



# Epileptic Seizures in Multiple Sclerosis Patients

## Multipl Skleroz Hastalarında Epileptik Nöbetler

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### Summary

**Objective:** The presence of epileptic seizures in patients with multiple sclerosis (MS) is a well-known phenomenon. The aims of our study, performed in our clinic are to point out the correlation of the mean age/gender and age of MS patients with the onset of seizures, to identify the types of epileptic seizures in MS patients by sex/age, to identify the correlation between relapses and seizures, and to identify the main electrophysiological / imaging changes.

**Material and Method:** The medical records of 300 MS patients observed between January 2000 and December 2009 in the Neurological Clinic of University Clinical Centre of Kosova were reviewed. All patients fulfilled the McDonald MS criteria Epilepsy diagnosis was based on the ILAE (International League against Epilepsy) (1983) criteria while epileptic seizures were classified based on the ILAE classification (1981).

**Results:** Out of 300 MS patients enrolled in this study, 49 (16.33%) were identified with seizures or epilepsy. In 23 (47%) patients out of 49, seizures or epilepsy appeared after the MS diagnosis. In 6 patients (12.2%), epileptic attacks preceded the MS diagnosis, while in 20 patients (40.8%), epilepsy was diagnosed before multiple sclerosis. These patients were treated with antiepileptics. Out of 23 patients (47%) in whom the epileptic seizures appeared after the MS diagnosis, 17 (74%) had simple partial seizures, and 6 (26%) had complex partial seizures. Based to our study, the epileptic seizures in MS patients appeared about 2.2 years after the MS diagnosis.

**Discussion:** Simple partial seizures were 2.8 times more frequent compared to complex partial seizures. In female patients the prevalence of complex partial seizures was higher than in male patients with multiple sclerosis. (*Turkish Journal of Neurology* 2013; 19:40-3)

**Key Words:** Epilepsy, multiple sclerosis, simple partial seizures, complex partial seizures, electroencephalography, magnetic resonance imaging

### Özet

**Amaç:** Multipl skleroz (MS) olan hastalarda epileptik konvülsiyonlar olduğu iyi bilinen bir fenomendir. Kliniğimizde yaptığımız çalışmanın amacı MS hastalarının ortalama yaşı ve cinsiyeti ile konvülsiyonlar arasındaki korelasyonu ortaya koymak, MS hastalarındaki epileptik konvülsiyonların tiplerini cinsiyet / yaşa göre belirlemek, relapslar ve konvülsiyonlar arasındaki korelasyonu belirlemek ve başlıca elektrofizyolojik / görüntüleme değişikliklerini belirlemektir.

**Gereç ve Yöntem:** Kosova Üniversitesi Nöroloji Kliniği'nde Ocak 2000 ile Aralık 2009 arasında izlenen 300 MS hastasının hastane dosyaları incelendi. Bütün hastalar Mc Donald MS kriterlerine uyuyordu. Epilepsi tanısı ILAE (International League Against Epilepsy) (1983) kriterlerine dayandırılırken, epileptik konvülsiyonlar ILAE sınıflandırmasına (1981) göre sınıflandırıldı.

**Bulgular:** Bu çalışmaya alınan 300 MS hastasından 49'unda (%16,33) konvülsiyon ya da epilepsi olduğu belirlendi. Kırkdokuz hastadan 23'ünde (%47) konvülsiyonlar ya da epilepsi MS tanısından sonra ortaya çıkmıştı. Altı hastada (%12,2) epilepsi nöbetleri MS tanısından önce görülürken, 20 hastada (%40,8) epilepsi tanısı multipl sklerozdan önce konmuştu. Bu hastalar antiepileptik(ler)le tedavi edilmekteydi. Epileptik konvülsiyonların MS tanısından sonra ortaya çıktığı 23 hastanın (%47) 17'sinde (%74) basit parsiyel konvülsiyonlar, 6'sında (%26) ise kompleks parsiyel konvülsiyonlar vardı. Çalışmamızda MS hastalarında epileptik konvülsiyonlar multipl skleroz tanısından yaklaşık 2,2 yıl sonra ortaya çıkmıştır.

