

# The prevalence of autoimmune diseases in patients with multiple sclerosis: A cross-sectional study in Qom, Iran, in 2018

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## Keywords

Multiple Sclerosis; Autoimmune Disease;  
Comorbidity; Prevalence

## Abstract

**Background:** Multiple sclerosis (MS) is one of the most common autoimmune diseases worldwide and various autoimmune comorbidities are reported with MS. The objective of this study is to estimate the prevalence of the autoimmune diseases' comorbidity in patients with MS.

**Methods:** In this cross-sectional study, we investigated a group of patients with MS in terms of age, gender, duration of MS, presence of simultaneous autoimmune diseases, such as Graves' disease, Hashimoto's thyroiditis, type 1 diabetes mellitus (DM), and systemic lupus erythematosus (SLE).

**Results:** This study included 1215 patients with MS, of

which 70.8% were women. The mean age of participants was  $33.70 \pm 27.63$  years. 55 patients (4.5%) had at least one autoimmune disease. The most common comorbidity was for Hashimoto's thyroiditis (30 patients). The frequency of simultaneous autoimmune disease was higher in women. Mean age ( $P = 0.01$ ), mean duration of MS ( $P = 0.03$ ), and mean age on MS diagnosis ( $P = 0.02$ ) were significantly higher in simultaneous MS and other autoimmune diseases.

**Conclusion:** Our study revealed that the probability of autoimmune diseases co-occurrence in patients with MS could be higher in older patients, in longer

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duration of disease, and also in patients with higher age at time of MS diagnosis.

### Introduction

Multiple sclerosis (MS) is the most common demyelinating disease caused by an autoimmune inflammatory process in the central nervous system (CNS).<sup>1-3</sup> The disease has hit 2.5 million people worldwide and the incidence rate is increasing.<sup>4</sup> The most common pathologic hallmark of disease is myelin destruction and axonal degeneration which is affected by genetic and environmental factors.<sup>5,6</sup>

Prevalence of various autoimmune and non-autoimmune diseases has been assessed in patients with MS compared to the general population.<sup>7</sup> Although autoimmune diseases are rare, some of them tend to occur together. Co-occurrence of MS and other autoimmune diseases and also presence of T and B lymphocytes which are active against myelin basic protein (MBP) antigen support the theory of the autoimmunity of MS.<sup>8,9</sup>

Some studies showed high prevalence of thyroiditis, psoriasis, and autoimmune thyroiditis as the most common diseases accompanied by MS.<sup>7-10</sup> Some other studies demonstrated high comorbidity of connective tissue diseases such as familial Mediterranean fever (FMF), rheumatoid arthritis (RA), Sjogren's syndrome, and systemic lupus erythematosus (SLE) with MS.<sup>11-15</sup>

The autoimmune diseases comorbidity in patients with MS can decrease the development of disability through an unknown change in the immune system, but some called the co-occurrence of MS and autoimmune diseases as a cause of increasing brain injury and atrophy.<sup>16,17</sup> On the other hand, flaring up of some autoimmune diseases occurs in patients with MS following the use of immune-modulators, such as interferon beta (IFN- $\beta$ ).<sup>18</sup>

The aim of this study is to investigate the frequency of autoimmune diseases in patients with MS.

### Materials and Methods

**Study design:** We conducted a cross-sectional study at Qom MS Society, Qom, Iran, during 2018. The executive protocol was approved by the Ethics Committee of Islamic Azad University, Qom Branch. The study was conducted in accordance with the Declaration of Helsinki (seventh revision, 2013). The medical documents of all patients, who were member of Qom MS

Society from the foundation of the society (February 2010) until 2018, were gathered as primary data. All patients with MS, who gave informed consent obtained by phone call, were included in the study. Patients whose document was incomplete were excluded from the study. The information was used privately and without mentioning patient's name.

**Data gathering:** The basic information including age (at the time of study), gender, age on MS diagnosis, and duration of MS was collected based on the data in the document. History of other autoimmune diseases including Graves' disease, Hashimoto's thyroiditis, psoriasis, ulcerative colitis (UC), Addison's disease, type 1 diabetes mellitus (DM), alopecia areata, celiac disease, pernicious anemia (PA), immune thrombocytopenic purpura (ITP), Sjogren's syndrome, RA, and SLE and duration of autoimmune disease were collected. History of autoimmune diseases was defined as presence of autoimmune disease from the time of MS diagnosis to the time of study which was asked by phone call. In case of document defect, additional history was also asked from the patient.

