Malaria in travellers returning or migrating to Canada: surveillance report from CanTravNet surveillance data, 2004–2014

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Abstract

Background: Malaria remains the most common specific cause of fever in returned travellers and can be life-threatening. We examined demographic and travel correlates of malaria among Canadian travellers and immigrants to identify groups for targeted pretravel intervention.

Methods: Descriptive data on ill returned Canadian travellers and immigrants presenting to a CanTravNet site between 2004 and 2014 with a diagnosis of malaria were analyzed. Data were collected using the GeoSentinel data platform. This network comprises 63 specialized travel and tropical medicine clinics, including 7 Canadian sites (Vancouver, Calgary, Toronto, Ottawa, Winnipeg and Montréal), that contribute anonymous, delinked, clinician- and questionnaire-based travel surveillance data on all ill travellers examined to a centralized Structure Query Language database.

Results: During the study period, 20 345 travellers and immigrants were evaluated, and 93% had a travel-related diagnosis. Of these, 437 (2.1%) patients received 456 malaria diagnoses, the most common species being Plasmodium falciparum (n = 282, 61.8%). People travelling to visit friends and relatives were most well-represented (n = 169, 38.7%), followed by business travellers (n = 71, 16.2%). Sub-Saharan Africa was the most common source region, accounting for 341 (74.8%) malaria diagnoses, followed by South Central Asia (n = 55, 12%). Nigeria was the most well-represented source country, accounting for 41 cases (9.0%). India, a high-volume destination for Canadians, accounted for 40 cases (9.0%), 36 of which were caused by Plasmodium vivax. Of 456 malaria diagnoses, 26 (5.7%) were severe. Of 377 nonimmigrant travellers with malaria, 19.9% (n = 75) travelled for less than 2 weeks, and 7.2% (n = 27) travelled for less than 1 week.

Interpretation: This analysis provides an epidemiologic framework for Canadian practitioners encountering prospective and returned travellers. It confirms the importance of preventive measures and surveillance associated with travel to sub-Saharan Africa and India, particularly by travellers visiting friends or relatives. Short-duration travel confers important malaria risk.
surveillance summary of malaria in a cohort of returned travellers and new immigrants presenting for care at CanTravNet sites over a 10-year period.

**Methods**

**Setting**

Seven Canadian sites from 5 provinces (British Columbia, Alberta, Manitoba, Ontario and Quebec), also belonging to the GeoSentinel Global Surveillance Network, constitute CanTravNet, as described. These sites are large referral-based outpatient centres staffed by specialists in travel and tropical medicine, which serve the Greater Vancouver–Victoria, Calgary, Winnipeg, Toronto, Ottawa and Montréal metropolitan areas and could account for service of almost 50% of the Canadian population. Network sites have been accrued over time, with inaugural sites in Toronto (1997) and Ottawa (1997), and more recent additional sites in Victoria–Vancouver (2009), Montréal (2007 and 2011), Calgary (2012) and Winnipeg (2016).

**Sources of data**

Data were collected using the GeoSentinel Surveillance Network data platform. This network comprises 63 specialized travel and tropical medicine clinics on 6 continents, which contribute denominализed clinician- and questionnaire-based travel surveillance data on all ill travellers who undergo examination to a centralized Structured Query Language database (for additional details see www.geosentinel.org). Collected data include patient demographics, details of recent travel, 5-year travel history, purpose of travel and pretravel encounter history. Final diagnoses are made by attending physicians at the CanTravNet site and assigned a diagnostic code selected from a standardized list of more than 500 diagnostic entities, including etiologic (e.g., *Plasmodium falciparum*) and syndromic (e.g., fever) diagnoses. All CanTravNet sites contribute microbiologically confirmed data, where available, based on the best national reference diagnostic tests (including molecular diagnostics) available at the time. Further details regarding CanTravNet can be found at www.istm.org/cantravnet, and additional details regarding the CanTravNet data source and definitions are as described.

**Definitions and classifications**

**Reason for most recent travel**

Six travel purpose designations were used, including immigration (including refugee), tourism, business, missionary/volunteer research/aid work, visiting friends and relatives and “Other,” which includes students, military personnel and medical tourists. Travel for the purpose of visiting friends and relatives is defined as travel by an immigrant who is ethnically or racially distinct from the majority population in their current country of residence who returns to his or her homeland to visit friends and relatives. Such travel also includes children of foreign-born parents (i.e., second-generation immigrants) who return to their parent’s homeland to visit friends and relatives. The term is typically applied to people travelling from a high-income country of current residence to a low-income country of origin.

