

THE EPIDEMIOLOGY OF PATIENTS WITH SEVERE MALARIA WHO DIED AT THE HOSPITAL FOR TROPICAL DISEASES, 1991-2004

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Abstract. This study is a retrospective case series of the causes of death among patients with severe malaria. Data from the medical records of patients who were admitted to the Intensive Care Unit (ICU) of the Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand between 1991 and 2004 were analyzed. The overall hospital mortality rate was 0.2% and the ICU mortality rate was 1.8% for patients with malaria. Thirty-five patients died of malaria in the ICU during the study period, while a total of 1,866 patients were treated for malaria in the ICU during the study period. The most common complication of malaria was cerebral malaria (77.1%). The socioeconomic and demographic characteristics of those who died are examined here, as well as the cost of their treatment.

INTRODUCTION

Malaria is a leading cause of morbidity and mortality worldwide, especially in developing countries. Every year malaria affects more than 200 million people worldwide, and it is estimated there are more than 1-2 million malaria related deaths annually (Storochler, 1989; Thomson and Connor, 2001). Forty percent of the world's population are at risk for getting malaria (WHO, 2005).

There were 424 reported deaths attributed to malaria in Thailand during the year 2001, out of a total of 63,528 cases. *Plasmodium falciparum* accounted for 29,061 cases (45.8%), with a case-fatality rate of 1.5% (Singhasivanon *et al*, 2003).

The aim of this retrospective case-series study was to evaluate the characteristics of pa-

tients who died due to severe malaria in the ICU at the Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand from 1991 to 2004. This study describes the epidemiological, demographic and geographic characteristics of 35 patients who died as a result of complicated malaria. The complications of these patients are summarized, as well as the financial cost of caring for these patients. Finally, a simple comparison is made between these patients and the 1,866 patients admitted to the ICU with severe malaria during the same time period who did not die to identify characteristics associated with death and to develop a profile for high-risk malaria patients.

MATERIALS AND METHODS

This study was conducted intermittently from 2002 to 2004 at the intensive care unit (ICU) of the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. Approval for the study was obtained from the Ethics Committee, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

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Hospital records for all malaria patients who were admitted to, and died in, the ICU between May 1991 and September 2004 were reviewed. The records were compiled by the ICU and the medical records unit based on data routinely collected on all ICU patients. Data collected on each patient who died included: age, sex, marital status, nationality, occupation, socioeconomic status, site of infection, length of hospital admission, initial parasitemia, initial diagnosis, treatment (including anti-malarials), complications and cost of care. Some results from laboratory tests and some data on signs and symptoms, such as splenomegaly and vomiting, were also available.

Patients were considered to be suffering from the complications of malaria if they satisfied the criteria for the systemic complications of malaria as set by the WHO (1990) as shown in Table 1. All patients who met any of these criteria were admitted to the ICU. All cases referred from other hospitals and patients with circulating schizonts were also admitted to the ICU.

Data from patients with malaria who were admitted to the ICU, and did not die, were com-

pared with data from patients with malaria who died, to look for any significant patterns unique to those who died. The specific categories compared included: age, sex, province, occupation, parasite count, jaundice, shock, presence of schizonts, HIV status, presence of acute renal failure, hypoalbuminemia, and reduced serum bicarbonate level.

Data were summarized and analyzed by SPSS (version 7.5) for Windows[®]; the means and standard deviations were calculated. The level of significance was set at $p < 0.05$.

RESULTS

Thirty-five (35) patients with falciparum malaria died at the Hospital for Tropical Diseases in the ICU from 1991 to 2004. During this same period of time 1,866 patients, who did not die, were treated for malaria in the ICU. Fig 1 shows the annual malaria mortality rate during the study period. There were 23 males (66%) and 12 females (34%), a male to female ratio of about 2:1.

Of the 1,866 patients admitted to the ICU who did not die, there were 1,329 males (71%)

Table 1
Criteria for severe manifestations and complications of malaria (WHO 1990).

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- Cerebral malaria (unarrousable coma not attributable to any other cause)
 - Severe normocytic anemia (hematocrit <15% or hemoglobin <5g/dl)
 - Acute renal failure [urine output <400 ml/24 hours in adults; <12 ml/kg/24 hours in children; failure to improve after rehydration; serum creatinine >265 μ mol/l (3 mg/dl)]
 - Pulmonary edema or adult respiratory distress syndrome
 - Hypoglycemia [whole blood glucose <2.2 mmol/l (40 mg/dl)]
 - Circulatory collapse, shock: hypotension (systolic BP <50 mmHg in children 1-5 years old; <70 mmHg in adults); cold, clammy skin or core/peripheral skin temperature difference >10°C
 - Spontaneous bleeding or disseminated intravascular coagulation (DIC)
 - Repeated general convulsions
 - Acidemia (arterial pH <7.25) or acidosis (plasma bicarbonate <15 mmol/l)
 - Macroscopic hemoglobinuria
 - Postmortem confirmation of diagnosis.

