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DIFFERENTIAL EPIDEMIC MODEL OF DENGUE VIRUS ATTACK IN HUMAN BODY

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Abstract

A differential Dengue Susceptible-Infectious-Removed-Susceptible (d-SIRS) epidemic model of DengueHaemorrhagic Fever (DHF) in human has been formulated latent period and time for self replication have been considered , stability of the result is stated in terms of the threshold parameters, We have derived an explicit formula for the reproductive number and have shown that the Dengue-virus-infection-free equilibrium, whose component of the infective is zero is globally asymptotically stable if threshold number is less than 1, and unstable if it is greater than 1.

Keywords: Severe DHF compartment –d-SIRS epidemic model-self replication-temporary immunity, Dengue virus

1 Introduction

Dengue, the most prevalent mosquito-borne viral disease affecting humans, results in about 50-100 million cases of dengue fever and 250,000 to 500,000 cases of the more severe dengue hemorrhagic fever/dengue shock syndrome each year, with about 20,000 deaths. The research team detailed critical changes that take place as the virus is assembled and moves from the inner to the outer portions of its host cell before being secreted so that it can infect other cells. Virus particles are exposed to progressively less acidic conditions as they traverse this "secretory pathway," and this changing acidity plays a vital role in the maturation of the virus. The dengue virus moves through compartments inside the cell called the endoplasmic reticulum and the trans-Golgi network. While immature, virus particles are incapable of fusing with cell membranes, preventing them from infecting their own host cells and ensuring their maturation. Once mature, however, the virus particle is able to fuse to cell membranes, a trait that enables it to infect new host cells. As a virus particle matures along the pathway through the host cell, it changes the protein structure, or "conformation," in its outer shell. The team mimicked the trans-Golgi network environment in test tubes, enabling them to study the virus's changing structure with increasing acidity.

There are several computational techniques that look to biology for inspiration. Some common examples evolutionary algorithms, immunological computation. Many researcher have taken to help of the biological model to understand the behaviour of spreading of virus in human body The action of virus attack can be studied by using epidemiological models for disease propagation[1, 2 ,3, 4, 5] based on the Kermack and McKendick SIR classical epidemic model[6 ,7 ,8], The kind of approach was applied to d-virus propagation schemes [9] and modification of SIR models generated guides for infection prevention by using the concept of epidemiological threshold.Richard et al[10] propose an improved SEI(Susceptible-exposed-infected) model to simulate virus propagation. However they do not show the length of latency and take into account the impact of anti-virus- Medicine. The model SEIR proposed by the authors[11] assumes that recovery hosts have a permanent immunization period with a certain probability. Which is not consist wit real situationIn order to over- come limitation, Mishra and Saini[12]present a SEIRS model with latent and temporary immune periods, which can reveal

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common virus propagation. Recently, more research attention has been paid to the combination of virus propagation models and antivirus countermeasuresto study the prevalence of virus, for example, virus immunization[18,19,20,21,22,23] and quarantine[24,25,26]. Hyman and Li[27] proposed a biological SIR model that describes the transmission dynamics of an infectious disease assuming susceptible population divided into different groups. Individuals in each group have homogeneous susceptibility but susceptibility of individual from different groups is distinct. Assuming homogeneous infectiousness of infected individuals so that they can beaggregated into one group, infected state, following system of differential equations were given.

$$\frac{dS_{H_i}}{dt} = \mu_H \left(p_i S_H{}^0 - S_{H_i}\right) - \lambda_{H_i} S_{H_i}$$

$$\frac{dI_H}{dt} = \sum_{k=1}^{n} \lambda_{H_k} S_{H_k} - (\mu_H + \gamma_H + \delta_H) I_H$$

$$\frac{dR_H}{dt} = \gamma_H I_H - (\mu_H + \xi_H) R_H$$

Where S_{H_i} is the susceptible individual humans in the i^{th} group, I_H is the infected individuals human, R_H is the recovered individual human , μ_H is the natural death rate of humans, $\mu_H S_H{}^0$ is a constant influx, λ_H is the rate at which infective are removed human δ and ξ are the disease-induced mortality rates for infective and removed

