Mathematical Model for The Transmission of Lymphatic Filariasis and Its Applications

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We have constructed a stochastic transmission model for lymphatic filariasis caused by Wuchereria bancrofti, and have analyzed its prevalence using computer simulations. In Pondicherry, India, where Wuchereria bancrofti has been spreading, the Vector Control Research Centre has carried out an integrated vector control strategy against malaria and filariasis for five years (1981 ~ 1985) with good results reported. Our study was aimed at evaluating the effect of vector control in the context of Pondicherry, and in particular the continuous effect for the post-control period. In this paper, we have used the LYMFASIM model proposed by Plaisier et al., the carrying capacity model by Rochet and the population dynamics model by us. In the LYMFASIM model and the carrying capacity model, we have modified the quantities of parameters in order to fit the models to the parasitological, entomological and epidemiological data in Pondicherry. We have combined the improved LYMFASIM model with the other models. Through simulations of our combined model, we have compared the prevalence rate in the human population as well as the mean number of L3-larvae in the mosquito population, with and without vector control. As a result, the simulations show that the prevalence rate would be restrained for a long time even if only a small continuous effect of the vector control remains in the post-control period. However, the mean number of L3-larvae would recovered within a short time comparatively. This is because of the differences in life spans between human and mosquito as well as the incubation periods between the adult worm in the human host and L3-larvae in the mosquito vector.

Keywords: Lymphatic filariasis, mathematical model, Pondicherry, vector control, Wuchereria bancrofti

1 INTRODUCTION

Lymphatic filariasis is a parasitic disease which prevails throughout the tropical belt, and most of patients are infected with Wuchereria bancrofti [1]. The acute manifestation of bancroftian filariasis is unperiodical attacks of adenolymphangitis with fever preceding or complicating the chronic manifestations that are hydrocele, lymphoedema, chyluria and/or elephantiasis which is the most severe. Adult male and female parasites of W. bancrofti (adult worms) live on the lymph channel of the human host, and a mature female produces a large number of microfilariae (mf) that circulate through the blood. A mosquito vector that belongs to Culex, Anopheles, etc. ingests mf when it bites an individual, and part of the mf in a vector develops through two intermediate stages (L1-larvae, L2-larvae) to the stage of infectious L3-larvae. L3-larvae develop into new adult worms

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in the human host when an infective vector with L3-larvae bites a host.

The control strategies for lymphatic filariasis in an endemic community can be divided into three methods: controlling the vector mosquito (vector control), reducing the parasite reservoir by means of chemotherapy (parasite control), and a combination of both. Vector control aims to reduce the rate where persons are bitten and receive L3-larvae. This can be achieved by preventing mosquitoes from breeding through a reduction in the area of stagnant polluted water, by the spreading of biological insecticides, and by other measures to prevent man-vector contacts. In parasite control, two drugs, diethylcarbamazine (DEC) and ivermectin, are generally used, which are effective in killing mf and also depressing the production of mf. Repeated treatment reduces the progress of disease symptoms, consequently, this can lead to a lowering in the reservoir of mf available to the vector, and thus to a reduced prevalence.

_**W. bancrofti** is widespread in India, especially in Pondicherry, the South-East India where it is an endemic disease. The dominant mosquito species is _Culex quinquefasciatus_. The Vector Control Research Centre (VCRC) has carried out an integrated vector control program against malaria and filariasis for five years (1981 ~ 1985), and have reported a substantial decrease in both the vector population size and the transmission index for _W. bancrofti_ during the period of vector control [2].

In this study, the LYMFA SIM model [3] was improved to cooperate with the population dynamics of mosquito vectors being acted on the carrying capacity model [4], while the parameters of the LYMFA SIM model and the carrying capacity model have been chosen to fit a prevalent situation in Pondicherry [5]. The initial distribution of worms in the human population has been determined on the basis of the pre-control parasitological, entomological and epidemiological data in Pondicherry, and human population dynamics is founded on the live-birth rate together with the life table in India [6].

