

The prevalence and clinical profile of multiple sclerosis in Timis County, Romania

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ABSTRACT

Introduction. Multiple sclerosis is a neurodegenerative disease for which correct prevalence and incidence data are mandatory to assess the long term health policy in terms of social and economic burden. The present study aims to evaluate the prevalence of MS and the distribution of clinical MS forms in Timis County, a region inhabited by 3.39% of the Romanian stable population according to the 2011 Romanian census, and is meant as a sample of the national situation. There have been no previous attempts to assess the MS prevalence status in Timis County.

Material and methods. This study was conducted in a well-defined geographical area (i.e the Timis County which lies in the Western region of Romania) exploring the prevalence of MS and the patients' clinical profile. The information regarding MS patients was obtained using hospital records and the files of the patients treated and followed up in the Romanian National MS Program for treatment of MS.

Results. The crude calculated prevalence was 53.6 per 100,000 inhabitants. The F:M ratio was 1.7 corresponding to a number of 220 (65.4%) females and 116 (34.5%) males.

Discussions. This study is the first attempt to estimate the prevalence of multiple sclerosis in Timis County as part of an ongoing project of the National Romanian Society of Neurology to build up the Romanian MS Registry and our results indicate higher prevalence values than expected, fact due to an increased diagnostic accuracy provided by clear cut diagnosis criteria and MRI standardized magnetic resonance imagery procedures currently available.

Keywords: epidemiology, multiple sclerosis, prevalence

INTRODUCTION

Geo-epidemiology aims to offer a comprehensive image of the geographical distribution, environmental and genetic factors that correlate with any chronic disease. Multiple Sclerosis, as a chronic neurodegenerative disorder of yet unproven etiology has been subjected to extensive epidemiological approaches.

In terms of prevalence, based on the results of prior studies, the highest MS prevalence lies within the temperate zone, in both northern and southern hemispheres while the subtropical zone has lower values (1,2). In the tropical regions, traditionally, MS has even been considered an uncommon disease (3).

Data gathered mostly from national registries became very useful in providing the follow-up opportunity. The temporal factor is a valuable parameter of assessment along with data regarding the geographic environment, socio-economic and ge-

netic structure of the population providing a more accurate dimension to the studied pathology (4,5).

This information also provided new insights in understanding the changes that occurred in the gradient (north to south) behavior of the disease prevalence.

Registry data also uncovered variations in the MS profile in terms of a steady increase in incidence and prevalence. Despite variation among countries, the impact of disease modifying therapies (DMT) on the natural history of the disease equally impact health resources distribution policies. (3)

As epidemiological data concerning MS in Romania are scarce, the present study was an epidemiological attempt to evaluate the prevalence of MS and the distribution of clinical MS forms in Timis County, a region inhabited by 3.39% of the Romanian stable population according to 2011 Romanian census, and is meant as a sample of the national situation. This project is part of an ongoing

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attempt to evaluate the Romanian national prevalence and incidence of multiple sclerosis, initiated by the Romanian Society of Neurology.

MATERIAL AND METHODS

This study was conducted in a well-defined geographical area, studying the patients' profile within this region.

Study area

Timis County lies in Western Romania, between 45°81 north latitude and 21°33 longitude. The climate in this region can be described as temperate oceanic, similar to the rest of the South Eastern part of the Pannonian basin. The mean annual temperature is 10.6°C. The warm season lasts from May 25 to September 14 with an average temperature ranging from 22.8°C to maximum 27.8°C. The cold season lasts from November 25 to March 12 with the average temperature varying from –4°C to 3°C. The mean UV index ranges between 1 in cold and 7 in warm season (6-8) (Fig. 1).

As to 20 Oct 2011, according to the last national census performed by the Romanian National Statistical Institute the population in Timis County was 683.540 persons out of which 329.176 males and 422.349 females, with a female per male ratio (F: M) of 1.28. Timis County has a significant positive rate of incoming migration based mainly on economic reasons. Between 2005-2010 the cross-country internal migration rate was 5.23‰ with a raw value of 3,642 people that migrated into the region, (9). Regarding ethnicity, Romanians represent 80.5% while the main ethnic minorities are: 5.1% Hungarians, 2.1% Gypsies, 1.4% Serbians, 1.2% Germans, 0.8% Ukrainians, 0.6% Bulgarians, 0.2% Slovaks and 8.1% others. A percentage of 62.1 % of the population lives in urban areas.

