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Preliminary investigation on the prevalence of malaria and HIV co-infection in Mae Sot District, Tak Province of Thailand

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ABSTRACT

Objective: To preliminarily investigate the prevalence of HIV co-infection in patients with malaria in Mae Sot District, Tak Province of Thailand.
Methods: The study was a retrospective study on blood samples collected from a total of 256 patients with malaria (all species and severity) who attended Mae Tao clinic for migrant workers, Tak Province during 2005-2007 (148 samples) and 2010-2012 (108 samples). Malaria diagnosis was performed based on microscopic examination of patients' blood smears. Chemiluminescent microparticle immunoassay and gel particle passive agglutination were employed for the detection of HIV antigen in patients' plasma.
Results: *Plasmodium falciparum* (*P. falciparum*) and *Plasmodium vivax* (*P. vivax*) are the two predominant malaria species with the ratio of about 1: 1 to 1.5:1. Most of the *P. falciparum* cases were presented with acute uncomplicated signs and symptoms with highest parasitemia of 1 045 000 asexual parasites/μL bloods. The prevalence of malaria and HIV co-infection during 2005-2007 was 1.35% (2/148 cases, 1 each for *P. falciparum* and *P. vivax* co-infection), but was increased to 2.78% (3/108 cases, 2 and 1 for *P. falciparum* and *P. vivax* co-infection, respectively) during 2010-2012.
Conclusions: The increasing trend of prevalence of malaria and HIV co-infection in Mae Sot, Tak province was of a great concern on either pharmacodynamics or pharmacokinetics aspect. The study in a larger numbers of malaria patients in different endemic areas throughout the country with different time periods is underway.

1. Introduction

Malaria is the world's most important parasitic infectious disease ranking among the major health and developmental challenges. Malaria is caused by the protozoan *Plasmodium* transmitted by the female *Anopheles* mosquitoes. Despite years of continual efforts, the disease remains one of the major causes of morbidity and mortality affecting third-world countries and still a threat to over 2 billion people, representing approximately 40% of the world's population in about 100 countries. Best estimates currently describe the annual global burden of malaria as 300-500 million cases and 1-2 million deaths. Over 90% of the disease burden is in sub-Saharan Africa[1].

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AIDS due to infection with HIV is a very serious contemporary pandemic. Millions of people are infected with high fatal rate each year. World statistics shows the estimated cases of individuals infected with HIV in 2010 as follows: people living with HIV/AID 34 million, new infection 2.7 million and death cases 1.8 million[2]. Malaria and HIV/AIDS have overlapping geographical distribution. Together, the two diseases account for 4 million deaths a year worldwide[3]. Malaria disproportionately affects young children and pregnant women and HIV/AIDS affects mostly adolescents and young adults. Since 2009, the CDC has included malaria in the list of AIDS-related opportunistic infections; even though malaria is not among the leading causes of death in HIV-infected patients, it has been identified as the third most important source of HIV-related morbidity in Africa. The major burden of malaria and HIV occurs in Sub-Saharan Africa, Southeast Asia, Latin America and the Caribbean. However, the prevalence of malaria and HIV as well as the extent of geographical overlap varies widely within each region. The prevalence of malaria-HIV co-infection reported from Africa is approximately 10%[1]. There has been, however, no information on the prevalence of malaria-HIV co-infection in Thailand. In

areas with stable malaria transmission, HIV increases risk of malaria infection and clinical malaria especially in individuals with advanced immuno-suppression and in areas with unstable malaria transmission; HIV-infected individuals are at increased risk for severe malaria and death[1]. Interactions between antimalarial and antiretroviral drugs in patients with co-infection of both diseases, either pharmacodynamically or pharmacokinetically could also have profound public health consequences. The aim of the study was to preliminarily investigate the prevalence of HIV co-infection in patients with malaria in Mae Sot District, Tak Province of Thailand, the area with highest malaria incidence of the country.