The purpose of this paper is to evaluate the effect of vector control on the prevalence of _W. bancrofti_ using computer simulations based on the stochastic transmission model, with the main focus being on the continuous effect of the post-control period. In the model, we adopted a month as the unit time. We have performed simulations on the prevalence of _W. bancrofti_ in the human population and the mean number of L3-larvae in the mosquito population in the Pondicherry context from 1981, when VCRC started vector control, until 1999, for cases with or without vector control. The age specific prevalence rate in the human population is also given in this paper. The simulations show that the prevalence rate would be restrained for a long time if a small continuous effect of vector control remains for the post-control period, while in contrast the mean number of L3-larvae would recover within a short time comparatively. This is due to differences in the life spans between human and mosquito as well as the incubation periods between the adult worm in human hosts and L3-larvae in the mosquito vector.

2 MATERIALS AND METHODS

2.1 Model of population dynamics

We have prepared the model of population dynamics in India based on the demographic data from [6], which would simulate the population movements from 1981 to 1999 by month. Fig.1 and Fig.2 showed the transition of live-birth rate (1981 ~ 1995) and life table in India (1981 ~ 1985) respectively.

In the population dynamics, we assume that the number of live-births depends on the total population number as well as the monthly live-birth rate without regard for parous histories and that deaths are assigned randomly to each age group in months following from its probability of dying at that time. For simplification, the model makes no distinction of sex.

The demographic data of population by age group in years for India in 1981 (Fig.3) and the age specific survival rate during 1981 ~ 1985
(Fig. 4) allowed us to assign the initial population by age in months from birth up to 70 years old (Fig. 5). The total size of the population at the beginning of the study (1981) was set at ten thousand.

![Figure 4: Age specific survival rate in India (1981 ~ 1985). The data being derived from [6]](image)

![Figure 5: Assignment of population by age (the initial size of total population being set at ten thousand)](image)

### 2.2 LYMFASIM model

#### 2.2.1 Dynamics of the transmission

When a vector mosquito bites an individual with mf in the blood, a certain number of mf are ingested by the mosquito and some can then develop into L3-larvae through the intermediate L1, and L2-stages. The LYMFASIM model described the relationship between the mf density in human blood and the number of L3-larvae in mosquitoes as a hyperbolic function, which was investigated in [7].

\[
L_3(t) = \frac{a \times m_i(t)}{1 + b \times m_i(t)}
\]  

(1)

where \(L_3(t)\) denotes the mean number of L3-larvae per mosquito that bites the person \(i\) in a given month \(t\) and \(m_i(t)\), the density of mf in
the blood of the person \(i\) in a given month \(t\) per 20 \(\mu\)l. The values of parameters \(a\), and \(b\) in (1) that stand for the slope of the function at low human mf densities and the saturation level for the number of L3-larvae at high mf densities are referred to [3] \((a = 0.09, b = 6.6)\).

The mean number of L3-larvae in the mosquito population at a given month \(t\) \(\langle L3(t) \rangle\) can be calculated by the average of \(L3_i(t)\) with the weight of the relative exposure of each person \(i\) in a given month \(t\) \((E_i(t))\) over the total human population \((N(t))\) being the size of total population in a given month \(t\) where \(\nu\) denotes the growth rate by which the mf in the infected mosquito develop into the infectious L3-larvae, and whose value is 0.1 [3].

\[ L3(t) = \frac{\sum_{i=1}^{N(t)} (E_i(t) \times \nu \times L3_i(t))}{\sum_{i=1}^{N(t)} E_i(t)} \]  

(2)

