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Research Paper: The Time-trend of Multiple Sclerosis Incidence and Prevalence in Khuzestan Province, Iran

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ABSTRACT

Background: The prevalence and incidence of Multiple Sclerosis (MS) have increased in Iran.

Objectives: This study aimed to observe the temporal trends and provide a predictive model in the prevalence and incidence of MS in Khuzestan Province, Iran.

Materials & Methods: This cross-sectional study was performed from 2006 to 2019 in Khuzestan Province, Southwestern Iran, on 2676 patients registered in the Khuzestan Multiple Sclerosis Center. The simple exponential smoothing model was used to study the time trends and predict the prevalence and incidence of MS in 2020.

Results: The mean±SD age of the examined patients with MS was 31.40±8.94 years; while the mean±SD age-incidence of MS was 29.19±9.16 years. The sex ratio (female to male) was measured as 3.05. The patients' prevalence and average annual incidences were 57.77 and 4.35per 100000 individuals from 2006 to 2019, respectively. The trend in the MS incidence has been upward with a very slight slope during the years 2006 to 2019. The slope of the increase from 2006 to 2019 was higher for women than men.

Conclusion: The collected results suggested that Khuzestan Province is a high-risk area for MS; the prevalence and incidence of the disease are increasing, especially in women. We prognosticate a slight increase in the incidence of MS in the age group of 20 to 50 years. However, the prevalence of the disease in this age group was similar to 2019.

Keywords: Multiple Sclerosis (MS), Prevalence, Incidence, Prognosis

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Highlights

• The prevalence and average annual incidence among the patients were 57.77 and 4.35 per 100000 individuals from 2006 to 2019, respectively, in Khuzestan Province.

• The MS incidence increased slightly from 5.01 to 4.87 per 100000 subjects from 2006 to 2019 in Khuzestan Province.

• The increase of MS incidence from 2006 to 2019 has been higher for women than men.

• The relevant results indicated that Khuzestan Province is a high-risk area for MS, and the prevalence and incidence of the disease are increasing.

Introduction

Multiple Sclerosis (MS) frequency distribution is measured by estimating prevalence and incidence. To determine the relative contribution of genetic and environmental factors in the development of MS, related studies compared the prevalence and incidence of MS among different populations [1]. The incidence rate of the disease refers to the number of new cases over some time (usually one year), while the prevalence rate refers to the number of individuals with the disease (usually per 100000 individuals). According to the latest update of Assessment of the MS Outbreak by the Atlas of MS, i.e., the most widely used source worldwide for MS epidemiology with universal access to resources for individuals with MS; the estimated number of individuals with MS in 2008 was 2.1 million subjects which increased to 2.3 million people in 2013. Moreover, the global average prevalence increased from 30 in 2008 to 33 per 100000 individuals in 2013 [2].

Recently, Iran has become a country with a high prevalence, and the prevalence continues to increase [3-5]. The study conducted by Hosseinzadeh et al. found that Iran is a high-risk area as regards MS. The MS incidence and the ratio of women to men (average annual incidence: 6.7 per 100000 individuals; the ratio of women to men: 10.5 & 3.0) are comparable to the dominant patterns in the developed countries [6]. In another study published at the end of July 2020, Abtahi et al. found that the frequency distribution of MS prevalence ranged from 7.40 to 101.39 per 100000 individuals. Twenty-One provinces in Iran are at high risk of MS (>25 per 100000 individuals), and 9 provinces are at moderate risk (5-25 per 100000 individuals) [7]. Despite several cross-sectional studies describing the past trend of the disease in Iran, studies related to predicting its prevalence and incidence in the coming years are few. A survey in Kohgiluyeh and Boyer-Ahmad Province used the curve estimation method to examine changes in the prevalence and incidence of the disease, and the univariate time series model for analysis [8]. Another study in Canada used a population-based longitudinal, micro-simulation model named POHEM-Neurological for identifying individuals with MS and for future prognosis and MS mortality. They used the incidence and mortality parameters of a British Columbia-based group [9].

The prevalence of MS is on the rise. Accordingly, addressing the issue of prevalence and incidence and focusing on the models of predicting the trend of MS could be helpful. Such data can be valuable in planning for the current situation, getting ready for unexpected conditions in the coming years, assessing the speed of disease spread, and identifying strategies for its prevention and treatment [8]. Therefore, this study performed an epidemiological analysis on the temporal trends of the prevalence and incidence rate of MS (2006-2019). Furthermore, we proposed a prognosis model for MS prevalence and incidence in Khuzestan Province based on data collected from the Khuzestan Multiple Sclerosis Center.

Materials and Methods

Khuzestan Province is located at the coast of the Persian Gulf in the southwest of Iran. It is considered the center of Iran's oil and gas production. The area of this province is 64.055 square kilometers with a population of more than 4.711 million (according to the 2016 census), is the fifth most populous province in Iran [10]. Khuzestan Province is located at 31.33˚N and 48.69 ˚E (Figure 1).