The main city in the region is Timisoara, an important academic and medical center of Western Romania.

The Neurological Clinic of the Clinical County Emergency Hospital "Pius Brinzeu" is currently a referral center for the diagnosis, follow up and treatment of MS in the Western region of Romania.

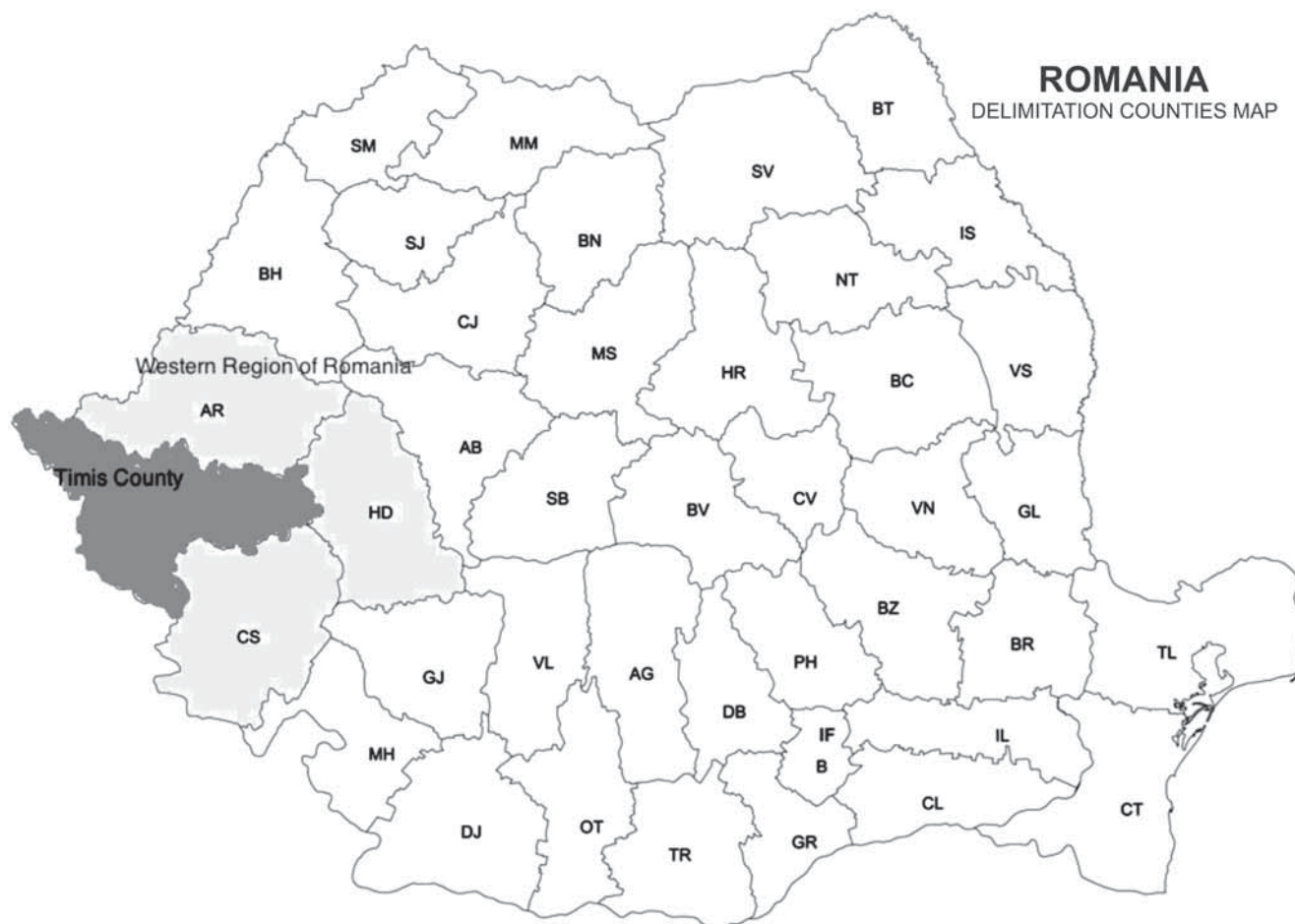


FIGURE 1. Timis County (dark grey) and the Western Region of Romania (light grey)

