CHAPTER TEN

Preparation for Malaria Resurgence in China: Approach in Risk Assessment and Rapid Response

Ying-Jun Qian[1], Li Zhang[1], Zhi-Gui Xia[1], Sirenda Vong[2], Wei-Zhong Yang[3], Duo-Quan Wang[1], Ning Xiao[1,*]

[1]National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention; Key Laboratory of Parasite and Vector Biology, Ministry of Health; WHO Collaborating Center for Malaria, Schistosomiasis and Filariasis, Shanghai, People's Republic of China
[2]World Health Organization, China Representative Office, Beijing, People's Republic of China
[3]Chinese Preventive Medicine Association, Beijing, People's Republic of China; Chinese Center for Disease Control and Prevention, Beijing, People's Republic of China
*Corresponding author: E-mail: ningxiao116@126.com

Contents

Abstract

With the shrinking of indigenous malaria cases and endemic areas in the People's Republic of China (P.R. China), imported malaria predominates over all reported cases accounting for more than 90% of the total. On the way to eliminate malaria,

Advances in Parasitology, Volume 86
ISSN 0065-308X
http://dx.doi.org/10.1016/B978-0-12-800869-0.00010-X

Malaria Control and Elimination Program in the People's Republic of China, First Edition, 2014, 267-288

prompt detection and rapid response to the imported cases are crucial for the prevention of secondary transmission in previous endemic areas. Through a comprehensive literature review, this chapter aims to identify risk determinants of potential local transmission caused by the imported malaria cases and discusses gaps to be addressed to reach the elimination goal by 2020. Current main gaps with respect to dealing with potential malaria resurgence in P.R. China include lack of cross-sectoral cooperation, lack of rapid response and risk assessment, poor public awareness, and inadequate research and development in the national malaria elimination programme.

1. BACKGROUND

Although many countries are on the way to malaria elimination with sharp reduction of autochthonic malaria infections, imported cases are the main source of increasing local malaria transmission as long as the environment is favorable. The People's Republic of China (P.R. China) is one of the countries targeting elimination of malaria by 2020, and the possibility of secondary transmission induced by increasing imported cases is a high risk. This review systematically evaluates the risks of sustained malaria transmission induced by the imported cases and response efforts in P.R. China since 2010, the year the national malaria elimination programme (NMEP) was launched (Ding, 2012).

2. MALARIA IN CHINA

In P.R. China, malaria has been known for more than 4000 years and was identified as one of the top five parasitic diseases that seriously affected socioeconomic development in the twentieth century. Thanks to great efforts made by the government and whole society, the malaria status in P.R. China changed quickly in terms of the number of malaria cases which has been reduced year by year recently. In 2010, the Chinese Government announced the malaria elimination action plan with the aim to eliminate malaria by 2020. Since then, surveillance and response activities have been strengthened, which has steadily reduced indigenous malaria cases. However, with developing globalization and increasing international population migration, imported cases of malaria have become the predominant threat to the NMEP in P.R. China (Zheng et al., 2013). Among the four species of imported *Plasmodium* spp., *Plasmodium falciparum* and *P. viviax* are dominant in P.R. China.

The number of nationwide reported malaria cases in 2011 was 4479, with 29.3% reported as indigenous cases and with a reduction by 43.0% compared to that in 2010 (7855). The confirmed cases were 81.7% of the total cases, while the other 18.3% were clinically diagnosed cases (Zhou et al., 2011a).

Compared to the reduced autochthonous malaria, the number of imported malaria has been sustained at a high level, accounting for a growing share of total malaria cases between 2010 and 2012 in the mainland of China. The areas that suffered from autochthonous malaria were significantly shrinking (Yin et al., 2013), while imported malaria cases were becoming dominant and widely distributed in the whole country with the four *Plasmodium* species. It is foreseeable that this situation could bring about high risk of reintroduction of malaria transmission in the areas where malaria has effectively been under control (Xia et al., 2012). A total of 651 counties in 23 provinces were affected by the imported malaria cases in 2010, 760 counties in 26 provinces in 2011, and 598 counties in 29 provinces in 2012. Most of these cases resulted from *P. falciparum* malaria were people who came back to China from African countries or Southeast Asian countries, especially Myanmar; and only a very small proportion of them were people who migrated from some provinces inside China where local transmission still occurs (Yin et al., 2013). Therefore, it is essential to understand the importance of this situation, through a literature review, in order to respond to the potential resurgence of secondary malaria transmission induced by these imported cases in this current stage of malaria elimination in P.R. China (Tambo et al., 2014a).

