Falciparum malaria in a South African Tertiary Care Hospital

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Abstract: Introduction. This study was a retrospective case series over one year. **Objectives.** The purpose was to review the clinical presentation, travel history, laboratory findings and outcome of *Plasmodium falciparum* malaria. **Patients and methods.** The study was conducted in the medical wards of Dr. George Mukhari Hospital, a teaching hospital in South Africa that serves mainly black patients. Fifty-nine patients were evaluated. The mean age was 34 years. Twenty-three patients (39%) had strictly defined severe malaria. Ninety-eight percent acquired *Plasmodium falciparum* in Sub-Saharan Africa. The death rate was 1.7%. Virtually all patients had a travel history obtained in the emergency department and the diagnosis was confirmed in all cases within 24 hours of admission. **Results.** In our study population, the differences in the percent parasitemia, platelet count, haemoglobin and bilirubin were not statistically significant between the cases with severe and those with less severe malaria. **Conclusions.** *Plasmodium falciparum* malaria should not carry a high mortality in adequately equipped centers, when the diagnosis is made early and therapy is instituted promptly.

Key words: malaria, mortality, tertiary centre

INTRODUCTION

Malaria remains a major public health problem, with approximately 1–3 million deaths each year [1]. *Plasmodium falciparum* malaria is the most severe type and is responsible for almost all the complications and deaths related to malaria [2]. Tropical African countries are estimated to contribute more than 90% of the total malaria incidence [2]. In Europe as well as other industrialized non-endemic areas, imported malaria remains a growing problem, with approximately 16,000 cases diagnosed in Europe annually [3]. The diagnosis is generally made in returning travellers, military personnel and immigrants from endemic countries.

Hospital-based data indicates that deaths from severe falciparum malaria vary 10–40% depending on the time-lag between initial symptoms and effective treatment, and hospital facilities for the management of complications [4,5].

In the management of malaria, early presentation to a health care facility, early and accurate diagnosis and early treatment with effective antimalarial drugs are fundamental components of strategy.

This study was undertaken to review the travel history, clinical presentation, laboratory findings and outcome of falciparum malaria in adults admitted to the medical wards of a teaching hospital.

PATIENTS AND METHODS

The study was performed in the medical wards of a 1500-bed University – affiliated teaching hospital. Patients who were admitted with a diagnosis of *P. falciparum* malaria between January 1, 2005 and December 31, 2005 were retrospectively evaluated. Fifty-nine cases of falciparum malaria were identified through review of the parasitology log reports, and medical records were available for all. Information obtained from the hospital records was used to complete a standardised case report form for each malaria episode. This medical centre serves a predominantly black South African community. From the medical records, we abstracted information on demographics, travel history, clinical presentation, laboratory findings and outcome. Falciparum malaria was classified as severe if one or more of the World Health Organization (WHO) major criteria (2000) were present at admission.

Laboratory methods

The initial evaluation of the patients involved the use of the rapid antigen detection test (ICT Malaria Pf – ICT DIAGNOSTICS), and the diagnosis of falciparum malaria

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Table 1. Symptoms at presentation

Symptoms	Number of patients	95% CI	
		UL	LL
Fever	55	58	49
Rigor	38	45	30
Headache	49	54	42
Confusion	5	11	2
Malaise	42	49	34
Diarrhoea	13	21	7
Vomiting	27	35	19
Nausea	20	28	13
Cough	2		
Photophobia	7		
Chest pain	2		
Abdominal pain	3		
General pain	1		
Dizziness	10		
Rash	1		
Dyspnoea	1		
Hematuria	1		
Pruritis	1		

LL – lower limit, UL – upper limit

was confirmed by microscopic examination of stained thick and thin blood films (Giemsa at pH 7.2).

Statistical analysis was performed with MS Excel. Comparisons were done using the Student t-test for continuous variables. Mortality as a variable was not analysed for related factors because the number of non-survivors was small.

