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# Neuromyelitis optica spectrum disorders in Iran

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ABSTRACT

*Background:* Neuromyelitys optica spectrum disorder (NMOSD) is a rare demyelinating disease; as a result, the epidemiological data on this disorder is scarce. In this regard, the aim of this study was to estimate the prevalence, serology, and clinical features of NMOSD in Caucasian population in Tehran, Iran.

*Method:* A cross sectional study was performed in Tehran from 2015 to 2016 among patients registered with NMOSD diagnosis, based on consensus criteria published in 2015. The researchers designed a questionnaire to cover the important epidemiological and clinical data of NMOSD in Tehran. Structured face to face interviews were conducted with 103 patients by trained interviewers to collect the data. The logistic regression was applied in analysis via SPSS software package.

*Result:* The prevalence of NMOSD in Tehran was 0.86 per 100,000 in 2016. Female to male ratio was 5:1 with mean age at the disease onset of 31.54. NMO-IgG were positive in 44 (46.8%) patients, and the primary presenting symptoms of TM were observed in 29 (28.2%) patients.

The adjusted odds ratio for sex was estimated for depression (OR = 6.83; 95% CI: 1.47, 31.71), migraine (OR = 1.27; 95% CI: 1.13, 1.42), and hypothyroidism (OR = 1.25; 95% CI: 1.12, 1.39).

*Conclusion:* The researchers indicated that the rate of NMOSD is significantly higher among females and younger age group. In addition, the history of depression, migraine, and hypothyroidism has been observed more among female patients in comparison to male patients.

## 1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is a rare severe autoimmune inflammatory disorder of the central nervous system that mainly targets the optic nerves and spinal cord (Wingerchuk et al., 2006; Pandit and Kundapur, 2014).

The spectrum of clinical appearance of NMOSD has been expounded and its diagnostic criteria have been refined in recent years. Clinical features, immunological and histopathological characteristics as well as the access to neuroimaging have contributed to the identification of and distinguishing NMOSD from multiple sclerosis (MS).

The essential clinical distinguishing criteria for the diagnosis of patients with NMOSD include the presence of serum immunoglobulin G (IgG) aquaporin 4 (AQP4) antibody (AQP4-IgG) and the findings of magnetic resonance imaging (MRI) or the appearance of clinical syndromes connected to spinal cord and optic nerve (Wingerchuk et al., 2015).

The principal clinical features of NMOSD include bilateral or unilateral optic neuritis (ON) and critical transverse myelitis (TM). The AQP4-IgG is an 85–99% specific serum biomarker for NMOSD (Wingerchuk et al., 2015; Fazio et al., 2009).

NMOSD causes longstanding disability in adults with a mean age of onset higher than multiple sclerosis (MS) and affects women more than men (Etemadifar et al., 2015; Eskandarieh et al., 2017a, 2016, 2017b). It is thought to be scarce in Caucasians (Cabre et al., 2009). NMOSD has a worldwide distribution affecting different nations and races; however, a few epidemiologic studies have indicated a diverse prevalence and incidence of NMOSD in different ethnic groups (Pandit et al., 2015).

As far as the authors of the present study are concerned, there are few studies on the prevalence rates of NMOSD which have been conducted in Isfahan (Etemadifar et al., 2014), Mangalore (Pandit and Kundapur, 2014), Merseyside (Jacob et al., 2013), Tokachi (Houzen et al., 2012), South East Wales (Cossburn et al., 2012), Southern Denmark (Asgari et al., 2011), Cuba (Cabrera-Gomez et al., 2009), French West Indies (Cabre et al., 2001), Mexico City (Rivera et al., 2008) and khuzestan (Kashipazha et al., 2015).

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Comorbidity and disease history are important part of patient characteristics and are associated with adverse outcomes which are related to the clinical appearance (Yurkovich et al., 2015).

The comparative clinical features and epidemiological characteristic of NMOSD are not yet well known. Despite the essential limitations to the evaluation process, the available context noted on the clinical and demographic features of NMOSD among different populations help a further global understanding of NMOSD and the approaches to address it. As far as the authors of the present study are concerned, there are no epidemiological studies on NMOSD and its prevalence in Tehran.

The aim of this study is to estimate the prevalence, clinical characteristics, and features of NMOSD in the large population of Tehran and to provide perceptions into the differences of clinical features and demographic characteristics of NMOSD among different genders.

## 2. Method

### 2.1. Study area and setting

This cross-sectional study was conducted in a referral hospital in Tehran, the capital of Iran. Tehran is located in the north of Iran (Latitude: 35° North, Longitude: 51° East) with an estimated population of 11950000 in 2016.

The researchers performed a population based study on patients with a definite diagnosis of NMOSD at Sina hospital, a tertiary care referral center in Tehran to assess the prevalence, clinical and baseline characteristics of registered NMOSD patients.

