system is locally asymptotically stable.

Table 1. Definition of parameters.

Parameter	Symbol	Value	Reference
- Biological existence genes present in human	ω	1.0	Variable
- Probability that at least one of the genetic factors could be responsible for host resistance from a number of genes	ρ	0.9	Variable
- Biological susceptibility genes present in human	σ	1.0	Variable
- Probability that at least one of the genetic factors could be responsible for susceptibility for a number of genes	τ	0.9	Variable
- Recruitment term of the genetically resistance humans	$\wedge_{hr}$	0.00215	Variable
- Recruitment term of the genetically susceptible humans	$\wedge_{hs}$	0.0314	Variable
- Treatment rate	ε	0.0013699	[19]
- Recovery rate	γ	0.05	[19]
- Bitting rate of the mosquito	b	0.12	[14]
- Probability that a bite by an infectious mosquito results in transmission of disease to human	β_h	0.1	[20]
- Probability that a bite results in transmission of parasite to a susceptible mosquito	β_m	0.09	[20]
- Recruitment term of susceptible mosquito	$\wedge_m$	0.07	[14]
- Per capital death rate of human	μ_h	0.00548	[19]
- Per capital death rate of mosquito	μ_m	0.06667	[19]
- Disease - induced death rate of human	δ_h	0.02	[15]
- Disease - induced death rate of mosquito	δ_m	0.01	[20]

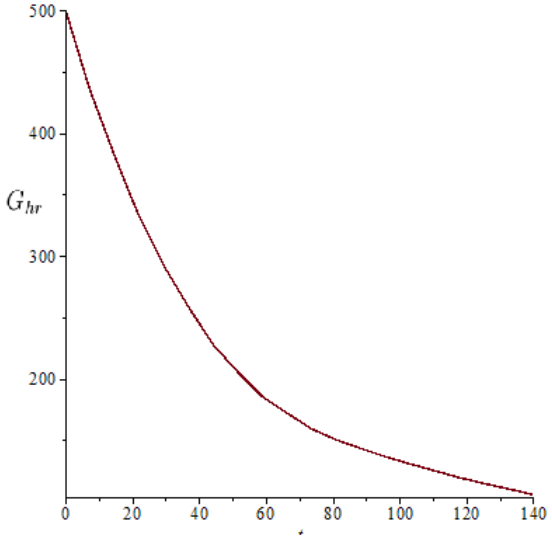

Fig. 1. The behavior of genetically resistant human when $R_0 < 1$ and $b = 0.12$

4. NUMERICAL RESULTS.

In this section, the behaviour of system (2) was investigated numerically using some of the parameter values compatible with malaria [3,8,10], as given in Table 1 by considering the initial conditions $G_{hr}(0) = 500$, $G_{hi}(0) = 100$, $S_h(0) = 500$, $I_h(0) = 100$, $R_h(0) = 0$, $S_m(0) = 2000$, $I_m(0) = 100$. The numerical simulations were conducted using Maple 18

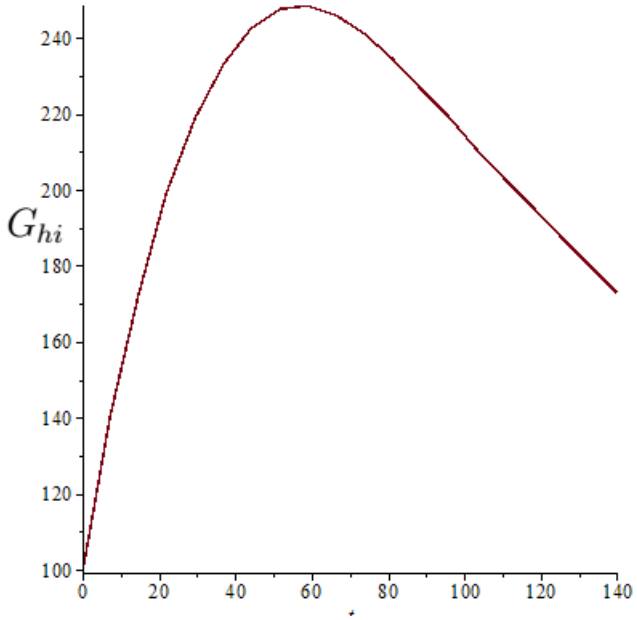

Fig. 2. The behavior of genetically resistant human infected by malaria parasite when $R_0 < 1$ and $b = 0.12$

