Epidemiology of Malaria Presenting at British Columbia's Children's Hospital, 1984-2001

Lessons for Prevention

Kirsten K. Miller, MD

Anna Banerji, MD, MPH, FRCPC, DTM&H

ABSTRACT

Background: Few studies have examined the epidemiology of imported malaria in Canadian children. Identifying populations at increased risk in Canada would enable targeted malaria prevention strategies within those groups. The study objective was to describe the epidemiology of malaria diagnosed at British Columbia's Children's Hospital (BCCH) between 1984 and 2001.

Methods: This was a retrospective chart review of malaria cases identified at BCCH and confirmed through the British Columbia Centre for Disease Control. Demographic and clinical data were recorded on a standardized form.

Results: Malaria was diagnosed 42 times in 40 children (age 24 days to 14.8 years). Thirty cases (71.4%) occurred in 28 Canadian residents, and 12 (28.6%) occurred in immigrant or refugee children. Twenty-six children (65%) were male. Thirty-one children (77.5%) were of East Indian descent. Thirty-three exposures (78.6%) to malaria occurred in the Indian subcontinent. *Plasmodium vivax* was identified in 37 cases (88.1%), *P. falciparum* in 3 (7.1%), and the species was unknown in 2 (4.8%). Fourteen cases in the resident children (46.7%) reported pre-travel counselling. Ten resident cases (33.3%) were prescribed chemoprophylaxis, primarily chloroquine, and at least six of them (60%) were non-compliant. The duration of symptoms prior to diagnosis was ≤ 7 days in 27 cases (64.3%), 8 to 30 days in 10 (23.8%), > 30 days in 4 (9.5%) and the duration was unknown in 1 (2.5%). Twenty-four of 36 cases (66.7%) had seen 2 to more than 4 doctors before the diagnosis of malaria was made.

Conclusion: The majority of children in our review were of East Indian origin and were exposed to malaria in India. Most had not sought or had received inadequate pre-travel counselling and had been non-compliant with chemoprophylaxis. As malaria is a potentially lethal but preventable disease, strategies to ensure adequate pre-travel counselling for high-risk groups are required.

La traduction du résumé se trouve à la fin de l'article.

Department of Pediatrics, University of British Columbia, Children's & Women's Health Centre of BC, Vancouver, BC

Correspondence and reprint requests: Dr. Anna Banerji, 12 Zealand Road, Toronto, ON M9R 3W4, E-mail: abanerji@post.harvard.edu

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Malaria is a major cause of morbidity and mortality in children throughout the developing world and kills approximately 1 million children world-wide each year.¹ Despite this, there have been few studies examining imported malaria in the pediatric population. As global travel increases, the rate of imported malaria will continue to rise in Canada. In recent years, British Columbia has had one of the highest per capita rates of imported malaria in Canada, with peaks in 1996 and 1997 when it was two to three times the average Canadian rate.²

The goal of this study was to describe the epidemiology of malaria diagnosed at British Columbia's Children's Hospital (BCCH) between 1984 and 2001. Understanding the demographics of this disease in children may support the implementation of targeted malaria prevention strategies for high-risk groups. As delays in the diagnosis and treatment of malaria are associated with increased morbidity and mortality³⁻⁵ it is important to emphasize the value of prevention strategies and early recognition and treatment of disease, particularly for populations at increased risk.

METHODS

This retrospective chart review was undertaken at BCCH in Vancouver, British Columbia, Canada. BCCH is the only tertiary pediatric referral centre in the province of British Columbia. This review recorded the epidemiologic factors and clinical presentation of all laboratory-confirmed episodes of malaria seen at BCCH between 1984 and 2001. Cases were identified by ICD-9 coding for malaria at BCCH and through the provincial reference laboratory (British Columbia Centre for Disease Control [BCCDC]). Cases were children (≤ 16 years of age) who were either admitted to BCCH, or who were seen in the hospital emergency department or outpatient clinic, with an episode of laboratory-confirmed malaria. Each episode of malaria is defined as a case. Malaria parasites were identified and speciated on thin or thick smears by an experienced hematopathologist at BCCH. Speciation was confirmed at the BCCDC. Medical records were reviewed and data were collected on a standardized form. The data were managed and summarized using Microsoft Excel.

RESULTS

Patient characteristics

Malaria was diagnosed 42 times in 40 children between 24 days and 14.8 years of age (median 6.7 years, mean 6.0 years). Two positive smears were detected by screening asymptomatic siblings of a case and were not included in our analysis. One child had three episodes of malaria following separate trips to Indonesia. It was not determined whether these episodes represented relapse or re-infection, but for the purpose of this analysis, each episode was considered a re-infection. There was one case of congenital malaria diagnosed at 24 days of age in a child whose mother had emigrated from India the day prior to delivery.

