Elimination of falciparum malaria from Sri Lanka: an epidemiological possibility?

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Malaria has been and continues to be one of the most important public health problems in Sri Lanka. Throughout the ages malaria has had a profound impact on the local population. It is generally believed that malaria was one of the important factors that led to the decadence of the ancient Sinhala civilizations (1). The massive epidemic of 1934/35 claimed over 1.5 million cases and 80,000 deaths (2). It is an accepted fact that malaria hinders human development in general and economic development in particular.

Organised malaria control activities in Sri Lanka started in the early twentieth century and have undergone several major changes in the strategies adopted. It first commenced as a control programme. Following the dramatic reduction in malaria incidence with the advent of DDT, an eradication programme was launched in 1958. Although near-eradication was reached around 1963, this status could not be maintained. The programme suffered a major setback which culminated in a major epidemic of malaria throughout the country in 1967/68. Since then, the programme has focussed on control rather than eradication. Today, the programme is based on the Global Strategy for Malaria Control adopted by the World Health Organization in 1993 (3).

In Sri Lanka, two human malarial parasites, namely *Plasmosium vivax* and *Plasmodium falciparum* are prevalent. *P. malariae* was also observed but transmission appears to have been interrupted since 1969. Of the two species, *P. falciparum* is the more virulent one causing severe disease which may be fatal. *P. falciparum* is also the species that has developed widespread drug resistance and continues to pose problems to control efforts. Elimination of this parasite will have beneficial effects not only in the health sector but also in other sectors as well. In this paper we review certain features related to transmission of *P.falciparum* that favour elimination of the parasite from Sri Lanka utilizing the currently available tools for malaria control.

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Parasitological considerations

1. Latent liver forms

A salient feature of *P.falciparum* infections is the absence of latent liver forms. This implies that there is only a single passage of the parasite through the liver and no relapses occur due to the persistence of hypnozoites. This phenomenon is very favourable for interrupting transmission of the disease.

2. Release of merozoites

Falciparum exo-erythrocytic forms release approximately 40,000 merozoites which is much more than those of other plasmodial species (4). The release of such a large number of merozoites from a tissue schizont is a major factor in falciparum malaria being the more severe form as compared to other plasmodial infections. In the Sri Lankan situation where endemicity of malaria is unstable and the immunity of the population is low, patients will present early during a falciparum infection. Early diagnosis and prompt treatment of falciparum infections will reduce transmission of the disease.

3. Incubation period

The incubation period of falciparum malaria is shorter than other plasmodial species. This is due to the shorter duration of the pre-erythrocytic stage in *P.falciparum* and the large number of merozoites released from tissue schizonts that would lead to early appearance of symptoms. As stated above, given the transmission dynamics of malaria in Sri Lanka, this fact can be exploited to reduce falciparum transmission.

4. Virulence

P.falciparum is the most virulent human malarial parasite. It gives rise to serious complications such as cerebral malaria which can be fatal. Due to the virulence of the parasite which gives rise to more severe disease at an early stage, patients usually seek treatment early and, hence, transmission may be curtailed.

5. Maturation of gametocytes

The duration of time taken for maturation of gametocytes in *P. falciparum* is 10-14 days, longer than for other plasmodial species. Very often examination of peripheral blood films of patients who present early for treatment, do not show gametocytes. In Sri Lanka, the treatment schedule adopted for falciparum malaria, which includes a stat dose of primaquine, will eliminate any gametocytes and will ensure interruption of transmission.

Considerations of the vector

1. Vector characteristics

Vector characteristics have a major impact on malaria transmission. Among the characteristics that are important are whether the vector is anthropophilic or zoophilic, endophagic or exophagic and endophilic or exophilic. The major vector in Sri Lanka is *A. culicifacies* which is primarily zoophilic, endophagic and endophilic. These current behavioural characteristics of the major vector of malaria in Sri Lanka are not major limiting factors for the elimination of malaria in Sri Lanka.

