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Research Paper

Association Between the Multiple Sclerosis Epidemic and Socioeconomic Status in Iran: A Descriptive-analytical Cross-sectional Study

Hossein Mozhdehipanah[1], Ali Emami[2], Shima Mohammadhoseini Targhi[2], Fatemeh Kazemi[2], Ali Sarbazi-Golezari[3], Monirsadat Mirzadeh[3*]

1. Department of Neurology, Bou Ali Sina Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.
2. Student Research Committee, Qazvin University of Medical Sciences, Qazvin, Iran.
3. Metabolic Diseases Research Center, Research Institute for Prevention of Non-communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran.

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ABSTRACT

Background: Multiple sclerosis (MS) is a key neurogenic cause of disability among young populations. Assessing the parameters affecting MS severity is vital to reduce the disease burden. **Objective:** This study aims to determine the relationship between socioeconomic status (SES) and MS severity among young Iranian adults.

Methods: A descriptive-analytical cross-sectional study was conducted on 180 patients (142 females and 38 males) with MS selected by non-probability and consecutive sampling from September 2018 to 2019. The socio-demographic and primary clinical data were collected by a self-developed questionnaire and face-to-face interviews, respectively. The expanded disability status scale (EDSS) was used to assess the physical disability and overall neurological function of patients.

Findings: The mean age of patients and MS onset were 27.54 and 35.58 years, respectively. The majority of the patients were married (68.3%) and lived in cities (74.4%). The mean values of unemployment, homeownership, and monthly income were 54.4%, 71.7%, and 11078330 IRR, respectively. The mean EDSS was 2.80±1.79 points. A weak positive correlation was found between EDSS and the age of the patient (P=0.001, r=0.246) and the number of children (P=0.001, r=0.250). There was no significant difference between EDSS and SES factors (i.e. disease onset age, treatment cost, and monthly income).

Conclusion: As SES was not related to MS severity, there is no need to take special treatment measures in patients with poor SES.

*** Corresponding Author:**
Monirsadat Mirzadeh, Associate Professor.
Address: *Metabolic Diseases Research Center, Research Institute for Prevention of Non-communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran.*
Phone: *+98 (912) 3986052*
E-mail: *monirdokht_mirzadeh@yahoo.com*

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Introduction

Multiple sclerosis (MS) is a chronic disease with specific characteristics, such as refractory inflammation, axonal damage to neurons, demyelinating process, and irreversible pathological changes in the central nervous system (CNS). This autoimmune disease demyelinates neurons, reduces nerve conduction velocity, and disrupts the CNS function [1]. MS has various symptoms, such as paresthesia, spasticity, bladder or sexual dysfunction, tremor, dystrophy, and visual impairment (e.g. optic neuritis or internuclear ophthalmoplegia) [2]. MS typically starts in the third or fourth decade of life and affects young females three times more than males. These decades are the reproductive years of women; therefore, their complications may also affect the fetus [3, 4]. The MS incidence depends on the geographical area and race and changes from 5.1 to 11.6 cases per 100000 people in a year [5]. This inflammatory demyelinating disease is the most common chronic disorder of the CNS, causing disability and loss of function in young people [6].

The prevalence of this disease in the world has been increasing in recent years. It is estimated that 2.5 million people worldwide suffer from this disease and 80% of patients experience disability [7].

According to Kurtzke's prevalence pattern of MS, Iran is classified as low-risk (less than 5 cases per 100000 population) [8]. However, some epidemiological studies in the central area of Iran (e.g. Isfahan City) have shown that the MS prevalence is about 35-45 per 100000 individuals; accordingly, the risk level for MS prevalence is moderate to high [9]. Therefore, there are several parameters involved in increasing the prevalence of MS, such as genetic (e.g. the HLA class I and II genes) [10, 11], lifestyle (e.g. dietary intake, exercise, drug abuse, smoking, and alcohol consumption) [12-14], and environmental risk factors (e.g. sun exposure and actinic damage) [15, 16]. Currently, MS is increasing in developed countries; hence, it is more common in high socioeconomic classes with higher education, income, and a good occupation [17, 18]. However, the role of socioeconomic status (SES) in the prevalence of MS in Iran has been evaluated less.