We searched for terms in two large databases, PubMed (http://www.pubmed.com) for English literatures and China National Knowledge Infrastructure (CNKI) (http://www.cnki.net/) for Chinese literatures. The search terms were *malaria*, *imported*, *risk*, *transmission*, *resurgence and elimination*, as well as combinations in both English and Chinese. Because of China's shifting malaria control to elimination from 2010 (Ministry of Health, 2010), we then searched papers published from 2010 to 2013. The search yielded 8466 papers, and then a four-step screening was used to establish the final database for paper review. In the first screening, papers written by authors who are non-Chinese were excluded. Second, we went through title screening, in which we established the exclusion criteria. Third, we screened papers through detailed abstract reading, and the fourth step was full-text reading and analyzing (Figure 10.1, Table 10.1).

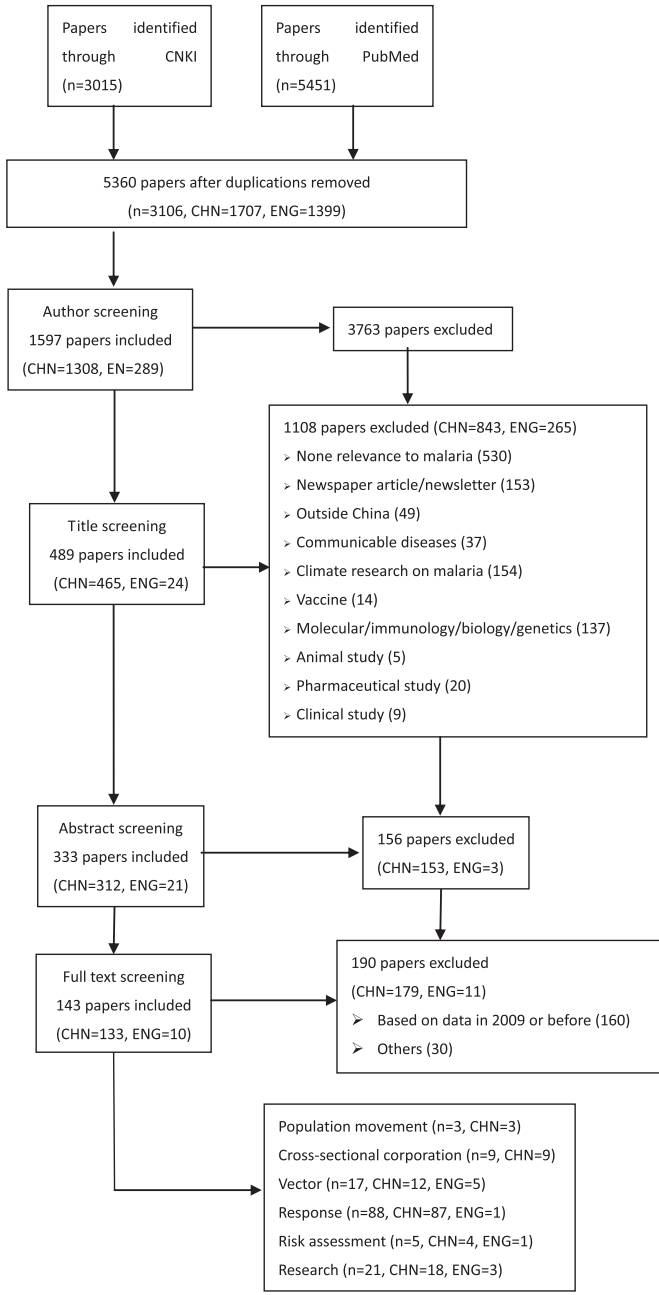

Figure 10.1 ***Diagram of literature selection flow chart.***

Table 10.1 Risk determinants and their roles

Risk determinants	Roles and function	References
Mobile populations	Mobile populations' contribution to reintroduction to malaria-free areas.	Bruce-Chwatt (1968), Prothero (1977).
Vectorial capacity	Biting behavior and capacity as well as insecticide-resistance of vectors are key factors that cause potential local transmission risk.	Liu and Liu (2010), Liu et al. (2011b), Yu et al. (2013), Wang et al. (2013b).
Cross-sectoral cooperation	Inter-sectoral cooperation contributes to good information sharing and joint efforts to prevent from reintroduction.	Li et al. (2011a), Chen et al. (2012a).
Response to reintroduction	Timely and appropriate response contributes to saving cases' life and to removing any potential reservoirs.	Ministry of Health (2011), Xie and Tan (2011), Chen et al. (2013).

