



Research Article

Epileptic Seizures in Multiple Sclerosis Patients

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Abstract

The presence of epileptic seizures in patients with multiple sclerosis (MS) is a well known phenomenon. The aims of our study performed in the Clinic of Neurology, University Clinical Centre of Kosovo, Prishtina are; to point out correlation between the mean age of MS manifestation in MS patients in general and according to gender (age/gender) and the mean age of manifestation of epileptic seizures in MS patients in general according to gender (age/gender); to identify the types of epileptic seizures in patients with multiple sclerosis, according to gender/age; to point out the correlation between relapses and seizures and to point out the main electrophysiological / imaging changes observed. The in-patients documents of 300 observed patients with multiple sclerosis in Prishtina during the period of January 2000 - December 2009 in the Neurological Clinic of University Clinical Centre of Kosova have been reviewed. All the observed patients have fulfilled the MS criteria of McDonald et al (2010). The epilepsy diagnosis has been set based on the criteria of ILAE (International League against Epilepsy) (1983) while epileptic seizures have been classified based on ILAE classification (1981). Out of the 300 patients with multiple sclerosis, in this study 49 (16.33%) have been identified with epileptic seizures. In 23 out of 49 patients or 47%, seizures or epilepsy appeared after diagnosing multiple sclerosis. In 6 patients (12.2%), epileptic seizures have preceded multiple sclerosis diagnosis while in 20 patients (40.8%) epilepsy diagnosis was set before diagnosing multiple sclerosis. These patients were being treated with antiepileptic therapy. Out of 23 patients (47%) in whom the epileptic seizures appeared after setting multiple sclerosis diagnosis, 17 (74%) had simple partial seizures, while 6 (26%) had complex partial seizures. According to our study, the epileptic seizures in MS patients appeared about 2.2 years after multiple sclerosis diagnosis.

Key words: Epilepsy, Multiple sclerosis, Simple partial seizures, Complex partial seizures, EEG, MRI

INTRODUCTION

Epilepsy prevalence 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 is a neurological chronic disease of the white brain matter with an unknown etiology and with a wide spectrum of symptoms and signs. Because it primarily involves the white brain matter, it is considered that epileptic seizures are not frequent in patients with multiple sclerosis.

The latest studies showed more about the brain grey matter involvement from the disease. The study emphasized that there is a connection between the number, localization and the volume of cortical and juxtacortical demyelinating lesion changes and epilepsy (3, 4). A possible an atomic substrate for seizures are the inflammation areas and demyelination in the cortex and the white juxtacortical substance (5). According to the investigatory team lead by Professor Edgar Meinl, the grey brain matter damage in multiple sclerosis is a consequence of the attack in protein Contactin 2 (which is produced by myelin sheath and by neurons of the brain grey matter) by immunological factors (6). For a long time it's been 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 from epileptic attacks appearance in comparison to the general population (8, 9). The prevalence of epileptic seizures in patients with multiple sclerosis changes in studies in Western countries from 1.9 to 7.5% (10, 11, 12).

There are different explanations regarding the appearance of epileptic seizures during multiple sclerosis such as the seizures from demyelization plaques on the cortical or sub cortical regions, the reactive *gliosis*, edema and the damage of Na⁺ K⁺ ATP enzyme activity (8, 9).

The aim of our study is to define the clinical and electrophysiological/imaging profile of epileptic seizures in patients with multiple sclerosis observed in the Neurological Clinical Center in UCC of Kosovo in Prishtina.

MATERIALS AND METHODS

The study is based on the review of the hospital/ stationary documentation of 300 patients with multiple sclerosis who were observed in the Neurology Clinic of UCC of Kosovo in Prishtina during the time period of January 2000 - December 2009. All the patients included in the study have fulfilled the MS McDonald criteria (2010). An inclusive criterion in the study was the epileptic seizures appearance after diagnosing multiple sclerosis, while the patients in whom the epileptic seizures have appeared before being diagnosed with multiple sclerosis and those in whom the seizures have preceded the diagnosis of multiple sclerosis were not included in the study. The exclusion of those patients from the study is done because in those patients we can suppose that etiological factor of seizures or epilepsy is different from multiple sclerosis. Similar criteria of inclusion and exclusion have been employed by the study in India (9).

