Co-infection Model Formulation to Evaluate the Transmission Dynamics of Malaria and Dengue Fever Virus

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ABSTRACT: A mathematical model of the co-infection dynamics of malaria and dengue fever condition is formulated. In this work, the Basic reduction number is computed using the next generation method. The disease-free equilibrium (DFE) point of the model is obtained. The local and global stability of the disease-free equilibrium point of the model is established. The result show that the DFE is locally asymptotically stable if the basic reproduction number is less than one but may not be globally asymptotically stable.

Malaria is a mosquito-borne disease caused by the Plasmodium parasite, which is transmitted through the bites of an infected *anopheles* mosquito. Malaria is caused by five different species of *Plasmodium*: *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale*, *Plasmodium vivax,* and *Plasmodium knowlesi*. However, *Plasmodium falciparum* is the most prevalent in Africa and it causes the highest mortality rate induced by the disease (Olumese P., 2005). The World Health Organization (WHO) world malaria report, an estimated 219 million cases of malaria occurred worldwide in 2017 with *Plasmodium falciparum* and *Plasmodium vivax* parasite species posing the extreme public health challenge. In the WHO African Region which has the world's greatest proportions of the population at high menace of malaria, *P. falciparum* is found to be most prevalent and accounts for 99.7% of estimated malaria cases while *P. vivax* is responsible for 74.1% of malaria cases in the WHO Region of Americas (WHO, 2018). Dengue is an infectious disease caused by any of the four dengue virus serotypes: DENVs 1–4. It is a mosquito-borne disease and is primarily transmitted to humans by the female *Aedes* mosquito. Dengue is highly prevalent in tropical and subtropical regions, reflecting the distribution of the vector, *Aedes aegypti* mosquitoes. Nearly one-third of the global population is at risk for infection (Messina *et al.*, 2014). Infection with DENV results in varying degrees of pathological conditions, ranging from mild asymptomatic dengue fever (DF) to severe dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) which may turn fatal (Murphy and Whitehead, 2011). Infected humans are the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes. Patients who are already infected with the dengue virus can transmit the infection (for 4-12 days) via Aedes mosquitoes after their first symptoms appear. When a person recovers from dengue infection they develop long-term immunity to that specific virus, but not the other three dengue viruses. If the person becomes infected again with a different dengue virus, there is an increased chance that they may develop into dengue hemorrhagic fever (Nyerere *et al.*, 2017). Dengue cannot be spread from human to human. Dengue and malaria are the most prevalence arthropod-borne diseases with an estimated global incidence of 390 million and 214 million cases a year, respectively (Chong *et al.,* 2017). Dengue viral and malaria parasitic co-infection in an individual is regarded as a 'severe malaria' case (Rao *et al.*, 2016). Mutua *et al.* (2015) developed a mathematical model to describe the co-infection dynamics of malaria and typhoid. Elmojtaba (2016) formulated a mathematical model to study the co-infection dynamics of malaria and visceral leishmaniasis. Bakare and Nwozo (2016)

developed and analyzed a mathematical model to explore malaria and schistosomiasis confection. Mensah *et al.* (2018) in their work proposed a mathematical model to study the transmission dynamics of Zika and Malaria in the malaria-endemic area. Aldia and Agustin (2018) formulated a mathematical model to understand the spread of dengue and chikungunya confection in a closed population. In this work, we proposed a mathematical model for the Co-infection dynamics of malaria and dengue fever.

