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Analysis of Malaria Epidemiological Characteristics in the People's Republic of China, 2004–2013

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Abstract. This study aims to explore and characterize the malaria-endemic situation and trends from 2004 to 2013, to provide useful evidence for subsequently more effective strategic planning of malaria elimination in China. A total of 256,179 confirmed malaria cases were recorded in this period, and 86.8% of them were reported during 2004–2008. Between 2004 and 2008, *Plasmodium vivax* was the major species (72.2%) of malaria parasite. Most cases (67.3%) were found in male, and mainly in the age group of 35–39 years. A total of 236 deaths resulting from malaria were reported and nearly half (45.3%) of them were in Yunnan province. In all, 204,760 local malaria (79.9%) and 51,419 imported malaria (20.1%) were observed during 2004–2013. However, afterward the proportion of imported malaria continuously increased from 2004 (16.2%) to 2013 (97.9%). Moreover, 9,285 imported malaria cases were recorded during 2011–2013 in China, of which 5,976 cases (64.4%) came back from Africa. Overall, China has made achievements in controlling malaria, the locally transmitted malaria significantly declined in the past decades, by which the incidence has achieved historically the lowest levels. On the other hand, imported malaria has increasingly become a severe threat to malaria elimination. Therefore, to prevent the reintroduction of malaria, surveillance systems need to be well planned and managed to ensure timely case detection and prompt response at the elimination stage.

INTRODUCTION

Malaria is caused by one or more of the five species of *Plasmodium* via the bite of positive female *Anopheles* mosquitoes. An estimated 198 million confirmed cases and 584,000 deaths were reported from 97 countries and territories in 2013. Most deaths (78.0%) were reported in children under 5 years of age.[1] However, China has made obvious achievements in controlling the locally transmitted malaria over the past decades and the incidence has been down to historically low levels in 2009.[2] Since 2010, China has initiated the National Malaria Elimination Action Plan, which aims to eliminate indigenous malaria except for border areas by 2015 and completely eliminate it nationwide by 2020.[3] In line with the goal, the strategy and interventions should be adjusted and transited from control to elimination, based on the better understanding of malaria status. At present, the local malaria cases are only reported in two regions, the counties along the border of China–Myanmar, and one county of Tibetan Autonomous Region of China. On the other hand, the proportion of imported malaria is increasing in recent years, and has become a great challenge to the public health in China.[4] For example, despite a 89.4% decrease in the total malaria cases reported from 2004 (N = 38,972) to 2013 (N = 4,128), the proportion of imported malaria was significantly increased from 16.2% to 97.9% in contrast.[5] Moreover, the imported malaria has brought out the high risks to the malaria-free localities where *Anopheles* mosquitoes still exist. The objective of this study was to characterize the situation and trends of malaria from 2004 to 2013, which was a very important transition period from control to elimination phase in China, to provide useful data to support the adjustment of appropriate strategies and interventions toward the malaria elimination goal in China.

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MATERIALS AND METHODS

Data collection. A retrospective study was conducted to explore malaria-endemic characteristics of year 2004–2013 in China. All individual cases from the Web-Based Reporting System (WBRS) were carefully reviewed and analyzed. The data were selected by onset of date, reporting area, and final confirmation, but the data from Hong Kong, Macao, and Taiwan were not included for this statistics. The WBRS parameters consist of species composition, geographical distribution, gender and age distribution of cases, and death numbers. Clinically diagnosed cases were defined as a patient with malaria-like symptoms but no parasites detected in blood examination, and the laboratory-confirmed cases were those defined by using any of the laboratory tests including polymerase chain reaction (PCR), rapid diagnostic tests (RDTs), and microscopy examination. Both of these cases were included in this analysis. For total number of the cases consisting of local infections and imported malaria cases, these data were obtained from another system, the Annual Reporting System (ARS). In China, any cases defined as imported malaria must meet all of the following criteria: 1) the patient was given a diagnosis of malaria; 2) the patient had a travel history to malaria-endemic areas outside China during malaria transmission season; and 3) the onset time was less than 1 month after returning to China during the local transmission season. This definition is based on the reasonable latent period for all *Plasmodium* species reported in China.

