



Abstract 303 Figure 3

304 **TNF- α PROMOTER POLYMORPHISMS (G-238A AND G-308A) ARE ASSOCIATED WITH SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS: A STUDY IN P. FALCIPARUM ENDEMIC AREA**

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Background and aims Tumour necrosis factor- α (TNF- α) is a proinflammatory cytokine associated with *P. falciparum* malaria and autoimmune disorders. Elevated plasma TNF- α has been linked to *P. falciparum* malarial severity and mortality. Higher levels of TNF- α has also been reported in systemic lupus erythematosus (SLE). Two functional common polymorphisms (G-238A and G-308A) at promoter region of TNF- α gene have been linked to SLE susceptibility in different population. In the present report, we conducted a case control study to investigate association of TNF- α (G-238A and G-308A) polymorphisms with susceptibility/resistance to SLE development in a *P. falciparum* malaria endemic cohort.

Methods A total of 204 female SLE patients and 224 age and sex matched healthy controls were enrolled in the study. TNF- α polymorphisms (G-238A and G-308A) were typed by polymerase chain reaction and restriction length polymorphism (PCR-RFLP). Plasma level of TNF- α was quantified by enzyme linked immunosorbent assay.

Results The prevalence of heterozygous mutants and minor alleles of TNF- α (G-238A and G-308A) polymorphisms were significantly higher in SLE patients compared to healthy controls. Furthermore, heterozygous (GA) and minor allele (A) of TNF- α (G-238A) polymorphism were associated with susceptibility to lupus nephritis. SLE patients displayed higher levels of plasma TNF- α compared to healthy controls. TNF- α (G-238A and G-308A) variants were associated with higher plasma TNF- α in both SLE patients and healthy control.

Conclusions The results of the present study demonstrate that TNF- α (G-238A and G-308A) variants are associated with higher plasma TNF- α level and increased susceptibility to development of SLE in malarial endemic areas.

305 **ASSOCIATION OF C4A AND C4B GENOMIC COPY NUMBER VARIATIONS IN ADULT AND PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background and aims C4 complement gene has been observed to be a susceptibility gene for SLE. Lower C4 gene (C4A and C4B) copy number (CN) is a risk factor for SLE, where as higher C4 CN is a protective factor. We investigated the association of C4 gene copy number variation in a north Indian cohort of SLE patients

Methods We recruited 112 aSLE and 52 pSLE patients with 115 healthy adult (CA) and 60 healthy paediatric (CP) controls and compared for C4A and C4B CN by RT-PCR, serum C3, C4 by nephelometry and ANA autoantibodies by line blot assay

Results C4A low copy number was higher in pSLE (OR=1.82, p=0.67) and aSLE (OR=1.51, p=0.41) as compared to their respective controls, pSLE had higher C4A low copy number than the aSLE (OR=1.33, p=0.58), though they were not statistically significant. C4A and C4B CN negatively correlated with several ANA autoantibodies. The total C4 (C4A +C4B) CN negatively correlated with Ro52 (r=-0.29, p=0.03), dsDNA (r=-0.32, p=0.02), SSB (r=-0.33, p=0.01), nucleosome (r=-0.28, p=0.04) and histone (r=-0.34, p=0.01) in pSLE and with nucleosome (r=-0.20, p=0.03) in aSLE. The total C4 CN positively correlated with serum C4 level (r=0.26, p=0.007) in both groups of patients

Conclusions We demonstrate that low copy numbers of complement genes correlate with the propensity for increased antibody secretion in both aSLE and pSLE. Thus, more productions of autoantibodies cause large number of immune complex formation with defective clearance process, due to low serum C4 level and low gene copy number