MATERIALS AND METHODS

Model Formulation: In this model, the total human population at any given time t denoted by N_h is divided into eight sub-classes which are susceptible humans (S_h), individuals exposed to malaria only (E_{hm}), individuals infected with malaria only (I_{hm}), individuals exposed to dengue fever only (E_{hd}), individuals infected with only dengue fever (I_{hd}), individuals exposed to malaria and dengue fever co-infection (E_{md}), individuals infected with malaria and dengue fever co-infection (I_{md}), individuals that recovered from malaria and dengue fever (R_h). The vector population includes the Malaria Parasite non-carrier vectors (S_m), Malaria parasite carrier vectors (I_m), Dengue virus non-carrier vectors (S_d), and Dengue fever carrier vectors (I_d). Susceptible individuals are recruited through constant Λ_h. Susceptible individuals are infected with dengue fever at through contact with the infectious mosquito at a rate α_d, infected with malaria at a rate α_m, individuals who recover from malaria returns to the susceptible class at a rate of γ_h, a susceptible individual have a natural death rate of μ_h. The class of individuals exposed to malaria only are generated by susceptible individuals infected with malaria only and reduced by the rate of contacting dengue fever at a rate α_d, the rate of progression to malaria only infected class κ_1 and natural death rate μ_h. The class of individuals infected with malaria (I_{hm}) is increased by κ_1 the rate of progression from malaria exposed class, reduced by the rate of contacting dengue fever at a rate α_d, disease-induced death rate

δ_1, malaria only recovery rate θ_1, and natural death rate μ_h. Individuals that are exposed to dengue fever only are generated by susceptible individuals infected with dengue fever at a rate α_d, reduced by the natural death rate μ_h, rate of progression to infected class for dengue fever only at the rate, κ_2 and the rate at which susceptible individuals contact malaria only. The population of individuals with dengue fever only (I_{hd}) is generated by individuals that progressed from the exposed class (E_{hd}) at the rate κ_2. It is also reduced by disease-induced death rate δ_2, recovery rate from dengue fever only θ_2 and the rate of contacting malaria only. The population of individuals exposed to malaria and dengue fever co-infection (E_{md}) is increased by the rate of acquiring malaria through contact with the parasite carrier vectors and dengue fever through contact with dengue virus carrier vectors but reduced by natural death rate and rate of progression to infected malaria and dengue fever co-infection class κ_3. Infected malaria and dengue fever co-infection class (I_{md}) are increased by κ_3 and reduced by the natural death rate, co-infection recovery rate θ_3, and disease-induced death rate δ_3. The recovery class (R_h) is generated by the individuals who recovery from malaria only at the rate θ_1, individuals who recover from dengue fever only at the rate θ_2, individuals who recover from both diseases at the rate θ_3, and reduced by natural death rate and individuals who return to susceptible class after recovery at the rate γ_h. The Malaria parasite non-carrier vector population (S_m) is generated by a constant Λ_m, reduced by the vector natural death rate μ_m and the rate at which the non-carrier vector acquires malaria parasite through contact with exposed and infected individuals with malaria only and co-infection of malaria and dengue fever given as α_{vm} The Malaria parasite carrier vector population is generated by the rate at which the non-carrier vector acquires malaria through contact with exposed and infected individuals with malaria only and co-infection of malaria and dengue fever and the natural death rate μ_m. The Dengue virus non-carrier vector

population (S_d) is generated by a constant Λ_d, reduced by the vector natural death rate μ_d, and the rate at which the Dengue virus non-carrier vector acquires dengue virus through contact with exposed and infected individuals with dengue fever only and co-infection of malaria and dengue fever given as α_{vd}

The Dengue virus carrier vector class (I_d) is increased by the rate at which the Dengue virus non-carrier vector acquires dengue virus through contact with exposed and infected individuals with dengue fever only and co-infection of malaria and dengue fever and reduced by the vectors natural death rate μ_d.

