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MALARIA IN KAMPUCHEA: CLINICAL COURSE OF FALCIPARUM MALARIA IN CHEMIN DE FER HOSPITAL, PHNOM PENH

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Abstract. To receive actual information about the clinical course of falciparum malaria case history of 373 patients hospitalized in Chemin de Fer Hospital in Phnom Penh from May 1 till October 1, 1985 were evaluated. No patients were infected in Phnom Penh. We estimated that only 8.3 % of patients had higher parasitaemia than 100,000 or more asexual parasites in μl of peripherial blood which is considered as a heavy infection. Complicated malaria was found in 39 patients (10.4 %). The most frequent complications were cerebral complications (80.0 %), renal failure (23.3 %), and liver failure (16.6 %). Ten patients had multiple organ complications and they represented 25.6 % of patients with complications. The 100 % mortality was observed in those in coma stage III; with haemoglobinuria, epistaxis and melena. Only coma stage III as a single symptom caused the death. In other cases death resulted from multiple organ complications.

For many reasons, but particularly because of the development of resistance to insecticides in mosquitos and development of resistance to some synthetic antimalarials in *Plasmodium falciparum*, the prevalence of malaria has been rising in many countries. In South-east Asia the prevalence is three and half times higher than in 1972 (Wernsdorfer 1980). According to the reports from Thailand (Panyagupta et al. 1974), falciparum malaria is becoming more serious in terms of clinical complications. One of the explanations could be the increase in parasitaemia (Boonpucknaving et al. 1984). In recent observations, examples with over 90.9 % of erythrocytes (Ery) infected frequently with double or triple infections in a single Ery were recorded.

In order to have precise information about falciparum malaria in Kampuchea, an initial evaluation of the course of clinical malaria due to P. falciparum was made.

MATERIALS AND METHODS

A total of 373 patients hospitalized with falciparum malaria in Chemin de Fer Hospital in Phom Penh from May 1 till October 1, 1985 were studied. All hospitalized patients came to the hospital from different provinces of Kampuchea. No autochtonous case from the Capital Phom Penh was hospitalized during this period.

We recorded the level of parasitaemia in different age groups, the clinical form of malaria depending on the parasitaemia.

The counting of asexual parasites in μl of blood was undertaken from thick blood film according to the formula

$$\frac{\text{asexual parasites count} \times 8{,}000}{\text{leucocytes counted}} = \text{asexual parasites count per } \mu\text{l of blood (Payne 1982).}$$

The percentage of Ery infected with asexual form of *P. falciparum* was calculated from 100 fields of thin blood films.

Because Chemin de Fer Hospital has no laboratory for haematological or biochemical examination, we were not able to evaluate the pathological changes in the above-mentioned criteria.

It was not possible to obtain exact histories of the disease in all patients. As some patients had gametocytes present in the peripheral blood on first examination, we considered that it was not the first attack. As an indicator of the duration of illness we used the time of appearance of the gametocytes in the peripheral blood after the first examination in the hospital.

RESULTS

The level of parasitaemia in different age groups of the 373 patients is presented in Table 1. Only 31 patients were infected with 100,000 and more asexual parasites (a.p.) in 1 μl of blood, which is considered a heavy infection. The majority of patients were infected with 50,000 a.p. μl of blood (81.5 %). We observed correlations between the age of patients and parasitaemia which decreased with the age.

The relationship between the parasitaemia and clinical picture in our 373 patients is presented in Table 2. For the evalution of the clinical condition we used two criteria: complicated and uncomplicated malaria. The cases which succumbed were included in the complicated malaria group. We also found a relationship between parasitaemia and frequency of complications in falciparum malaria. The critical number of 100,000 and more a.p. of *P. falciparum* per μl blood was found in 8.3 % of patients, which approximately correlates with the 10.4 % of total complicated malaria.

