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Genomic Screening Of Immune-Related Genes In Association Of Hla-B Allele And Leukemia Some North Indian States

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ABSTRACT

The current investigation was initiated to investigate the "potential relationship between leukemia and the HLA-B allele in the North Indian population", as a result of the deficiencies of such studies in the Indian context. DNA extraction was followed by HLA genotyping using the Sequence-Specific Oligonucleotide (SSO) method on the Luminex 200 system platform, as outlined in the kit insert [Lifecodes®HLA-SSO, USA]. The bulk run was prepared for each batch of samples before the samples were analyzed on the Luminex instrument. In leukemic patients, 293 HLA-B genotypes (allelic combinations) were identified out of the 69 HLA-B allelic variants that were identified. HLA-B*07:02 has 24 genotypes, followed by HLA-B*08:01 (19), B*35:01 (19), B*35:03 (18), and HLAB*40:06 (14) among the total identified genotypes. The initial evidence of the HLA-B allele association with leukemia in the North Indian population is provided by our findings. It may be employed for additional analysis of leukemia susceptibility investigations...

Keywords: Genomic screening, Leukemia, HLA-B, Genes, Allele.

INTRODUCTION

Since the first revelation that HLA-B allele diversity was connected with the occurrence of lymphoma Hodgkin, a wide range of disorders involving HLA have been found (Tran et al., 2023). A large number of illnesses, including auto immune disorders, have HLA alleles as a major genetic predictor (Nagler and Mohty, 2022). What diversity and molecular activity are and how important they are "HLA-G has been investigated in a variety of autoimmune diseases, including rheumatoid arthritis (RA), multiple sclerosis (MS), systemic lupus erythematosus (SLE), and type 1 diabetes mellitus (T1DM) (Deshpande, 2017). The genetic association, molecular function, and mechanisms of HLA-G-mediated immune tolerance in autoimmune diseases are the primary focus (Mehra and Baranwal,2016).

"The molecular mechanism that underpins the associations between autoimmune diseases and MHC (HLA) has not yet been completely elucidated (Hurley, 2021). In numerous instances, it is indicative of LD phenomena between HLA alleles and the physically mapped gene disease in the MHC region (Rani et al., 2023). However, in other instances, the association discovered is indicative of the amino acid composition of the HLA molecule. In reality, the principal function of HLA class II antigens is to bind the peptide antigens and expose them to CD4+ and CD8+ cells (Kankonkar, 2022). Other mechanisms that have been suggested include the capacity to influence the clonal selection of T cells at the thymic level through the stimulation of various cytokines or the presence of specific HLA alleles (Aggarwal et al., 2017)". In this manner, the aim of the present investigation to assess the relationship between HLA and leukemia in India, particularly in relation to the "HLA-B locus.

2. MATERIAL AND METHOD

A healthy individual aged 18 to 55 was enrolled in the study. Any individual with a history of significant surgery, blood disorders, diabetes, or high blood pressure was excluded.

"Genotyping 3 ml of whole blood was collected from each enrolled participant (cases and controls) in ethylene diamine tetra-acetic acid (EDTA) coated vials".

DNA was extracted from each blood sample collected from participants in the control and cases groups using a commercial reagent "(NucleoSpin® Blood DNA Extraction reagent, Germany). Prerequisites for HLA-B genotyping with the LIFE CODES HLA-B SSO

- Typing Kit include a Luminex instrument and an XY platform.
- Luminex sheath fluid • Veriti™ 96-Well thermal cycler
- "Lifecodes HLA-B master mix • Lifecodes HLA-B probe mix"
- Dilution solution
- Lifecodes Taq polymerase
- Costar plate
- R-Phycoerythrin conjugated streptavidin (SAPE)

Each sample was subjected to the subsequent stages in the preparation of the PCR mixture:

Allowed the HLA-B master mix to reach room temperature (18 to 30°C). For approximately 10 seconds, vortexed it vigorously. the amplification mixture to the PCR tubes that contained the genomic DNA. To prevent condensation during PCR, the containers were securely caped.

The Luminex instrument was activated 30 minutes prior to analyzing any of the samples during the entire session, as the samples were analyzed up to 30 minutes after being diluted.

Result and Discussion

The variation in frequency by OR and its significance value, as well as the frequency of HLA-B alleles in the patient and control groups, are detailed in Table 4.6. We have found that leukemia is positively associated with "HLA-B*15:25 (p=0.048, OR=4.49, 95% CI), B*38:02 (p=0.002, OR=3.97, 95% CI), and B*44:03 (p=0.003, OR=1.48, 95% CI), and negatively associated with HLA-B* 08:01 (p=<0.001, OR=0.48, 95% CI). Leukemia was not associated with any other main significant HLA-B allele."

"In leukemic patients, 293 HLA-B genotypes (allelic combinations) were identified out of the 69 HLA-B allelic variants that were identified. HLA-B*07:02 has 24 genotypes, followed by HLA-B*08:01 (19), B*35:01 (19), B*35:03 (18), and HLAB*40:06 (14) among the total identified genotypes, as illustrated in Figure 4.3."