2. Sporogonic cycle

The sporogonic cycle of *P.falciparum* is longer than the other *Plasmodium sp.* On an average it takes 12 days at 26^0 C for the sporogonic cycle of *.P.falciparum* which is approximately three days longer than *P.vivax* (5). The longer sporogonic cycle implies that the probability of transmission is less as compared to *P.vivax* when survival of the mosquito is considered. If the average duration of the lifespan of the mosquito is considered to be 25 days and mortality of the mosquito is constant throughout this period, then the probability of survival of the mosquito at 9 days, calculated as $(1-(1/25))^9$, is 0.69 and at 12 days is 0.61. This implies that a maximum of only 61% of infected mosquitoes with *P.falciparum* will be capable of transmitting a new infection.

3.Biting habits

The biting behaviour of mosquitoes has shown that younger mosquitoes bite earlier during the evening and night as compared to older mosquitoes. Although this has not been demonstrated for *An. culicifacies*, it is likely to be of a similar nature. A late biting pattern implies that the human host will be less susceptible to mosquito bites as they will be less active later at night. The use of impregnated bed nets as a control measure will have a greater impact on transmission of falciparum malaria as the mosquitoes which are late biters will have less chance of transmitting the disease as more people will be protected. In fact, studies on the impact of impregnated bed nets on malaria incidence in areas where both *P.falciparum* and *P.vivax* exist have shown that the impact on the incidence of *P.falciparum* is much greater as compared to that of *P.vivax* confirming this hypothesis (6).

Host Factors

1. Immune response

The epidemiology of malaria in Sri Lanka can at best be described as unstable (7). In such a situation the exposure of the population to malaria is not as intense as in places such as tropical Africa and as a result the population is relatively non-immune. The majority of infections result in clinical disease and patients on the average seek treatment within 3-4 days of the onset of symptoms (8). Due to the early presentation of patients at health care facilities, only 4 percent of falciparum patients have gametocytes in the peripheral blood (9). It has also been shown that only about 8% of patients presenting with falciparum malaria are infective to mosquitoes (10). Hence, control measures based on early diagnosis and treatment will undoubtedly lead to a reduction in the transmission of the *P.falciparum.*

2. Asymptomatic states

P.falciparum is a parasite species that depends on the chronicity of its infection for transmission and probably depends on the induction of symptomatic chronic infections of a very mild degree for its propagation (11). It has been shown that for an infection to become subclinical, a previous infection with the same species is required within a short period of the current infection. If the incidence of malaria can be reduced by a significant amount in a very short period of time, then the potential of this group to contribute to the infectious reservoir of falciparum malaria that will be responsible for transmission will be minimal.

3. Knowledge of the community

The Sri Lankan population is relatively literate and our experience in the field suggests that almost all patients in malarious areas are aware of the importance of getting a blood smear examined in case of fever, the correct drug

regimen and methods of control. Besides, the role of the Ayurveda and traditional medicine in the treatment of malaria is limited and not very popular. These points should and can be exploited in great measure in a renewed effort to eliminate *P.falciparum* malaria from Sri Lanka.

Epidemiological Considerations

1. Incidence of falciparum malaria

The incidence of falciparum malaria for selected years is given in Table 1. The proportion of falciparum malaria of all malaria cases reported in the country has shown a gradual increase since the mid eighties. Based on the data in Table 1, it appears that this increase probably started in the early to mid seventies but was contained due to the introduction of malathion island wide in 1977. Even during the height of the '67/'68 malaria epidemic, the proportion of falciparum cases was less than 1% of all malaria cases (12). A possible reason for the gradual increase in the proportion of falciparum cases in Sri Lanka is the development of drug resistance, which was first reported in Sri Lanka in 1984 (13). The current percentage of falciparum malaria of all malaria cases which is approximately 30 percent is probably a reflection of the selective advantage of transmission of drug resistant strains of *P.falciparum* rather than improved conditions for malaria transmission.

