6th MENACTRIMS CONGRESS
December 10-11, 2021
Intercontinental Hotel, Dubai
Hosted by MENACtrims
Middle East North Africa Committee for Treatment and Research in Multiple Sclerosis

POSTER PRESENTATION

First study in Iraq about (HLA)-DRB1 * 15:01 as a genetic risk factor for MS initiation

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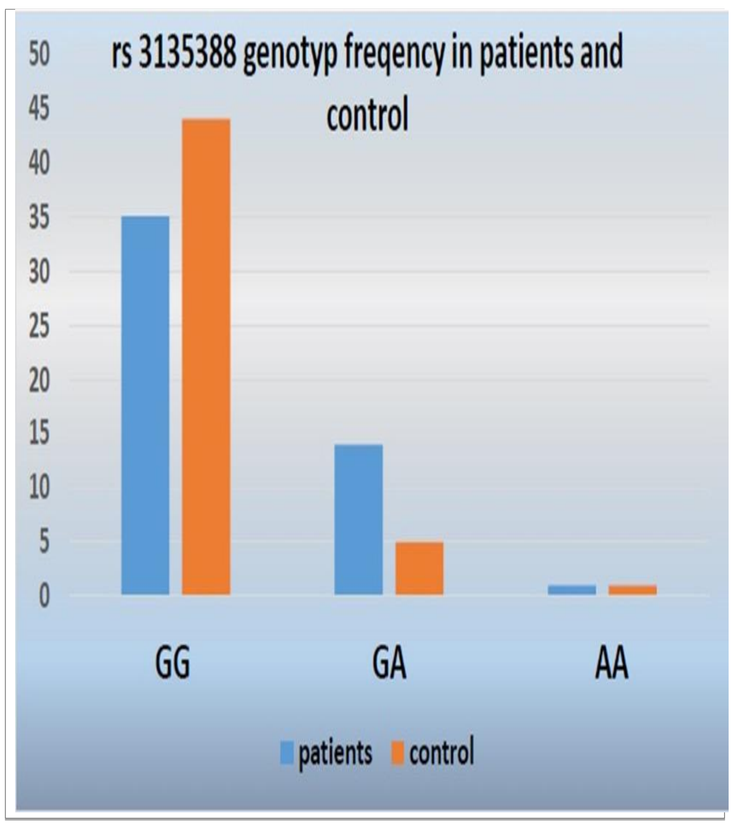
INTRODUCTION

Multiple sclerosis is a demyelination autoimmune disease, which affects the central nervous system. Definite cause for MS initiation is still unknown However, genetic factors are known to participate in the MS risk; the majority of genetic studies have concentrated on the susceptibility variant. The human leukocyte antigen (HLA)-DRB1 * 15:01 has been studied as genetic risk factor in some population. The main players in the disease pathogenesis are the activated immune cells The HLA association with MS is consistent with the idea that MS is –at its core- an antigen-specific autoimmune disease. With features common to MS are related with certain human leukocyte antigen (HLA), specifically autoimmune diseases. HLA system supply a set of genetic loci their proteins that have important role in immune response. HLA-DRB1*15:01 has been confirmed to have the strongest association with MS risk in many population.

