Antibody Responses of Naturally Infected Individuals to Asexual Erythrocytic Stage Vaccine Candidates of *P. vivax* in Sri Lanka

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Recombinant proteins, p42, p19 and PV66/AMA-1 representing native Merozoite Surface Protein 1 and Apical Membrane Antigen-1 of *P. vivax*, were used in an indirect microplate ELISA to assess the total immunoglobulin (IgG and IgM) responses and titers of patients (15 years and above) with acute *P. vivax* malaria infections. These individuals were from two malaria endemic areas of the island, Anuradhapura (n=96; mean ± SEM , number of past malaria infections = 3 ± 0.5) and Kataragama (n=127; 6 ± 1.25), and from a non-endemic area Colombo (n=103; 2.0 ± 0.91). The proportion of responders for p42 was significantly higher ($P<0.05$) than that for p19 and PV66/AMA-1 while there was no such difference between p19 and PV66/AMA-1 ($P>0.05$), in each test area. No significant differences were apparent ($P>0.05$) among responding proportions, magnitude of total antibody levels and antibody titers to p42, p19 and PV66/AMA-1, between the two endemic areas or between endemic and non-endemic areas. Significant correlations ($P<0.001$) existed between the responses to combinations of all three antigens in each of the three test populations. Sera from patients randomly selected from the three test areas screened positive to anti-PV66/AMA-1 (n=40, 46 & 47), anti-p19 (n=55, 48 & 40) and anti-p42 (n=44 & 48) antibodies, respectively, were assessed in a sandwich ELISA for IgG1 and IgG3 cytophilic isotypes against the three recombinant proteins. The proportion of responders for both IgG1 and IgG3 for PV66/AMA-1 were significantly higher ($P<0.01$) than that for p19 and p42 in Anuradhapura. In contrast, the proportion of responders for both isotypes from Kataragma, for both p42 and p19 were significantly higher ($P<0.05$) than that for PV66/AMA-1. Both responding proportions and magnitude of isotype responses for p42 were significantly higher ($P<0.01$) in Kataragama than in Anuradhapura. For p19, these parameters were significantly lower ($P<0.01$) in Anuradhapura than the other two test areas. Responding proportions and isotype levels for PV66/AMA-1 were significantly higher ($P<0.05$) in Colombo than in the two endemic areas. In order to develop *in vivo* correlates of protection for MSP-1 and AMA-1 of *P. vivax*, attempts were made to establish associations between antibody parameters and host factors. Antibody parameters to all three recombinant proteins were independent of the age of patients in all test areas. Total antibody levels and titers for p42 and p19 of the residents of the two endemic areas confer a positive correlation ($P<0.05$) with parasitaemia that was not evident for their isotypic responses. Nevertheless, individuals from Colombo showed correlation with this host factor ($P<0.05$) for IgG1 and IgG3 responses to p19, and IgG1 responses to PV66/AMA-1.In Colombo, a positive correlation ($P<0.05$) was observed between total antibody levels and titers for p42 and p19 with the number of previous malaria infections.