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Abstract Topic: - Clinical Genetics

Abstract Title: - Association of HLA DR/DQ Haplotypes with Malaria Infection: A Pilot Study

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Aims: - Major Histocompatibility complex II (MHCII) expressed on the surface of antigen presenting cells (APCs) play an important role in inducing adaptive immune responses. Its association with autoimmune, inflammatory and infectious diseases is well established. Allelic variations in MHCII lead to diverse range of immune cell interactions and T cell repertoire formation. However, allelic polymorphism in the upstream regulatory regions of MHCII gene may cause impaired antigen presentation; inadequate expression of MHC class II molecules contributes to insufficient CD4+ T-cell responses, thus increases disease susceptibility.

Methods: - Load of Parasite Infection: The parasitic load was checked by real-time PCR analysis using the isolated Genomic DNA from malaria patients, for which the standards were prepared in the range of 0.1-1010copy number of P. vivax/P.falciparum specific genes cloned plasmid; a standard graph was prepared.

Genotyping: HLA DR/DQ genotyping was performed for 25 samples' DNA isolated from whole bloods of Malaria patients and healthy individuals by PCR using sequence specific primers. Purified PCR products of DQB promoters were sequenced by the 1st base DNA sequencing Division, Malyasia. Multiple Sequence Alignment was done with the use of the CLUSTAL W tool for polymorphism search in the HLA-DQB promoter samples. All 25 samples were aligned with reference sequence (Genebank sequence ID: X55423.1, X55426.1, X55425.1). The genotype and allele frequency were calculated by direct counting.

Statistical Analysis: Statistical analysis was performed using Graphpad Prism software. Fisher's exact test was used for comparison of genotype, allele frequencies distribution among malaria patients and healthy controls. Comparison of two groups was performed by Chi square test and for more than two groups one-way ANOVA was performed. For two grouping variables two-way ANOVA was used.

Results: - In this study we report allelic variation in the upstream regulatory region of MHCII-DQB gene and their association with malaria. Nucleotide sequencing of MHCII-DQB regulatory regions reveals three different haplotypes (DQB3.3, DQB3.1 and DQB2.0) are among twenty-five individuals in Ahmedabad. HLA DQB3.3 is the most and HLADQB2.0 is the least prevalent haplotype in the study population. HLADQB2.0 haplotype patients show low parasitaemia compared to HLADQB3.3 and 3.1 haplotype patients. Further, we studied the probable association between HLA-DR/DQ alleles with the load of malaria infection.

Conclusions: - To our knowledge, this is the first report linking the haplotypes DRB1/DQB1 with malaria infection. A future study in plan involving larger number of samples would validate the present findings of the possible susceptible risk of HLA DR/DQ in malaria and other infectious diseases.

Keywords: - In this study we report allelic variation in the upstream regulatory region of MHCII-DQB gene and their association with malaria. Nucleotide sequencing of MHCII-DQB regulatory regions reveals three different haplotypes (DQB3.3, DQB3.1 and DQB2.0) are among twenty-five individuals in Ahmedabad. HLA DQB3.3 is the most and HLADQB2.0 is the least prevalent haplotype in the study population. HLADQB2.0 haplotype patients show low parasitaemia compared to HLADQB3.3 and 3.1 haplotype patients. Further, we studied the probable association between HLA-DR/DQ alleles with the load of malaria infection.