All data were analyzed by SPSS software (version 24, IBM Corporation, Armonk, NY, USA). Continuous variables were described using mean  $\pm$  standard deviation (SD) and categorical variables were described using frequency and percentage. In order to evaluate the association of qualitative variables with each other, chi-square test or Fisher's exact test was used. One-way analysis of variance (ANOVA) and independent t-test were applied to analyze the relation between categorical and continuous variables. Significance level was set at  $P < 0.05$  in all analyses.

### Results

Documents of 1223 patients with MS disease were investigated in the present study. 8 patients were excluded from the study due to document defect and 1215 patients enrolled in the study. 860 participants (70.8%) were women. Age range of the study was 19 to 55 years with a mean of  $33.27 \pm 7.63$  years. The mean age of participants with autoimmune disease comorbidity ( $35.76 \pm 8.40$  years) was significantly higher than participants without autoimmune disease comorbidity ( $33.15 \pm 7.58$  years) ( $P = 0.01$ ).

Mean age on MS diagnosis was  $29.60 \pm 5.85$  years. The mean age on MS diagnosis was significantly higher in participants with

autoimmune disease comorbidity ( $31.34 \pm 5.92$  years) than participants without autoimmune disease comorbidity ( $29.52 \pm 5.84$  years) ( $P = 0.02$ ).

Mean duration of MS was  $3.66 \pm 2.75$  years with minimum and maximum of 1 and 15, respectively. The mean duration of MS was significantly higher in participants with autoimmune disease comorbidity ( $4.41 \pm 3.57$  years) than participants without autoimmune disease comorbidity ( $3.63 \pm 2.71$  years) ( $P = 0.03$ ).

None of the participants had UC, celiac disease, Addison's disease, or PA. Among the studied patients, 55 (4.5%) had at least one autoimmune disease comorbidity and the most common autoimmune disease in both genders was Hashimoto's thyroiditis with the total frequency of 30 persons (2.46%). The distribution of simultaneous autoimmune disease in two genders showed that the rate of simultaneous autoimmune disease was higher in women. However, the relationship between simultaneous autoimmune disease and gender was not statistically significant ( $P > 0.05$ ) (Table 1).

## Discussion

The presence of immunoglobulin G (IgG) oligoclonal bands (OCBs) is one of the most common immunologic findings in patients with MS and confirms an autoimmune process in these patients.<sup>19</sup> Many studies named autoantibodies that are associated with autoimmune disorders with a prevalence of 4% to 21%. This implies the autoimmunity of MS.<sup>20,21</sup>

On the other hand, the study by Dal-Bianco et al. showed that among 176 patients with MS, 18.8% had autoantibodies of autoimmune diseases while in 12.0% of them, an autoimmune disease was actually found.<sup>22</sup>

Our study showed that the prevalence of MS

in women was higher than men. In general, the prevalence of autoimmune diseases is 3% to 8% worldwide and between 78% to 85% of them are women.<sup>23</sup>

MS, as an autoimmune disease, has also higher prevalence in women than men. Various epidemiological studies in past two to six decades reported that incidence of MS in women had more ascending increase than that in men.<sup>24</sup>

Our study revealed that the prevalence of co-occurrence of MS and other autoimmune diseases was 4.5% among which the most common ones were hypothyroidism and RA, respectively. A study by Cooper et al. in Denmark showed that type 1 DM, UC, pemphigus vulgaris, and thyroiditis were the most prevalent autoimmune diseases in patients with MS but no relationship between RA and MS was found.<sup>25</sup>

Langer-Gould et al. conducted a study on 5296 patients with MS and 26478 controls in northern part of California, United States of America (USA). They found that the prevalence of autoimmune diseases such as uveitis, Bell's palsy, Guillain-Barre syndrome (GBS), and inflammatory bowel disease (IBD) in patients with MS was more than the control group but there was no relationship between MS and RA, SLE, or thyroiditis.<sup>26</sup>

While in a study by Sahraian et al. in Tehran, Iran, on 1700 patients with MS, only 28 of them had simultaneous autoimmune disease of which the most common was RA.<sup>16</sup>

In many studies, thyroid disorders were reported as the most common autoimmune diseases accompanied by MS with a prevalence of 2.5% to 10.0%.<sup>10</sup>

Main cause of difference in the prevalence and type of autoimmune diseases and MS is unknown but it can be due to the similarity of genetic factors, immune pathways, and environmental factors.<sup>26,27</sup>

