HLA & NON-HLA Gene Polymorphisms In A Cohort Of AIH Type-1 Adult Patients In North India

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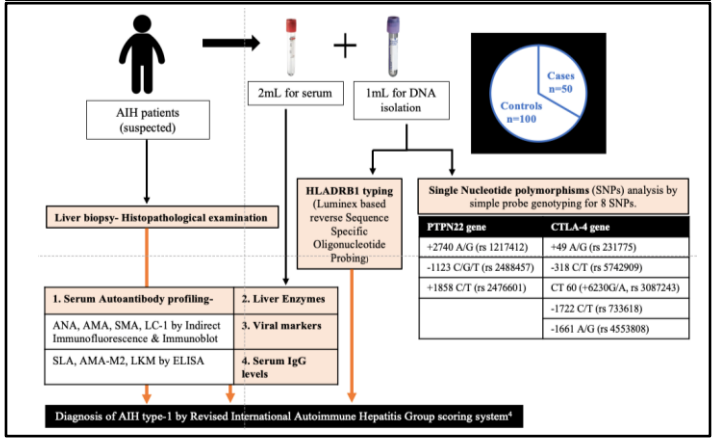
I. Introduction

- Autoimmune Hepatitis- a multifactorial disease affected by both environmental and genetic factors.
- Both HLA and Non-HLA gene polymorphisms are involved in the immunopathogenesis[1].
- There is ethnic variation in these polymorphisms and susceptibility to develop AIH type 1 in different populations.
- No study has been stated from India regarding the non-HLA gene polymorphisms and only a few studies have talked about the HLA DRB1 typing in the same disease[2,3].

II. Aim

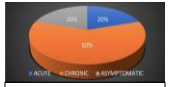
- To analyze CTLA-4, PTPN22 gene polymorphisms and HLA DRB1 typing in a cohort of adult AIH type 1 patients in North India.

III. Methods

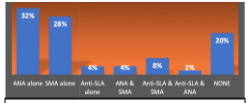


IV. Results & Observations

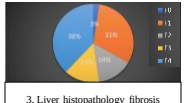
❑ *Clinical profile of cases-*



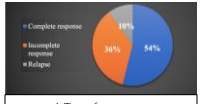
1. Type of clinical presentation of the cases



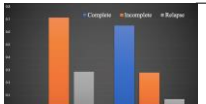
2. Type of autoantibody positivity in cases



3. Liver histopathology fibrosis score (METAVIR) of the cases

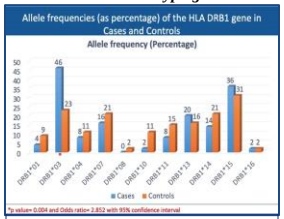


4. Type of response to immunosuppression in cases



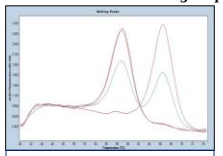
5. Response to immunosuppression was significantly poor in cases with SLA positivity, p value= 0.007

❑ *HLADRB1 typing-*

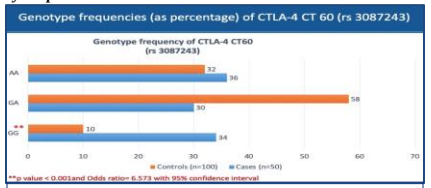


HLA DRB1*03 significantly higher in cases than controls especially in female cases as compared to female controls

❑ *Non-HLA gene polymorphisms-*



Representative melting curves of SNP CTLA-4 CT 60 (rs 3087243), when derivative of fluorescence over temperature is obtained. The three clusters in the above figure segregate into three different kinds of peaks.



❖ Genotype frequencies of all the 8 SNPs assessed in cases and controls.
❖ GG genotype of CTLA-4 CT 60 significantly increased in cases (34%) as compared to controls (10%).
❖ Multinomial analysis showed that CTLA-4 CT 60 is an independent predictor for cases. If GG genotype is present then Odds of becoming patient is 24.528 with 95% CI.

- Association analysis of all the 8 SNPs were done with reference to age at presentation, clinical features at the time of presentation, presence or absence of cirrhosis and response to immunosuppressive therapy. No significant association was found.
- Association Analysis between HLA DRB1 typing of all the cases and all the eight SNPs was separately done but it was not significant.

V. Conclusions

1. Anti-SLA positive AIH type1 are poor responders to immunosuppression
2. HLA DRB1*03 is the susceptibility allele for AIH type1.
3. CTLA-4 CT60 is an independent predictor of the disease in North Indian population.

VI. Strength &Limitation of Our Study

- **Strength**- For the first time in North-Indian population we have been able to analyze HLA along with non-HLA genotype of Type 1 AIH patients and their correlation with clinical phenotype of the disease.
- **Limitation**- This is a pilot study and it needs to be validated in a larger cohort.

VII. References

1. Czaja AJ, Manns MP. Advances in the Diagnosis, Pathogenesis, and Management of Autoimmune Hepatitis. Gastroenterology. 2010;139:58-72.
2. Kaur N, Minz RW, Anand S, Saikia B, Aggarwal R, Das A, et al. HLA DRB1 Alleles Discriminate the Manifestation of Autoimmune Hepatitis as Type 1 or Type 2 in North Indian Population. J Clin Exp Hepatol. 2014;4:14-8.
3. Amarapurkar DN, Patel ND, Amarapurkar AD, Kankonkar SR. HLA genotyping in type-I autoimmune hepatitis in Western India. J Assoc Physicians India. 2003;51:967-9.
4. Alvarez F, Berg PA, Bianchi FB, Bianchi L, Burroughs AK, Cancado EL, et al. International Autoimmune Hepatitis Group Report: review of criteria for diagnosis of autoimmune hepatitis. Journal of Hepatology. 1999; 31: 929-38.

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