All study data were extracted from the database of the Khuzestan MS Center. Khuzestan MS Center records

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Figure 1. The location of Khuzestan Province in Iran

information concerning MS patients from all parts of the province after the final diagnosis. The Khuzestan MS Center is in Ahvaz Jundishapur University of Medical Sciences. It is a referral for all patients residing in Khuzestan Province whose disease is diagnosed for the first time by neurologists. In the center, MS patients are evaluated by neurologists supervising the MS Center, and the final diagnosis is confirmed based on clinical and radiological evidence. Patient data in this study included the following: age, diagnosis age, duration, the first symptom of the disease, sex, education, employment status, race, marital status, and MS type. These data were retrieved from the database of the Khuzestan Multiple Sclerosis Center since the establishment of this association since 2006 entered the study by the end of 2019. To estimate the prevalence and incidence of MS by gender (female, male) and age groups (under 20, 20-50 years, & over 50 years) in different years according to the census, the study used census population. However, to obtain the number of populations between the census years, the natural population growth rate in the base population was used. The simple exponential smoothing model was used to study time-trends and predict the prevalence and incidence of MS, in Khuzestan, in 2020.

The simplest exponential smoothing method is called Simple Exponential Smoothing (SES) (in some books, it is called "single exponential smoothing"). It can be viewed either as an adaptive-forecasting algorithm. Exponential smoothing is implemented to predict a time series with no linear trend and seasonal pattern. The observation of the short-range time series has an aperiodic variation and fluctuates around a stable mean over time. The equation for this method is as follows:

$$E_T=\alpha(Y_T+\sum_{i=1}^{T-1}(1-\alpha)^i Y_{T-i})$$

The Y_T and E_T are the observed and forecasted value of the series at time T, and α is the smoothing constant. The above equation shows that the method constructs a weighted average of the observations [11-13], introducing single-exponential smoothing as a modern time-series method. It can produce optimal forecasts for several underlying models, including ARIMA (0,1,1) and the random-walk-plus-noise and state-space models [13].

The procedures of the Single Exponential Smoothing Method (SESM) are presented as per below:

Step 1: Compute the initial estimate of the series at period t=0.

There is no theoretical justification for estimating the initial values. It is common to calculate initial estimates of exponential smoothing procedures using historical data; however, it is not applicable in all situations. Setting it to Y_1 is a method of initialization. The average of the first four or 5 observations could be another possible way of initialization.

Step 2: Compute the updated estimate using the smoothing equation.

$$E_T=\alpha Y_T+(1-\alpha)E_{T-1}$$

The smoothing parameter or smoothing constant that takes values between zero and one. Note that:

$$E_T=\alpha Y_T+(1-\alpha)\,E_{T-1}$$

$$=\alpha Y_T+(1-\alpha)[\alpha Y_{T-1}+(1-\alpha)\,E_{T-2}$$

$$=\alpha Y_T+(1-\alpha)\alpha Y_{T-1}+(1-\alpha)^2\,E_{T-2}$$

$$=\alpha Y_T+(1-\alpha)\alpha Y_{T-1}+(1-\alpha)^2\,Y_{T-2}+\ldots+(1-\alpha)^{T-1}\,\alpha Y_1+(1-\alpha)^T E_0$$

The coefficients measuring the contributions of the observations decrease exponentially over time. The smoothing parameter controls the trade-off between the closeness of smoothed data to the observed data.

Although there is no generally accepted statistical procedure for choosing α, a small value for α., i.e., close to 0, has a greater smoothing effect and weighs the more distant past observations. In contrast, the value of close to one gives more weight to the recent observations. As a great suggestion to choose α, the value that made smaller Root

Mean Square Error (RMSE) of the forecast, the square root of squared deviations between the forecasts and the realized values could be a proper selection. Eventually, we used the Augmented Dickey-Fuller test for unit root to find the stationary of the data. All analysis was done by Stata12 software.

The simple exponential smoother is a special case of a simple moving average. In the moving average, all data points are assigned equal weights. Arguably, recent observation provides more relevant information than the observation in the past. Therefore, the exponential-smoothing method can give larger weights to more recent observations, and weight decreases exponentially as the observation becomes more distant. This method is more effective when the observations change slowly over time. The simple exponential smoothing method is used for short-range forecasting, usually just one lag into the future.

Results

In total, 2676 patients with MS were registered in the Khuzestan Multiple Sclerosis Center from its establishment (2006) until the end of December 2019, i.e., included in the study. The mean and SD score for the MS patients' age was 31.40 and 8.94 years. The youngest and oldest patients were 10 and 75 years old, respectively. The sex ratio (female to male) was 3.05, meaning

Table 1. The demographic and clinical variables of patients with MS in Khuzestan province from 2006 to 2019 (N=2676)

