Increasing Plasmodium falciparum malaria in southwest London: a 25 year observational study

J P Williams, M Chitre, M Sharland

Aims: To identify changes in the presenting number and species of imported malaria in children in southwest London.

Methods: A prospective single observer study over 25 years (1975–99) of all cases of paediatric malaria seen at St George’s Hospital.

Results: A confirmed diagnosis was made in 249 children (56% boys; 44% girls; median age 8.0 years). Of these, 53% were UK residents and 44% were children travelling to the UK. A significant increase was noted in the number of cases over the 25 years (1975–79: mean 4.8 cases/year; 1990–99: mean 13.7 cases/year). Over the 25 years Plasmodium falciparum was seen in 77%, P vivax in 14%, P ovale in 6%, and P malariae in 3% of cases. P falciparum had increased in frequency (1975–79: P falciparum 50%, P vivax 50%; 1990–99: P falciparum 82%, P vivax 6%), associated with an increase in the proportion of children acquiring their infection in sub-Saharan Africa. Median time between arrival in the UK to the onset of fever was: P falciparum, 5 days; P ovale, 25 days; P malariae, 37 days; and P vivax, 62 days. Median time interval between the onset of fever to commencement of treatment was 4 days. This had not improved over the 25 year period. Only 41% of UK resident children presenting to hospital had taken prophylaxis and the overall number of symptomatic children taking no prophylaxis was increasing.

Conclusion: Imported childhood P falciparum malaria is increasing in southwest London associated with increasing travel from sub-Saharan Africa. Over the 25 year period there has been no improvement in chemoprophylaxis rates or time to diagnosis.

RESULTS

Between August 1975 and December 1999, 249 children were diagnosed as having malaria (56% boys, 44% girls). The median age of presentation was 8.0 years (range 1 month to 17 years). Children fell into two groups: UK residents travelling abroad (53%), and children resident abroad travelling to the UK (44%). Overall, 36% of the total cohort had been born in the UK, and 22% were new immigrants arriving in the UK. Details were not known for 3% of children. There was one case of congenital malaria. Over the 25 year period a significant increase was observed in the number of cases of malaria diagnosed, with a mean number of cases/year in 1975–79 of 4.8, 1980–89 of 8.8, and 1990–99 of 13.7 (p = 0.042; 95% CI 4.8 to 56.17). There was a biphasic distribution, with the main peak in summer (21% cases in September, 17% in August, 12% in July, 9% in October) and a second rise in winter (8% in January), following holiday patterns.

Malaria species

Over the 25 year period, Plasmodium falciparum caused 77%, P vivax 14%, P ovale 6%, and P malariae 3% of all cases. There was a notable increase in the proportion of cases caused by P falciparum over the study period (see table 1). In 1975–1979 P falciparum was seen in 50%, and P vivax in 50% of cases, compared to 1990–99, when P falciparum caused 82% of all malaria cases, and P vivax only 6%.

Countries visited

Over the study period, 84% of all malaria cases were acquired in sub-Saharan Africa (SSA), with the majority from Ghana, Nigeria, and Uganda. Overall, 98% of P falciparum, 100% of P

Abbreviations: ISC, Indian subcontinent; SSA, sub-Saharan Africa

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ovale, and 83% of P malarium cases came from SSA. Only 15% of all malaria cases were acquired in the Indian subcontinent (ISC), with the majority from Pakistan and India. Overall 94% of P vivax cases came from the ISC. During the period of this study the proportion of cases from the ISC has been decreasing, while the proportion from SSA has increased (see table 1).

Latent period
The overall median time interval between arrival in UK and the onset of fever for all cases of malaria was 7 days (range 0–11 months).

For P falciparum, the median was 5 days (range 0–330 days). In three children there was an unusually long latent period of 150, 294, 330 days, respectively; after careful scrutiny of the travel history, these were confirmed as genuine cases. For P vivax, the median was 62 days (range 0–330 days). For P ovale, the median was 25 days (range 0–120 days). For P malarium, the median was 37 days (range 0–188 days).

Delay in diagnosis
The median time between the onset of fever and confirmation of a malaria infection with commencement of treatment was 4 days (range 0–32 days). There was no significant difference between children resident in the UK, and those visiting from abroad. Over the 25 year period there was no evidence of improvement towards an earlier diagnosis of malaria, with the time interval between onset of symptoms and treatment remaining constant.

Prophylaxis
Information on prophylaxis was available for 94% of children. Only 41% of all UK resident children took some form of prophylaxis during their travel period, and only 3% continued their prophylaxis after returning to the UK: 94% of these were visiting SSA and 6% were visiting ISC. Of those taking prophylaxis, chloroquine was taken by 57%, proguanil by 24%, both chloroquine and proguanil by 4%, pyrimethamine by 13%, maloprim by 5%, and mefloquine by 1% of patients.

Over the study period, the proportion of symptomatic children returning from SSA who had taken prophylaxis remained constant at 24%, but the total number not taking prophylaxis has been increasing (see table 1).

Clinical data
The majority of patients showed anaemia, mild neutrophilia, and thrombocytopenia (median platelet count 112, range 13–513 × 10^9/l). The parasite percentage was measured in 30% of all children. A median parasite percentage of 1% was recorded, with a range of 0.1–25%. All patients were successfully treated with either quinine or chloroquine. Only one child, with a parasite count of 23%, had an exchange transfusion. There were no deaths.

