A Five-Year Review on Malaria Cases in Hospital Universiti Sains Malaysia

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ABSTRACT: This is a five-year retrospective study (2007-2011) on the prevalence of malaria in Hospital Universiti Sains Malaysia (Hospital USM), Kelantan, Malaysia. Out of 1307 blood specimens requesting for microscopic examination of malaria parasites, only 13 blood smears were positive for the presence of *Plasmodium* species. The overall slide positivity rate was 1% constituting of *Plasmodium knowlesi* (n=6, 0.46%), *P. vivax* (n=4, 0.31%) and *P. falciparum* (n=3, 0.23%). The levels of parasitemia at initial blood sampling ranged from 200 to 40200 parasites per microliter blood. The mean parasitemia level for *P. knowlesi, P. vivax and P. falciparum* were 15400, 9025 and 9027 parasites per microliter blood respectively. Affected patients were all adults and predominantly male (92%, 12 cases). All infected patients presented with fever for a few days prior to admission. Majority had hepatomegaly (92%, 12 cases), anemia (69%, 9 cases) and thrombocytopenia (69%, 9 cases). All patients recovered after treatment with the standard anti-malarial drugs. The data have shown a low prevalence of malaria in this tertiary teaching hospital.

Keywords: Anti-malaria drugs, blood smears, malaria, parasitemia, *Plasmodium* species

Introduction

Malaria has been one of the tropical diseases worldwide that causes significant morbidity and mortality. The disease is still an important threat to public especially in Malaysian Borneo (Sabah and Sarawak) as well as in interior central areas of Peninsular Malaysia where Perak, Pahang and Kelantan states share their borders. There are four well-known malaria-causing *Plasmodium* parasites, namely, *Plasmodium falciparum, P. vivax*, *P. malariae* and *P. ovale.* Following the discovery of the fifth human malaria species, *P. knowlesi* infection was found to be widely distributed across Malaysian Borneo and Peninsular Malaysia (Cox-Singh *et al*., 2008).

Many reports in Malaysia focused on malaria prevalence in the Orang Asli (aborigines) population of Peninsular Malaysia (Norhayati *et al*., 2001; Jamaiah *et al*., 2006; Kaur, 2009). Malaria infection may give rise to a wide spectrum of clinical manifestations, ranging from asymptomatic to severe illness with complications or even death. Paroxysm of fever, hepatomegaly and anemia are among the major clinical presentations of malaria. The objectives of this study were to determine the prevalence of *Plasmodium* species identified in the blood specimens and to review the clinical presentations, as well as treatment outcome among positive malaria cases in Hospital Universiti Sains Malaysia (Hospital USM).

Material and Methods

This retrospective study was conducted by reviewing the results of microscopic examination for malaria parasites in non-repeated blood specimens received from January 2007 to December 2011. Positive samples for malaria, *Plasmodium* species and level of parasitemia at first blood sampling were analysed based on the routine blood smear reports prepared by qualified medical laboratory staff in Medical Microbiology and Parasitology Laboratory, Hospital USM. Positive blood smears which preliminarily diagnosed as *P. malariae* morphologically were subjected to PCR analysis in the reference laboratory (Institute of Medical Research Laboratory, Kuala Lumpur). Demographic data and relevant clinical information of each malaria case were obtained from patient's clinical record.

Results

A total of 1307 blood specimens were received for microscopic examination of malaria parasites. Thirteen specimens were positive for the presence of *Plasmodium* species giving rise to overall slide positivity rate of 1%. **Figure 1** shows the distribution of *Plasmodium* species detected in the positive samples in Hospital USM from 2007 to 2011 which comprised *P. knowlesi* (n=6, 0.46%), *P. vivax* (n=4, 0.31%) and *P. falciparum* (n=3, 0.23%). There was no *P. malariae, P. ovale* or mixed infection reported from the microscopic examination. Demographic characteristics of the malaria patients admitted to Hospital USM from 2007 to 2011 are shown in **Table 1**.

