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Mathematical Modeling of malaria

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ABSTRACT

The work to fight malaria effectively started in early twentieth century with mathematical models. These models work on mosquito borne pathogen transmission. Ross Macdonald theory was established in 1970. Mosquito borne pathogens affect public health and finances in many ways. The work of controlling and guiding with the help of models started after that. The theory dealing with public health challenges is changing day by day and so are the ways to control the diseases.

1. Introduction

The history of malaria is age old. It has very high impact on public health, socially and economically. It is mainly present in tropical countries. Even the investigation is going for so many years, the mosquitoes remains a major problem for health department. Till 2008, 109 countries have been declared endemic as regards to malaria. Many older anti-malarial medicines are considered ineffective as drug resistance is an emerging problem. It is also gaining importance in recent times because of global warming, which is suitable for mosquitoes. Vector and parasite life cycle is greatly affected by temperature fluctuation. Malaria is caused by protozoan bacteria. According to the author in human it is caused by Plasmodium falciparum and other species like it [8]. In India, the main pathogen responsible for malaria is P. vivax. But in recent times P. falciparum is also gaining attention. The life cycle of the parasite is competed by two stages, that is, vector female anopheles mosquito and other human. The transmission between two humans is done by the bites/blood meals by infected mosquitoes. The role of mosquito in parasite's life cycle is discovered by Grassi and Ross. In about last hundred years, so much efforts and scientific research is done to understand host-parasite- vector interaction. But there are so many factors on which morbidity and mortality relating to disease depends. Some of the factors are drug resistance of parasite, the endemic and non-endemic areas, the migration of population between the areas, climate change etc. are the new challenges for researchers and health professionals. Biology researchers who work in infectious diseases realized the importance of mathematical models in providing important information about transmission of the disease. In disease transmission, the main factors to be investigated are incorporated in mathematical models as simple terms to predict the process of transmission and explore new facts. These models helps us to predict the facts that are not known completely. Whether a disease will be endemic or turn into epidemic, mathematical models can predict to a great extent.

2. Literature review

Malaria, one of the diseases since ages has been studied and vast literature exists that gives information about modelling. Epidemiologists are working on eradication of malaria globally and efforts to control are being done. Compartmental modeling, one of the approaches, focuses on transmission of infection in host and vector population. We cannot deny the importance of the models which are concerned with 'within host' biology [2], [3] and [4]. The interaction of parasite and immune cells is being studied in these models. Inspite of the wide range of these models and their approaches, the major one in modelling is transmission of infection from one compartment to other [5]. In the light of climate change globally, it is very important to predict the transmission of the infectious disease through mathematical models. Sir Ronald Ross was the one among the first to publish papers with mathematical functions regarding study of Malaria transmission. He demonstrated the life cycle of malaria parasite in mosquito. His simple model on malaria, that is, classical “Ross Model” well demonstrated the relation between malaria in humans and number of mosquitoes. But when new data become available, the simple model do not predict satisfactorily. Hence many new models have been developed by taking new factors into consideration to give better research. Important key words which are used in modelling are:

- Latent Period: It is the period from start of infection to the state of infectiousness. During this time the individual is in the exposed class.
- Inoculation Period: It is the period between infections in an individual caused by pathogen and manifestation of the illness it causes.
- Basic reproduction number: It is the number of average infections caused by an infected in a totally susceptible population[7].
- Incubation period: The period between start of infection and appearance of symptoms of disease is called Incubation period.

The pioneer in the compartmental models is Karmack and McKendrick. In infectious disease transmission, compartmental models are studied [11]. The transmission of infection in host community categorises the individuals in partitions depending on the density of parasite and type of infection. These compartments are represented by standard notation S-E-I-R [1]and [6]. The first group consists of susceptible host population, E stands for exposed class, that is, the number of individuals affected by pathogen. But they are not capable of passing infection to others during that period. The size of the compartments may vary depending upon disease. I is class of individuals infected and R is the class which recovers temporarily or permanently. The plasmodium parasite needs humans and mosquito to complete its life cycle. When infected mosquito bites susceptible human, the infection is transferred. The mosquito gets infected through a blood meal from infected human. In malaria models, compartments are made both in case of humans (S_h,E_h,I_h,R_h) and mosquitoes (S_m,E_m,I_m) . The mosquito population die of infection, hence no recovery class but in case of humans, after end of infection, the fraction of class becomes recovered class. In the first mathematical model of Ronald Ross [12], he used the word, ‘pathometry’ which means “quantitative study of a disease either in the individual or in the community”. In his model, he showed that there is a certain number of mosquitoes below which malaria can be eradicated. After many years, the model of Ross was modified by the fact that due to parasitic infection in mosquitoes, female mosquitoes, cannot survive much that is, it is the weakest link. This fact helped in the use of DDT, for elimination of mosquitoes that caused malaria among 500 million people in Africa. There are three basic models for malaria:

- Ross model
- Macdonald Model
- Anderson-May Model.

