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Research Article

Relationship of HLA-DRB1 Alleles and Rheumatoid Arthritis in West South of Iran

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ABSTRACT

Background: Rheumatoid arthritis is a systemic multifactor disease that presented with symmetrical polyarthritis more preferably in small wrist joint and ankle. Synovial pannus cause destruction and deformities in joints. The main reason of this disease in unknown, but past researches showed that genetically factor play important role beside environmental factors in susceptibility to this entity. Method:100 patients with rheumatoid arthritis diagnosed upon ACR 2010 criteria enrolled study. 92 healthy patents also enrolled DNA studying. of both group was extracted through DNA extraction kits by blood sampling. HLA-DRB1 typing was done by PCR-SSP method. Results: There were no significant differences in HLADRB1 *04, HLADRB1*08 and HLADRB1*11 alleles presentation between patients and healthy controls. Only there were statically significant correlation between HLA-DRB1*08 and Rheumatoid factor positive patents. (P = 0.025).

Keywords: Rheumatoid arthritis, HLA-DRB1*08, HLADRB1 *04, HLADRB1*11, Rheumatoid Factor.

INTRODUCTION

Rheumatoid arthritis has prevalence about 1 %. this balance become more in older age. Prevalence is more in fourth and fifth decades. And women involved three fold rather than men[1].

Familial studies indicated that there is a genetically susceptibility on affection of disease. Prevalence of disease is 4 folds in relative with auto antibodies of rheumatoid factor. About 10 percent of patients with RA have minimum 1 kinsman affected from this disease[2]. Monozygotic sibling has 4 folds' possibility of affection to disease rather than dizygotic sibling. This fact indicated that genetically process have responsible for about 60 percent of affection to disease[3].

Although main immunogenic process of RA is unknown, but HLA class II play important role. for the first time in 1970, correlation between RA and HLADRB1*0401 was reported. In Most mutual agreement found in sibling with HLADRB1 and HLADRB1*0401that thought to be responsible for disease affection[4,5].

Risk of incidence of RA in HLADRB1*0401 positive patients is 1 in 35 people and in HLADRB1*0404 is 1 to 20 persons. If person have 2 alleles together this chance of affection become very high[6]. 75 % of African person have not this allele. Spanish patients have HLADRB1*10:01 alleles while Chilean person have HLADRB1*0901 and Arabian patients have HLADRB1*0301 alleles[7].

METHOD

This study is an analytic epidemiological one.100 patients with diagnosis of rheumatoid arthritis upon ACR2010 criteria enrolled study, 92 healthy people also were analyzed. the control group consist of healthy persons more than 16 years old that referred to blood transfusion organization and all of them had no history of genetically or Collagen vascular in themselves and thief first degree family. All of them had deliberately consent for enrollment. Non probability sampling and Convenient sampling was done because of the both group should be matched with age and gender.

Inclusion criteria consist of: patients with diagnosis of RA upon ACR2010 criteria more than 16 years old. Participants with history of genetically disorder or other simultaneous collagen vascular disease in themselves and their first degree family excluded from study.

Genomic DNA of them extracted from their blood sample.sillisian fibre kits were obtain before.DNA in presence of chemotropic salt connected to Silesian

Table 1: relation between HLADRB typing and disease presentation.

HLA Typing	RA patients	Control group	P value
HLADRB1 *04	64 (64 %)	58 (63%)	0.923
HLADRB1*08	68 (68%)	54 (58%)	0.344
HLADRB1*11	60 (60%)	44 (47%)	0.232

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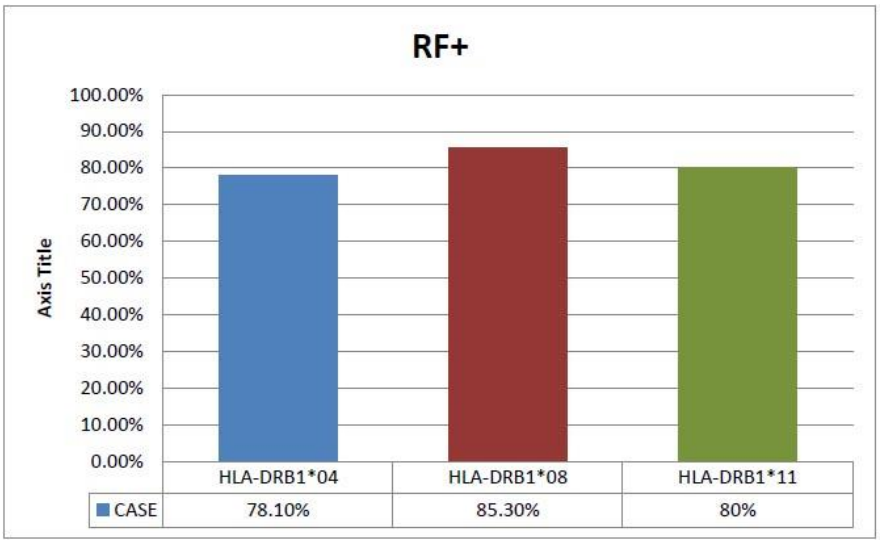

