(IJRST) 2016, Vol. No. 6, Issue No. III, Jul-Sep **e-ISSN: 2249-0604, p-ISSN: 2454-180X**

STATE SPACE MODEL ON MALARIA INFECTION WITH MISDIAGNOSIS

K.M. Sharma* and Neetu Srivastava
B.S.A. College, Mathura (U.P.) India

ABSTRACT

In this paper mathematical modeling of Malaria infection has been done on the basic of possibility of relapses. The misdiagnosis in terms of false negatives is taken into account. The analysis consists of the derivation of state probabilities and the estimation processor. The model provides an understanding of the process of Malaria infection of human host. The out comes may be useful for the medical doctors for the prevention of Malaria disease.

Keyword: *Malaria infection, Human host, Markov chain, Misdiagnosis, Transition probability.*

1. INTRODUCTION

The process of infection of the malaria in human host is an important one with a view to find ways to eradicate this disease from root. The mathematical study to provide the process information in this regard has been done by many researchers. **Macdonald (1950)** introduced super infection as an important concept in malaria modelling, but the fact that super infection occurs in malaria infections has not yet been proved. Before this study, relapses were not studied previously in malaria host models. **Vessel (1986)** studied a model, where the concept of super infection without relapses is used to estimate infection and recovery rates. This model for the infection of a human host was a Markov chain version of the human host model developed by **Ross (1910, 1911).**

The Ross model was further discussed by **Bailey (1982)** and **Nasell (1985). Nedelman (1988)** derived estimates of misclassification probabilities, based on data from Garki project discussed in **Molineaux and Gramiccia (1980).** The data we used for the estimation are from the paper by **Anderson (1988).** The use of maximum likelihood (ML) method for estimating the parameters of the model is made. The estimation procedure is an extension of the path-breaking ideas introduced by **Anderson (1988).** This chapter is organized as follows: Section 2 is devoted to the description of the model. In section 3, misdiagnosis is taken into account. In section 4, we presented the out line of the estimation procedure. Finally conclusion has been drawn in section 5.

(IJRST) 2016, Vol. No. 6, Issue No. III, Jul-Sep **e-ISSN: 2249-0604, p-ISSN: 2454-180X**

2. MODEL FOR INFECTION OF A HUMAN HOST

The model studied in this chapter for the infection of a human host is based on a Markov chain version X(t) of the Ross Transmission Model that deals with the human host. The state space of X(t) is {0, 1}. These states represent the absence and presence respectively, of malaria parasites in the blood of the host. The host is said to be in state "1" when an infection bite is present due to by an infected mosquito or due to a relapse of malaria. The host is in state "0" if the same has recovered from the infection or if he is in latent sate i.e., host still is infected, but there are no malaria parasites in his blood. Let us consider a time interval {0, T} taking the parameters as constant. The rate of transition from state '0' to state '1' is $h = h_1 + h_3$, where h_1 is the rate of acquisition of new infections and h_3 is the relapse rate. The rate of transition from state 1 to state 0 is clearly the recovery rate r. All three rates depend on the age of the host. , However, let us take the rates as constant in each of the seven age bands defined by the Garki data. But the infection rate h_1 is assumed to vary with the five seasons (time periods) identified in the Garki baseline data, while both the relapse rate h_3 and the recovery rate r are assumed constant over the seasons. For analysis purpose these assumptions mean that the rates are the piecewise constant as a function of time.

Let us denote the probabilities of being patent at the beginning and at the end of the time interval [0, T] by p_1 and p_2 respectively. Therefore

$$P_1 = P\{X(0) = 1\}, P_2 = P\{X(T) = 1\} \quad \ldots(1)$$

The transition probabilities during the time interval are denoted by P_{mn}, where

$$P_{mn} = P\{X(T) = n \mid X(0) = m\}, m,n = 0, 1 \quad \ldots(2)$$

The transition probabilities P_{mn} in terms of the parameters h and r in the time interval of length T can be easily written [Nasell, 1986]. The data give the number of occurrences of the four events {00, 0I, I0, II},We denote the probabilities of these events by P_1, P_2, P_3 and P_4 respectively. Then

$$\left.\begin{aligned} P_1 &= P\{X(0) = 0, X(T) = 0\} \\ P_2 &= P\{X(0) = 0, X(T) = 1\} \\ P_3 &= P\{X()) = 1, X(T) = 0\} \\ P_4 &= P\{X(0) = 1, X(T) = 1\} \end{aligned}\right\} \quad \ldots. (3)$$

Let us determine the time when the host was born and divide the time interval from this moment until the beginning of the presently considered time interval into contiguous time intervals in which the parameters are constant. Let us also assume that the five "seasons" occur during the same time each year. At the time of birth the host is assumed to be uninfected with $p_1=0$ Then after in caching the contiguous intervals p_1 can be determined successively to be equal to p_2 in preceding interval. The state probability p_2 in any time interval can be obtained from p_1 and the transition probabilities Pmn during the same time interval.

