asm microbe 2019
JUNE 20 – 24 ● SAN FRANCISCO, CA

Control/Tracking Number: 2019-A-3184-MICROBE
Activity: Abstract
Current Date/Time: 1/19/2019 2:07:17 PM

Low Sequence Heterogeneity of *Plasmodium falciparum* Isolates Imported to Ontario, Canada from West Africa over a 10-year Period with Increased Molecular Markers of Resistance to Proguanil

Author Block: E. Shao[1], R. Lau[2], M. Dong[1], J. Kwan[1], R. Kariyawasam[3], F. Ralevski[2], A. K. Boggild[1]; [1]Tropical Disease Unit, Toronto Gen. Hosp., Toronto, ON, Canada, [2]Publ. Hlth.Ontario, Toronto, ON, Canada, [3]Univ. of Toronto, Toronto, ON, Canada

Abstract:

Approximately 200 cases of malaria are imported to the province of Ontario annually, with the majority due to *Plasmodium falciparum (Pf)* originating from West Africa. We performed sequence analyses of *Pf* isolates returning from Ghana and Cameroon over a 10-year period to understand patterns of genetic heterogeneity and molecular drug resistance markers over time. We identified 36 *Pf* isolates from Ghana (18 from 2006-2008 and 18 from 2014-2016); and 16 from Cameroon throughout 2006-2016. DNA was extracted and regions commonly used for strain typing were analyzed including: merozoite surface potein (*msp*) 1 and 2; erythrocyte binding antigen (*eba*) 175; and glutamate-rich protein (*glurp*) regions. Molecular resistance markers including: *cytochrome B* (*cytB*) and *dihydrofolate reductase (dhfr)* for resistance to atovaquone-proguanil (Malarone®); *atpase6* and *kelch13* for artemisinin and derivatives; and c*hloroquine resistance transporter (Pfcrt)* for chloroquine were analyzed. Phylogenetic tree analysis revealed some sequence heterogeneity within Ghanian and Cameroonian isolates, however, there was no clustering of isolates over time. All isolates were wild type on *cytB* codon 268. Isolates from Cameroon all had triple codon 51, 59, and 108 mutations at *dhfr* conferring resistance to proguanil, whereas isolates from Ghana had an increase of such mutations from 39% (7/18) in 2006-2008 to 83% (15/18) in 2014-2016 (p=0.0153). Eight percent (3/36) of Ghanian isolates had a mutation in codon 623 of *atpase6,* while all Cameroonian isolates were wild type. No mutations were observed at *atpase6* codon 769 or *kelch13* codons >440. In *Pfcrt* codon 76, 27% (7/26) of Ghanian isolates were mutant compared to 50% (6/12) of those from Cameroon. *Pf* isolates from Ghana demonstrated increasing molecular markers of resistance to proguanil, but remain wild type to the partner drug atovaquone in Malarone. The relatively high percentage of molecular mutants to chloroquine resistance still predominates throughout West Africa. The low sequence heterogeneity suggest there was no major evolutionary genetic changes over the years.