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Prevalence of Diabetes Type 1 in Patients Suffered From Multiple Sclerosis

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Abstract

Background: Because IL2RA is considered a predisposing factor in the incidence of both type I diabetes and multiple sclerosis (MS), and considering that both are autoimmune diseases, some studies suggest a correlation between type I diabetes and MS.
Objectives: The aim of this study was to examine the prevalence of type I diabetes among people with MS.
Patients and Methods: The study subjects comprised 100 patients with MS from the Khuzestan multiple sclerosis center at rehabilitation school of Jundishapur University of Medical Sciences, whose diagnosis of MS had been confirmed by a specialist, and were not being treated with steroids. Subjects were selected from patients younger than 30 years old. After filling out an application form, 5 mL fasting venous blood and 5 mL after 2 hours were taken. The blood glucose level was measured with a kit (Zist Shimi) using the enzymatic method.
Results: The mean age of the participants was 24.28 years. The rate of type I diabetes was equal to 4% of the total sample, while 18% of all patients had impaired fasting glucose.
Conclusions: Given the high level of impaired fasting glucose among patients in this study, it is likely that MS provides the basis for the incidence of glucose metabolism disorders. To prove this, further studies with larger sample sizes are required.

Keywords: Type I Diabetes, Multiple-Sclerosis, Auto-Antibody, Prevalence

1. Background

Multiple sclerosis (MS) is one of the most common diseases of the central nervous system. The disease is caused by auto-antibodies attacking myelin tissue of the central nervous system. Many factors have been introduced as stimulants for the attack of auto-antibodies on myelin tissues, including Epstein-Barr Virus (Herpes Simplex Virus), A3, B7, and DW2 HLA antigens, and vitamin D deficiency. Following damage to myelin (demyelination), transmission of message along the nerves is disrupted and slowed down. When the damage is severe, nerve message transmission is completely stopped. The most common symptoms at the onset of disease include weakness in motor system, feeling of pins and needles, impaired vision, sudden unilateral reduced or blurred vision (optic neuritis), diplopia, involuntary eye movement, aphasia, tremor, impaired deep senses and loss of balance, partial paralysis of lower extremities and changes in emotional responses, cramp, tingling and imbalance in one limb, bladder dysfunction either as urgency or hesitancy. These symptoms are predominantly transient and disappear within days or weeks. However, in time, these symptoms may persist and cause problems in speech, cognition, mood, and memory of the patient (1). According to statistics published by the ministry of health and medical education (MOHME) in 2011, the prevalence of MS in Iran was 45/100,000. Thus, Iran is considered among countries with medium to high prevalence of MS (1). Previous studies have demonstrated that heredity is an important factor in the incidence of MS. Other risk factors include age between 20 and 40, female gender, ethnicity, and geographical location of residence (2). Some studies have shown a correlation between MS and type I diabetes (TID). Multiple sclerosis and TID are two autoimmune diseases. In both diseases, specific alleles make the person more susceptible to the disease (3). In 2002, a study in Sardinia, Italy on people with TID proved a correlation between TID and MS, while researchers realized DQA1 0102-DRB1 15- DQB1 0602, which prepared the grounds for the incidence of MS is considered a protective factor against diabetes. Thus, some studies conducted in other geographical locations did not show such correlation (4). At the time, the interpretation researchers provided for this problem was that in Sardinia HLA haplotypes of DRB1 0405-DQA1 501-DQB1 0301 and DRB1 0301-DQA1 501-DQB1 0201 were responsible for predisposing peo-

ple to MS and the same haplotypes were responsible for the incidence of TID, while in other parts of the world MS is associated with haplotypes DRB1 15-DQA1 0102-DQB1 0602, which does not increase the risk of diabetes (5). Later studies showed that familial autoimmune and diabetes (FAD) increased the prevalence of MS in adults with TID or with first degree family relation with diabetes (6). Similarity of the results led to researchers' seeking another genetic cause that was common in both TID and MS. Continued studies led to discovery of the gene IL2RA as the gene responsible for the correlation between MS and TID (7). Later studies showed that IL2RA was not the only factor responsible for the correlation between the two diseases, and other unknown genetic and environmental factors were also involved (8). Given that diabetes adds secondary complications such as nephropathy, neuropathy, and retinopathy to MS complications, and have major physical, and socioeconomical losses, creating public awareness toward the correlation between the two diseases and proper education to avoid environmental risk factors of diabetes to prevent incidence of MS seems to be necessary.

