Singapore Med J 2004 Vol 45(1) : 28-36

A Retrospective Study of Malaria Infections in an Intensive Care Unit of a General Hospital in Malaysia

K H Koh, P H Chew, A Kiyu

ABSTRACT

Aims: To study the clinical and demographic aspects as well as the outcomes of severe cases of malaria infections managed in the intensive care unit of the Sarawak General Hospital, Kuching from January 1996 to December 2001.

Methods: All cases of malaria admitted to the intensive care unit of the Sarawak General Hospital from January 1996 to December 2001 were identified from the intensive care records and retrospectively reviewed.

Results: A total of 31 cases of malaria were managed in the intensive care unit of the Sarawak General Hospital in the six-year period. Twenty-eight cases were *P. falciparum* infections; two were *P. vivax* and one was a mixed infection of *P. falciparum* and *P. vivax*.

Fever with or without chills and rigors, headache, abdominal pain and vomiting were the four commonest presenting complaints for *P. falciparum* infections. Patients with both abdominal pain and hepatomegaly have significantly higher mortality. The fatal cases, at presentation, had higher parasite counts, higher bilirubin, aminotransferase, potassium and urea levels, but lower haemoglobin and platelet counts, and more deranged coagulation profiles compared to surviving patients. The major complications include acute renal failure, acute respiratory distress syndrome, cerebral malaria and disseminated intravascular coagulopathy, haemolytic anaemia and liver dysfunction.

A single case of vivax malaria, which was complicated by septicaemic shock and disseminated intravascular coagulopathy was also documented. Higher mortality rate was documented if the antimalarial medication was not commenced on the day of admission into hospital.

Conclusion: Several infections of *P. falciparum* are still associated with significant mortality. Other confounding factors include the patient's own pre-morbid general health status and delay in initiating quinine therapy. Aggressive and appropriate therapy is life saving. Earlier anti-malaria treatment may improve the survival rate for falciparum malaria. The isolated case of death from *P. vivax* infection argues against complacency in the management of even the "benign" form of the infection.

Keywords: ICU infections, intensive care unit (ICU), malaria, malaria complications, plasmodium falciparum

Singapore Med J 2004 Vol 45(1):28-36

Medical Department
Sarawak General Hospital
30, Lorong Sky Garden 2,
Off Green Road
93150 Kuching
Malaysia

K H Koh, MBBS MRCP
Physician

P H Chew, MBBS, FAMM, FRCP
Head

Sarawak Health Department

A Kiyu, MBBS, MPH, DrPH
Deputy Director

Correspondence to:
Dr Koh Keng Hee
Tel: (60) 82 276666
Fax: (60) 82 240767
Email: kohkenghee@yahoo.com

INTRODUCTION

Malaria is widely distributed in tropical and subtropical countries. It is endemic in most areas of South East Asia. The malaria parasites are protozoa of the genus Plasmodium. Of the four species that are pathogenic in man, i.e. *P. vivax, P. ovale, P. malariae* and *P. falciparum*, Sarawak is endemic for *P. falciparum, P. vivax* and *P. malariae* infections. Infections with *P. falciparum* are prone to complications and associated with significant mortality.

There were 16,184 malaria cases reported in Sarawak[1] from 1996 to 2001. Most of them were treated in government clinics (of which there were over 200) and hospitals (of which there were 21) throughout the state. Over the same period, a total of 712 cases were admitted into Sarawak General Hospital, either directly or via referral from the other smaller hospitals (refer Table I).

The majority of cases admitted into Sarawak General Hospital were managed in the general medical wards and paediatric wards. Those ages above 12 years old with serious complications were managed in the intensive care unit (ICU).

We undertook a retrospective study of malaria cases admitted over a six-year period into the ICU of Sarawak General Hospital, looking into their demographic and clinical profiles, in order to study the prognostic factors and possible ways of modifying the clinical outcomes.

Table I. Number of cases of malaria notified in Sarawak state and number admitted to Sarawak General Hospital by species and year, 1996-2001.