**Sonuç:** MS hastalarında basit parsiyel nöbetler kompleks parsiyel nöbetlere göre 2.8 kat daha sıktır. Kadın hastalarda kompleks parsiyel nöbet prevalansı erkeklere göre daha fazladır. (*Türk Nöroloji Dergisi* 2013; 19:40-3)

**Anahtar Kelimeler:** Epilepsi, multipl skleroz, basit parsiyel konvülsiyonlar, kompleks parsiyel konvülsiyonlar, elektroensefalografi, manyetik rezonans görüntüleme

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## Introduction

The prevalence of epilepsy in industrialized countries is about 3 to 9 per 1000 residents, while the age-adjusted incidence is from 28.9 to 53.1 in 100000 residents (1,2).

Multiple sclerosis (MS) is a chronic neurological disease of the white brain matter with an unknown etiology, with a wide spectrum of symptoms and signs. Because it primarily attacks the white brain matter, epileptic seizures do not frequently occur in patients with multiple sclerosis.

The latest studies have helped substantially in clarifying how this disease attacks the brain grey matter. These studies emphasize the connection between the number, localization and the volume of cortical and juxtacortical demyelinating lesion changes and epilepsy (3,4). A possible anatomic substrate for seizures is the inflammation areas and demyelination in the cortex and the juxtacortical white matter (5). According to the investigatory team lead by Edgar Meinl, the grey brain matter damage in multiple sclerosis is a consequence of the attack of the protein contactin2 (which is produced by myelin sheath and by neurons of the brain grey mass) by immunological factors (6). For a long time it's, known that epilepsy is part of the spectrum of multiple sclerosis symptoms (7). Based on the previous study reports it has been documented that patients with multiple sclerosis are at a higher risk for epileptic seizures than the general population (8,9). The prevalence of epileptic seizures in patients with multiple sclerosis varies in studies in Western countries from 1.9 to 7.5% (10,11,12).

There are various explanations as to, about the reasons of the epileptic seizures occur in multiple sclerosis, including damage of the cortical or sub cortical regions from demyelinating plaques, the reactive gliosis, edema and the damage of Na<sup>+</sup>K<sup>+</sup>ATP-ase enzyme activity (8,9).

Our aim is to define the clinical and electrophysiological/ imaging profile of epileptic attacks in patients with multiple sclerosis observed in the Neurological Clinical Center in UCC of Kosova in Prishtina.

## Material and Methods

Our study is based on the review of the hospital documentation of 300 MS patients who were observed in the Neurology Clinic of UCC of Kosova in Prishtina from January 2000 to December 2009.

All of the patients included in the study have fulfilled the MS McDonald et al. criteria (2010). The inclusive criteria in the study was the appearance of epileptic seizures following a diagnosis of multiple sclerosis. Patients in whom epileptic seizures appeared before being diagnosed with multiple sclerosis, and those in whom seizures preceded the disease diagnosis, were not been included in the study (similar inclusion and exclusion criteria have been employed by the study in India) (9).

The diagnosis of epileptic seizures was based on the ILAE criteria of 1983, while the seizures were classified based on the ILAE classification of 1981. EEG, brain MRI and cerebrospinal fluid analyses were performed on all patients.

## Results

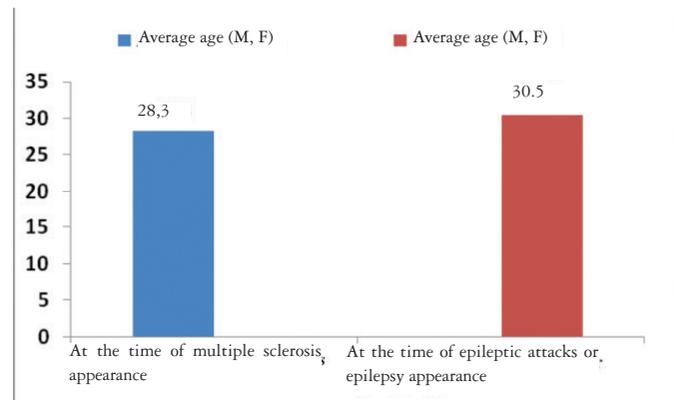
All of the medical records of the 300 MS patients observed in the Clinic of Neurology from January 2000 to December 2009 were reviewed. Out of these patients, 94 (31.33%) were male and

206 (68.67%) were female. Forty-nine (16.33%) of these patients were diagnosed with epileptic seizures. In 23 (47%) of these 49 patients, the epileptic seizures appeared after the diagnosis of multiple sclerosis, in 6 (12.2%) other patients the epileptic seizures preceded the MS diagnosis. These 6 patients were not included in the study because there were positive data about other injuries in their medical history. In 20 other patients (40.8%), the epileptic seizures appeared before the MS diagnosis and these patients were under antiepileptic treatment. They are also excluded from this study. Out of 23 patients with epileptic seizures and MS who were enrolled in this study, 8 patients (34.8%) were male and 15 patients (65.2%) were female (Table 1).