Assumptions of the Model: The following Assumptions are made in formulating the model: (i) Recruitment into the susceptible population is constant (ii) The recovery population include those jointly infected with Malaria and Dengue fever only (iii) Recovery from Dengue fever is permanent.
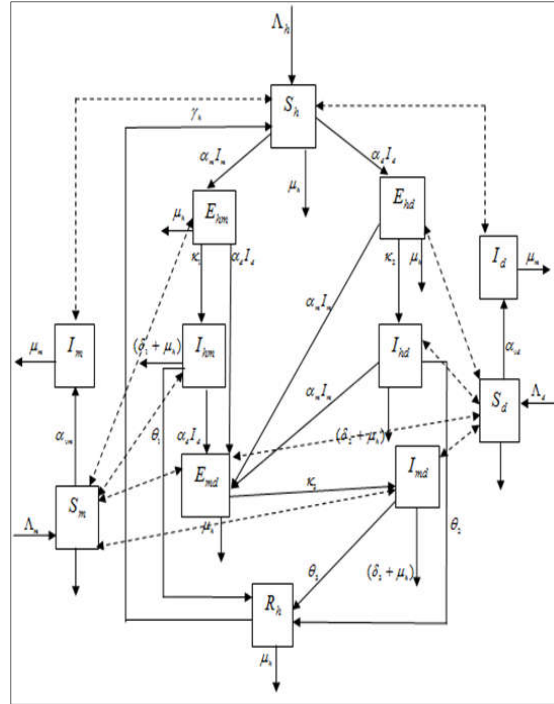

Fig 1: Schematic Representation of the Model

With the assumptions, the co-infection model equations is given below as:

$$\frac{dS_h}{dt} = \Lambda_h + \gamma_h R_{hm} - (\alpha_d I_d + \alpha_m I_m)S_h - \mu_h S_h \qquad (1)$$

$$\frac{dE_{hm}}{dt} = \alpha_m I_m S_h - (\alpha_d I_d + \kappa_1 + \mu_h)E_{hm} \qquad (2)$$

$$\frac{dI_{hm}}{dt} = \kappa_1 E_{hm} - (\alpha_d I_d + \delta_1 + \theta_1 + \mu_h)I_{hm} \qquad (3)$$

$$\frac{dE_{hd}}{dt} = \alpha_d I_d S_h - (\alpha_m I_m + \kappa_2 + \mu_h)E_{hd} \qquad (4)$$

$$\frac{dI_{hd}}{dt} = \kappa_2 E_{hd} - (\alpha_m I_m + \delta_2 + \theta_2 + \mu_h)I_{hd} \qquad (5)$$

$$\frac{dE_{md}}{dt} = \alpha_d I_d E_{hm} + \alpha_d I_d I_{hm} + \alpha_m I_m E_{hd} + \alpha_m I_m I_{hd} - (\kappa_3 + \mu_h)E_{md} \qquad (6)$$

$$\frac{dI_{md}}{dt} = \kappa_3 E_{md} - (\delta_3 + \theta_3 + \mu_h)I_{md} \qquad (7)$$

$$\frac{dR_{hm}}{dt} = \theta_1 I_{hm} + \theta_2 I_{hd} + \theta_3 I_{md} - (\gamma_h + \mu_h)R_{hm} \qquad (8)$$

$$\frac{dS_m}{dt} = \Lambda_m - \alpha_{vm}(E_{hm} + I_{hm} + E_{md} + I_{md})S_m - \mu_m S_m \qquad (9)$$

$$\frac{dI_m}{dt} = \alpha_{vm}(E_{hd} + I_{hd} + E_{md} + I_{md})S_m - \mu_m I_m \qquad (10)$$

$$\frac{dS_d}{dt} = \Lambda_d - \alpha_{vd}(E_{hd} + I_{hd} + E_{md} + I_{md})S_d - \mu_d S_d \qquad (11)$$

$$\frac{dI_d}{dt} = \alpha_{vd}(E_{hd} + I_{hd} + E_{md} + I_{md})S_d - \mu_d I_d \qquad (12)$$

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Table 1: Variables of the Model