		Year						
		1996	1997	1998	1999	2000	2001	Total
Sarawak state	Number of cases	1,900	2,416	2,557	3,155	3,011	3,145	16,184
	Parasite species							
	P. falciparum	397	396	318	786	690	593	3,180
	P. vivax	1,101	1,651	2,061	2,030	1,923	2,134	10,900
	P. malariae	392	347	153	270	334	359	1,855
	Mixed infection	10	22	25	69	64	59	249
SGH admission	Number of cases	115	97	56	108	134	202	711
(includes all wards)	Parasite species							
	P. falciparum	47	36	17	57	62	85	304
	P. vivax	66	58	35	46	71	110	386
	P. malariae	2	1	0	0	0	3	5
	Mixed infection	0	2	4	5	1	4	16
SGH	Age >12 years	37	32	12	40	53	71	245
P. falciparum cases	Age 12 years	10	4	5	17	9	14	59
	Subtotal	47	36	17	57	62	85	304
ICU admissions		6	0	1	4	8	12	31

Source: Vector-bone Diseases Control Unit, Sarawak Health Department

METHODS

All malaria cases that were admitted into the ICU of Sarawak General Hospital, from 1996 to 2001 are included in this study. Cases were identified from the computer records in the records office as well as from the ICU records of Sarawak General Hospital. Individual case notes were then retrieved and data abstracted using a format that was developed for this study. The data were analysed using SPSS[2].

Blood parasites count on thick film was calculated based on World Health Organisation (WHO) established method, i.e. converting the parasite count per µL in relation to the leukocyte count based on a standard figure of 8,000 leukocytes per µL of blood[3].

Daily percentage of dropping total parasite count was assessed with calculation demonstrated in Appendix I.

Severe malaria is defined as a complicated case of falciparum malaria infection following WHO criteria[4,5]. Thus, complicated vivax malaria cases were not described as severe malaria.

Controversies still exist in defining impaired consciousness of cerebral malaria and the underlying mechanism[6]. We have limited the term cerebral malaria to patients with *P. falciparum* asexual parasitemia, who satisfy the WHO criteria of being in a deep coma (not attributable to any other cause), from which a patient is unable to be aroused (>30 minutes if after convulsion), and unable to make a localising response[4].

Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) were diagnosed based on the timing (acute onset), refractory hypoxaemia (Pa02/FI02 <200 mmHg for ARDS. Pa02/FI02 ≥200 mmHg but <300 mmHg for ALI) and typical chest radiography view (bilateral lungs infiltrates)[7]. We did not perform pulmonary capillary wedge pressure measurement in these series.

Acute pulmonary oedema was diagnosed based on clinical findings, chest radiograph and the appropriate clinical circumstances (underlying aetiology)[8]. It may be due to acute renal failure, acute heart failure or overhydration.

Acute renal failure was defined as a urine output of less than 400 ml in 24 hours in adults (or 12 ml/kg/24 hours in children) failing to improve after rehydration and a serum creatinine of more than 265 micromol per litre[4].

Statistical analyses were done for symptoms, signs, admitting laboratory parameters, and complications, with respect to the outcome (e.g. survival or rate of complication). Fisher's exact test (two-sided) was used in non-parametric test when the expected value(s) was less than five. Two-tailed t-test for independent samples was used in comparison of means, without assuming equal variances.

Death was arbitrarily grouped into early if it occurred within one week of admission and late if it occurred after 14 days of admission.

APPENDIX I

Highest parasite counts either from District or General Hospital were taken as pretreatment parasite count, named as "highest total count". To calculate the daily percentage of dropping total parasite count, we used the ratio of the first total parasite count when asexual parasite count dropped below 10,000/μL (named as "lower total count") to the highest total parasite count. If the patient died before the asexual parasite count dropped below 10,000/μL, we took the latest reported parasite count as "lower total count". The day that was taken to reach this number was used as inverted power (root) for the ratio to derive the daily ratio. The percentages of dropping parasite count was one minus daily ratio. Below is the calculation:

$$\text{Daily percentage of dropping parasite count} = \left(1 - \sqrt[\text{day}]{\text{lower total count/highest total count}}\right) \times 100\%$$

The formula in Microsoft Excel is

ratio = lower total count/highest total count

daily ratio = power (ratio, 1/day taken)

Daily percentage of dropping parasite count = (1 – daily ratio) x 100%

As an example of the formula used, if the highest total parasite count of 100,000/mL took one day to become 1,000/μL (as first total parasite count when asexual parasite count fell below 10,000/μL), then the daily percentage of dropping parasite count would be 99%. If it took two days, then the daily percentage of dropping parasite count would be 90%.