Variable	Class/Mean±SD	Median±IQR/No. (%)	Variable	Class/ Mean±SD	Median±IQR/ No. (%)
Gender	Female	2015(75.3)	Race	Persian	891(33.3)
	Male	661(24.7)		Turkish	61(2.3)
Job	Employed	697(26.0)		Kurd	63(2.4)
	Unemployed	749(28.0)		Lor	922(34.5)
	Disabled	91(3.4)		Arab	704(26.3)
	Housewife	1139(42.6)		Other	35(1.3)
Education	Illiterate	144(5.4)	Marital	Single	931(34.8)
	Under diploma	679(25.4)		Married	1661(62.1)
	Diploma	782(29.2)		Divorced	62(2.3)
	Post-diploma and bachelor's degree	940(35.1)		Widower/ Widow	22(0.8)
	Master's degree and higher	131(4.9)			
The first sign of MS	Sensory-sign	992(37.1)	MS-Type	RR-MS	2041(76.3)
	Motor-sign	462(17.3)		PP-MS	93(3.5)
	Equilibrium-sign	344(12.9)		SP-MS	132(4.9)
	Visual-sign	1013(37.9)		RP-MS	25(0.9)
	Urinary disorder-sign	73(2.7)		DEVIC	67(2.5)
	Fatigue-sign	126(4.7)		CIS	318(11.9)
Age, y	31.40±8.94	30.00±11	Age-incidence of MS	29.19±9.16	(28.00±12)
EDSS	1.857±1.7846	(1.500±1.5	The time between the onset of symptoms and definitive diagnosis (months)	14.84±31.601	(2.00±12)
Duration of MS disease (Years)	1.95±3.658	0.0±2			

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MS: Multiple Sclerosis; RR-MS: Relapsing Remitting MS; PP-MS: Primary Progressive MS; SP-MS: Secondary Progressive MS; PR-MS: Progressive Relapsing MS; DEVIC: Devic's Syndrome; CIS: Clinically Isolated Syndrome MS; EDSS: Expanded Disability Status Scale; SD: Standard Deviation; IQR: interquartile range.

Table 2. The number of multiple sclerosis patients and total population in Khuzestan according to gender

Year	Female		Male		Total	
	No. MS	Population	No. MS	Population	No. MS	Population
2006	156	2184968	58	2090011	214	4274979
2007	169	2204633	55	2119271	224	4323904
2008	74	2224474	20	2148941	94	4373415
2009	132	2244495	41	2179026	173	4423521
2010	144	2264695	44	2209532	188	4474227
2011	155	2286209	41	2245511	196	4531720
2012	157	2306785	52	2261230	209	4568015
2013	131	2327546	58	2277058	189	4604604
2014	144	2348494	50	2292998	194	4641492
2015	154	2369630	56	2309049	210	4678679
2016	167	2388674	43	2321835	210	4710509
2017	149	2410172	46	2338088	195	4748260
2018	190	2431864	66	2354454	256	4786318
2019	176	2453750	59	2370936	235	4824686

No. MS: Number of Multiple Sclerosis

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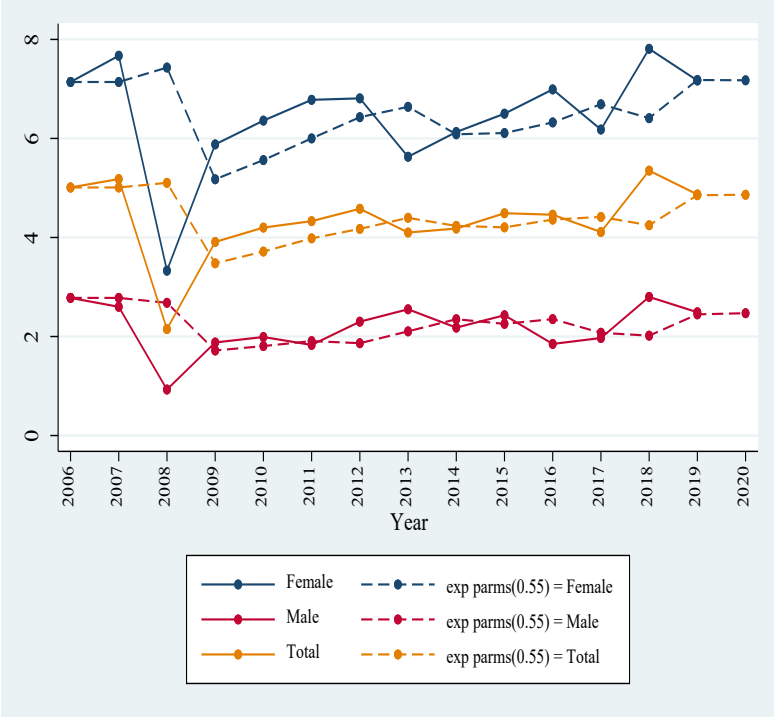

Figure 2. The gender-wise incidence rate and smoothed values of MS

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Table 3. Multiple sclerosis incidence and prevalence rate and smoothed values according to gender