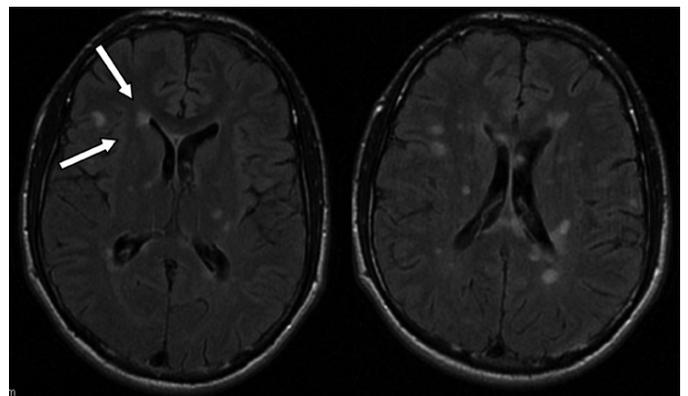
The male-female ratio of MS patients is 1:1.87 in favour of females. The average age of onset for MS in the 23 patients was around 28.3 years (SD=4.1), while the average age of onset for epileptic seizures was 30.5 years (Figure 1). The average age of onset for MS in our study is a little higher than the study performed in Albania, which averaged around 25.8 years (13).

In females the average age of onset for multiple sclerosis was 26.4 years, while the average age of onset for epileptic seizures was 28.6 years.

In males, the average age of onset for multiple sclerosis was 31.6 years, whereas the average age of onset for epileptic seizures was 34.1 years.



**Figure 1:** The patients' mean age at MS and seizures onset according to gender



**Figure 2:** Juxta-cortical localization of demyelinating plaques

In 10 (43.5%) of the patients enrolled in the study, epileptic seizures appeared during acute relapses of multiple sclerosis, while in 13 (56.5%) of the patients enrolled in this study the seizures continued appearing during the remission period.

Patients with seizures during the remission period had an EDSS considerably higher than the patients who had attacks primarily during an acute relapse of multiple sclerosis (Table 2).

As far as the frequency of the type of the epileptic seizure is concerned, 17 patients (73.9%) had simple partial epileptic seizures, while 6 other patients (26.1%) had complex partial seizures.

**EEG Findings**

In 8 patients changes in EEGs have been recorded. In 3 of 8 patients with these changes there was a diffuse slowing of the electrocerebral activity (slow waves in groups) and in 5 there was a slowing down of the electrocerebral activity and of theta activity, all localized in frontal and temporal regions (frontal 2 cases, temporal 3 cases).

**MRI Findings**

Ten (43.5%) of 23 patients had a brain MRI performed within 24 hours of an epileptic seizure. In 6 (60%) of these patients, the

brain MRI showed the presence of demyelinating lesions with juxtacortical localization (Figure 2), while in the other 4 patients (40%), cortical atrophy was present. None of the 6 patients with juxtacortical localized demyelinating lesions have shown active plaques in the brain MRI at the time of examination.

Our study showed that simple partial seizures in patients with multiple sclerosis were about 2.8 times more frequent than complex partial seizures.

Ten female patients (67%) had simple partial seizures, whereas 5 female patients (33%) had complex partial seizures. In contrast, 7 male patients (87%) had simple partial seizures, while 1 male patient (13%) had a complex partial seizures (Figures 3, 4).

**Discussion**

The analyses of serial studies of epileptic seizures have shown that the prevalence in patients with multiple sclerosis is not clear. Epilepsy appears in the general population at a rate of about 0.5 to 1%. Studies on the relationship between epilepsy and multiple sclerosis show that the risk of a patient with multiple sclerosis having epilepsy is 3 to 6 times higher than for the general population (1,5,10).

Despite varying theories, providing different possible reasons for the appearance of epileptic seizures in MS patients, a consequential relationship between seizures and MS has so far not been documented. However, some authors support the theory that epilepsy in MS patients could be related to the severity and course of the disease itself (15).