Table II. Characteristics of 31 malaria patients admitted to ICU in Sarawak General Hospital, 1995-2000.

Characteristics	Died	Survived	Total
Malaria species			
P. falciparum	10	18	28
Others	1	2	3
Gender			
Male	4	12	16
Female	7	**8	15
Ethnic group			
Bidayuh	5	11	16
Iban	5	5	10
Others*	1	4	5
Age group (years)			
10-19	3	2	5
20-29	1	4	5
30-39	2	5	7
40-49	1	4	5
50-59	1	4	5
60+	3	1	4
Source of referral			
District hospital	7	11	18
Private or Government outpatient clinic	2	6	8
Direct admission to SGH	2	3	5

* Two patients each were from the Malay and Chinese ethnic groups and one patient's ethnic grouping was uncertain and labelled as "others".

** Two of the females were pregnant at 25 and 30 weeks of gestation.

RESULTS

Thirty-one cases of malaria were admitted to the ICU within this six-year period. The characteristics of these patients are shown in Table II. There were 16 male (51.6%) and 15 female (48.4%) patients. Of these, 13 male and 15 female patients had *P. falciparum* infections. Two of the female falciparum malaria patients were pregnant at 25 weeks and 30 weeks of gestation. Two female patients were infected by *P. vivax* and one male patient by a mixed *P. falciparum* and *P. vivax* infection. Over 80% of patients were from two ethnic groups: i.e. Bidayuh (16 patients) and Iban (10 patients).

Eighteen (58.1) of the cases were referred from district hospitals while eight cases (25.8%) were referred by private and government outpatient clinics. Only five cases (16.1%) presented directly to the Sarawak General Hospital.

The ages of patients with falciparum malaria ranged from 15 to 75 years with a mean of 38.6 years old. There was no statistical difference in the age and sex distributions between fatal and non-fatal cases.

Patients with falciparum malaria presented with fever (96.4%), chills and/or rigors (78.6%), abdominal pain (42.9%), headache (39.3%), vomiting (35.7%), diarrhoea (14.3%), seizure (10.7%), cough (7.1%), bleeding tendency (7.1%). Statistically, these symptoms showed no correlation with survival. The mean onset

Table III. Laboratory parameters on admission for falciparum malaria cases.

	Overall				Died				Survived			
	N**	Minimum	Maximum	Median	N**	Minimum	Maximum	Median	N**	Minimum	Maximum	Median
Asexual count of parasites (per μL) *	27	0	400,000	160,000	9	0	400,000	224,385	18	0	362,060	55,280
Sexual count of parasites (per μL) *	27	0	5,120	400	9	0	5,120	800	18	0	2,400	220
Highest total parasites count (per μL) *	28	80	404,800	***189,920	10	121,000	404,800	***242,298	18	80	362,300	127,800
Haemoglobin concentration (g/dL)	28	5	16.2	9.35	10	5.0	13.7	8.95	18	6.3	16.2	9.35
Total white cell count (per μL)	28	2,500	12,600	6,450	10	3,100	12,000	7,900	18	2,500	12,600	6,050
Platelet (per μL)	28	11,000	249,000	31,000	10	11,000	220,000	28,500	18	11,600	249,000	42,500
Prothrombin time (seconds)	25	10.6	33.4	15.7	9	13.5	33.4	20.0	16	10.6	19.5	14.1
Partial thromboplastin time (seconds)	25	27	110.7	41	9	27.0	110.7	50.0	16	30.0	58.6	29.25
Creatinine (μmol/L)	25	63	687	156	7	111	283	157	18	63	687	124.5
T Bilirubin (μmol/L)	23	6.8	457.0	68	6	15.0	457.0	95.3	17	6.8	330.0	67
C Bilirubin (μmol/L)	21	0	245.0	56.0	5	34.2	245.0	85.5	16	0	240.0	49
Unconjugated Bilirubin (μmol/L)	21	6.8	212.0	29.0	5	17.1	212.0	32.5	16	6.8	173.0	27.0
AST (U/L)	24	36	924	94.5	7	36	924	144	17	40	689	91
ALT (U/L)	24	15	258	39.5	7	30	258	68	17	15	257	37
NA (mmol/L)	28	117	142	130	10	117	142	126.5	18	125	139	131.5
K (mmol/L)	28	3	6.5	4	10	3.2	6.5	4.2	18	3	4.5	3.9
UREA (mmol/L)	28	4	38.1	17.35	10	8.1	38.1	17.85	18	4	33.5	16.4

* The asexual and sexual counts were recorded from the highest available parasite count either from district or our general hospital. If the on-call technician did not report the stage of parasite on highest parasite count, then the asexual and sexual count will be taken from the subsequent highest parasite count.