The details of 30 patients with complicated falciparum malaria are presented in Table 3. As a criterion for the evaluation of parasitaemia we used the percentage of infected Ery. Because of the lack of the exact history of the disease, it was not possible to establish a relation between the level of parasitaemia and severity of clinical conditions. Complicated malaria appeared in two cases with only gametocytes present

Table 1. Level of parasitaemia in different age groups of 373 patients with falciparum malaria in Chemin de Fer Hospital, Phnom Penh, May 1 — October 1, 1985

Age group	Total infected	Asexual parasites in μl of blood/cumulative %						
		10,000	10,001—50,000	50,001—100,000	100,001—200,000	200,001—500,000	500,001—1.000,000	1 million
1—10	1	1	0	0	0	0	0	0
11—20	26	8 30.8 %	10 69.2 %	4 84.6 %	2 92.3 %	1 96.1 %	0	1 100 %
21—30	167	73 43.7 %	62 80.8 %	20 92.8 %	10 98.8 %	1 99.4 %	1 100 %	0
31—40	111	49 44.1 %	43 82.9 %	10 91.9 %	7 98.2 %	1 99.1 %	1 100 %	0
41—50	59	30 50.8 %	19 83.7 %	4 89.8 %	4 96.6 %	2 100 %	0	0
51—60	8	6 75.0 %	2 100 %	0	0	0	0	0
60	1	0	1	0	0	0	0	0
TOTAL (cumulative %)	373	167 44.8 %	137 81.5 %	38 91.7 %	23 97.9 %	5 99.2 %	2 99.7 %	1 100 %

Table 2. Parasitaemia and clinic of 373 patients with falciparum malaria in Chemin de Fer Hospital, Phnom Penh, May 1 — October 1, 1985

Trophozoit (μl of blood)	TOTAL	Men	Women	Falciparum malaria	
				complicated/%	uncomplicated/%
10,000	167	151 90.4 %	16 9.6 %	6/3.6 %	161/96.4 %
10,001—50,000	137	132 96.3 %	5 3.7 %	10/7.3 %	127/92.7 %
50,001—100,000	38	35 92.1 %	3 7.9 %	8/21.0 %	30/80.0 %
100,001—200,000	23	22 95.6 %	1 4.4 %	9/39.1 %	14/60.9 %
200,001—500,000	5	4 80.0 %	1 20.0 %	4/80.0 %	1/20 %
500,001—1,000,000	2	2 100 %	0	1/50 %	1/50 %
1,000,000	1	1 1,338,666	0	1	1
TOTAL	373	347 (93.0 %)	26 (7 %)	39 (10.4 %)	334 (89.6 %)

in the blood (No. 3.21) and also in one case with very low parasitaemia (No. 10). Eleven cases had multi-organ involvement (36.6 %). The organ involvement observed is shown in Table 4. The most frequent complications were cerebral malaria (in 24 of 30 patients), renal failure and liver failure. Other complications included haematological complications, melena, convulsion and severe dehydration. To demonstrate the importance of various clinical manifestations, we evaluated the associated mortality. 100 % mortality was associated with coma stage III, haemoglobinuria, epistaxis and melena.

During the period from January 1—October 1, 1985, 13 patients died due to complicated falciparum malaria. Because of incomplete data we were only able to evaluate 9 cases. Table 4 gives details of clinical complications in these cases. Cerebral malaria was observed in patients with high parasitaemia, but it may be found also in cases with few parasites in the blood.

DISCUSSION

In general, our patients were not suffering from high parasitaemia, as only 8.3 % had 100,000 and more asexual forms of *P. falciparum* per μl of peripherial blood. At this density around 40.4 % of patients had complicated falciparum malaria. Table 3 shows the level of parasitaemia on admition to the hospital, but the outcome of the disease cannot be predicted in all patients. In the patients infected with strains of *P. falciparum* multi-resistant to antimalarials we observed more rapid multiplication

Table 3. Clinical complications in 30 falciparum malaria cases, Chemin de Fer Hospital, Phnom Penh, May 1 — October 1, 1985