Year	Incidence in 100000						Prevalence in 100000					
	Female		Male		Total		Female		Male		Total	
	OD	SES	OD	SES	OD	SES	OD	SES	OD	SES	OD	SES
2006	7.14	7.14	2.78	2.78	5.01	5.01	7.14	7.14	2.78	2.78	5.01	5.01
2007	7.67	7.14	2.60	2.78	5.18	5.01	14.74	7.14	5.33	2.78	10.13	5.01
2008	3.33	7.43	0.93	2.68	2.15	5.10	17.94	14.36	6.19	5.20	12.16	9.87
2009	5.88	5.18	1.88	1.72	3.91	3.48	23.66	17.76	7.99	6.14	15.94	12.05
2010	6.36	5.56	1.99	1.81	4.2	3.72	29.81	23.36	9.87	7.89	19.96	15.74
2011	6.78	6.00	1.83	1.91	4.33	3.98	36.30	29.49	11.53	9.77	24.03	19.75
2012	6.81	6.43	2.30	1.86	4.58	4.17	42.79	35.96	13.75	11.44	28.41	23.81
2013	5.63	6.64	2.55	2.11	4.1	4.40	48.03	42.45	16.21	13.63	32.29	28.18
2014	6.13	6.08	2.18	2.35	4.18	4.23	53.74	47.75	18.27	16.08	36.22	32.08
2015	6.5	6.11	2.43	2.26	4.49	4.20	59.76	53.44	20.57	18.16	40.42	36.01
2016	6.99	6.32	1.85	2.35	4.46	4.36	66.27	59.44	22.31	20.45	44.60	40.19
2017	6.18	6.69	1.97	2.08	4.11	4.42	71.86	65.93	24.12	22.22	48.35	44.38
2018	7.81	6.41	2.80	2.02	5.35	4.25	79.03	71.56	26.76	24.02	53.32	48.15
2019	7.17	7.18	2.49	2.45	4.87	4.85	85.50	78.66	29.06	26.62	57.77	53.06
2020		7.17		2.47		4.86		85.16		28.94		57.53
RMSE	1.27		0.56		0.88		6.16		2.08		4.15	
Unit root tests to find the stationary of the data												
Test statistics (P)	-2.93(0.042)		-3.23(0.018)		-3.09(0.027)		2.57(0.998)		2.61(0.998)		3.47(0.999)	

OD: Observed Data, SES: Single Exponential Smoothing, RMSE: Root Mean Square Error.

that one-third of the patients were male. The mean±SD age of incidence of MS was 29.19±9.16 years. Overall, 75% of patients were under 35 years of age at diagnosis. The majority had post-diploma and bachelor's degrees (35.10%), were married (62.10%), and concerning ethnicity, were Lor (34.50%). In terms of the type of MS, RRMS was the most common type among the patients (76.3%); however, only 3.5% had the PPMS type, and 4.9% had the SPMS type (Table 1). Other details are presented in Table 1.

Table 2 shows the number of patients with MS and the total population by gender in different years of the study. Overall, the prevalence and average annual incidence of MS disease were 57.77 and 4.35 per 100000 individuals from 2006 to 2019, respectively.

The estimated incidence and prevalence rate per 100000 individuals are displayed in Table 3. We used the single exponential smoothing method to consider these time series data and forecast appropriately. In this regard, to have a minimum Root Mean Square Error (RMSE) for incidence and prevalence rate, the smoothing constant α is equal to 0.75 and 0.9, respectively. The first observation was used as the initial value. The trend of incidence and prevalence rate in total population, females, and males are shown in Table 3 and Figures 2 and 3. The forecasting of incidence and prevalence rate in 2020 is reported in Table 3. The study used the Augmented Dickey-Fuller test for unit root to check the linear trend and find the data's stationery. The data for incidence had stationary in all categories. For prevalence data, the unit

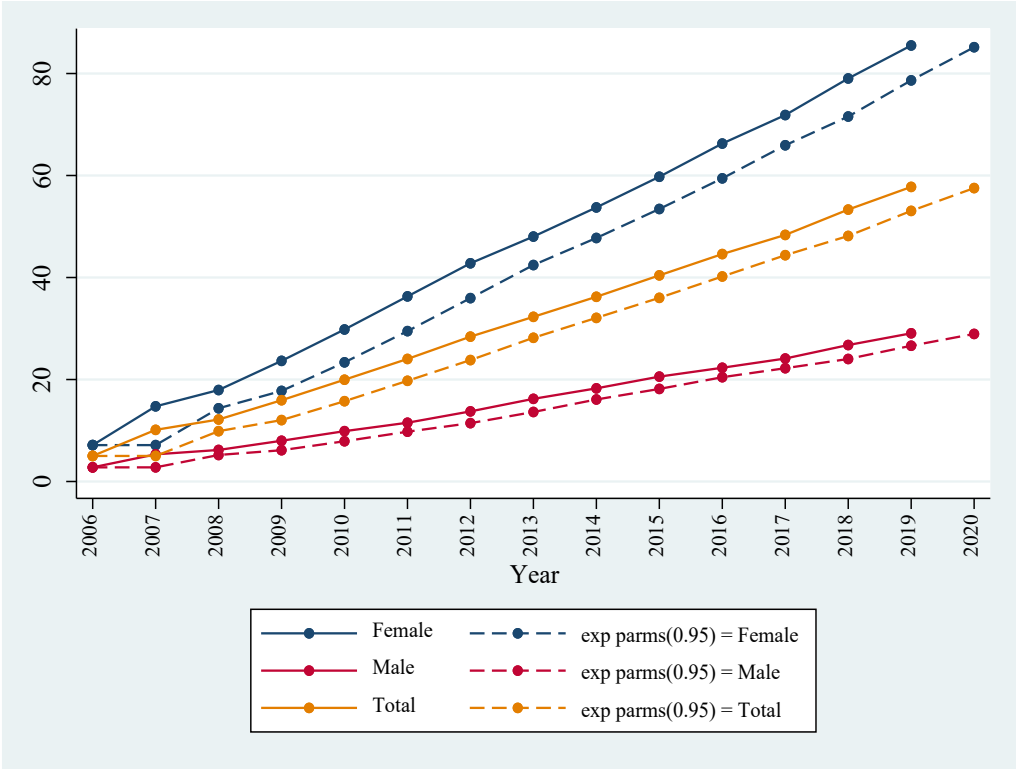

Figure 3. The gender-wise prevalence rate and smoothed values of MS

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root test shows no stationary, i.e., attributed to the increasing nature of this data type.