Statistical analysis. A descriptive analysis was processed using Microsoft Excel and SAS software (Version 9.2; SAS Institute Inc., Cary, NC). The χ^2 test was used to assess differences, the P value < 0.05 was considered statistically significant. The distribution maps of imported malaria in 2004 and 2013 were created by ArcGIS 10.1 (Environmental Systems Research Institute, Inc., Redlands, CA).

RESULTS

A total of 256,179 malaria cases were recorded by WBRS during 2004–2013, of which 222,490, accounting for 86.8% of all cases, were reported from 2004 to 2008.[5–13] During this

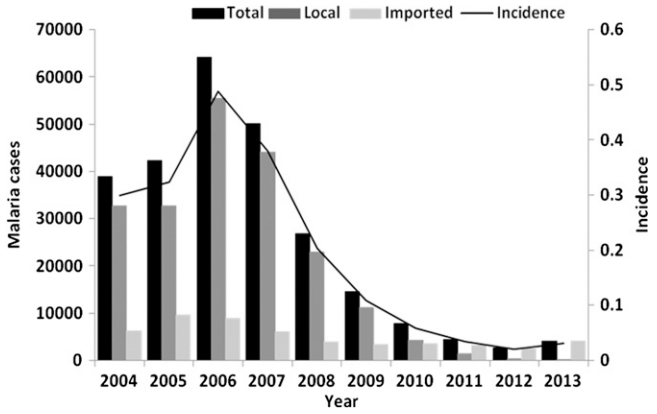

FIGURE 1. Malaria prevalence in China, 2004–2013. The columns of different colors show the change trend of total cases (black), local cases (gray), and imported from other countries (hoary). The black line indicated the malaria incidence during 2004–2013.

period, the reported malaria cases reached to peak in 2006 (N = 60,193) with the highest incidence (0.49/10,000) (Figure 1), and these cases were particularly focused in central China along Huai River covering Anhui (58.1%), Henan (8.4%), Hubei (2.9%), and Jiangsu provinces (1.1%).[14] The malaria outbreak of central China contributed significantly to nationwide malaria resurgence, and the main reason was due to the accumulation of residual loci, in which *P. vivax* was the predominant species (72.2%). Also the WBRS reported that the ratio of *P. vivax* to *P. falciparum* cases was 10.4 to 1 from 2004 to 2013 (Figure 2).

To solve the problem, China had adopted integrated control and prevention interventions. The malaria cases in Anhui, Henan, Hubei, and Jiangsu were 8,627 in 2009, which was decreased by 79.8% when compared with 2006 cases (N = 42,626). Because of this, the whole reported cases in China with a 76.6% decrease was noted from 2006 (N = 60,193) to 2009 (N = 14,098), of which local transmission was 79.9% decrease from 2006 (N = 55,335) to 2009 (N = 11,119). However, since 2007, the proportion of imported cases have begun increasing due to the more and more Chinese workers going and coming back from abroad. According to the data by National Bureau of Statistics of China, the number of migrant workers was 255,674 in 2013, which was a 47.8% increase compared with that in 2004 (173,000). In contrast to sharply decline of local malaria, the imported malaria accounted for 16.2% of total cases in 2004, whereas in 2012, the proportion increased to 91.0%. In 2013, because of the clustered migrant workers coming back from Ghana to Shanglin County of Guangxi Zhuang Autonomous Region, the imported malaria cases rose significantly, contributing greatly to the nationwide reported malaria numbers that year.

Regarding the spatial distribution of *Plasmodium* species during 2004–2013, most provinces had a higher proportion of *P. vivax* except in Guangxi where *P. falciparum* was the predominant species (*P. vivax* to *P. falciparum* = 1:2.1). This was because of the large number of migrant workers coming back from Ghana in 2013, and 88.2% of whom (N = 1,104) were infected with *P. falciparum* in Guangxi.

Malaria cases occurred in 67.3% males and 32.7% females with similar distribution for all age groups. The highest malaria cases were observed in the age group of 35–39 years, in 71.4% males and 28.6% females (Figure 3).

In addition, WBRS had reported 79,728 clinically diagnosed (31.1%) and 176,451 laboratory-confirmed cases (68.9%) from 2004 to 2013. The proportion of clinically diagnosed cases had been decreased since 2006, and in 2013, it was only 1.0% of the whole malaria cases.

