Is There an Association Between Multiple Sclerosis Epidemic and Socioeconomic Status in Iran? - A Descriptive-analytical Cross-sectional Study

Hossein Mozhdehipanah  
Bou Ali Sina Hospital, Qazvin University of medical sciences

Ali Emami  
Qazvin University of Medical Sciences

Shima Mohammadhoseini Targhi  
Qazvin University of Medical Sciences

Fatemeh Kazemi  
Qazvin University of Medical Sciences

Ali Sarbazi-Golezari  
Qazvin University of Medical Sciences

Monirsadat Mirzadeh (monirdokht_mirzadeh@yahoo.com)  
Qazvin University Of Medical Sciences

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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. The objective of this study is to determine the relationship between socioeconomic status (SES) and MS severity among Iranian young adults.

**Methods:** A descriptive-analytical cross-sectional study was conducted by 180 patients (142 females and 38 males) with MS selected by a non-probability and consecutive sampling was conducted during September 2018-2019. 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 degree and the overall neurological function of patients.

**Results:** The mean age of patients and MS onset was 27.54 and 35.58 years, respectively. The majority of patients were married (68.3%) while were living in cities (74.4%). The mean values of unemployment, homeownership, and monthly income were determined to be 54.4%, 71.7%, and 11,078,330 IRR, respectively. The mean EDSS was 2.80±1.79 points. A weak positive correlation between EDSS and patients’ age (P = 0.001, r = 0.246) and number of children (P = 0.001, r = 0.250) was found. There was no significant difference between EDSS and SES factors (i.e., disease onset age, treatment cost, and monthly income).

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

Background

Multiple sclerosis (MS) is a chronic disease with specific characteristics such as the refractory inflammation, the axonal damage of neurons, the demyelinating process, and the irreversible pathological changes in the central nervous system (CNS). This autoimmune disease demyelinates neurons, reduces the nerve conduction velocity, and disrupts the CNS function(1). MS has variant 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 for women so its complications may affect the fetus too (3, 4). The MS incidence depends on the geographical area and race is variable and changes from 5.1 to 11.6 cases per 100,000 people in a year(5). This inflammatory demyelinating disease is the most common chronic disorder of the CNS causing disability and loss of functions in young people(6)

The prevalence of this disease in the world has been increasing in recent years, while it is estimated that 2.5 million people worldwide suffer from this disease and 80% of patients experience disability(7).
According to the Kurtzke's prevalence pattern of MS, Iran is classified at a low-risk level (less than 5 cases per 100,000 population) (8). However, some epidemiological studies in central area (e.g., Isfahan city) of Iran have shown that the MS prevalence is about 35-45 per 100,000 population, and accordingly, the risk level for MS prevalence is moderate to high (9). Therefore, there are a number of 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 (e.g., sun exposure and actinic damage) (15, 16) risk factors. Nowadays, the incidence of MS is increasing in developed countries so that it is more common in high socioeconomic classes with higher education, income, as well as good occupation (17, 18). However, the role of socioeconomic status (SES) on the prevalence of MS in Iran has been less evaluated.

This complex neurological disorder due to arising many physical and mental problems and the need for multiple hospitalizations of patients causes high medical costs for them and their families and the overall health care system in the country (19). As a result, identifying and controlling the factors exacerbating this nervous disorder can have a significant effect on reducing the burden of MS (20). Due to the contradictory results of different studies on the relationship between SES and MS and also the lack of a similar study in Iran, the present study was aimed to determine the epidemiology of MS among Iranian people with a specific emphasis on the role of socioeconomic variables on MS severity.

Methods

Study design and participants

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

Inclusion and exclusion criteria

The criteria for patients in this study included the following: people with a confirmation letter from neurologists who diagnosed MS based on the described criteria worldwide (21, 22), and people who lived in Qazvin province for at least ten years before the disease onset. On the other hand, the patients with any physical disability and a history of the disease less than 6 months were excluded. Also, the cases with 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, the number of family members, occupational status,
and the level of family support. The written informed consent for each patient was obtained after presenting enough explanations about 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, the pattern of refractory and regression periods, and family history of autoimmune diseases confirmed by a neurologist.

**Expanded disability status scale (EDSS)**

The most common tool to assess the disability of patients with MS is “expanded disability status scale (EDSS)” (23). This tool has 0-10 scores, which changes 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 way, the scores of 1 to 4.5 was awarded to people who had MS with defect criteria in functional systems while 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 IBM SPSS Statistics software version 20.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to examine the normality of data distribution. Pearson’s correlation coefficient and Chi-square parametric tests were used according to the distribution of quantitative variables in the population. The significant level was set at 0.05.