Countries of exposure and travel were assigned to 1 of 8 hard-coded regional classifications (within the GeoSentinel database) where malaria is transmitted: Central America, the Caribbean, South America, North Africa, sub-Saharan Africa, South Central Asia, Southeast Asia and Oceania.

**Inclusion criteria**

Demographic, clinical and travel-related data on Canadian citizens and new immigrants to Canada encountered after completion of their international travel or residence abroad and seen in any of 6 CanTravNet sites from September 2004 to September 2014 were extracted and analyzed. Only patients with a probable or confirmed final diagnosis of malaria (specific cause as described previously) were included. A “returned traveller” refers to a single travel episode within the database, where patients could appear more than once if they had more than 1 episode of malaria related to different trips, or if their illness was diagnosed with more than 1 species of malarial infection.

**Statistical analysis**

Extracted data were managed in a Microsoft Access database and analyzed descriptively. Travellers were described by purpose of travel, demographics and travel metrics (including pretravel encounters, diagnoses, country of exposure and region of travel). Differences between groups of travellers were compared using a Fisher exact test or χ² analysis. All statistical computations were performed on SigmaStat 2.03 software (SPSS Inc., Chicago, Ill.) or GraphPad Prism software (GraphPad Software Inc., La Jolla, Calif.).

**Results**

During the study period, 20 345 travellers and immigrants presented to a CanTravNet site, 93% of whom had a travel-related diagnosis. Of these, 437 (2.1%) patients received 456 diagnoses of malaria, which accounts for 10.9% of the total number of malaria cases (n = 4190) reported in Canada through the national notifiable disease surveillance system over a similar 10-year period; 63.7% of patients with a malaria diagnosis were male. The most common malaria species imported by returned travellers and new immigrants in this analysis was *P. falciparum* (n = 282, 61.8%). Four cases of *P. falciparum–Plasmodium vivax* coinfection, and 2 cases of *P. falciparum–Plasmodium ovale* coinfection were documented. People travelling for the purpose of visiting friends and relatives were the most well-represented (n = 169, 38.7%), followed by business travellers (n = 71, 16.2%), missionaries, volunteers or aid workers (n = 69, 15.8%), immigrants (n = 60, 13.7%), tourists (n = 52, 11.9%) and students or military personnel (n = 16, 3.7%). Demographic characteristics of the malaria patients presenting to CanTravNet sites are summarized in Table 1. Sub-Saharan Africa was the most common region of acquisition for malaria, accounting for 326 (n = 71.5%) cases, followed by South Central Asia (n = 55, 12.6%), South America (n = 10, 2.2%) and North Africa (Sudan and South Sudan) (n = 10, 2%) (Table 1). Nigeria was the most well-represented source country, accounting for 41 cases (9.4%). India, a partic-
Table 1: Demographic characteristics of 437 returned travellers or new immigrants with 456 malaria diagnoses who presented to a CanTravNet site for care, 2004–2014*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Purpose of travel; no. (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All cases (456 diagnoses; 437 patients)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 278 (63.6) 101 (59.8) 62 (87.3) 38 (55.1) 39 (65.0) 26 (50.0) 12 (75.0)</td>
</tr>
<tr>
<td>Age, yr, median (range)</td>
<td>33.5 (1–82) 37 (2–82) 42 (21–71) 28 (12–68) 22 (1–64) 39 (1–75) 22 (14–48)</td>
</tr>
<tr>
<td>Children and adolescents (age &lt; 18 yr)</td>
<td>27 (6.2) 10 (5.9) 0 (0) 1 (1.4) 14 (23.3) 1 (1.9) 1 (6.3)</td>
</tr>
<tr>
<td>Type of patient</td>
<td>Inpatient 141 (32.3) 52 (30.8) 28 (39.4) 21 (30.4) 18 (30.0) 16 (30.8) 6 (37.5)</td>
</tr>
<tr>
<td>Travel duration, d, median (range)</td>
<td>35 (0–7256) 34 (0–884) 33 (0–1065) 61 (3–831) NA 19 (0–547) 90 (1–7256)</td>
</tr>
<tr>
<td>Pretravel medical encounter</td>
<td>Yes 131 (30.0) 29 (17.1) 39 (54.9) 39 (56.5) NA 16 (30.8) 6 (37.5)</td>
</tr>
<tr>
<td>Geographic region of exposure</td>
<td>Sub-Saharan Africa 326 (74.6) 133 (78.7) 57 (80.3) 58 (84.1) 38 (63.3) 28 (53.8) 11 (68.8)</td>
</tr>
<tr>
<td>Birth country</td>
<td>Canada 148 (33.9) 11 (6.5) 43 (60.6) 59 (85.5) 0 (0) 29 (55.8) 6 (37.5)</td>
</tr>
</tbody>
</table>

Note: NA = not available.

