



**ORIGINAL RESEARCH PAPER**

**Pharmacology**

**CHALLENGES FOR MALARIA CONTROL AND ELIMINATION IN THE LAO PEOPLE'S DEMOCRATIC REPUBLIC (LAOS).**

**KEY WORDS:** Malaria, control, elimination, Lao PDR

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**ABSTRACT** Lao People's Democratic Republic (Laos) is a landlocked country, one of the mainland Southeast Asia which bordered by malaria endemic countries. Southeast Asia is known as the starting point of the emerging resistance in *Plasmodium falciparum* since the Chloroquine, Sulfadoxine-Pyrimethamine, Mefloquine and Artemisinin-resistant have been first reported in the Cambodia. Eliminating malaria from the country by 2030 is the goal set in Lao PDR National Strategic Plan for malaria control and elimination. However, challenges facing the control and elimination of malaria still exist due to anti-malarial resistance, collaboration between relevant organizations, health system and human resources, health education factors. In this paper, these main challenges are discussed and suggestions are recommended.

**INTRODUCTION**

Malaria is endemic in many countries of the world, despite the fall in malaria cases globally, the rate of decline in malaria morbidity and mortality are slower in high burden countries. In 2015, an estimated 212 million cases of malaria occurred worldwide (range: 148-304million), a decline of 41% since 2000. In the same year, number of malaria deaths globally fell from an estimated 839,000 in 2000 to 429,000, with the increasing number of countries are moving towards malaria elimination phase (WHO, 2016). Although, substantial progress has been made in the malaria elimination across the globe, malaria in the Lao People's Democratic Republic (Laos) is still considered as a serious public health issue. In 2013, with nearly 2,090,000 population which accounts for 31% of the total population has lived in high transmission areas (WHO, 2015). Malaria is endemic throughout Laos with variable transmission intensity, is more intense and more entrenched in southern part than other parts of the country. Between 2006 and 2008, five southern provinces namely Xekong, Attapeu, Savannakhet, Saravane and Champasack ranked the highest incidence of *P. falciparum* with an estimated incidence of 32.7, 24.7, 11.5, 9.6 and 3.3 per 1,000 population respectively (Jorgensen *et al*, 2010). These incidence rates imply the challenges presented for malaria controlling in Laos. In this paper, past, current and progress of malaria control are reviewed and identified the key challenges for eliminating malaria in Laos are discussed.

**KEY CHALLENGES**

**Inadequate health system and human resources**

Lao People's Democratic Republic had an estimated population of 6.4 million (Lao Statistics Bureau, 2016). It is a landlocked country with a predominant natural resource-based. 66.8% of the population living in rural where are no road to access and far from public health facilities. Four administrative strata in the health system are: Central (Ministry of Health), provincial, district and health centers level. Most of the health services are delivered by public sectors (Lao National Report, 2010). There are about 894 health centers, 130 district hospitals, 12 provincial hospitals, 4 central hospitals, 222 clinics and 1,993 pharmacies, while clinics and pharmacies are mainly in urban areas. There are around 18,072 health workers in Laos, 70% of them are under the Ministry of Health, with the average of 3.2 health workers per 1,000 population. Of them, only 2,992 obtained high and mid degree of medical education and they concentrated in better socioeconomically regions, while in district and health centers almost served by the low and mid level staff (WHO, 2012). Therefore, each village need to have two Village Health Volunteers (VHVs) that selected by village committee. VHVs are key persons to improve prompt delivery of effective malaria treatment. Nevertheless, some misconceptions regarding severe malaria,

malaria transmission and prevention were found among village health volunteers (Phommanivong *et al*, 2010).

