Original article

Do diabetes and family history influence the rheumatoid arthritis? - results from a case-control study

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Abstract

Introduction: Up to now, several studies have been performed about the role of dif ferent factors on incidence and severity of Rheumatoid arthritis (RA) in the world. This 2009 study was carried out to investigate the association between History of diabetes and Family history of RA with RA incidence in Hamedan, a western city of Iran. ***Methods:*** As a case-control study , information from 128 cases and 130 controls, matched for age and Sex, were collected by questionnaire and analyzed using SPSS (chi-square test). ***Results:*** In case and control groups, females were 116 and 118 persons respectively and the rest were males. Statistical analysis showed that there is significant and no significant association between Family history of RA and history of diabetes with RA respectively. ***Conclusion:*** Considering previous global investigations on these topics and the results of our study , it seems that more studies will be needed to describe the association between history of diabetes and RA, but about another checked risk factor, there is a definite significant association between family history of RA and RA.

Keywords: Rheumatoid arthritis, diabetes, family history, risk factors.

Introduction

Rheumatoid arthritis (RA) as an autoimmune disease with unknown etiology af fects is assumed to involve several genetic as well as environmental factors. The incidence rate of this disease in the world is about 1% and based on previous studies, women are more susceptible than men. [1-4]. the main genetic risk factor is the shared epitope (SE) of HLA-DR, but several proposals have been presented about environmental risk factors [1-4]. On the other words, RA is believed to occur as a result of the interaction between genetic constitution and environmental triggers However, as in most other complex diseases, few such interactions have been described and it has been assumed that more studies will be needed to describe significant gene-environment interactions in these diseases. One of the most important of studied risk factors should be the history of particular infections such as Epstein-Barr virus (EBV) [2]. This virus causes the polyclonal activation of infected B lymphocytes followed by rheumatoid factor (RF) production. RF is a kind of IgM autoantibody against IgG that reacts with it, precipitates in joints and damage them. In connection with RA etiology there are also other microor ganisms such as, cytomegalovirus, micoplasma and rubella that probably enroll in the appearance of RA following a history of infection by them[2]. In this case, super anigen presentation or cross-reaction between microbial antigens and joint proteins should be noted. [1-4]. Familial studies have also shown that genetic susceptibility is important in this connection and, as mentioned previously, the role of shared epitope of HLA has been proved [1-4]. Several other areas of research about other risk factors have identified coffee consumption[5-7], blood transfusion history[8,9], kind of sex[1-4, 10,] sex hormones [2, 11,] diet [2, 12-14,] weather [2, 15,16] and smoking [2-4, 17-21]. Since in diabetes as one of the most complex health problems in the world, the balance between biochemical reactions and endocrine system is targeted, this is an area of study that merits more research. Although in most previous reports in different area of world it has been shown that there is a significant association between family history of RA (or genetic contribution) and RA incidence [22,23], we decided to investigate this relation in another parts of the world in hamedan. We think that the results of different studies about risk factors cannot be generalized to all parts of world because RA is a multifactorial disease and some known and unknown area-dependent factors should have an effect. As shown in other reports, 80% of RA cases begin in the fourth and fifth decades of life, and information about relative risk factors and useful

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instruction should assist in preventive methods and decrease the incidence of RA. Thus in 2009 we start to study the relation of some risk factors (such as history of diabetes and Family history of RA) with RA in Hamedan, a city located in the west of the Iran.

Materials and Methods

Design of Study

This research was designed as a case-control study involving incident cases of RA that were derived from the population ages 20-55 years in a geographically defined city in the western parts of Iran, Hamedan. The recruitment period for the cases and controls was 2009.

Selection of the Cases and Controls

All referring potential cases were examined and diagnosed by a rheumatologist in Mobasher hospital, the centre of rheumatology care in this aforementioned city. Definite RA diagnosis was completed on 128 individuals after RA latex examination on blood samples, physical exam, clinical symptoms and study of personal history . Primary statistical analysis was then conducted in order to calculate the average of sex and age in the case group. A total of 130 control populations were selected by physicians among healthy persons matched for age and sex with the case group after examination.

Data Collection

All needed data about family history of RA and history of diabetes were collected by standard questionnaire with the consent of both patients and controls in the presence of physician.

Statistical Analysis

Statistical analysis was carried out by SPSS version 16 with Pearson's chi-square tests. p value lower than 0.05 was considered as a significant result. Results were analyzed and studied by cross-tabulation.