3. MODEL FOR INFECTION WITH MISDIAGNOSIS

Let Y (t) be an observed state as stochastic process in the space {0,1}. The observed state Y (t) may differ from the true state X (t) because of misdiagnosis in the form of false negatives. Singer and Cohen (1980, 1982) also discussed misdiagnosis in terms of these two stochastic processes. Here Y (t) is considered in a time interval (o, t) where the parameters of the process X (t) are constant. The extent of misdiagnosis at each survey and age band has been estimated by **Nedelman (1988)**. Nedelman establishes three models in which false negatives one allowed by both the microscopist and the supervisor.

Misclassification probabilities can be defined in two ways.

Following Nedelman we first defined the misclassification probability τ as the probability that a host who is observed negative is truly positive. For fixed age band and time interval the use of subscripts 1 and 2 is made to denote the misclassification probabilities at the beginning and the end of the time interval. Thus

$$\tau_1 = P\{X(0) = 1 \mid Y(0) = 0\}, \quad \ldots. 4(a)$$

$$\tau_2 = P\{X(T) = 1 \mid Y(T) = 0\} \quad \ldots.4(b)$$

If the conditional events 4(a) and 4(b) have positive probabilities, then above definition is meaningful. This condition leads us to the requirement that the state probabilities q_1 and q_2 are strictly less than one, i.e.

$$0 \leq q_i < 1 \qquad i = 1,2 \quad \ldots..(5)$$

Following Singir and Cohen (1980), let us define the misclassification probability π as the probability that a truly positive host is observed negative. Let the new classification probabilities at the beginning and end of the time interval be denoted by π_1 and π_2 respectively. Then

$$\pi_1 = P\{Y(0)=0 \mid X(0)\} \quad \ldots. 6(a)$$

$$\pi_2 = P\{Y(T)= o \mid X(T) = 1\} \quad \ldots. 6(b)$$

These definitions are meaningful only when

$$0 \leq p_i \leq 1, \qquad i = 1, 2, \qquad \ldots..(7)$$

Thus we arrive at the relation

$$p_i \pi_\iota = (1 - q_i) \tau_{n,} \qquad i = 1,2 \qquad \ldots. (8)$$

Here it is assumed that here are false negatives but no false positives. It implies that the sample space at any time (t = 0 or t = T) is partitioned into a union of three disjoint events as follows.

$$\Omega = \{X(t) = 0\} \cup \{X(t) = 1, Y(t) = 0\} \cup \{Y(t) = 1\} \qquad \ldots.(9)$$

The first of these events can be considered as "true negative", the second one as "false negative", and the third one as "observed positive". Hence it implies that whenever a host is truly free from parasites in his blood, then he will also be observed free of parasites i.e.

$$\{X(t) = 0\} \subset \{Y(t) = 0\} \qquad \ldots.(10)$$

Furthermore, whenever a host is observed patent then he is truly patent, so that we have

$$\{Y(t) = 1\} \subset \{X(t) = 1\} \qquad \ldots.(11)$$

The event of being truly patent at either the beginning or the end of the time interval is the union of two disjoint events, i.e. that of being observed patent and that of being a false negative. By computing the probabilities of these events, we have the relation

$$p_i = q_i + p_i \pi_\iota \qquad i=1,2 \qquad \ldots.(12)$$

From relations (5) and (6), we can obtain relation between the probabilities of being patent p_i and of being observed patent q_i at the beginning and the end of the time interval. Thus

$$p_i = q_i \ (1 - i) \tau_\iota \qquad i=1,2 \qquad \ldots.(13)$$

This relation (9) is also given by Nedelman.We extend the restrictions of the state probabilities p_i and q_i by requiring that the state probabilities all lie in the open unit interval:

$$0 < p_i < 1, \qquad 0 < q_i < 1, \ i = 1,2. \qquad \ldots. (14)$$

In this case $q_i = 0$ and $p_i = 1$ are excluded. It follows from relations (12) and (13) that the restrictions (14) of the state probabilities mean that the misclassification probabilities are strictly less than one i.e.

$$0 \leq \tau_\iota < 1, \qquad 0 \leq \pi_\iota < 1, \qquad i = 1,2 \qquad \ldots.(15)$$

The transition probabilities P_{1n} for the process X (t) are unaffected if the conditioning event {X (o) = 1} is replaced by any subset. Therefore

$$\begin{aligned} P_{1n} &= P\{X(T) = n \mid X(0) = 1\} \\ &= P\{X(T) = n \mid Y(0) = 1\} \\ &= P\{X(T) = n \mid X(0) = 1, Y(0) = 0\}, \; n = 0 \end{aligned} \qquad \ldots.(16)$$