The relative exposure of a person is influenced by age and sex as well as other factors such as behavior, and attractiveness to mosquitoes, etc. The composite of the latter factors for the person \(i\) \((E_{i1})\) is stochastically treated as following the gamma distribution with the mean value at 1.0 and the shape parameter at 1.0. For simplicity, \(E_{i1}\) does not vary throughout the life span. On the other hand, the contribution of the former factors for the person \(i\) \((E_{ai}(a,s))\) which is assumed to only depend on age \(a\) regardless of sex \(s\), may be represented as a linear function from 0.18 at birth up to 1.0 at 187 months old, while above this age a constant function value of 1.0 is used. It is prescribed that \(E_i(t)\) is the product of \(E_{i1}\) and \(E_{ai}(a,s)\).

\[ E_i(t) = E_{ai}(a,s) \times E_{i1} \]  

(3)

Generally, the number of mosquito bites is large enough to ignore differences in L3-larvae load among mosquitoes, so it seems that the mean number of L3-larvae released per mosquito bite is equal for every person. On the assumption that an infective mosquito releases all L3-larvae in its body, the monthly transmission potential of the person \(i\) in a given month \(t\) denoted by \(mtp_i(t)\) is given by the following formula:

\[ mtp_i(t) = K(t) \times L3(t) \times E_i(t) \]  

(4)

\(K(t)\) stands for the carrying capacity of the larval environment in a given month \(t\), to which the density of mosquito population is in proportion. Although Plaisier et al. [3] applied a stationary monthly biting rate, we considered the variable monthly transmission potential with the annual and seasonal fluctuations by using the carrying capacity model. A detailed explanation of the carrying capacity is given in subsection 2.3.

\[ H_{i1}(t) = mtp_i(t) + \beta \times H_{i1}(t - 1) \]  

(6)
\[ R_l(t) = 1 - \exp \left[ -\gamma \times \rho_i \times H_l(t) \right] \]  
(7)

The quantity of \( \gamma \) was chosen as \( 9.2 \times 10^{-4} \) through our simulations to fit the prevalence level in Pondicherry.

We assume that the distribution of newly acquired adult worms with a discrete quantity follows a negative binomial pattern whose mean value is given by the force of infection with the shape parameter \( 1.3 \times 10^{-3} \). \( T_{ij} \), and \( T_{lj} \) are the growth period from L3-larvae to adult worm of a parasite \( j \), and the survival period of a parasite \( j \) respectively. The mode of an adult worm and the maximum are estimated at 5.42 years and 10.0 years respectively [4]. We assume that the distribution of \( T_i \) and \( T_l \) follow the Weibull distribution with the mean values at 12.0, and 62.62 and the shape parameters at 1.0, and 68.47 respectively. \( M_i(t) \) approximates to:

\[ M_i(t) \approx M_i(t-1) + M_i(t - \overline{T_i}) - M_i(t - \overline{T_l}) \]  
(8)

(\( \overline{T_i}, \overline{T_l} \) being the means on \( T_{ij} \), and \( T_{lj} \)).

On the assumption that the sex ratio of adult worms is 0.5, the mf density in 20 \( \mu \)l blood is given by:

\[ m_r(t) = \frac{1}{2} M_i(t) \times \frac{r}{1 - s} \]  
(9)

where \( r \), and \( s \) denote the mf production of one female per 20 \( \mu \)l, and the survival rate of mf respectively, \( (r = 1.56, s = 0.57) \) [4], (note that \( 1/(1 - s) \) is the life expectancy).

### 2.3 Carrying capacity model

The density of the mosquito population is closely related to meteorological variables such as precipitation, temperature and humidity, because the combination of meteorological variables controls the size of the open water surface and therefore determines the transmission capacity of the larval environment for the mosquito vector (carrying capacity). Rochet [4] reported that the size of the open water surface could be estimated by the evaporation during the current month \( (V) \) and the sum of rainfall during the current month and the two previous ones \( (P) \). Fluctuations in the density of the mosquito population tracks that of the carrying capacity. For the carrying capacity model, we use a multiple linear regression with \( \log(\text{carrying capacity}) \) which was adopted in [4].

\[ \log K = n_1 P + n_2 V + n_3 \]  
(10)

where \( n_1 \) are the coefficient parameters. We put the quantities of \( n_1 \), and \( n_2 \) listed in [4] in our simulations ((11), and (12)) and that of \( n_3 \) (13) which is modified by the baseline of Madras data, noting that \( e^{n_3} \) means the basic carrying capacity.