**Table 1.** Demographic characteristics of the patients with psychogenic non-epileptic seizures (PNES)

Simultaneous autoimmune disease	Total	Men	
		n (%)	
Hashimoto's thyroiditis	30 (2.5)	10 (2.8)	20 (2.3)
Graves' disease	3 (0.2)	1 (0.3)	2 (0.2)
SLE	5 (0.4)	0 (0)	5 (0.6)
RA	8 (0.7)	4 (1.1)	4 (0.5)
Psoriasis	3 (0.2)	1 (0.3)	2 (0.2)
Alopecia areata	2 (0.2)	2 (0.6)	0 (0)
Type 1 DM	2 (0.2)	0 (0)	2 (0.2)
ITP	1 (0.1)	0 (0)	1 (0.1)
Simultaneous Hashimoto's thyroiditis and Sjogren syndrome	1 (0.1)	0 (0)	1 (0.1)
No autoimmune disease	1160 (95.5)	337 (27.7)	823 (67.7)

SLE: Systemic lupus erythematosus; RA: Rheumatoid arthritis; DM: Diabetes mellitus; ITP: Immune thrombocytopenic purpura

Investigation of demographic data conducted in our study showed that the prevalence of autoimmune disease comorbidities in MS was higher in women than men. Also, mean age of patients, mean years of MS duration, and mean age on MS diagnosis were higher in patients with simultaneous autoimmune disease.

A study by Sloka et al. investigated the relationship of MS with Graves' disease or Hashimoto's thyroiditis and found that the prevalence of simultaneous autoimmune diseases was higher in women but it was not statistically significant. Also, the age on MS diagnosis in patients with simultaneous autoimmune diseases was higher but the relationship was also not statistically significant.<sup>28</sup>

Another study by Zivadinov et al. showed that the prevalence of autoimmune diseases in women with MS was lower than men but the mean age on MS diagnosis was higher in these patients.<sup>17</sup> Munteis et al. assessed the prevalence of hypothyroidism in patients with MS in a cohort study. They showed that positive anti-thyroid peroxidase antibody (anti-TPO antibody) and subclinical hypothyroidism (SCH) were significantly higher among women.<sup>29</sup>

Most studies explained that the differences in demographic findings might be influenced by geographic or racial factors and different sample sizes.

Although the exact mechanism of autoimmune diseases is unknown, genetic and environmental factors are always of paramount importance. Importance of genetic factors is undeniable due to the co-occurrence of many autoimmune diseases. The immune cells and immunologic pathways are common in many of these diseases. On the other hand, environmental factors such as ultraviolet (UV) radiation and cigarette are other effective factors in the simultaneous occurrence of autoimmune diseases.<sup>30,31</sup>

In a study conducted by Nageeb et al., genomes of 40 patients with MS and 40 patients with SLE were compared with 40 patients in control group without any disease. They showed that signal transducer and activator of transcription 4 (STAT4) polymorphism was significantly higher in the genome of patients with MS and SLE.<sup>32</sup>

Another factor supporting the genetic effect is higher incidence of autoimmune diseases among the family members of patients with autoimmune diseases. Heinzlef et al. studied autoimmune diseases in the first-degree relatives of 357 patients with MS. They showed that 6.2% of

patients had MS in their first-degree relatives, 8.4% had other autoimmune diseases, and 0.8% had both MS and other autoimmune diseases.<sup>33</sup>

The importance of investigation of the co-occurrence of autoimmune disease and MS is primarily the answer to the question "whether autoimmune disease comorbidity has any effect on course of MS and brain function or not". In various studies, the presence or absence of this effect is a subject of controversy. A study conducted by Lorefice et al. on 286 patients with MS and autoimmune disease comorbidity suggested that the evidence of brain atrophy in magnetic resonance imaging (MRI) was more significant in patients with MS and type 1 DM than the control group, but its effect on clinical features and disease prognosis was not clarified.<sup>18</sup>

In the study of Marrie et al., patients with MS who had DM showed more progressive trend in their clinical symptoms compared to the control group.<sup>34</sup>

On the other hand, other studies indicated that autoimmune diseases comorbidities in patients with MS could improve the clinical process of MS through making a tolerance in the immune system with an unknown mechanism.<sup>16</sup>

## Conclusion

In our study, autoimmune disease comorbidity in patients with MS was relatively higher than other studies. We also revealed that the probability of autoimmune diseases co-occurrence in patients with MS could be higher in older patients, in longer duration of disease, and also in patients with higher age at time of MS diagnosis. Further studies are needed to confirm our results and also clarify the underlying mechanism of this comorbidity.

**Limitations:** Since the study was a cross-sectional study, there was no access to some variables such as type and route of medication consumption, subtype of MS, and nutrition patterns. Comparing the relationship between autoimmune disease comorbidities and different variables was not statistically possible because of the low prevalence of autoimmune disease in patients with MS.

## Conflict of Interests

The authors declare no conflict of interest in this study.

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