Beside the Timis County, there is a large capture area for such patients including three more neighboring counties: Arad (2.14%), Caras Severin (1.46%), and Hunedoara (2.08%), representing 5.68% out of the Romanian population.

The center is also involved in data collection for the Romanian National MS Registry since 2014, a fact that ascertains the reliability of the data.

Patients

We analyzed data regarding MS patients using hospital records and the files of the patients being treated within the Romanian National MS Treatment Program using the date of 16 Aug 2016 as the cross section analysis date. Duplicate entries were excluded if the case. MS patients were identified using the ICD 10 codes for the following diagnosis: MS, optic neuritis, paraparesis (plegia), myelitis and cerebellar ataxia.

RESULTS

We identified a total of 346 MS patients out of which 336 were actually living in the county at the analysis time, the difference given by 4 patients that emigrated and six that died. The patients were identified either from the data available in the MS National Registry [(267 cases (77.2%)] and the Neurology Clinic records' cases for the remaining 79 cases (22.7%). All of the remaining 336 patients met the McDonald 2010 diagnosis criteria.

There are five foreigners who live and work in Timisoara in our group – three from Serbia, one from the Republic of Moldova and one from India.

The crude prevalence value was 53.6 at 100,000 inhabitants. The F: M ratio was 1.7 with 220 (65.4%) females and 116 (34.5%) males respectively (Table 1).

The mean age at onset was 35.86 years (sd 10.28) ranging from 14.35 to 56.49. There were no significant differences in-between the male and the female group regarding the mean age at onset (35.09 – sd 10.13 vs. 36.26 – sd 10.49 with a p-value 0.164) (Fig. 2).

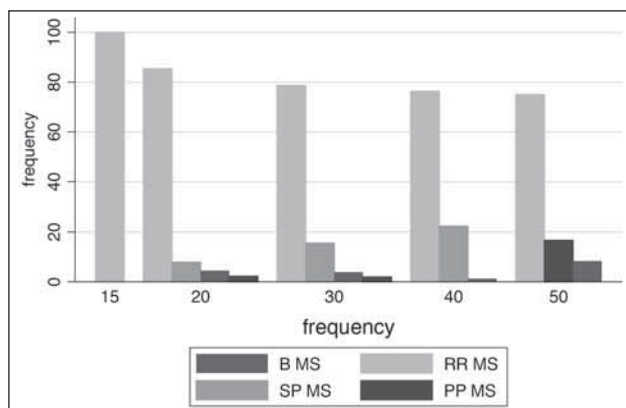


FIGURE 2. The distribution of MS clinical forms frequency and age groups (Age groups are defined as follows <15 years, 15-19 years, 20-29 years 30-39 years, 40-49 years, >50 years) (B MS – benign MS, RR MS – relapsing remitting MS, SP MS – secondary progressive MS, PP MS primary progressive MS)

In our group, there were three pairs of first-degree relatives diagnosed with MS (two sisters, two brothers and a mother and daughter).

The mean duration of the disease as to the 16th of Aug 2016 was 9.72 years (sd 6.49), ranging from 2 months to 34.6 years.

The MS clinical form could be ascertained only for 331 cases (98.5%) due to insufficient reliable documents for five patients (Fig. 3).