\[ n_1 = 2.986 \times 10^{-4} \]  
(11)

\[ n_2 = -8.993 \times 10^{-3} \]  
(12)

\[ n_3 = 10.8 \]  
(13)

Due to the signs of the parameters, the carrying capacity goes up or down on an increasing \( P \) or \( V \). Using the meteorological data of Madras [9] that is a city near to Pondicherry (Fig. 6, 7), we have estimated the transition in carrying capacity from 1981 to 1999 (Fig. 8). Fig. 8 shows that it tracked the annual and seasonal fluctuations.

**Fig.6** Precipitation in Madras (1981 ~ 1999). The data being derived from [9]

### 2.4 Vector control

In Pondicherry, the principal species of mosquito which transmits \emph{W. bancrofti} is \emph{Culex quinquefasciatus} [2]. Rajagopalan et al. [2] reported that the average daily emergence of \emph{Culex quinquefasciatus} mosquitoes ranged from 172,000
in the rainy month of November to 9.6 million in the post-rainy month of January. This high density of mosquitoes is maintained by mosquito breeding in over 100 km of drains, thousands of cesspits, pools and wells, as well as a large swamp. In addition, the urban population in the study area has grown enormously, from about 50,000 in 1961 to 272,000 in 1981. This rapid urbanization has increased the movement of mf carriers and susceptible populations into the town. The Vector Control Research Centre (VCRC) carried out a Filariasis Control Demonstration Project from 1 January 1981 to 31 December 1985, and in their report [2], the indoor resting density of *Culex quinquefasciatus* as well as the transmission index for *W. bancrofti* were both reduced by 90% (Table 1). The effect of vector control on the basis of their data has been investigated by our model. The curves in Fig. 9 show the annual fluctuations in the carrying capacity, according to whether vector control operation was in or not. It demonstrated the efficacy of the vector control project against Lymphatic filariasis during the period of the study.

Our simulations were performed stochastically in monthly steps from January 1981, when VCRC launched the vector control in Pondicherry, to December 1999 on the basis of demographic data in India [6], meteorological data in Madras [9] which refers to the carrying capacity of mosquitoes, and epidemiological data of the *W. bancrofti* in Pondicherry [5]. The initial size of the total human population was set at ten thousand. The simulations were repeated one hundred times for various random seed numbers. Their averages were used in the our figures.

### 3 RESULTS

For each age group, the distribution of mf density was assigned to patients who were chosen randomly from the age grouped individuals, so as to follow the zero truncated negative binomial distribution grounded on the pre-control data in Pondicherry [5]. For each mf positive person, the initial number of adult worms harbored in his body was determined by equation (9).
Table 1 Annual transmission Index for Wuchereria bancrofti in Pondicherry during the 5 years of the VCRC vector control project

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated no. of mosquitoes biting a single man in one year (a)</td>
<td>26203</td>
<td>8238</td>
<td>3181</td>
<td>3222</td>
<td>1662</td>
<td>3617</td>
</tr>
<tr>
<td>Proportion of infective mosquitoes (from biting collections only) (b)</td>
<td>0.0086</td>
<td>0.006</td>
<td>0.004</td>
<td>0.0066</td>
<td>0.0079</td>
<td>0.0061</td>
</tr>
<tr>
<td>Estimated no. of infective bites a man receives in one year</td>
<td>225</td>
<td>49</td>
<td>13</td>
<td>21</td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td>Number of infective larvae per infective mosquito (c)</td>
<td>2.0</td>
<td>4.0</td>
<td>2.6</td>
<td>2.9</td>
<td>3.72</td>
<td>3.5</td>
</tr>
<tr>
<td>Annual transmission index (a x b x c)</td>
<td>450</td>
<td>197</td>
<td>33</td>
<td>62</td>
<td>49</td>
<td>77</td>
</tr>
</tbody>
</table>

Derived from Rajagopalan et al. (1987)

shows the comparison of our initial age specific distribution to the age specific prevalence rate during Pondicherry in the pre-control period (Table 2).

