MALARIA: AN AUDIT OF 56 CASES ADMITTED TO A HOSPITAL

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ABSTRACT

A 2-year prospective audit on the profile and outcome of malaria cases admitted to a general hospital was performed. Fifty-six cases were seen from January 1991 to December 1992, 52 of which were due to monoinfections with Plasmodium vivax. The main presenting complaints were fever, chills, sweats, myalgia, dry cough and headache. A significant percentage had anaemia (64.3%), thrombocytopaenia (57.1%), hyponatraemia (42.9%), and liver dysfunction (44.7%). Diagnosis rests on the demonstration of parasites in stained peripheral blood smears. None of the patients developed major complications. A high index of suspicion of malaria must be maintained in the medical evaluation of all patients and in particular, of returning travellers.

Keywords: *malaria, parasites, demography, blood film, chemoprophylaxis*

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INTRODUCTION

Imported malaria is an increasing problem throughout the western world. Over 2,000 cases of malaria are reported in the UK every year[1]; in the United States, malaria is primarily acquired by immigrants and travellers who visit endemic areas. Approximately 1,000 cases per year were reported to the Centers for Disease Control from 1987-1991, although the actual number of cases may be significantly higher[2]. In Singapore, the reported incidence of imported malaria among foreign workers has been increasing from 25 cases in 1989 to 116 cases in 1993[3]. However, localised outbreaks have also occurred in 1993 and 1994, despite well established disease and vector surveillance systems and epidemic control measures to ensure a malaria-free status in the country.

This prospective study looked at the demographic profile, clinical features and outcome of 56 patients with a parasitological diagnosis of malaria admitted to the Alexandra Hospital over a two-year period from Jan 1991 - Dec 1992. The study was not intended to influence the investigation or management of suspected or confirmed cases of malaria admitted to hospital. An analysis of the cost-expenditure involved in treating malaria will be presented in a subsequent paper.

PATIENTS AND METHODS

All patients with malaria confirmed on peripheral blood film were included into the 2-year prospective study, which was carried out between Jan 1991 and Dec 1992. Altogether 56 cases were documented and studied. The main purpose was to record the profile and outcome of the typical patient with malaria who seeks treatment at hospital. No cases of transfusion-induced malaria or malaria associated with intravenous drug abuse were seen during the study period.

Details of patients' background, nationality, period of residence in Singapore, travel history, clinical presentation, physical signs, method of diagnosis, laboratory investigations performed and their results, duration of hospitalisation and outcome of treatment were documented into a standard 2-page survey questionnaire. This was reviewed and updated in all cases before discharge of the patient from hospital. Altogether 50 items were recorded for each individual patient entered into the malaria study. All subjects throughout the course of their hospital stay had laboratory investigations for haemoglobin, white cell count and platelets, blood films for malarial parasites, urea and creatinine, sodium, potassium and blood sugar level. Liver function tests and blood cultures were performed in the majority of patients. Additionally, where relevant, coagulation studies, bacterial investigation of stool or urine and dengue or hepatitis serologies were also performed.

The presenting complaints of all patients were also carefully charted. Particular attention was directed at whether there was a history of fever, chills or sweats, malaise, headache, nausea or vomiting and any symptoms referrable to the central nervous system (eg. drowsiness, fits, etc.). The clinical signs to which particular attention were directed were: temperature on admission, maximum temperature recorded during hospitalisation, pallor, jaundice, blood pressure on admission to the ward, hepatomegaly, splenomegaly, and the presence of central nervous system manifestations such as delirium. The duration of hospitalisation (within this hospital) and the response to treatment were recorded. The response to therapy was documented both in terms of the number of days it took before fever subsided and the number of days for the blood film to become negative for the malarial parasite.