The trend of incidence rate changes in Figure 2 represents that the incidence rate in females is higher than males in all years. However, these rates get closer at the beginning of 2006, in the middle at the end of 2013, and 2019. We predict that the incidence rate in 2020 will be more or less similar to 2019 in total and for both generations.

The trend of incidence rate changes in Figure 2 represents that the incidence rate in females is higher than males in all years. However, these rates get closer at the beginning in 2006, in the middle in 2013, and at the end in 2019.

The prevalence rate changes in Figure 3 represent that multiple sclerosis is more prevalent in males. The graph shows that the prevalence rate gets more over time. However, the increasing slope is higher for women. Our forecast for the prevalence is the same for 2020 compared to 2019.

MS, from 2006 to 2019, is more prevalent in individuals aged between twenty to fifty years old in Khuzestan province. The new cases and total populations in a 3-age category are displayed in Table 4.

The estimated incidence and prevalence rate per 100000 individuals for the three-age categories are in Table 3. The single exponential smoothing method was used to consider these time series data. To minimize the MSE and properly forecast the incidence and prevalence rate, the smoothing constant α is equal to 0.7 and 0.95, respectively. The estimated smoothing values can be seen in Table 5 and Figures 4 and 5. The forecasting of incidence and prevalence rate in 2020 is reported in Table 5. To check the linear trend and find the data's stationery, we used the Augmented Dickey-Fuller test for unit root. It showed that the data for incidence had stationary in all categories. For prevalence data, the test of the unit root shows no stationery.

The incidence rate of MS in three age categories is represented in Figure 4. As we consider for individuals under 20 and above 50 years old, the incidence rate of MS had increased just slightly over time and is less than 2 per 100000 individuals. In the 20 to 50 years old individuals, the incidence rate is higher and close to 8 per 100000 individuals. We forecast that the incidence rate will increase slightly in 2020 than 2019, just for the 20-50 age category.

Figure 5 represents that MS's prevalence rate is very high for between twenty to fifty people. It gets more over time; however, the increasing slope is much higher for

Table 4. The age-wise number of MS patients and total population in Khuzestan

Year	Under 20		20-50		Above 50		Total	
	No. MS	Population	No. MS	Population	No. MS	Population	No. MS	Population
2006	14	1058316	198	2001255	2	449457	214	3509028
2007	11	1009739	204	2051507	9	469921	224	3531167
2008	3	963393	87	2103966	4	491568	94	3558927
2009	19	919175	152	2158721	2	514470	173	3592366
2010	16	876988	166	2215870	6	538712	188	3631570
2011	19	835452	171	2275397	6	564292	196	3675141
2012	11	808500	191	2290944	7	585139	209	3684583
2013	10	782998	172	2309838	7	607103	189	3699939
2014	14	758865	176	2332089	4	630246	194	3721200
2015	10	736025	190	2357711	10	654639	210	3748375
2016	12	714577	188	2383354	10	680062	210	3777993
2017	10	694146	172	2415773	13	707163	195	3817082
2018	15	674800	230	2451645	10	735748	255	3862193
2019	13	656480	210	2491010	12	765907	235	3913397

No. MS: Number of Multiple Sclerosis cases

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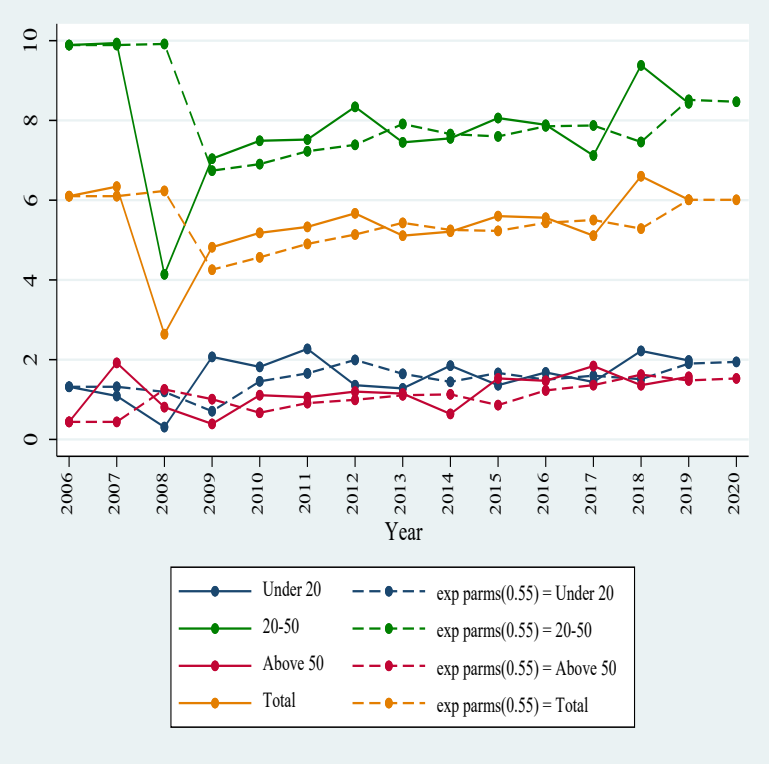