3. RISK DETERMINANTS OF SECONDARY TRANSMISSION BY IMPORTED MALARIA

3.1 Population movement

In the past, population movement has often contributed to the spread of disease (Prothero, 1977). Lack of consideration of this factor contributed to failure of malaria eradication campaigns in the 1950s and 1960s (Bruce-Chwatt, 1968). The movement of infected people from areas where malaria was still endemic to areas where the disease had been eliminated led to resurgence of the disease (Service, 1991). Imported malaria cases have been a major part of reported malaria in P.R. China in recent years, indicating that provinces with more mobile populations and imported cases need to pay greater attention to rapid response action (Xia et al., 2012).

Statistics showed that more and more malaria cases were found in workers who had returned from malaria endemic countries overseas. For example, in Guangdong ports, the malaria incidence among incoming passengers was 0.27 per 100,000 from 2010 to 2011, which was 2.7 times higher than reported malaria incidence in Guangdong Province in the same time period. Of all the imported cases, 57.5% were Chinese exported labors returning from Africa, which indicates that migrant labors become predominant in the imported malaria cases (Dai et al., 2012). It was also found

that a great proportion of workers stay in malaria endemic areas all year round since they work for big engineering projects. For instance, in Xiamen, Fujian Province, there are around 4000 export labourers annually, and 10,000 workers stay abroad all year round (Chen et al., 2010). In Jiangdu District of Yangzhou City, Jiangsu Province, a total of 5000 people work abroad each year, and 2000 of them work in high malaria endemic areas overseas (Zhu and She, 2012). As a central governmental enterprise with 36,000 staff, over 2000 people participate in international projects abroad in the Gezhouba Group Corporation. Among 700 returnees to Xilin District, Yichang City, 14 malaria cases were reported in 2010 (Yang, 2011). Currently labor export management is not standardized in P.R. China due to the following three reasons (Zhu and She, 2012). First, many intermediaries that dispatch labourers to relevant companies have not been authorized. Second, labour export organizations or companies sometimes change the destination countries for labourers without authorization. Third, returnees always return in batches without valid information, all of which makes the management of imported malaria difficult.

3.2 Vectorial capacity of transmission

Anopheles is the vector of malaria and there are more than 60 species of anopheline mosquitoes reported in P.R. China, of which the four dominant vectors are *Anopheles sinensis*, *An. anthropophagus*, *An. minimus* and *An. dirus* (Liu and Liu, 2010). *An. sinensis* is the most widely distributed malaria vector in P.R. China except for in Qinghai and Xinjiang. *An. anthropophagus* has proven to be one vector with a high capacity to transmit *P. falciparum* malaria, which inhabits more than 30 counties of 18 provinces. *An. minimus* acts as the main vector living in the hilly areas. *An. dirus* is mainly distributing in Hainan Province, as well as in southern Yunnan Province and southwest Guangxi Zhuang Autonomous Region.

Most of the literatures on vectors in P.R. China focussed on the population and seasonal distribution, biological characteristics and flight range (Liu et al., 2011a,b; Shang, 2012; Wang et al., 2012a,b), and very little is about the resistance to insecticides (Wang et al., 2013b). For the most widely distributed *An. sinensis*, by using the mark-release-recapture (or capture-recapture) method, the flight range of *An. sinensis* is proved to be within 400 m, and 80% were captured from the center point of the range of 100 m (Liu et al., 2011a). *An. sinensis* plays a major role in the maintenance of *P. vivax* malaria transmission in P.R. China. Host-seeking behavior survey of culicine species and *An. sinensis* was conducted in *P. vivax* distributed areas and the results

indicated that pigs, goats and calves were more attractive to *An. sinensis* and *Culex tritaeniorhynchus* than what dogs, humans, and chickens done (Liu et al., 2011b).

Malaria around the China–Myanmar border is an important issue in the elimination stage. As the principal malaria vector with a wide geographic distribution in this area, many studies showed anopheline mosquito is abundant with *An. minimus* being the dominant species and having a high human blood index along the China–Myanmar border (Yu et al., 2013).