Source of infection. The data from ARS of 2004–2013 indicated 204,760 local malaria (79.9%) and 51,419 imported malaria (20.1%) cases. During this period, the local transmission was sharply decreased by 99.7% from 2004 (N = 32,678) to 2013 (N = 85). The total local cases were mainly reported in Anhui (N = 108,482; 53.0%), Yunnan (N = 33,553; 16.4%), and Hainan (N = 23,742; 11.6%). At present, the local vivax malaria in China was mainly reported in two regions, the counties along the border of China–Myanmar and Motuo County of Tibetan Autonomous Region, while the local

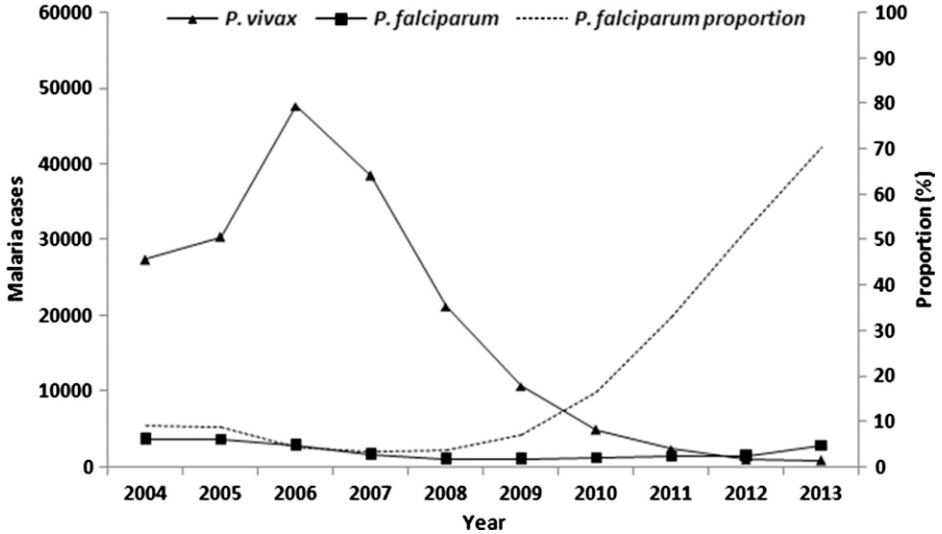

FIGURE 2. Trend of *Plasmodium vivax* and *P. falciparum*, China, 2004–2013. The lines of different shapes show the change trend of *P. vivax* (triangle) and *P. falciparum* (square). The dash line represents the proportion of *P. falciparum* in the total cases.

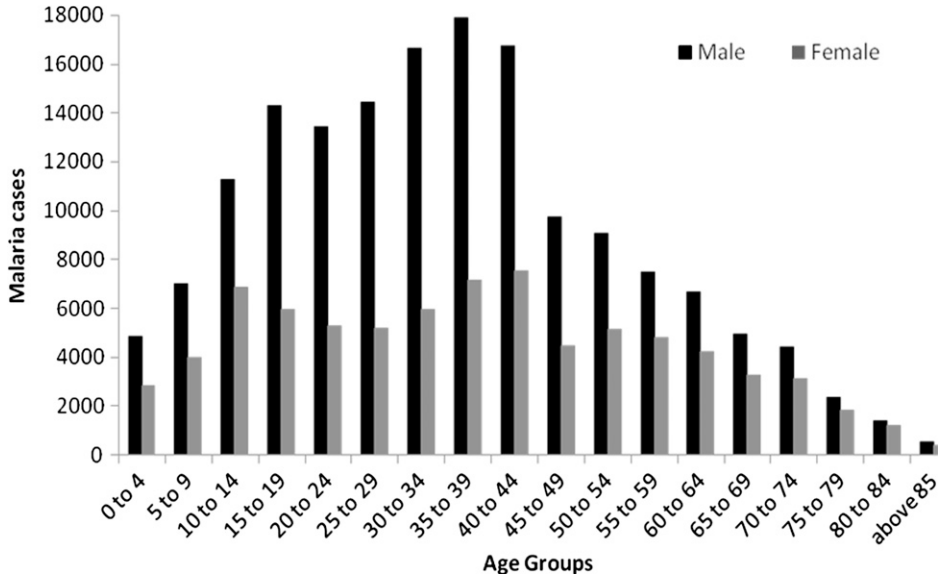

FIGURE 3. Malaria cases by gender and age, China, 2004–2013.