*The total cohort of travellers consisted of 18 870 travellers with a definitive travel-related diagnosis, 931 with a non-travel–related diagnosis, and 544 with a diagnosis for which relation to travel could not be ascertained. This analysis includes only those travellers with a final diagnosis of malaria, except where indicated otherwise.

†Unless otherwise specified.
‡Includes 15 cases in students and 1 case in military personnel.
§Among patients born outside of Canada, people who travelled for the purpose of visiting friends and relatives were defined as immigrants who were ethnically or racially distinct from the majority population in their current country of residence and who returned to their homeland to visit friends and relatives. This group also included children of foreign-born parents (i.e., second-generation immigrants) who returned to their parents’ homeland to visit friends and relatives.
ularly high-volume destination for Canadians, accounted for 40 cases (9.2%), 36 of which were caused by \textit{P. vivax}. In total, 60.7\% of \textit{P. vivax} cases were imported from the Indian subcontinent (51/84). Five cases of \textit{P. falciparum} were imported from Haiti and 3 from Dominican Republic. Source regions by purpose of travel are listed in Table 1, and source countries by type of malaria are listed in Table 2. Table 3 lists source countries by year of import to Canada.

Of 456 diagnoses among returned travellers or new immigrants with malaria who presented for care at a CanTravNet site, fever was the presenting symptom in 83.1\% (\(n = 379\)), although this presentation varied by causative species (Table 2). Malaria was also the more common specific cause of fever in this analysis, occurring in 15\% of returned travellers or new immigrants presenting with fever. Other common presenting symptoms in those with malaria diagnoses included fatigue (\(n = 153, 33.6\%\)), abnormal laboratory tests (\(n = 146, 32\%\)) and gastrointestinal problems (\(n = 114, 25\%\)). Of the total 456 malaria diagnoses, 26 (5.7\%) were classified as severe, but varied by travel reason, with 9.6\% (7/73) of cases in missionaries classi-
fied as severe, 9.1% (7/77) in business travellers, 7.4% (4/54) in tourists, 3.2% (2/62) in immigrants and 2.9% (5/174) in travellers visiting friends and relatives (Table 4). Collectively, severe malaria was overrepresented among travellers not visiting friends and family and nonimmigrant travellers (19/221 diagnoses) compared with the immigrants or travellers who were visiting friends and relatives (7/236 diagnoses) \( (p = 0.014) \). About one-third of travellers and new immigrants with malaria \( (n = 154) \) required inpatient management of their illness, 81.2% of which cases were caused by \( P. falciparum \) \( (n = 125) \) (Table 1).

About 30% \( (n = 131) \) of travellers with malaria had received pretravel care (Table 1). The most well-represented group of travellers with malaria, travellers visiting friends and relatives, had the lowest rate of pretravel encounters (Table 1). The next most well-represented groups of travellers, those travelling for business and missionary, volunteer, research or aid work, had the highest uptake of pretravel encounters (54.9% and 56.5%, respectively). Of travellers with malaria who had received pretravel care \( (n = 131) \), only 68 (51.9%) reported taking some sort of chemoprophylaxis (Table 4). Although it is unknown how many travellers with malaria were adherent to prophylaxis, at least 5 (1.1%) were specifically noted as having either missed doses of doxycycline throughout travel or run out of pills before departure from the malaria-endemic area (Table 4).

Of 377 returned nonimmigrant travellers with malaria presenting for care at a CanTravNet site, 19.9% \( (n = 75) \) had a trip duration of less than 2 weeks, and 7.2% \( (n = 27) \) had travelled for less than 1 week. Of malaria diagnoses among nonimmigrant travellers with short-duration travel \(< 2 \text{ weeks}\), 68.0% were caused by \( P. falciparum \) \( (51/75) \), and 9.3% were severe \( (7/75) \). Pretravel advice had been obtained by 34.7% \( (26/75) \) of travellers with malaria who had travelled for less than 2 weeks, which was similar to those with any duration of travel (Table 1).