3.3 Cross-sectoral cooperation

In order to promote the NMEP, in May 2010 the National Health and Family Planning Commission (NHFPC, previously called Ministry of Health, MOH) of P.R. China issued the National Malaria Elimination Action Plan (2010–2020) in collaboration with 12 other central ministries and commissions. In this document, the responsibilities of each department are clarified and close cooperation is highlighted, which include the National Development and Reform Commission, Ministry of Education, Ministry of Science and Technology, Ministry of Information Industry, Ministry of Public Security, Ministry of Finance, Ministry of Commerce, General Administration of Quality Supervision, Inspection and Quarantine, State Administration of Radio, Film and Television, National Tourism Administration, Health Department of General Logistics Department and the Logistics Department of Armed Police Force (Ministry of Health, 2010).

However, lack of close coordination between health and other sectors may delay effective response to imported malaria. In 2012, for instance, some imported malaria cases were identified by Ezhou Center for Disease Control and Prevention (CDC), Hubei Province. Active case detection, foci investigation and response were then conducted quickly. However, until the completion of the response, the local bureau of exit–entry inspection and quarantine and the relevant labor export agency did not contact CDC to provide any detailed information, which directly delayed the process of case finding (Chen et al., 2012a).

To further prevent imported *P. falciparum* cases among returnees, Yangzhou City government issued the 'Management project of imported falciparum malaria in Yangzhou' to carry out labor export surveys in 2010, and a database was then established that includes information on both labour export agencies and export labourers (Xu et al., 2011). By the end of 2012, the information on 159 agencies and 9999 export workers was put into the local disease control system; this information showed that 84.3%

(5639/6687) returnees received the health services from 2011 to 2012. Meanwhile, health education and services were provided by the team of entry–exit inspection and quarantine authorities, CDCs, health facilities and labour export companies to the export labourers. As a result, malaria awareness was greatly improved among those workers one year after the implementation of the project, and prompt diagnosis and treatment were received without deaths or complicated cases.

It is worth mentioning that besides incorporation of malaria control in the national health system, malaria elimination should consider the health system in the army. As an independent entity, the army has its own health system. Integrating information between the public health services and army system is very important in the stage of malaria elimination. In 2011, it was reported that the Air Force General Hospital treated pilots infected with *P. falciparum* malaria (Li et al., 2011a). Although timely, standardized diagnosis and treatment were applied, there was no further information on the follow-up of the case reporting. Therefore, the interaction between the hospital, public health, and entry–exit inspection and quarantine units need to be strengthened.

4. RESPONSE TO REINTRODUCTION OF MALARIA

Effective and timely responses to the reintroduction of malaria due to population movement reflect the capacity of a health system to provide timely action for public health issues (Zhou et al., 2013). Malaria is one of infectious diseases not only worldwide distribution particularly in the tropical areas, but is also characterized by transmission quickly in some environmental settings where the intervention and surveillance is week (Tambo et al., 2014a). There are at least following 5 challenges currently in the response to the reintroduction of malaria in China, indentified based on the surveillance data.

4.1 Prompt diagnosis and treatment

At the current stage of malaria elimination, prompt case identification and treatment is crucial to the follow-up activities (Ministry of Health, 2011). However, the quality of diagnosis and treatment is still need to be improved in some of malaria endemic areas. The misdiagnosis or improper treatment sometimes caused patient died of malaria, specifically occurred mainly in the imported *P. falciparum* cases before launching the NMEP. For example, some imported malaria cases were not diagnosed on a timely basis, and