RESULTS

A total of 56 cases were recorded over the two-year study period. Of these, 49 patients were male, 7 female. Ages of the patients ranged from 18 to 72 years, with a mean of 30 years (Table I). Forty-four patients were foreigners who were either working or residing in Singapore, with 8 from Bangladesh, 24 from India, 4 from Thailand, 2 from Sri Lanka, 3 from Burma, 2 from Malaysia and one from Indonesia. Forty patients gave a history of recent travel within the preceding 6 months (in most instances to their

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Table I - Age distribution of 56 malaria cases

Age (yrs)	Sex M	Sex F	No	%	Cumulative %
10-19	3	1	4	7.1	7.1
20-29	27	3	30	53.6	60.7
30-39	11	1	12	21.4	82.1
40-49	5	0	5	8.9	91.0
50-59	1	1	2	3.6	94.6
60+	2	1	3	5.4	100.0

country of origin) and of these, only 3 were on malaria chemoprophylaxis; all 3 patients were Singaporeans. It was not possible to determine from the survey of these 40 cases why individuals did not take malaria chemoprophylaxis or, for individuals who took such prophylaxis, what recommendations were followed. Most claimed ignorance to the need for such preventive measures.

Of the 56 cases, 52 were infected with the *P. vivax* strain of malaria while 3 had *P. falciparum* malaria (one Thai, one Indian national and one Bangladeshi); one patient had mixed infection with both the *P. vivax and P. falciparum* strain of the parasite. No cases of *P. malariae* or *P. ovale* were seen. Malaria was the first diagnosis in 30 of the 56 cases at presentation to the hospital. Of the remaining 26 cases, hepatitis was the provisional diagnosis in 5 cases, while 9 patients were thought to have viral fever. Pyrexia of undetermined origin (PUO) was the first diagnosis in 7 cases. In addition to these, one case was initially suspected to have typhoid, while another was suspected to have liver abscess. Of the remaining 3 cases, one was thought to have meningitis, one chest infection and another a urinary tract infection (Table II). Persistent fevers in all patients prompted evaluation for malaria.

Table II – Admitting diagnosis for malaria cases

Diagnosis	No. of cases	Percentage
Malaria	30	53.6
Viral fever	9	16.1
PUO	7	8.9
Hepatitis	5	12.5
Meningitis	1	1.8
Chest infection	1	1.8
UTI	1	1.8
Liver abscess	1	1.8
Typhoid	1	1.8

Although all cases were eventually confirmed on blood film, the diagnosis was strongly suspected on clinical grounds alone (before blood film confirmation) in 24 of the 56 cases. In the majority of instances (42 out of 56 cases or 75%) the diagnosis of malaria was suspected or confirmed only in the medical wards. Of the 56 cases, the accident and emergency (A&E) doctors made the correct diagnosis of malaria in 9 cases, and the general practitioner (GP) suspected or made the diagnosis in 4 cases, despite not having the benefit of the blood film for the malarial parasite. One case was diagnosed at the Government Polyclinic. The major presenting complaints were fever, chills, night sweats, malaise, myalgia, dry cough, headache and gastrointestinal symptoms like vomiting and abdominal pain (Table III). All cases gave a history of fever; this ranged from 1-22 days, with a mean duration of 6 days (1 S.D. = 4.4). Fifty of those cases with fever

Table III – Presenting features of 56 malaria cases

Symptoms	No. of cases (n = 56)	%
Fever	56	100.0
Chills	50	89.3
Headache	32	57.1
Cough	16	28.6
Night sweats	12	21.4
Gastrointestinal symptoms	11	19.6

also had chills, while 12 had fever with night sweats. Thirty-two patients also complained of headache while 20 gave a history of vomiting prior to hospitalisation. Myalgia was present in 11 (19.6%) and 16 (28.6%) had dry cough as one of their complaints. Other common complaints were abdominal pain (11 patients), dark/tea-coloured urine (5 patients) and malaise (11 patients). A history of a previous episode of malaria was noted in 6 of the 56 cases.

Fever was documented in 50 of the 56 cases on admission, and this was common in all patients regardless of which species of malaria was found. The temperature recorded on admission ranged from normal (37°C) to 40.5°C. None of the patients were delirious or disorientated from hyperpyrexia. All but one case eventually had fever documented during hospitalisation. Pallor was present in 6 cases, jaundice in 9 cases. One patient was hypotensive on admission, with a blood pressure of 85/60 mm Hg. He recovered quickly with fluid therapy. None of the patients in the study had haemorrhagic manifestations. Hepatomegaly was found in 14 patients, splenomegaly in 7 and hepatosplenomegaly in 16 patients (Table IV).