Symbols	Description
S_h	Susceptible Humans
E_{hm}	Exposed Humans with Malaria
I_{hm}	Humans infected with Malaria only
E_{hd}	Exposed Humans with Dengue Fever
I_{hd}	Humans infected with Dengue Fever only
E_{md}	Exposed Humans jointly infected with Malaria and Dengue Fever
I_{md}	Humans jointly infected with Malaria and Dengue Fever
R_h	Humans Recovered from Malaria and Dengue Fever
S_m	Malaria Parasite carrier vectors
I_m	Malaria Parasite non-carrier vectors
S_d	Dengue virus non-carrier vectors
I_d	Dengue virus carrier vectors

Table 2: Parameters of Model

Symbols	Description
Λ_h	Recruitment rate of Human Population
Λ_m	Recruitment rate of Malaria Parasite Vectors
Λ_d	Recruitment rate of Dengue Virus Vectors
θ_1	Recovery rate for Humans infected with Malaria only
θ_2	Recovery rate for Human infected with Dengue only
θ_3	Recovery rate for Human jointly infected with Malaria and Dengue
γ_h	Rate at which recovered becomes susceptible
κ_1	Rate at which E_{hm} becomes I_{hm}
κ_2	Rate at which E_{hd} becomes I_{hd}
κ_3	Rate at which E_{md} becomes I_{md}
α_m	Transmission rate of Malaria Parasite Vectors per human per unit time
α_d	Transmission rate of Dengue Virus Carrier Vectors per human per unit time
α_{vm}	Probability for Malaria Parasite Vectors to be infected
α_{vd}	Probability for Dengue Virus Vectors to be infected
δ_1	Disease induced death for I_{hm}
δ_2	Disease induced death for I_{hd}
δ_3	Disease induced death for I_{md}
μ_h	Natural death rate for Humans
μ_m	Natural death rate of Malaria Parasite Vectors
μ_d	Natural death rate of Dengue Virus Vectors

Disease Free Equilibrium (DFE) Point: This is the state solution where is no infection in the population. The DFE of the model is obtained when the right-hand side of the model equation (1) – (12) is set to

zero. Thus, the DFE point of Malaria-Dengue Fever co-infection is given as in equation 13.

Basic Reproduction Number: The basic reproduction number is defined as the expected number of secondary infections produced by an index case in a completely susceptible population. For this research, the basic reproduction number is defined as the number of secondary malaria (or dengue) infections due to single malaria (or a single dengue-infective) individual. Applying the next generation method, the basic reproduction number is the spectral radius of the matrix FV^{-1} where F and V are transmission and transition matrices respectively defined as in equation 14.

$$\varepsilon_0 = \left(S_h^0, E_{hm}^0, I_{hm}^0, E_{hd}^0, I_{hd}^0, E_{md}^0, I_{md}^0, R_{hm}^0, R_{hd}^0, S_m^0, I_m^0, S_d^0, I_d^0\right)$$
$$= \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Lambda_m}{\mu_m}, 0, \frac{\Lambda_d}{\mu_d}, 0\right) \tag{13}$$

$$F = \begin{pmatrix}
0 & 0 & 0 & 0 & 0 & 0 & \alpha_m \dfrac{\Lambda_h}{\mu_h} & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_d \dfrac{\Lambda_h}{\mu_h} \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\alpha_{vm} \dfrac{\Lambda_m}{\mu_m} & \alpha_{vm} \dfrac{\Lambda_m}{\mu_m} & 0 & 0 & \alpha_{vm} \dfrac{\Lambda_m}{\mu_m} & \alpha_{vm} \dfrac{\Lambda_m}{\mu_m} & 0 & 0 \\
0 & 0 & \alpha_{vd} \dfrac{\Lambda_d}{\mu_d} & \alpha_{vd} \dfrac{\Lambda_d}{\mu_d} & \alpha_{vd} \dfrac{\Lambda_d}{\mu_d} & \alpha_{vd} \dfrac{\Lambda_d}{\mu_d} & 0 & 0
\end{pmatrix} \tag{14}$$

$$V = \begin{pmatrix}
\eta_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & z_1 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & \eta_2 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & z_2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \eta_3 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & z_3 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & \mu_m & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_d
\end{pmatrix} \tag{15}$$

