Intercurrent Flaviviral Viremia in Ill Returned Travelers with *Plasmodium vivax* Malaria

Ruwandi Kariyawasam[1], **Katherine Tan**[2], Min Qun Chen [3], Ruben Cuidamat [3], Aisha Khatib [4,5], Rachel Lau[3], Filip Ralevski[3], Andrea K. Boggild[1,3,4,5]

[1]Institute of Medical Sciences, University of Toronto, Toronto, ON, Canada, [2]Department of Human Biology, University of Toronto, Toronto, ON, Canada, [3]Public Health Ontario Laboratories, Toronto, ON, Canada, [4]Tropical Disease Unit, UHN-Toronto General Hospital, Toronto, ON, Canada, [5]Department of Medicine, University of Toronto, Toronto, ON, Canada.

Introduction

- Flaviviruses: transmitted to humans through infected bites of *Culex* spp. and *Aedes* mosquitoes[1]
- *Plasmodium vivax*: spread by the bite of *Anopheles* mosquito[2]
- Flaviviral infection could precipitate a *P. vivax* relapse[3]
- Given overlap of epidemiological and clinical presentations of both flaviviral and malaria infections, diagnostic testing where malaria is confirmed or excluded, without subsequent flaviviral testing may mask true epidemiology of co-infections[4]

Objective: We aim to understand the incidence of intercurrent flaviviral infection in confirmed *Plasmodium vivax* infection.

Methods

- DNA extracted from whole blood specimens and tested for malaria by microscopy and rapid diagnostic test (RDT) between 2006 and 2019 at Public Health Ontario Laboratory-Toronto[5,6]
- RNA extracted from *P. vivax* positive whole blood specimens and examined by real-time PCR (qPCR) for the following targets: flaviviruses (pan-FLAV) and dengue virus types 1-4 (DEN1, DEN2, DEN3, DEN4)[7-9]

696 whole-blood specimens tested with confirmed *P. vivax* from 2006-2019 → 502 unique specimens of *P. vivax* with documented travel history tested for dengue and flavivirus by qPCR

Figure 1: Workflow highlighting *P. vivax* confirmed diagnostic testing for intercurrent flaviviral infection using qPCR.

Results

Table 1: Clinical and parasitological characteristics of *P. vivax* cases.

	Total [n=175 (%)]
Median Age, years (range)	34 years (4 – 88 years)
Median Parasitemia, % (range)	0.1 % (< 0.01 % - 1.1 %)
Sex	
Male	121 (69 %)
Female	50 (29 %)
Unknown	4 (2%)
Travel History	
Yes	68 (39%)
Unknown	107 (61%)

Table 2: Known travel history

	Total [n=68 (%)]
Sub-Saharan Africa	5 (7%)
Indian Subcontinent	53 (78%)
India	34 (50%)
Latin America	9 (13%)
Southeast Asia	1 (2%)

Table 3: DENV and Flavivirus qPCR positive results.

DENV qPCR	Flavivirus qPCR
1/175 (0.6%)	1/175 (0.6%) untypeable

Discussion & Conclusions

- Both the Pan-FLAV and the Pan-DENV assays yielded a 0.6% positivity rate (1/175) each (Table 3)
- Type-specific real-time PCR revealed DEN1, detected on both Pan-FLAV and Pan-DENV assays
- *P. vivax* infections rates are highest from India, Pakistan and Guyana[10]
- Intercurrent flaviviral viremia was noted in 0.6% of specimens, suggesting primary flaviviral infection could have triggered relapse of *P. vivax*
- Alternatively, co-infections may suggest primary infection with both organisms given the overlap of vector populations in these endemic areas
- Consideration of flaviviral co-infection should be given to *P. vivax* patients to appropriately manage clinical manifestations including deep thrombocytopenia, lymphopenia, and high yield arboviral symptomology including rash and retro-orbital headache[4]

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Contact: Dr. Andrea K. Boggild | andrea.boggild@utoronto.ca | www.boggildlab.ca | @BoggildLab