Individuals respectively, and λ is the infectivity rate given by $\lambda_H = \frac{\alpha\beta c}{N_H}$ where α is the susceptible rate, β as the infectious rate; as the average number of contacts per individuals and $\frac{1}{N_H}$ is the probability that a random contact is infectious with $N_H = S_H + I_H + R_H$ as the total population size. In the above model full immunity of recovered individuals is assumed such that these individuals are no longer susceptible after they recovered. But there is no permanent immunity for the people. The temporary recovered people enter the susceptible class after certain interval of time. We propose a differential compartment for d-SIRS epidemic model in which susceptible and infected population are divided into different groups. People are susceptible due to Dengue virus. Virus in each group has homogeneous susceptibility but susceptibility of virus from different group isdistinct. Virus in each infected group (as per their susceptible behavior group) has homogeneous infection but infection of virus from different group is distinct. We also assume the self-replication possibilities of virus.

2 Differential d-SIRS Epidemic Model

After the virus enters the human body, the people become susceptible and in later course of time become infected and hence infective. There is a certain time lag for the people to become infective once it is in the human body and it is termed as latent period ω_H .After the people becomes infected, the malicious object in it may/may not self-replicate. Hence after the medicine taken to the people recovers and attains temporary immunity for a time period termed as period of temporary immunity τ_H

Assumptions:

1. The natural death rate (crashing of the human due to the reason other than attack of virus) of the human as they are once susceptible virus decreases.
2. Death rate of the human due to dengue virus is constant.
3. Latent period ω_H immunity period τ_H and period of "self-replication Φ_{H_k} are "considered as constants.
4. When a human is infected, it may self-replicate with a probability p_{H_k} and may not self-replicate with a probability $1 - p_{H_k}$
5. When a person is removed from infected class, it may recover with a probability q_{H_k} and may not recover with a probability $1 - q_{H_k}$ and that recovery is temporary.
6. Susceptible Humans are divided into different groups.Human may be susceptible due to dengue virus. Dengue virus in each group have homogeneous susceptibility but susceptibility of dengue virus from different group is distinct.

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7. Infected Humans are also divided into different groups (as per their susceptible behavior group). Dengue Virus in each group has homogeneous infection but infection of malicious objects from different group is distinct.

We assume that the total number of human at any instance *t* is $N_H(t) = S_H(t) + I_H(t) + R_H(t)$

Dengue Virus is assumed to be in the affected Human places for at least a time $\theta_H = \max(\omega_H, \tau_H)$, So that the initial stage of dengue virus affected have ceased. The systems of equations for the model as per our assumptions take the following forms for $t > \theta$.

$$\frac{dS_{H_k}(t)}{dt} = m_k(bN_H(t)) + (\gamma_H I_{H_k}(t-\tau_H)e^{-\mu_H t}) - \mu_H S_{H_k}(t) - \lambda_{H_k} S_{H_k}(t)$$

$$\frac{dI_{H_l}(t)}{dt} = \alpha\beta c \frac{I_H(t-\tau_H)}{N_H(t-\tau_H)} S_H(t-\tau_H)e^{-\mu_H t} + \left[p_{H_k}\alpha\beta \frac{I_H(t-(\tau_H+\omega_H+\phi_{H_k}))}{N_H(t-(\tau_H+\omega_H+\phi_{H_k}))} . S_H(t-(\tau_H+\omega_H+\phi_{H_k})) . r_{H_k} . e^{-\mu_H(\omega_H+\phi_{H_k})} \right]$$

$$\frac{dR_{H_k}(t)}{dt} = \sum_{j=1}^{n} \left[q_{H_k}\gamma_{H_{ki}} I_{H_k}(t) - \gamma_{H_{ki}} I_{H_k}(t-\tau_H)e^{-\mu_H \tau_H} - \epsilon_{H_k} R_H(t) \right] - \mu_H R_H(t).$$