Table 1: Malaria incidence in Sri Lanka in selected years

Year	Total No. of Malaria cases	No. of *Pf* Infections	Percentage of *Pf* Cases*
1970	468202	1613	0.34
1972	132604	3495	2.64
1974	315448	26207	8.31
1976	304487	18792	6.17
1978	69685	1876	2.69
1980	47949	1475	3.08
1982	38566	1599	4.15
1984	149470	3758	2.51
1985	117816	13057	11.08
1986	412521	84078	20.38
1988	383294	94239	24.59
1990	279172	57390	20.56
1992	399349	82655	20.70
1994	273502	47638	17.42
1996	184319	44957	24.39
1998	211691	42396	20.03

Source: Anti-Malaria Campaign, Sri Lanka
* Microscopically confirmed cases

If the percentage of falciparum cases has increased due to more favourable conditions for malaria transmission, then a similar pattern should also be seen for *P.vivax*, which has a greater propensity for transmission.

2. Drug Resistance

Drug resistant strains of *P.falciparum* have a selective advantage in malaria transmission (14). The possible mechanisms include presentation of patients with atypical symptoms, which mislead clinicians or the patients. Some patients do not have parasites in the peripheral blood film when the parasitaemia is very low. Ironically, patients with late recrudescent infections due to RI drug resistance are the most effective transmitters of drug resistant strains as they are undetected for a longer period of time while carrying gametocytes. Patients with RII and RIII resistance are likely to come earlier for re-treatment and be cleared of gametocytes. As already stated earlier drug resistance is a probable cause of the increase in the proportion of falciparum malaria. The use of an effective drug either alone or in combination should drastically reduce the transmission of falciparum malaria.

3. Effective chemotherapy

During epidemics we have observed that the incidence of *P. falciparum* is higher than *P. vivax* initially. As effective treatment is administered, there is a significant drop in the incidence of *P.falciparum*. However, the decline in the incidence of *P.vivax* is not so marked probably due to relapses. It has been shown that the proper management of foci of drug resistant infections with effective second line drugs results in a significant decrease in the incidence of *P.falciparum* infections. Gunawardena has shown that the introduction of sulphadoxine/pyremathamine, a second line antimalarial, in the Kataragama area resulted in a decrease in the percentage of *P.falciparum* infections with gametocytes from 53.5 % to 22.1% (15). These findings demonstrate that the use of effective chemotherapy will significantly reduce the incidence of *P.falciparum* infections.

4. Low mortality

Mortality from *P.falciparum* in Sri Lanka is extremely low as compared to other countries in the region with similar epidemiological characteristics. The main reason for the low mortality in Sri Lanka is a literate population and early diagnosis and treatment provided by the extensive network of health care institutions in the malaria endemic areas of the country. In

addition, absence of multi-drug resistance and relatively good drug compliance has contributed to the low mortality.

5. Environmental considerations

Environmental factors play a major role in malaria transmission. Of the environmental factors, the most important are rainfall, humidity and temperature. Excessive rainfall or the lack of it may precipitate a malaria epidemic by increasing vector density. Humidity is closely associated with rainfall and affects the longevity of the mosquito, a high humidity favouring a greater survival. Temperature affects both the longevity of the mosquito and the duration of the sporogonic cycle of the parasite in the mosquito. These factors have not changed significantly in Sri Lanka in the past 30 - 40 years to provide a more favourable environment for transmission of malaria. If this were not the case, a similar increase should also have been observed for vivax malaria.