Twenty-nine children (72.5%) were admitted to BCCH while 11 children (27.5%) with 13 episodes of malaria were seen in the emergency or outpatient departments and discharged home. All children survived without significant long-term sequelae. Twenty-six children (65%) were male. Thirty-one children (77.5%) were of East Indian descent, of whom 16 were born in Canada, 7 in India, 1 in Pakistan, 1 in England and the birthplace was unknown for 6.

Twenty-eight of the children (70%) resided in Canada (referred to as *resident children*), and their purpose for travel to an endemic region was to return to the country of origin, presumably to visit friends or relatives (VFR). Twelve children (30%) were new immigrants or refugees who were exposed to malaria in their native country or in refugee camps before their arrival in Canada. Thirty-three of all of the exposures (78.6%) occurred in South Asia, (30 in India, 2 in Pakistan and 1 child had travelled to both countries).

Chemoprophylaxis

For the 30 cases of malaria that occurred in the 28 resident children, 14 (46.7%) had reported receiving pre-travel counselling (Table I). Ten cases (33.3%) indicated that they were prescribed chemoprophylaxis, 14 (46.7%) were not prescribed chemoprophylaxis, and it was not documented for 6 cases (20%). The medication used for prophylaxis was chloroquine for 6 cases (60%) and was unknown for the other 4 (40%). Six of those who took prophylax-

TABLE I

Summary of Demographics, Plasmodium Species, Exposure and Prophylaxis for Resident and Non-resident Cases (Immigrant/Refugee)

	Resident Cases	Non-resident Cases	Overall
Numbers (%)	30 (71.4%)	12 (28.6%)	42 (100%)
Age (years)			
Mean	7.4	5.0	6.7 years
Median	6.5	4.6	6.0 years
Range	1.3-14.8	0.1 - 9.8	0.1 to 14.8
Sex (%) male of cases	20* (66.7%)	8 (66.7%)	28 (66.7%)
Region of Exposure	Species	Species	Overall Species (%)
India/Pakistan	25 <i>P. vivax</i>	7 <i>P. vivax</i> 1 unknown	32 (76.1) <i>P. vivax</i> 1 (2.4) unknown
Asia outside India/Pakistan	4* <i>P. vivax</i>	1 unknown	4* (9.5) <i>P. vivax</i> 1 (2.4) unknown
Africa	0	3 <i>P. falciparum</i>	3 (7.1) <i>P. falciparum</i>
South/Central America	1 <i>P. vivax</i>	0	1 (2.4) <i>P. vivax</i>
Total	30	12	42 (100)
Malaria Prophylaxis in Resident Cases (N=30)	N (%)		
Pre-travel advice	14 (46.6)	—	
Prophylaxis prescribed†	10 (33.3)	—	
Non-compliance documented	6 (60)	—	
Unknown compliance	4 (40)	—	
Known compliance	0 (0)	—	

* One male child, who had 3 episodes of malaria after 3 separate trips to Indonesia, counted as 3 cases.

† Adequate or inadequate regimen

is (60%) admitted to non-compliance, and compliance was not documented for the remaining 4 (i.e., none of the cases were documented to be compliant with the prescribed drug regimen). None of the immigrant or refugee children reported using malaria chemoprophylaxis.

Diagnostic information

Plasmodium vivax was identified in 37 cases (88.1%), *P. falciparum* in 3 (7.1%), and the species was unknown in 2 (4.8%) (Table I). All 3 cases with *P. falciparum* malaria had emigrated from Africa. Platelet counts were measured in 40 of 42 cases at the time of diagnosis. The platelet counts were $<80 \times 10^9/L$ in 8 cases (20%), $80-100 \times 10^9/L$ in 7 (17.5%), $101-130 \times 10^9/L$ in 12 (30%) and $>130 \times 10^9/L$ for 13 (32.5%).

Thirty-five of the 42 cases of malaria (83.3%) had the onset of their symptoms in Canada. The time between departure from the malaria-endemic area and onset of symptoms was inconsistently documented. Twelve cases (28.6%) were diagnosed on their first visit to a physician. Sixteen cases (38%) had contacts with 2 different doctors before a diagnosis, 4 (9.5%) had 3 contacts, 2 (4.8%) had 4 contacts, and 2 (4.8%) had seen more than 4 physicians before a diagnosis of malaria was made. The number of contacts was unknown in