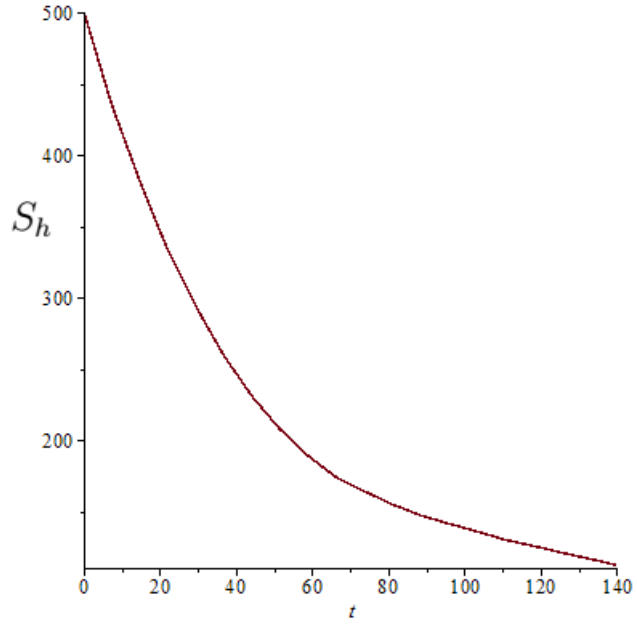

Fig. 3. The behavior of genetically susceptible human when $R_0 < 1$ and $b = 0.12$

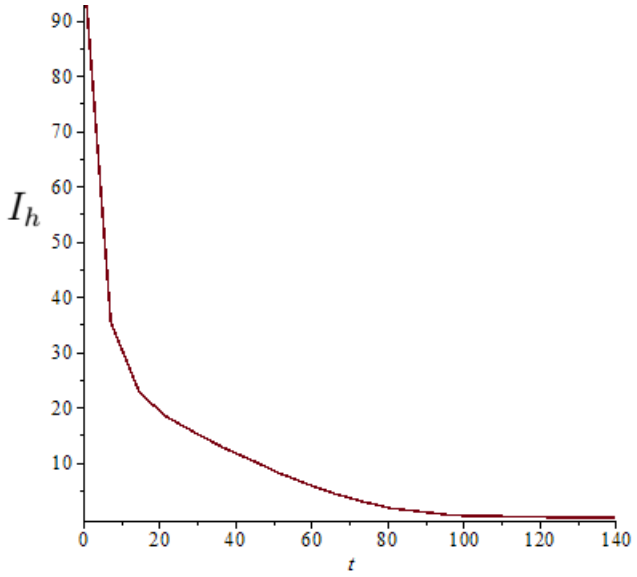

Fig. 4. The behavior of infected human when $R_0 < 1$ and $b = 0.12$

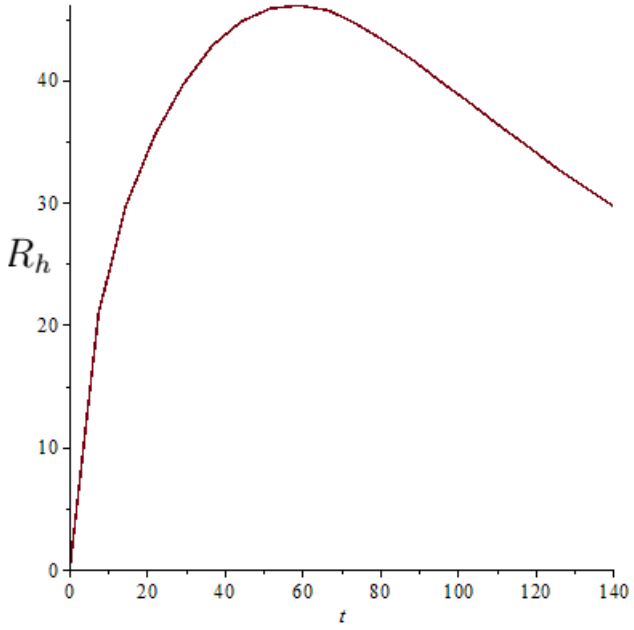

Fig. 5. The behavior of recovered human when $R_0 < 1$ and $b = 0.12$

Software and results are given in Figures 1-7 to illustrate the system's behaviour. Figures 1-4 shows the effects of genes ω and δ present on human population when $R_0 < 1$ and $b = 0.12$. In particular, Figure 1 shows the behaviour of the genetically resistant human population G_{hr}.