P. falciparum only occurred in the border counties of Yunnan province.

Contrary to the decreasing local transmission, the proportion of imported malaria has significantly increased in the recent years. For instance, the proportion of imported malaria continuously increased from 2004 (16.2%) to 2012 (91.0%), and in 2013, it was as high as 97.9% ($P < 0.05$). Further, the distribution of imported malaria has become wider, only 22 provinces in 2004 but extending to 30 provinces even to the western and northern China in 2013, where most have been nonendemic areas and no imported malaria was reported before (Figure 4). The imported malaria cases had been reported in 651 counties of 23 provinces (2010), 760 counties of 26 provinces (2011), 598 counties of 29 provinces (2012) and 607 counties of 30 provinces (2013), respectively.[15] This may bring out the high risks to the malaria-free

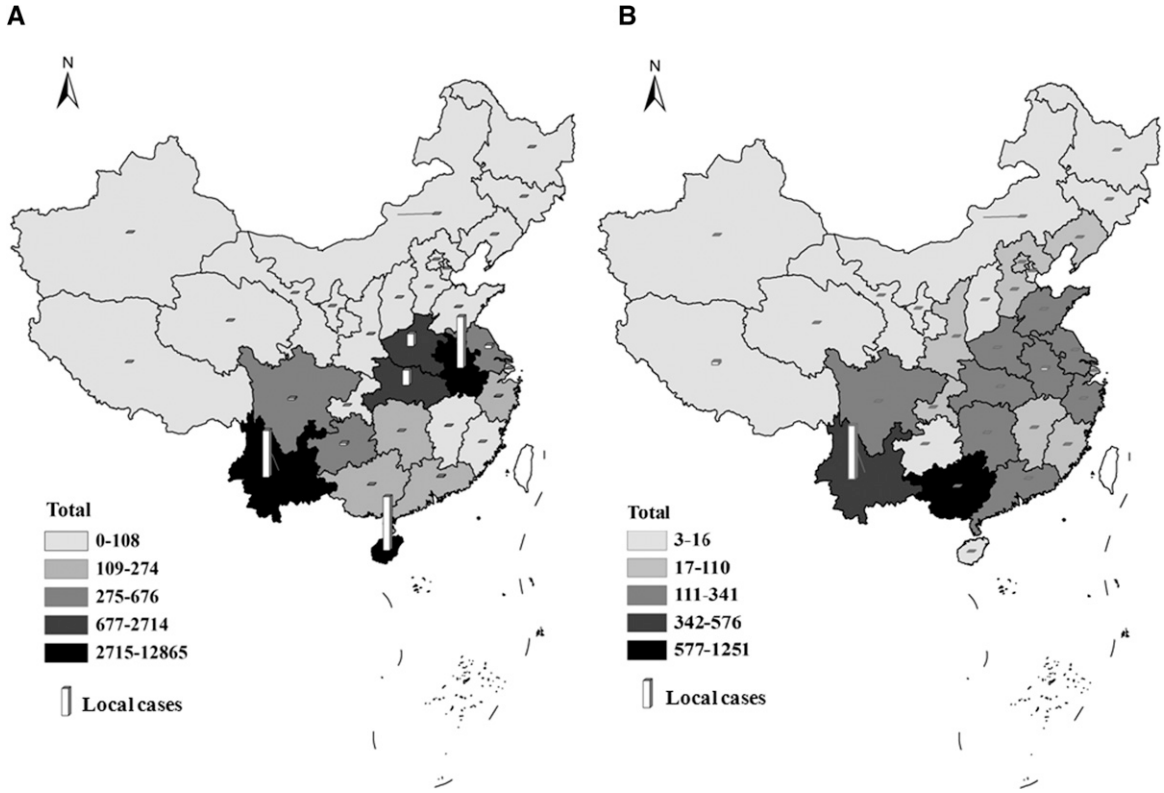

FIGURE 4. Distribution of malaria, China, in 2004 (**A**) and 2013 (**B**). Map was created by ArcGIS 10.1. The numbers following by the different color of squares indicate the reported case number ranges. Local cases were indicated with white columns in the map for each year.

localities, in which *Anopheles* mosquitoes are prevalent as usual during the transmission season. The importation of the malaria cases has become a great challenge to the national malaria elimination.