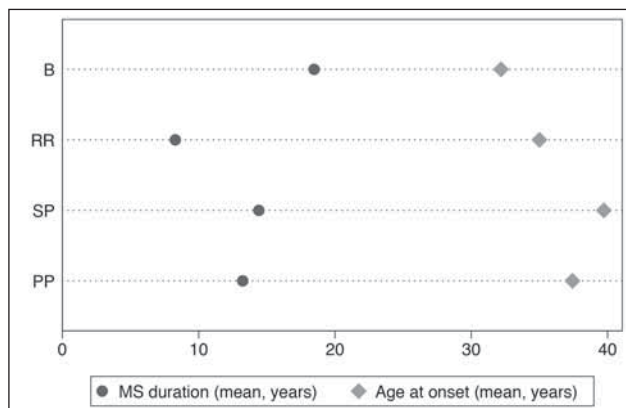


FIGURE 3. The distribution of MS clinical forms, mean disease duration and mean age at onset (B MS – benign MS, RR MS – relapsing remitting MS, SP MS – secondary progressive MS, PP MS primary progressive MS)

TABLE 1. Age and sex specific prevalence rates (per 100 000) and the reference population in Timis County on August 1st, 2016

Age groups at onset	Female population	Female cases	Male population	Male cases	Female crude prevalence	Male crude prevalence	Prevalence by age groups
≤19	34,031	13	35,157	6	38.20	17.06	27.46
20-29	59,723	48	59,267	36	80.37	60.74	70.59
30-39	53,620	76	55,018	38	141.73	69.06	104.93
40-49	47,374	51	47,329	26	107.65	54.93	81.30
≥ 50	49,883	32	45,018	10	64.15	22.21	44.25
Total	244,631	220	241,789	116	89.93	47.97	69.07

Six patients (2%) met the criteria for the primary progressive MS (F: M ratio 2.0), 279 (84.2%) belonged to the relapsing remitting form (F: M 2.1) while 45 (13.8%) were in the secondary progressive form (F: M ratio 1.1). Ten patients (F: M ratio 2.33) could be considered as having a “benign” MS clinical course (EDSS score below 3.5 even 15 years after onset).

In our study, 246 (74.5%) patients have been assessed with the EDSS score. All the patients in the “benign” group and those with the relapsing remitting MS form had had an EDSS score below 4.0 [56.5% (n=139)]. Six patients (2.43%) in the secondary progressive MS group had an EDSS score between 5 to 6, while 35 patients (14.22%) had an EDSS score higher than 6.0. All the patients within the primary progressive MS form had an EDSS score ranging from 4.0 to 5.5.

DISCUSSIONS

The role of the epidemiological data in MS research has been well proven (21), epidemiological studies being a reliable source of information by quantifying different parameters such as geographical, environmental, clinical, etc.

Most of the studies available have been conducted in Northern Europe, especially in the Scandinavian countries (10-14).

Some authors tried to explain (in serial epidemiological studies) the constant increase of both MS incidence and prevalence, independently of the geographic and environmental setting (10,11).

In 1975 Kurtzke rated Romania as a country of “medium prevalence” ranging between 5 – 30/100,000, opinion re-confirmed by Morariu et al. in 1974 (15). He found prevalence data ranging from 14.5 (Satu Mare County) to 28.8 (Mures County), while Verdes et al. in 1978 found a MS prevalence of 41.3/1,000,000 of so called “probable cases” (16,17) facts that placed Romania (Bucharest actually, as it was compared with other large cities at the time) within the high range of prevalence in Europe (17,18). We should point that the diagnosis accuracy at the time could have biased the data.

As for the Timis County, there are no other published epidemiological data concerning MS. The last two published epidemiological studies regarding the prevalence of MS patients were performed in the Mures County in 1994. Our colleagues, Becus and Popoviciu (19) found a prevalence of 22.6 (ranging from 19.14 to 26.69) while Balasa et al., in 2007, outlined a prevalence of 26.1/100,000 within the county (Fig. 4). (20)