**Results**

Some demographic and SES properties of MS patients at the disease onset are shown in Table 1. This table shows that 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%). 26.1% of the patients were the last child in their family. The average number of children and family members was 1 and 4, respectively. The percentage of immigration history and family support was 15.6% and 72.2%, respectively. 3.5% of women had a history of abortion, while one-third of them had a history of pregnancy during MS. Also, there was a family relationship between parents in 15.6% of cases (Table 1). Some socio-demographic properties of MS patients including age, marital status, occupational status, residential location, and housing situation between the disease onset and study time are compared in Fig. 1. Results showed that the percentage of marriage, divorce, unemployment, ruralization, and living in rented houses were increased from the disease onset to the study time (Fig. 1). Fig. 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 were reported to be 8.9 and 27.2%, respectively. However, there was no family history of lupus. (Fig. 2b). The history of autoimmune diseases in the family of patients revealed that there was MS in 9.8 and 68.8% among their family members and 1st-degree relatives, respectively. Besides, the frequency distribution of 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 (Fig. 2c).
Table 1
Frequency distribution of demographic and SES characteristics of patients with MS (n = 180) at the disease onset

| Variable                      | Sub-variable | MS onset                          |
|-------------------------------|--------------|-----------------------------------|
|                               | Frequency (n) | Percentage (%)                    |
| Age (years)                   |              | 27.54±8.27 (min = 9, max = 52)    |
| Monthly income (IRR)          |              | 11,078,330.3±2,018,190.2 (min = 0, max = 20,000,000) |
| Monthly treatment cost (IRR)  |              | 993,500.0±17,904.4 (min = 0, max = 15,000,000) |
| Children number (n)           |              | 1.11±0.99 (min = 0, max = 4)       |
| Family members number (n)     |              | 4.08±1.84 (min = 1, max = 12)      |
| Gender                        | Men          | 38                                 |
|                               | Women        | 142                                |
| Education level               | Illiterate   | 1                                  |
|                               | Primary      | 23                                 |
|                               | Under diploma| 28                                 |
|                               | Diploma      | 75                                 |
|                               | Academic     | 53                                 |
| Marital status                | Single       | 55                                 |
|                               | Married      | 123                                |
|                               | divorced     | 0                                  |
|                               | Widow        | 2                                  |
| Occupational status           | Student      | 28                                 |
|                               | Unemployed   | 98                                 |
|                               | Employed     | 54                                 |
|                               | Retired      | 0                                  |
| Residential location          | Metropolis and city | 134                                 |
|                               | The suburbs  | 31                                 |
|                               | Village      | 15                                 |
| Variable                      | Sub-variable | Frequency (n) | Percentage (%) |
|-------------------------------|--------------|---------------|----------------|
| Housing situation             | Own 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 or more  | 47            | 26.1           |
| 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           |

The average monthly treatment cost and income of patients were 993,500 and 11,078,330 IRR, respectively. The mean ages of patients and MS onset were 27.54 (±8.27) and 35.58 (±8.95) years, respectively. There was no significant difference in the mean age of MS onset between women (27.39
±8.10 years) and men (28.08±8.80 years) (Fig. 3a). But, 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 (Fig. 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. As well, 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, no considerable relationship between the EDSS and the age of the disease onset, the treatment cost, as well as the patient's income. Nonetheless, there was a weak, positive correlation between EDSS and patients' age (P = 0.001, r = 0.246) and number of children (P = 0.001, r = 0.250) (Table 3).
Table 2
The relationship between EDSS and demographic and SES characteristics of MS patients

| Parameter                | EDSS value | p-value |
|--------------------------|------------|---------|
|                          | Men       | Women   | Total population |
| Current age (yrs)        |            |         |                  |
| < 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     |           |         | 0.45 |     |
| Student                  | -         | -       | 2.60±1.80 |
| Unemployed               | -         | -       | 2.90±1.80 |
| Employed                 | -         | -       | 2.60±1.70 |
| Retired                  | -         | -       | 2.30±1.90 |
| Residential location     |           |         | 0.91 |     |
| Metropolis and city      | -         | -       | 2.8±1.80 |
| The suburbs              | -         | -       | 2.9±1.90 |
| Village                  | -         | -       | 2.6±1.70 |
| 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        |           |         | 0.42 |     |
| Yes                      | -         | 2.81±1.82 | - | - |
| No                       | -         | 2.78±1.70 | - | - |
| Abortion history         |           |         | 0.74 |     |
| Yes                      | -         | 2.78±1.78 | - | - |
| No                       | -         | 3.80±2.07 | - | - |
Table 3
The significance and correlation coefficients between some SES parameters and SDSS of MS patients

| SES Parameter          | EDSS value | r-value | p-value |
|------------------------|------------|---------|---------|
| Age (yrs)              |            | 0.246   | 0.001   |
| MS onset age (yrs)     |            | 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   |