AIM

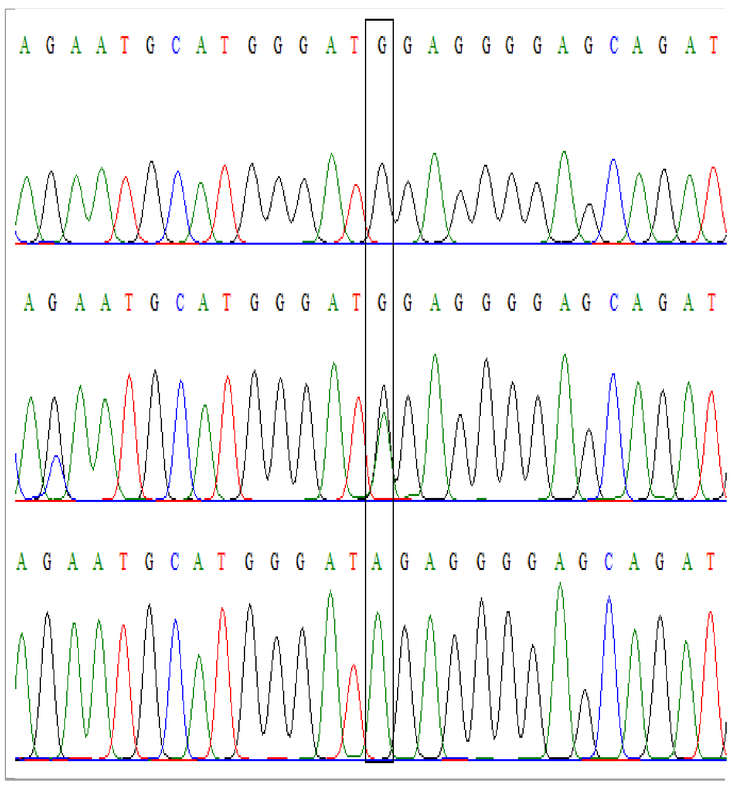
To assess the genotypes of (HLA)-DRB1 * 15:01 as ge netic risk factor for MS development in samples of Iraqi MS patients.



The frequency of different genotypes of rs3135388 in MS patients and controls.

rs2213585

Like the two previous SNPs, this SNP had three genotyp es in both patients and controls. These genotypes were GG, AG and AA

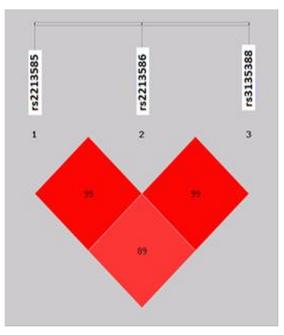


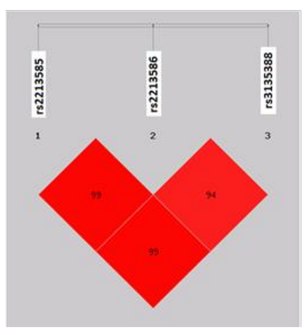
sequence analysis of the rs2213585, forward strand. The bases in the frame s represent the polymorphism sites. The G in the upper frame represents homozygous wild type genotype (GG), the A in the middle frame represents the heterozygous genotype (AG), while the A in the lower frame represents mutant genotype (AA).
Logistic regression analysis showed that this polymorphism had no significan t association with MS neither at genotype nor at allelic level

METHODS

This Case control study involved; fifty MS patients for HLA-DRB1 15:01 investigation; their age were ranged from 14 to 69 years. They attended to seek treatment in the MS out patient's clinic at Medical City- Baghdad Teaching Hospital in the period, which extended from December 2018 to March 2020. The diagnosis of each case was established according to MC Donald criteria done by a neurologist and confirmed by MRI and certain cases by oligoclonal band test of the CSF. Patients were subjected to a questionnaire about name, age, sex smoking, family history, the control group involved 50 apparently healthy person. Patients were.

Haplotype blocks	Controls (n=50)	Patients (n=50)	p-value	OR(95%CI)
AAG	2(2%)	14(14%)	0.027	7.98(0.94-67.45)
GAG	21(21%)	15(15%)	0.213	0.59(0.26-1.35)
GGA	70(70%)	66(66%)	0.271	0.66(0.32-1.39)





The most frequent haplotype blocks in gene HLA-DRB1 in patients and controls
Haplotype blocks for HLA-DRB1 gene were constructed using SHESIS software. Table (6) shows the most frequent haplotypes of HLA-DRB1in patients and contro ls. The frequency AAG block was significantly higher in patients than controls (14% vs. 2%) (OR=7.98, 95%CI= 0.94-67.45, p=0.027). The other two haplotypes were comparable between the two groups with no significant difference.

The association of genotypes and alleles of rs 3135388 with MS compared to control.