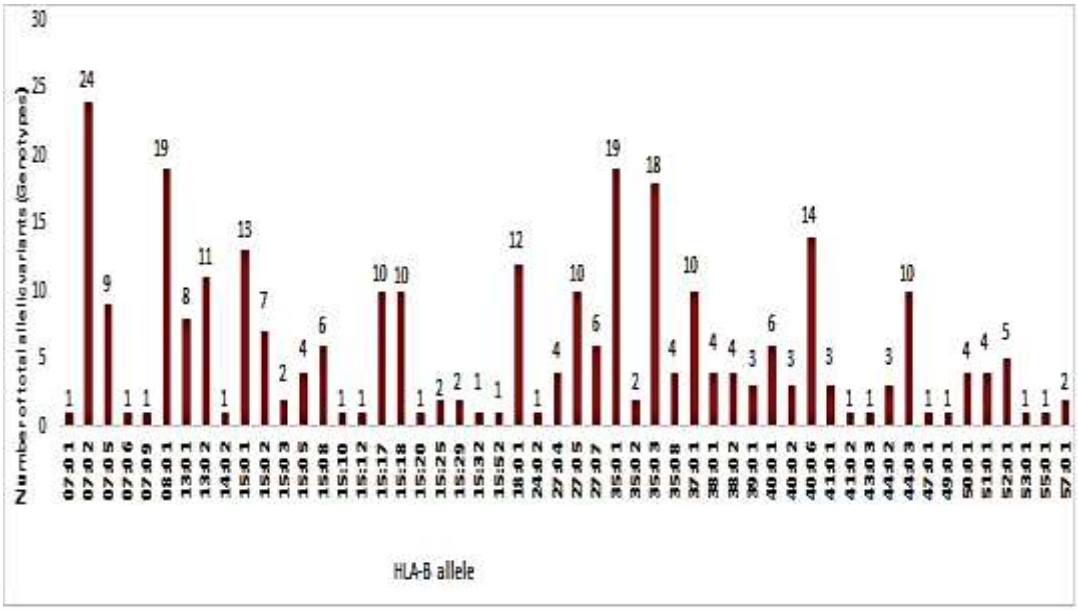

Figure 4.3: Summary of allelic combinations (genotypes) on each HLA-B allelic variants in Patients (N=583)

The most prevalent HLA-B genotypes were identified as HLA-B*35:03- B*44:03 (1.71%) and B*40:06- B*52:01 (1.71%). Consequently, the most prevalent were HLA-B*08:01-B*40:06 (1.54%) and B*08:01-B*51:01 (1.54%). Table 4.7 displays the frequency and total quantity of genotypes.

In order to compare our findings with those from other regions of India and abroad and to observe the diversity and distinctiveness of North Indian populations, "we have extracted the HLA-B allele frequency from the allele frequency net database (AFND). (www.allelefrequencies.net) The AFND provides a repository that is freely accessible for the storage of immune gene frequencies, including the HLA system, in a diverse global population. The HLA-B data was extracted from 200 Austrian individuals. In the same vein, HLA-B encompasses 264 individuals from China. Canton Han was also incorporated to gain a better understanding of the diversity of the North Indian population in these regions.

"It was evident from our results that the HLA-B locus of the North Indian population is characterized by a significant degree of diversity. The pattern of HLA-B alleles that was identified suggested that the North Indian population is similar to the oriental genotype in contrast to Caucasian individuals. The most prevalent HLA-B*08:01 (10.39%), B*40:06 (9.46%), B*51:01 (9.38%), B*35:03 (7.99%), and B*52:01 (6.52%) were identified in this context. The most frequently identified genotypes in the sample under investigation were HLA-B*08:01-B*40:06 (1.94%), B*40:06-B*51:01 (1.94%), B*08:01-B*51:01 (1.77%), and B*08:01-B*08:01 (1.68%)."

"In North Indian populations, a study conducted by Rani et al. (2023) identified 47 allelic variants of HLA-B, with the most prevalent being HLA-B*52:01, B*35:01, B*44:02, B*44:03, B*18:01, and B*58:01. Kankonkar (2022) This is consistent with other HLA alleles that have been disclosed in the western Indian population. The HLA-B*35, B*44, B*51, and B*52 alleles were prevalent in the south Indian population, and they are partially different from those of North Indians. Additionally, the most prevalent antigens in the eastern region of India were HLA-B*44 and B*51, similarly to the North Indian population. (Dedhia et al., 2015) In general, the Indian population exhibited the highest prevalence of HLA-B *35 and B*51".

In contrast to another recognized HLA-B allele, "HLA-B*15 among the North Indian populace has 13 allelic variants and was found to be more polymorphic". Consequently, 5 allelic variations were identified for HLA-B*35 and B*40, respectively. Furthermore, four allelic variations of HLA-B*27 were observed, which are believed to be associated with ankylosing spondylitis (AS). The published report suggested a robust correlation between carbamazepine-induced hypersensitivity reactions and HLA-B*15:02 genes (Aggarwal et al., 2017; Chong et al., 2017; Sukasem et al., 2021).

Conclusion

In the total number of samples (cases) examined, 95.56% were heterozygous, while homozygosity was observed in only 4.43%. In comparison to the other homozygous genotypes, HLA-B*52:01- B*52:01 was the most prevalent (0.51%), followed by "HLA-B*08:01- B*08:01 (0.34%), HLA-B*15:01- B*15:01 (0.34%), and B*15:18- B*15:18 (0.34%)."

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