TABLE II

Reported Symptoms and Physical Signs, Platelet Count at Diagnosis

Symptom or Sign	N	%
Fever	42	100
Nausea/vomiting	26	62
Chills/rigors	22	52
Headache	22	52
Anorexia	20	48
Abdominal pain	11	26
Malaise	9	21
Cough	7	17
Myalgia/arthritis	6	14
Lethargy	5	12
Diarrhea	4	9.5
Fever ($\geq 38^\circ C$)	32	76
Splenomegaly	16	38
Abdominal tenderness	7	17
Hepatomegaly	6	14
Fever alone	10	24
No physical findings	6	14
Splenomegaly alone	2	4.8
Platelet count* ($\times 10^9/L$)		
<80	8	20
80-100	7	17.5
101-130	12	30
>130	13	32.5

* the child with 3 separate episodes of malaria had a CBC done only with the first episode

6 cases. The duration of symptoms prior to the diagnosis of malaria was from 0 to 7 days in 27 cases (64.3%), 8 to 30 days in 10 (23.8%), greater than 30 days in 4 (9.5%), and was unknown in 1 case (2.5%).

The most common signs and symptoms reported at the time of presentation are listed in Table II. A history of fever was

present in 100% of the cases, although only 32 cases (76.1%) were febrile ($T \geq 38^\circ\text{C}$) at the time of presentation. Other common symptoms were nausea or vomiting (62%), headache (52%), chills or rigors (52%). Splenomegaly was found in 16 of the cases (38%). In 10 cases (23.8%), fever was the only physical finding.

DISCUSSION

This study identified Canadian-born children of East Indian origin who travelled to India as a population at increased risk of imported malaria in the Vancouver, British Columbia area. This is consistent with another study, which documented a disproportionate number of malaria cases in the South Asian population in British Columbia (98% of malaria cases).⁶ Both studies identified *Plasmodium vivax* as the causative parasite in the majority of cases.⁶ This contrasts with results from other North American studies in which higher rates of *P. falciparum* malaria were found, primarily due to a population with more travel to Africa.^{3,4,7-10} Our study corresponds with numerous other studies, where travellers received inadequate pre-travel counselling, were prescribed inappropriate malaria chemoprophylaxis, and were non-compliant with prophylaxis prescribed.^{4,6,9,10}

Malaria prophylaxis, which typically continues for 4 weeks after leaving the malaria-endemic area, serves a primary goal of preventing the more serious *P. falciparum* malaria, but also provides protection against *P. vivax*. Although the incubation period for *P. vivax* is usually 7 to 14 days, it can be as long as several months to years. In our series, there was general non-compliance with chemoprophylaxis, although it is recognized that, given the lengthy incubation period, even adequate prophylaxis may not have prevented all cases of *P. vivax*.

This study demonstrated that there was a failure by health care professionals to recognize the need for adequate chemoprophylaxis for travel to India. Within our small sample of malaria cases acquired in India, we identified only infections with *P. vivax*. The absence of *P. falciparum* may lead to the false impression that chloroquine prophylaxis is adequate for travel to

India. Since the early to mid-1990s,¹¹ there have been several epidemics of chloroquine-resistant *P. falciparum* malaria in India. There have also been reports of chloroquine-resistant *P. vivax* malaria in India since 1995.¹² The emergence of chloroquine-resistant *P. falciparum* malaria in India had made chloroquine alone inadequate prophylaxis¹³ since the early 1990s, yet where documented, chloroquine was the drug prescribed during this time interval. Chloroquine-resistant *P. falciparum* malaria is increasing at an alarming rate in India and inappropriate chemoprophylaxis will inevitably result in imported *P. falciparum* cases in children travelling to India.

Appropriate chemoprophylaxis and personal protection measures can reduce the incidence of imported malaria.^{7,13,14} Physicians who prescribe anti-malarial medications for travellers must be aware of the changing drug-resistant patterns of malaria. Numerous studies have shown that travellers are inadequately prepared or ignore measures that may reduce their risk of acquiring malaria during travel.^{3,4,6,8-10} In particular, travellers returning home to visit friends and relatives (VFRs) often do not seek pre-travel counselling or are not compliant with the advice.^{13,14} Several studies have demonstrated that VFRs are at increased risk of acquiring malaria when they return to their place of origin.^{3,13-16}

A recent survey of Canadians of South Asian origin departing for travel to India found that only 54% had sought pre-travel advice, 31% intended to use chemoprophylaxis, and the majority of them had been inappropriately prescribed chloroquine.¹⁴ Only 24% of that study's cases were prescribed a drug regimen recommended by Health Canada.¹⁴ Our study did not find any cases that were compliant with a drug regimen recommended by Health Canada.

Due to its non-specific presentation and a lack of familiarity in areas of low endemicity, the diagnosis of malaria can be missed.^{3,4,9,10} In this study, only 12 episodes of malaria (33.3%) were diagnosed during the first visit with a physician. The remaining 20 cases (66.7%) had seen 2 to more than 4 doctors before the diagnosis of malaria was made. The diagnosis was delayed by more than one week in 33.5% of the cases. Although the majority of children in our study had *P. vivax*

infection, young children generally suffer increased morbidity due to malaria compared to adults,¹⁷ and a prompt diagnosis is essential to prevent prolonged suffering due to this illness.