**Table 1. Health human resources in highest malaria incidence rate provinces**

Province	Malaria incidence rate (per 1000 inhabitant)	Medical health worker (per 1000 inhabitant)
Xekong	32.7	1.22
Attapeu	24.7	0.84
Savannakhet	11.5	0.74
Saravan	9.6	1.07
Champasack	3.3	0.72

**Community knowledge and awareness of malaria**

Evidence from previous study revealed that more than 60% of the residents near city and rural still had incorrect knowledge about malaria transmission (Khamlome *et al*, 2007). The low degree of malaria knowledge of residents remains a critical challenge for the malaria controlling, especially in remote areas where the rate of illiteracy is high. Moreover evil spirits is perceived among ethnic minority groups, due to their cultural, linguistic barriers, indigenous health beliefs and animist practices, therefore they considered as key risk population and reported more malaria episodes than others (Shirayama *et al*, 2006). Malaria incidence closely related with people's knowledge and behavior, though health education can reduce the malaria cases, to achieve the goal of malaria eliminating. Especially, in Laos where both dengue and malaria are endemic (Nalongsack *et al*, 2009), there were some confusion between the mosquito vectors for malaria and dengue such as: their species and biting time (Mayxay *et al*, 2013). This confusion may led to the misconception of malaria prevention and treatment. Therefore, there is the need to develop a more effective health information with a comprehensive scientific explanation of malaria transmission, including its entomology and epidemiology in simple language and in the way that at risk population could understand.

**Anti-malarial drugs resistance**

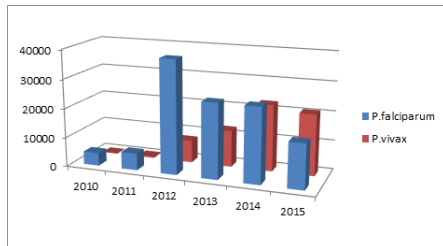
Resistance to anti-malarial drugs is an importance challenge for malaria control and eliminating, Southeast Asia is recognized as the epicenter of the emerging resistance in *P. falciparum*, since the first CQ-resistant has been reported in 1957 (Eyles *et al*, 1963) in the Cambodian-Thai border, later there were reports of SP-resistant in the 1960s, mefloquine in the 1990s (Vinayak *et al*, 2010) and artemisinin-resistant in 2006 (WHO, 2014) in the same region. In Laos, the mutation in the *kelch13* mainly C580Y that associated with reduced susceptibility to artemisinin was found (Phommasone K *et al*, 2016). In recent years, there was record the

increasing in the cases of malaria in Laos, from 22,800 in 2009 to 48,071 cases with 4 death in 2014 (WHO, 2015). Furthermore, there is increasing resistance to multiple partner drugs in Cambodia( Leang *et al*, 2015), and the containment of this resistance parasites to border regions including Laos is unfeasible due to its multiple resistance (Lover *et al*, 2016). Despite the different of first line treatment between GMS countries, Laos is the only one that AL remains as first line treatment for uncomplicated *falciparum*, and its efficacy has remained high since 2005(Mayxay *et al*, 2012). However as the recommended by the WHO, the ACT therapeutic efficacy must be monitored every 2 years(WHO, 2015), especially at the border region in southern Laos, regular monitoring of AL therapeutic efficacy is required.

**Increasing of Plasmodium vivax**

In Laos, despite a drop in *P. falciparum*, there has been an increasing in the proportion of *P. vivax* since 2010 (Mayxay *et al*, 2012). This increasing of *P. vivax* has also been reported in Cambodia, in contrast with Myanmar, Thailand and Vietnam where *P. vivax* prevalence has decreased, however the number of *P. vivax* cases still considered high in this region (WHO, 2016).

**Figure1: Incidence cases of P. falciparum and P. vivax malaria in Lao PDR, 2010-2015**



Since malaria control practices in Laos are more effective in the control of *P. falciparum* than *P. vivax*, in order to develop appropriate intervention strategies, therefore in 2016 primaquine was introduced as intervention for radical curative treatment by giving 0.25mg base/kg/day for 14 days and 0.25mg base/kg single dose as a gametocytocide. However primaquine may cause haemolytic toxicity in people who are glucose-6-phosphate dehydrogenase(G6PD) deficient, and the prevalence of G6PD in Lao population has not been determined. In 2015, the first assessment of using rapid G6PD test and primaquine for *P. vivax* treatment efficacy was conducted in Luangprabang, Savannakhet and Champasack provinces, the study showed the prevalence of G6PD deficiency ranges from 3-7% in those 3 provinces (CMPE unpublished data, 2015). Prospective studies should be conducted to identify the G6PD variants that causing G6PD deficiency in Lao population and to confirm the safety of primaquine as a radical curative regimen, since the severity deficiency of G6PD related to the G6PD variant (Ashley *et al*, 2014).

