

# SURVEILLANCE OF RISK FACTORS FROM IMPORTED CASES OF FALCIPARUM MALARIA IN SICHUAN, CHINA

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**Abstract.** With a sharp increase of the number of imported cases of falciparum malaria, the potential risk of the reemergent transmission of this kind of malaria is approaching imminently in Sichuan Province, China, where falciparum malaria had completely been eliminated by the 1960s. It has been of concern whether the epidemic would appear again, because there still exist malaria vectors and vulnerable populations in Sichuan. By undertaking surveillance on 31 cases returning from the endemic areas with falciparum malaria, and on their family members and neighbors, we have not found out any introduced case of falciparum malaria who was contracted from the imported ones. The vector monitoring results suggested that the use of insecticide-impregnated bednets interfered with malaria vectorial capacity and expectation of infective life. The epidemiological characteristics of the imported cases and reasons why no consequent malaria case was detected were analysed at dynastic level in detail.

## INTRODUCTION

By the 1960s, native falciparum malaria had completely been eliminated in Sichuan. Since then, through undertaking long-term surveillance on the population, we have not found out any indigenous falciparum malaria case yet. However, with rapid development of the social economy and opening to the outside world in the recent two decades, there have been a great number of floating people going out and coming in, some of whom were infected with malaria and became the cases or carriers. In this way, it is hardly avoided malaria parasites to hypoendemic areas by the travel of the population. At the same time, following these person's movement, malaria vectors may also emigrate and colonize some new areas. Most floating people who go to hyperendemic areas have taken no effective preventive measures (WHO, 1984; Steffen *et al.*, 1987). All these factors mentioned above are no doubt quickening the speed as well as widening the scale of malaria resumption in the areas where malaria has been completely eliminated or has been under control. So imported malaria more and more poses a public health problem. WHO (1984) regularly publishes manuals to warn travellers or other floating populations against malaria infection. Sichuan was once an endemic area of falciparum malaria, and still has suitable transmission conditions now. Since

1980, imported cases of falciparum malaria have increasingly been detected and reported, especially in recent years (Xiao *et al.*, 1994). Whether the resurgence of falciparum malaria will happen due to the imported cases has been paid high attention. To master the action regularity of the imported cases and to seek for some effective control strategies for potential risk factors of falciparum malaria infection, this project related to surveillance and management of imported malaria cases was carried out.

## MATERIALS AND METHODS

### Case selection and surveillance

Whoever returned from the endemic areas with falciparum malaria at home and abroad was investigated. House visits were conducted one by one to record general information, working and living conditions, malaria infection history, disease course and treatment status, and to collect blood samples for examination. The clinical recordings of their treatment were collected at local medical facilities as well. The criteria of cases used were: 1) with typical clinical symptoms and the parasites detected positive in blood film; 2) without clinical symptoms but the parasites positive on blood examination. All the cases identified were then admitted to hospital for a detailed health examination, close observation and timely treatment if possible. During the observation, when their health conditions were permissible, they were checked by the standard *in vivo* drug-susceptibility test (Chinese Ministry of Public Health, 1998) under a close supervision in hospital to as-

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certain the drug-resistant status of *Plasmodium falciparum* strains being carried by them to chloroquine (China Ministry of Public Health, 1988).

#### Focus selection and survey

Each focus in which an imported malaria case was found was subjected to survey. At those foci, besides the case investigation, their family members and neighbors were also subjected to epidemiological study and blood examination to find whether there was any consequentially introduced case.