Considering the origin of the infection regions, among the WBRS-recorded 9,285 imported malaria cases during 2011–2013 in China, 5,976 cases (64.4%) were from Africa. Only in 2013, there were 3,167 imported cases from Africa, which was 134.4% more than that in 2011 (N = 1,351; $P < 0.05$). The increasing cases mainly came from west and central Africa, including Ghana (N = 1,660; 17.9%), Angola (N = 843, 9.1%), and Equatorial Guinea (N = 720; 7.8%) (Supplemental Table 1).

Simultaneously, the imported cases from another major infection source, the southeast Asia, were declined gradually. A total of 2,965 cases (31.9%) were reported in the recent 3 years and a 46.4% decrease from 2011 (N = 1,348) to 2013 (N = 722) was noted in this region ($P < 0.05$) (Supplemental Table 1), probably because the decrease of malaria cases also occurred in the southeast Asia accordingly. For example, Myanmar, the major imported source of the southeast Asia, the cases were reported 333,871 in 2013, which was decreased by 30.2% compared with 2012 cases (N = 478, 084).[1,16]

Malaria in children under 5 years of age. Of all the cases reported from 2004 to 2013, 7,700 (3.0%) were children under 5 years of age (Figure 5). According to the data, 2,105 (27.3%) were at age of 3–4 years who was a higher group at risk. The male to female patient ratio was 1.7 to 1 (N = 4,846 male patients to 2,854 female patients). Parasite species distribution showed that *P. vivax* accounted for 83.2% (6,403) and *P. falciparum* for 4.9% (374). Malaria cases in children under 5 years of age were concentrated in four provinces: Anhui (N = 3,069; 39.9%), Yunnan (N = 1,788; 23.2%), Henan (N = 567; 7.4%), and Hainan (N = 520; 6.8%).

Death from malaria. From 2004 to 2013, WBRS had reported 236 malaria deaths (0.09%; 236/256,179) and most of them died of *P. falciparum* infection (N = 207; 87.7%) The highest death occurred in 2003 (N = 37) and most of the deaths (N = 107; 45.3%) happened in Yunnan province, while only one death was reported in children under 5 years of age in 2004.

DISCUSSION

China has succeeded in controlling malaria and has shifted from control to elimination phase since 2010.[17] The number of locally transmitted malaria cases has significantly declined. To take Hainan province for example, as a very highly endemic area in the history of China, it has cut local transmission since 2011. In 2013, only 16 imported malaria cases were reported there and 75% of them were diagnosed as *P. falciparum*, which decreased by 99.8% when compared with 2004 (N = 9,382) cases. On the other hand, how to prevent reintroduction of the imported malaria has been a great challenge to the national malaria elimination in China, particularly because *P. falciparum* is a deadly species and mainly responsible for the increasing impact. The importance of the imported malaria is that it may bring out the high risks to the malaria-free localities in which *Anopheles* mosquitoes still exist in the transmission season, and severe malaria, mainly caused by *P. falciparum*, would be catastrophic if diagnosis and treatment could not be carried out effectively.

Despite the remarkable decrease of local malaria in China, the border area of China–Myanmar is still a great challenge for malaria elimination. First, malaria was the most important public health problems in Yunnan province over the years, the proportion of total malaria cases in Yunnan accounted for 26.2% of the whole country during 2004–2013 (ranged from 14.0% to 35.6%), and up to 70% of the cases were clustered in the bordering 25 counties (Figure 6).[18,19] In 2013, the local transmission was still severe in this region, and 51 local cases were reported in the six border counties, taking up 59.3% of total local cases over the country. Second, how to identify imported infections from neighboring countries was crucial

