*Original Report*

# Imported Malaria in a Singapore Hospital: Clinical Presentation and Outcome

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**ABSTRACT**

*Objective:* To evaluate the clinical presentation and outcome of imported malaria.

*Methods:* A retrospective chart review was conducted of patients with imported malaria admitted to the Communicable Disease Centre (CDC), Singapore (a 130-bed tertiary referral center) from January 1992 to December 1993. An imported case was defined as a smear-positive infection that was acquired in another country.

*Results:* Among 200 malaria patients hospitalized at CDC, 168 imported cases (137 males and 31 females, 131 nonresidents and 37 residents) were studied. The mean age was 31.6 ± 10.5 years. The countries visited were India (49.4%), Indonesia (16.7%), and Bangladesh (13%). Five patients had chemoprophylaxis and 36 patients had experienced previous malaria infection. The predominant symptoms were fever (97.6%), chills (79.2%), and rigors (67.9%). Hepatomegaly was detected in 56 (33.3%) and splenomegaly in 49 patients (29.2%). *Plasmodium vivax* was present in 132 patients, *Plasmodium falciparum* in 29, and mixed *P. vivax* and *P. falciparum* in 7 patients. Parasitemia ranged from 0.1% to 8.0%. Of the vivax cases, 130 were treated with chloroquine, followed by primaquine in 123 patients. Quinine was given to 36 patients (29 falciparum malaria and 7 mixed infections). Median time to fever defervescence was 2 days. Complications occurred in three patients (2 with shock and 1 with pulmonary edema). According to World Health Organization gravity criteria, body temperature over 40°C was detected in six patients, bilirubinemia higher than 50 μmol/L in nine, parasitemia over 5% in five, glycemia less than 2.2 mmol/L in two patients. There were five relapses. No death was recorded.

*Conclusion: Plasmodium vivax* is the most common cause of imported malaria, with the majority acquired from the Indian subcontinent. Only a few patients presented with severe malaria.

Key Words: *chemoprophylaxis, imported,* P. falciparum, P. vivax

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Malaria still remains a leading cause of morbidity and mortality in the developing world.[1] The increasing movement of travellers from developed countries to the malaria endemic tropical countries and the migration of workers from malaria endemic countries to the industrialized countries are responsible for the emergence of imported malaria.[2] Malaria may pose a diagnostic challenge to the physician who does not have experience with the disease. These cases also pose a therapeutic challenge because of the emergence of multiple-drug-resistant *Plasmodium falciparum* in Southeast Asia.[3] Malaria is now primarily an imported disease in Singapore. A total of 221 cases were reported in 1992 and 354 cases in 1993 of which 100% and 82% were imported, respectively. There were two local outbreaks of vivax malaria in 1993, originating from imported cases.[4]

The objective of the present study was to evaluate the clinical presentation and outcome of imported malaria at the Communicable Disease Centre (CDC), Ministry of Health, Singapore.

## PATIENTS AND METHODS

The Communicable Disease Centre, a 130-bed hospital, is the only tertiary referral center for infectious diseases in Singapore. Medical records were retrospectively analyzed of all patients with imported malaria admitted to the CDC from January 1992 to December 1993. The patients were located from a computerized database of medical records that were analyzed for travel history, chemoprophylaxis use, clinical features, species of *Plasmodium* detected, complications, treatment, and outcome.

An imported case of malaria was defined as a smear-positive infection that was acquired in another country. Severe malaria was defined according to the World Health

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Organization (WHO) criteria.[5] The time to fever defervescence was defined as the interval from initiation of appropriate antimalarial treatment until the documentation of normal body temperature for more than 24 hours. Significance testing between groups was done where applicable with Fisher's exact test.

## RESULTS

Of 200 patients with smear-positive malaria admitted to CDC during the 2-year study period, 168 (84%) fulfilled the definition of imported malaria and were included in the analyses.

There were 137 male and 31 female patients (male-to-female ratio 4.4:1). The mean age was 31.6 ± 10.5 years (range, 3–70 y). The 168 patients studied included 37 (22%) local residents and 131 (78%) foreigners, consisting of tourists and nonimmigrant foreign workers (Table 1).

Four patients had underlying medical conditions: two had diabetes mellitus, one had hypertension, and one had ischemic heart disease. Chemoprophylaxis was used by five patients, three of whom developed vivax, and two falciparum malaria. Most of the infections were acquired in India (49.4%), followed by Indonesia (16.7%), Bangladesh (13%), Thailand (7.7%), and Sri Lanka (5.4%) (see Table 1).

