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No association between socioeconomic status and risk of multiple sclerosis: A population-based incident case-control study in a developing country

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ABSTRACT

Background: Evidence on the association between socioeconomic status (SES) and multiple sclerosis (MS) is inconsistent. We examined the association of several indicators of SES with MS in an Iranian population.
Methods: We conducted a population-based incident case-control study with 547 incident cases and 1057 general population controls in Iran, 2015. Data was collected using telephone interviews and indicators of SES i.e. parental education, and household SES during adolescence using asset variables. Adjusted odds ratios (AORs) were estimated using multiple logistic regression model.
Results: Parental education levels were not significantly associated with MS development. Household SES during adolescence was insignificantly associated with an increased risk of MS diagnosis ($P = 0.575$).
Conclusion: We did not identify an association between household SES during adolescence, parental education levels, and a subsequent risk of developing MS in an Iranian population.

1. Introduction

Multiple sclerosis (MS) is the most common inflammatory disorder of the central nervous system, and one of the leading causes of disability in young adults (Milo and Kahana, 2010). A growing body of global evidence indicates the increasing trend of MS incidence and prevalence rates (Browne et al., 2014). Consistent with the international literature, an increased rate of people with MS has been reported in Iran. Reports show that Tehran, the capital of Iran, has a prevalence of more than 70 per 100,000 (Elhami et al., 2011; Etemadifar and Maghzi, 2011). Although the etiology of MS still remains poorly understood, epidemiologic research highlights the role of genetic and environmental factors associated with its increased risk such as smoking (6), waterpipe smoking (Abdollahpour et al., 2017; Handel et al., 2011), vitamin D deficiency (Munger et al., 2004), infectious mononucleosis (Thacker et al., 2006), high body mass index (BMI) (Hedström et al., 2012), low sunlight exposure (Munger et al., 2004), as well as socioeconomic status (SES) (Bjørnevik et al., 2016; Briggs et al., 2014, 2015; Hammond et al., 1996; Lauer, 1994).

Out of the environment and socio-structural factors associated with the risk of MS, the potential role of SES has received particular attention (Bjørnevik et al., 2016; Briggs et al., 2014, 2015; Hammond et al., 1996; Lauer, 1994). However, evidence for fundamental SES-MS association is still inconsistent. While the greater risk of developing MS had been linked with the high level of SES (Hammond et al., 1996; Lauer, 1994), recent studies have suggested that high gradients of SES may play a protective role in the development of MS (Bjørnevik et al., 2016; Briggs et al., 2014, 2015). Childhood SES has also been studied as a potential factor for the risk of MS. For example, Briggs et al. in a prevalent case-control study in Northern California showed that individuals whose parents were renters were more likely to develop MS (odds ratio (OR) = 1.48) than those whose parents were home-owners during the person's childhood (Briggs et al., 2014). Also, education level as a proxy for current SES of the individuals has been shown to play a role in MS development. For example, Bjørnevik et al. in a case-control study in Norway, demonstrated that individuals with high education

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were 39% less likely to get MS (odds ratio (OR): 0.61 (95% confidence interval (CI): 0.44, 0.83) (Bjørnevik et al., 2016). Using a registry-based 50-years–follow up-sibling study, Bjørnevik et al. replicated their findings and found a protective role for high education (OR 0.73; 95% CI: 0.59–0.90) (Bjørnevik et al., 2017). Unlike such protective associations, a recent systematic review showed, on overall, no substantial link between SES and increased risk of MS (Goulden et al., 2015). However, inconsistent findings were apparent in countries with more in-equivalent and equivalent SES (Goulden et al., 2015). In a nationwide Danish cohort study followed 1.5 million individuals, Nielsen and colleagues identified no important role of childhood SES and the following risk of MS (Nielsen et al., 2013).

Although a higher MS incidence and prevalence has been reported in countries with high income level (Buchter et al., 2012), the underlying association of SES-MS is still controversial, particularly in developing countries such as Iran. It appears that the formerly reported inconsistent findings may be in part due to the contextual nature of the socioeconomic measures that could change across time and space. In addition, methodological issues in the previous studies may also explain some levels of the inconsistencies. For example, using prevalent rather than incident cases (Briggs et al., 2014; Koch-Henriksen, 1989) may tend to increase the possibility of recall bias as a major source of information bias (Rothman et al.) even in the context of chronic diseases such as MS. Also, some researches provided estimations with wide confidence intervals arising from a small employed sample size that may limit the generalizability of the findings (Kurtzke et al., 1997; Poskanzer et al., 1980).