The basic reproduction number R_0 is given as

$$R_0 = \max\left\{ \sqrt{\frac{\alpha_m \alpha_{vm} \Lambda_h \Lambda_m}{\eta_1 \mu_h \mu_m^2}}, \sqrt{\frac{\alpha_d \alpha_{vd} \Lambda_h \Lambda_d}{\eta_2 \mu_h \mu_d^2}} \right\} \tag{16}$$

RESULT AND DISCUSSION

Local Stability of the Disease-Free Equilibrium:
Theorem: The Disease-Free Equilibrium of the Model Equations (1) – (12) is locally asymptotically stable if $R_0 < 1$ and unstable if otherwise.

Proof: The system (1) – (12) at DFE is given as

$$J(\varepsilon_0) = \begin{pmatrix} A & B \end{pmatrix} \tag{17}$$

Components in are given as

$A =$

$$\begin{pmatrix}
-\mu_h & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & -\eta_1 & 0 & 0 & 0 & 0 & 0 \\
0 & \kappa_1 & -z_1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -\eta_2 & 0 & 0 & 0 \\
0 & 0 & 0 & \kappa_2 & -z_2 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & -\eta_3 & 0 \\
0 & 0 & 0 & 0 & 0 & \kappa_3 & -z_3 \\
0 & 0 & \theta_1 & 0 & \theta_2 & 0 & \theta_3 \\
0 & -\alpha_{vm}\dfrac{\Lambda_m}{\mu_m} & -\alpha_{vm}\dfrac{\Lambda_m}{\mu_m} & 0 & 0 & -\alpha_{vm}\dfrac{\Lambda_m}{\mu_m} & -\alpha_{vm}\dfrac{\Lambda_m}{\mu_m} \\
0 & \alpha_{vm}\dfrac{\Lambda_m}{\mu_m} & \alpha_{vm}\dfrac{\Lambda_m}{\mu_m} & 0 & 0 & \alpha_{vm}\dfrac{\Lambda_m}{\mu_m} & \alpha_{vm}\dfrac{\Lambda_m}{\mu_m} \\
0 & 0 & 0 & -\alpha_{vd}\dfrac{\Lambda_d}{\mu_d} & -\alpha_{vd}\dfrac{\Lambda_d}{\mu_d} & -\alpha_{vd}\dfrac{\Lambda_d}{\mu_d} & -\alpha_{vd}\dfrac{\Lambda_d}{\mu_d} \\
0 & 0 & 0 & \alpha_{vd}\dfrac{\Lambda_d}{\mu_d} & \alpha_{vd}\dfrac{\Lambda_d}{\mu_d} & \alpha_{vd}\dfrac{\Lambda_d}{\mu_d} & \alpha_{vd}\dfrac{\Lambda_d}{\mu_d}
\end{pmatrix} \quad (18)$$

$B =$

$$\begin{pmatrix}
\gamma_h & 0 & -\dfrac{\alpha_m\Lambda_h}{\mu_h} & 0 & -\dfrac{\alpha_d\Lambda_h}{\mu_h} \\
0 & 0 & \dfrac{\alpha_m\Lambda_h}{\mu_h} & 0 & 0 \\
0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \dfrac{\alpha_d\Lambda_h}{\mu_h} \\
0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 \\
-z_4 & 0 & 0 & 0 & 0 \\
0 & -\mu_m & 0 & 0 & 0 \\
0 & 0 & -\mu_m & 0 & 0 \\
0 & 0 & 0 & -\mu_d & 0 \\
0 & 0 & 0 & 0 & -\mu_d
\end{pmatrix} \quad (19)$$

Where $z_4 = \left(\gamma_h + \mu_h\right)$ (20)