From the description of the misclassification in terms of false negatives given above it is easy to derive the event probabilities Q_i of the observed process in terms of the probabilities P_3 of the true process. Now

$$\begin{aligned} Q_1 &= P_1 + \pi_2 P_2 + \pi_1 P_3 + \pi_1 \pi_2 P_4, \\ Q_2 &= (1 - \pi_2)(P_2 + \pi_1 P_4) \\ Q_3 &= (1 - \pi_2)(P_3 + \pi_1 P_4 \\ Q_4 &= (1 - \pi_1)(1 - \pi_2) P_4. \end{aligned} \qquad \ldots. (17)$$

We note that if there are no misclassifications then

$$\pi_1 = \pi_2 = 0 \text{ and therefore } Q_i = P_i, = 1 \qquad \ldots.(18)$$

It is useful to express the misclassification probabilities π_ι in terms of the misclassification probabilities τ_ι estimated by Nedelman and the state probabilities p_i. From (7) and (8), we get .

$$\pi_i = \frac{\tau_i (1 - p_i)}{(1 - \tau_i) p_i}, \; i = 1,2 \qquad \ldots.(19)$$

4. THE ESTIMATION PROCEDURE

The estimation procedure is based on the method of successive ML, We discuss Malarial lymphocytes estimates in each age band over all five-time intervals, as studied discussed by **Nasell (1986).** The likelihood function for a given age band is the product of the likelihood functions for that age band each of the five time intervals. In a given age band and time interval the data, giving the number of occurrences of each of the four events {00, 0I, I0, II} are denoted by $N_{00,}$ N_{0I} , N_{I0}, N_{II} , respectively. The likelihood function for these data is determined by the multinomial distribution. By omitting a term that depends only on the data we find that the contribution from each time interval to the logarithm of the likelihood function for a given age band can be written as

$$\log L = N_{00} \log Q_1 + N_{0I} \log Q_2 + N_{I0} \log Q_3 + N_{II} \log Q_4 \quad \ldots.(20)$$

where $Q_1 - Q_4$ are the event probabilities for the observed process Y (t). We note that an explicit expression for the likelihood function in any age based is difficult to obtain be too complex, a computational processor can be employed.

5. CONCLUDING REMARKS

The result presented by **Nasell (2000)** show that Markov Chain Model works well for the study of infection of a human host together with the longitudinal data form the Garki project for the purpose of estimating model parameters. The model presented here is very simple and can be used by medical doctors even without having a deep mathematical knowledge. In fact this is a model that gives an understanding of the process of malaria infection of human hosts that accounts for both super infection and relapses. Misdiagnosis, which is also an important factor, is incorporated established in the model discussed. The analysis of Nasell approves that the estimation of misclassification probabilities is useful for understanding the infection of human hosts.

REFERENCES

1. Ahlgren D.J. and Stein A.C. (1990): Dynamic models of the AIDS epidemic, J. Simulation, Vol. 54, No.1, pp 7-20.
2. Anderson R.M. (1981): Population ecology of infectious diseases agents, Theo. Ecol., 2nd Edn., Oxford, pp 318-355.
3. Anderson R.M. (1982): Population dynamics of infectious diseases theory and applications, Chapman and Hall London.

4. Anderson R.M. (1988): The epidemiology of Malaria infection: variable incubation plus infectious periods and heterogeneity in sexual behavior, J. Roy. Stat. Soci., Vol. 151, pp. 66-93.

5. Bailey N.T.J.(1980a): spatial models in the epidemiology of infectious diseases. Lecture notes in biomathematics, vol. 38, pp. 233-261. new york: springer.

6. Herbert, J. and Isham, V. (2000): Stochastic host-parasite population models. JMB 40, 343–371.

7. Macdonald G. (1950): The analysis of infection rates in diseases in which super infection occurs, Trop. Dis. Bull., Vol. 47, pp. 907–915.

8. Molineaux and Gramiccia, (1974): A malaria model tested in the African Savannah Bull, World Health organization, Vol. 50, pp. 347 –357.

9. Nasell I. (1985): Hybrid models of tropical infections, Lect. Notes Biomat, Vol .59, PP. 1-206.

10. Nasell I. (1986): Hybrid models of tropical infections, Lect. Note. Biomat., Vol .59, pp. 185-206.

11. Nasell I. (2000): On the quasi-stationary distribution of the Ross Malaria model, Math. Boise, Vol. 107, pp. 187-208.

12. Nedelman (1988): The prevalence on malaria in Garki, Nigeria, Double sampling with a fallible expert. Biometrics, vol. 44, pp. 635-655.

13. Ross R. (1910): The prevention of malaria. London: murray.

14. Ross R. (1911): The prevention of malaria (2^{nd} edn). (with addendum on the theory of happenings.) London: murray.

15. Hethcote, H. W. (2000) The mathematics of infectious diseases. SIAM Review 42, 599–653.