** N: Number of cases recorded

*** One of the fatal patients had "too numerous parasites" that the technician failed to report an exact number. We exclude his data in the calculation of median for asexual and sexual count. Nevertheless, we include his data in highest total parasites count assuming that he has high parasite count that definitely higher than the median.

of symptoms in both fatal and non-fatal cases was seven days prior to admission.

On admission to the intensive care, nine (32.1%) out of 28 patients with plasmodium falciparum have sinus tachycardia (pulse rate >100/minute). Three patients (10.7%) have systolic blood pressure readings less than 90 mmHg while 10 patients (35.7%) have diastolic blood pressure readings below 60 mmHg. Five patients (17.8%) were severely oliguric. Four out of 10 fatal cases and one out of 18 surviving patients have urine output less than 25 ml/hour on admission (Two-sided Fisher's Exact test p=0.041).

Among the 28 cases with falciparum infection, hepatomegaly was noted in 15 patients (53.6%) with four patients (14.3%) having splenomegaly. Two patients (7.1%) have both hepatomegaly and splenomegaly. Abdominal pain was one of the frequent complaints for patients with hepatomegaly.

Table IV. Laboratory parameters on admission for falciparum malaria cases – analysis.

			Died		Survived		t-test **
	No. of cases with records	Overall Mean	No. of cases	Mean	No. of cases	Mean	p value
Asexual count of parasites (per μL) *	27	153,300	9	171,384	18	112,815	0.035
Sexual count of parasites (per μL) *	27	926	9	3,081	18	460	0.076
Highest total parasites count (per μL) *	27	178,981	9	214,283	18	143,697	0.038
Haemoglobin concentration (g/dL)	28	9.3	10	9.0	18	9.5	0.581
Total white cell count (per μL)	28	7,361	10	7,697	18	7,174	0.683
Platelet (per μL)	28	55,679	10	44,820	18	61,711	0.487
Prothrombin time (seconds)	25	16.3	9	19.5	16	14.5	0.041
Partial thromboplastin time (seconds)	25	46.8	9	57.4	16	40.8	0.096
Creatinine (μmol/L)	25	189.5	7	184.7	18	191.3	0.889
T bilirubin (μmol/L)	23	117.2	6	169.7	17	98.6	0.363
C bilirubin (μmol/L)	21	80.0	5	124.5	16	66.0	0.234
Unconjugated bilirubin (μmol/L)	21	46.9	5	76.1	16	37.8	0.364
AST (U/L)	24	171.3	7	258.9	17	135.2	0.348
ALT (U/L)	24	72.1	7	96.7	17	62.0	0.347
NA (mmol/L)	28	130.1	10	127.7	18	131.4	0.149
K (mmol/L)	28	4.1	10	4.6	18	3.9	0.106
UREA (mmol/L)	28	17.8	10	19.5	18	16.8	0.529

* The asexual and sexual counts were recorded from the highest available parasite count either from district or our general hospital. If the on-call technician did not report the stage of parasite on highest parasite count, then the asexual and sexual count will be taken from the subsequent highest parasite count. The parasite counts data of fatal case with "too numerous parasites" that the technician failed to report were excluded from the data in this table.

** Statistical analysis for comparison of the means was using independent sample 2-tailed t-test without assuming equal variances.

Seven out of 11 patients with both hepatomegaly and abdominal pain died, compared to three out of 17 other patients without hepatomegaly and abdominal pain (Two-sided Fisher's Exact test p=0.02).

There was a wide range of the laboratory parameters on admission of the falciparum cases, as demonstrated in Table III, IV, V and VI.

At the time of presentation, fatal cases had higher parasite counts, higher bilirubin, aminotransferase, potassium and urea levels, but lower haemoglobin and platelet counts, and more deranged coagulation profiles compared to the non-fatal cases. Prothrombin time more than 18 seconds; potassium level more than 5.5 mmol/L and sodium level less than or equal to 125 mmol/L were significant predictors for high mortality.

Table VII records the daily percentage of dropping total parasite count.

