SEVERITY OF MALARIA CASES REPORTED IN URBAN AND RURAL HOSPITALS IN MALAYSIA

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Abstract. The age distribution, types of infection and clinical patterns of malaria were compared in patients admitted to an urban and a rural hospital. Analysis of the cases seen in urban setting characteristically indicated a relatively low transmission rate of the disease, whereas the mean inoculation rate in patients from the rural hospital was found to be at least twenty folds higher. *Plasmodium vivax* was the predominant causative species in the urban hospital (p=0.01), infecting mostly adult (p=0.001) males (p=0.01). The geometric mean parasite count at 3,432/μl among the urban patients was significantly higher than that in the rural patients at 1,422/μl (p=0.04). Coma and death were more common among the cases seen in the urban hospital (p=0.003), while severe anemia was the significant complication in the rural setting. Overall, the provisional diagnosis of malaria was relatively low in the urban hospital (p=0.02). The results from this study highlighted the need to define the extent of malaria in urban areas. This report attempts to identify the non-climatic determinants of the infection and, furthermore, to provide a more informed basis to describe the burden of the disease.

INTRODUCTION

Indigenous malaria remains a major public health problem in the interior areas of Malaysia where the infection rates are highest among the aboriginal Orang Asli. In the eastern states of Sabah and Sarawak, the emergence of chloroquine-resistant cases poses a major problem in the control of the disease. These problems are being compounded by the continuous influx of migrant workers from malaria endemic countries. The migrant population usually lives in poor environmental conditions conducive to mosquito breeding and malaria transmission and is not covered by active surveillance (Robert *et al,* 2003). Undetected imported cases among this group of population may trigger new foci of outbreak thus further undermines the efforts in the control of the disease.

Malaria follows a very definite geographic pattern as it is dependent on both the anopheline mosquito and human host to continue its lifecycle. Those living in low-lying tropical areas are most at risk for contracting the disease where access to health care is less available and mosquito prevention programs are sparse (Guthmann *et al,* 2002).

Most studies on the transmission have been carried out in rural environments (Vijayamma *et al*, 1980; Vythilingam *et al*, 1986; Henderson and Rixom 2004). As a result of extensive urbanization in Malaysia in the recent years that elevates the standard of living conditions and infrastructures, malaria control in urban environments may be more efficient than in the rural areas; however, much

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of what is known of the disease transmission in the rural environments might not be relevant in the urban context. In addition, little is known about individual predisposing characteristics and disease presentations in those cases reported in the urban areas.

The present study examined two sets of malaria patients that represented cases in urban and rural settings, respectively. In particular, the clinical presentations and the final outcome of these patients were investigated.

MATERIALS AND METHODS

This study was a retrospective investigation between the period 1998 to 2003 on all malaria patients admitted to two referral hospitals, one each in an urban and a rural setting, respectively. The study utilized the retrievable case records, stained thick and thin Giemsa blood smears of the patients. Laboratory diagnosis of malaria at the urban hospital was based on both thick and thin blood films, whereas in the rural hospital, the diagnosis was based on thick blood films only.

The study conducted at the urban teaching hospital in Kuala Lumpur city examined 49 out of a total of 52 cases from the general population. Cases investigated in the rural hospital represented the Aborigine community that generally lives in the mountainous interiors of the country, where control intervention strategies are less successfully implemented due to the difficult geographical accessibility and the high mobility of the Aborigine population (MOH, 2003). A total of 333 cases were admitted during the study period. Due to the incomplete recording in some cases, the clinical presentations, complications and laboratory investigations were investigated in only 110 Aborigine patients.

Case definition was adapted from the WHO classification (1990). Data were double entered in EPI-INFO 6.0. Analysis was performed in SPSS 10.0.

RESULTS

From the biodata gathered (Table 1), a majority of the patients seen in the urban hospital were older than 16 years of age. Seventy-three percent of these patients were male. The cases in the rural hospital were mainly younger patients. More than half of the cases (59.2%) at the urban hospital contracted the infection outside Kuala Lumpur, whereas all cases at rural hospital were indigenous. ($p<0.001$).

Of the parasite species identified by blood film examination (Table 2), *Plasmodium vivax* was the predominant species responsible for clinical sickness in the urban hospital, whereas *P. falciparum* contributed to 52% of the cases seen in the rural hospital. Throughout the study period, only 2% of cases in the urban hospital were attributed to *P. malariae* infection. No cases of quartan malaria were reported in the rural hospital. To a lesser extent, mixed infec-

Table 1
Comparison by biodata.

Variables	Urban, N=49	Rural, N=333	p-value
Age ≥ 16 years	47 (95.9%)	65 (19.5%)	p=0.001
Male	38 (73.1%)	157 (46.8%)	p=0.01
Non-indigenous cases	29 (59.2 %)	0 (0%)	p<0.001

N = total number of cases

tions by any two of the three species of parasites were reported in both hospitals. No cases of *P. ovale* infection were reported in both hospitals.

Table 3 presents the various clinical signs and symptoms presented by the patients in both hospitals. Except for pallor and splenomegaly, all other clinical presentations were more prominent among patients admitted to the urban hospital.