There is few, if no, study has ever reported SES-MS link in a developing country as the most information available concerning this association have come from developed nations. Here, in a large population-based case-control study enrolled only incident MS cases, we collected data on multiple variables measuring adolescence SES when the study participants were at their 15th birthday including father and mother education levels and asset variables. We also obtained individuals' education level. We investigated the possible link between adolescence SES and MS onset adjusted for a several number of well-known confounders in an Iranian population. The result of current study would fill an important gap in the literature with respect to the MS-SES association.

2. Materials and methods

2.1. Study participants

We conducted a population-based incident case-control study from August 17, 2013, through February 17, 2015, in Tehran, the most populous city in Iran. The study design has been previously described elsewhere (Abdollahpour et al., 2018a, b, 2017). Briefly, the entire 15–50 years old individuals residing in 22 municipality areas of Tehran (nearly 5.1 million) were considered as the source population of the current study. The Iranian Multiple Sclerosis Society (IMSS), the only registry center available in Tehran, was used to recruit the study cases with an acceptable completeness (Abdollahpour et al., 2017). We defined an index date for each participant as the exact date, by year and month, of confirmed diagnosis. The eligibility criteria to be included as control in the study were non-diseased 15–50 years old, and living in Tehran at the time of case diagnosis. Controls were selected proportional to population size of 22 areas of Tehran (Wacholder et al., 1992). First, 4457 randomly generated phone numbers were obtained, of which 2856 numbers were either non-residential or inactive at the time of study development. Of the 1601 remaining numbers, 91 (5.7%) were excluded as there was no eligible person within their household, leaving 1510 contactable households. Of the contactable households with eligible people, 1057 (70.0%) agreed to a full interview. We used the Kish method to select one person from all eligible people living in the same household (Kish, 1949). The Research Ethics Committee (REB) at the Tehran University of Medical Sciences approved this study.

2.2. Data collection protocol

The phone interviews were conducted by 10 trained staff, selected for interview skills have used the standardized data collection procedures. The data collection activities were monitored for any interviewer bias by randomly recording interviews. At the start of each interview, the main study objectives were fully explained to both MS cases and controls. In order to decrease the possibility of misclassification of undetected cases among controls, the clinical signs and characteristics of MS were explained to the control sample.

2.3. Measurement

2.3.1. Outcome - MS

The main study outcome was being diagnosed with MS or not. Applying the 2010 McDonald criteria for case definition criteria, all MS diagnosed cases were confirmed by at least one neurologist (Polman et al., 2011).

2.3.2. Exposures - SES

The following SES indicators for both individual and household levels were measured:

Parental educational level at the individual's 15th birthday- participants were asked to provide information about their parents' level of education when they were at 15th birthday as; "What was the highest educational level of your parents when you were 15 years old?" The level of education for their mother and father was measured. Each of these educational levels was categorized as, Illiterate or primary school, completed guidance school, completed high school, and "University degree". We also created a single variable combining the education level of both participants' parents during their adolescence. This was a 3-level variable coded as: 1; if none of the parents had University educational level, 2; when one of them had University educational level and 3; when both of them had University educational level.

Asset variables- Information about asset variables of paternal home during adolescence, at 15th birthday, including having any of these amenities: car, freezer, washing machine, TV, vacuum cleaner, personal computer/ laptop, LED/LCD, dishwasher, microwave and mobile. A binary measure for each asset variable was created: having the corresponding asset (coded 1) vs. not having (coded 0).

Participants' level of education- The highest level of education and the number of education year completed were obtained. The highest level of completed education was categorized as, (Illiterate or primary school (age 7–11 years) guidance school (age 12–14 years), high school (age 15–18 years), associate's or Bachelor's degree and Master's degree and higher. The number of successfully passed years of education was also obtained for each of participants.

Potential confounders- Data on substance use were collected as: lifetime tobacco smoking history defined as pack-years cigarette smoking, lifetime waterpipe smoking defined as at least once a week for a minimum 6 months, history of passive smoking exposure defined as ever lived with anyone who regularly smoked, drug use measured as "Have you ever used any type of illicit drugs [opioids, cannabis, hallucinogens and stimulants) for at least once a month during at least 6 month period?" Detailed information on the type, duration (in years), and frequency (per month) of each drug was also obtained. Lifetime drug use was defined as the average frequency of a drug per month × 12 × duration (years), and then summed the different drug types. Sunlight exposure during adolescence (age 13–19 years) (Pugliatti et al., 2012) was collected for summers asking the following question, "During adolescence (age 13–19 years), how many hour/day on average did you have outside