2. Materials and methods

2.1. Study site and patients

The study was a retrospective study on blood samples collected from a total of 256 patients with malaria (all species and severity) who attended Mae Tao clinic for migrant workers, Tak Province during 2005-2007 (148 samples) and 2010-2012 (108 samples). Malaria is a serious imported medical problem in this area with a low and stable disease transmission with two seasonal peaks and forest-related during May-August and November-January of each year. *Anopheles minimus* and *Anopheles dirus* are the principal vectors. The study was approved by the Ethics Committee of the Institute for the Development of Human Research Protection, Thailand. Demographic and parasitological data of all patients are recorded.

2.2. Malaria diagnosis

The diagnosis of malaria was done according to clinical and parasitological examination[4]. Finger-pricked blood samples (100 μL each) were obtained from all patients on enrolment and blood smears were prepared and stained with Giemsa. Thick films were screened for 200 oil-immersion fields. Asexual parasites and gametocytes were separately counted against 200 white blood cells; if the parasite density was too numerous to count on the thick film, the number of parasites per 2 000 red blood cells on the thin film was counted.

2.3. HIV diagnosis

The chemiluminescent microparticle immunoassay was performed to detect HIV antigen using 500 μL plasma samples. The assay principle combines a two-step sandwich chemiluminescent immunoassay to determine the presence of HIV p24 antigen and antibodies to HIV-1 in human plasma. A chemiluminescence signal is generated and photons are counted. The result was measured in relative light unit which was directly proportional to amount of HIV-1 p24 antigen present in sample. The result was expressed as sample/cut off (S/CO); S/CO value <1 is considered non reactive and S/CO value ⩾ 1 is considered reactive. It was confirmed by gel particle passive agglutination in which antigen-coated particles are allowed to react with serum antibodies to form visible clumping[5]. A result is regarded as positive reaction to HIV when control particles (final dilution 1:16) are not agglutinated and sensitized particles (final specimen dilution 1:32 or more) give a definite agglutination pattern.

2.4. Data analysis

Categorical data are presented as number and proportion (%).

3. Results

Results of the present study (Table 1) showed that the majority of patients were Burmese (71.6% and 100% of total cases in 2005-2007 and 2010-2012, respectively). The minority of the cases were Karen and Thai (24.3% and 4.1% in 2005-2007, respectively). The infection was found in all age groups, but was most common in adults aging 15-24 years. The proportion of male was higher than female patients during the year 2005-2007 (72.3% *vs*. 27.7%) but was inversed during 2010-2012 (43.5% *vs*. 56.5%). *P. falciparum* and *P. vivax* were the two predominant malaria species with the ratio of about 1:1 to 1.5:1. *Plasmodium malariae* is occasionally found and *Plasmodium ovale* is rare. All age groups are affected and nearly all the *P. falciparum* infections are symptomatic. Most of the *P. falciparum* cases were presented with acute uncomplicated signs and symptoms with highest parasitemia of asexual parasites/μL blood. The prevalence of HIV-malaria co-infected cases in this malaria endemic area of the country was 1.35% (2/148 cases, 1 each for *P. falciparum* and *P. vivax* co-infection) during 2005-2007 to 2.78% (3/108 cases, 2 and 1 for *P. falciparum* and *P. vivax* co-infection, respectively) during 2010-2012.

Table 1

Demographics, prevalence of malaria infection and malaria-HIV co-infection in the population in malaria endemic area of Mae Sot District, Tak province, Thailand.