6. Vectorial capacity

The vectorial capacity is a measure of malaria transmission and gives the number of new infective bites a mosquito will make given that it has taken an infectious bite from a person having gametocytes. In Sri Lanka, the vectorial capacity has been estimated to be in the range of 0.3 to 0.4 (16). This implies that at least 3 to 4 mosquitoes have to bite an individual for malaria to be transmitted. It also implies that malaria transmission is maintained by vector density and man-vector contact. This fact is confirmed by the dramatic reduction of malaria transmission evidenced by the decline in the incidence of malaria during the malaria eradication era in Sri Lanka where blanket house spraying with DDT was carried out (12). In tropical Africa especially South of the Sahara, the vectorial capacity is high which is one reason why eradication was never attempted. If vector density and / or man-vector contact can be reduced,. a substantial reduction in the incidence of malaria can be expected.

7. Surveillance

Surveillance is one of the most important facets in the elimination of disease. The surveillance system for malaria (a vestige of the eradication era) is an excellent one. Although it is primarily geared towards monitoring programme performance and being reactive rather than proactive, the changes that have been recommended and the computerization of data that is expected in the near future, will make it a vital tool in the quest for elimination of *P.falciparum* transmission in Sri Lanka.

8. Infrastructure

A legacy of the malaria eradication era was the establishment of a sound and extensive network for malaria control. The infrastructure for malaria control in Sri Lanka is well established, organized and widespread. It does not lack in human resources at the managerial level as it is administered by qualified and experienced staff. There are a few constraints such as operational limitations that need to be addressed which do not appear to be major obstacles in the quest for elimination of *P.falciparum*.

9. New Control Methods

In the past decade three new developments have revolutionized malaria control worldwide, namely, the use of insecticide treated nets, development of Rapid Diagnostic Tests (RDTs) for the diagnosis of malaria and development of artemisinin derivatives for the treatment of malaria.

a. Insecticide Treated Nets (ITNs) or Bed Nets

The use of insecticide treated nets has been shown to be effective in reducing both the morbidity and mortality due to malaria. This is an excellent control strategy for high risk groups in communities where access is not easy and where the health infrastructure is not well developed.

b. Rapid Diagnostic Tests

Rapid Diagnostic Tests originally developed for only *P.falciparum* have now incorporated *P.vivax* as well. These tests, though more expensive than traditional microscopy and have certain limitations, are easier to perform and probably excludes possible human error that is associated with microscopy. These tests can easily be used in areas where health infrastructure is not well developed.

c. Artemisinin Derivatives

The development of artemisinin derivatives revolutionized treatment of malaria being the only choice for multi-drug resistant malaria. Artemisinin derivatives have a short half life and are effective in rapidly reducing the parasite load and temperature of malaria patients (17). Today, these drugs are used in combination with traditional first and second line drugs to delay the development of resistance of first and second

line drugs. Combination therapy is recommended with the introduction of second line antimalarials as a first line measure. In Sri Lanka, it will only be a matter of time before it is introduced. In order to reap the maximum benefits of the expected change in drug policy for treatment a vision of the elimination of falciparum malaria is essential to enable the country to afford this change.

Other Considerations

1. Improvement of social standards

Malaria in Sri Lanka is primarily a disease of the rural poor. It has been shown that people living in poorly constructed houses are at a higher risk of developing malaria (18, 19). The construction of these houses itself has been shown to favour the resting mosquitoes and reduce the effectiveness of indoor residual spraying. Poor communities also find it more difficult to adopt personal protection measures such as use of repellents for control and bed nets are costly. With urbanization and improvement of living standards of the population a reduction in malaria transmission is expected.

2. Experiences of other countries

If we look at countries in the tropics which have successfully eradicated malaria such as Taiwan, Singapore, the Caribbean countries and the Maldives, all these countries have been islands. Other countries in the temperate zones which have eliminated malaria have been countries where malaria transmission was seasonal. Although Sri Lanka is a tropical country with perennial transmission, the geographic features of being an island makes elimination not impossible.

3. Information Technology

The rapid development and expansion of information technology and use of new tools such as GIS have opened new vistas for public health. These tools have a wide array of applications which range from forecasting and early detection of epidemics to targeting control measures in a more cost effective manner. Currently the national malaria control programme has embarked on a project to use these tools for its routine surveillance which would make malaria control more effective and efficient.

