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Intercurrent Flaviviral Viremia and *Plasmodium ovale* Infection in Ill Returned Travelers to Ontario

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Introduction

- Flaviviruses: transmitted to humans through infected bites of *Culex* and *Aedes* mosquitoes[1]
- *Plasmodium ovale*: spread by the bite of *Anopheles* mosquito[2]
- Flaviviral infection could precipitate a *P. ovale* 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 ovale* infection in whole blood specimens from ill returned travelers

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. ovale* 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]

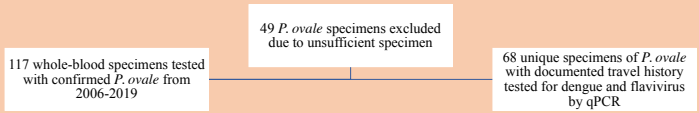

Figure 1: Workflow highlighting *P. ovale* confirmed diagnostic testing for intercurrent flaviviral infection using qPCR.

Results

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

	Total [n=68 (%)]
Median Age, years (range)	27.4 years (22 months – 72 years)
Median Parasitemia, % (range)	<0.01 % (< 0.01 % - 0.8 %)
Sex	
Male	37 (54.4 %)
Female	30 (44.1 %)
Unknown	3 (4.4%)
Travel History	
Yes	39 (57.4%)
Unknown	29 (42.6%)

Table 2: Top countries of travel

	Total [n=68 (%)]
Nigeria	23 (33.8%)
Africa, unspecified	5 (7.4%)
Congo	3 (4.8%)
Tanzania	3 (4.8%)

Table 3: DENV and Flavivirus qPCR positive results.

DENV qPCR	Flavivirus qPCR
0/68 (0%)	1/68 (1.5 %) untypeable

Discussion & Conclusions

- Pan-FLAV yielded a 1.5% positivity rate (1/68), while the DENV assays did not yield a positive result (Table 3)
- *P. ovale* infections are commonly imported to Ontario from West Africa, especially from Nigeria which was our top country of travel (Table 2)
- Intercurrent flaviviral viremia was noted in 1.5% of specimens, suggesting that primary flaviviral infection could have triggered a relapse of *P. ovale*
- Alternatively, co-infection 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. ovale* patients to appropriately manage clinical manifestations including deep thrombocytopenia, lymphopenia, and high yield arboviral symptomology including rash and retro-orbital headache[3]

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