Figure 4. Multiple sclerosis incidence rate and smoothed values according to age

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Table 5. Multiple sclerosis incidence and prevalence rate and smoothed values according to age

Year	Incidence in 100000								Prevalence in 100000							
	Under 20		20-50		Above 50		Total		Under 20		20-50		Above 50		Total	
	OD	SES	OD	SES	OD	SES	OD	SES	OD	SES	OD	SES	OD	SES	OD	SES
2006	1.32	1.32	9.89	9.89	0.44	0.44	6.10	6.1	1.32	1.32	9.89	9.89	0.44	0.44	6.10	6.1
2007	1.09	1.32	9.94	9.89	1.92	0.44	6.34	6.1	2.48	1.32	19.60	9.89	2.34	0.44	12.40	6.1
2008	0.31	1.19	4.14	9.92	0.81	1.25	2.64	6.23	2.91	2.42	23.24	19.11	3.05	2.24	14.95	12.08
2009	2.07	0.71	7.04	6.74	0.39	1.01	4.82	4.26	5.11	2.89	29.69	23.03	3.30	3.01	19.62	14.81
2010	1.82	1.46	7.49	6.90	1.11	0.67	5.18	4.57	7.18	4.99	36.42	29.36	4.27	3.29	24.59	19.38
2011	2.27	1.66	7.52	7.23	1.06	0.91	5.33	4.91	9.82	7.07	42.98	36.07	5.14	4.22	29.63	24.33
2012	1.36	1.99	8.34	7.39	1.20	0.99	5.67	5.14	11.50	9.68	51.03	42.63	6.15	5.09	35.23	29.36
2013	1.28	1.65	7.45	7.91	1.15	1.11	5.11	5.43	13.15	11.41	58.06	50.61	7.08	6.09	40.19	34.94
2014	1.85	1.44	7.55	7.66	0.64	1.13	5.21	5.25	15.42	13.06	65.05	57.69	7.46	7.03	45.17	39.93
2015	1.36	1.67	8.06	7.59	1.53	0.86	5.60	5.23	17.25	15.30	72.40	64.68	8.71	7.44	50.45	44.91
2016	1.68	1.49	7.89	7.85	1.47	1.22	5.56	5.43	19.45	17.15	79.51	72.01	9.85	8.65	55.61	50.17
2017	1.44	1.59	7.12	7.87	1.84	1.36	5.11	5.50	21.47	19.33	85.56	79.14	11.31	9.79	60.15	55.34
2018	2.22	1.51	9.38	7.46	1.36	1.62	6.60	5.29	24.30	21.36	93.69	85.24	12.23	11.23	66.05	59.91
2019	1.98	1.90	8.43	8.52	1.57	1.48	6.01	6.01	26.96	24.15	100.64	93.27	13.32	12.18	71.19	65.74
2020		1.94		8.47		1.53		6.01		26.82		100.27		13.26		70.92
RMSE	0.57		1.68		0.54		1.07		2.08		7.15		1.07		5.11	
Unit root tests to find the stationary of the data																
Test statistics (P)	-2.96(0.038)		-4.74(< 0.001)		-3.77(0.003)		-3.33(0.013)		2.52(0.997)		2.44(0.996)		1.84(0.998)		2.66(0.998)	

OD: Observed Data, SES: Single Exponential Smoothing, MSE: Root Mean Square Error

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individuals aged 20 to 50. The increase in the prevalence rate of MS for under 20 years of age and above 50 has a slight slope. Moreover, our forecast for the prevalence is the same for 2020 compared to 2019 in 3 age categories.

Discussion

Our results indicated that the patients' prevalence and average annual incidence were 57.77 and 4.35 per 100000 people from 2006 to 2019, respectively. Therefore, Khuzestan has been one of the high-risk areas for MS (prevalence of >25 per 100000 subjects).

MS prevalence and incidence have been increasing over time. Meanwhile, there is a slight change in the annual incidence of MS from 5.01 per 100000 individuals in 2006 to 4.87 per 100000 subjects in 2019. The slope of the increase in all years (from 2006 to 2019) has been higher for women than men. The number of new cases and the total population of women with MS is almost three times higher than men. However, this ratio was closer in the early years (2006), in 2013, and later in 2019. The MS incidence in women and men had increased slightly from 7.14 and 2.78 per 100000 individuals in 2006 to 7.17and 2.49 per 100000 individuals in 2019, respectively.