This complex neurological disorder, because of many physical and mental problems and the need for multiple hospitalizations of patients, causes high medical costs for the patients, their families, and the overall healthcare system in the country [19]. As a result, identifying and controlling the factors exacerbating this nervous disorder can significantly reduce the burden of MS [20]. Due to the contradictory results of different studies on the relationship between SES and MS and the lack of similar studies in Iran, the present study aims to determine the epidemiology of MS among Iranians, with a specific emphasis on the role of socioeconomic variables in MS severity.

Materials and Methods

Study design and participants

A descriptive-analytical cross-sectional study was conducted with 180 patients with MS living in Qazvin (Qazvin Province, Iran), who were referred to the clinic of Bou-Ali Hospital for general and critical care from September 2018 to September 2019. A non-probability and consecutive sampling were used in this study.

Inclusion and exclusion criteria

The inclusion criteria for patients in this study were as follows: Patients with MS with a confirmation letter from neurologists based on the worldwide described criteria [21, 22], and people who lived in Qazvin Province, Iran, for at least 10 years before the onset of the disease. On the other hand, patients with any physical disability, history of the disease less than 6 months, and insufficient or missing information were excluded.

Data collection

Socio-demographic data

A self-developed questionnaire was designed to answer a set of demographic and midwifery characteristics, including gender, age, marital status, education level, and SES such as income, living place address, housing status in terms of ownership, number of family members, occupational status, and level of family support. The written informed consent was obtained from each patient after presenting enough explanation of the study objectives. A single code number was assigned to each participant to maintain the confidentiality of personal and medical data as well as to prevent the duplication of information.

Clinical data

A face-to-face interview was conducted with each MS patient to record the clinical data, including the onset time of MS, diagnosis, pattern of refractory and regression periods, and family history of autoimmune diseases confirmed by a neurologist.

Expanded disability status scale

The most common tool to assess the disability of patients with MS is the Expanded Disability Status Scale (EDSS) [23]. The scores range from 0 to 10, changing with 0.5-point steps based on functional systems, including cerebellar, pyramidal, sensory, brainstem, mental, visual, and bowel or bladder functions examined by a neurologist. The EDSS scores range from 0 (no disability and normal neurological function) to 10 (MS-related death). In other words, scores from 1 to 4.5 are given to people who had MS with defect criteria in functional systems while they could walk without any assistance. The score of 5.0 to 9.5 was determined by gait disturbance [23, 24].

Statistical analysis

The collected data were analyzed using SPSS software, version 20 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to examine the normality of the data distribution. The Pearson correlation coefficient and the chi-square parametric tests were used according to the distribution of quantitative variables in the population. The significance level was set at $P<0.05$.

Results

Some demographic and SES characteristics of the MS patients at disease onset are provided in Table 1. Accordingly, the majority of patients at the onset of MS were women (78.9%), married (68.3%), unemployed (54.4%), and urban residents (74.4%), with a diploma degree (57.2%) and private housing (71.7%). Meanwhile, 26.1% of the patients were the last child in their family. The mean numbers of children and family members were 1 and 4, respectively. The percentages for immigration history and family support were 15.6% and 72.2%, respectively. Also, 3.5% of women had a history of abortion, while one-third of them had a history of pregnancy during MS. In addition, there was a family relationship between parents in 15.6% of cases (Table 1). Some sociodemographic characteristics of MS patients, including age, marital status, occupational status, residential location, and housing situation between disease onset and study time are compared in Figure 1. The results showed that the percentages of marriage, divorce, unemployment, rural residence, and living in rented houses increased from disease onset to the study time (Figure 1). Figure 2a depicts that the most frequent clinical signs at the onset of MS among Iranian patients were imbalance (10.6%), diplopia (16.7%), blurred vision (28.9%), paresthesia (43.3%), and paresis (23.9%) disorders, respectively. Also, a family history of rheumatoid arthritis and hypothyroidism was reported at 8.9% and 27.2%, respectively. However, there was no family history of lupus (Figure 2b). The history of autoimmune diseases in the family of patients revealed that there was MS in 9.8% and 68.8% of their family members and first-degree relatives, respectively. In addition, the frequency distribution of the history of infectious diseases in patients with MS proved that they had 16.7% measles, 5.6% rubella, 30% mumps, 67.8% chickenpox, and 9.3% hepatitis (Figure 2c).

