TITLE PAGE

The impact of the COVID-19 pandemic on malaria in returning travelers in Canada: a retrospective population-based cohort study

RUNNING TITLE:

Impact of the COVID-19 Pandemic on Malaria in a Canadian Urban Center

AUTHORS:

Anthony Lieu MD,[1] Jordan Mah MD,[1] Noémie Desgagnés MD,[2] Dylan Pillai MD PhD[1,3]

AFILLIATIONS:

1. Division of Infectious Diseases, Department of Medicine, Cummings School of Medicine, University of Calgary, Calgary (Canada),

2. Division of Internal Medicine, Department of Medicine, Cummings School of Medicine, University of Calgary, Calgary (Canada)

3. Department of Pathology and Laboratory Medicine, Cummings School of Medicine, University of Calgary, Calgary (Canada)

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CORRESPONDING AUTHOR:

Dylan Pillai, MD, PhD

Department of Pathology and Laboratory Medicine, Cummings School of Medicine, University of Calgary, Calgary

Phone: (403) 770 3578

Email: drpillai@ucalgary.ca

AUTHOR STATEMENTS

AUTHOR CONTRIBUTIONS

Anthony Lieu: Methodology, Data Collection, Statistical Analysis, Writing, Reviewing and Editing **Jordan Mah:** Writing, Interpretation of Results, Reviewing and Editing **Noémie Desgagnés:** Original draft preparation and critical appraisal **Dylan Pillai:** Conceptualization, Methodology, Interpretation of Results, Reviewing, Editing and Supervision

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CONFLICT OF INTEREST/DISCLOSURE

The authors have declared no conflicts of interest

HIGHLIGHTS

In high-income, low-prevalence settings, travel patterns largely govern malaria transmission; the COVID-19 pandemic has led to travel restrictions resulting in a decrease in malaria case incidence. The proportion of travellers seeking pre-travel has decreased; with the easing of borders, an increase in malaria cases may occur.

Malaria is a life-threatening illness that remains a global burden, with an estimated 241 million malaria cases in 2020.[1] The coronavirus disease (COVID-19) pandemic has disrupted worldwide efforts to reduce malaria's global burden, leading to more cases and deaths in highly endemic countries.[1] The impact of the COVID-19 pandemic on malaria epidemiology in low-prevalence settings has not been previously studied.

Over the last decade, malaria incidence has increased in low-prevalent countries due to higher rates of immigration and travel from malaria-endemic countries, mainly from visiting friends and relatives (VFRs), a group less likely to seek pre-travel advice and chemoprophylaxis.[3-5]

In Canada, the COVID-19 pandemic led to nationwide travel restrictions imposed by the federal government on March 16, 2020, to control the virus, as early transmission dynamics were driven mainly by returning travelers.[5] This study aims to describe the impact of the COVID-19 pandemic on malaria epidemiology in Canada, a high-income low-prevalence setting.

We conducted a retrospective population-based cohort study at a centralized regional microbiology laboratory serving Calgary and surrounding areas, covering a population of 1.9 million. All patients who tested positive for malaria from January 2018 to December 2021 were enrolled and included for analysis. We compared the epidemiological characteristics of the pre-pandemic period (January 2018 – March 15th, 2020) to the peri-pandemic period (March 16th, 2020 – December 2021).

Clinical data was retrieved from the standardized travel form, which physicians are required to complete prior to malaria testing. This included sex, age, reason(s) for travel, country visited, whether pre-travel advice was sought, whether chemoprophylaxis was

taken, symptoms, and onset of symptoms. Regions of travel are defined according to the United Nations geoscheme.

When multiple history forms were submitted for the same patient, only the original form was collected. Relapsing infections (within two months) and cases with a mixed *Plasmodium* infection were counted as a single case. The algorithm used to test malaria includes a Loop-Mediated Isothermal Amplification (LAMP) screen (Alethia® Malaria, Median Bioscience, Cincinnati, OH) followed by standard Giemsa-stained thick and thin film microscopy for speciation.[6] We classified as *Plasmodium spp*. cases where *Plasmodium* could not be speciated.