Results

Results after filling out the questionnaire were cross-tabulated including sex distribution in two groups, case and control and are shown in Table 1. The study of relation between family history of RA and R.A. was analyzed using Pearson's chi square test and p value was 0.002, meaning that there is a significant relation between the family history of RA and R.A (Table 2), but another part of our results, which have been analyzed by aforementioned test, showed that there is no significant association between history of diabetes and RA (p value=0.97) (Table 3).

Table 1: Cross-Tabulation for sex distribution in case and control groups

Studied groups	Male		Female		Total	
	Number	Percent	Number	Percent	Number	Percent
Case	12	9.4	116	90.6	128	100
Control	12	9.2	118	90.8	130	100
Total	24	9.3	234	90.7	258	100

Table 2: Cross-Tabulation between family history of RA and R.A in case and control groups

Studied groups	Without family history of RA		With family history of RA		Total		p.value
	Number	Percent	Number	Percent	Number	Percent	
Case	95	74.2	33	25.8	128	100	0.002 significant
Control	113	89	14	11	127	100	
Total	208	81.6	47	18.4	255	100	

Table 3: Cross-Tabulation between history of diabetes and R.A in case and control groups

Studied groups	With history of diabetes		Without history of diabetes		Total		p.value
	Number	Percent	Number	Percent	Number	Percent	
Case	5	3.9	122	96.1	127	100	0.97 Non-significant
Control	5	3.6	125	96.2	130	100	
Total	10	3.9	247	96.1	257	100	

Discussion

This 2009 study revealed that there is a significant association between family history of RA and RA incidence in Hamedan, a western city of Iran. It has been proved that there is a tendency for RA to run in families. Based on a report from Norfolk located in the UK, If one member of a pair of identical twins has RA then the other member has a 15% chance of developing the disease [21, 23]. This rate is substantially higher than risk in general population, which is about 0.8% [21-22]. According to results of another study which has been performed in Finland and the UK, the genetic contribution to RAsusceptibility has been estimated at around 60% [24]. However, more results will be needed to distinguish the genes enroll for susceptibility from those that enroll for persistence or disease severity. Several studies have been done in the context of understanding of RA genetics in recent decades. First of all was the observation of a high concordance in monozygotic twins and the next was the discovery of the link between HLA-DR4 and RA incidence [21-25]. Other studies found links between RA and different HLA-DRB1 allels. In 1987, the "shared epitope (SE)" hypothesis has been proposed to describe these associations [21-26]. It has been show previously that HLA-DRB *0101, *0102, *0401, *0404, *0405, *0408, *1001 and *1402 which have association with RA, share a highly conserved sequence of amino acid residues in the third hypervariable region of their DRB1 chain [21-26]. Individuals with homozygote shared epitope have a substantially higher risk of RA than those with heterozygote SE [27]. In 1997, scientists tried to investigate the risk of RA in the first degree relatives using an interview based case-control study [28]. Their results confirm the familial clustering of RA and suggest that mothers confer susceptibility to RA on their offspring more often than fathers. Considering previous investigations on this topic and the results of our study, it seems that there is a significant association between RA history and RA incidence. Another part of our study was to investigate the association between history of diabetes and RA. The results showed that there is no significant relation between mentioned factors. It should be noted that both diseases (RA and Diabetes) are Th1-mediated autoimmune diseases and it is proved that most of autoimmune diseases are polygenic. It means that several genes may contribute in a particular autoimmune disease formation; also one particular gene may have causal role in several autoimmune diseases. For this reason, existence of two or three (or more) autoimmune diseases in one person is expectable. In 1988, as a case report, a patient is described who had insulin-dependent diabetes mellitus for 2 years, prior to developing rheumatoid arthritis and then subsequently ankylosing spondylitis and dermatomyositis [29]. In 2001, it has been shown that there is a positive association between RA and insulin treatment in women using a case-control study in Sweden [30]. In spite of our expectation, we did not find any significant relation between RA and history of diabetes. It should be attributed to racial differences in genomic construction. For this reason, as aforementioned, we think that the results of different studies about risk factors cannot be generalized to all parts of world because RA is a multifactorial disease and some known and unknown factors should have an ef fect. It seems that more studies will be needed to describe the association between history of diabetes and RA.

Conclusion

It seems that there is a significant association between RA history and RA incidence, but about another checked risk factor , more studies will be needed to describe the association between history of diabetes and RA.

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Conflict of interest:

We have not any conflict of interest.

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