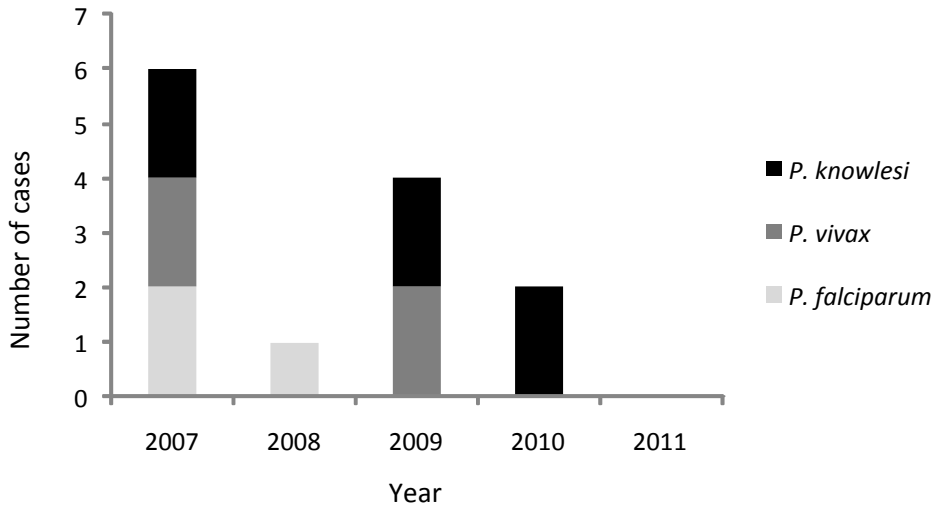

Figure 1: Distribution of *Plasmodium* species among positive cases of malaria in Hospital USM from 2007-2011 (n=13)

Table 1: Demographic characteristics of malaria patients admitted to Hospital USM from 2007-2011 (n=13)

Socio-demographic characteristics	**Frequency (%)**
Age group (years)	
<15	-
15 – 40	9 (69)
41 – 60	3 (23)
>60	1 (8)
Gender	
Male	12 (92)
Female	1 (8)
Ethnicity	
Malay	10 (77)
Chinese	1 (8)
Indian	-
Others	2 (15)
Occupation	
Army	2 (15)
Agricultural sector	1 (8)
Trading sector	1 (8)
*Others	6 (46)
Unemployed/student	3 (23)

*odd job, restaurant staff, lorry driver

The levels of parasitemia at initial blood sampling ranged from 200 to 40200 parasites per microliter blood. The mean parasitemia level for *P. knowlesi*, *P. vivax and P. falciparum* were 15400 (range: 1200 to 40200), 9025 (range: 600 to 17360) and 9027 (range: 120 to 24000) parasites per microliter blood respectively. Clinical characteristics, laboratory findings and anti-malarial treatment outcome were as shown in **Table 2**.

Table 2: Clinical characteristics, laboratory findings and treatment outcome (n=13)

Variables	Frequency (%)
Recent history of being in forested area	7 (54)*
Recent history of travel abroad[a]	3 (23)
Symptoms	
Fever	13 (100)
Headache	7 (54)
Body aches	9 (69)
Abdominal pain	4 (31)
Clinical signs	
Body temperature on admission	9 (69)
Jaundice	5 (38)
Hepatomegaly	12 (92)
Splenomegaly	6 (46)
Laboratory investigations	
Anemia[b]	9 (69)
Thrombocytopenia[c]	9 (69)
Anti-malarial treatment outcome	
Clinical & laboratory response	13 (100)
Clinical & laboratory failure	-
Death	-

[a]Ghana, Cambodia, Papua New Guinea; [b]Hb <12.0 g/dl; [c]platelet count of less than 150,000 per microlitre; *five patients were infected with *P. knowlesi*

Discussion

According to Malaysia Ministry of Health Annual Report (2009), the prevalence of malaria in Peninsular Malaysia was relatively low as compared to the states in Malaysian Borneo namely Sabah and Sarawak. There were 7010 malaria cases notified and 60% of the cases were indigenous cases mainly from remote areas. Hospital USM is a tertiary hospital located in Kelantan state, Peninsular Malaysia. The incidence rate of malaria in Kelantan was 1.68 per 10,000 populations. The overall prevalence of malaria cases was low (1%) and the number of cases were steadily declining in the past 3 years (2009 to 2011). This could be a reflection of the effective Malaria Control Program employed in the state. The program utilises a primary

healthcare approach, chemoprophylaxis, as well as focal spraying activity in localities with outbreaks in both malaria-prone and non-malarious area.