More than half patients were diagnosed as having contracted malaria at the time of admission to the rural hospital. On the contrary, the accuracy of clinical diagnosis was relatively low when the patients were admitted to the urban hospital. Table 4 indicates the list of provisional diagnosis provided in both hospitals.

Anemia was more prominent among the aborigine patients admitted to the rural hospital; the hemoglobin levels of these patients were consistently lower, with the mean value at 0.7±2.6 g/dl. Thrombocytopenia was more prominent among patients in the urban hospital (Table 5).

Table 2
Comparison by parasite species.

Parasite species	Urban N=49	Rural N=333	p-value
P. falciparum	34.7%	52.3%	p=0.02
P. vivax	57.2%	38.1%	p=0.01
P. malariae	2.0%	0%	p=0.28
Mixed infection	6.1%	9.6%	p=0.67

N = Total number of cases

Table 3
Comparison by clinical presentation on admission.

Findings	Urban N=49	Rural N=110	p-value
Fever [a]	49 (100%)	81 (73.6%)	p<0.001
Chills	35 (71.4%)	47 (42.7%)	p=0.001
Sweating	22 (44.9%)	28 (25.5%)	p=0.002
Headache	21 (42.9%)	22 (6.6%)	p=0.001
Pallor [a]	20 (40.8%)	61 (55.5%)	p=0.11
Jaundice [a]	20 (40.8%)	23 (20.9%)	p=0.01
Hepatomegaly [a]	31 (63.3%)	20 (18.1%)	p=0.001
Splenomegaly [a]	16 (32.7%)	49 (44.5%)	p=0.21
Right hypochondrial pain	7 (14.3%)	5 (4.5%)	p=0.053
Gastrointestinal symptoms [a]	34 (69.3%)	46 (41.8%)	p=0.002
Dark urine	6 (12.2%)	1 (0.9%)	p=0.06

N = Total number of cases

[a] The signed clinical findings are defined as follow:

Fever as manifested by an internally originated increase in core temperature (above 37ºC).

Pallor, indicative of anemia with a decrease in hemoglobin (adult male <13.5g/dl; adult female < 12g/dl)

Jaundice, as indicated by yellow discoloration of skin and sclera detectable; serum bilirubin > 3mg/ dl

Hepatomegaly and splenomegaly as manifested by palpable enlargement of liver and spleen, respectively, below the costal margin by abdominal examination.

Gastrointestinal symptoms included diarrhea, abdominal pain, nausea and vomiting.

Table 4
Comparison by provisional diagnosis on admission.

Provisional diagnosis	Urban N=49	Rural N=110	p- value
Malaria	19 (38.8%)	65 (59%)	p= 0.02
Dengue fever	15 (30.7%)	9 (8.2%)	p< 0.001
Viral hepatitis	5 (10.2%)	0 (0%)	p< 0.001
Leptospirosis	3 (6.1%)	0 (0%)	p< 0.001
Lymphoma /Leukemia	3 (6.1%)	0 (0%)	p< 0.001
Gastrointestinal diseases	2 (4.1%)	17 (4.3%)	p=0.71
Typhoid	1 (2.0%)	1 (0.3%)	p=0.88

N = Total number of cases

Table 5
Comparison of FBC of malaria patients in the hospitals.

Full blood count	Urban N=49	Rural N=110	p- value
Mean hemoglobin	11.9±2.2 g/dl	7.7±2.6 g/dl	p=0.04
Mean white blood count	6.9±2.8 $x10^9$/liter	10.1±5.0 $x10^9$/liter	p=0.13
Mean platelet count	84.9±38.2 $x10^9$/liter	229.9±118.4 $x10^9$/liter	p=0.01

N = Total number of cases

Table 6
Comparison between malaria cases by complications.

Complications	Urban N=49	Rural N=110	p- value
Severe anemia, <5 g/dl	4 (8.2%)	30 (27.3%)	p=0.01
Renal impairment	3 (6.1%)	1 (0.9%)	p=0.17
Bleeding and clotting disorders	2 (4.0%)	3 (2.7%)	p=0.84
Cerebral malaria	3 (6.1%)	0 (0%)	p=0.05
Malarial hepatitis	2 (4.0%)	0 (0%)	p= 0.18
Ruptured spleen	1 (2.0%)	0 (0%)	p=0.69

N = Total number of cases

Laboratories in both hospitals assumed the normal total white blood count to be 8,000/μl for parasite count in a thick blood film. Based on this assumption, the urban hospital reported an overall significantly higher parasite count, at 3,432, than the rural hospital, at geometric mean 1,422 (p=0.04).

Table 6 presents the various complications encountered in the patients in both hospitals. Severe anemia was commonly seen

Table 7
Comparison between malaria cases by outcomes.