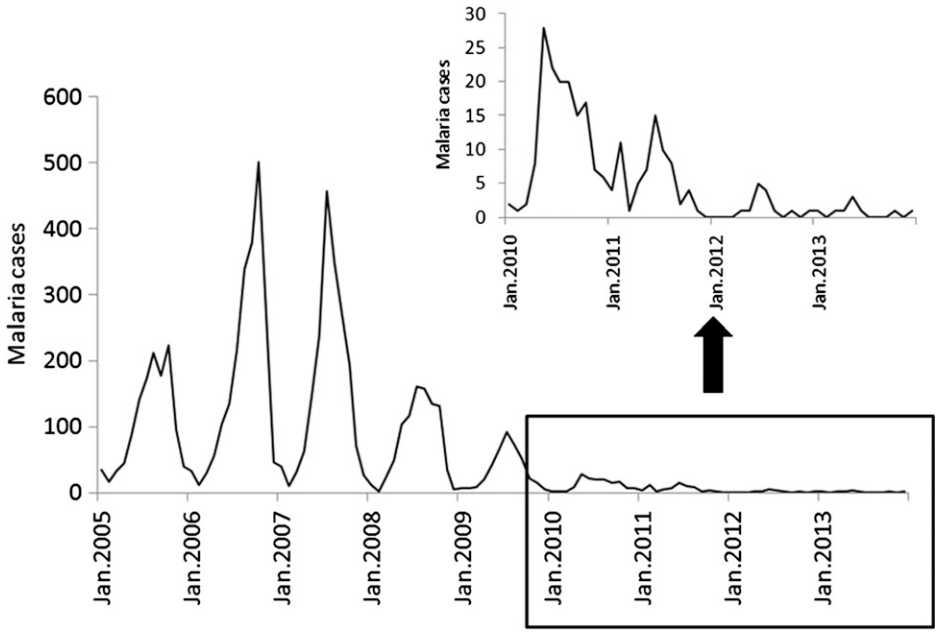

FIGURE 5. Malaria in children under 5 years of age, China, 2004–2013.

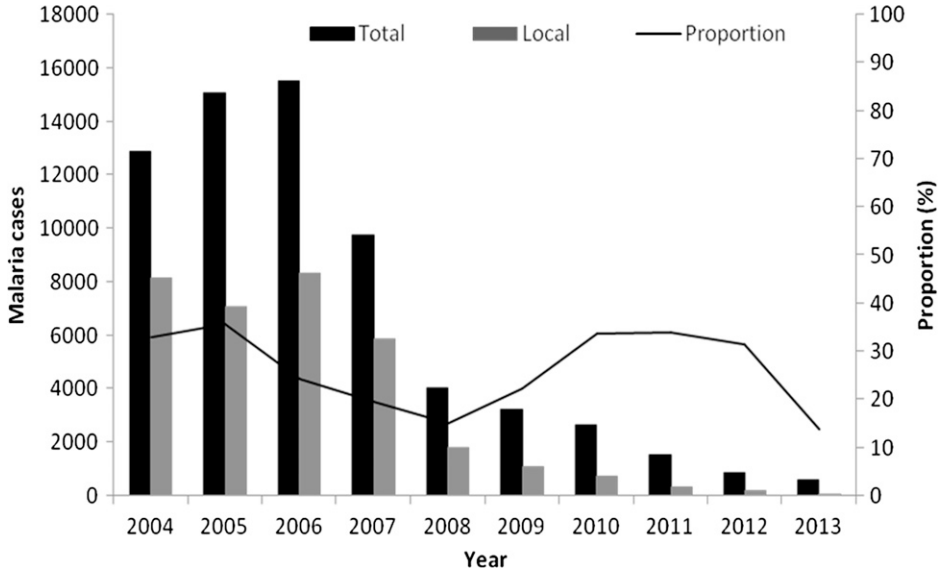

FIGURE 6. Malaria in Yunnan province, 2004–2013. The columns of different colors show the change trend of total cases (black) and local cases (gray). The black line indicated the proportion of malaria in Yunnan and the whole country.

since the borders are porous and migrant populations pass over daily. Recently, World Health Organization (WHO) recommends the screening for malaria infection at border immigration checkpoint not only to identify and treat malaria cases, but also to set up the response measures to prevent reintroduction across the border. Therefore, the more active measures may be needed at the border immigration checkpoint, which target longer-term migrant workers.[20] Third, the emergence of artemisinin resistance originally in the Thai–Cambodian border has spread and become a great concern for malaria control and elimination in the Great Mekong Subregion (GMS),[21] and the spread of artemisinin resistance may pose a great threat to the bordering counties further.[22] Although artemisinin-based combination therapies (ACTs) is generally still effective in treating *P. falciparum* at the China–Myanmar border, there has been some indication of reduced sensitivity of parasites to artemisinin and its derivatives.[23] Also, the declined sensitive of parasites against artesunate and dihydroartemisinin has been detected in Laiza City of Myanmar, and the resistance is gradually increasing.[24] As Yunnan had once the longest history of artemisinin usage mostly in the form of monotherapy for several decades, rigorous clinical efficacy studies are warranted in this region.