often were misdiagnosed as other diseases or confused with other *Plasmodium* species by health facilities at different levels (Cao, 2012; Chen et al., 2010; Chen, 2012; Chen et al., 2012b; Cui et al., 2011; Miao and Chen, 2011; Wang et al., 2013c; Yao et al., 2013; Ye and Li, 2010; Wang et al., 2013; Zhou et al., 2013a). This may delay or misdirect treatment, cause death (Chu et al., 2011; Cui et al., 2011; Gao et al., 2013; Ke et al., 2011), and result in continuous transmission (Chen et al., 2013). In 2011, 145 imported *P. falciparum* cases were reported in Henan Province, of which the longest time interval from onset to confirmed diagnosis was up to 125 days, and only 13.1% patients were diagnosed within 24 h (Chen et al., 2012c). In Hubei Province, among 28 imported *P. falciparum* cases in 2010, only 50% of cases were correctly diagnosed by health facilities at the county level or above (Huang et al., 2012). On the other hand, due to the low educational level and poor awareness of malaria, most patients usually self-medicate after the onset of symptoms (Lu et al., 2011; Liu et al., 2011; He et al., 2011), or go to private clinics as well as other primary care health facilities, such as village clinics or township health centers (Chen et al., 2011a; Li et al., 2010; Xie et al., 2011; Feng and Jiang, 2012). In most settings, these institutions do not carry out microscopy examination for malaria confirmation and treat patients as upper respiratory tract infections, gastritis or liver disease (Cui and Fang, 2011; Wang et al., 2013a; Yu et al., 2013; Ministry of Health, 2011). In one extreme case in 2010, a patient was treated as common infection at a local health facility and then clinically diagnosed as *P. falciparum* malaria in a provincial hospital without microscopy. When the provincial CDC read the blood film, it was full of *P. falciparum* in each visual field. Because of the delayed diagnosis, the patient died finally (Xie and Tan, 2011). The same story happened in Luoyang City, Henan Province, in 2010 where two *P. falciparum* malaria cases were misdiagnosed at the village clinic, township health centre, county hospital and city hospital and finally led to death (Li, 2013). With the development of symptoms, patients were then referred to another hospital at a higher level where confirmed diagnosis could be done (Chen, 2012; Cui et al., 2011; Li et al., 2010; Ministry of Health, 2011; Rao and O, 2011; Ying et al., 2011). In case of missed or delayed diagnosis, some papers attributed the situation to that most of patients did not tell their migrant history (Ke et al., 2011; Lu and long, 2011). Nevertheless, it was the responsibility of clinic doctors who should be aware and ask whether the patients had visited malaria endemic countries (Huang et al., 2012; Ke et al., 2011; Zhou et al., 2011b).

Moreover, the literature shows that there is a serious shortage of microscopists in P.R. China (Li et al., 2013; Gao et al., 2012). In a baseline survey conducted in Yunnan Province in 2010, only 58.78% (77/131) health facilities were able to carry out malaria microscopy (Li et al., 2013). In Guizhou Province, 40.3% cases were misdiagnosed (27/67) in 2011 (Zhou et al., 2013b). Among the total reported cases, 49% had conducted microscopy after presumptive treatment. Only 25.37% blood films were qualified, among which 70.59% were qualified at county CDC, 12.50% at township hospitals and zero at village clinics. As one of the pilot sites of malaria elimination, a baseline survey was performed in Chengan County, Hebei Province, in 2010, results showed there was no staff working on microscopy for malaria examination in whole county. There was a huge shortage of professionals working on malaria diagnosis and treatment (Ya-min et al., 2012).

In terms of treatment, it was often seen that uncomplicated cases or clinically diagnosed cases were treated as inpatients and given intravenous or intramuscular injections at different levels (Chen et al., 2012d; Tong et al., 2011; Wang, 2011; Liu et al., 2011; Wang et al., 2013), which was not right protocol in accordance with the National Malaria Elimination Action Plan (2010–2020) sometimes (Li et al., 2011b). In addition, according to recommendations of World Health Organization (WHO) and the national protocol (Ministry of Health, 2009; WHO, 2010), *P. falciparum* malaria cases should take primaquine for radical treatment. However, this is not usually seen in some hospital or CDCs (Quan et al., 2011; Wang et al., 2013). In terms of treatment, some clinical doctors are confused about different malaria species or have no idea of radical and preventive treatment. Some one consider that chloroquine plus primaquine is used for radical treatment of all malaria (Wu et al., 2011), and there still accidently occurred cases that clinical doctors treated as cases with monotherapy (Yu et al., 2012). Therefore, more training on standard diagnosis and treatment for malaria cases in clinics and hospitals at various levels is urgently required, in order to improve the capacity on diagnosis and treatment in the stage of malaria elimination.