#### Vector observation

One focus at Yibin was selected to monitor malaria vectors, where two imported falciparum malaria cases were detected and reported in 1995. The following observations were made: 1) *Anopheles* density in human dwellings: 50 bednets in a natural village with an identified imported case were selected. All *Anopheles* species in these bednets were collected during 08.00-10.00 hours. 2) *Anopheles* density in cattle sheds: all species of *Anopheles* in two cattle sheds were caught in 30 minutes during 08.00-10.00 hours. 3) Man-biting rate: all species of *Anopheles* in 50 bednets were collected during 04.30-05.30 hours. Man-biting rate was calculated by the formula: No. mosquito with newly-ingested blood/No. persons sleeping in nets. At the same time, the rate by the overnight man-bait inducing method was also done for comparison (Liu *et al*, 1986; Xue *et al*, 1995). 4) Human blood index: at the same village, all female *Anopheles* with newly-ingested blood were collected in human dwellings and cattle sheds in the early morning in July of 1995 to make blood filter samples of *Anopheles* stomach contents and then to identify the source of the blood. 5) Parous rate: dissecting all collected female *Anopheles* in human dwellings and livestock sheds, and identify the parous female mosquitos.

## RESULTS

#### Case surveillance

During 1993 - 1997, about 15 - 35 imported cases of falciparum malaria were officially reported in Sichuan every year. As these cases moved in and out irregularly and lived scatteredly in rural areas over the whole province, and many of them had been cured before the reports were received, finally a total of only 31 cases were surveyed, among whom 29 persons were the cases infected with falciparum malaria (including 1 mixed infection of falciparum

and vivax malaria), 1 quartan malaria and 1 vivax malaria case. All of the cases were male workers, average age of 31.4 (19-61 years old). The areas which they went to and returned from were mainly in Hainan and Yunnan, China, Africa and Southeast Asia. At working spots, they slept in crowded, simple rooms without bednet or any effective mosquito-proof device. Their hometown-return date was mostly in January (43.1%), May (25.8%) and August (22.6%), owing to diseases, agricultural activities or festivals. Most of them went to see doctor due to the symptoms of shivering, fever, headache or anemia. At the clinic, they were mostly diagnosed in error as other diseases such as heavy cold, hepatitis and septicemia at their first visit. Of the surveyed cases, 5 persons died of cerebral malaria due to delayed clinic-visits or treatment, but the others survived on timely diagnosis and treatment. At the duration of observation in hospital, 19 cases with relatively good health were given the *in vivo* drug-susceptibility test. The results showed that *Plasmodium falciparum* strains from 12 cases had resistance to chloroquine, accounting for 63.2% (12/19), 5 RII, 1 with RIII resistance.

#### Epidemic focus investigation

A total population of 524 were given detailed interviews, blood examinations and follow-up visits in the transmission seasons. Fortunately, no case of locally acquired falciparum malaria has yet been recorded.

#### Vector monitoring

The survey results of vector densities showed that only *An. anthropophagus* and *An. sinensis* were caught at the village of Yibin County, and *An. anthropophagus* was predominant in human dwellings but *An. sinensis* was predominant in cattle sheds (Tables 1, 2).

Based on the number of mosquitos caught at human dwellings in the morning, the average man-biting rates were *An. anthropophagus* 0.88 and *An. sinensis* 0.13 respectively. However, the man-biting rates obtained by the overnight man-bait inducing method were 15.00 and 3.67. The ratio of the man-biting rates of *An. anthropophagus* and *An. sinensis* was 2.08:1 by the latter method. To take into consideration of outdoor-flying behavior of *An. sinensis* in the early morning, this ratio was used to revise the former man-biting rate of *An. sinensis*. The revised rate was 0.42 (0.88 x 1/2.08).

**Human blood index and man-biting habit:** the stomach blood filter samples of *An. anthropophagus*

Table 1  
Vector density in human dwellings in Yibin County in 1995  
(No. mosq/net).

Date (MM)	No. <i>Anopheles</i>	Density	<i>An. anthropophagus</i>		<i>An. sinensis</i>	
			No (density)	No (density)	No (density)	No (density)
05	51	1.02	37 (0.74)		14 (0.28)	
06	74	1.48	50 (1.00)		24 (0.48)	
07	81	1.62	49 (0.98)		32 (0.64)	
08	81	1.62	63 (1.26)		18 (0.36)	
09	8	0.16	6 (0.12)		2 (0.04)	
10	6	0.12	5 (0.10)		1 (0.02)	

Table 2  
Vector density at cattle sheds in Yibin County in 1995  
(No. mosq/person/hour).