Figure 1: prevalence of RF positive in patients with HLA –DRB1*04, 08, and 11.

fiber.proteins were eliminated through washing and centrifuge and Genomic DNA extracted in a low salt solution.

HLA-DRB1 typing was done with PCR-SSP protocol. for assurance of extracted data and deletion false negative results, we used internal control of beta Actin in each PCR reaction. This Gen is Housekeeping and presented in all cells.

RESULTS

In this study 100 patients with RA and 92 healthy patients assessed. 20 % of them were male and 80 % were female. Average age in control group was 43.3 and in patients were 43.6 years old.

In RA patients 64 person and 58 people in control group had HLADRB1 *04 that there was no difference between two groups. (OR = 1.042, p value =0.923)

Otherwise 68 cases in RA patients and 54 in control group were HLADRB1*08 positive that in this issue there were no significant difference between them. (OR = 1.49, P value=0.344).

Prevalence of HLADRB1*11 in RA group was 44 and 60 in control group that describes no correlation between RA and HLADRB1*11 (OR. =1.636 p value= 0.232).

Among 64 patients with HLA-DRB1*04, 50 case had positive Rheumatoid Factor that shows there is no correlation between RF and HLA-DRB1*04 (p=0.137). relation between subtyping of HLADRB and disease presentation showed in table 1.

From 68 RA patients with HLA-DRB1*11, 48 of them had positive Rheumatoid Factor that shows there is no significant relation between HLA-DRB1*11 and Rheumatoid factor (P =0.825).

That is necessary to said that there was no significant correlation between HLA-DRB1*11 and Rheumatoid factor (P =0.825).

From 68 patients with RA, 58 had positive Rheumatoid factor that shows there is significant relation between HLA-DRB1*08 and RF (P = 0.025). relation between HLADRB subtyping and rheumatoid factor was shown in figure 1.

DISCUSSION

Rheumatoid arthritis is chronic and progressive disease and because of Genetic factors played an important role in predisposing people for affliction, therefor understanding of Genetic facts of this disease cause better recognition of disease (8,9). Otherwise this Genetic allele play an important role in disease prognosis and severity. Therefore, by better comprehension of these topics, we can reach earlier diagnosis, better treatment and prevention of complication and disabilities (10,11,12).

In a study that done by Batmaz I, and et al in 2013 in turkey, they showed that there is significant correlation between HLADRB1*10 and rheumatoid arthritis (p=0.001). while penetration of HLADRB1*7, HLADRB1*11 alleles was less in patents groups. (p=0.02 and p<0.001). HLADRB1*08 incidence had no difference in two groups (13). Results of this study were similar to us about HLADRB1*08 alleles. But about other alleles mentioned there is no agreement in our study and this one.

In 1997 S WAKITANI and ET al showed that, there were significant correlation between HLADRB1*01 HLADRB1*0405 alleles and rheumatoid arthritis incidence while in our study there were no relation. However, these differences may differ because of ethics differences (14).

van Gaalen FA and et al showed in 2004 that HLA-DRB1*0401, DRB1*1001, DQB1*0302, and DQB1*0501 accompanied with presentation of anti ccp , and presence of at least two HLA DRB alleles anticipate progression and severity of disease(15). while our study suggests that HLA-DRB1*08 alleles correlate with RF positive in RA patients. However in van Galen FA study rheumatoid factor was not assessed while in our study anti ccp was not assessed. both study showed that alleles of HLADRB can correlate with some antibodies in serum of rheumatoid arthritis patients and therefore anticipate more disease severity and activity.

However, our study has limitations. In our study correlation between HLA alleles and disease activity or severity was not evaluated. Second the relation between

HLA DRB alleles and RF was assessed and its relation to anti ccp was not evaluated.

CONCLUSION

This study shows that there is no relation between HLA B alleles and disease presentation. The other result is that, between HLA II alleles, only there is significant correlation between HLA-DRB1*08 alleles and Rheumatoid factor in patients with rheumatoid arthritis.

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CONFLICT OF INTEREST

None declared

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