The average monthly treatment cost and income of patients were 993 500 and 11078330 IRR, respectively. The mean ages of patients and MS onset were 27.54±8.27 and 35.58±8.95 years, respectively. No significant difference was found in the mean age of MS onset between women (27.39±8.10 years) and men (28.08±8.80 years) (Figure 3a). However, there was a significant relationship between patients' current age and gender ($P=0.005$). The majority of patients with the same diversity of marital status were in the age range of 30 to 39 years (Figure 3). The mean EDSS of patients was 2.80±1.79. Table 2 shows the relationship between EDSS and gender according to the current age of MS patients. No significant difference in the EDSS amount among different age groups in both genders was found. In addition, there were no significant differences between the EDSS and socioeconomic variables, such as marital status, monthly income, pregnancy and abortion history, residential location, and occupational status (Table 2). The correlation test demonstrated that the EDSS had no significant association with the monthly income of men and women. Moreover, there is no significant relationship between EDSS and age at disease onset, treatment cost, or patient income. Nonetheless, there was a weak, positive correlation between EDSS and the patient's age ($P=0.001$, $r=0.246$) and the number of children ($P=0.001$, $r=0.250$) (Table 3).

Discussion

Finding a notable relationship between demographic characteristics, SES, and MS severity in Iran allows policymakers to present appropriate planning to improve the living conditions of patients. As the pro-inflammatory phenotype is directly related to adverse SES in childhood and adulthood, MS as a complicated neuro-inflammatory autoimmune disorder can be reduced by improving SES variables [25]; however, the etiological role of this issue requires longitudinal studies, such as case-control studies, and it could not be examined in the present cross-sectional study. Our findings showed no statistically significant relationship be-

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Table 1. Frequency distribution of demographic and socioeconomic status characteristics of patients with multiple sclerosis (n=180) at the disease onset

Variables	Sub-variables	Mean±SD (Max-Min)/No. (%)
Age (y)	-	27.54±8.27 (9-52)
Monthly treatment cost (IRR)	-	993500.0±217904.4 (0-15000000)
Children number	-	1.11±0.99 (0-4)
Family members number	-	4.08±1.84 (1-12)
Gender	Men	38(21.1)
	Women	142(78.9)
Education level	Illiterate	1(0.6)
	Primary	23(12.8)
	Under diploma	28(15.6)
	Diploma	75(41.6)
	Academic	53(29.4)
Marital status	Single	55(30.6)
	Married	123(68.3)
	Divorced	0(0.0)
	Widow	2(1.1)
Occupational status	Student	28(15.6)
	Unemployed	98(54.4)
	Employed	54(30.0)
	Retired	0(0.0)
Residential location	Metropolis and city	134(74.4)
	Suburbs	31(17.2)
	Village	15(8.4)
Housing situation	Personal	129(71.7)
	Rental	51(28.3)
Birth rank (in the family)	1st	34(18.9)
	2nd	44(24.4)
	3rd	34(18.9)
	4th	21(11.7)
	≥5th	47(26.1)

Variables	Sub-variables	Mean±SD (Max-Min)/No. (%)
Disease control	Yes	152(84.4)
	No	28(15.6)
Disease follow-up place	Qazvin	166(92.2)
	Tehran	8(4.4)
	Others	6(3.3)
Immigration history	Yes	28(15.6)
	No	152(54.4)
Family support	Good	130(72.2)
	Medium	31(17.2)
	Week	19(10.6)
Parents' relative marriage	Yes	28(15.6)
	No	152(84.4)
Pregnancy history (during MS)	Yes	59(32.7)
	No	121(67.3)
Abortion history (during MS)	Yes	6(3.3)
	No	174(96.7)

Abbreviations: MS: Multiple sclerosis; Min: Minimum; Max: Maximum.

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tween EDSS and SES factors. Goulden et al. [26] assessed the association between SES and MS in a case-control study with 2144 cases and 3859 controls from Norway, Italy, and Canada. They found no consistent relationship between parental SES and MS risk. In a systematic review, Goulden et al. [27] evaluated the role of SES as a risk factor for MS and concluded that only three studies reported MS had an association with low SES, while the other 13 surveys showed no significant relationship between MS and SES. Overall, there was inconsistent evidence regarding the correlation between high SES and increased MS risk. However, a more powerful effect can be found in some countries with higher inequality [27]. According to Nielsen et al. [28], although there was no robust association between the social class difference in childhood and MS risk, a slightly lower risk of developing MS was observed in children from families with higher education, especially educated mothers.