The first deterministic differential equation model in malaria given by Ross explains the idea of dividing the human population into three compartments namely Susceptible (S_h), Infected (I_h) and again susceptible class, which is SIS model. In case of mosquitoes, there are only two compartments (S_m,I_m) because they do not recover from infection. Increase in mosquito mortality and decrease in biting rate of mosquitoes can reduce malaria transmission which in turn reduces the basic reproduction number R_0. In the simple Ross model, the latency period, that is, the period of 10 days in which parasite remains inside a mosquito, was not considered which resulted in fast progress of malaria epidemic in humans. Macdonald considered this latency period and introduced exposed class compartment giving rise to SEI model for mosquitoes. This new class changed the value of R_0 to the lower side. Again, Anderson and May extended the latency period to 21 days in humans and introduced exposed class E_h for humans. Now there were three in case of host, that is, humans (S_h,E_h,I_h) and again three compartments in case of mosquitoes (S_m,E_m,I_m). From the comparative study of three models Ross (RR), Macdonald (MC) and Anderson May (AM), it is clear that the inclusion of latency period in mosquitoes and humans gave better results. In the basic model many factors like demographic heterogeneity, population distribution geographically, social interaction, climate change, ecology of area were not considered in details. The system is so complex that it is not possible to incorporate all variables and factors. To make a better model, we can go step by step. Then comes the next model, that is, next generation mathematical models which evolved from basic models. The immunity against malaria also depends on age. In African children, deaths due to malaria mostly occurs under the age of 5 years. But continuous exposure and developing immunity to disease is lesser in older Africans. But outside Africa, the disease burden extends into adulthood where continuous exposure of malaria is not there. Macdonald considered this latency period and introduced exposed class compartment giving rise to SEI models for mosquitoes. This new class changed the value of R_0 to the lower side.

In case of an epidemic, the dynamics of birth and death are often slower than that of a epidemic, therefore, birth and death are mostly not considered in

Figure 1: Flow diagram of the system

simple compartmental models. A simple SIR model can be described in the form of differential equations given below:

$$\frac{dS}{dt} = -\frac{\beta IS}{N},$$
$$\frac{dI}{dt} = \frac{\beta IS}{N} - \gamma I,$$
$$\frac{dR}{dt} = \gamma I.$$

Where S denotes the susceptible population, I denotes the infected, and R denotes the recovered population. Here β is the transmission rate and γ is the death rate.

The dynamics of an infectious disease in which both birth rate and death rates are included is given in the form of differential equations a

$$\frac{dS}{dt} = N - \mu S - \beta IS,$$
$$\frac{dI}{dt} = \beta IS - \alpha I - \mu I,$$
$$\frac{dR}{dt} = \alpha I - \mu R.$$

Here N is the total population through birth or immigration, μ is the death rate, β is the transmission rate and α is the force of infection.

Here $S + I + R = N$.

To make model more realistic to give better predications, it is important to incorporate immunity [10]. Also considering immunity, that is, effect of vaccines can give better directions to vaccination programmers. One more factor which determines the transmission of disease is how the host and parasite respond to infection. Earlier it was considered that all individuals, host and parasites in the population have equal probability of transmitting the disease or becoming immune to the infection. But actually there exists difference among them. Further long term use of DDT and other drugs have affected the transmission of malaria in negative way. But on the other side, drug resistance to parasites have also evolved. So in modelling these factors should also be considered. Climate change is among very favourite topic in research of malaria because to understand better the malaria transmission, it is necessary to consider them in epidemiology host, vector and pathogens. Environmental factors such as wind patterns humidity, rainfall, temperature have great impact on mosquito reproduction, survival and its development. One of the other important factors is socio economic factors. It is fairly evident that where the malaria prospers most, human societies have prospered least [9]. Malaria and poverty are positively correlated using mathematical modelling it was shown by Yang that basic reproduction number R_0 of malaria transmission changes with social and economic changes and global warming.