Outcome	Urban N=49	Rural N=333	p- value
Recovery	39 (79.6%)	289 (86.8%)	p=0.28
Complication	7 (14.3 %)	27 (8.1%)	p=0.26
Death	3 (6.1%)	1 (0.3%)	p=0.003
Incomplete data	0 (0%)	16 (4.8%)	-

N = Total number of cases

among patients who were infected with *P. falciparum* and those who had high parasite density at both hospitals. However, the complication was significantly more common at the urban hospital. Severely anemic patients were found to have hemoglobin readings lesser than 5g/dl. Six percent of the patients in the urban hospital were found to present with signs of renal impairment with abnormal findings related to the urinary system, such as edema, black urine and hemoglobinuria. Bleeding and clotting disorders related to thrombocytopenia were observed in both hospitals, though there was no noted significant difference in the number of cases. Two patients (4%) in the urban hospital were noted to have hepatitis associated to the infection; their bilirubin and liver enzymes were notably elevated (data not shown). No similar cases of hepatitis were noted among the rural patients. Two out of the 49 malaria patients in the urban hospital succumbed to cerebral malaria; whereas none was seen in all patients admitted to the rural hospital. Throughout the study, there was only one single case of spontaneous ruptured spleen, as reported in the urban hospital.

Most patients in both hospitals were discharged with complete recovery and negative blood film for malaria parasite. The patients in the urban hospital, however, were noted to have presented with complications more frequently during the admission period than those in the rural hospital. The death rate appeared to be higher in the urban hospital. Based on the available complete records in the rural hospital, there was only one death among the 317 admitted cases with complete data between the period 1998 through April 2003. The details are summarized in Table 7.

DISCUSSION

The rapid urbanization in the third world has major implications on the epidemiology of malaria. A review of malaria transmission in sub-Saharan African cities shows the strong likelihood of transmission occurring within these sprawling cities, whatever the size or characteristics of their bioecologic environment (Shomakhov, 1999). In the present investigation, the high number of male patients of age older than 16 years seen at the urban hospital may have reflected the high mobility and inclination for outdoor recreation activities among the older male population in the urban areas. The activities may have resulted in their exposure to the infection when they traveled to the malaria endemic foci in the peninsular Malaysia. This observation in the urban hospital was consistent to the study done at another urban hospital in Kuala Lumpur (Sidhu and Ng, 1991). The occurrence of 57.2% of malaria cases caused by *P. vivax* in the urban hospital and 52.3% of cases by *P. falciparum* in the rural hospital was compa-

rable with the actual statistics reported to the Ministry of Health (MOH, 2003).

In children admitted to the rural hospital, fever, pallor and splenomegaly were found to be strongly associated with malaria parasitemia, whereas parasitemia appeared to be the influencing factor on the severity of fever in adult patients of the urban hospital (Personal observation). The clinical presentations reported in the present study may have been influenced by the epidemiological variables, especially by the locations where malaria was acquired. This was indicated by the finding that more than half of the patients in the urban hospital had acquired the infection from outside of the city after having traveled to the malaria endemic areas. In contrast, all cases at the rural hospital were indigenous cases, whereby the patients were infected by the malaria parasite in the environment where active transmission was ongoing. Similar observations on the influence of epidemiologic variables on the clinical presentations and severity of malaria had been reported by other workers (Modiano *et al*, 1998; Tatem and Hay, 2004).

Overall, the urban hospital in the present study reported significantly higher parasitemia levels ($p=0.04$). The correlation between parasitemias and severity of malaria was well noted (Field and Niven, 1937). In this study, two patients in the urban hospital were found to have high parasitemias of more than 100,000/μl. The disease in both cases developed rapidly to cerebral malaria, with ensuing death. Muhlberger *et al*, (2000) reported differing clinical outcomes between adults and children and noted that the severity of disease, the need for hospitalization, and the risk of death due to falciparum malaria increased significantly with each decade of life. In cases with complications or where the infections were fatal, there was an indication in our data of comparable findings. Further extensive analysis on more data is needed before we are able to draw a similar conclusion or otherwise.

Due to the lack of specific components of clinical picture and the complications in malaria, clinical diagnosis of the infection based on physical examination can be difficult and imprecise. In the urban hospital of present study, patients with dengue fever, especially those with positive HESS test, were among the myriads of febrile cases admitted daily. The overlapping presenting features of these febrile diseases in the hospital complicated the diagnosis of malaria. This is expected since the country is endemic for both malaria and dengue fever. Most patients usually seek medical help within few days of having fever when the classical malaria paroxysms have not yet occurred. Under the circumstances, confirmatory diagnosis of malaria therefore depends heavily on the detection and identification of the causative agent in stained blood smears in the laboratory. On the other hand, the presence of the parasite does not necessarily establish a diagnosis of clinical malaria especially in patients from the endemic areas where low parasitemia may be common in those who have developed some form of resistance to the disease. This may have explained the low accuracy of clinical diagnosis of malaria in an urban setting.

From our investigation of the available medical records, some cases were noted to be city dwellers who admitted to having visited the malaria endemic areas. However, the source of infection in a handful of local residents could not be determined. We were unable to confirm these cases were urban or imported malaria. As it is established that *Anopheles* vector is absent in the city, it was unlikely that they could have been urban malaria cases.

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