Standard descriptive statistics was performed. Categorical data was compared using the $\chi 2$ test; continuous data were compared using the rank-sum test. A p-value <0.05 was considered statistically significant. Ethics approval was obtained from the Conjoint Health Research Ethics Board at the University of Calgary.

The mean incidence rate for positive malaria cases for the study period was 1.74 per 100,000 person-year [95% CI,1.47-2.05] (Figure 1). From the pre-pandemic to the peri-pandemic period, the incidence rate significantly decreased from 2.31 [95% CI,1.89-2.79] to 1.02 cases per 100,000 person-year [95% CI,0.73-1.40]. We identified 138 cases, 102 (73.9%) were from the pre-COVID-19, and 36 (26.1%) were peri-COVID-19 period (Table 1). The median age was 38-years-old for the entire study period with no significant difference pre- or per-pandemic. Men represented the majority of cases (68.8%), and most travelled to Africa (87.6%), followed by Southern Asia (5.8%). *Plasmodium falciparum* was the most frequently detected species (90, 65.2%), followed equally by *P.ovale* and *P. vivax* (14.5%) with no significant difference pre- or per-

pandemic. Overall, VFRs was the most common reason for travel during both periods (52.6%) but represented a higher proportion in the pre-pandemic group (56.9 vs. 38.9%, [P= .042]). The proportion of new immigrants increased during the peri-pandemic period (14.7 vs. 27.8%, [P= .028]). Significantly fewer patients during the peri-pandemic period sought pre-travel advice (30.0 vs. 11.1%, P= .048). While malaria chemoprophylaxis was sought less frequently during the peri-pandemic phase, it was not statistically significant (25.9% vs. 12.9%, P= .204). The duration from symptom onset to malaria testing was similar in both groups, with a median of 4 days (IQR 3-8). Visits to the Emergency Department were the most common presentation site during the study period (72.1.3%). There was no statistical difference between ED and outpatient visits between periods.

In high-income low-prevalence settings, immigration or travel patterns largely govern malaria transmission dynamics.[2,3,4,7,8] We observed a significant drop in malaria cases in the peri-pandemic period, likely caused by several public health measures to slow down COVID-19 transmission, including avoidance of non-essential travel and mandatory quarantines.[5] The decrease in the proportion of VFRs and increased travel related to new immigrants during the peri-pandemic period is likely related to travel restrictions deterring the general population from non-essential travelling.[5] More alarmingly, during the peri-pandemic period, there was a further decrease in those seeking pre-travel advice and a trend towards decreasing malaria chemoprophylaxis. Possible explanations for this include the stigma associated with travel during the pandemic, lack of publicly funded pre-travel clinics in times of economic scarcity, and avoidance of healthcare utilization due to fear of COVID-19. Pre-travel advice is beneficial for all travelers as these individuals are less likely to be diagnosed with malaria and other infectious diseases.[4,7,9]

If these trends continue, with resuming travel and the easing of border measures, this could lead to higher malaria rates in a low-prevalent setting. Targeted pre-travel health care services should be emphasized in these populations to prevent malaria cases.

Our results endorse previous findings that adult males are at highest risk of acquiring malaria, *P. falciparum* is the most reported malaria species, and cases are mainly imported from Africa.[4,7,8] Interestingly, we detected an increase in the proportion of patients presenting with cough, arthralgias/myalgias, and diarrhea in the peri-COVID-19 period. The presence of cough and diarrhea is associated with a decreased odds of having malaria.[10] However, we attributed this finding to patients and healthcare providers being sensitized to screening for a broad list of COVID-19 symptoms during the pandemic, which include cough, arthralgia/myalgia, and diarrhea. This could also be potentially explained by COVID-19 co-infection or recall bias in a period of high SARS-CoV-2 endemicity.

Some limitations of our study include the retrospective nature and single-center design, which may not be generalizable to other low-prevalent malaria settings. Nevertheless, to our knowledge, this is the first study describing the impact of the COVID-19 pandemic on the epidemiology of malaria in a low-prevalent setting. Pre-travel advice and malaria chemoprophylaxis was even lower during the peri-pandemic period, which may increase the proportion of vulnerable population at risk for malaria. This could bear important public health considerations and targeted pre-travel health care services for this group should be considered.