**Table 4: Cases of malaria by travel reason among 18 870 ill returned travellers presenting to a CanTravNet site, 2004–2014**

<table>
<thead>
<tr>
<th>Reason for travel</th>
<th>Total no. of malaria diagnoses (no. of travellers)</th>
<th>Type of malaria; no. of diagnoses</th>
<th>Top 3 countries of exposure</th>
<th>Received prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ( (n = 18 870) )</td>
<td>456 (437)</td>
<td>Plasmodium falciparum 282</td>
<td>Ghana, Uganda, Ivory Coast</td>
<td>68*</td>
</tr>
<tr>
<td>Tourism ( (n = 8 136) )</td>
<td>54 (52)</td>
<td>Severe malaria 26</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Immigration ( (n = 4 967) )</td>
<td>62 (60)</td>
<td>Plasmodium vivax 16</td>
<td>India, Nigeria, Liberia</td>
<td>NA</td>
</tr>
<tr>
<td>Visiting friends and relatives ( (n = 1 966) )</td>
<td>174 (169)</td>
<td>Plasmodium ovale 15</td>
<td>Nigeria, India, Cameroon</td>
<td>28</td>
</tr>
<tr>
<td>Missionary, volunteer, research or aid work ( (n = 1 656) )</td>
<td>73 (69)</td>
<td>Species unknown 4</td>
<td>Ghana, Burkina Faso, Cameroon</td>
<td>19</td>
</tr>
<tr>
<td>Business ( (n = 1 643) )</td>
<td>77 (71)</td>
<td>Plasmodium malariae 5</td>
<td>Burkina Faso, Ghana, Guinea</td>
<td>7</td>
</tr>
<tr>
<td>Other† ( (n = 498) )</td>
<td>16 (16)</td>
<td></td>
<td>India, Benin, Burkina Faso, Tanzania</td>
<td>2</td>
</tr>
</tbody>
</table>

Note: NA = not applicable.
*Includes 5 travellers who either missed doses of doxycycline during travel or ran out of doxycycline before the end of travel.
†Includes 355 students, 122 military personnel and 21 people travelling for medical tourism.

**Interpretation**

Our analysis of surveillance data on ill returned Canadians provides an epidemiologic framework for Canadian practitioners encountering prospective travellers. About two-thirds of malaria cases in this analysis occurred in men, a phenomenon noted previously. Higher rates of malaria and deaths due to malaria among male travellers may reflect both biological
(e.g., attractiveness to vectors) and behavioural (e.g., adherence to chemoprophylaxis) risk factors, although their continued overrepresentation in epidemiologic analyses speaks to the need for better, targeted prevention initiatives.

Business travellers were overrepresented among returned travellers with malaria presenting for care at a CanTravNet site. As a group, these travellers tended to be born in Canada and conducting business in West Africa, the region with the highest overall relative risk of malaria. Most cases of malaria in business travellers in this analysis were caused by potentially fatal *P. falciparum*. Although more than half of business travellers with malaria had received pretravel advice, few reported taking chemoprophylaxis. Thus, there is a clear disconnect between known travel to a risk area and adherence to chemoprophylaxis in this group. Understanding barriers to uptake of malaria preventive measures, which includes chemoprophylaxis and insect precautions after the pretravel encounter among business travellers should be strategically prioritized to reduce morbidity and potential mortality.

Travellers visiting friends and relatives constitute a particular group at high-risk for malaria, and were the most well-represented group of travellers with malaria in our analysis. Unlike business travellers, these travellers had the lowest rates of pretravel encounter of any type of traveller, a finding that has been noted in previous studies. Because malaria is preventable with appropriate chemoprophylaxis and insect precautions, poor uptake of pretravel advice and intervention may translate into a proportionately higher burden of malaria among travellers visiting friends and relatives. Understanding the barriers to obtaining a pretravel consultation in this population is necessary to inform strategic initiatives aimed at reducing the burden of imported malaria in this group of highly mobile Canadians and their children.

Our data confirm the overwhelming importance of travel to sub-Saharan Africa and the Indian sub-continent, particularly by travellers visiting friends and relatives, but also other travellers, to the importation of malaria to Canada. The top represented source countries in this analysis were Nigeria and India, although countries such as Ghana, Ivory Coast, Cameroon and Burkina Faso were also well-represented, and mostly accounted for imports of *P. falciparum*. Although most cases of malaria in this analysis were imported from sub-Saharan Africa, only about half of tourist travellers acquired their malaria in this region. Compared with other types of traveller, tourists appeared to acquire malaria in regions such as Central America, the Caribbean and Oceania, which may reflect the perception of low malaria risk in these areas and consequent poor adherence to prophylaxis and personal protective measures. Continued reinforcement of personal protective vigilance, including insect precautions, in the pretravel setting, even for possibly low-risk itineraries, is important.