4. Roll Back Malaria Initiative (RBM)

The Roll Back Malaria Initiative of the World Health Organisation which commenced in 1999 is a renewed effort with novel strategies to combat malaria (20). Important features of RBM include use of evidence-based multiple prevention strategies revolving around sustainable partnerships. Sri Lanka is way ahead in the RBMI as compared to other countries in the region. The launch of this initiative is expected to reduce malaria morbidity by as much as 50% by the end of 2004.

Interruption of transmission and elimination of *P.falciparum* from any country requires a massive control effort that should be extensive and highly focussed in the short term and sustained in the long term. It requires complete dedication from a committed team. At the present time, elimination of *P.falciparum* looks promising given the renewed initiative on malaria control launched by the World Health Organization and the fact that new strategies will be adopted by the malaria control programme in Sri Lanka. The three major developments with regard to malaria diagnosis, treatment and control in the last decade, namely rapid diagnostic tests, artemisinin and bed nets, if used judiciously, will complement each other in the control effort. These strategies have still not been used extensively as major control startegies in Sri Lanka. Of these, bed nets and rapid diagnostic tests have been used on a limited scale. Artemisinin is still to be registered in Sri Lanka. However, it will only be a matter of time before it is evaluated, as current strategy in countries which use it is to combine it with current second line drugs, if the current first line treatment is ineffective. Rapid diagnostic tests though relatively costly at the moment will probably become cheaper with time. International and bilateral donor agencies should be able to provide assistance initially. This will probably be an important diagnostic method in communities that have limited access to health care.

We have intentionally omitted reviewing the case of vaccines in the equation as an effective and safe vaccine that can be used in the field is currently not available. However, the emergence of an effective and safe vaccine will dramatically affect the equilibrium, tilting the balance definitely in favour of elimination. The potential use of a vaccine in, and its contribution to, the elimination of falciparum malaria from Sri Lanka should not be overlooked at this point in time.

For an elimination programme to be effective, there should be no obstacles in the implementation of the programme. The ongoing terrorist war will probably be the biggest obstacle. In 1998, more than 50% of malaria cases were reported from three districts in the North that are affected by the war, namely, Jaffna, Kilinochchi and Mullaitivu. Nevertheless, the objective of elimination of *P.falciparum* should not be discarded at least for the rest of the country. Should the war end early, elimination should be the only concern.

It may be argued that if an effort is made for elimination of *P. falciparum* why should the efforts not be extended to *P.vivax* as well. From the points that have been raised in this article it is clear that elimination of *P.vivax* is more difficult and complex. For example, given the existing infrastructure where malaria cases are diagnosed by activated passive case detection, by the time a vivax malaria case is diagnosed (s)he may already have infected a mosquito which may transmit the disease to a healthy person. Latent liver forms of *P.vivax* will give rise to relapses and initiate more infections in the community. Given these negative characteristics of *P.vivax* infections for elimination, it will be more productive if elimination of *P.falciparum* infections is prioritized as it is the species that causes more severe disease which may be fatal. It is also the species that is currently posing more problems and will continue to do so in the future too due to rapid spread of drug resistance.

The benefits of elimination of *P.falciparum* infection will be numerous. An important source of morbidity in Sri Lanka will be eliminated. The impact of this programme will trickle down to *P.*vivax infections as well and will result in a further reduction of morbidity. The impact on communities living in malaria endemic areas will be immense not only in terms of reduction of morbidity and mortality but also in economic terms. Although not a major objective, the programme itself may precipitate the development of the health infrastructure in rural areas which will have a significant impact on the well being of the community. The acceptance of this challenge by public health officials and its successful completion will be a tremendous boost to public health in this country and would be another laudable landmark in the annals of the history of public health in Sri Lanka.

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