Case No.	Age/ sex	Parasi-taemia in % of infected Ery	Death	Duration of illness	Gameto-cytes appear after 1 examin. in the hospital	Clinical complications				Semi-immune/ non immune population	Used anti-mala-rial drug
						renal failure	cerebral compli-cation tion	liver failure	other		
1	22 M	0.5 %		?	3 days		coma I			non	Q
2	26 M	20.9 %		?	9 days		coma I			non	Q
3	23 M	0.01 Fg		10 days	0	oligouria	coma I		dehydr.	semi	Q
4	50 M	9.0 %	+	4 days	0	haemoglo-binuria			melena	non	Q
5	40 M	4.3 %		2 weeks	3 days		coma I			semi	
6	32 M	4.5 %		2 weeks	4 days		coma I			non	F + Q
7	15 M	2.6 %		15 days	4 days		coma I			semi	F + Q
8	46 M	1.0 %		1 week	1 day		coma I		splenomegalia	non	F + Q
9	37 M	3.7 %		4 weeks	4 days		coma I			non	F + Q
10	27 F	0.09 %		2 weeks	1 day		coma I		convulsion	non	Q
11	30 M	3.0 %		6 weeks	0		coma I			non	Q
12	27 M	3.6 %		2 weeks	2 days		coma I			semi	Q
13	29 F	—	+	?	—		coma III	death after 1 hour in hospital		semi	
14	40 M	0.2 %		1 week	2 days		coma II			non	Q
15	33 M	1.3 %		?	2 days		coma I			non	Q
16	35 M	0.5 %		?	1 day		coma I			non	Q
17	23 M	2.2 %	+	2 months	0		coma III			semi	
18	46 M	0.3 %	+	3 weeks	1 day		coma III			non	F + Q
19	47 M	6.8 %	+	?	3 days	haemoglo-binuria		icter		non	F + Q
20	24 F	2.0 %	+	?	2 days		coma I		convulsion	non	Q
21	27 M	0.005 Fg	+	?	0		coma I		epistaxis	non	Q
22	20 M	33.5 %	+	1 week	2 days	oligouria	coma I	icter	epistaxis	non	F + Q
23	22 M	3.0 %		?	8 days			icter	splenomegalie	non	F + Q
24	35 M	1.0 %		?	2 days		coma I			non	F + Q
25	42 F	1.0 %		?	2 says	oedema	coma I			non	F + Q
26	28 M	1.0 %		?	4 days	oedema	coma I	icter	convulsion	non	F + Q
27	29 M	0.8 %		?	0	oligouria				non	Q
28	43 M	2.3 %		1 week	3 days	oedema of face				non	F + Q
29	38 M	0.01 %		?	0			icter		semi	Q
30	50 M	8.4 %	+	4 days	0	oligouria haemoglo-binuria	coma II		melena	non	F + Q

Q — Quinine F — Fansidar

Table 4. Frequency of clinical manifestations in 30 coplicated falciparum malaria cases and associated mortality

Organ involved	Clinical manifestation	No of cases	%	No of death	%
Cerebral complications n = 24	coma stage I	19	79.1	3	12.5
	coma stage II	2	8.3	1	50.0
	coma stage III	3	12.5	3	100
Renal failures n = 7	oligo anuria	4	13.3	2	50.0
	haemoglobinuria	3	10.0	3	100
Liver failures n = 5	icter (jaundice)	5	16.6	2	40.0
Haematology complications n = 4	splenomegaly	2	6.6	0	
	epistaxis	2	6.6	2	100
Gastrointestinal tract n = 2	melena	2	6.6	2	100
Other n = 7	oedena (generalized or in the face)	2	6.6	0	
	convulsion	4	13.3	1	25.0
	dehydration	1	3.3	0	

of parasites at the beginning of the recrudescence period. This resulted in a rapid increase in parasitaemia which was usually higher than in the first attack. Rosario et al. (1978) showed that resistant parasites overgrew the sensitive ones. Boonpucknaving et al. (1984) state that patients who had more than 50 % of Ery infected with *P. falciparum* never survived, while those with 10—15 % parasite density had a 50 % chance to survive. Trape et al. (1985) emphasize the importance of the parasite density determination for the diagnosis of clinical malaria. They also observed parasite density decreasing significantly with the age. The parasitaemia in patients from Congo over 20 years of age was 5,000 and more a.f. of *P. falciparum* per µl of blood.