In 2008, we observed a decrease in the incidence. One of the significant reasons for this decrease in 2008 was the occurrence of dust in Khuzestan province and con-

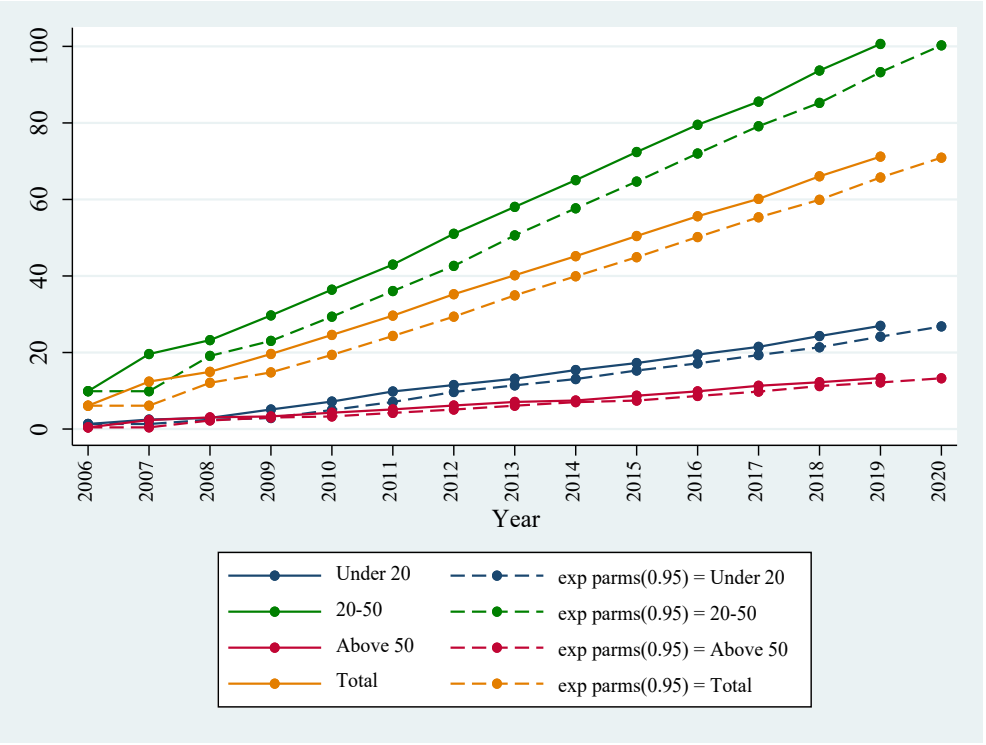

Figure 5. Multiple sclerosis prevalence rate and smoothed values according to age

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sequently the migration of some patients to neighboring provinces, such as Isfahan and Shiraz. We later saw the names of these migrating patients in the MS registration canters of those cities.

Similarly, the prevalence of MS increased from 5.01 per 100000 individuals in 2006 to 57.77 per 100000 people in 2019. Meanwhile, the MS prevalence in females and males has increased from 7.14 and 2.78 per 100000 subjects in 2006 to 85.50 and 29.06 per 100000 subjects in 2019, respectively.

Prior to this study, two other studies investigated the prevalence or incidence of the disease in Khuzestan Province; however, in smaller populations and smaller areas. Radmehr et al. estimated the prevalence of MS in northern Khuzestan at 15 per 100000, with a female-to-male ratio of 2.08 to 1 [14]. In Sharafaddinzadeh's study, which identified 696 patients with MS in Ahvaz (Khuzestan's capital), the prevalence and incidence of MS were 16.28 and 2.20 per 100000, respectively [15]. In other regions of Iran, in Asmarian's study conducted on 5468 patients with MS in Fars Province, the incidence significantly increased from 1991 and 2016. At the beginning of the study (1991), the incidence rate was 0.61, and at the end (2016), it was 11.20 per 100000 individuals, and this ratio was higher in women than men in all years studied [16]. A study aimed at estimating the prevalence and incidence of MS in the Persian Gulf region, which reviewed 39 articles published from January 1985 to December 2018 in this region, reported the average age of patients with MS as 23.11 years. The disease incidence was estimated at 5.03 per 100000 and the prevalence at 39.31 per 100000, increasing by 2.3% from 1985 to 2018 [17]. In other parts of the world, the results of a study by Patti et al. in Biancavilla, Sicily, southern Italy, suggested an increase in the average annual incidence for the period 2012-2018 (16.8 per 100000 individuals), compared to the period 1992-1996 (4.5 in 100000 subjects). As of December 31, 2018, the prevalence of the disease was 292.3 per 100000 individuals (198.2 for men & 380.7 per 100000 for women), indicating a high-risk area for MS [18]. In Brola et al.'s study in Swietokrzyskie Province (central Poland), the results were similar. The prevalence of MS on December 31, 2015, was 121.3 per 100,000 people (167.1 per 100000 women, 73.2 per 100,000 men) and the average annual incidence of MS between 2010 and 2015 was about 4.5 per 100000 individuals. This rate was estimated to be much higher than in 2010 and previous studies in Poland [19].

Concerning the MS incidence in the three age groups in the present study, for individuals under 20 and over 50 years, the incidence over time has been constant and less than 2 per 100000 subjects. While in the age group of 20

to 50 years, the incidence rate was higher and close to 8 per 100000 individuals. Our age-wise results indicated a mean age of 31.40 years for patients with MS. Moreover, 75% of patients were below 35 years of age at diagnosis.