Table IV – Findings present on admission in 56 malaria cases

Findings	No. of cases (n = 56)	%
Fever	50	89.3
Pallor	6	10.7
Jaundice	9	16.1
Hepatomegaly	14	25.0
Splenomegalay	7	12.5
Hepatosplenomegaly	16	28.6

Of the 56 cases, 87.5% were found to have haematological abnormalities, either anaemia (64.3%) or thrombocytopaenia (57.1%). The white blood cell count was normal in 80.4% and decreased in 12.5%. Renal impairment was evident in 7.1% while hyponatremia (Na < 130 mEq/L) was noted in 42.9%. Two patients were hypoglycaemic (blood sugar level < 50 mg%) on random blood (plasma) sugar testing. Both however were asymptomatic at the time of blood taking. Liver function tests were performed in 38 of the 56 cases (67.9%). Of these, total bilirubin levels were elevated in 50% while 44.7% had impairment of liver function, with raised liver enzyme markers. Fifty-four of the 56 cases were treated with a chloroquine/primaquine regime. One patient was given only chloroquine because he was found to be G6PD deficient on the second day after initiation of therapy. He did not suffer any adverse consequences. One patient with *P. falciparum* malaria was treated with quinine and tetracycline for a week and primaquine for 2 weeks as he was suspected to have double infection, although this was not proven. The average time taken for fever to settle (clinical remission) was 3 days (standard deviation 1.7). This

ranged from 1-6 days. The average time taken for clearance of malarial parasites on blood film was 4 days (1 S.D. = 2.0).

None of the patients developed major complications like cerebral malaria, renal failure, haemorrhagic sequelae or splenic rupture. Nine patients were subsequently transferred to the Communicable Disease Centre (CDC) after 2-3 days' treatment at our hospital. These patients were followed-up at CDC. The rest of the cases were reviewed at our hospital's outpatient medical clinics. Hospital stay ranged from 3-16 days, with an average of 6 days (CDC cases were excluded). One case had concomitant amoebic liver abscess. No complications due to treatment for malaria was noted in the study. None of the patients involved in the study died.

DISCUSSION

This study documents the profile and typical features of malaria cases who seek treatment at a local hospital, and their outcome. It shows that malaria can be a variable disease and mimic a whole variety of disease syndromes and it can cause dysfunction of various organ systems. The typical patient is likely to be male (male to female ratio 7:1 in this study), about 30 years old and a foreigner or immigrant worker who has travelled to a malaria endemic region recently. In about 30% of patients the illness will start with a dry cough; other common symptoms include fever, chills or night sweats, headache, malaise, myalgia and loss of appetite. Abdominal symptoms and mild jaundice may also feature early in the presentation. Organomegaly was found in more than half the patients (37 out of 56) and this has to be carefully assessed as it may not be present on admission and may be subtle. Like hepatomegaly, malarial splenomegaly has to be differentiated from the many other causes of splenic enlargement in the tropics. In the early stages the spleen is often tender, giving place to painless enlargement when the infection has become chronic.

Haemorrhagic manifestations and signs referable to the central nervous system were not common in our cases. This may reflect the type of strain-infections seen here, the parasite density, the relatively more benign course of *P. vivax* infection and the ready response to chloroquine therapy. The clinical picture of malaria may also resemble hepatitis or dengue fever, two other common illnesses seen here. The diagnosis may be missed if an inadequate history (including travel history) is obtained and the possibility of malaria is not entertained.

Our data indicate that most (37 out of 40) who had travelled did not take malaria chemoprophylaxis. This may be due to ignorance; other reasons could include decreased access to medical care and pretravel advice, language or cultural barriers, or the mistaken impression that they possess 'immunity' to malaria. It is therefore important that immigrants from countries where malaria is endemic be advised that they are susceptible to malaria and should receive chemoprophylaxis when visiting their country of origin or travelling to another endemic area. Locally, all work permit applicants are medically examined and those working in receptive areas are routinely screened for malaria parasites to help minimise the number of cases.