The epileptic attack diagnosis is set based on the ILAE criteria of 1983 while the attacks have been classified based on the ILAE classification of 1981. In all the patients EEG, brain MRI and the cerebrospinal fluid analyses have been executed. Testing of parametric data was done with T-test and those of non-parametric with Fisher test and X2-test. The difference is significant if P <0.05.

RESULTS AND DISCUSSION

During the study, all the hospital/ stationary documents of 300 observed patients with multiple sclerosis in the Neurological Clinic from the time period of January 2000 to December 2009 were reviewed. Out of these patients, 94 (31.33 %) were male while 206 (68.67%) were female. 49 (16.33%) patients are diagnosed with epileptic seizures. In 23 (47%) of 49 patients, the epileptic seizures appeared after the diagnosis for multiple sclerosis was done, in 6 (12.2%) other patients the epileptic seizures preceded multiple sclerosis diagnosis. As a result this, the 6 patients were not included in the study because they were having positive data about other injuries in their life history of diseases. In 20 other patients or 40.8%, the epileptic seizures appeared before multiple sclerosis diagnosis and they were under antiepileptic treatment. They were excluded from the study too because it can be supposed that etiological factor of seizures or epilepsy is different from multiple sclerosis. Out of 23 patients with epileptic seizures and multiple sclerosis involved in this study, 8 patients or 34.8% were male while 15 patient or 65.2% were female with no significant difference (X2-test =2.13 , P>0.05), (Table 1).

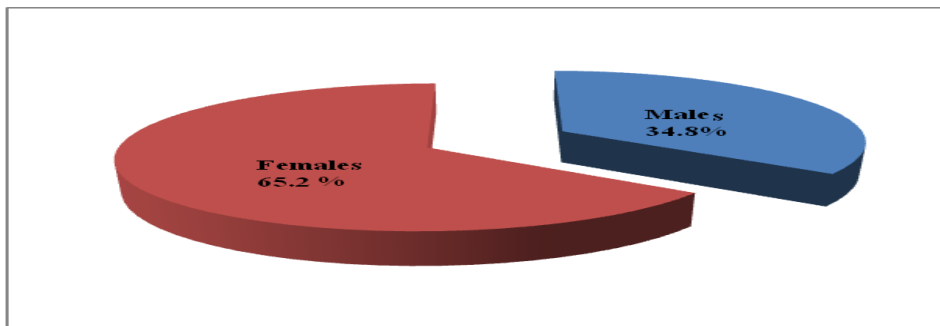
Table 1. The cases of patients at the time of multiple sclerosis appearance according to gender

Gender	Cases	%	X ² -test
Male	8	34.8	X ² =2.13 P=0.144
Female	15	65.2	
Total	23	100.0	

The male/female ratio regarding patients with multiple sclerosis is 1: 1.87 in favor of females according to our study in graph 1.

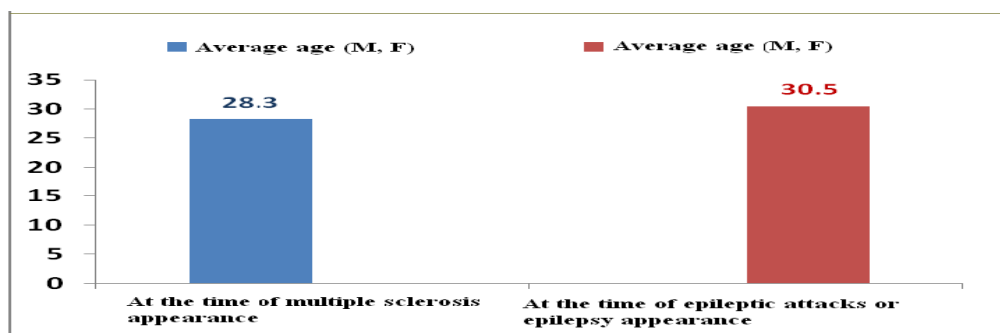
The average age of multiple sclerosis appearance in our study is a bit higher than the study done in Albania which has resulted to be 25.8 years old (13). The average age of epileptic seizures appearance in our study has resulted to be slightly higher compared to those of literature. In females the average age of multiple sclerosis appearance was 26.4 years old (SD ± 4.1) while the average age of epileptic seizures appearance was 28.6 years old (SD ± 1.8) with no significant difference (T-test = 1.91, P=0.06), (graph 3).