2. Objectives

Given the high prevalence of MS in Iran (8), this study aimed to assess the prevalence of TID in patients with MS in Khuzestan Province, Iran, and examine the likelihood of the incidence of TID in MS patients in terms of risk factors of age, gender, ethnicity and education.

3. Patients and Methods

The present study was conducted on 100 people with MS whose disease had been confirmed by a specialist physician at MS center at rehabilitation school of Jundishapur University of Medical Sciences in Ahvaz City, Iran. The study was designed based on the principles of the ethics committee of the University of Medical Sciences in Ahvaz. All subjects received and signed a written consent form for voluntary participation in the study. The inclusion criteria were age under 30 years, and no use of steroids. The questionnaire was completed by all subjects. Data relating to age, gender, height, weight, ethnicity, education, marital status, familial diabetes and level of education were recorded. Subjects attended the clinic fasting, and 5 mL venous blood sample was taken from each. Then, they received 70 g glucose syrup in 100 mL water. Two hours later, blood sampling was repeated. Blood samples were centrifuged at 3000 rpm. After separation of serum from clot, serum was kept in the freezer at -20°C. Glucose concentration was measured for both fasting and the glucose tolerance test with a glucose kit (Zist Shimi, Iran), using the enzymatic glucose oxidase method. Data obtained were processed with SPSS-17 (Statistical Package for the Social Sciences; Nie, Bent and Hull, USA). The chi-square test was used to determine the correlation between the variables.

4. Results

Study population included 54% women and 46% men with MS. Mean age of the participants was 24.28 years. Eighteen percent of the subjects had impaired fasting glucose. Also, 4% of people with MS showed an impaired glucose tolerance test and thus diagnosed as diabetic patients. There was a significant correlation between the incidence of diabetes and MS ($P < 0.001$) with relative risk of 0.043. Moreover, there was a significant correlation between the incidence of impaired fasting glucose and MS ($P < 0.001$) with relative risk of 0.329. Among risk factors of diabetes, family history of diabetes, age, and gender were significant factors in the incidence of impaired fasting glucose and diabetes (Tables 1 and 2). This meant that with family history of diabetes in MS patients, risk of diabetes in these people increased by threefold compared to other subjects. With every year's age increase, risk of diabetes in MS patients increased by 1.3 times, and risk of diabetes in women with MS was nearly twice as that in men. According to tables 1 and 2, no significant correlation was found between the incidence of impaired fasting glucose and factors of ethnicity (Persian or non-Persian), body mass index (BMI), marital status, or education level (diploma or under).

5. Discussion

According to previous studies, MS is on an ascending trend in Iran. A study by Etemadifar et al. in Isfahan revealed that a rate of incidence of MS in Isfahan has increased from 9.1 per 100,000 in 2009 to 9.22 in 100,000 in 2011 (9). In the study by Moghtaderi et al. conducted in the Southeast of Iran, the incidence rate of MS was 2.4 times in women and 2.7 times in men in 2009 as compared with that in 2006 (10). Thus considering the growing trend of MS in Iran, and also given the damaging effects of diabetes on patients with MS, the present study was conducted to assess a rate of prevalence and factors affecting the incidence of TID in patients with MS. According to the results obtained in this study, 4% of all patients with MS also had diabetes. The correlation between first degree family history of diabetes in patients with MS and the incidence of impaired fasting glucose and diabetes in these patients was significant ($P < 0.001$), and the rate of impaired fasting glucose was 18% of all patients with MS. It is

Table 1. Association Between Risk Factors of Diabetes and Impaired Fasting Glucose in Patients With Multiple Sclerosis

Variables	P Value	Relative Risk (RR)	95% CI for RR
Familial history of diabetes	0.014[a]	3.06	22.18 - 1.42
Age, y	0.034[a]	1.36	2.99 - 1.13
Gender	0.050[a]	2.01	40.99 - 1.88
BMI	0.440	0.99	1.28 - 0.77
Ethnicity	0.815	0.58	4.59 - 0.07
Marital status	0.726	1.68	14.54 - 0.19
Education	0.367	1.20	18.19 - 0.08

[a] $P < 0.05$: Significant relation.

