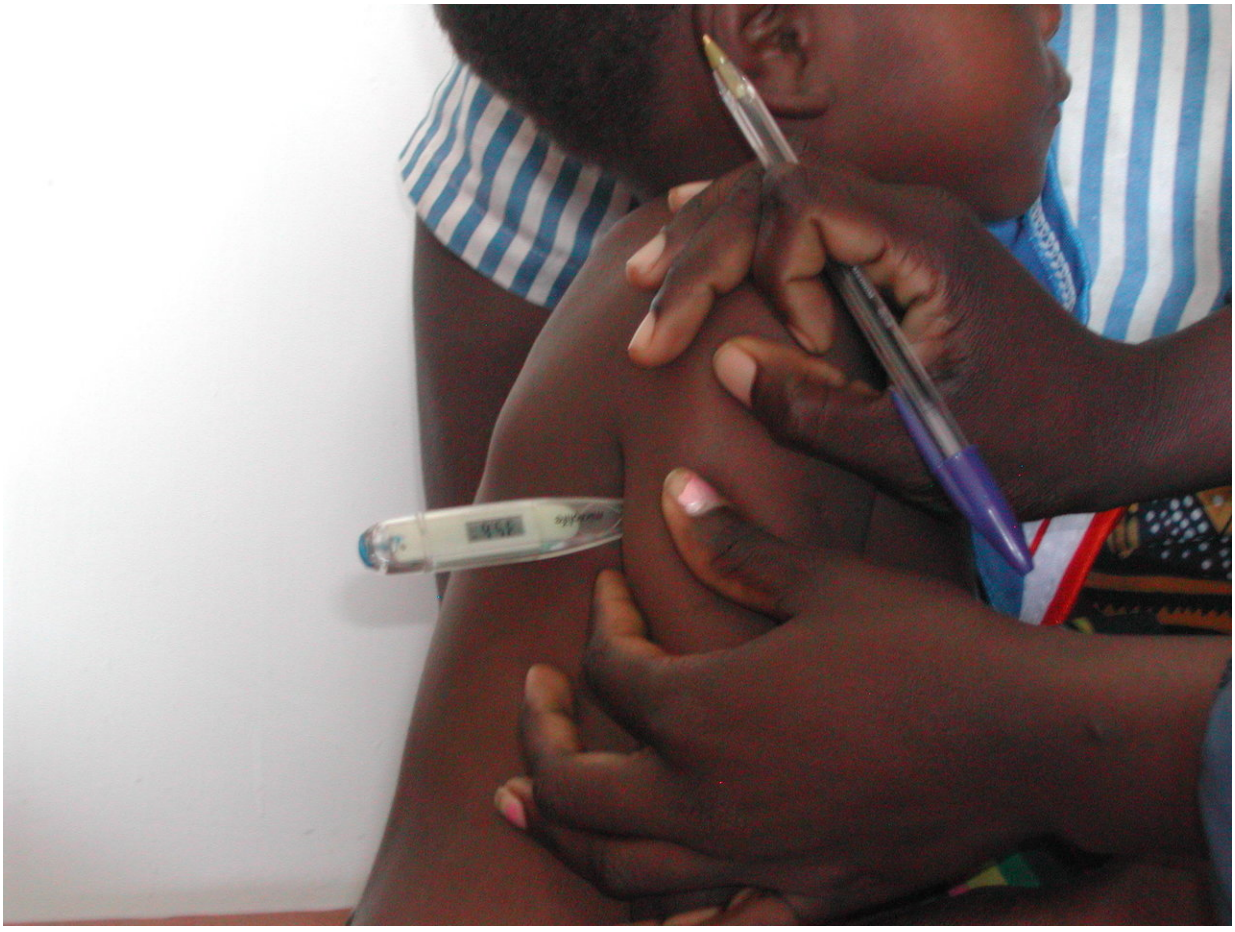
A study identifies new markers associated with protection by the RTS,S malaria vaccine

October 31 2018



A child is attended at a health care center in Southern Mozambique in the framework of the RTS,S phase 3 clinical trial Credit: ISGlobal

Protection conferred by the RTS,S malaria vaccine depends greatly on the amount and subclass of antibodies generated upon vaccination and on previous exposure levels to the parasite, according to a study led by ISGlobal. The results, published in *BMC Medicine*, shed new light on the mechanisms by which RTS,S confers protection and provide the basis for developing more efficacious vaccines.

Malaria elimination will require the right combination of interventions, including an effective vaccine. The RTS,S vaccine (MosquirixTM), approved by the European Medical Agency, has shown partial effectiveness—31 percent in infants six to 12 weeks old, and 56 percent in children aged five to 17 months. ISGlobal researcher Carlota Dobaño and her group have been working in recent years to understand the reasons for this variability and identify vaccine protection correlates.

In this study, an international team led by Dobaño investigated not only the levels but also the types of antibodies induced by the vaccine, thanks to a quantitative assay developed by her group. In particular, they measured levels of antibody subclasses against fragments of the CSP parasite protein and the Hepatitis B virus surface antigen (HBsAg), the two proteins comprised in RTS,S. They analysed serum and plasma from almost 200 infants and children from Kintampo, Ghana (an area with high malaria transmission) and Manhiça, Mozambique (low malaria transmission), vaccinated during the phase 3 clinical trial for RTS,S/AS01E.

The results confirm that the vaccine induces significant levels of IgG antibodies against both proteins (CSP and HBsAg), which are higher in children than in infants. However, not all subclasses of CSP antibodies seem to protect—IgG1 and IgG3 antibodies were associated with protection, while IgG2 and IgG4 were associated with higher disease risk. "The balance between the different subclasses seems to be more important than the total IgG levels," explains lead author Itziar Ubillos.

"This could be because IgG1 and IgG3 antibodies have the capacity to stick to the parasite and give an 'eat-me' signal to cells of the immune system," she adds.

The results also indicate that children with higher pre-vaccine levels of CSP antibodies were less protected against disease post-vaccination. "This means that the vaccine will exert a larger benefit to infants who have not been exposed to the parasite in utero or during the first weeks of life," explains Dobaño. "This study, the fruit of many years of work and many collaborators, identifies new correlates of vaccine success and failure in African children and provides a basis for designing more efficacious vaccines," says the researcher.

More information: Itziar Ubillos et al, Baseline exposure, antibody subclass, and hepatitis B response differentially affect malaria protective immunity following RTS,S/AS01E vaccination in African children, *BMC Medicine* (2018). DOI: 10.1186/s12916-018-1186-4

Provided by Barcelona Institute for Global Health (ISGlobal)