Applying Gauss Jordan elimination method we have the following from the characteristics equation:

$$\left.\begin{aligned}
&\lambda_1 = -\mu_h < 0,\, \lambda_2 = -\eta_1 < 0,\, \lambda_3 = -z_1 < 0,\, \lambda_4 = -\eta_2 < 0,\, \lambda_5 = -z_2 < 0,\, \lambda_6 = -\eta_3 < 0, \\
&\lambda_7 = -z_3 < 0,\, \lambda_8 = -z_4 < 0,\, \lambda_9 = -\mu_m < 0,\, \lambda_{10} = -\left(\mu_m - \frac{\alpha_{vm}\alpha_m\Lambda_m\Lambda_h(\kappa_1 + z_1)}{\eta_1 z_1 \mu_m \mu_h}\right) < 0, \\
&\lambda_{11} = -\mu_d < 0,\, \lambda_{12} = -\left(\mu_d - \frac{\alpha_{vd}\alpha_d\Lambda_d\Lambda_h(\kappa_2 + z_2)}{\eta_2 z_2 \mu_d \mu_h}\right) < 0
\end{aligned}\right\} \quad (21)$$

From λ_{10} we have

$$\lambda_{10} = -\left(1 - R_{0m}^2\right) < 0 \qquad (22)$$

It, therefore, implies that $\lambda_{10} < 0$ if $R_{0m} < 1$

Also from λ_{12} we have

$$\lambda_{12} = -\left(1 - R_{0d}^2\right) < 0 \qquad (23)$$

It shows that $\lambda_{12} < 0$ if $R_{0d} < 1$

Therefore, the model system is locally asymptotically stable at DFE if and only if $R_0 < 1$ i.e. $R_{0m} < 1$ and $R_{0d} < 1$.

Global Stability of the Disease-Free Equilibrium: The global asymptotic stability (GAS) of the disease-free equilibrium is investigated using theorem in [2]. We re-write the model as

$$\frac{dX}{dt} = H(X,Z) \qquad (24)$$

$$\frac{dZ}{dt} = G(X,Z), \quad G(X,0) = 0 \qquad (25)$$

Where $X = (S_h, R_{hm}, S_m, S_d)$ (26)

and $Z = (E_{hm}, I_{hm}, E_{hd}, I_{hd}, E_{md}, I_{md}, I_m, I_d)$ (27)

With the components X denoting the uninfected population and components Z denoting the infected population.

The disease-free equilibrium is now denoted as

$$E^0 = (X^*, 0); \quad X^* = \left(\frac{\Lambda_h}{\mu_h}, 0, \frac{\Lambda_m}{\mu_m}, \frac{\Lambda_d}{\mu_d} \right) \qquad (28)$$

The following conditions must be satisfied to guarantee global asymptotical stability:

i. $\frac{dX}{dt} = H(X,0)$; X^* is globally asymptotically stable

ii. $G(X,Z) = PZ - \hat{G}(X,Z), \ \hat{G}(X,Z) \ge 0$ for $(X,Z) \in \Omega$,   (29)

Where $P = D_z G(X^*, 0)$ is a M-matrix (the off-diagonal elements of P are non-negative) and Ω is the region where the model makes biological sense.

If the system satisfies the condition above, then the theorem below holds.

Theorem: The fixed point $E^0 = (X^*, 0)$ is globally asymptotically stable equilibrium of the system provided $R_0 < 1$ that and the conditions in (29) are satisfied.

Proof: From the model system, we have

$$H(X,0) = \begin{pmatrix} \Lambda_h - \mu_h S_h + \gamma_h R_{hm} \\ 0 \\ \Lambda_m - \mu_m S_m \\ \Lambda_d - \mu_d S_d \end{pmatrix} \qquad (30)$$