Sina hospital of Tehran provides comprehensive services for patients with demyelinating disorders who are referred to this hospital by neurologists. The hospital has 4 units with neurology departments including the only NMOSD specialist clinic in Tehran, Iran. The services contain: physical and cognitive rehabilitation, nutrition consultant, physiotherapy and free hospitalization, and medication and injection.

### 2.2. Patient identification and selection strategy

Clinical records of all prevalent patients were included in this preliminary investigation. The researchers designed a structured questionnaire in MS research center of Tehran university of medical sciences to measure the baseline characteristics, severity of symptoms, significant epidemiological variables, and self-report diseases history diagnosed by a physician (Horton et al., 2010), which were associated at the individual level with NMOSD risk factors according to the questionnaire designed for multinational case-control studies of environmental risk factors in multiple sclerosis (EnvIMS-Q). The content validity and reliability of the questionnaire were determined (Sahraian et al., 2016; Abdollahpour et al., 2016).

NMOSD diagnosis was based on international 2015 consensus criteria (Wingerchuk et al., 2015). The definite diagnosis was confirmed in the NMOSD clinic by neurologists, in case report form (CRF) for each patient.

The enzyme-linked immunosorbent assay (ELISA) was used for AQP4 (Waters et al., 2016). Most of the tests have been completed during the relapse before receiving corticosteroid.

The goals of the study were described by a trained interviewer to all participants and data were collected from hospital database registry system. The required information was obtained from patients through face to face interviews by an expert interviewer.

### 2.3. Protocol approvals, registrations, and patient consents

The study protocol, questionnaire, and consent form were approved by the institutional review boards (IRB) at Tehran University of medical sciences (ref.no. IRTUMSREC13941195).

The Entire patients filled out the written informed consent.

### 2.4. Statistical analysis

The prevalence rate was estimated in 2016 as a percentage of the number of inflammatory demyelinating disease patients registered from 2000 to 2016.

The prevalence was calculated based on annual population census conducted by the Iranian central bureau of statistic.

The Means, median, sex ratio, and clinical characteristics of the participants were estimated. The study made use of the chi-square test to analyze the association among variables. Moreover, the logistic regression was applied to test the interactions between variables.

The odds-ratio (OR) and 95% confidence intervals (CI) were calculated. P values $< 0.05$ were considered significant. All data analyses were performed via SPSS software package, version 23.

## 3. Results

### 3.1. NMOSD prevalence

For the period that the study procedure was followed, a total of 103 patients met the NMOSD diagnostic criteria. The point prevalence of NMOSD among the Iranian population living in Tehran was 0.86 (95% CI: 0.76, 0.91) per 100,000 with point prevalence of 1.35 and 0.26 per 100,000 for female and male rates, respectively.

The most prevalence of NMOSD, 1.61 per 100000 populations, was observed among 40–49 age groups. This rate appeared in both genders (2.72 and 0.56 per 100000 populations in females and males, respectively) (Table 1).

### 3.2. Baseline characteristics and clinical features

Baseline characteristics and clinical features of patients are presented in Table 2.

Among all patients, 86 (83.5%) were females and 17 (16.5%) were males. Female to male ratio was 5:1. The majority of patients (i.e., 63 patients (61.2%)) were married.

The presence of NMO-IgG was checked in all patients. The results were positive for 44 (46.8%) patients and negative for 50 (53.2%) patients.

The first presenting symptoms among patients were symptoms of

**Table 1**
Prevalence of NMOSD per 100000 populations in Tehran, 2016.

| Variable | Female N (%) | Population 5924000 | prevalence | Male N (%) | Population 6026000 | prevalence | Total N (%) | Population 11950000 | prevalence |
|---|---|---|---|---|---|---|---|---|---|
| **Age group** | | | | | | | | | |
| ≤19 | 3 (3.5) | 1471000 | 0.20 | 2 (11.8) | 1550000 | 0.12 | 5 (4.9) | 3022000 | 0.16 |
| 20–29 | 16 (18.6) | 1021000 | 1.56 | 4 (23.5) | 1031000 | 0.38 | 20 (19.4) | 2051000 | 0.97 |
| 30–39 | 33 (38.4) | 1280000 | 2.57 | 4 (23.5) | 1285000 | 0.31 | 37 (35.9) | 2564000 | 1.44 |
| 40–49 | 23 (26.7) | 845000 | 2.72 | 5 (29.4) | 887000 | 0.56 | 28 (27.2) | 1732000 | 1.61 |
| 50–59 | 10 (11.6) | 664000 | 1.50 | 1 (5.9) | 659000 | 0.15 | 11 (10.7) | 1323000 | 0.83 |
| 60≥ | 1 (1.2) | 643000 | 0.15 | 1 (5.9) | 614000 | 0.16 | 2 (1.9) | 1258000 | 0.15 |

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