**Table 2. Number of P. vivax cases in Laos and bordering countries from 2010-2015**

Country/Year	2010	2011	2012	2013	2014	2015
Laos	122	442	7,634	12,537	22,625	20,804
Cambodia	4,794	5,155	19,575	11,267	10,356	13,146
Myanmar	29,944	28,966	135,388	98,850	41,866	26,316
Thailand	13,401	8,608	17,506	15,573	20,513	4,655
Vietnam	4,466	5,602	7,220	6,901	7,220	4,756

**Collaboration between relevant organizations**

During the last decades, the emerging and growing of *P. falciparum* resistance to artemisinin and its derivatives, fake artesunate tablets and its distribution network have been reported along border regions(Newton *et al*, 2006). Border malaria has become a major challenge in malaria control and elimination, since it is difficult to monitor and the movement of populations between both side of the border is very common(Pongvongsa *et al*, 2012). In order to combat these scourges, more strength collaboration between drug regulatory authority, education, security, commerce and travel will be required (Yong *et al*, 2012).

Otherwise, in Laos poor condition of National laboratory and Minilab on the border checkpoint need to upgrade with high quality techniques and instruments for detection and identification of fake anti-malarial, good maintenance and proficient staff.

**Asymptomatic malaria infections**

The first survey on asymptomatic and sub-microscopic *plasmodium* infection was conducted in 2015 in Savannakhet province. This survey found the considerable number of the afebrile population was carrying *plasmodium* infection. Of them, the number of asymptomatic *P.vivax* was higher than *P.falciparum* infections and those *P.falciparum* infections found K13 mutant that may be resistant to artemisinin derivatives(Phommasone K, 2016). Another cross-sectional surveys but focused on the prevalence of malaria in pregnancy in southern Laos found the asymptomatic and sub-microscopic malaria in pregnant women, therefore the overall number of malaria incidence in pregnancy may underestimated, since the screening for malaria in pregnant women is not performed in Laos(Briand *et al*, 2016). The asymptomatic malaria may produce low parasitaemia that maintained the transmission either by infection anopheles female mosquitoes(Schneider *et al*, 2007) or accidental blood transfusion as reported in Malaysia(Antony *et al*, 2013). Transfusion-transmitted malaria represent an important risk, since it can cause a severe and fatal disease, particularly in pregnant women(Parekh *et al*, 2010) and thalassaemia patients(Bird *et al*, 2016). Although no any published data on transfusion-transmitted malaria in Laos, since the low parasitaemia level need more sensitive tool than microscopic examination for detecting parasites(Shrestha *et al*, 2015) while just a limit number of microscopic available in district, province and central health facilities(Pongvongsa *et al*, 2012), hence the transfusion-transmitted malaria is unquestionably ignored. Furthermore, microscopic examination were being dependent on the reader's skills of microscopists, therefore errors can be reduced by periodic microscopists-training that would improve the microscopists' skills and techniques.

**CONCLUSION**

In Laos, malaria control and elimination is challenged by inadequate health system and human resources, community knowledge and awareness of malaria, anti-malarial drugs resistance, increasing of *Plasmodium vivax*. These factors may consequence of poverty, and poverty may aggravate above mentioned challenges. Therefore, investments are needed in basic-infrastructure, education, which is the most important for improving population living conditions that may reduce malaria incidence(Junior *et al*, 2014). Regarding to the increasing of *P. vivax*, further studies on G6PD variants, safety and adherence to primaquine radical curative regimen are urgently required. Further screening for asymptomatic in the rest of southern provinces of Laos where malaria transmission even higher than Savannakhet province is required. Furthermore microscopic examination were being dependent on the reader's skills of microscopists, the false negative and false positive microscopies can be reduced by periodic microscopists-training that would improve the microscopists' skills and techniques (Ashraf *et al*, 2012).

Some factors can be greatly changed through current global supporting such as anti-malarial drugs quality monitoring, improve access to diagnostics and rational treatment with ACTs, invest in artemisinin-resistance research, increase collaboration and coordination for artemisinin resistance containment(WHO, 2011), but the effective of these programmes must be evaluated and measured through the reduction of malaria incidence in the Lao PDR.

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