The common reason for the high MS rate at low SES may be increased vulnerability and exposure to pathogens in early life. In addition, MS risk may be remarkably increased by several stressors [28, 29]. These psychological risk factors, by enhancing the expression of inflammatory cytokines and the secretion of stress hormones (e.g. cortisol), intensify viral infections in patients' bodies at later ages [30]. In our study, 76% of patients had a history of infectious diseases, including chickenpox, mumps, and measles, in childhood. Besides, the higher unemployment rate of patients (68.3%) compared to the unemployment rate (10.4% and 18.9% for women and men, respectively) can considerably increase mental disorders (e.g. stress, dispersion, anxiety, etc.) in the studied population. This can be due to various factors, such as the inability of patients, the unwillingness of centers and companies to hire these patients, and the inability to attend work because of the need for regular use of drugs. As a result, this evidence suggests a link between viral infection or chronic stress and MS. Rezaali et al. [31]investigated the epidemiology of MS in Qom City, Iran, and reported that the prevalence of MS in married people was three times higher than single people, although divorced people had a lower risk than single ones. These findings were in line with the results of our study. In addition, there was a similarity between the two studies from the viewpoint of the ratio of females to males (3.4 vs 3.0) and the lower MS onset age in women than in men [31].

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Table 2. Relationship between EDSS, demographic, and socioeconomic characteristics of multiple sclerosis patients

Parameter		EDSS Value			P
		Men	Women	Total Population	
Current age (y)	<20	3.25±3.18	1.75±1.06	-	0.59
	20-29	2.10±1.68	2.05±1.35	-	0.85
	30-39	3.30±1.51	2.61±1.78	-	0.15
	≥40	3.54±2.00	3.47±1.86	-	0.91
Occupational status	Student	-	-	2.60±1.80	0.45
	Unemployed	-	-	2.90±1.80	
	Employed	-	-	2.60±1.70	
	Retired	-	-	2.30±1.90	
Residential location	Metropolis and city	-	-	2.8±1.8	0.91
	Suburbs	-	-	2.9±1.9	
	Village	-	-	2.6±1.7	
Marital status	Single	2.50±1.60	2.60±1.70	-	0.86
	Married	3.30±1.90	2.70±1.80	-	0.12
	Divorced	-	-	3.70±1.90	-
	Widow	-	2.00±0.70	-	-
Pregnancy history	Yes	-	2.81±1.82	-	0.42
	No	-	2.78±1.70	-	
Abortion history	Yes	-	2.78±1.78	-	0.74
	No	-	3.80±2.07	-	

EDSS: Expanded disability status scale.

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Table 3. Significance and correlation coefficients between some socioeconomic status parameters and EDSS of multiple sclerosis patients

SES Parameter	r	P
Age (y)	0.246	0.001
MS onset age (y)	0.009	0.910
Treatment cost (IRR)	-0.020	0.791
Monthly income (IRR)	-0.048	0.519
Children number (n)	0.250	0.001

SES: Socioeconomic status; EDSS: Expanded disability status scale.