In other studies, the prevalence and incidence at a young age have been reported more than in other age groups. In Hosseinzadeh study in Iran, the mean age of patients with MS for men and women was 31.3 and 32.3 years, respectively [6]. In Cheraghmakani's study in Mazandaran, Iran, the highest MS incidence rate is reported among the 30-34-year-old age group (28.5 per 100000 subjects), while the lowest rate was reported for above 65-year olds (0.2 per 100000 individuals) [20]. However, in Rotstein's study, the MS prevalence increased mainly for individuals aged 35 years and older, especially individuals over 50 years [21].

Regarding some demographic and clinical variables, including the higher MS prevalence in women and the youth and the higher prevalence of relapsing-remitting MS, the results of this study are consistent with other studies.

Another variable focused in this study was the racial-ethnic aspect of patients with MS. In this study, most individuals with MS were Lors (34.5%), Persians (33.3%), and Arabs (26.3%). In this regard, Sharafaddinzadeh's study on the impact of Persian and Arab ethnics living in Khuzestan Province on MS it was shown that the prevalence and incidence of MS were higher in the Persian population. However, the progressive nature of MS with motor symptoms and cerebellar involvement was more common in the Arab population [15]. In our study, ocular and sensory disturbances were reported as the first MS symptom more than other symptoms. Some other studies have emphasized this [15, 22]. The relationship between occupation and MS prevalence rate survey reported the highest frequency for homemakers. This is because housewives are more than working women in Iran. The MS prevalence in people with "diplomas" and "post-diploma and bachelor" has been higher than others, indicating the dominant population of Iranian society with this level of education.

Most studies evaluated the prevalence and incidence and description of the temporal trends of MS, and few have predicted the prevalence and incidence of MS in the coming years. The present study predicted that the incidence of MS in 2020 will be more or less the same compared to 2019 and will reach 4.86 per 100000 individuals, i.e., more for women than men (7.17 & 2.47 per 100000 individuals, respectively), and only in the 20-50-year-old age group. However, it is predicted that the prevalence of MS in 2020 for all age and sex groups will be more or less the same as in 2019. In this regard, in Canada, Nana et al. reviewed and presented a prognosis model over 20 years and estimated that MS cases will increase from 4051 in 2011 to 4794 in 2031. The prevalence of MS will exceed 400 per 100000 and is 3 times more common in women than in men [9]. Likewise, in Mousavizadeh's study in Kohgiluyeh and Boyer-Ahmad, Iran, on 421 patients between 1990 and 2016, the MS prevalence was estimated to be 60.14 per 100000 the average annual incidence was 3.8 per 100000 individuals. The MS incidence was projected to increase from 8.5 per 100000 at the end of 2016 to more than 17 per 100000 individuals in 2025, and in 2025 MS will exceed 1,250, representing a nearly threefold increase in the diagnosed cases over 10 years [8].

Several factors may increase the prevalence and incidence of MS in the region between 2006 and 2019. Despite its sunny weather, vitamin D deficiency remains among the most critical health issues in Khuzestan Province [23, 24]. Further epidemiological studies have shown that serum vitamin D deficiency can be a potential environmental predisposing factor for MS in Iran [25]. Furthermore, this area's inhabitants encounter dust particles and high temperatures. The adverse effect of Particulate Matter of 10 (PM_{10}) on dusty days on people's health in Ahvaz is more than days without dust [26]. A positive association between exposure to air pollution and multiple sclerosis has been reported in some studies [27-30]. Lifestyle changes, increasing urbanization, and industrialization of cities can be other factors [31]. According to studies, provinces with less urbanization, such as Sistan-Baluchestan and South Khorasan in Iran, have the lowest prevalence of MS. In contrast, provinces with high urbanization, such as Tehran and Isfahan, have the highest prevalence [32].

This study has its strengths and limitations. The first study presented the prevalence and incidence of MS and presented a predictive model in all of Khuzestan Province. On the other hand, the actual number of individuals with MS may not be identified for various reasons, as follows: The elderly with long-term illness, primarily secondary progressive MS, are few. There are problems in accessing people who rarely communicate with medical services or have difficulty communicating with a physician. In addition, some young patients with mild forms of MS might avoid contacting medical services or do not require medical treatment during the study years.

Conclusion

Khuzestan Province is a high-risk area for MS. In the province, the overall prevalence has increased from 2006 to 2019. The overall incidence has been increasing with a very slight slope. The increase in prevalence and incidence was more noticeable in women than in men. The present study also predicts an increase in the incidence of MS in the coming years in the age group of 20 to 50 years. However, MS prevalence is similar to 2019. Establishing a national registry for comprehensive long-term follow-up studies is recommended.

Ethical Considerations

Compliance with ethical guidelines

The proposal of this study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (Code: IR.AJUMS.REC.1397.640).

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Authors contributions

Conceptualization, methodology, supervision and project administration: Maryam Dastoorpoor; Investigation: Nastaran Majdinasab and Majid Soltani; Writing – original draft: Narges Khodadadi; Writing – review & editing: Narges Khodadadi and Maryam Dastoorpoor; Formal analysis and software: Saeed Ghanbari and Maryam Dastoorpoor.

Conflict of interest

The authors declared no conflicts of interest.

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