In Kosovo, there is a lack of information about the prevalence of epilepsy in the general population. Therefore, we could not evaluate the risk of seizures in MS patients compared to the general population. The data in our study match the data reported from the studies in other states related to the prevalence of the type of epileptic seizures within the partial seizures.

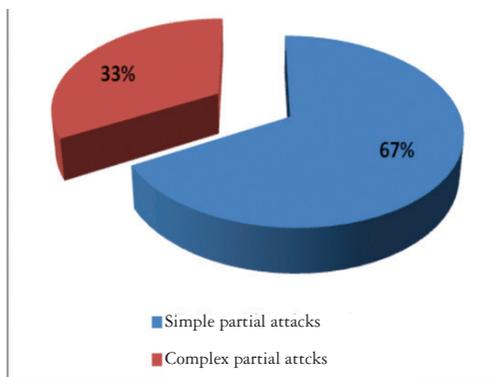
The frequency of epileptic seizures in MS patients in our study is higher than that in similar studies conducted in India (9), Finland (10), and Iceland (11), but the frequency of the seizures reported in this study is similar to that seen in other countries in the region (Serbia) (14).

**Table 1. Patients at the time of MS onset by sex**

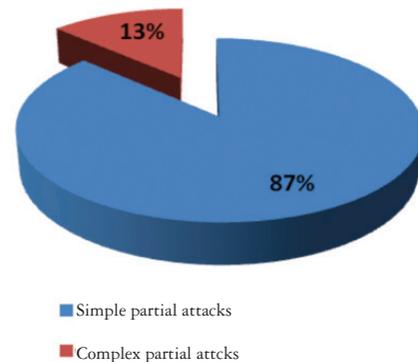
Sex	Cases	%
Male	8	34.8
Female	15	65.2
Total	23	100.0

**Table 2. Presentation of epileptic seizures, by sex and relapses and mean EDSS**

Period of attack or epilepsy manifestation	Sex		Total	EDSS (median)
	F	M		
During acute relapses	7	3	10	2
Any phase	8	5	13	4



**Figure 3:** The percentage of frequency of epileptic attacks type in females  
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**Figure 4:** The percentage of frequency of epileptic attacks type in males

Our study has shown that in 10 (43.5%) patients out of 23 enrolled in the study, epileptic seizures occurred during the acute relapses of multiple sclerosis, while in 13 others (56.5%) the seizures appeared regardless of the stage of disease.

In our study, the average age that multiple sclerosis appears in women is 26.4 years, whereas in men it is 31.6 years. Multiple sclerosis manifested itself on an average of 2.2 years after the onset of the disease, whereas for men it occurred 2.5 years after onset of the disease.

Most studies done in other countries on patients with multiple sclerosis having seizures have reported that the frequency of simple partial seizures is about twice as high as complex partial seizures. This is in contrast with studies on seizures in the general population, where complex partial seizures are more frequent (16). In this study, simple partial seizures are 2.8 times more frequent than complex partial seizures.

Ten female patients (67%) had simple partial seizures, whereas 5 patients (33%) had complex partial seizures. In males 7 patients (87%) had simple partial seizures, while only 1 patient (13%) had complex partial seizures.

In 5 patients out of 8 (62.5%) with EEG changes, we observed a slowing of electrocerebral activity and of theta range, which was primarily localized in the frontal and temporal regions. In majority of cases, i.e. 6 out of 10 (60%), the presence of demyelinating lesions with juxtacortical localization was observed in MRI findings.

## Conclusion

Our research showed that the prevalence of simple partial seizures in patients with multiple sclerosis is about 2.8 times higher than in patients with complex partial seizures. Our study also found that the prevalence of complex partial seizures is higher in female patients with multiple sclerosis than in male patients.

Our study therefore concludes that there are more simple partial seizures in both sexes than complex partial seizures. Simple partial seizures were diagnosed in 10 female patients (67%) and in 7 male patients (87%).

It is clear that complex partial seizures appear more frequently in female patients with multiple sclerosis (33%) than in male patients (13%). This ratio is about 1-2.6. At present there is nothing in the literature regarding the frequency of the epileptic seizure type in patients with multiple sclerosis based on sex.

Therefore, it is impossible to make comparisons with the results of this study and to draw any conclusions. Further work is needed in this area.

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