Graph1. The number of patients with multiple sclerosis included in the study according to their gender



The average age of multiple sclerosis appearance in the 23 patients was about 28.3 years old (SD ± 4.1) while the average age of epileptic seizures appearance was 30.5 years old (SD ± 1.9), with significant difference (T-test = 2.33, P=0.024), (graph 2).

Graph 2. Patients mean age at MS and seizures onset according to gender

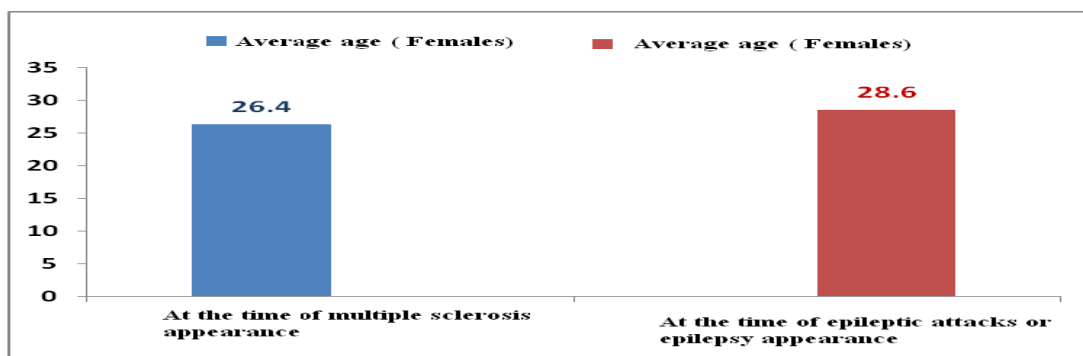


In males the average age of multiple sclerosis appearance was 31.6 years old (SD ± 4.8), whereas the average age of epileptic seizures was 34.1 years old (SD ± 1.9) with no significant difference (T-test = 1.37, P=0.192), (Graph 4).

In 10 (43.5%) of the patients involved in the study, epileptic seizures have appeared during acute relapses of multiple sclerosis while in 13 (56.5%) others the seizures have appeared even during the remission period. Patients with seizures during the improvement period have an EDSS scale considerably higher in comparison to the patients in whom the seizures were manifested mostly during the acute relapses of multiple sclerosis (Table 2). With regard to the frequency of the type of the epileptic seizure, 17 patients (73.9%) had simple partial epileptic seizures while 6 others (26.1 %) had complex partial seizures with no significant difference (Fisher test P>0.05).

EEG findings In 8 patients, changes in EEG was recorded, in 3 out of the 8 patients with changes in EEG, a diffuse slowing of the electro cerebral activity (slow waves in groups) was seen and in 5 there was a slowdown of the electro cerebral activity, localized in frontal and temporal regions (frontal 2 cases, temporal 3 cases).

