CHAPTER 5

CONCLUSION AND DISCUSSION

5.1 Conclusion

Clinical criteria for diagnosing malaria are developed to be introduced in places where fever alone is the diagnostic criterion for giving presumptive treatment. Oral temperature equal to or higher than 38° C and enlargement of the spleen are found to be significant predictors for blood slide positivity. Probability of blood slide positivity given, oral temperature equal to or higher than 38° C and enlargement of the spleen in the rainy season is higher than that in the nonrainy season. It means rainy season influences these clinical features in predicting slide positivity. Other factors like endemicity, measured in this study in terms of area of residence with regards to risk of contracting malaria, and age of the patients are expected to have effects on these clinical features in determining or predicting blood slide positivity. But this could not be demonstrated in this study.

Although nine variables are included in the analysis only three are significant. There are a number of variables found to be significant statistically as predictors for blood slide positivity in the study by Genton and others (1994). As the data used in the present study are hypothetical in nature no definite conclusion can be drawn here. On the other hand the objective here is to develop an approach to produce a set of clinical criteria to predict blood slide positivity so as to make the presumptive treatment more specific in selecting cases. Another objective is to develop a method to evaluate benefits and costs that can arise from introducing these clinical criteria into practice. It is expected that by using the empirical approach more definite conclusions can be drawn.

Relying only on the clinical features in reaching the decision to give treatment may not be appropriate as species identification cannot be done. But by being more specific in selecting cases for giving presumptive treatment substantial amount of resources can be saved by reducing the number of cases

treated unnecessarily. In places where the slide positive rate is low, giving presumptive treatment to all cases on clinical evidence of fever alone is not a good practice. This presumptive treatment approach may be reasonable in places where the slide positive rate is high and the risk of missing malaria cases is not desirable. If the slide positive rate is low one should be more selective in giving presumptive treatment. This problem can be solved by developing clinical criteria to select cases to be given presumptive treatment. In developing this, the economic implication is one of the factors that are to be taken into consideration. The professional skills of health workers in peripheral areas can be upgraded by improving their clinical acumen. Although they are intended to be used more in preventive work, early and correct diagnosis and treatment is also one way of prevention. It is undeniable that technology for diagnosis of malaria is advancing. But this advanced technology is not available everywhere and especially in places where malaria is a major public health problem. While waiting for this advanced technology to get within their capacity developing countries should try to develop appropriate technology which is practical, within their means and easy to sustain. It is expected that the approach developed in this study is one way of attaining it.

5.2 Discussion

5.2.1 Clinical Criteria

Genton and others (1994) included length of history of fever, history of malaise, headache, loss of appetite, nausea, vomiting, abnormal stools as well as temperature, level of consciousness, respiratory rate, spleen size, cough and chest indrawing as explanatory variables in their model to predict blood slide positivity and parasite density. Their final model retained spleen size, no cough, temperature, no chest indrawing and abnormal stools as significant predictors in children. They found that normal stools and no cough were predictors in adults. Analysis was done separately for children and adults. In this study the explanatory variables included were temperature equal to or higher than 38° C, enlargement of the spleen, cough, vomiting and normal motion. Other background variables expected also to determine slide positivity were included in the study. They were area of residence with respect to risk of getting

malaria, time of the year with regards to rain, and age and sex of the patients.

Temperature was expected to be positively associated with blood slide positivity. Delfini (1973) also found the same association. He found that as temperature rises it is more likely to be associated with blood slide positivity. This is said to be influenced by age. It is said that the difference is less well marked in the older age group. As expected, temperature was found to be a significant variable. As the scale of measurement in this study was nominal, a trend could not be shown definitely. Age was found to have no effect in determining the slide positivity. No definite conclusion can be drawn as the data used were hypothetical and the study was not done separately for the two age groups as was done by Genton and others.

Another variable found to be significant was enlargement of the spleen. The scale of measurement was nominal only and the effect of the degree of enlargement of the spleen on blood slide positivity cannot be determined although an association between splenic enlargement and the blood slide positivity can be demonstrated. Although it is expected that the significance of splenic enlargement in determining blood slide positivity may not be the same in different age groups, this cannot be demonstrated. This may be due to the fact that separate study and analysis has not been undertaken. Enlargement of spleen is common in malaria endemic areas and inclusion of this sign as predictor in the model should also take into consideration the prevalence of splenomegaly in the population. It usually denotes chronicity of the disease rather than the acute attacks (Kidson, personal communication).

Cough and normal stools were found to be negatively associated with blood slide positivity in the study by Genton and others. This was not so in this study. But as the results in the present study were based only on hypothetical data no definite inference should be drawn. An empirical study may yield a different result. Vomiting was found to be associated with *P. falciparum* parasitaemia $\geq$ 10,000/μl in the study by Genton and others and it can also be related to the severity of the

disease. Association was not found in this study, where the dependent variable, unlike in the study by Genton, was blood slide positivity only.