In 24 cases (42.9%), the primary diagnosis of malaria was correctly made on admission. The other frequent diagnoses were viral fever (16.1%), hepatitis (8.9%) and pyrexia of undetermined origin (12.5%). Our findings are similar to those of a previous (retrospective) study of 64 patients with malaria seen over a 5-year period, admitted to the University Hospital, Kuala Lumpur from Jan 1984 to Dec 1988[4]. In that study, the primary diagnosis of malaria was correctly made in 40 cases out of 64 (62.5% of the total). The other primary diagnoses were: viral fever (9.4%), typhoid (7.8%), and hepatitis (3.1%). Also in that study, 41 cases (64%) out of 64 were found to have haematological abnormalities either anaemia (23 cases) or thrombocytopaenia (29 cases); renal impairment was evident in 7 cases (11%) in that study. Our data reveal the following comparison: haematological abnormalities in 87.5% of cases, and 7.1% of cases had renal impairment.

Twenty-four of 56 cases (42.9%) studied in our review had a serum sodium value less than 130 mEq/L; in the Malaysian study[4], 39% of all cases showed sodium levels below 132 mEq/L. Hyponatremia, usually associated with hypoosmolality, correlates in many studies with more severe symptoms and higher parasitaemias, and tends to occur more commonly with *P. falciparum* infections[5]. These electrolyte changes have been attributable to a mixture of mild salt depletion and water retention, and in some cases to an inappropriate secretion of antidiuretic hormone[6]. Hypoglycaemia, with blood sugar level less than 50 mg%, occurred in 2 of our patients. Both had mono-infections with *P. vivax* strain and both were asymptomatic. This feature is also more commonly seen with *P. falciparum* infections; it is more common in pregnant women and in other patients with severe disease, especially when treatment with intravenous quinine is used[7]. The hypoglycaemia associated with falciparum malaria must be differentiated from other well-known causes of hypoglycaemia, eg. reactive postprandial hypoglycaemia and fasting hypoglycaemia. The convulsions associated with hypoglycaemia are also often mistaken for cerebral malaria. Hypoglycaemia must be excluded in every malaria patient who has impaired consciousness, fits, or who is pregnant.

The majority of our cases were infections with the *P. vivax* strain of malaria. This may reflect the regions where the majority of our patients came from or visited, namely India and Bangladesh, where *P. vivax* is known to predominate. However, species distribution of malaria does not, in general, follow well defined geographic distributions. The diagnosis of malaria currently rests upon the demonstration of parasites in stained peripheral blood smears. Such smears should be examined by a trained observer as soon as the diagnosis is suspected. This method is highly sensitive and is species and stage-specific in experienced hands[8]. A negative smear does not exclude the diagnosis as chemotherapy may suppress parasitaemia; the symptoms of malaria may also precede detectable parasitaemia by a few days. Serial smears should be examined and a diagnosis of malaria can only be excluded by obtaining negative blood smears on several successive days[8]. Newer methods such as DNA probes and acridine orange fluorescence may provide more sensitive and rapid techniques to diagnose malaria in the future but are currently only research tools[9].

Clinical and parasitical remission was achieved quickly in our patients, averaging 3 and 4 days respectively. Treatment was uncomplicated and the morbidity from the disease itself was minimal. Ideally, accurate parasite counts should be performed on admission and daily during therapy, particularly for severe infections. The average hospital stay was less than a week (6 days).

There are clear limitations to an audit-study of patients presenting with malaria. These include a bias in the excess of immigrant population within the hospital, defects in symptom recall, over reporting of key symptoms, inadequacies of case records and changes in investigation and management practice, all or any of these may have led to possible bias in the results of the study. Nonetheless, the study highlights that physicians must be aware that malaria is still a major problem throughout the world, and it is a potentially fatal parasitic disease. The majority of the cases as in this study were imported, and due to the *P. vivax* strain. A history of travel to a malarial endemic area, however short, should immediately alert the doctor that infection might have occurred, regardless of the clinical picture. Symptoms of malaria are protean and nonspecific, and it often presents as a

viral syndrome. The most important step in the differential diagnosis is to think that malaria may be the cause of the patient's illness, once the history of recent exposure/travel has been elicited. The typical patient may have anaemia, thrombocytopaenia, liver dysfunction, hyponatraemia and mild renal impairment. However, blood smears must be performed for demonstration of the parasite so that effective anti-malarial treatment can be instituted early. A single negative blood smear examination does not exclude the diagnosis of malaria. While early diagnosis remains crucial to minimise morbidity and mortality, the need for prophylaxis and education of the susceptible population has to be highlighted.

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