Table 2 presents the clinical features of the patients at presentation. The predominant symptoms were fever, chills, and rigors. Hepatomegaly and splenomegaly were the predominant signs. A majority of the patients reported fever of 2 to 7 days duration. At presentation, 100 (59.5%) patients were thrombocytopenic (i.e., platelets <150,000/mm$^3$) and 63 (37.5%) were anemic (Hb <12 g/dL).

*Plasmodium vivax* was detected in 132 cases, *P. falciparum* in 29 cases and mixed infection (*P. vivax* and *P. falciparum*) in 7 cases. Parasitemia ranged from 0.1% to 8.0%. Five (3%) patients had parasitemia over 5%.

**Table 1.** Epidemiologic Characteristics of Imported Malaria

| *Characteristic* | *Number of Patients n = 168 (%)* |
|---|---|
| Population group | |
| Local residents | 37 (22) |
| Foreigners | 131 (78) |
| Country of origin | |
| India | 83 (49.4) |
| Indonesia | 28 (16.7) |
| Bangladesh | 22 (13.0) |
| Thailand | 13 (7.7) |
| Sri Lanka | 9 (5.4) |
| Philippines | 4 (2.4) |
| Africa | 4 (2.4) |
| Others | 5 (3.0) |
| Chemoprophylaxis | |
| Received chemoprophylaxis | 5 (3.0) |
| None | 162 (96.4) |
| Unknown | 1 (0.6) |
| Previous history of malaria | 36 |

**Table 2.** Clinical and Laboratory Findings at Presentation in Patients with Imported Malaria

| *Findings* | *Number of Patients n = 168 (%)* |
|---|---|
| Clinical symptoms | |
| Fever | 164 (97.6) |
| Chills | 133 (79.2) |
| Rigors | 114 (67.9) |
| Arthralgia | 13 (7.7) |
| Diarrhea | 11 (6.5) |
| Abdominal pain | 11 (6.5) |
| Clinical signs | |
| Hepatomegaly | 56 (33.3) |
| Splenomegaly | 49 (29.2) |
| Pallor | 29 (17.3) |
| Jaundice | 15 (8.9) |
| Laboratory | |
| Thrombocytopenia | |
| < 150,000 / mm$^3$ | 100 (59.5) |
| < 50,000 / mm$^3$ | 32 (19.0) |
| Leukopenia | |
| < 3500 / mm$^3$ | 10 (6.0) |
| Anemia | |
| < 12 g/dL | 63 (37.5) |
| Hypoglycemia | |
| < 3.6 mmol/L | 5 (3.0) |
| Urea | |
| > 7 mmol/L | 29 (17.3) |
| Creatinine | |
| > 140 μmol/L | 4 (2.4) |

Chloroquine was administered to 130 patients with vivax malaria; of these, 123 patients received additional primaquine. Quinine was given to 36 patients (29 with falciparum malaria and 7 with mixed infections), sulfadoxine-pyrimethamine and mefloquine each were

**Table 3.** Therapy and Outcome in 168 Patients with Imported Malaria

| *Therapy or Outcome* | *Number of Patients n = 168 (%)* |
|---|---|
| Antimalarial therapy | |
| Chloroquine | 7 (4.2) |
| Chloroquine + primaquine | 123 (73.2) |
| Sulfadoxine-pyrimethamine | 1 (0.6) |
| Mefloquine | 1 (0.6) |
| Quinine (including 3 with additional doxycycline and 14 with additional tetracycline) | 36 (21.4) |
| Days to fever defervescence (median) | 2 |
| Complications | |
| Shock | 2 (1.2) |
| Pulmonary edema | 1 (0.6) |
| Outcome | |
| Cure | 162 (96.4) |
| Relapse | 5 (3.0) |
| Death | 0 |
| WHO gravity criteria: | |
| Body temperature > 40°C | 6 (3.6) |
| Bilirubinemia > 50 μmol/L | 9 (5.4) |
| Parasitemia > 5% | 5 (3.0) |
| Consciousness impairment | 0 |
| Systolic blood pressure < 70 mmHg | 0 |
| Hypoglycemia < 2.2 mmol/L | 2 (1.2) |
| Hemoglobin < 5 g/dL | 0 |
| Renal failure (serum creatinine > 140 μmol/L) | 4 (2.4) |

administered to one patient (Table 3). None required exchange transfusion.