Rs3135388	Controls (50)	MS patients (50)	P-value	OR(95%CI)
Genotypes				
GG GA AA	44(88%)	35(70%)	0.086	1.0 Reference
HWE	5(10%)	14(28%)	0.027	3.52(1.16-10.72)
	1(2%)	1(2%)	1.0	1.25(0.07-20.82)
	0.1	0.768		
Alleles				
G A	93(93%)	84(84%)	0.032	1.0 Reference
	7(7%)	16(16%)		2.69 (1.06-6.8)

Analysis of allele distribution exposed a higher frequency of A allele among patients than controls (16% versus 7%) with a significant difference (OR= 2.69, 95%CI= 1.06-6.8, p= 0.032) as shown

RESULTS

The Polymerase chain reaction (PCR) products HLA-DRB1 Genes were subjected for Sanger sequencing technique. In addition, the resultant sequences were compared with reference sequences in national center for biotechnology information NCBI. All the genotypes of HLA-DRB1 were analyzed for link age disequilibrium. There was a very high linkage disequilibrium in rs2213585, rs2213586 and rs3135388 in both patients and control. In concern to the rs313538 8, which tags for HLA-DRB1*15:01 the heterozygous genotype (GA) was more frequent in MS patients (28%) than controls (10%) (OR= 3.52, 95%CI=1.16-10.72, p=0.027). Regarding the rs2213585, rs2213586 there were no significance associations between control group and patients.

The frequency of different genotypes and allele of rs22 13585 polymorphism in MS patients and controls

Rs2213585	MS patients(50)	Controls (50)	P-value	OR(95%CI)
Genotypes				
AA GA GG	27(54%)	26(52%)	0.459	1.0 Reference
HWE	19(38%)	16(32%)	0.759	0.87(0.37-2.06)
	4(8%)	8(16%)	0.276	2.08(0.58-7.74)
	0.798	0.061		
Alleles				
G A	73(73%)	68(68%)	0.438	1.0 Reference
	27(27%)	32(32%)		1.27 (0.7-2.34)

CONCLUSIONS

This is the first study that revealed that HLA-DRB1 15. 01genotyp may be considered as genetic risk factor for MS susceptibility in Iraqi MS patients until 2020

BIBLIOGRAPHY

1. EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP). Regulatory perspective on real world evidence (RWE) in scientific advice https://www.ema.europa.eu/documents. Accessed 25 11 2018.
2. Lublin FD, Reingold SC, Cohen JA. et al . Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2018; 83:278– 286.
3. Luchetti S, Fransen NL, van Eden CG. et al . Progressive multiple sclerosis patients show substantial lesion activity that correlates with clinical disease severity and sex: a retrospective autopsy cohort analysis. Acta Neuropathol.2018 ; 135:511–528
4. Hasan Z N. Disability and prognosis of relapsing remitting multiple sclerosis, is it different in Iraqi patients?; Neurosciences.2011 ; 16(3):233-236.
5. Ascherio A, Munger KL. Epidemiology of Multiple Sclerosis: From Risk Factors to Prevention-An Update. Semin Neurol 2016;36 (2):103–14.
6. Ascherio, A., K. L. Munger. Environmental risk factors for multiple sclerosis. Part I: the role of infection. Ann. Neurol.2007 ; 61:288–299.
7. Thompson AJ, Baranzini SE, Geurts J, et al. Multiple sclerosis. Lancet. 2018; 391:1622–36.
8. Sawcer S, Franklin RJ, Ban M. Multiple sclerosis genetics. Lancet Neurol. 2014; 13:700–709.
9. Reich DS, Lucchinetti CF and Calabresi PA. Multiple sclerosis. N Engl J Med. 2018 ; 378:169 –80.
10. Mitchell T. Wallin, William J. Culpepper, Jonathan D. Campbell, et al . The prevalence of MS i n the United States. Neurology. 2019 ; 92 (10).

ACKNOWLEDGEMENTS

A greeting for medical staff and sub staff in the MS clinic in Baghdad teaching hospital, for their help in samples collection and providing data co ncerning patients and eliminating all difficulties