In our series, the rate drop in parasite counts with treatment was not significantly associated with survival rate in falciparum malaria infection. In fact, six of the fatal cases (three cases of early and three cases of late mortality) had recorded downward trends in parasite counts with treatment. Among the fatal falciparum cases, the patients who died within seven days, had a mean for daily percentage of dropping parasite count of 90.5%, in comparison to the patients who died after two weeks of hospital stay, had a mean of 87.5%. One isolated patient who was treated with chloroquine in a district hospital had successful eradication of the asexual stage and was admitted to our ICU, only with a sexual parasite count of just 200/μL (which cleared off in subsequent days). He developed complications of acute respiratory distress syndrome and died after 16 days of intensive care management.

Table V. Geometric mean of highest total parasites count.

			Died		Survived		t-test for log value **
	No. of cases with records	Overall Geometric Mean	No. of cases	Geometric Mean	No. of cases	Geometric Mean	p value
Highest total parasites count (per μL) *	27	68,077	9	229,087	18	37,102	
Log_{10} of above value	27	4.8330	9	5.3600	18	4.5694	0.011
Platelet count	28	38806	10	29,854	18	44,895	
Log_{10} of above value	28	4.5889	10	4.4750	18	4.6522	0.211

* The parasite count data of fatal case with "too numerous parasites" that the technician failed to report was excluded from the data in this table.

** Statistical analysis for comparison of the log_{10} values was using independent sample 2-tailed t-test without assuming equal variances.

Table VI. Number of cases in different group of laboratory parameters on admission for falciparum malaria cases.

Laboratory parameter		Number of cases				p value***
Item	Group	Survived	Died*	MR**	Total	
Asexual parasite	>100,000/μL	7	8	53%	15	0.019
	100,000/μL	11	1	8%	12	
Sexual parasite count	>500/μL	5	7	58%	12	0.037
	500/μL	13	2	13%	15	
Total parasite count	>100,000/μL	9	10	53%	19	0.010
	100,000/μL	9	0	0%	9	
Prothrombin time	>18 seconds	1	5	83%	6	0.012
	18 seconds	15	4	21%	19	
Potassium level	>5.5 mmol/L	0	3	100%	3	0.037
	5.5 mmol/L	18	7	28%	25	
Sodium level	125 mmol/L	1	4	80%	5	0.041
	>125 mmol/L	17	6	26%	23	

* There were 10 deaths. Data on the asexual parasite count, asexual parasite count, and prothrombin time were not available in all cases.

** MR – abbreviation for Mortality Rate.

*** Fisher's exact test (2-sided) was used to derive p-value.

Table VII. Daily percentage of dropping total parasite count for falciparum malaria cases.

	Daily percentage of dropping total parasite count (%)		
	All falciparum cases	Survived cases	Fatal cases
Recorded cases*	19	13	6
Mean**	90.3	90.9	89.0
Median	92.7	92.7	93.4
Range	34.2	28.4	34.2
Minimum	65.6	70.8	65.6
Maximum	99.8	99.1	99..8

* In this statistical analysis, cases were only recorded if there were a series of parasite count recorded and highest total parasite counts were more than or equal to 10,000/mL. Five survived cases of highest parasite count less than 10,000/mL were excluded. Three fatal falciparum malaria cases were excluded in analysis because of merely single reading of parasite count. One fatal case of single reading of "too numerous parasite count" was excluded. Please refer to the note in Appendix I.

** P-value on comparing the mean of survived and died cases was 0.756 using 2-tailed t-test for independent samples not assuming equal variances.

In terms of referral and prior treatment, the 28 cases of falciparum malaria could be divided into three groups in terms of referral, prior treatment and outcome, namely: (i) Nine patients whose treatment of quinine was initiated in district hospital (two died; mortality: 22%); (ii) Seven patients referred from district hospitals without quinine treatment prior to admission into Sarawak General Hospital (four died; mortality: 57%); and (iii) twelve patients presenting directly to the Sarawak General Hospital (four died; mortality: 33.3%). Thus, among the referral cases from district hospital, there were documented higher mortality for patients without quinine treatment in district hospital (comparing first and second group: Two-sided Fisher's Exact Test p=0.302).