RESULTS

Fifty-nine patients (mean age 34.8 ±10.7 years) were admitted to the medical wards for *Plasmodium falciparum* malaria infection during the study period. The gender distribution showed a male predominance (76%). Ninety-seven percent of the patients were self-referred. All but 2 patients had a recent (one month or less) history of travel to a malaria endemic area. Ninety-eight percent of the patients acquired *P. falciparum* malaria in Sub-Saharan Africa (Fig.). Travel history was obtained in the emergency care department in 95% of the cases. The mortality rate was 1.7%.

The initial clinical features and laboratory findings are summarised in Tables 1 and 2, respectively. Fever, headache and malaise were the most common symptoms documented on the day of admission. The mean duration of symptoms prior to presentation at the emergency department was 4.5 ±3.4 days. In all the cases the diagnosis was confirmed within 24 hours of admission. None of the patients appear to have had superimposed secondary bacterial infections.

Table 2. Laboratory findings

Parameter	Mean ±SD	Min.	Max.
Platelets (10^9/l)	81.78 ±47.53	25	169
Hemoglobin (g/dl)	11.26 ±2.69	3.8	18
Bilirubin (total) (mmol/l)	40.64 ±27.90	20	125
Parasitemia (%)	4.33 ±5.24	0.9	33

Table 3. Laboratory findings

Parameter	Severe malaria (n = 23)	Less severe (n = 36)	p
Platelets (10^9/l)	82.82 ±38.38	81.09 ±53.34	0.896
Hemoglobin (g/dl)	11.78 ±2.56	10.92 ±2.76	0.252
Bilirubin (total) (mmol/l)	35.10 ±16.13	44.66 ±33.72	0.190
Parasitemia (%)	4.19 ±5.75	4.41 ±4.98	0.875

Twenty-three patients (39%) met the WHO (2000) criteria for severe malaria. The WHO major defining criteria in these patients were: jaundice (n = 10), severe anemia (n = 2), renal failure (n = 5), coma (n = 4), ≥4% parasitemia (n = 15), respiratory failure (n = 2). Eight patients had at least 2 major criteria and three had at least 3 criteria. A comparison of the mean values of the platelet count, hemoglobin, total billirubin and percentage parasitemia revealed no statistically significant differences between patients with severe and those with less severe malaria (Tab. 3).

Serology for the human immunodeficiency virus was performed in one patient and was found to be non-reactive.

All patients were treated with quinine sulphate (650 mg 8 hourly) and doxycycline (100 mg bid) for 7 days. The mean time from symptom onset to antimalaria therapy initiation was 4.5 ±3.4 days. Two patients required, in addition to the standard antimalaria therapy, transfusion of blood products: one received three units of packed red cells for severe anemia (hemoglobin of 3.8 g/dl) and the other a mega unit of platelets for a platelet count of 19×10^9/l. Three patients were admitted to the intensive care unit and two of these required ventilatry support. The mean length of stay in the intensive care unit was 3 ±3.5 days. Two patients required renal replacement therapy in the form of intermittent hemodialysis. No patient underwent exchange transfusion.

DISCUSSION

Mortality among adults with severe falciparum malaria treated by highly trained teams ranges 10–25% [6,7]. The death rate has not decreased during the past two decades despite numerous therapeutic approaches. Mortali-