India was the second most common source country in our analysis and contributed mostly to the burden of imported *P. vivax* infection, which raises the issue of how to best address malaria prevention in Canadian travellers to the Indian subcontinent. Although clearly a risk in many parts of the Indian subcontinent, the true epidemiology of malaria in India is complex owing to seasonal variability, widespread urban and rural transmission and the difficulty in separating multiple relapses of *P. vivax* from new infections. These factors contribute to confusion and inconsistent recommendations around malaria prevention strategies for travellers to India. An individualized approach to malaria prevention is needed for travellers, taking into account multiple relevant factors including the season, duration, regions visited and type of travel.

Risk of malaria to Canadian travellers is a complex combination of local transmission intensity, type and duration of travel, total numbers of Canadian travellers to the malaria-endemic regions and other factors. For example, India has far lower transmission intensity than most countries in sub-Saharan Africa, yet it was the second most common source country in this analysis. Thus, local transmission intensity, while important when advising travellers, does not directly translate into overall risk for importing malaria into Canada.

Short duration travel to malaria risk areas was confirmed to require malaria prevention, which may include chemoprophylaxis and personal protective measures, such as insecticide-treated bed nets and clothing, and the use of insect repellents. About one-fifth of malaria cases in this analysis were acquired on trips lasting less than 2 weeks, most of which were caused by *P. falciparum* and some of which were severe. Even trips lasting less than 1 week carried risk. Again, poor uptake of pretravel consultation, the perception of lower risk with shorter itineraries and poor translation of pretravel counselling into preventive action on the part of the traveller may have contributed to the malaria burden among short-term travellers.

Serial short-term travellers (e.g., frequent business traveller) present a challenge to the current standard of pretravel care. Many of these travellers anecdotally report that they are loathe to be on antimalarial agents continuously or near continuously, and are either nonadherent to posttravel 1- or 4-week dosing of chemoprophylaxis, or do not take chemoprophylaxis at all. Business travellers had the highest rates of hospital admission for their malaria among all groups of travellers and new immigrants presenting for care at a CanTravNet site. Similarly, missionaries, volunteers, researchers and aid workers, most of whom were Canadian-born, had high rates of severe malaria. Conversely, very few cases in immigrants or travellers visiting friends or relatives were severe, supporting the hypothesis that at least some long-term semi-immunity to malaria in people born and raised in an endemic area persists and translates into less severe clinical manifestations of disease. Additional clinical context of this report’s findings can be found in Appendix 1, available at www.cmajopen.ca/content/4/3/E352/suppl/DC1.

**Limitations**

Analysis of CanTravNet data has several limitations, which have been described previously. This analysis pertains only to the sample of ill returned travellers and new immigrants who presented to a CanTravNet centre, thus, our conclusions may lack generalizability. Our network captured 11% of all malaria cases imported to Canada over a 10-year period, with 19% captured during the final year of this analysis, and we noted similar rates of severe and complicated malaria to those noted.
previously.10 Our ability to comment on changing rates of imported malaria over time is hindered by our accrual of additional sites in the network. Our data cannot estimate incidence rates or destination-specific numerical risks for malaria.8,22 Because the Calgary site was new to CanTravNet in 2012, travellers and new immigrants to Alberta are under-represented, which may have introduced bias given the inter-provincial variation in travel patterns and preferences. In addition, owing to the nonnominal and delinked nature of the database, we cannot exclude the possibility of bias due to case-clustering within family units, for example. Data on pre-travel medical consultation was missing for 20% of ill returned travellers. Finally, our network does not capture substantial numbers of pediatric malaria cases; for this reason, our data may not be generalizable to the pediatric population in Canada.

Conclusion

The data collected by the CanTravNet Surveillance Network can be used to better inform pretravel malaria risk assessment, and posttravel management, and to illuminate changing patterns of imported malaria. Malaria remains the top specific cause of fever in returned travellers, and although still mostly acquired in sub-Saharan Africa, India was the second most common source country of imported malaria over the 10-year period studied. The lack of pretravel counselling continues to be noted in groups of high-risk travellers, such as those travelling to visit friends and relatives. Barriers to the uptake of effective chemoprophyaxis by particular risk groups and the use of insect repellent, bed nets, and other preventative measures should be systematically assessed through future research.

References


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