Table 5. Clinical complications in 9 deaths with falciparum malaria

No.	Age/sex	Parasitaemia (asexual form in µl of blood)	Duration of illness	Complications
1	29 F	death 1 hour after arrival to hospital		coma III
2	23 M	88,266	2 months	coma III
3	46 M	12,735	3 weeks	coma III
4	24 F	80,451	?	coma I, convulstion
5	27 M	207 Fg	?	coma I, epistaxis
6	20 M	1,338,666	1 week	coma I, icter, epistaxis
7	50 M	360,251	4 days	haemoglobinuria, melena
8	47 M	272,081	?	haemoglobinuria, icter
9	50 M	336,636	4 days	coma II, haemoglobinuria, melena, diarrhea, oliguria

Cerebral complications were the most frequent manifestations in our patients with complicated malaria (80.0 %) with a mortality of 29.2 %. Among all the patients with falciparum malaria, 6.4 % developed cerebral malaria. Daroff et al. (1967) reported cerebral involvement in 0.25—2.3 % of cases, Boonpucknaving et al. (1984) in 82.3 % of complicated cases of falciparum malaria with a 33.0 % mortality. Vassalo et al. (1985) observed cerebral malaria in 1.7 % of patients in Saudi Arabia. Tapchaisri et al. (1985) found that patients with cerebral malaria had relatively less challenge with malaria antigen and were probably less immune to malaria than were patients with acute uncomplicated malaria. Out of our 30 patients with complicated malaria 23 were from nonendemic area and 7 from an endemic area (3,2 : 1). Cerebral malaria occurred in 18 patients from the nonendemic area and in 6 from endemic area (3 : 1).

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МАЛЯРИЯ В КАМПУЧИ: КЛИНИЧЕСКОЕ ТЕЧЕНИЕ *FALCIPARUM* МАЛЯРИИ В БОЛЬНИЦЕ *CHEMIN DE FER* В Г. *PHNOM PENH*

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Резюме. С целью получить информации о клиническом течении малярии, вызванной *Plasmodium falciparum*, обследовали 373 пациентов в больнице Chemin de Fer в г. Phnom Penh от 1 мая до 1 октября 1985 г. Ни один из пациентов не получил инфекцию в г. Phnom Penh. Только у 8,3 % пациентов было обнаружено 100000 или больше бесполых паразитов в 1 µл периферической крови, что считалось высокой степенью заражения. Сложная малярия была обнаружена у 39 пациентов (10,4 %). Самые частые компликации были расстройства мозга (80,0 %), почек (23,3 %) и печени (16,6 %). У 10 пациентов (25,6 % из всех пациентов с компликациями) встречались сложные расстройства органов. 100 % смертность была у пациентов в 3-ей стадии комы, сопровождаемой гемоглобинурией, носовым кровотечением и меленой. Кома 3-ей стадии, как единственный симптом, стала уже причиной смерти. В других случаях смерт была причинена сложными расстройствами органов.

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EXTINCTION OF A DERMACENTOR VARIABILIS (SAY) TICK INFESTATION (ACARI: IXODIDAE)

Infestations of *Dermacentor variabilis* in interior Massachusetts were characterised by, 1. extream localization within a tick-free region, 2. their occurence after rural areas were built up with house, 3. their location in a winter survival microhabitat with a high water table, and 4. the presence of pet dogs (McEnroe W. D., 1974: Acarologia 19: 618—625). Such an infestation was followed for 3 tick seasons by tick burdens on a dog with total collections of 942, 1,480, and 1,196 ticks. The infested area was ca 3 ha (McEnroe W. D., 1974: Acarologia 16: 207—219).

This area, after the dog was absent for 5 years, was found to be tick free. The absence of the infestation was not due to climatic regulation because similar infestations survived extream winter regulation (McEnroe W. D., 1984: Z. ang. Ent. 97: 481—484).

In its daily rounds, the dog traversed the infested area. Although the dog was groomed every evening, some females compleated engorgment because engorged females were found in the house. The limited home range of the dog resulted in some engorged females dropping off in the survival area. The limited movement of the immature hosts, *Microtus pennsylvanicus*, maintained the local population. Only a few engorged females were required because of their large egg production (McEnroe W. D., 1981: Folia parasitol. 28: 381—383) and the constant presence of the adult host.

Not only did the dog support the infestation, but also its habit of dropping off unattached ticks in the house and automobile exposed the occupants to risk of tick exposure.

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