2.1 No dengue virus induced Mortality

For the simplicity of the model, we neglect the dengue virus induced crashing of the Human such that $\delta_H = O_H = \epsilon_H$. Thus we have the system of the model as

$$\begin{bmatrix} \frac{dS_{H_k}(t)}{dt} = m_k(bN_H(t)) + (\gamma_{H_k} I_{H_k}(t-\tau_H)e^{-\mu_H t}) \\ -\mu_H S_{H_k}(t) - \lambda_{H_k} S_{H_k}(t) \\ \frac{dI_{H_l}(t)}{dt} = \alpha\beta c \frac{I_H(t-\tau_H)}{N_H(t-\tau_H)} S_H(t-\tau_H)e^{-\mu_H t} + \\ \left[p_{H_k}\alpha\beta \frac{I_H(t-(\tau_H+\omega_H+\phi_{H_k}))}{N_H(t-(\tau_H+\omega_H+\phi_{H_k}))} . \right. \\ \left. S_H(t-(\tau_H+\omega_H+\phi_{H_k})) . r_{H_k} . e^{-\mu_H(\omega_H+\phi_{H_k})} \right] \\ -(\mu_H + r_{H_k}) I_H(t). \end{bmatrix} \quad \text{-----(2)}$$

As the dynamics of the system is unaffected by the equation of *R*, we omit it. We further assume, $\frac{c(S_H^0)}{S_H^0} = \eta$. System (2) is positively time invariant in the set $G = \{S_{H_i} \geq 0, I_i \geq 0\}$.

2.2 Reproductive Number

System (2) has dengue virus infection-free equilibrium in which the components of infective are zero and other susceptible components are positive. We denote this infection-free equilibrium by $E_{H0} := (S_{H_i} = m_i S_H^0, i = 1,2,...n; I_H = 0)$ Analyzing the local stability of E_{H0} gives the epidemic threshold conditions under which the number of infected person will either increase or decrease to zero as a small number of infective introduced into a fully susceptible Humans. These threshold conditionsare characterized by the reproductive number, denoted by R_{H0} such that E_{H0} is locally asymptotically stable if $R_{H0} < 1$ and unstable if $R_{H0} > 1$. The Jacobian of Equation (3) at E_{H0} has the form

$$\begin{bmatrix} -\mu_H & 0 & . & . & 0 & -\eta\beta S_H^0 \alpha_1 m_1 (1 + p_{H1} r_{H1}) \\ 0 & -\mu_H & 0 & . & 0 & -\eta\beta S_H^0 \alpha_2 m_2 (1 + p_{H2} r_{H2}) \\ . & . & . & . & . & . \\ . & . & . & . & . & . \\ . & . & . & . & . & . \\ 0 & 0 & . & . & -\mu_H & \eta\beta S_H^0 \alpha_n m_n (1 + p_{Hn} r_{Hn}) \\ 0 & 0 & . & . & 0 & -(\mu_H + \gamma_H) + \eta\beta S_H^0 \alpha_i m_i (1 + p_{Hi} r_{Hi}) \end{bmatrix} \text{----(3)}$$

All Eigen values of J have negative real part if and only if,

$$-(\mu_H + \gamma_H) + \eta\beta S_H^0 \sum_{i=1}^{n} \alpha_i m_i (1 + p_{Hi} r_{Hi}) < 0$$

Therefore, the reproductive number can be defined as

$$R_{H0} = \frac{\eta\beta S_H^0}{\mu_H + \gamma_H} \sum_{i=1}^{n} \alpha_i m_i (1 + p_{Hi} r_{Hi})$$

$$= \frac{c(S_H^0)\beta}{\mu_H + \gamma_H} \sum_{i=1}^{n} \alpha_i m_i (1 + p_{Hi} r_{Hi})$$

The mean number of contact is $c(S_H^0) = z$ the mean duration of the infection is $\frac{1}{\mu_H + \gamma_H}$, and the mean infectivity rate of each group is

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$\bar{\beta}_i = \beta\alpha_i$. Wedefine the reproductive number for each group is

$$R_{H0_i} = \frac{z\beta\alpha_i}{\mu_H + \gamma_H}(1 + p_{Hi}r_{Hi}) - - - (3)$$

The reproductive number of infection for the entire peoples can be expressed as the weighted average of the reproductive numbers of the groups such that

$$R_{H0} = \sum_{i=1}^{n} m_i R_{H0i.}$$

Theorem 1. Define the reproductive number of infection, R_{H0}, for System (1) as in Equation (3). Then the infection free-equilibrium E_{H0} is globally asymptotically if $R_{H0} < 1$ and unstable if $R_{H0} > 1$[13].