P. falciparum and *P. vivax* have been reported as the two main malaria-causing parasites in Peninsular Malaysia (Norhayati *et al*., 2001; Mahdy *et al*., 2004; Jamaiah *et al*., 2006). *P. knowlesi* infections have been prevalent especially in East Malaysia (Sabah and Sarawak) and widespread in other parts of West Malaysia (Singh, 2010; Joveen-Neoh *et al*., 2011). It was recommended that any positive blood smear microscopically similar to *P. malariae* necessitates confirmatory evaluation using nested PCR (Joveen-Neoh *et al*., 2011). In this study, we found that *P. knowlesi* was the most common *Plasmodium* detected among the patients presented to Hospital USM between 2007 and 2010. Human knowlesi malaria cases have substantially been reported in the Kapit Division of Sarawak since 2000 (Singh *et al*., 2004). This is a major concern especially due to the zoonotic nature of *P. knowlesi*, as monkeys were incriminated to harbor and transmit the parasite through *Anopheles leucosphyrus* group of mosquitoes (Vythilingam *et al*., 2008).

Most malaria patients (77%) were Malay, the major race group of population residing in Kelantan state. All cases were adult patients with age ranged between 18 to 63 years old (median age of 27 years old). This is in contrary to the previous reports of high malaria susceptibility among Orang Asli children or young age groups due to low immunity level as compared to adult or older age groups (Norhayati *et al*., 2001; Jamaiah *et al*., 2006). Majority of patients in this study had no specific risk factors for malaria susceptibility except for being to the high risk areas in Kelantan and abroad (Ghana, Cambodia and Papua New Guinea). Five out of 6 patients with *P. knowlesi* infection had recent history to the forested area. Humans acquire knowlesi malaria when they visit the forested area with the presence of macaques and the mosquito vectors (Singh and Daneshvar, 2010). Male patients were predominant, most probably because they have been involved in most outdoor activities related to their occupation or recreation in remote parts of the country. This finding was consistent with other studies where the incidence of malaria was reportedly higher among men (Norhayati *et al*., 2001; Tangpukdee *et al*., 2011).

The main clinical feature in a typical case of malaria is paroxysms of fever. In areas where malaria transmission is low, the proportion of individuals who present with fever and clinical symptoms of malaria is likely to be high (Norhayati *et al*., 2001). In this study, fever was the main presenting symptom in all malaria cases which occurred a few days prior to hospital admission ranging from 2 to 14 days. Majority of the cases had hepatomegaly (92%), anemia (69%) and thrombocytopenia (69%). These findings were also consistent with other studies showing significant association between malaria and other clinical or laboratory features of malaria such as hepatomegaly, anemia and thrombocytopenia (Norhayati *et al*., 2001; Tangpukdee *et al*., 2011). Thrombocytopenia was seen in all knowlesi malaria cases in this study and it is a consistent feature found in many reported cases of *P. knowlesi* infections (Singh and Daneshvar, 2010). Hence fever cases presented with thrombocytopenia in dengue endemic region warrant laboratory testings to exclude malaria as well. Mean parasitemia levels were also high in those patients with *P. knowlesi* infection. Parasitemia level can serve as one of the predictors for severe malaria which might be useful for its clinical management, particularly in areas of unstable transmission or hypo-endemicity (Tangpukdee *et al*., 2011).

In this study, the length of hospital stay for all patients was less than a month (ranged from 5 to 21 days). Duration of hospital stay among admitted patients was used as a measure to grade the severity of infection; the longer the duration, the more severe the infection (Jamaiah *et al*., 2006). All patients in this study were treated with the standard anti-malarial drugs. Chloroquine was initiated in 10 out of 13 patients. Majority (92%) had responded well clinically followed by subsequent parasite clearance after a few days (ranged from 3 to 21 days) of anti-malarial drugs combination treatment. There were two *P. knowlesi* patients (15%) presented with complications of acute renal impairment. The parasitemia levels of the patients with severe knowlesi malaria on admission to hospital were 16000 and 24000 parasites per microliter blood. There was no mortality related to malaria documented in our hospital for the past 5 years.

In conclusion, the study showed a low prevalence of malaria in Hospital USM and *P. knowlesi* was the predominant species detected. Fever and other clinical presentations of malaria in a high risk patient are useful criteria for clinicians to make prompt clinical diagnosis. Although no treatment failure or anti-malarial drug resistance were noted in our hospital, continuous clinical

and laboratory monitoring should always be considered since acquired resistant strains can be easily transmitted across the neighbouring countries.

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