Table 2. Association Between Risk Factors of Diabetes and Diabetes in Patients With Multiple Sclerosis

Variables	P Value	Relative Risk (RR)	95% CI for RR
Familial history of diabetes	0.02[a]	3.02	20.20 - 1.75
Age, y	0.028[a]	1.15	2.87 - 1.06
Gender	0.053[a]	2.44	36.32 - 1.88
BMI	0.329	0.80	1.63 - 0.65
Ethnicity	0.610	0.38	5.49 - 0.05
Marital Status	0.413	1.83	15.31 - 0.14
Education	0.319	1.35	14.92 - 0.17

[a] $P < 0.05$: Significant relation.

known that impaired fasting glucose increases risk of diabetes in future years. Extensive studies conducted across the world to investigate the correlation between MS and diabetes confirms the results of the present study. A study by Marrosu et al. in 2002 on patients with MS and their first degree family members showed that the prevalence of diabetes in patients with MS was 3 times their first degree family members and 5 times ordinary people in the society. This study also showed that risk of diabetes in patients whose first degree family members also have MS is 6 times as much as that in patients with healthy families (3). Results of prospective epidemiological studies conducted in Italy in 2003 by Dorman et al. on patients with TID and their first degree family members showed that 2% of women with TID and 0.5% of their sisters with MS in future (6). In studies by Maier et al. in 2009 in America, IL2RA variants had been collected from DNA of patients with diabetes, patients with MS, their families, and healthy people, and it was demonstrated that two alleles of IL2RA were effective in predisposition to both diabetes and MS (7). A study by Nielsen et al. in 2006 in Denmark, which investigated risk of MS in patients with TID and risk of TID in first degree relatives of MS patients showed an increase in the incidence of MS in diabetes patients of more than 3 times, and 63% increase in risk of TID in first degree relatives of patients with MS (11). This study also showed that predisposed women to MS are exposed to higher risk of impaired fasting glucose and diabetes compared to men (11). In a study by Bechtold et al. conducted prospectively from 1995 to 2012 on 56635 TID patients in Germany and Australia, relative risk of MS in patients with TID was found between 3.35 and 4.79 (12). Considering that both MS and TID are autoimmune diseases, similarity of immunological patterns of these diseases could also be involved in their correlation (11). Both diseases are caused by T-helper lymphocytes attacking body tissues, and studies by Winer et al. show that pancreatic and nervous system auto-antigens are both affected by T-helper cells, and thus some existing auto-antibodies against both tissues may be the same (13). Given that TID is a multi-factorial disease, thus, incidence of this disease may be intensified under the influence of factors other than MS autoimmune disease. Factors such as race, geographical location of residence, family history of diabetes, nutritional type, and various viral infections can affect the incidence of TID (14). The present study showed a significant effect of increasing age and fe-

male gender in increased incidence of impaired fasting glucose and diabetes in patients with MS. However, the correlation between the incidence of impaired fasting glucose and diabetes with ethnicity (Fars or Arab), BMI, education, and marital status was insignificant. Previous studies revealed that the prevalence of TID varies in different ethnicities. The lowest prevalence was reported in China, and the prevalence in natives of Finland and Sardinia of Italy was nearly 100 times that of China (15). A study by Jeffcoate et al. showed that older age, female gender, low education level, abnormal BMI, and white race were factors affecting the incidence of diabetes (15). The insignificant correlation between the incidence of diabetes and some of these factors in the present study could be attributed to the small sample size. The small sample size was a limitation which resulted from lack of cooperation of the majority of patients. Generally, results indicate that MS can be considered a predisposing factor in the incidence of TID. The incidence of impaired fasting glucose and ultimately diabetes in patients with MS who are genetically predisposed to diabetes is higher than in other people. Thus, diabetes prevention and education of correct methods to avoid risk factors of diabetes are suggested to patients with MS for prevention of diabetes. Also, given the results, screening MS patients for timely diagnosis of diabetes is recommended.

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Footnote

Authors' Contribution: Abdollahzadeh: Doing the experiments; Naderi: Doing the experiments; Madji Nasab: Data interpretation.

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