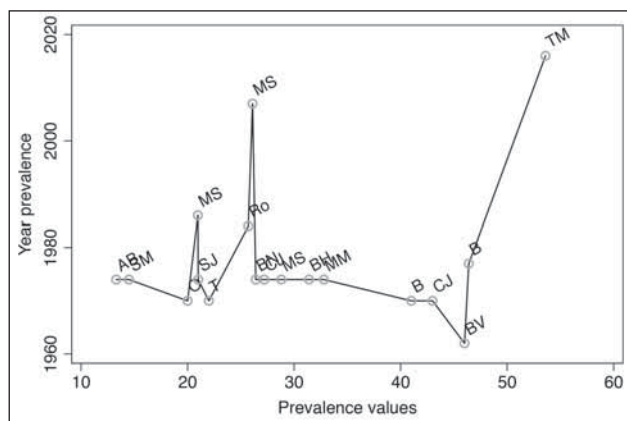


FIGURE 4. Prevalence indices in different periods across the country

(Country: Ro – Romania, Regions: T – Transilvania, O – Oltenia Counties: AB – Alba, SM – Satu Mare, SJ – Salaj, BN – Bistrita Nasaud, CJ – Cluj, BH – Bihor, MM – Maramures, B – Bucuresti, BV – Brasov, TM – Timisoara)

Data from <http://www.mult-sclerosis.org/about-thissite.html> estimate an approximate number of 7,000 MS diagnosed cases in Romania, meaning a prevalence of 33.4/100,000 inhabitants (21).

Our prevalence data (53.6/100,000 persons) are higher than the results available from the last published studies i.e. those regarding the disease profile in Mures County (2007).

On the other hand, our data are similar to the epidemiologic results found across the neighboring Csongrad County (Hungary) between 1992 and 1996. They found a MS prevalence ranging from 32 to 65 per 100,000 (22,23). Zsiros et al., in 2013, found a crude prevalence of 89.9/100,000, in line with the increasing tendency of prevalence all across the European countries (24)

The increasing prevalence has been linked to several interacting factors such as the change in the population structure, the higher accuracy of diagnosis (by procedures and criteria) the reliability of the raters and last but not least the increasing financial resources endorsed for this disease.

An analysis from Rosati, in 2001, regarding the MS prevalence in the USA, outlines the importance of genetic variability versus the geographic distribution, the migration patterns of the population and the south to north gradient ratio (25). This data have been extrapolated into the European setting by Alonso et al. 2008 as he did not find a statistical relevant significance of the geographical gradient ratio (5).

Keeping in mind the size of our group, we also found migration tendencies as four of the patients (1.4%) from the initial group emigrated (all after 2011) while five foreigners were diagnosed and treated at the MS Center in Timisoara. The ethnical

structure of the patients in our center is as follows: 306 (91.07%) Romanians, 8 (5%) Hungarians, 12 (3.5%) Serbians, 7 (2%) Germans and others 1 patient (0.003%).

In his meta-analysis of 69 MS prevalence studies and 22 MS incidence studies, conducted between 1980-1989, within the 40 to 60 latitude across the world, Zivadinov et al. (2003) found a weaker impact of the latitude factor in MS variance when data were adjusted and standardized by age and sex (26). Alonso et al., in 2008, had also brought into questions the consistency of the latitude variation impact when incidence and prevalence data were adjusted for age and sex (27).

There are also findings that showed the increase of prevalence rates in regions closer to the equator, concomitantly with an attenuation of the latitude influence and a consistent increase of female to male ratio (from 1.4 in 1955 to 2.3 in 2000) (5).

The increase in prevalence and incidence along the time in the same region can be explained by the following: more accurate databases, increasing interest towards MS in the area, better diagnosis procedures available, longer survival rates, migration patterns.

Simpson and his collaborators, in 2015, included the time factor (the longitudinal follow up) into

the MS features' analysis and at the same time combined prevalence and incidence data with the geographical distribution. By doing so, they found that the increasing trend of prevalence and incidence still respects a geographical distribution pattern (with statistical significance) (28).

CONCLUSIONS

This study is the first attempt to estimate the prevalence of multiple sclerosis in Timis County as part of an ongoing project of the National Romanian Society of Neurology to build up a Romanian MS Registry, and our results indicate higher prevalence values than expected, fact possibly owed to a more accurate diagnosis of the disease by means of improved diagnosis criteria, enhanced MRI accuracy and increased awareness of the burden of the disease.

Abbreviation list

MS – multiple sclerosis

RR MS – relapsing remitting MS

B MS – benign MS

SP MS – secondary progressive MS

PP MS – primary progressive MS

EDSS – Expanded Disability Status Scale

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