References

1. World Health Organization. More malaria cases and deaths in 2020 linked to COVID-19 disruptions. Accessed January 19, 2022. https://www.who.int/news/item/06-12-2021-more-malaria-cases-and-deaths-in-2020-linked-to-covid-19-disruptions
2. Lee CS, Gregson DB, Church D, et al. Population-Based Laboratory Surveillance of Imported Malaria in Metropolitan Calgary, 2000–2011. PLoS One 2013;8(4):e60751. doi:10.1371/JOURNAL.PONE.0060751
3. MacLean JD, Demers AM, Ndao M, et al. Malaria epidemics and surveillance systems in Canada. Emerg Infect Dis 2004;10(7):1195-1201. doi:10.3201/EID1007.030826
4. Angelo KM, Libman M, Caumes E, et al. Malaria after international travel: A GeoSentinel analysis, 2003-2016. Malar J 2017;16(1). doi:10.1186/s12936-017-1936-3
5. Government of Canada. Prime Minister announces new actions under Canada's COVID-19 response | Prime Minister of Canada. Published March 16, 2020. Accessed January 19, 2022. https://pm.gc.ca/en/news/news-releases/2020/03/16/prime-minister-announces-new-actions-under-canadas-covid-19-response
6. Rypien C, Chow B, Chan WW et al. Detection of Plasmodium Infection by the illumigene Malaria Assay Compared to Reference Microscopy and Real-Time PCR. J Clin Microbiol 2017;55(10):3037-3045. doi:10.1128/JCM.00806-17

7. Marasinghe DH, Cheaveau J, Meatherall B, et al. Risk of malaria associated with travel to malaria-endemic areas to visit friends and relatives: a population-based case–control study. CMAJ Open 2020;8(1):E60. doi:10.9778/CMAJO.20190070

8. Boggild AK, Geduld J, Libman M, et al. Malaria in travellers returning or migrating to Canada: surveillance report from CanTravNet surveillance data, 2004-2014. CMAJ Open 2016;4(3):E352. doi:10.9778/CMAJO.20150115

9. Weiss DJ, Bertozzi-Villa A, Rumisha SF, et al. Indirect effects of the COVID-19 pandemic on malaria intervention coverage, morbidity, and mortality in Africa: a geospatial modelling analysis. Lancet Infect Dis2021;21(1):59-69. doi:10.1016/S1473-3099(20)30700-3

10. Taylor SM, Molyneux ME, Simel DL, Meshnick SR, Juliano JJ. Does This Patient Have Malaria? JAMA 2010;304(18):2048-2056. doi:10.1001/JAMA.2010.1578

252 **FIGURE LEGEND:**

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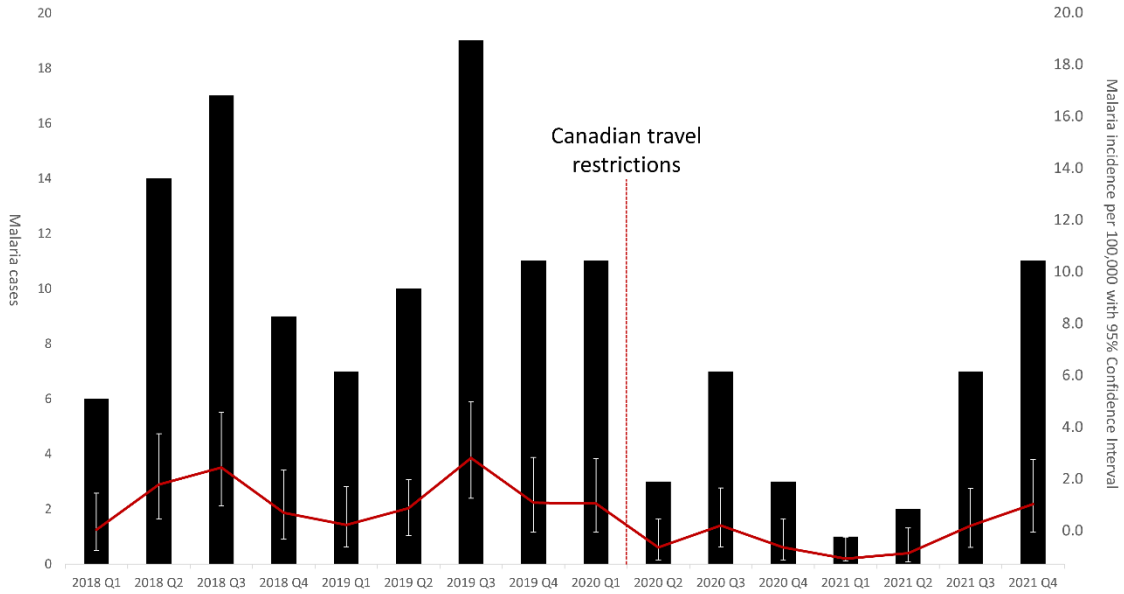