Graph 3. The graphical presentations of the patients' mean age at the time of multiple sclerosis appearance and at the time of seizures or epilepsy appearance in females



Graph 4. The graphical presentation of the patients' average age at the time of multiple sclerosis appearance and at the time of a seizures or epilepsy appearance in males

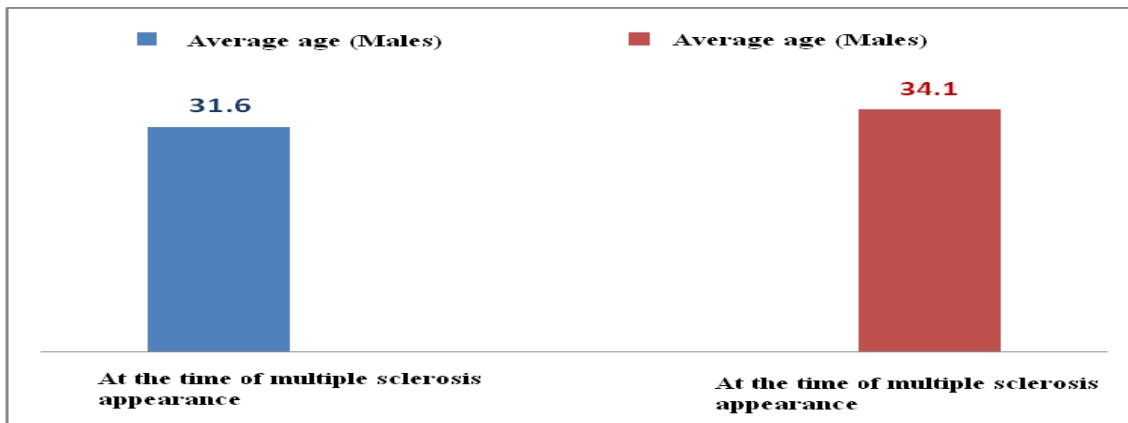


Table 2. Presentation of epilepsy seizures, according to gender and relapses phase

The period of seizures or epilepsy manifestation	Gender		N	Mean EDSS
	F	M		
During acute relapses	7	3	10	About 2
Not considering the stage	8	5	13	About 4
Total	15	8	23	
Fisher test	P>0.05			

MRI findings

An analyzed brain MRI of 10 (43.5%) patients out of 23 in who brain MRI was done within 24 hours after the epileptic seizure occurred. In 6 or 60% of the patients out of 10, the brain MRI showed the presence of demyelinating lesions with juxtacortical localization (figure 1) while in other 4 patients or 40% cortical atrophy was present. However none of the 6 patients with juxtacortical localized demyelinating lesions have shown active plaques in the brain MRI at the time of examination. According to our study, simple partial seizures in patients with multiple sclerosis are about 2.8 times more frequent in comparison to complex partial seizures.