All patients recovered and no death was recorded. Five patients with vivax malaria suffered relapse, two of whom had been noncompliant with primaquine treatment. The mean time to fever defervescence was 2 days. Of the three patients who developed complications, one of the two patients with shock and the only patient with pulmonary edema had falciparum malaria (see Table 3).

According to the WHO gravity criteria, body temperature over 40°C was detected in six patients, bilirubinemia over 50 μmol/L in nine, parasitemia over 50% in five, glycemia less than 2.2 mmol/L in two patients, and serum creatinine over 140 μmol/L in four patients (see Table 3).[5]

## DISCUSSION

In spite of vigorous efforts to eradicate malaria, there are about 300 to 500 million cases reported yearly, with 80% of these occurring in sub-Saharan Africa.[6] Imported malaria commonly is diagnosed in other industrialized countries that, like Singapore, have had successful malaria eradication programs.[7,8]

Malaria is a notifiable infectious disease in Singapore, where it is usually an imported disease occurring in Singaporeans who visit or work in endemic areas and in nonimmigrant foreign workers, mainly from Indonesia and the Indian subcontinent.

In this study, there were 200 patients with smear-positive malaria admitted to the CDC in 1992 and 1993, in whom 84% of cases were imported. This accounts for 35% of total malaria cases and conforms to the average of 90 to 95% imported malaria cases reported in Singapore during the 2-year study period.

Chemoprophylaxis was used in only five patients; 97% of patients travelled without chemoprophylaxis. It has been suggested that chemoprophylaxis has been associated with less frequent severe malaria and lower parasitemia.[9,10] Foreign workers as a group are less likely to take necessary preventive measures for visits to their countries of origin. More attention should be devoted to Singaporean travellers when promoting the importance of malaria prevention. The majority of individuals reported travel to India, Indonesia, and Bangladesh. This reflects the country of origin of many nonimmigrant foreign workers in Singapore and the high incidence of malaria transmission throughout Asia. Indeed the risk of infection is highest in India, calculated to be 1:1900 travellers as compared to 1:4000 for Southeast Asia.[11]

The frequency of clinical symptoms in the present study is consistent with findings in various studies except for a lower frequency of gastrointestinal symptoms.[12,13] Hepatomegaly and splenomegaly were the major physical findings. About 60% of patients were thrombocytopenic. Thrombocytopenia also has been noted frequently in previous studies.[12,13]

*Plasmodium vivax* was the species most often identified (78.5%) in the present study. Other studies have noted an increase in falciparum malaria in recent years.[13,14] These differences can be explained by the prevailing destination of travel. Most cases of *P. vivax* in this study originated in Asia, which is the preferred destination of the Singapore traveller, whereas in the other studies, the falciparum infection was acquired in Africa.

Falciparum malaria is known to cause more serious illness, with symptoms varying from a mild flu-like illness to severe hemolysis and multiorgan failure. All five patients with parasitemia over 5% and three of the four patients with raised serum creatinine (> 140 μmol/L) had falciparum malaria. Parasitemia appears to be a reliable prognostic factor.

Complications were detected in three patients, namely shock and pulmonary edema. Cerebral malaria did not occur in this series, and no death was recorded. Only a few of the patients presented with severe malaria, which probably explains the absence of fatality. Other studies report a fatality rate around 1%.[15,16]

The majority of patients with vivax malaria were treated with chloroquine and primaquine. Quinine in combination with tetracycline was the main antimalarial treatment for falciparum malaria. In the follow-up of 107 patients at 4 weeks, relapses were detected in five patients with vivax malaria. Only two of these five patients required re-admission for treatment. Travellers to malaria endemic areas should receive malaria prophylaxis, and patients with malaria should receive adequate treatment according to the drug-resistance patterns in that region.

## CONCLUSIONS

This study has defined the characteristics of imported malaria in Singapore. *Plasmodium vivax* is the most common cause of imported malaria, with the majority of cases acquired from the Indian subcontinent. Singapore is both vulnerable and receptive to the re-introduction of malaria because of the constant influx of travellers and foreign workers and the presence of the *Anopheles* vector. It is vital that pre-travel advice on pre-exposure chemoprophylaxis and personal protection measures be provided, especially to travellers visiting the Indian subcontinent, since malaria is, to a large extent, a preventable disease.

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