In their study Genton included *P. falciparum* parasitaemia ≥ 10,000µl as a dependent variable in addition to blood slide positivity. He argued that the small difference in blood slide positivity between presumptive cases of malaria and the random survey meant that the presence of parasitaemia is not a useful indicator of morbidity and does not really help to diagnose a malaria attack. But parasite density may denote the severity of the disease only (Kamol-Ratanakul, personal communication). They concluded in their study that the clinical examination did not help with the diagnosis in adults but an enlarged spleen was a good predictor for a positive blood slide.

Apart from the clinical symptoms and signs it is expected that the background variables like endemicity, age and season will also influence these clinical features in predicting blood slide positivity. But in this study only the season can be demonstrated to have influence on this. In the rainy season it was found that the probability of blood slide positive, given temperature ≥ 38° C and splenic enlargement was 0.36 while this was only 0.19 in the nonrainy season. A similar study done in different endemic regions in different seasons on different age groups may yield a different outcome.

Malaria distribution between genders varies from place to place and from year to another, depending on many interrelated factors. There is marked preponderance of malaria among males as compared to females. Sex difference in malaria incidence might well be influenced by local socio-economic status, ethnic origin, attitudes of parents especially mother towards male and female children, ignorance and access to free medical services in the villages (Kondrashin and Rooney, 1992). Whether gender influences clinical signs and symptoms in predicting slide positivity cannot be demonstrated in this study.

5.2.2 Benefits and Costs

It is seen that benefits (costs saved) are determined by the specificity of the diagnostic process or procedure, slide positivity at that time , total number of patients to be given presumptive treatment and the drug costs. The more specific the procedure or process the lesser will be the number of false positive cases. Blood slide positivity is usually low in the low endemic region and this is the place where the clinical criteria will be useful because the lower the slide positivity the greater will be the costs saved. If the drug used for presumptive treatment is expensive more benefit can be accrued from using the clinical criteria rather than fever alone in selecting cases for presumptive treatment. But cheap and safe drugs are usually recommended to be used for presumptive treatment.

Additional costs of introducing these clinical criteria are a function of the fixed costs (X), number of new cases infected by each false negative case, sensitivity of the criteria and the slide positive rate at that time. Under different scenarios it can be seen that number of new cases determine additional costs and the benefit cost ratio (Table 4.7). The great majority of studies on the resource cost of malaria concentrate on treatment costs, days of work lost, leaving aside the more intractable issues of demographic consequences, attitudes to risk and innovation and effect on intellectual development (Mills, 1984). It is quite desirable that these resource costs should be measured. But it is difficult to pinpoint definitely these resource costs are mainly due to malaria because they are multifactorial in origin. Another problem lies in the difficulty one has to face in measuring these costs.

In considering costs, costs of missing other serious illnesses also need to be addressed. This depends on the prevalence of these illnesses which may concurrently exist with malaria in the same patient. As stated earlier in the section on population and sampling those with obvious evidence of other illnesses will be excluded from the study. It means that the approach developed in this study will only take into consideration those without other overt illnesses.

It is found here that benefit cost ratios are more than one in both seasons if the number of new cases and slide positive rates are small. The number of new cases that can be infected by each false negative case depends on many factors: number of vectors, their longevity and their capacity to transmit the parasite; immunity of the people, their health seeking behavior and their socio-economic status; the environmental conditions are among these factors. From the equations for determining benefits and costs it is seen that slide positive rate is the common determinant for both benefits and costs. More benefits can be accrued if the slide positive rate is low, see equation 3.4.3(c). In places where the slide positive rate is low the additional costs of introducing the clinical criteria will be less. This can be seen from the equation 3.4.4(f) showing the relationship between additional costs and these factors. Levels of slide positive rates under different scenarios and a given sensitivity and specificity of the clinical criteria, at which the benefit cost ratios will be high had been determined. Figures 4.3 (a), (b), (c) and 4.4 (a), (b), (c). On the basis of these it may be possible to determine various circumstances under which the clinical criteria will be applicable.

