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ASSOCIATION STUDY OF SINGLE-NUCLEOTIDE POLYMORPHISM RS10865331 AND THE RISK OF ANKYLOSING SPONDYLITIS IN AN IRANIAN AZARI POPULATION

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ABSTRACT

Ankylosing Spondylitis (AS) is a common cause of inflammatory arthritis. The disease is associated with the gene HLA-B27; however, only 1%–5% of HLA-B27-positive individuals develop ankylosing spondylitis, and there is increasing evidence to suggest that other genes must also be involved. Over the last few years, the development of high-throughput microarray-based single-nucleotide polymorphism (SNP) genotyping techniques and genome-wide association studies (GWAS) have helped to highlight non-HLA genetic risk factors associated with AS. In this study, we investigated the association between SNP rs10865331 and Ankylosing Spondylitis in Iranian Azari patients. 57 AS patients who fulfilled the selection criteria, were solicited sequentially at Tabriz University of Medical Sciences Hospitals, Tabriz, Iran. Also, 50 cases as control group were participated in this study. There were 45 men (79%) and 12 women (21%) in the patient group. Mean age of patients was 38 ± 10.4 years (ranging 20-62). The mean BASFI score of AS patients was 7.74. Also, the mean BASDAI score was 20.11.All of the patients were heterozygote for rs10865331 SNP. Also, all of the cases in the control group were heterozygote for rs10865331 SNP. This lack of association could be related to a small sample size or racial issues. Because of this, This SNP cannot have a diagnostic application in our population and therefore complementary study with larger sample size is necessary to unravel this intergenic AS-associated SNP.

INTRODUCTION

AnkylosingSpondylitis (AS) is a common cause of inflammatory arthritis, with a prevalence of5 per 1,000 in European populations(Braun, Bollow, *et al*., 1998). It is characterized by inflammation of the spine andsacroiliac joints causing pain and stiffness and ultimately new bone formation and progressive joint ankylosis. Hip and peripheral joint arthritis is common, and inflammation may also involve extra-articular sites such as the tendon insertions,uveal tract, proximalaorta and, rarely, the lungs and kidneys. The disease is associated with the geneHLA-B27; however, only 1%–5% of HLA-B27-positive individuals develop ankylosingspondylitis, and there is increasing evidence to suggest that other genes must also beinvolved(Brown, Laval, *et al*., 2000, Brown, Kennedy, *et al*., 1997, Calin, Marder, *et al*., 1983, van der Linden, Valkenburg, *et al*., 1983). Over the recent years, the development of high-throughput microarray-based single-nucleotide polymorphism (SNP) genotyping techniques and genome-wide association studies (GWAS) have helped to highlight non-HLA genetic risk factors associated with AS(Brown, Edwards, *et al*., 2000, Burton, Clayton, *et al*., 2007, Pazár, Safrany, *et al*., 2010, Safrany, Pazar, *et al*., 2009, Timms, Crane, *et al*., 2004). In this study, we investigated the association between SNP rs10865331 andAnkylosing Spondylitis in Iranian Azari patients.

MATERIALS AND METHODS

AS patients who fulfilled the selection criteria, were solicited sequentially at Tabriz University of Medical Sciences Hospitals, Tabriz, Iran.57 patients who fulfilled

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the New York Modified Criteria(Fauci, 2008, Mitra, Elvins, *et al*., 2000)and 50 cases as control group signed an informed written consent and the study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences which was in compliance with Helsinki declaration.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were applied to evaluate the disease activity, physical function and global well-being.

The SNPrs10865331 were genotyped using ARMS and RFLP PCR. Association were performed by chi-squared test and Fisher Exact test. Also, we used Kruskal-wallis and Mann-whitney U as non-parametric tests, using SPSS (version 18) software. Statstical significance was set at $p<0.05$.

RESULTS AND DISCUSSION

There were 45 men (79%) and 12 women (21%) in the patient group. Mean age of patients was 38 ± 10.4 years (ranging 20-62).

The mean BASFI score of AS patients was 7.74 (Figure 1). Also, the mean BASDAI score was 20.11 (Figure 2).

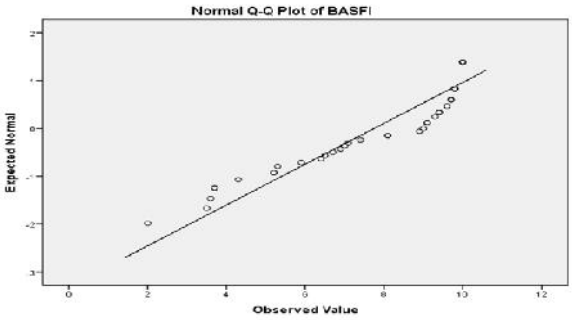

Figure 1 Data distribution of BASFI in patients with AS.

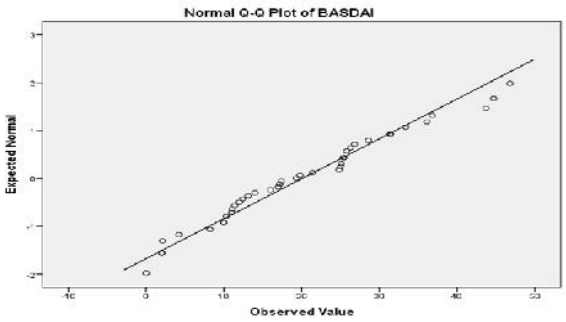

Figure 2 Data distribution of BASDI in patients with AS.

All of the patients were heterozygote for rs10865331SNP. Also, all of the subjects in control group were heterozygote for rs10865331SNP.

We examined in Iranian Azari population the association of rs10865331 SNP with AS. All of the patients and control group were heterozygote for this SNP. This lack of association could be related to a small sample size or racial issues. Because of this, we suggest that this SNP cannot have a diagnostic application in our population and complementary study with larger sample size is necessary. In contrast to this study, Sanchez *et al*, provided evidence of the association of the rs10865331 intergenic variant with AS in a Spanish population, replicating the results recently obtained in a GWAS. They suggested further research is necessary to unravel the functional significance and the biological processes altered by this intergenic AS-associated SNP (Sánchez, Szczypiorska, *et al*., 2010). The closet protein-coding genes to rs10865331 are B3GNT2 (UPD-GlcNAc: betaGal beta-1, 3-N-acetylglucosaminyltransferase 1) and COMMD1 (copper metabolism domain containing 1), which codify for a type II transmembrane protein involved in the biosynthesis of poly-N-acetyl-lactosaminechains and for a protein known to inhibit nuclear factor-kB activation, respectively.

Conflict of Interest

There is no conflict of interest.

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