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99 - HIGHER AFRICAN ANCESTRY PROPORTION IS ASSOCIATED WITH GREATER VIVAX MALARIA INCIDENCE IN YOUNG AMAZONIANS: A POPULATION-BASED COHORT STUDY

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Resumen

Background/Objectives: The malaria parasite *Plasmodium vivax* originated from Africa, where human genetic variants that reduce the susceptibility to malaria - e.g., at the ackr1 locus that encode the Duffy blood group antigen - have been selected in local populations over the past 10,000 years. Five centuries after its introduction in the Americas, P. vivax infects local admixed populations with American native (AMR), African (AFR), and European (EUR) ancestral sources. How genetic ancestry influences malaria risk remains little explored in admixed populations form the New World.

Methods: We analyze data from a cohort of 1,454 Brazilian Amazonians (mean, 29.1 yr), who contributed 6578.4 person-years of follow-up. The main study outcome is P. vivax infection diagnosed from 1 January 2014 through 31 December 2018. Participants were genotyped with the Axiom Precision Medicine Diversity Research Array. We used principal components analysis of 211,428 genotyped variants to estimate individual's global genetic ancestry. Mixed-effects negative binomial regression models were run to quantify the impact of genetic ancestry on malaria incidence, while adjusting for sex, age, socioeconomic status, and ackr1 genotype, including an interaction term age vs. AFR ancestry.

Results: The average proportions of global AFR, AMR, and EUR ancestry in the study population were 0.226 (95%CI, 0.223 to 0.229), 0.280 (95%CI, 0.274 to 0.286) and 0.494 (95%CI, 0.488 to 0.500), respectively. Cohort participants experienced 1,717 infections with P. vivax, iwith an average incidence of 26.1 (95%CI, 24.9 to 27.4) cases/100 person-years at risk. Somewhat surprisingly, we found that AFR ancestry proportion > 20% - but not higher AMR ancestry - was associated with twice the risk of vivax malaria in children and adolescents, but this effect was significantly attenuated among older participants. We hypothesize that cohort participants at increased risk of vivax malaria, such as those with higher AFR ancestry, are repeatedly infected throughout childhood and develop clinical immunity earlier than their low-risk counterparts.

Conclusions/Recommendations: These results point to genetic ancestry as a major contributor to vivax malaria risk in Amazonians and highlight the value of including admixed populations in studies of genetic determinants of malaria susceptibility.

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