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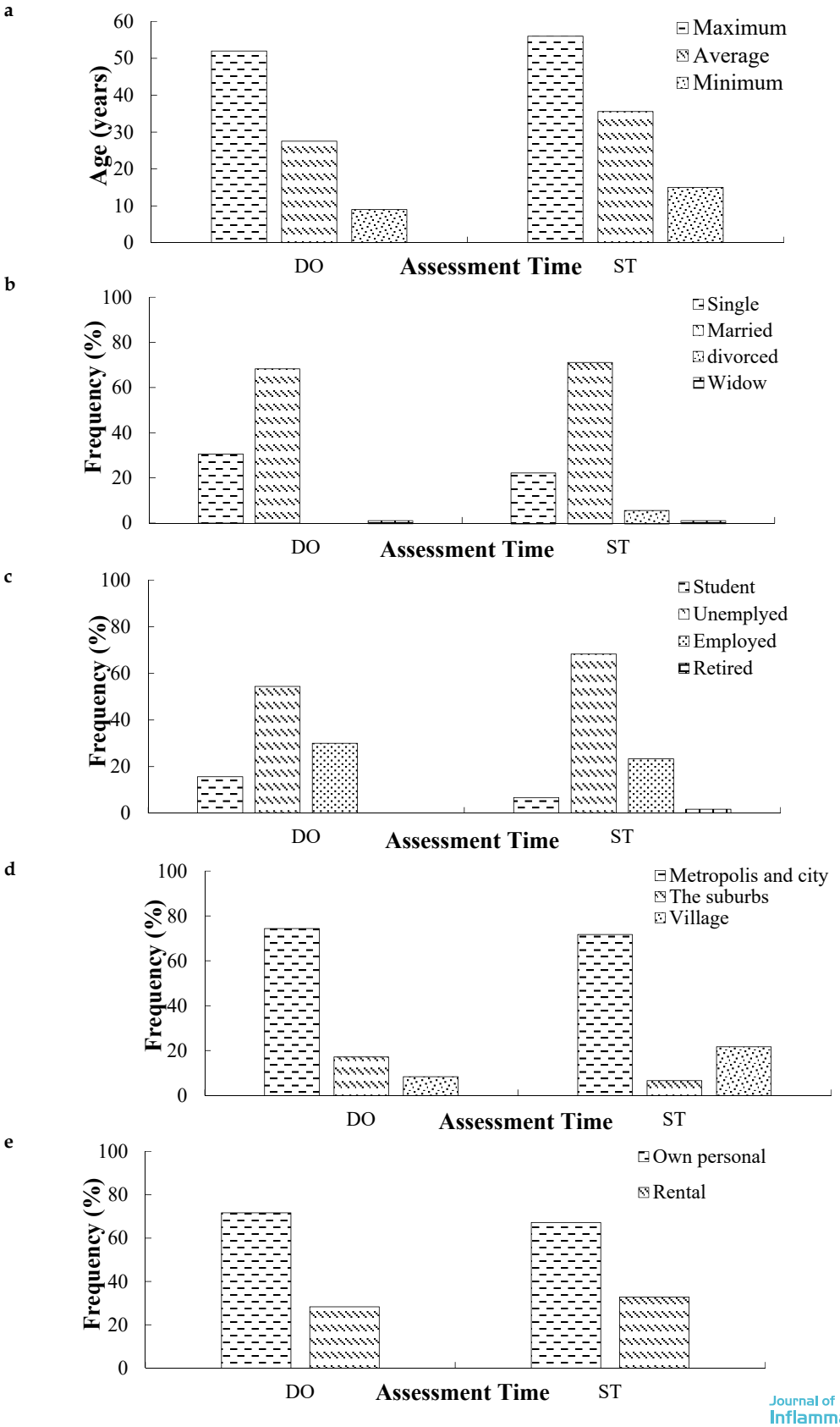

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Figure 1. A comparative illustration on some socio-demographic characteristics of multiple sclerosis patients between the disease onset (DO) and study time (ST)

a) Age, b) Marital status, c) Occupational status, d) Residential location, e) Housing situation