Characteristics		2005-2007 (n = 148)		2010-2012 (n = 108)	
		n	(%)	n	(%)
Sex	Male	107	72.300	47	43.50
	Female	41	27.700	61	56.50
Age (years)	15-19	44	29.700		
	20-24	35	23.700		
	25-29	21	14.200		
	30-34	13	8.800	No data	No data
	35-39	11	7.400		
	40-44	12	8.100		
	45-49	6	4.000		
	50-54	2	1.400		
	55-60	4	2.700		
Ethnic	Burmese	106	71.600	108	100.00
	Karen	36	24.300	0	0.00
	Thai	6	4.100	0	0.00
Malaria species	*P. falciparum*	87	58.800	55	50.90
	P. vivax	52	35.100	53	49.10
	Plasmodium malariae	1	0.700	-	-
	P. falciparum/*P. vivax* mixed	8	5.400	-	-
Parasite density (/μL)	None	1	0.700	1	0.90
	< 1 000	6	4.100	6	5.60
	1 000 - < 10 000	34	23.000	75	69.40
	⩾10 000	107	72.300	26	24.10
HIV co-infection		2	1.350	3	2.78
	with *P. falciparum*	1	0.675	2	1.85
	with *P. vivax*	1	0.675	1	0.93

4. Discussion

Mae Sot District on the western border of Thailand has been continuously reported as the province with highest malaria incidence of the country since 1996[6]. Results obtained from the two investigation periods suggested the increasing trend of HIV-malaria co-infected cases in this malaria endemic area of the country from 1.35% during 2005-2007 to 2.78% during 2010-2012. This was

considered relatively low comparing with that reported in Africans[1] and Indians[7], of which co-infection rates of approximately 10% and 9.8% respectively, were reported. Unfortunately, most of the cases included in the present study were Burmese population and thus actual information on the prevalence of co-infection in the Thai population could not be estimated. The study in a larger numbers of malaria patients in different endemic areas throughout the country is underway.

HIV is a retrovirus that belongs to the genus *Lentivirus*. There are two major HIV subtypes, *i.e.*, type 1 (HIV-1) and type 2 (HIV-2). HIV-1 is most widespread in the world, while HIV-2 was mostly found in West Africa[8,9]. The major concern of malaria and HIV co-infection is that both may synergetically affect the pathogenesis of each other. In addition, either infection might also influence the clinical course of the other. HIV infection has been reported to increase the parasitemia in patients which will in turn facilitate the transmission of malaria infection[10]. Several *in vitro* and *in vivo* studies demonstrated that *P. falciparum* co-infection rapidly enhanced the expression of HIV proteins, mRNA and p24, as well as stimulation of interferon alpha, interferon gamma and macrophage inflammatory protein 1 alpha production. The later led to up-regulation of CD4 expression that could be the driving factor in the HIV replication[11,12]. The observation was later confirmed by the following cohort studies in Northern Uganda which showed that HIV-1 RNA concentration was nearly doubled from the baseline value (96 215 copies per mL) and the cases with only malaria infection (168 901 copies per mL)[13]. It is also claimed that HIV-1 viral burden is tenfold higher in patients with *P. falciparum* malaria than in controls in Zambian adults[14]. Furthermore, it is argued that antimalarial treatment failure may be more common in HIV-infected adults with low CD4-cell counts compared to the non-infected individuals[15].

The influence of HIV infection and malaria severity remains however, controversial. Based on the results of the present study, the association between HIV-malaria co-infection and severity of malaria disease could not definitely assess. In a previous study in Zambia, cases of severe malaria clearly attributable to malaria could not be confirmed in patients co-infected with malaria, because several opportunistic infections of AIDS patients could have clinical presentations similar to those of severe malaria[15]. On the other hand, the prospective studies of severe malaria from Mozambique and Zambia both suggested that HIV-infected adults have a higher malaria case-fatality rate[15,16]. Moreover, Hochman and Kim claimed that HIV infection tends to increase episodes of symptomatic malaria and risk of severe or complicated malaria including death in both children and adults. These conflicting conclusions on the effect of HIV infection on malaria severity could be explained by variability in the CD4 lymphocyte counts of the patients[17]. A study in Nigerian showed a greater prevalence of parasitemia episodes and severity of fever in HIV-infected patients with low CD4-cell count[10].

Conflict of interest statement

We declare that we have no conflict of interest.

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