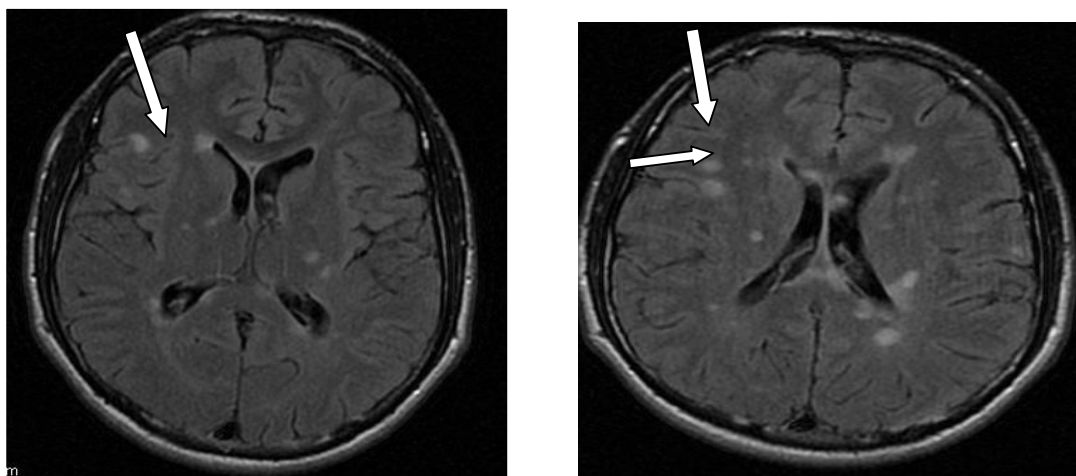
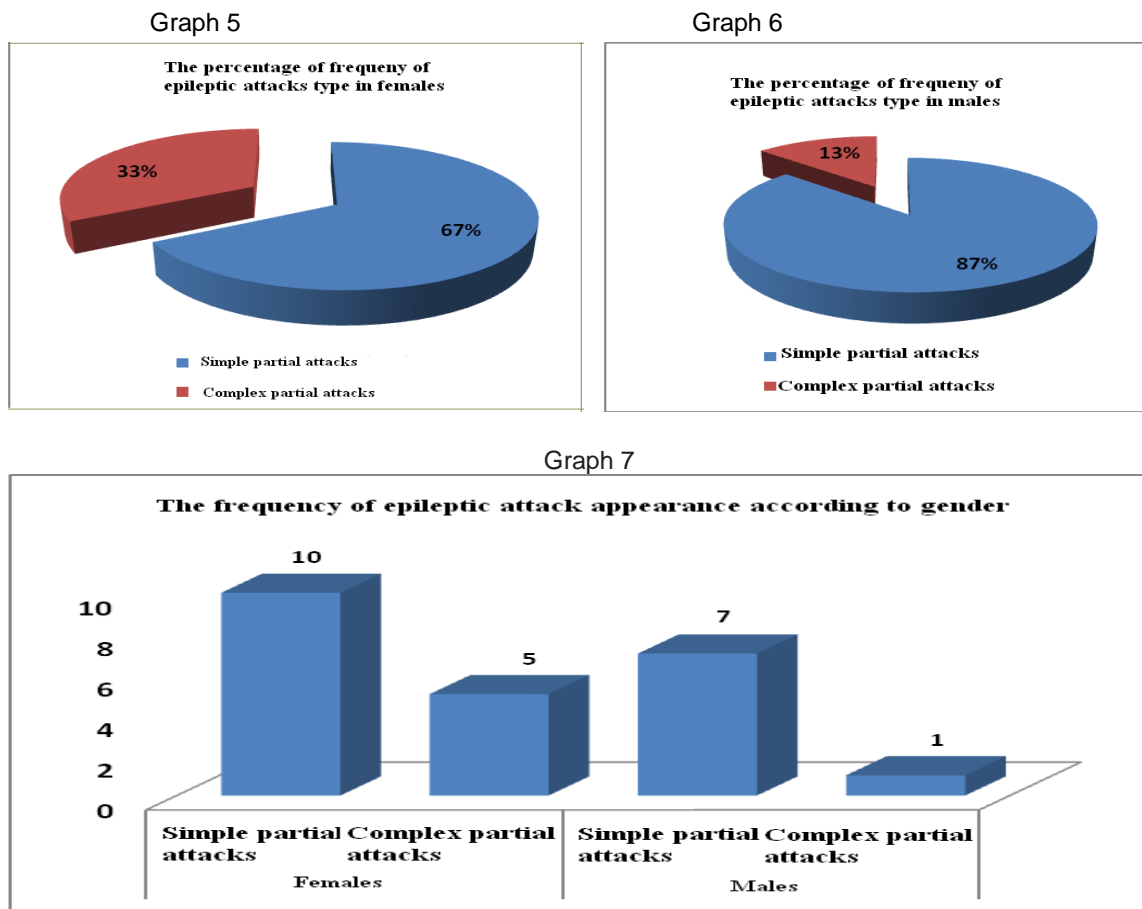


Figure 1 Juxta-cortical localization of demyelinating plaques

In females 67% (10 patients) simple partial seizures are observed, whereas 33% (5 patients) had complex partial seizures. In males however, 87% (7 patients) were identified with simple partial seizures while in 13% (1 patient) the complex partial seizures was diagnosed (Graphs 5, 6 and 7).