In our series, 25 cases had documented day of initiating antimalarial medication. (Three cases that were referred from district hospitals had no documentation on the day of initiating antimalarial medication.) Five out of 19 patients (26%), who had been treated with antimalarial medication even on the day of admission (either into district or our general hospital) died, in comparison to four out of six other patients (67%) who had later treatment died (Two-sided Fisher's Exact Test: p=0.142). Thus, higher mortality was documented for cases which antimalarial treatment was not initiated on the day of admission.

Twenty-five of the 28 falciparum malaria patients were treated with quinine, initially intravenously, and subsequently changing to oral route. Three of the patients were treated with oral quinine from the start. One of the three patients subsequently developed perforated bowel due to peritoneal dialysis while the remaining two patients recovered smoothly. All patients with serial blood testing of their parasitaemia during the treatment period demonstrated reducing parasite counts. Some patients had prolonged QT intervals (suspected to be quinine toxicity) during their ICU stay, especially among the elderly or those patients with liver or renal impairment. Blood quinine level was not measured due to lack of facility.

One isolated case with a high total asexual parasite count reaching 362,060/μL received "exchange transfusion" besides intravenous quinine. This was a 39-year-old man who recovered well despite hyperparasitaemia, and without any documented complication during his five-day ICU stay. This was two days below the average stay of other falciparum cases in the series.

Eight patients (28.6%) out of 28 patients with *P. falciparum* infection developed cerebral malaria with a mortality rate of 62.5%, compared to 25% for those who did not develop cerebral malaria (p=0.091). Eight patients (28.6%) developed disseminated intravascular coagulopathy (DIVC). Falciparum malaria patients who developed DIVC had highest total parasite count of 227,150/μL, in comparison to others with highest total parasite of 158,700/μL. (Two tailed independent samples t-test, not assuming equal variances: p=0.210.)

Thirteen (46.4%) of the 28 falciparum malaria patients developed acute renal failure. Eight patients underwent acute dialysis, with three patients receiving haemodialysis, three receiving peritoneal dialysis and the remaining two patients receiving both peritoneal and haemodialysis (one because of inadequate fluid extraction with peritoneal dialysis, and the second because of perforated ascending colon). Nine (69.2%) out of 13 acute renal failure patients had fatal outcomes, compared to one (6.7%) of 15 without acute renal failure (Two-sided Fisher's Exact, p=0.001). Patients with acute renal failure had a mean parasite count of 228,503/μL. compared to 125,651/μL for those without renal failure (t-test for equality of mean, not assuming equal variance p=0.042). Other documented complications include haemolytic anaemia and liver dysfunction.

Twenty-one patients (75.0%) received ventilatory support. This was done for acute respiratory distress syndrome (eight patients), acute pulmonary oedema (three patients) and acute lung injury (two patients). The rest were ventilated for acute respiratory failure secondary to septicaemic shock and deepening coma complicating cerebral malaria. The causes of acute pulmonary oedema include one case of acute heart failure (evidenced with echocardiogram) due to non-OT-myocardial infarction (not directly related to his malaria infection or treatment), one case of acute renal failure and one case of overhydration.

Treatment related complications include a case of bacterial peritonitis following peritoneal dialysis, a case perforated ascending colon requiring emergency laparatomy due to peritoneal dialysis, a case of ventilator-associated pneumonia due to *Klebsiella pneumoniae*, and one case of vocal cord damage from prolonged intubation.

The average length of hospital stay was 11.2 days with a range of one to 31 days. Surviving patients had an average length of stay of 13.1 days in comparison to 7.6 days for fatal cases. Of the 10 fatal falciparum cases, seven died early, i.e. within six days of admission with the remaining three cases occurring after 14 days. The early fatalities had initial total malaria parasite counts higher than 150,000/μL, while the two out of three late fatalities all had initial total malaria parasite counts less than 150,000/μL.

The immediate causes of death for those who died within six days of admission included disseminated

intravascular coagulopathy (four cases) and algid malaria (three cases) as opposed to those who died after 14 days of admission, where cerebral malaria (two cases) and multiple organ failure (one case) secondary to perforated bowels during peritoneal dialysis accounted for the immediate cause of death.

