Association between selected single nucleotide polymorphisms (SNPS) in chromosome 5 and anti-malaria antibodies in a malaria endemic area in southern Sri Lanka

[1]RL Dewasurendra, [2]P Suriyaphol, [1]SD Fernando, [3]R Carter, [1]ND Karunaweera

in collaboration with the MalariaGEN Consortium

[1]Department of Parasitology, Faculty of Medicine, University of Colombo

[2] Faculty of Medicine, University of Mahidol, Bangkok, Thailand [3]University of Edinburgh, UK

Introduction

Malaria incidence, at present, is low in Sri Lanka and the cases reported from Moneragala District, which was a malaria endemic area, have reduced; but a study of host factors associated with protection is important to achieve targets for malaria elimination. This study planned to investigate the antibody profile of some specific anti malarial antibodies and study its association with host genetic mutations in chromosome 5.

Objectives

To investigate the relationship between selected anti-malaria antibodies and polymorphisms in human chromosome 5

Methods

Based on the previous census, every household in eight villages near the Malaria Research Station, Kataragama was listed and every individual living in these households was selected. Blood was collected from 1011 individuals to extract sera and DNA. Data on age, sex, bed net use and history of malaria was collected and thick /thin blood smears were examined for malaria. 80 SNPs in 16 genes in chromosome 5 were genotyped using the Sequenom iPLEX Platform and antibody titres against *P. falciparum* AMA1, MSP1, MSP2, NANP and *P. vivax* AMA1, MSP1 were determined by ELISA. Antibody levels were analyzed in relation to age, history of malaria and association between antibody titres and SNPs were tested.

Results

Ages ranged from 14 to 89 years with approximately equal numbers of males and females (514:497). Over 99% of the population was Sinhalese with only seven being Tamil. The majority of individuals (>95%) used bed nets. Only 18.4% (186/1,011) had had clinical malaria within the past 10 years and none within the past five years. At the time of sample collection, blood smear examinations were negative for malaria in all subjects. Sero-positivity rate against *P.falciparum* and *P.vivax* was 80% and 97% respectively. A positive association between antibody levels and age was observed (which was highest at 59 years), but not with gender. Significant associations were seen between high levels of anti-AMA1 (Pf) with SNPs rs25882 (CSF2) and rs1881457 (IL13); anti-MSP1 (Pf) with SNP rs2706348 (RAD50); anti-NANP (Pf) with SNPs rs25887 (CSF2), rs156029

(P4HA2), rs272867 (SLC22A4) and rs1881457 (IL13). Levels of anti-MSP2 (Pf) was not associated with any of the tested SNPs. High levels of anti-AMA1 (Pv) was associated with SNP rs1801033 (C6) and anti-MSP1 (Pv) with SNPs rs156029 (P4HA2) and rs848 (IL13). High linkage disequilibrium was observed between SNPs rs1801033 and rs1881457 (D'=0.858, LOD=164.96, r2=0.646), rs25882 and rs2706348 (D'=0.86, LOD=146.5, r2=0.667), rs2706348 and rs272867 (D'=0.662, LOD=54.79, r2=0.279).

Conclusions

High anti-malaria antibody levels are maintained despite low malaria transmission. Positive association between sero-prevalence of anti-malarial antibodies with increasing age suggests an age specific acquired immunity. Genetic basis for serological response could be suggested with SNPs acting individually or together with evidence of strong linkage between these markers.

This work has been previously published in an international conference in early 2012.