The progress of the disease in which host and vector (which is mosquito here)is considered in a cycle is described by the following set of differential equations

$$\dot{S_H} = b_H N_H - a\beta_1 \frac{S_H I_m}{N_m} - \mu_H S_H - \epsilon S_H,$$
$$\dot{I_H} = \frac{a\beta_1 S_H I_m}{N_m} - (\alpha + \mu_H) I_H,$$
$$\dot{R_H} = \epsilon S_H - \mu_H R_H,$$
$$\dot{S_m} = b_m N_m - a\beta_2 S_m \frac{I_H}{N_H} - \mu_m S_m,$$
$$\dot{I_m} = a\beta_2 S_m \frac{I_H}{N_H} - \mu_m I_m.$$

The total population N_H and N_m can be determined from

$N_H = S_H + I_H + R_H,$

$N_m = S_m + I_m.$

Also upon adding all the equations in the model for human and mosquito populations, we get

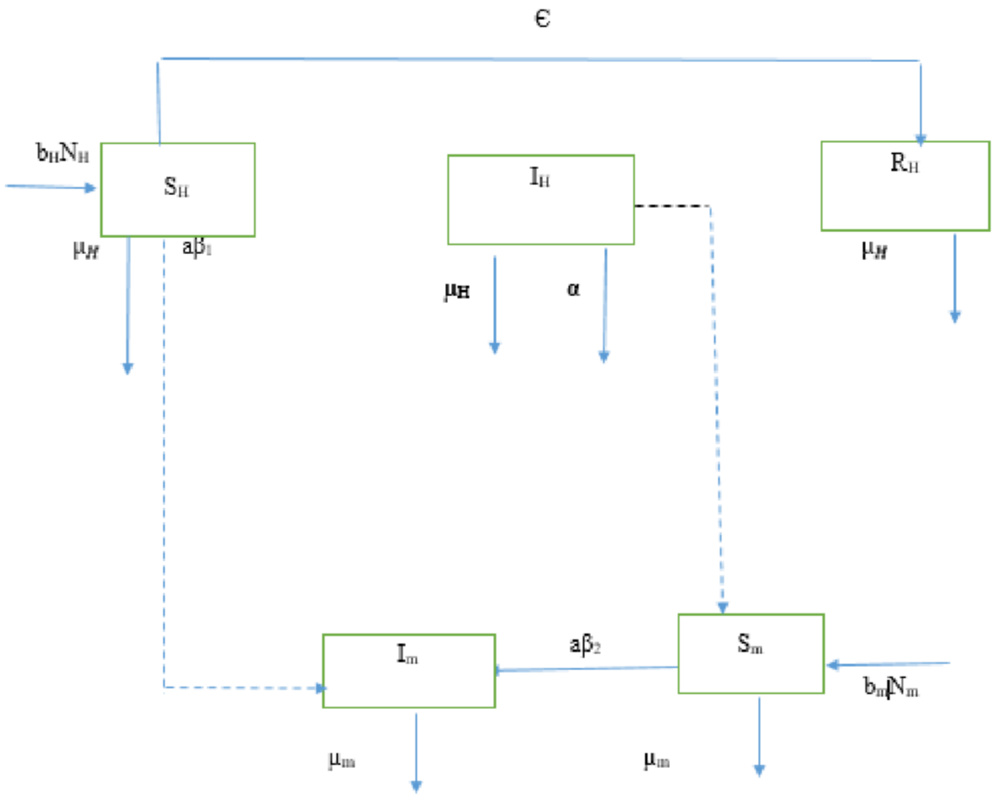

Figure 2: Flow diagram of the above system

Table 1: Table for parameters.

Parameters	Description
a	Mosquito biting rate
β_1	Transmission probability of disease from mosquito to human
β_2	Transmission probability of disease from human to mosquito
μ_H	Natural death rate for human
μ_m	Natural death rate for mosquitoes
b_H	Birth rate of humans
b_m	Birth rate of mosquitoes
α	disease induced death rate
N_H	Total human population
N_m	Total mosquito population

Here N_H is the total population. S_H is the susceptible class. I_H is infectious class. R_H is the recovered class. S_m denotes the susceptible population of mosquito, the vector in the disease transmission and I_m is the infected mosquito population.Similarly, there can be many models in which different parameters like temperature, immunity, weather etc can be considered to find their dependence on each other and also how they can affect the disease transmission.

3. Conclusion

A model is used to predict reality the models tries to match the result with epidemiological data available, where the deaths due to infection determines the status of an epidemic in population. Therefore, the basic purpose of R_0, basic reproduction number is to determine whether the infection will die or persists in population. It is important for the epidemiological models, to consider the factors predicted by molecular studies. In this review, we have tried to mention the factors which affect the completion of infection process. The models about which we have discussed are only indicative not exhaustive. The role of moderate factors, such as, economic status, social status play important role in malaria transmission. If heterogeneity in the locality is not considered, local differences in ecology due to poverty are not considered, it may result in failure of control strategies. Therefore, we need to consider many more factors to better understand the malaria transmission.

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