

Malaria and other infections induce polyreactive antibodies that impact SARS-CoV-2 seropositivity estimations in endemic settings

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Abstract

Anti-SARS-CoV-2 seroprevalence is used as marker of viral exposure to estimate the proportion of previously infected population, track transmission, and monitor naturally- and vaccine-induced protection. However, in sub-Saharan African settings, antibodies induced by higher exposure to pathogens may increase unspecific seroreactivity to SARS-CoV-2 antigens, resulting in false positive responses. To investigate the level and type of unspecific seroreactivity to SARS-CoV-2 in Africa, we measured IgG, IgA and IgM to a broad panel of antigens from different pathogens by Luminex in 659 plasma samples from African and European subjects differing in COVID-19, malaria and other exposures. Seroreactivity to SARS-CoV-2 antigens in pre-pandemic African was higher compared to European samples, and positively correlated with antibodies against HuCoV, helminths, protozoa, and especially *P. falciparum*. African subjects presented higher levels of autoantibodies, a surrogate of polyreactivity, which correlated with *P. falciparum* and SARS-CoV-2 antibodies. Finally, we found an improved sensitivity in the IgG assay in African samples when using urea as chaotropic agent. In conclusion, our data suggests that polyreactive antibodies induced mostly by malaria are important mediators of the unspecific anti-SARS-CoV-2 responses, and that the use of dissociating agents in immunoassays could be useful for more accurate estimations of SARS-CoV-2 seroprevalence in African settings.

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