5.2.3 Possible Place of Clinical Criteria in Diagnosis of Malaria

Presumptive treatment is best used when the laboratory examination results are available in less than one week's time and the patients return for radical treatment, if found positive. In practice the time lag between taking the blood slide and examination has increased considerably resulting in delayed and incomplete treatment of cases. The average time for slides to reach township laboratories is 16.9 days (1-60 days), the average duration of time from receiving to examination of slides takes 11.2 days (1-30 days) and feedback of laboratory results to the patient is 17 days (1-99 days) (VBDC Myanmar, 1996, cited by Naing, 1996). The proportion of *P. falciparum* continues to average about 40% of the total malaria cases in WHO South East Asian Region nations but the range is wide, the highest being in Myanmar (85%) and the lowest in Nepal

(approximately 10%) (Kandrashin and Rooney, 1992). Falciparum malaria accounted for more than 80% of cases in Myanmar. Severe and complicated malaria is almost always due to *P. falciparum*. The response of *P. falciparum* to chloroquine like drugs and other antimalarials according to *in vivo* results from 1987-1990 indicated that 4-aminoquinolines (chloroquine) and sulfadoxine/pyrimethamine combinations are still effective for treatment of semi-immune living in endemic areas (Tin, 1992).

From figure 4.3 (a) it can be seen that in rainy season if the number of new cases infected by each false negative case is low, the benefit cost ratio is higher than one if the slide positive rate is less than 0.6. Higher benefit cost ratios can also be expected if slide positive rates are lower though the number of new cases may be higher, Figures 4.3 (b) and (c). In nonrainy season high benefit cost ratios can be expected at much lower levels of slide positive rates under similar rates of infecting new cases by false negative cases as in the rainy season, Figures 4.4 (a), (b) and (c). In general using the clinical criteria thus developed, instead of fever alone in selecting cases for presumptive treatment, in places where slide positive rates and disease transmission rate are low may have more benefits in terms of costs saved, and will also be less costly. Feasibility of using these clinical criteria in diagnosing and giving radical treatment for malaria in places where prevalence of *P. falciparum* is high and parasites are still sensitive to cheaper and safe drugs like chloroquine; microscopy is not available or delayed; there is possibility of low slide positive rate; should be considered.

5.3 Strength of the Study

This study is based on methods that are practical, easy to follow and inexpensive. The model developed in this study can be understandable by nonexperts. The outcomes of the intervention are not remote from it and are possible to measure. It is important that approaches and options for health care interventions and their decision criteria should be presented to the policy makers in such a way that they are simple and easy to understand. The mathematical equations in this study are simple and easily understandable to nonexperts. Many health status outcomes are not easy to measure and even if they can be

measured it cannot be claimed with confidence that these outcomes are due to that particular intervention. The outcome and intervention in this study are in close proximity and this may be convincing for the authorities. Although the findings in this study were based on data which are hypothetical, they are generated on sound and realistic basis.

In introducing a new diagnostic technique it should be made sure that the new technique will be less risky, less uncomfortable, less embarrassing to the patient and less costly (Kamol-Ratanakul, 1996). The clinical criteria that could be developed by this study can fulfill all these requirements. It is noninvasive, needs no reagents or instruments, is easy to perform and not harmful to the patient.

The technical qualities (i.e. sensitivity and specificity) of the clinical criteria are based on the stable properties. They do not change with prevalence of the disease. Both technically and economically the criteria are acceptable. Other advanced diagnostic techniques are not attainable in less developed countries. Petersten and Marbiah (1994) in evaluating the quantitative buffy coat (QBC) malaria diagnostic system stated that the price of the QBC tubes is beyond that affordable in most malaria endemic countries and the system is less robust under field conditions than conventional thick blood films. On the other hand thick blood film examination, even by an expert microscopist, is time consuming and labor intensive, especially when the parasites are infrequent in the blood or absent at the time of testing (Tranpradist and others, 1995)

5.4 Limitations of the Study

Most of the data used in this study are hypothetical in nature. A definite conclusion cannot be drawn as regards to the significance of the clinical features in predicting blood slide positivity. But the aim here is to find ways to develop a set of clinical criteria and an approach to determine costs and consequences arising from introducing them. The clinical criteria developed will not be able to identify species of malaria parasites. It will also call for upgrading the clinical acumen of the health workers in the periphery and this approach

can possibly be resisted by those who are more oriented to preventive health.

The findings in this study are based on patients coming to the public sector only. About 80% of malaria cases are seeking care from nonformal sectors. The results therefore may not reflect the whole situation. Costs and consequences (benefits) are measured only on provider aspect in this study. The findings do not reflect aggregate costs or consequences.

5.5 Recommendations for Further Research

This approach to develop a set of clinical criteria is based on hypothetical data. It is also based on a situation where the survey is done only once and encompasses endemicity, season and age. An attempt should be made to conduct the survey separately for different regions, seasons and age groups (i.e. adults and children).

The methodology should be incorporated into other economic or technical evaluation of new diagnostic procedures or techniques. Costs and benefits that could arise from introduction of a new diagnostic procedure or technique can be evaluated using this method with modification when necessary.

As a substantial proportion of patients including malaria cases are seeking care in the private sector, feasibility of developing and applying clinical criteria for diagnosis of malaria in this sector should be explored.