DISCUSSION
This study has shown an increasing number of children with P falciparum malaria presenting to St George’s Hospital, associated with travel to sub-Saharan Africa. Nationally there are around 300 children presenting each year with imported malaria in the UK, with P falciparum causing around 56% of

Table 1: Species, countries visited, median time to diagnosis, and prophylaxis over time

<table>
<thead>
<tr>
<th>Year</th>
<th>Species</th>
<th>Countries visited</th>
<th>Median time to diagnosis (days)</th>
<th>Prophylaxis over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>P falciparum</td>
<td>ISC</td>
<td>11</td>
<td>4</td>
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</tr>
<tr>
<td>P falciparum</td>
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<td>19</td>
<td>4</td>
<td></td>
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<tr>
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<td>5</td>
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<td></td>
</tr>
<tr>
<td>P malariae</td>
<td>ISC</td>
<td>9</td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>

Cases with simultaneous infection:

Box 1: Numerical data for results

- 249 children diagnosed: 140 (56%) boys, 109 (44%) girls
- UK residents travelling abroad: 132 (53%)
- Children visiting the UK: 110 (44%), including new immigrants which are 55 (22%)
- Details not known: 7 (3%)
- Children born in the UK: 89 (36%)
- Distribution of cases over the year: January, 21 (8%); February, 11; March, 6; April, 11; May, 13; June, 19; July, 31 (12%); August, 42 (17%); September, 53 (21%); October, 13 (5%); November, 7; December, 12 (see fig 1)
- Over 25 years malaria cases caused by P falciparum = 195 (77%); P vivax = 36 (14%); P ovale, 16 (6%); P malariae, 6 (3%); four children with two simultaneous species present
- 1975–79, cases caused by P falciparum = 12 (50%); P vivax = 12 (50%); 1980–89, P falciparum = 71 (79%), P vivax = 15 (17%); 1990–99, P falciparum = 112 (82%), P vivax = 9 (6%)
- Over 25 years, cases acquiring malaria in sub-Saharan Africa = 210 (84%); P falciparum = 191 (98%), P ovale = 16 (100%), P malariae = 5 (83%)
- Cases acquiring malaria in the Indian subcontinent = 37 (15%); P vivax = 34 (94%)
- Information on prophylaxis available in 233 (94%) children: prophylaxis taken by 54 (41%) UK residents; of these, 7 (13%) continued taking on return
- Number of children taking chloroquine = 36 (57%); proguanil = 15 (24%); pyrimethamine = 8 (13%); maloprim = 3 (5%); mefloquine = 1 (1%)
- Children taking prophylaxis over 25 years = 59 (24%)
- Parasite percentage measured in 74 (30%) children
- Statistical analysis performed using Stata, version 5
- Statistically significant increase in malaria cases over the three decades (p = 0.042)
- 95% confidence intervals 4.82 to 56.17

Figure 1: Distribution of cases according to time of year.
cases in the early 1990s. The increase in the proportion of cases caused by *P. falciparum* is of concern because of the increased morbidity and mortality associated with *P. falciparum* childhood malaria over other species. The majority of cases of malaria reported here were diagnosed in the summer and winter, showing a seasonal variation coinciding with school holiday periods. Despite a local awareness/advertising campaign on the advisability for malaria prophylaxis, it is of concern that no improvement in the proportion of children taking prophylaxis was seen over the 25 year period. Around two thirds of children acquiring their malaria in sub-Saharan Africa were resident in the UK, and could have taken prophylaxis. It is not clear why so few families give malaria prophylaxis to their children. One study has suggested that the cost of chemoprophylaxis against malaria might prevent travellers from taking any or the most appropriate drug when travelling abroad, although chemoprophylaxis for children is free. Bradley and Warhurst noted that over a third of cases of malaria in Britain occur in families originating from endemic areas who travel abroad to visit friends and relatives. Chemoprophylaxis among this group of travellers is lower than among other tourists visiting the tropics. It is our experience that families regard their children as being “immune” to malaria, despite them being brought up in the UK. The taste and formulation of paediatric antimalarial agents is poor, and this may influence compliance. The increasing number of malaria cases seen in Wandsworth remains of great concern, despite repeated local malaria information campaigns which have been widely disseminated to the public and healthcare professionals.

Children are particularly at risk of developing severe *P. falciparum* malaria; symptoms can develop rapidly and the clinical presentation is often more atypical than that seen in adults, with cerebral, paraintestinal, and respiratory presentations seen more frequently. Increased efforts need to be made to educate families, healthcare professionals, travel agents, and airlines of the importance of malaria prophylaxis when visiting endemic countries, and the prompt evaluation of fever on return from endemic areas. While we have had no deaths from *P. falciparum* malaria, it is worth highlighting that in UK adults dying from malaria in the year 2000, the majority had not taken any prophylaxis, even though some were frequent travellers to malaria areas. Because of increasing resistance to antimalarial medications, prophylaxis regimes are becoming more complicated. Up to date advice can be obtained from the PHLS Malaria Reference Laboratory (www.malaria-reference.co.uk or www.fco.gov.uk/knowbeforeyougo).

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JPW collected and stored the data, established a clinical database at St George’s Hospital, discussed the analysis, and edited the manuscript; he will act as guarantor for the paper. MC analysed and interpreted the data and wrote the manuscript. MS initiated the study, directed the analysis, discussed core ideas, and edited the manuscript.

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