Date (MM)	No. <i>Anopheles</i>	Density	<i>An. anthropophagus</i>		<i>An. sinensis</i>	
			No (density)	No (density)	No (density)	No (density)
05	157	314	49 (98)		108 (216)	
06	263	526	71 (142)		192 (384)	
07	387	774	81 (162)		306 (612)	
08	178	356	65 (130)		113 (226)	
09	97	194	53 (106)		44 (88)	
10	74	148	43 (86)		31 (62)	

101 and *An. sinensis* 315 were collected at both human dwellings and livestock sheds. The index were *An. anthropophagus* 0.84, *An. sinensis* 0.055 respectively. It was estimated that the gonotrophic cycle of both anopheles species were 2.5 days. So the calculated man-biting habit was *An. anthropophagus* 0.336 and *An. sinensis* 0.022.

**Parous ratio:** by dissecting the female anopheles of *An. anthropophagus* 109 and *An. sinensis* 125, the parous ratios were 0.68 and 0.62 respectively. Based on the results above, the vectorial capacities of two vectors were calculated and were shown in Table 3.

The results listed in Table 3 indicate that the vectorial capacity, mean expectation of life and expectation of infective life of both *Anopheles* species in this survey were all lower than those reported by Liu *et al* (1986).

## DISCUSSION

For the imported cases of malaria, a special group of the population, can cause the reemergence of malaria transmission in the non-endemic or hypoendemic areas and the spread of drug-resistant

*Plasmodium* strains. It is very difficult to know the cases' moving schedule and to give them timely diagnosis and treatment. In addition, the typical symptoms of malaria infection were often hidden because patients used some drugs to control this disease unknown for themselves. On the other hand, as there has been no falciparum malaria transmission in Sichuan for more than 30 years, clinicians lack adequate attention and have very poor experience of detection and treatment, especially the cure of drug-resistant strains of *Plasmodium falciparum*. These factors interfered with timely treatment and could easily bring about introduced transmission. So it is necessary to ascertain risk factors and to carry out health education for imported malaria cases.

This investigation showed that 31 cases were all men working in the endemic areas with falciparum malaria, and most of them were farmers, whose hometowns were in the rural areas with poor economic and transportation status. At their first time of clinic consultation, they all were diagnosed in error as heavy cold, hepatitis or septicemia. In particular, 5 cases eventually died of cerebral malaria due to either error diagnosis or unsuitable antimalarial treatment. Although no introduced case has been detected yet, it is still worrying fact that 31 cases

Table 3  
The vectorial capacity of two *Anopheles* species at Yibin in 1995.

Species	Man-biting rate (ma)	Man-biting habit (a)	Daily-survival rate (p)	MEL (day)	EIL (day)	Vectorial capacity (Vc)
<i>An. anthropophagus</i>	0.88 (0.91)	0.336 (0.330)	0.86 (0.88)	6.6 (7.8)	1.5 (2.2)	0.434 (0.654)
<i>An. sinensis</i>	0.42 (0.41)	0.022 (0.021)	0.83 (0.88)	5.4 (7.8)	0.8 (2.2)	0.008 (0.091)

MEL: mean expectation of life

EIL: expectation of infective life

$Vc=ma*a*p/Lnp$

n: sporoponic cycle in *P. falciparum* =10 days the same as that in *P. vivax*

The figures in ( ) stand for the calculated survey results by Liu *et al* (1986).