Other manifestations of severe malaria which do not, in themselves, define the condition in all geographic areas and age groups, include:

- Impaired consciousness (but arousable)
 - Prostration or extreme weakness
 - Hyperparasitemia
 - Jaundice [serum bilirubin >50 μ mol/l (3 mg/dl)]
 - Hyperpyrexia (rectal temperature >40°C in adults and children)
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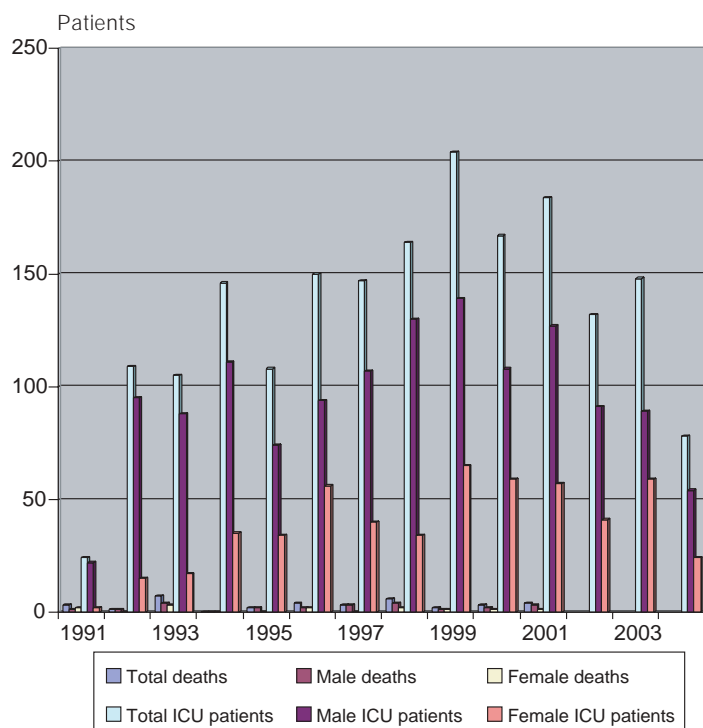


Fig 1—Total ICU patients and deaths.

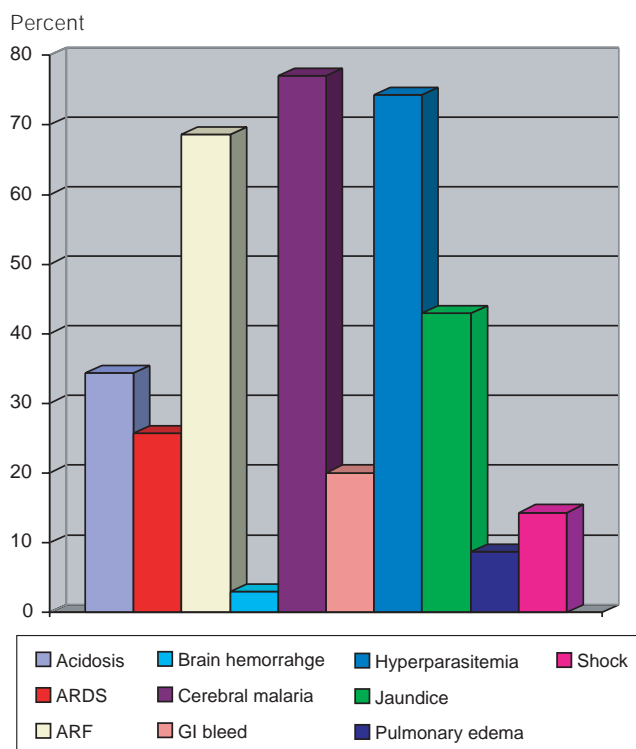


Fig 2—Complications of severe malaria in the ICU at the Hospital for Tropical Disease, 1991-2004.

and 537 females (29%) (Fig 1). There was no significant difference in male to female ratios between fatal and non-fatal cases ($p > 0.5$).

The socioeconomic characteristics of those who died are shown in Table 2. Most of the patients had contracted their malaria in Central Thailand. Three of the patients had been infected along the borders (Lao PDR 2.9%, Myanmar 5.7%). The majority of the patients were Thai nationals (62.9%).

The mean length of time from admission to death was 3.3 days ($SD \pm 3.0$ days). The longest period of hospitalization was 12 days. The cost for admission and treatment varied greatly, from 7,900 to 193,600 baht (US\$1.00=41.00 baht). The mean cost per hospital stay was 35,175.86 baht ($SD \pm 36,082.60$ baht).

The complications of malaria in these patients are shown in Fig 2. In many of the cases the patients suffered from more than one complication. The most common complication was cerebral malaria (77.1%), followed by hyperparasitemia (74.3%), acute renal failure (68.6%), jaundice (42.9%), and acidosis (34.3%).

DISCUSSION

This study aimed to establish the causes of malaria-related deaths that occurred in the ICU at the Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand. A variety of possible risk factors for death were assessed, including clinical complications, medical treatment, nursing care, and the patients' demographic, geographic and socioeconomic backgrounds. The financial cost of treatment for each of the patients was also calculated.