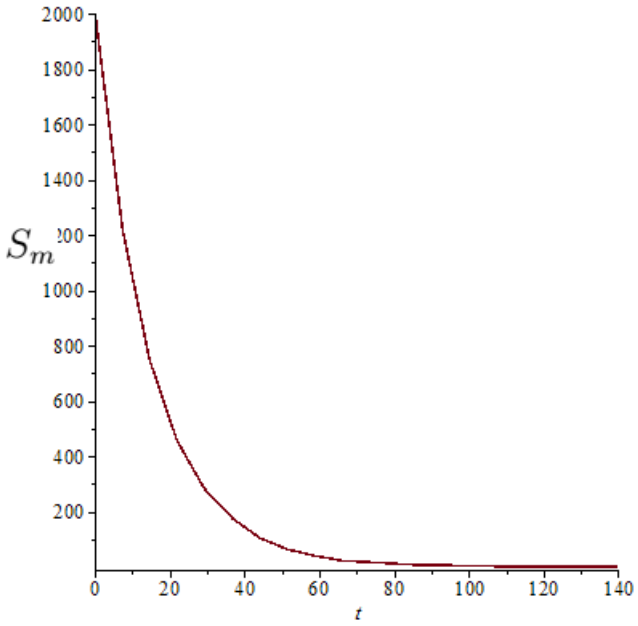

Fig. 6. The behavior of susceptible mosquito when $R_0 < 1$ and $b = 0.12$

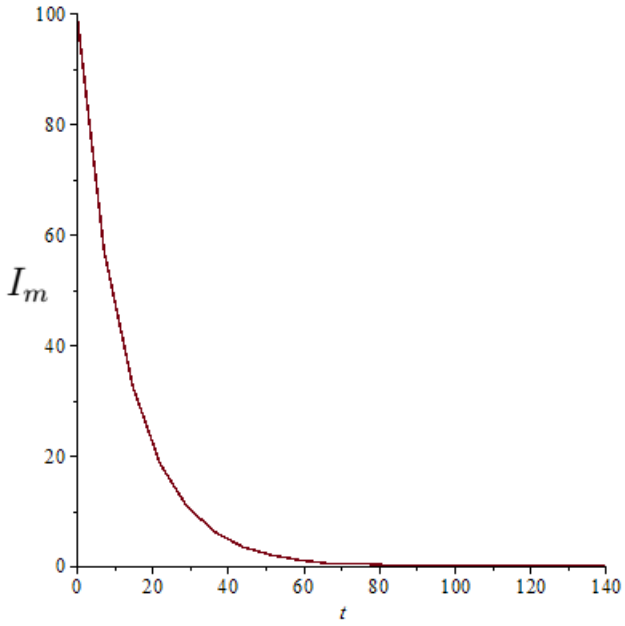

Fig. 7. The behavior of infected mosquito when $R_0 < 1$ and $b = 0.12$

It was observed that the genetically resistant humans decline as a result of infection by infected mosquitoes and leads to increase in the number of genetically resistant humans infected by malaria parasites G_{hi}, because of the presence of resistant gene against malaria parasites. The presence of resistant genes also stabilizes population of the genetically resistant humans infected by malaria parasites as given in Figure 2.

The magnitude of genetically susceptible and infected human population in Figures 3 and 4 respectively decreases because of the presence of the genes that make them to be highly susceptible. Thus, the decrease number of infected human contributes to the increase in the number of recovered human in Figure 5. Finally, the magnitude of susceptible and infected mosquitoes decreases with time due to death after oviposition. See Figures 6 and 7.

4. CONCLUSION.

This study highlighted a compartmental modelling for the transmission dynamics of malaria in genetically resistant and susceptible populations and focussed on two populations: human and vector. d A region where the model is epidemiologically feasible and mathematically well-pose was established. The autonomous model was analysed for disease-free equilibrium, the basic reproduction number R_0 was deduced and local stability of the non-trivial equilibrium was determined using Routh-Hurwitz criterion. The analysis reveals that the disease-free equilibrium E_0 is stable if $R_0 < 1$. The numerical simulations were performed to see the effects of the two different genes present in human population and other key parameter on the spread of the disease. Our results showed that there was a reduction in the number of death of genetically resistant human, increase in the number of infected susceptible humans, increase in the number of death cases of susceptible human and increase in the number of infected mosquitoes. This is because genetically resistant humans serves as a reservoir host of malaria parasite.

In view of the above, genetically resistant persons should be encouraged to take prophylactic treatment so that they will not serve as a reservoir host, thereby reducing the number of infected mosquitoes.

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