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255 Figure 1: Incidence of malaria by quartile (2018 Q1 to 2021 Q3)

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257 Table 1: Characteristics of laboratory-confirmed malaria case from malaria-endemic areas
258 stratified by pre-pandemic and peri-pandemic group.

Demographic	All N (%) N = 138	Pre-Pandemic N (%) N = 102	Peri-Pandemic N (%) N = 36	P. value
Age (y), Median (IQR)	38.0 (28.0-50.0)	39.0 (30.0-52.0)	35.0 (24.3-48.0)	.223
Sex (F)	43 (31.2)	30 (29.4)	13 (36.1)	.456
Region of Travel WHO				
Western Africa	48 (34.8)	40 (39.2)	8 (22.2)	.066
Eastern Africa	24 (17.4)	18 (17.6)	6 (16.7)	.894
Northern Africa	30 (21.7)	21 (20.6)	9 (25.0)	.581
Middle Africa	18 (13.0)	11 (10.8)	7 (19.4)	.185
Southern Asia	8 (5.8)	4 (3.9)	4 (11.1)	.113
Other	4 (2.9)	4 (3.9)	0	.228
Initial Site				
Calgary ED visits	81 (59.6)	60 (58.8)	18 (58.3)	.959
Rural ED visits	17 (12.5)	11 (10.8)	6 (16.7)	.356

Outpatient visits	40 (29.5)	31 (30.4)	9 (25.0)	.540
Pre-travel Care				
Received pre-travel advice	27/107 (25.2)	24/80 (30.0)	3/27 (11.1)	.048
Received prophylaxis	25/122 (20.5)	21/81 (25.9)	4/31 (12.9)	.204
Reason for travel				
Tourism	18 (13.1)	14 (13.7)	5 (13.9)	.990
Business	6 (4.4)	5 (4.9)	1 (2.8)	.579
New Immigrant	26 (19.0)	15 (14.7)	10 (27.8)	.028
VFR	72 (52.6)	58 (56.9)	14 (38.9)	.042
Visitor to Canada	5 (3.6)	5 (4.9)	0	.172
Missing Travel Form	18 (13.0)	11 (10.8)	7 (19.4)	.199
Symptoms				
Fever/chills/rigor	119/124 (96.0)	92/94 (97.9)	27/30 (90.0)	.166
Headache	85/124 (68.5)	68/94 (72.3)	18/30 (60.0)	.170
Sore Throat	16/124 (12.9)	11/94 (11.7)	5/30 (16.7)	.253
Cough	20/124 (16.1)	11/94 (11.7)	9/30 (30.0)	.022
Arthralgia/ Myalgia	63/125 (50.4)	54/94 (57.4)	9/30 (30.0)	.012
Diarrhea	21/124 (16.9)	12/94 (12.8)	10/30 (33.3)	.009
Splenomegaly	2/124 (1.6)	1/94 (1.1)	1/30 (3.3)	.226

*Highlighted in grey indicate differences between periods with statistical significance