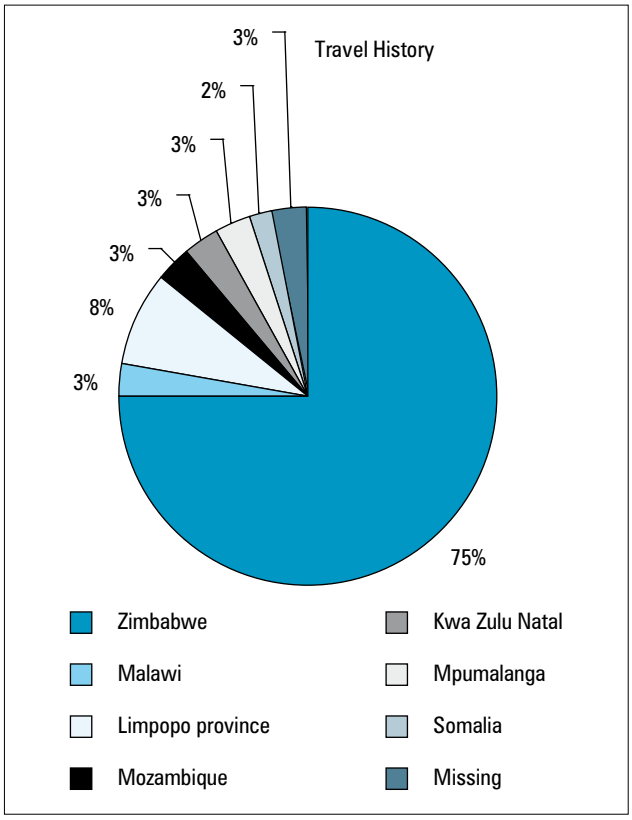

Fig. Travel history

ty from *P. Falciparum* malaria in this study was comparatively low (1.7%). The case fatality rate of cases of severe and complicated malaria managed at the King Edward VIII hospital, South Africa, was 11.1% [8]. In this study, the mean duration of symptoms before presentation was 8 days and chloroquine was the most frequently used antimalarial agent.

Whiles the average case fatality rate of imported malaria is reported at around 1%, severe imported malaria appears to still have a relatively high mortality [7,9,10].

In our view, the low case fatality rate in this study was due to: early diagnosis, early institution of potent antimalarial therapy and availability of appropriate facilities. The diagnosis of malaria was established in the emergency care department in 95% of the cases, with the result that effective antimalaria therapy was commenced timeously. Misdiagnosis of malaria is said to be frequent, and to contribute to increased mortality [11,12]. One of the possible reasons for the frequent misdiagnoses is the non-specific nature of the clinical features of malaria. The frequent occurrence of gastrointestinal symptoms in patients with malaria has also been cited to be responsible for the failure to diagnose malaria early, as they have the potential to divert the unwary clinician from the correct diagnosis [13]. Travel history was elicited in all but 2 cases. Failure of the physician to obtain or properly consider the patient's travel history could be one of the factors responsible for the frequency of misdiagnoses of malaria [13].

All patients received a combination of intravenous quinine and doxycyline. The effectiveness of quinine for severe falciparum malaria is well-known [5]. Artemisinin derivatives are alternatives and have been widely used in Asia. Parasite and fever clearance times may be significantly more rapid with this group of agents [14]. A recent meta-analyses suggested that artesunate may be superior to quinine in the treatment of severe malaria [15]. Other studies found artemeter to be similar to quinine with regards to mortality and coma resolution times, but superior in terms of overall serious adverse events [16]. Artemisinin derivatives have been shown to be equally effective when administered rectally or intramuscularly, making them useful alternatives in patients who cannot take orally or where intravenous therapy is delayed [17,18].

Exchange transfusion was not performed in any of our patients. This technique has been suggested for the treatment of severe malaria in patients with high parasite counts, although no well-designed, prospective controlled studies of its use in this setting are available. A recent meta-analysis suggested lack of survival benefit for patients treated with adjunct exchange transfusion [19].

Some limitations of this study need to be considered. Information on the use of chemoprophylaxis and the degree of immunity to malaria were not studied. Prior chemoprophylaxis has been associated with a reduction in the severity of falciparum malaria [20]. Severe malaria tends to be common in non-immune individuals, whereas partially – or semi-immune patients tend to have a lower risk of severe malaria and a better prognosis [21]. The possibility that these two factors either singly or in combination contributed to the low mortality observed in this study cannot be ruled out.

Plasmodium falciparum malaria infection should not carry a high mortality when treated under optimal conditions in a tertiary care centre. A high index of suspicion is required as the presenting features can mimic many infections. Elicitation of the patients' travel history is vital as it may alert the clinician to the possibility of malaria and allow for an early diagnosis. Travellers should be sensitized to the risk of malaria, and advised to pay attention to the malaria prevention methods.

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