$$G(X,Z) = PZ - \hat{G}(X,Z) \qquad (31)$$

$$P = \begin{pmatrix} -\eta_1 & 0 & 0 & 0 & 0 & 0 & \alpha_m S_h^0 & 0 \\ \kappa_1 & -z_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\eta_2 & 0 & 0 & 0 & 0 & \alpha_d S_h^0 \\ 0 & 0 & \kappa_2 & -z_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\eta_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \kappa_3 & -z_3 & 0 & 0 \\ \alpha_{vm} S_m^0 & \alpha_{vm} S_m^0 0 & 0 & 0 & \alpha_{vm} S_m^0 & \alpha_{vm} S_m^0 & -\mu_m & 0 \\ 0 & 0 & \alpha_{vd} S_d^0 & \alpha_{vd} S_d^0 & \alpha_{vd} S_d^0 & \alpha_{vd} S_d^0 & 0 & -\mu_d \end{pmatrix} \quad (32)$$

$$PZ = \begin{pmatrix} -\eta_1 E_{hm} + \alpha_m S_h^0 I_m \\ \kappa_1 E_{hm} - z_1 I_{hm} \\ -\eta_2 E_{hd} + \alpha_d S_h^0 I_d \\ \kappa_2 E_{hd} - z_2 I_{hd} \\ -\eta_3 E_{md} \\ \kappa_3 E_{md} - z_3 I_{md} \\ \alpha_{vm} S_m^0 (E_{hm} + I_{hm} + E_{md} + I_{md}) - \mu_m I_m \\ \alpha_{vd} S_d^0 (E_{hd} + I_{hd} + E_{md} + I_{md}) - \mu_d I_d \end{pmatrix} \quad (33)$$

$$G(X,Z) = \begin{pmatrix} \alpha_m S_h I_m - (\eta_1 + \alpha_d I_d) E_{hm} \\ \kappa_1 E_{hm} - (z_1 + \alpha_d I_d) I_{hm} \\ \alpha_d S_h I_d - (\eta_2 + \alpha_m I_m) E_{hd} \\ \kappa_2 E_{hd} - (z_2 + \alpha_m I_m) I_{hd} \\ \alpha_d I_d (E_{hm} + I_{hm}) + \alpha_m I_m (E_{hd} + I_{hd}) - \eta_3 E_{md} \\ \kappa_3 E_{md} - z_3 I_{md} \\ \alpha_{vm} S_m (E_{hm} + I_{hm} + E_{md} + I_{md}) - \mu_m I_m \\ \alpha_{vd} S_d (E_{hd} + I_{hd} + E_{md} + I_{md}) - \mu_d I_d \end{pmatrix} \quad (34)$$

$$\hat{G}(X,Z) = \begin{pmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \\ \hat{G}_3(X,Z) \\ \hat{G}_4(X,Z) \\ \hat{G}_5(X,Z) \\ \hat{G}_6(X,Z) \\ \hat{G}_7(X,Z) \\ \hat{G}_8(X,Z) \end{pmatrix} = \begin{pmatrix} \alpha_m I_m (S_h^0 - S_h) + \alpha_d I_d E_{hm} \\ \alpha_d I_d I_{hm} \\ \alpha_d I_d (S_h^0 - S_h) + \alpha_m I_m E_{hd} \\ \alpha_m I_m I_{hd} \\ -(\alpha_d I_d (E_{hm} + I_{hm}) + \alpha_m I_m (E_{hd} + I_{hd})) \\ 0 \\ \alpha_{vm} S_m (E_{hm} + I_{hm} + E_{md} + I_{md})(S_m^0 - S_m) \\ \alpha_{vd} S_d (E_{hd} + I_{hd} + E_{md} + I_{md})(S_d^0 - S_d) \end{pmatrix} \quad (35)$$

From (35), it shows $\hat{G}_5(X,Z) < 0$ so the conditions are not met. Therefore, E^0 may not be globally asymptotically stable when $R_0 < 1$.

Conclusion: In this work, a co-infection model is formulated to study the transmission dynamics of Malaria and Dengue fever virus. The basic reproduction number of the model is derived using the next generation method, local and global stability of the Disease-free equilibrium (DFE) is carried out. It was observed that the DFE is locally asymptotically stable if $R_0 < 1$ but may not be globally asymptotically stable.

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