Twenty-seven falciparum malaria patients fulfilled the WHO criteria for severe malaria. Therefore, the severe malaria cases stand for 11.0% out of 245 falciparum malaria admissions with age above 12 years in Kuching Sarawak General Hospital. (A single case of uncomplicated falciparum malaria was admitted into ICU due to suspicion of cerebral malaria.) The mortality rate among severe malaria cases in our series was 37% (10 out of 27). The mortality rate for falciparum malaria cases for age above 12 years old in Kuching Sarawak General Hospital, a tertiary referral centre for Sarawak, is 4.1% (10 out of 245 falciparum malaria admission). (The complicated malaria cases with age below or equal to 12 years old were managed in an intensive care setting of a paediatric ward.)

Two pregnant female patients who were infected with falciparum malaria developed complication of ARDS requiring mechanical endotracheal assisted ventilation; both had survived. One of the fatal falciparum cases was a 52-year-old man who was a known case of steroid dependent nephrotic syndrome and was still on prednisolone 20 mg bd in tailing down trend before admission.

The lone fatal vivax case died on the day of admission as a result of both disseminated intravascular coaglopathy and algid malaria despite having a low initial total malaria parasite count of 32,000/μL, dropping down to 1440/μL asexual and 40/μL sexual parasite count. She also had hypoglysaemia, glucose 1.3 mmol/L, which was managed by dextrose infusion. All surviving patients recovered fully without any long term sequelae.

DISCUSSION

In this retrospective descriptive study, we identified 28 cases of falciparum malaria, two cases of vivax malaria and one case of mixed infection of falciparum and vivax malaria, who were admitted into the intensive care unit of the Sarawak General Hospital in Sarawak, Malaysia. The case records of these 31 cases were thoroughly studied to gather relevant demographic and clinical data. Unfortunately in most cases, the history of previous travel of the malaria patients were incomplete, making it impossible to analyse this aspect of demography. In view of the small size of this sample and various other factors, such as pregnancy and steroid treatment, extrapolation of the findings to other institutions have to be done with caution.

Fever with or without chill and rigor, headache abdominal pain and vomiting were the four commonest presenting complaints for our cases of falciparum malaria. This is nearly the same as reported in review article of past journal[5,9]. In view of the finding that patients with both abdominal pain and hepatomegaly had significantly higher mortality compared to other patients, further study is needed to determine whether the size of liver *per se* has any significant impact in mortality rate. The epigastric and right hypochondriac pain is probably due to the rapid stretching of the capsule of liver as a result of the acute malaria infection.

The wide range laboratory parameter demonstrated that the patients had a wide spectrum of presentation depending on the type of complications. The fatal cases, at presentation, had higher parasite counts, higher bilirubin, aminotransferase, potassium and urea levels, but lower haemoglobin and platelet counts, and more deranged coagulation profiles compared to surviving patients. Most of these findings are consistent with other studies[10,11].

Cases with parasite counts of more than 150,000/mL showed a tendency towards early mortality (within six days) after admission. The immediate causes of death were documented as disseminated intravascular coagulopathy and algid malaria whereas immediate causes of death in patients with late mortality (after 14 days of admission) included cerebral malaria and other complications.

In this series, the daily percentage of dropping parasite count did not seem to have significant impact on survival rate. Further studies are needed to determine the association between the rate of decrease in parasite counts with survival rates and whether higher rates of decrease in parasite counts might be associated with higher rates of acute haemolysis, quinine toxicity and other destructive metabolic and systemic effects.

Our study documented a high mortality rate of 35.7% for falciparum malaria cases in the ICU or 37% for severe falciparum malaria cases. The mortality rate in this series is higher than the usual documented rates of 10-20% in the literature[4,9,10,11]. Among the referred falciparum malaria cases from district hospital, the mortality rate is lower if the quinine treatment was initiated in the referring hospital. The mortality rate was documented to be higher if the antimalarial treatment was not commenced on the day of admission into hospital. Delay in initiating treatment is due to delay in diagnosis or unavailability of treatment in district hospitals, resulting in an increased mortality rate.

Ideally falciparum malaria should be diagnosed and treated as early as possible.

Cerebral malaria in adults is normally part of a multi-organ disease, with features comparable with a systemic inflammatory response syndrome[12]. Our series demonstrate higher mortality in patients with cerebral malaria and this is consistent with other studies[4,13]. Cerebral oedema was demonstrated with CT brain in one patient with cerebral malaria. This has been reported in other studies[14,15].

High parasitaemia was associated with acute renal failure in our series. Our study demonstrated that the development of acute renal failure was a poor prognostic factor[16]. It was associated with higher mortality in this small group of patients. This is consistent with findings of Trang et al[17].