From 1991 to 2004, a total of 1,866 patients were admitted to the

Table 2
The socioeconomic and demographic characteristics of the 35 patients who died of malaria.

Characteristic	Number	Percent
Sex		
Male	23	65.7
Female	12	34.3
Age in years		
<20	4	11.4
21-40	19	54.3
41-60	9	25.7
61-80	3	8.6
>80	0	0
(Mean age=37 years; SD=±15.3)		
Employment		
Employed	5	14.3
Unemployed	30	85.7
Occupation		
Laborer	21	60.0
Civil/government	5	14.3
Housewife	5	14.3
Farmer	1	2.9
Businessman	2	5.7
Monk	1	2.9
Place of infection		
East Thailand	4	11.4
Northeast Thailand	1	2.9
North Thailand	4	11.4
Central Thailand	23	65.7
Lao PDR	1	2.9
Myanmar	2	5.7
Nationality/Ethnicity		
Thai	22	62.9
Mon	11	31.4
Burmese	1	2.9
Karen	1	2.9

ICU with severe malaria. Only 35 patients died, giving an ICU mortality rate for malaria patients of only 1.8%. From 1991 to 2001 at total of 15,822 patients were admitted to the Hospital for Tropical Diseases with a diagnosis of malaria. Therefore, the overall hospital mortality rate for malaria is only 0.2%. These hospital and ICU mortality rates are significantly lower than that reported by other researchers. Luxemburger *et al* (1997) working in the Shoklo refugee camp in Northwest Thailand documented a hospital mortality rate of 3.0%. The mortality rates at the

Hospital for Tropical Diseases in Bangkok and the Shoklo camp are lower than the national average. Shoklo is a research center, and the ICU at the Hospital for Tropical Diseases in Bangkok is a tertiary level malaria care center. Both places are specially equipped to manage critical malaria patients and their complications.

Harbarth *et al* (1997) found that the complications of severe malaria, rather than the malaria itself, were the cause of death for most patients. These complications included cerebral malaria, acute renal failure, severe anemia, disseminated intravascular coagulation and pulmonary involvement (ARDS).

Several studies (Nguyen *et al*, 1993; Lobovska *et al*, 1999) have shown that the death of malaria patients is secondary to multiple organ failure. It follows that the reduction of complications is a precursor to the reduction of mortality; if complications can be prevented or adequately treated, then deaths can be avoided. The treatment and nursing care of patients with, or at risk for, severe malaria should be planned and regularly reviewed. It is vital that correct antimalarial treatment be instituted promptly and at correct dosages. Delayed or ineffective treatment is likely to allow an increase in the parasite load, which can overwhelm the immune response. Vigilant monitoring of the patient's progress is important. Complications can be detected early or prevented. The lower mortality rates in the Hospital for Tropical Diseases show that early and correct treatment, along with careful monitoring can result in improved survival.

Our study identified a number of demographic, geographic, and socioeconomic determinants of mortality. Patients who contracted malaria in a non-endemic region of Thailand (the Central Region) were more likely to suffer from complications. Of the patients from this region, 77.1% went on to develop cerebral malaria and 68.8% developed acute renal failure. This suggests either a lack of immunity and/or a delay in diagnosis and treatment. Patients from Northwest Thailand, an endemic area, fared better. The overall mortality rate of 2.9% for this region reflects natural immunity and prompt diagnosis and management of malaria. Of the 35 patients who died from severe malaria, 62.9% were Thai and

the rest were of Burmese extraction: Mon (31.4%), Karen (2.5%), and other ethnic Burmese (2.9%). The vast majority contracted malaria in and around the central region of Thailand (65.7%). Very few contracted malaria in the endemic Northeast (2.9%).

Most of those who died were men, and the average age of death was 37 years old (range 16-71 years). Most were unemployed (85.7%). Of those who worked (14.3%), the majority were laborers (60%) or agricultural workers (29%). It is possible that poorly paid workers, whose outdoor occupations put them at increased risk for mosquito bites, delayed going to the doctor due to fear of the cost of diagnosis and treatment (Chuna *et al*, 2001). The education of manual workers is limited, which may have lead to overlooking the early symptoms of malaria.

The mean cost of care for each patient was 35,175.86 baht (range: 7,920-193,600 baht). The high cost was due to the need for intensive monitoring, nursing care, a wide range of pathology tests and the implementation of special supportive therapy, including hemodialysis and ventilation.

In conclusion, the prognosis of those with severe malaria is largely dependent on the complications of the disease and their prevention and management. Awareness of and prompt responses to the complications of malaria are as important as an accurate diagnosis and effective treatment.

ACKNOWLEDGEMENTS

We would like to thank Dr Nick Walters, volunteer at the Hospital for Tropical Diseases,

Faculty of Tropical Medicine, Mahidol University, Bangkok for his help with this paper.

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