4.2 Foci investigation and intervention

According to the national guidelines (Ministry of Health, 2010; China CDC, 2011), malaria cases reported through the website must be verified immediately through blood tests for confirmation of *Plasmodium* species by county-level CDCs. Epidemiological investigation should be completed within three working days, and foci investigation and treatment are to be

done within one week by county CDCs. Active case detection and relevant interventions should be conducted at all households of the epidemic site, and malaria prevention and consultation services should be provided. In Xiaochang and Xiantao, local CDCs of Hubei Province performed prompt case detection and foci intervention soon after the imported cases were identified, which was a quick and adequate response (Ye et al., 2013; Zhao et al., 2012). However, foci investigation and follow-up intervention in many imported malaria episodes sometimes do not strictly adhere to these guidelines (Quan et al., 2011). For example, active case detection is only focused on those who were on the same flight instead of neighborhoods after patients went home (Chen et al., 2010, 2012a). In other cases, vector interventions were not adequately conducted even during malaria transmission season (Chen et al., 2012d), or necessary health education was neglected (Yang et al., 2013). It is essential that the response to imported cases, even one imported case, must be taken as quickly as possible within one week.

4.3 Prophylaxis

WHO recommends that international travelers may also need to take preventive medication prior to, during, and upon return from their travels. Prior to their travel to malaria-endemic countries or regions, individuals should consult their national disease control centres, or other institutions offering travel advices, for information regarding preventive measures. In the Chinese national guidelines for malaria treatment, both chloroquine and piperaquine phosphate are recommended for malaria prophylaxis for no more than four consecutive months due to side effects (Ministry of Health, 2009).

In practice, the preventive medication was taken differently in different population. Prophylaxis by taking preventive drugs was significantly higher among managers, technicians, and businesspeople than that among workers (Jiang et al., 2013). Data shows that non-prophylaxis often leads to malaria infection within 15 days or 1 month for individuals without immunity.

4.4 Risk assessment

Risk assessment is one of important components in the response to the malaria reintroduction (Agomo and Oyibo, 2013; Tambo et al., 2014b). With the implementation of the NMEP, risk assessment has been applied in those areas where malaria elimination goal is nearly to be achieved. In 2011, risk assessment for malaria elimination in Guangdong Province was

conducted to explore any potential risks in achieving malaria elimination (Lin et al., 2011). Two counties were selected as pilot sites in class II and III, respectively, based on the stratification of malaria endemic areas (Ministry of Health, 2010). In comparison with a class II county, the proportion of basic equipment and diagnostic technology, human resources, skilled medical personnel armed with malaria knowledge as well as basic awareness among village residents were significantly higher than those in a class III county, which indicated that the class III counties may have a relatively higher risk of reintroducing malaria because of low capacity to diagnosis and treat malaria in local health systems.

In Yunnan Province, the risk assessment conducted in 2010 indicated that class III counties were at high risk in terms of the target of malaria elimination (Li et al., 2013). The results showed that many local residents had no knowledge about malaria prevention, especially in class III counties where malaria was not endemic for continuous 3 years, and very few health education activities were conducted. Nearly 50% of health facilities were unable to carry out malaria microscopy, and the coverage of technical training was low, especially in the class III counties.

Another risk assessment conducted in 2011 was based on mosquito surveillance (Liu et al., 2012). It was concluded that there was quite low risk of local continuous transmission due to imported malaria around Beijing Capital Airport (Li et al., 2013a).

4.5 Public awareness

Public awareness of diseases, including malaria, plays an important role in disease control and prevention. A lack of reasonable knowledge of disease leads to low detection rate, and the interruption of treatment and discrimination (Becker et al., 2002; Liu et al., 2013a). Health education aims to gradually improve populations' healthy behavior (Chang and Wang, 2008). In malaria prevention and treatment, health education helps improve public awareness and knowledge of malaria, community compliance with control measures, and facilitate collaborations between health facilities and individuals to achieve the given targets (Ministry of Health, 2007). With the development of economic globalization, management of imported malaria becomes more and more important. As a developing country with an increasing tourism economy, China is now facing big challenges of management for the imported malaria cases, particularly in non- or low- endemic areas, where the disease burden may be increased due to lack of necessary awareness (Du and Wu,

2010). Dynamics of influence on malaria by social factors have been widely reported, anthropological characteristics such as age and gender, and community knowledge and awareness of malaria have proven to be strong indices of malaria infection (Beck and Davies, 1981). Medication and professional health services are not the effective way to control parasitic diseases. Instead, the best way is to improve social and economic conditions, health education, health policy and necessary medical services (Jiao and Meng, 2006). In the current settings, large numbers of export labourers returning to China after the closure of abroad projects often result in malaria outbreaks or re-transmission within two months. High awareness and knowledge of malaria among the mobile population, local residents, as well as qualified skills of malaria management in health practitioners undoubtedly improve the timely identification of malaria cases and deter the reintroduction or continued transmission of malaria (Beck and Davies, 1981).