Discussion

Finding a notable relationship between demographic characteristics or SES and MS severity in Iran allows policymakers to present appropriate planning for improving the living conditions of patients. As the proinflammatory phenotype is directly related to the adverse SES in childhood and adulthood, MS as a complicated neuroinflammatory autoimmune disorder may be reduced by improving the SES variables (25). However, the etiological role of this issue requires longitudinal studies such as case-control research and could not be examined in the present cross-sectional study. Our findings showed that there was no statistically significant relationship between EDSS and SES factors. Goulden et al. (26) by assessing the association between SES and MS in a case-control study with 2144 cases and 3859 controls from Norway, Italy, and Canada found that there was 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 thirteen surveys showed no significant relationship between MS and SES. Overall, there was inconsistent evidence for the correlation between high SES and increased MS risk. However, a more powerful effect in some countries with higher inequality could be found (27). Nielsen et al. (28) found that although there was not a 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 high MS rate at low SES may be more vulnerability and exposure to pathogens in early life. Also, MS risk may be remarkably increased by a number of 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’ body 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 country
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 fact may be due to factors such as the inability of patients, the unwillingness of centers and companies to hire these patients and also the inability to attend work because of the need for regular use of drugs. As a result, this evidence suggests that there was a link between viral infection or chronic stress and MS. Rezaali et al. (31) earlier investigated the epidemiology of MS in Qom city (north-central of Iran) and reported that the MS prevalence 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 in two studies on the viewpoint of the ratio of females to males (3.4 vs. 3.0) and lower MS onset age in women than men (31).

The positive association between patients’ age and EDSS was previously reported by Koch et al. (32), who explained the 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, the functional disability in elder 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-sectional spinal cord area (CS-SCA). However, degenerative processes in higher ages might be more influential for cervical CS-SCA than thoracic CS-SCA. Achiron et al. (36) also proved that there was a significant relationship between greater disability and higher number of children prior to MS onset. Overall, the MS population have fewer children compared to the general one (37). Alwan et al. (38) pointed out that 72.5-75.2% of Canadian and American persons with MS did not prefer to have any/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 declined SES (38).

The MS risk assessment in young women, especially women of childbearing age, is very 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 the course of the 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 disease onset. In addition, Lai et al. (40) concluded that pregnancy can effectively protect females from MS relapse. Thus, the reduced severity of MS during pregnancy probably is due to the secretion of female sex hormones like estrogens and progesterone, as well as prolactin. These hormones gradually increase until the third trimester and subsequently decrease remarkably to relapse MS after the delivery (40, 41). This fact was also proved in some animal studies so that the secretion of sex-related hormones could improve relapses and regulate the immune system signaling in many animals with experimental autoimmune encephalomyelitis (42, 43). The MS reactivation after delivery may be owing to the breakdown of immunotolerance towards 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 for American (20.9%) and French (21.2%) women with MS was earlier reported (39, 45). This discrepancy may be contributed to the difference 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 thanks to the considerable secretion of pro-inflammatory cytokines (e.g., IL-6, IL-8, MCP-1, etc.) enhancing decidualization and implantation of the embryos (46, 47). Besides, a profound imbalance between pro-inflammatory and anti-inflammatory cytokines probably causes a recurrent miscarriage (44, 48).

Conclusions

The present study showed that the 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 be undertaken for improving health status in patients with MS. However, it is recommended to perform more studies with a higher sample size in a wider geographical area for the assessment of other affecting variables on the 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 physical disability degree and also required actions for stopping the conversion process to secondary progressive MS type.

Abbreviations

CNS: central nervous system, CS-SCA: cervical and thoracic cross-sectional spinal cord area, EDSS: expanded disability status scale, MS: multiple sclerosis, SES: socioeconomic status

Declarations

Ethical Approval and consent to participate

Before the patient s were enrolled in this study, informed consents were obtained by participant. The research's procedure entirely was consistent with the Human Ethics Committee of the Qazvin University of Medical Sciences with an ethical code of IR.QUMS.REC.1396.458. The protocols used in all stages of the study were based on principle recommendations in the last version of the Helsinki Convention for Ethics.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request. The datasets generated during and analyzed during the current study are not publicly available due to policy of our hospital which do not permit us to share the raw data but they are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

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**Authors' contributions**

Conceptualization: H.M & M.S; Writing and data analysis: S.M & F.K; Editing, supervision and project administration: M.S; Initial draft preparation by: A.S & A.E

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**Conflict of interest**

The authors declare no conflicts of interest.

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Figures
Figure 1

A comparative illustration on some socio-demographic properties of MS patients between the disease onset (DO) and study time (ST) [a, age; b, marital status; c, occupational status; d, residential location; e, housing situation].
Figure 2
The frequency of clinical symptoms (a), infectious disease history (b), and autoimmune disease history (c) among the studied MS population.
Figure 3

A comparison of patients' current age with gender (a) and marital status (b) in the studied MS population.