Graphs. The complex partial seizures



The analyses of serial studies have shown that the prevalence of appearance of epileptic seizures in patients with multiple sclerosis is disputable. Epilepsy appearance in the general population is about 0.5 to 1 % while the studies over the ratio between epilepsy and multiple sclerosis show a risk 3 to 6 times higher for the appearance of epileptic seizures in patients with multiple sclerosis, compared to the general population (1, 5, and 10).

Despite different theories which tend to give an answer to the appearance of epileptic seizures in patients with multiple sclerosis, so far it has not been documented that it is a consequence of multiple sclerosis.

However, a big number of studies in the world have reported that the incidence of epileptic seizures appearance in patients with multiple sclerosis is higher in comparison to the general population. Out of 23 patients with epileptic seizures and multiple sclerosis involved in this study, 8 patients or 34.8% were male while 15 patient or 65.2% were female with no significant difference (X2-test =2.13 , P>0.05).The average age of multiple sclerosis appearance in the 23 patients was about 28.3 years old (SD ± 4.1) while the average age of epileptic seizures appearance was 30.5 years old (SD ± 1.9), with significant difference (T-test = 2.33, P=0.024)

Our study has shown that in 20 or 87% of patients with multiple sclerosis out of 23 involved in the study, there has been an appearance of epileptic seizures during the acute relapses of multiple sclerosis while in 3 others or 13 % the seizures have appeared regardless of the stage of disease. The average age of multiple sclerosis appearance in women, according to our study is 26.4 years old, (SD ± 4.1) while the average age of epileptic seizures appearance was 28.6 years old (SD ± 1.8) with no significant difference (T-test = 1.91, P=0.06). In males the average age of multiple sclerosis appearance was 31.6 years old (SD ± 4.8), whereas the average age of epileptic seizures was 34.1 years old (SD ± 1.9) with no significant difference (T-test = 1.37, P=0.192).The average of the years of epileptic seizures appearance in women is 2.2 years after multiple sclerosis manifestation whereas in men it is 2.5 years after multiple sclerosis manifestation.

Regarding the frequency of the epileptic seizure type in patients with multiple sclerosis, most studies done in different countries have reported that the frequency of simple partial seizures is about 2.5 times higher than that of complex partial seizures in comparison to the general population where the complex partial seizures are more frequent. In our study,

In our study the frequency of the type of the epileptic seizure showed that, 17 patients (73.9%) had simple partial epileptic seizures while 6 others (26.1 %) had complex partial seizures with no significant difference (Fisher test $P > 0.05$). The simple partial seizures in patients with multiple sclerosis involved in the study are 2.8 times more frequent than complex partial seizures. In females 67% (or 10 patients) of epileptic seizures have simple partial seizures while 33% (or 5 patients) have complex partial seizures. In males 87% (7 patients) have simple partial seizures while 13% (or 1 patient) have complex partial seizures.

CONCLUSION

In Kosovo there is lack of evidence about the prevalence of epilepsy in general population. Therefore, we could not evaluate the rate of the dangerousness of seizures appearance in patients with multiple sclerosis in comparison 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 when it comes to partial seizures in patients with multiple sclerosis. According to the results of our research the prevalence of simple partial seizures is about 2.8 times higher in comparison to the complex partial seizures. Also, in our study it has resulted that the prevalence of complex partial seizures is higher in female patients with multiple sclerosis than in male patients.

Thus, from the results of our study it can be concluded that simple partial seizures have a higher tendency of appearance compared to complex partial seizures in both genders, in females 67% (10 female patients) and in males 87% (7 male patients).

As it can be seen, in female patients with multiple sclerosis the frequency of the appearance of complex partial seizures is higher (33%) than the frequency of appearance in male patients (13%). This ratio is about 1-2.6. So far, no literature or study has been found regarding the frequency of the partial epileptic seizures type in patients with multiple sclerosis according to gender. Therefore, there can be no comparisons made and it cannot be said that the conclusion drawn in our study is accurate. This issue may remain important to be investigated in the future so that the conclusion we drew can be proven right or wrong.

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