Since the issue of the National Malaria Control Programme (2006–2015), the malaria awareness rate among residents and school-aged children in endemic areas has become one of the key indicators for assessing the programme (Ministry of Health, 2006). In 2010, the National Malaria Elimination Action Plan (2010–2020) was issued to achieve the goal of eliminating malaria by 2020 throughout China. This document lays out a huge challenge to achieve an awareness rate of 80% and 85% among residents and school-aged children, respectively, in endemic areas by 2015 (Ministry of Health, 2010).

Through door-to-door investigations by uniformed surveyors, the public awareness of malaria could be assessed at different levels (Cao et al., 2011; Wu et al., 2012; Jiang et al., 2013; Lian, 2012; Zhang et al., 2012). In general, the awareness of malaria, symptoms, prevention and treatment were higher among school-aged children than local residents, although some differences remained in certain areas. However, awareness was lower than expected in the action plan in these areas (Cao et al., 2011; Jiang and Zhang, 2011; Jiang et al., 2013; Zhang et al., 2012). In Chongqing, for example, only 42.02% and 27.69% of respondents were aware of the serious consequences of *P. falciparum* malaria, and the best way to prevent malaria (Wu et al., 2012). As a class III county, no malaria has occurred in Chengan of Hebei Province for the past 30 years. Consequently, low malaria awareness was identified in local residents with only 2.86%, 5.71% and 6.19% for the knowledge on malaria endemic areas, transmission route and prevention skills, respectively (Ya-min et al.,

2012). In Hainan, where *P. falciparum* malaria was once hyper-endemic, only 20% residents were aware of the free treatment policy for malaria, and the ownership of insecticide-impregnated nets per family was as low as 20%. Reports showed that the proportion of doctor-seeking behavior and blood examination, as well as individual protection awareness after going back were not satisfied among exported labourers (Jiang et al., 2013; Liu et al., 2013b). It shows doctor-seeking behavior was more popular in both elderly and higher educated people, while the awareness of malaria was lower among younger people (Jiang et al., 2013). In terms of awareness among school-aged children, a survey conducted in Changyang County, Hubei Province, in 2010 showed that it was significantly higher among children living in cities than those in villages (Jiang and Zhang, 2011).

In Fujian Province, researchers conducted a survey on malaria awareness targeting health practitioners, including doctors and public health staff (Lian, 2012). The total awareness rate was as low as 51.5%, with the rate in clinical doctors (49.2%) much lower than that among public health practitioners (68.3%). Not surprisingly, public health practitioners tended to better understand basic malaria knowledge, clinic knowledge and prevention. The results revealed a huge gap between the requirements of the national malaria elimination programme and the current status. It also revealed that malaria training is the key impact factor in awareness, indicating training is an effective way to improve the awareness among health practitioners (Lian, 2012).

5. RESEARCH NEEDS IN THE NATIONAL MALARIA ELIMINATION PROGRAMME

In recent years, due to the decline in malaria cases and lower infection, it is urgent to conduct confirmed diagnosis promptly for each case, but it seems that traditional microscopy cannot meet the requirement. More sensitive diagnostic tools are urgently needed to meet the demands of the NMEP (Zheng et al., 2013). Most domestic researchers are focusing on the development of new diagnostic tools, including new diagnostic reagents, PCR and LAMP technology (Zhang et al., 2013; Shen et al., 2011; Wang et al., 2012b; Yi et al., 2010). Currently, malaria blood film microscopy and rapid diagnostic test strips are widely used at the grass roots level. Microscopy is the gold standard for malaria diagnosis, which requires skilled personnel. But it may cause misdiagnosis or improper judgment between species if the parasite density is