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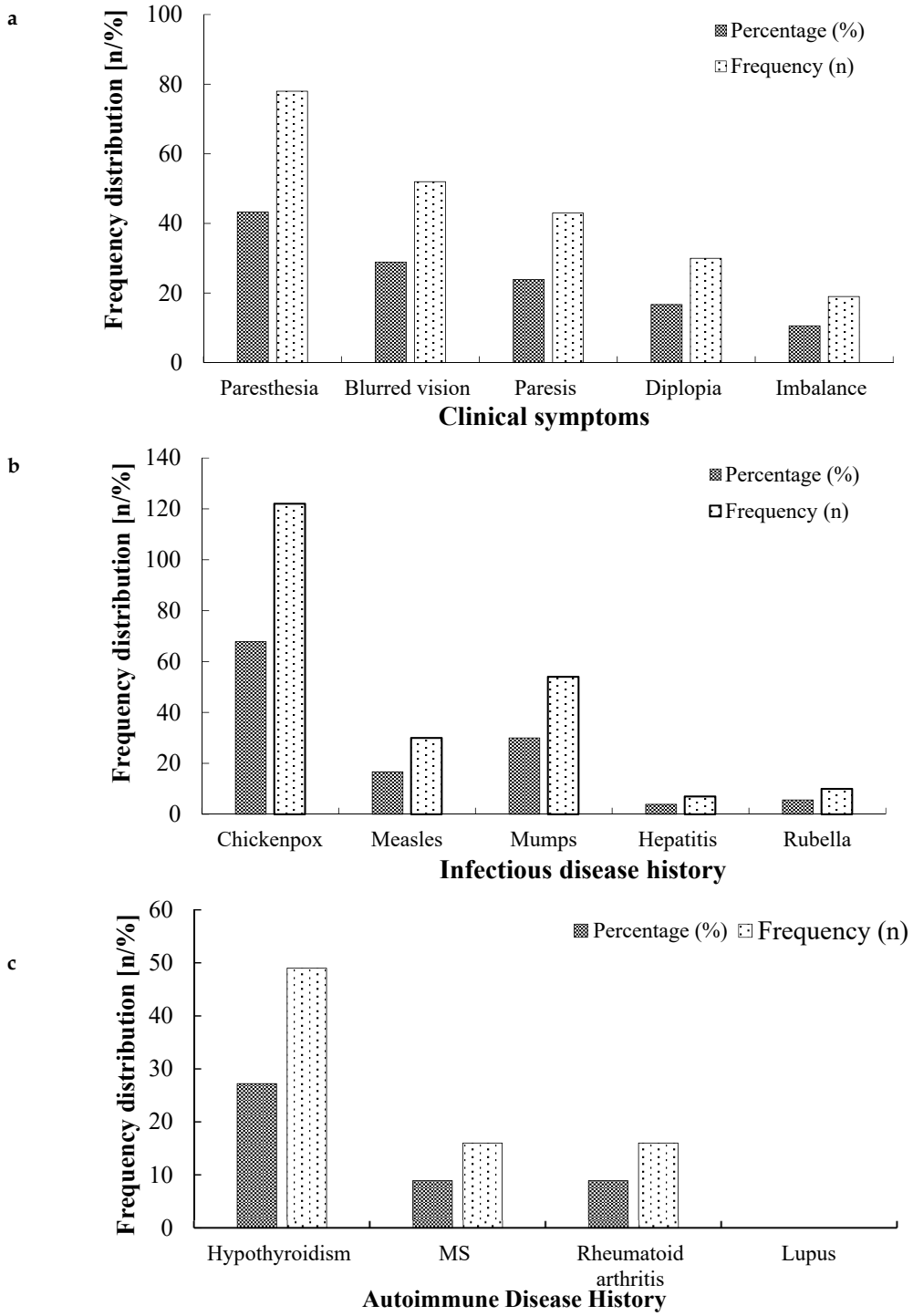

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Figure 2. Frequency of a) Clinical symptoms, b) Infectious disease history, and c) Autoimmune disease history among the studied multiple sclerosis population

The positive association between patients' age and EDSS was previously reported by Koch et al. [32], who explained that MS progression is an age-dependent process. The long-term duration and high disability severity at higher ages may be due to the severity of cognitive impairment [33]. Moreover, functional disability in elderly MS patients can be affected by chronic neurodegenerative processes and focal recurrent inflammation [34]. Nakamura et al. [35] stated that disability in MS patients is related to the cervical and thoracic cross-sec-