The node takes a time period of $\omega \geq 0$ before it gets infective [14, 15, 16]. The self replication of dengue virus starts after the human ϕ_{Hk} gets infected and thus it is infective only after the time for self-replication. The human gains a temporary immunity $\tau_H \geq 0$ before it gets susceptible again.

We have the following non-negative conditions for a shift of time θ to new time $t > 0 : S(t) \geq 0\ on\ [-\omega,0], I_H(t) \geq 0\ on [-\theta,0], R_H(t) \geq 0\ on\ [-\tau_H,0]$.

$$R_{Hk}(t) = \int_{t-\tau}^{t} q_{Hk} r_{Hk} I_{Hk}(u) e^{-\mu_H(t-u)} du$$

$$R_{Hk}(0) = \int_{-\tau}^{0} q_{Hk} r_{Hk} I_{Hk}(u) e^{-\mu(-u)} du$$

Our e-SIRS model formulated in Equation (1) is different from SIR model proposed by Hyman and Li [13] which only temporary immunity is assumed for recovered person such that a recovered persons again gets susceptible after certain interval of time. We also assume the infected people to be divided into different groups in which individual persons are a group and have homogeneous infectiousness which is different from that of individuals in other group. The self replication behavior of the malicious virus is also considered in infected stage. When it undergoes temporary immunity period.

The infection is initially very less andas the person spends time to have medicine, the infectivityincreases exponentially and at a certain time increasesabruptly before it reaches a maximum level. As thetemporary recovery starts after the run of anti-malicious medicine, the infection decreases and reaches a minimumpoint and the person body remains there for a short time whichis due to the immunity and latency periods. In order to set an efficient strategy in controlling dengue virustransmission in the human body, we canidentify more susceptible groups and make efforts to reduce the influx into those groups with the help of theformula developed in Equation (3) for $R_{H0i.}$ [17]

3. Conclusion

We have formulated a differential d-SIRS epidemic model in which susceptible and infected humanare divided into different groups. The susceptible and infected human is subdivided into *n* subgroups based on the attack due to dengue virus. Dengue Virus in each group has homogeneous susceptibility but susceptibility of dengue virus from different group is distinct. Dengue Virus in each infected group (as per their susceptible behavior group) has homogeneous infection but infection of malicious objects from different group is distinct. For the case where the number of contacts is proportional to the total population, we derived an explicit formula for the reproductive number R_{H_0}, and had shown that the infection-free equilibrium, whose component of infective is zero, is globally asymptotically stable if $R_{H_0} < 1$ and unstableif $R_{H_0} > 1$. Also we have defined the reproductive number in each subgroup, mean infectivity, and the mean duration of infection. The reproductive number for the whole population, R_{H_0}, is defined as a weighted averageof those R_{H_0}, weighted by the distribution of the influx into the susceptible subgroups.

For a class of population, d-SIRS model with constant latent period ω_H, immunity period τ_H and replication period Φ_{H_k} is developed keeping in view the replication concept of malicious agents. Whenever a human is infected there is chance of malware getting replicated with replication factor

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r_{H_k} . After a node has been included in the infective class, it may self replicate with a probability p_{H_k} and may not self-replicate with a probability $1-p_{H_k}$. In our model when a node is removed from infected class it recovers temporarily and acquires temporary immunity with probability q_{H_k} or the node may vanish with probability $1-q_{H_k}$ which considered the recovery from infected class acquiring permanent immunity with probability q_H. The recovered human remains in state of temporary immunity for a time period of τ_H before it becomes susceptible again. The future work will address on the endemic equilibriumand its stability & Disease-induced mortality.

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