It was also observed that patients with higher parasite counts had a higher tendency to develop disseminated intravascular coagulopathy (DIVC) although it was not statistically significant. Severe malaria can predispose to bacterial (especially gram negative) septicaemia[18,19]. The cases that we have seen presented in the mode of hospital acquired bacterial infection, i.e. ventilator associated pneumonia and bacterial peritonitis secondary to peritoneal dialysis.

One of the patients with vivax malaria had a fatal outcome because of DIVC and prolonged algid malaria shock while in the district hospital. Although vivax malaria are generally benign, they can and do cause death. This argues strongly against complacency in the management of cases due to "benign" strains of malaria.

In conclusion, our series demonstrated that mortality is high in complicated malaria cases. Clinicians working in Sarawak, where malaria is endemic must quickly learn to recognise and diagnose malaria speedily, and promptly institute appropriate anti-malarial therapy. There is a need to remember that during therapy we have to monitor for treatment complications, prevent them from occurring, and treat them if mortality is to be reduced.

ACKNOWLEDGEMENTS

The authors would like to thank all clinicians and staff of Intensive Care Unit and General Medical Wards who helped in managing the cases. The authors are grateful to the laboratory and radiology technicians for their kind services. The authors thank Madam Ivy Wong, Record Officer of Kuching General Hospital, and her staff who assisted in retrieving the case notes and also to Vector-borne Diseases Control Unit of Sarawak Health Department, in providing the epidemiology data.

REFERENCES

1. Vector-borne Diseases Control Unit, Sarawak Health Department (Unpublished data).
2. SPSS. SPSS Inc. 233 South Wacker Drive, 11th Floor, Chicago, Illinois 60606-6307.
3. World Health Organization. Management of uncomplicated malaria and the use of antimalarial drugs for the protection of travellers. Report of an Informal Consultation Geneva, 18-21 September 1995. WHO, MAL, 96.1075 Rev.1 1997.
4. Warrell DA, Molyneux ME, Beales PF. World Health Organization. Severe and complicated malaria. Trans Roy Soc Trop Med Hyg 1990; 84 Suppl 2:1-65.
5. World Health Organization. Management of Severe Malaria. A Practical Handbook. 2nd ed., 2000.
6. Clavier N. No evidence for cerebral hypoperfusion during cerebral malaria. Crit Care Med March 1999; 27:628-32.
7. Bernard GR, Artigas A, Brigham KL, et al. The American-European consensus conference on ARDS: Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994; 149:818-24.
8. Milne ENC, Pistolesi M, Miniati M, et al. The radiologic distinction of cardiogenic and non-cardiogenic pulmonary edema. Am J Roentgenol 1985; 144:879-94.
9. White NJ. Current concepts: the treatment of malaria. N Engl J Med 1996; 335:800-6.
10. Marsh K, Forster D, Waruiru C, et al. Indicators of life-threatening malaria in African children N Engl J Med 1995; 332:1399-404.
11. Modiano D, Sawadogo A, Pagnoni F, Sarkar S, Marsh K. Indicators of life-threatening malaria. N Engl J Med 1995; 333:1011-2.
12. Brown HC. Blood-brain barrier function in cerebral malaria and CNS infections in vietnam. Neurology 2000; 55:104-11.
13. Kochar DK. Cerebral malaria in Indian adults: a prospective study of 441 patients from Bikaner, north-west India. J Assoc Physician India 2002; 50:234-41.
14. Looareesuwan S, Warrell DA, White NJ, et al. Do patients with cerebral malaria have cerebral oedema? A computed tomography study. Lancet 1983; 434-7.
15. Patankar TF. Adult cerebral malaria: prognostic importance of imaging findings and correlation with postmortem findings. Radiology 2002; 224:811-6.
16. Barsoum RS. Malarial Acute Renal Failure. J Am Soc Nephrol 2000; 11:2147-54.
17. Trang TTM, Phu NH, Vinh H, et al. Acute renal failure in patients with severe falciparum malaria. Clin Infect Dis 1992; 15:874-80.
18. Goodall HB. Three aspects of disseminated intravascular coagulation in subtertian malaria. Trans Roy Soc Trop Med Hyg 1981; 75:884-5.
19. Bygbjerg IC, Lanng C. Septicaemia as a complication of falciparum malaria. Trans Roy Soc Trop Med Hyg 1982; 76:705.