lower than 50 /μL or mixed infection occurs. The malaria rapid diagnostic test strip is simple, fast, and has high sensitivity and specificity in the diagnosis of *P. falciparum* and *P. vivax* infections, but may provide false-negative diagnosis in detection of *P. ovale* and *P. malariae* infections. Nested PCR is of high sensitivity and accuracy in detections, but requires special equipment with skilled operation and high detection costs for each sample. For instance, the performance assessment on a domestic malaria diagnosis kit showed high agreement with the results of microscopy, and it was proved to be suitable for grass-roots application in malaria-endemic areas (Shen et al., 2011). In response to the increasing imported malaria, nested PCR could be used as an effective complement to microscopy and display its advantages of high sensitivity and specificity (Zhang et al., 2013; Li et al., 2013b). Shi YX established a nested PCR method that proved to be useful in the detection and identification of malaria species compared to microscopy (Shi et al., 2011). In Zhejiang Province, five samples from the imported *P. vivax* malaria cases misdiagnosed initially were retested by nested PCR for identification (Yao et al., 2013). Results showed four infections with *P. ovale* malaria and one mixed infection with *P. ovale* and *P. vivax* malaria. However, the rapid diagnosis test results were all negative. With the development of loop-mediated isothermal amplification technology (LAMP), it was found LAMP is suitable to replace nested PCR in the field, since it is a rapid, sensitive and promising diagnostic tool for *P. falciparum* and *P. viviax* detection (Chen et al., 2011b; Wang et al., 2012b). Yi et al. (2010) established a simple, rapid and highly sensitive fluorescent quantitative LAMP, which showed high sensitivity (90.00%), specificity (93.33%) and correction rate (91.67%), which took only 30 min.

Besides the research and development of new diagnostic tools, new antimalarial drugs, and the surveillance tools on drug resistance and insecticide resistance are also needed in the stage of malaria elimination (Fu, 2013; Wang et al., 2013b; Liu, 2014). As the broad distributed vector, it has been found that *An. sinensis* was resistant to both deltamethrin and DDT, and resistance to pyrethroid has risen strikingly recently.

6. DISCUSSION

In this chapter, the following four gaps have been identified in the national malaria elimination programme in P.R. China, through the literature review. First, in the current stage of malaria elimination, lack of cross-sectoral cooperation is a major gap. It seems that limited information is delivered at the grass-roots CDC level, resulting in the aggregation

of individual imported cases, as well as delayed responses. Therefore, it is urgent to tighten and strengthen the interactive activities among the multi-sectors, including departments of inspection and quarantine, health, commerce, foreign affairs, and export labour agencies, to jointly involve them in the national malaria elimination programme (Tambo et al., 2012).

Second, rapid response and risk assessment are necessary to protect the population from potential reintroduction of malaria transmission locally, after imported malaria cases are identified (Liu et. al., 2012; Tambo et al., 2014a,b). However, there is lack of routine risk assessment activities and the response is always delayed or inadequate with poor diagnosis and treatment, which is so crucial in the stage of malaria elimination. Moreover, a significant number of clinically diagnosed but unconfirmed cases still exist in the malaria elimination stage, which need to be addressed through strengthening local laboratory diagnostic capabilities (Xia et al., 2012).

Third, improvement of the public awareness level is urgent, and it is particularly necessary to enhance health education among low educated populations, and clinical doctors (Bhutta et al., 2014; Salam et al., 2014). Misdiagnosis and overtreatment are frequent in grass-roots hospitals due to lack of malaria training. In addition, private sectors should be paying greater attention to malaria diagnosis and treatment.

Fourth, research and development is the backbone of the NMEP, due to the innovative tools that are able to accelerate and sustain the achievement of malaria elimination (Zheng et al., 2013). New diagnostic tools are widely developed and evaluated at various levels in P.R. China, but the development of antimalarial drugs is limited in the context of potential artemisinin resistance spreading from the Greater Mekong Subregion (Cui et al., 2012; Chen, 2014).

7. CONCLUSIONS

The impact factors of reintroduction or continuous malaria transmission induced by imported cases include population movement, cross-sectoral coordination and corporation, vector biology, health services and response to imported malaria, as well as research achievements. Some factors, such as vector biology and population movement may not change in a short term. However, others could be greatly improved through many efforts, such as strengthening prompt, qualified diagnosis and treatment, and enhancing public awareness. It is very crucial that an effective management mechanism should be made and a nationwide surveillance system be established to

monitor returning exported workers (Salam et al., 2014; Zofou et al., 2014). It is important to have adequate coverage with well-qualified laboratory and clinical services for malaria detection, treatment and case management. People, especially clinical doctors, need to be trained about malaria prevention, diagnosis and treatment. It is urgent that these gaps be addressed if the goal of malaria elimination is to be achieved by 2020.

ACKNOWLEDGEMENTS

The project was supported by the National S & T Major Programme (grant no. 2012ZX10004220), by the National S & T Supporting Project (grant no. 2007BAC03A02) and by China UK Global Health Support Programme (grant no. GHSP-CS-OP1) and by WHO (2012/269948-0).

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