surveyed were all found at the distribution areas of *An. anthropophagus*, while, according to the vector-monitoring results done at Yibin by Liu *et al* (1986, 1990), *An. anthropophagus* is a highly competent vector with a high natural infection rate and with high sensibility to both *Plasmodium vivax* and *P. falciparum*; moreover the vectorial competence of *An. anthropophagus* was 20 times as high as that of *An. sinensis* (Liu *et al*, 1990; Nie *et al*, 1996). Sichuan has been the endemic areas of vivax malaria, and used to have epidemic falciparum malaria historically. The distribution and the density of *An. anthropophagus* in Sichuan is the widest and highest in China. In Sichuan such an area is suitable for falciparum malaria transmission so there has been concern why there is no introduced spread. From the case surveillance, epidemic focus survey, and vector observations done in Yibin, the results suggested that the following factors may exert some active effect on suppressing the introduced transmission: 1) the damage of primaquine to the gametocyte: when caught with malaria and appeared some malaria or malaria-like symptoms at the hyperendemic areas, the cases are usually given a course of antimalarials, chloroquine plus primaquine. Primaquine can impair the development of gametocytes. In this survey, 21 cases, accounting for 67.4%, once received this measure for treatment; 2) timely in-patient cure and focus management: because of the aggravating health status and high attention to the danger of falciparum malaria, 19.4% of cases (6/31) rapidly went to see doctor and left for hospital as soon as they were back home. In addition, the timely preventive measures at epidemic foci were taken owing to high attention to the death caused by this kind of malaria; 3) Insecticide influence: since 1987, the malaria and mosquito control strategy by using insecticide-impregnated bednets have

successfully been applied on a large scale in Sichuan (Chen *et al*, 1995); and following the situation of improved economic conditions and annual income, the usage of agricultural insecticides also increased to control pests. So it is very impressive that the population and longevity of *Anopheles* species decreased in particular *An. anthropophagus* which is highly sensitive to insecticides. Up to now, no insecticide-resistant *Anopheles* species was found and reported in Sichuan. The survey results at Yibin showed that the vector capacity and the expectation of infective life reduced in recent years, compared with the results of Liu *et al* in 1986. Another reason, of course, is that many cases, about 43.1%, returned home in uninfected seasons. All the factors mentioned have some important effect on the transmission. On the other hand, based on the investigations by Lu *et al* (1993) and Liu *et al* (1986), the subspecies of *Anopheles* indeed exist, and they also seem to be different in the sensibility to *Plasmodium vivax* and *P. falciparum*. It still remains to ascertain whether the subspecies of *An. anthropophagus* in Sichuan are distinct from those in other areas of China. Epidemic falciparum malaria in Sichuan once occurred in history, but the relationship between the transmission and the vector role of *An. anthropophagus* was not studied in detail; nor whether *An. anthropophagus* gradually changed its characteristics as a *Plasmodium falciparum*-specific vector following long-term evolution and environmental pressure is still an interesting topic.

In China, drug-resistant *Plasmodium falciparum* strains to chloroquine were firstly found and reported in Gengma County of Yunnan Province, China in 1973. After that, the strains with higher degrees of the drug-resistance were detected in Hainan Province. At present, the source of imported malaria in

Sichuan is mainly from Yunnan of China, Africa and Southeast Asia. At this field surveillance of drug-resistance of malaria, we originally planned to use the method of micro-test *in vitro*, because this test is accurate. Status of the patient does not exert an obvious effect on the result of the test. But the *in vitro* method requires that the targets tested should not take any antimalarial in 14 days. In fact, most imported cases surveyed in field, however, had taken some sort of antimalarials within 14 days. So it was inappropriate to monitor the resistance by this method. The *in vivo* method is simple and practical. In this survey, there were 12 cases, accounting for 63.2% (12/19), found with resistance, 6 cases having more than I-degree resistance. The results indicated that the spread of the drug-resistant strains was being expedited. This phenomenon needs attention, because Sichuan Province belongs to the endemic area of only vivax malaria, and chloroquine is effectively used over the whole province. Therefore, it is a crucial point to detect timely identify the species exactly and cure correctly. According to our clinical experience, as soon as an exact diagnosis has been made, it is strongly recommended that artemisinin be chosen for the treatment so as to avoid delaying chemotherapy, as the cases' health status was quickly changeable. Moreover it is also necessary to observe closely the change of symptom control, parasitic stages and parasitemia during chemotherapy.

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