Background: Despite several interventions in the malaria control programs, one of the major barriers to this intervention is asymptomatic malaria. Asymptomatic malaria is a major barrier to the malaria control program as individuals who harbour parasites serve as reservoirs to re-infect others. The mechanism by which these individuals remain asymptomatic is not well understood. A lot of work has been done in relation to human genes and its association to severe, mild and uncomplicated malaria. However, there is limited knowledge regarding host genetic factors and asymptomatic malaria.

Method: In this study, we investigated the association between host genetic polymorphisms of glucose-6-phosphate dehydrogenase gene (G6PD), mannose binding lectin (MBLG54A), tumor necrotic factor alpha (TNF-G308A) and nitric oxide synthase 2 (NOS2-G954C) and the outcome of asymptomatic *P. falciparum* malaria in 150 healthy individuals in Southern Ghana.

Results: We found a significant association between G6PDd and asymptomatic malaria with a prevalence of (9.6% and a P=0.035, by chi-square test). All the individuals who were heterozygous and hemizygote deficient (5.3%, 4.3%) were found to be asymptomatic. Individuals homozygous (GG) for TNF (G308A) were found to be highly asymptomatic (P= 0.019, by chi-square test). With regard to MBL (G54A) and NOS (G954C), no significant association was found between these markers and asymptomatic malaria.

Conclusion: Upon reviewing our data with others from published work, we conclude that both heterozygous and hemizygous individuals with G6PD A- and homozygous individuals (GG) of TNF (G308A) polymorphisms could be predisposed genetically to asymptomatic malaria.