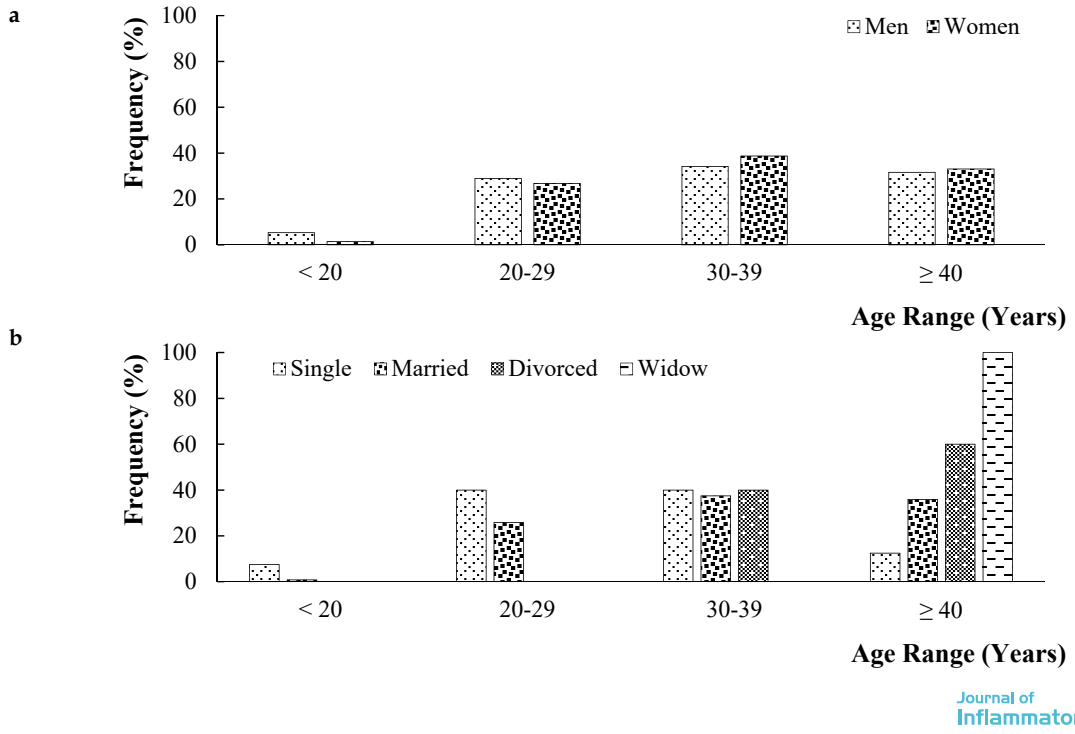

Figure 3. Comparison of patients' current age with a) Gender and b) Marital status in the studied multiple sclerosis population

tional spinal cord area (CS-SCA). However, degenerative processes at higher ages might be more influential for cervical CS-SCA than thoracic CS-SCA. Achiron et al. [36] also confirmed a significant relationship between greater disability and a higher number of children before MS onset. Overall, the MS population has fewer children compared to the general ones [37]. According to Alwan et al. [38], 72.5%-75.2% of Canadian and American people with MS did not prefer to have more children after the MS diagnosis. The risk of having additional children under this condition may be increased by the lack of a stable partner and declining SES [38].

MS risk assessment in young women, especially women of childbearing age, is important because pregnancy rates in different populations of women with MS have been substantially increasing. In this study, one-third of women with MS mentioned a pregnancy history during their disease. Similarly, Houtchens et al. [39] reported that one-third to one-fifth of American women with MS had a successful history of pregnancy after the onset of the disease. In addition, Lai et al. [40] concluded that pregnancy can effectively protect females from MS relapse. Thus, the reduced severity of MS during pregnancy is probably due to the secretion of female sex hormones, such as estrogen, progesterone, and prolactin. These hormones gradually increase until the third trimester and subsequently decrease remarkably to relapse MS after delivery [40, 41]. This was also confirmed in some animal studies showing that the secretion of sex-related hormones could improve relapses and regulate immune system signaling in many animals with experimental autoimmune encephalomyelitis [42, 43]. MS reactivation after delivery may be due to the breakdown of immunotolerance toward the fetus and the immunocompetence recovery [44]. In the present study, only 3.5% of patients pointed out a history of abortion during this demyelinating disease. In contrast, a higher abortion rate in American (20.9%) and French (21.2%) women with MS has been previously reported [39, 45]. This discrepancy may be attributed to the differences in lifestyle patterns, environmental risks, and the type and dose of MS drugs (e.g. fingolimod, azathioprine, and rituximab) taken during the disease course. The high abortion rate in some MS communities, particularly in early pregnancy, can be due to the considerable secretion of pro-inflammatory cytokines (e.g. IL-6, IL-8, MCP-1, etc.), which enhances the decidualization and implantation of embryos [46, 47]. In addition, a profound imbalance between pro-inflammatory and anti-inflammatory cytokines causes recurrent miscarriages [44, 48].

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Conclusions

The present study showed that SES did not have any significant effect on the MS severity among Iranian young adults. Accordingly, it would not be necessary to plan key managerial actions to improve the health status of patients with MS. However, it is recommended to perform more studies with a larger sample size in a wider geographical area for the assessment of other affecting variables on MS severity. Even though EDSS provides a practical, risk-dependent stratification in daily clinical practice to recognize patients with different disabilities, integrating EDSS with the results of inflammation markers and neurological symptoms might be more efficient for evaluating an improved endpoint to identify the degree of physical disability and also the required actions for stopping the conversion process to the secondary progressive MS type.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the Qazvin University of Medical Sciences (Code: IR.QUMS.REC.1396.458).

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Authors' contributions

Conceptualization and supervision: Hossein Mozhdehipanah; Methodology: Monirsadat Mirzadeh; Data collection: Shima Mohammadhoseini Targhi, Fatemeh Kazemi and Ali Sarbazi-Golezari; Data analysis: Ali Emami and Monirsadat Mirzadeh; Investigation, writing original draft, review & editing: All authors.

Conflict of interest

The authors declared no conflict of interest.

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