Fig.10 Comparison of our initial age specific distribution to the age specific prevalence rate of Pondicherry in 1980. ■ being the actual data, and the column being value estimated by our model

3.2 Transition of human population

Fig.11 shows a comparison of the transitions in the human population described by the model simulation with that of the demographic census data in India from 1981 to 1996 (the initial population size being set at ten thousand). This assured our model conformed with the real data.

3.3 Analysis of the LYMFASIM model

Fig.12 shows the transitions in the prevalence rate in the presence and absence of vector control from 1981 to 1985 obtained by the model simulations, without considering any continuous effects in the post-control period. Fig.13 shows the average of the age specific prevalence rate in 1985 with execution of vector control over 100 simulations. By contrast, Fig.14 shows the average without vector control.

For the post-control period, we simulated the transitions in the prevalence rate of the human population (Fig.15) and that of the mean number...
Table 2 Analysis of age and sex distribution of microfilaria rate in the Pondicherry rural population

<table>
<thead>
<tr>
<th>age group</th>
<th>males</th>
<th>females</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no.</td>
<td>mf</td>
<td>no.</td>
</tr>
<tr>
<td>0 - 5</td>
<td>371</td>
<td>3 (0.8)</td>
<td>336</td>
</tr>
<tr>
<td>6 - 10</td>
<td>1309</td>
<td>31 (2.4)</td>
<td>1040</td>
</tr>
<tr>
<td>11 - 20</td>
<td>2412</td>
<td>80 (3.3)</td>
<td>1163</td>
</tr>
<tr>
<td>21 - 30</td>
<td>1184</td>
<td>65 (5.5)</td>
<td>653</td>
</tr>
<tr>
<td>31 - 40</td>
<td>512</td>
<td>28 (5.5)</td>
<td>453</td>
</tr>
<tr>
<td>41 - 50</td>
<td>301</td>
<td>21 (6.9)</td>
<td>283</td>
</tr>
<tr>
<td>51 - 60</td>
<td>168</td>
<td>7 (4.2)</td>
<td>139</td>
</tr>
<tr>
<td>61 +</td>
<td>143</td>
<td>6 (4.2)</td>
<td>55</td>
</tr>
<tr>
<td>total</td>
<td>6400</td>
<td>241 (3.8)</td>
<td>4122</td>
</tr>
</tbody>
</table>

*mf rate % is shown in parentheses.
Derived from Rajagopalan et al. (1981)

Fig.12 Transitions of the prevalence rate with or without vector control. Solid line being with vector control, and the broken line without

of L3-larvae in the mosquito population (Fig.16) for several cases with the continuous vector control effect lasting at rate of 2%, 4%, 10% and 50%.

4 DISCUSSION

The model predicts that the prevalence rate will hold almost stable if there are no vector control projects (Fig.12). This is reflected in the fact that an increase in cases of W. bancrofti is balanced with a natural increase in population. On the other hand, it also predicts that, if the vector control project is enforced, the prevalence rate will gradually decrease with the reduction in carrying capacity during the execution period but that it will rally and rebound beyond the initial preva-
The transition of the prevalence rate in the human population, with the continuous effect of vector control lasting at a rate of 2%, 4%, 10% and 50%

The reason for this is due to differences in the life spans between individuals and mosquitoes as well as the incubation periods between adult worms and L3-larvae.

The distribution of adult worms harbored in the parasitemia population is not known. Therefore the initial distribution in our model were based on the data of the mf density distribution in Pondicherry. The process for acquiring adult worms should follow the negative binomial distribution, which is more appropriate for the real mf distribution than the Poisson distribution.

Finally follow-up studies on the prevalence of W. bancrofti will be anticipated on the bases of the post-control data in Pondicherry.

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