In this series, the clinical presentation of imported malaria was non-specific and, although a history of fever was present in all cases, 27% were afebrile when they were seen. In a child returning from a malaria-endemic area, a history of fever alone should prompt an evaluation for malaria. In our review, 15 episodes of malaria (37.5%) had platelet counts less than $100 \times 10^9/\text{L}$, and 12 (30%) had low normal platelet counts of $100-130 \times 10^9/\text{L}$. Although non-specific, thrombocytopenia can be an important early clue to the diagnosis of malaria.

Limitations to this study include its small size, retrospective nature and biases created by parent and family self-reporting. This study does not have a denominator for the number of children who received adequate malaria counselling and chemoprophylaxis, and represents a biased population. This study examined only cases seen at BCCCH and did not include pediatric cases from other hospitals in the Vancouver region. Reportable disease data from BCCDC suggest that a significant number of pediatric cases of malaria present to other hospitals in the greater Vancouver area.

CONCLUSION

This study identified that South Asian VFR children in the Vancouver region who travel to India are a population at increased risk of travelling without adequate malaria protection. The development of more innovative and creative approaches for reaching this VFR community who regularly travel without seeking pre-travel advice is essential. Clearly, there is an urgent need for education of both travellers and health care providers about personal protection measures, appropriate chemoprophylaxis, and the necessity for prompt medical evaluation of fever in a returning traveller.

Due to the constantly changing situation with drug-resistant malaria, physicians must have access to up-to-date evidence-based recommendations such as the most recent *Committee to Advise on Tropical*

Medicine and Travel (CATMAT) Canadian recommendations for the prevention and treatment of malaria among international travelers, Health Canada (www.TravelHealth.gc.ca), or they should refer patients to travel health specialists. Last, physicians need to have a high index of suspicion for malaria in any individual with a history of fever after returning from a malaria-endemic area.

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RÉSUMÉ

Contexte : Rares sont les études qui portent sur l'épidémiologie de la malaria importée chez les enfants canadiens. En cernant les populations les plus vulnérables au Canada, on pourrait élaborer des stratégies ciblées de prévention de la malaria dans ces groupes. Dans notre étude, nous avons voulu décrire l'épidémiologie de la malaria diagnostiquée à l'Hôpital pour enfants de la Colombie-Britannique (BCCH) entre 1984 et 2001.

Méthode : Nous avons procédé à l'examen rétrospectif des cas de malaria enregistrés au BCCH et confirmés par le British Columbia Centre for Disease Control. Les données démographiques et cliniques ont été enregistrées dans un formulaire normalisé.

Résultats : La malaria a été diagnostiquée 42 fois chez 40 enfants (âgés de 24 jours à 14,8 ans). Trente cas (71,4 %) se sont produits chez 28 résidents canadiens, et les 12 autres (28,6 %) chez des enfants immigrants ou réfugiés. Vingt-six enfants (65 %) étaient des garçons. Trente et un enfants (77,5 %) étaient originaires des Indes orientales. Trente-trois (78,6 %) avaient été exposés à la malaria dans le sous-continent indien. *Plasmodium vivax* a été décelé chez 37 enfants (88,1 %), *P. falciparum* chez 3 enfants (7,1 %), et une souche inconnue chez 2 enfants (4,8 %). Dans 14 cas relevés chez des enfants résidents (46,7 %), les parents ont dit avoir reçu des conseils médicaux avant de partir en voyage. Dans 10 cas relevés chez des résidents (33,3 %), on avait prescrit une chimioprophylaxie, principalement de la chloroquine, et au moins six de ces personnes (60 %) n'avaient pas pris le médicament. La durée des symptômes avant le diagnostic était inférieure ou égale à 7 jours dans 27 cas (64,3 %), de 8 à 30 jours dans 10 cas (23,8 %), supérieure à 30 jours dans 4 cas (9,5 %) et inconnue dans un dernier cas (2,5 %). Vingt-quatre cas sur 36 (66,7 %) avaient consulté au moins deux et parfois plus de quatre médecins avant de recevoir un diagnostic de malaria.

Conclusion : La majorité des enfants compris dans notre étude étaient originaires des Indes orientales et avaient été exposés à la malaria en Inde. Dans la plupart des cas, les parents n'avaient pas demandé de conseils médicaux avant de voyager ou avaient reçu des conseils inadéquats, et ils n'avaient pas observé la chimioprophylaxie. Comme la malaria est une maladie potentiellement mortelle, mais évitable, il faudrait mettre en place des stratégies pour conseiller adéquatement les voyageurs dans les groupes très vulnérables.