Another challenge as described above is that the imported malaria has become a major threat to malaria elimination in China. This is mainly due to the globalization and increasing mobile population between different countries.[25] For the countries that are approaching or have achieved elimination, imported malaria is always a great risk for resurgence or reintroduction.[26] The total number of Chinese laborers and travelers abroad in 2013 was estimated 0.5 and 98.2 million persons, respectively, increasing by 15.2% and 239.8%, respectively, compared with those in 2004.[27] At present, Africa and southeast Asia were the two major imported sources, and the former was responsible for increasing imported *P. falciparum*. Moreover, migrant workers going to and coming back from the west and central Africa were becoming a main population for the imported malaria. For instance, 765 migrant workers back from Ghana with *P. falciparum* (18.5%; 765/4,128) were reported in Shanglin county of Guangxi just within 2 months of June to July in 2013, contributing to a very high proportion of the imported cases that year.

On the basis of the data available, the imported malaria was widespread in China. Compared with reported imported malaria cases in 22 provinces in 2004,[6] it was found in 29 provinces in 2012,[28] and in 2013, it was increased to 30 provinces. Even imported malaria cases were found in some nonendemic areas in western China such as Xinjiang Uygur Autonomous Region, Qinghai, and Inner Mongolia Autonomous Region. Therefore, the case management for those who return from overseas is required to further strengthen weekly reporting via individual questionnaire or other blood detection reports.[29] All the strategies in current use were to aim at the prevention of a large-scale malaria reintroduction and the fatal infection or transmission risk it would cause. Till now, there is little secondary transmission of imported malaria in China, but the surveillance systems should also be strengthened to ensure timely recognition and prompt response for effective management.[30]

Only a limited proportion (3.0%) of the cases presented children under 5 years of age, and no death from malaria was reported since 2005 in this age group. This was different from the hyperendemic regions in Africa and southeast Asia where greater morbidity and mortality occur in children and infants.[1] It is not surprising that the low mortality rate occurred in China since early diagnosis and timely treatment was implemented strictly. Another factor that may contribute to this low mortality is *P. vivax* as a predominant species in China.

Despite the total malaria cases have declined during 2004–2013, the proportion of imported malaria was sharply increased.[31] To deal with this situation, surveillance systems should be well established to ensure timely recognition, prompt response, and effective management of imported malaria. What is also needed is good cooperation between various sectors, such as health services, immigration and quarantine services, customs, and police, to acquire and share the information on the entry of possibly infected sources. For instance, the entry–exit inspection and quarantine agencies

can carry out malaria screening for febrile travelers and inform the local CDC of positive malaria cases. More attention should be paid by Chinese medical staffs to the imported cases reported particularly from west and central Africa. Additional steps taken to prevent malaria resurgence should include mosquito control measures in the areas with high receptivity. If these strategies are well taken, it will greatly reduce the risk of malaria reintroduction, and speedup to achieve the goal of malaria elimination in different local settings and in the whole country.

CONCLUSION

The locally transmitted malaria in China has significantly declined in the past decade. However, the increasing proportion of imported malaria will significantly make adverse influence on malaria elimination program in China. Therefore, surveillance systems need to be carefully planned and well managed to ensure timely recognition and prompt response to each imported cases as well as removal of any residual local cases. In addition, effective mechanism of multisectoral coordination and cooperation should be strengthened further. One of the major tasks in the elimination phase is capacity building and maintaining. Sustainable training is necessary to make local medical staff including physicians to be able to give their accurate diagnosis and appropriate treatment to every reported malaria cases. Furthermore, the local health authority should strengthen the verification and trace investigation toward any malaria cases, indigenous and imported ones, which are required to ensure elimination of any potential reservoir and prevention of local retransmission caused by imported pathogens.

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