



Comorbidities in Multiple Sclerosis, Results of a Retrospective Algerian Study

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ABSTRACT

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS). It usually affects young adults and can have dramatic consequences on the functional, emotional and financial course of the patient's life. Comorbidities are common in MS patients. This combination of pathologies causes a decrease in quality of life and long-term disability, further worsening the prognosis of MS.

We carried out a retrospective study of the files of 137 patients followed for MS, all forms combined, in specialized consultation at the Neurology department of the University Hospital Mustapha Pasha, during the period between the year 2000 and 2018.

The results obtained show that certain comorbidities are more frequent in patients with multiple sclerosis, such as autoimmune pathologies, with a clear predominance of dysthyroidism (19.5%), hypertension and cardiovascular disorders (12.03%), ophthalmic diseases (9.77%), psychiatric disorders (depression, anxiety, psychosis, etc.) (7.5%) and epilepsy (5.26%).

Several parameters can be affected in the event of association of one or more comorbidities such as diagnostic latency, clinical presentation of MS, acceleration of disability progression, increased mortality and reduced quality of life.

Comorbidities complicate the management of patients with multiple sclerosis and have a real impact on their health as well as on the social and economic aspects of their lives. Consequently, a multidisciplinary approach to this pathology and better monitoring remain mandatory.

Keywords: multiple sclerosis, comorbidity, diagnosis delay.

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS). It generally affects young adults, and can have dramatic consequences on the functional, emotional and social course of the patient's life [1]. It is characterized by intermittent, recurrent and focal episodes of CNS demyelination caused by an inflammatory process initially affecting the myelin sheath and secondarily the axon [2].

Environmental, genetic and epigenetic factors play a causal role in MS, potentially interacting with other modifiable risk factors.

Comorbidities are common in MS patients. This combination of pathologies is at the root of reduced quality of life and long-term disability, further worsening the prognosis of MS. Depression, anxiety, cardiovascular disease, epilepsy, metabolic disease, gastroenterological disease and autoimmune disease are the most common comorbidities.

These pathologies are an added problem for clinicians treating MS, as they can delay diagnosis and management, but also worsen prognosis. Consequently, a multidisciplinary approach and rapid recognition of the conditions most frequently associated with MS are essential for rapid diagnosis and effective treatment. Both can be directly or indirectly affected by these diseases.

Objectives

- Identify the comorbidities most frequently associated with MS.
- Identify the frequency of the various associated conditions and compare them with data from literature series.
- Investigate the potential effects of these comorbidities on MS (delay in diagnosis, acceleration of disability progression, possible increase in mortality and reduction in quality of life).

Methods

This is a retrospective study of patients with MS treated at the Neurology Department of Mustapha Pacha Hospital, during the period from 2000 to 2018. All forms of MS were included (relapsing-remitting, progressive and secondarily progressive).

All patients included met the clinical and radiological diagnostic criteria for MS (McDonald 2017 criteria) [3].

Several parameters were studied during this analysis, in addition to comorbidities:

- Demographics, including patient age and gender,
- clinical form of MS,
- time to diagnosis,
- The degree of disability assessed by the Expanded Disability Status Scale (EDSS) [4] at the time of diagnosis.

Results

137 cases of patients with comorbidities were studied out of 706 patients diagnosed with MS between 2000 and 2018 at Mustapha Pacha Hospital: 18.8% of patients had at least one comorbidity at the time of diagnosis. Among these cases, 4 pediatric forms were reviewed but did not present any comorbidity at diagnosis or in the 2 years following diagnosis.

The average age of the patients was 39.9 years, with extremes ranging from 6 to 60 years. The sex ratio was 1 man to 3.7 women on average.

In our series we noted a clear female predominance (79.70%), more marked indeed in autoimmune diseases (100%), hypertension (87.5%) and psychiatric diseases (80%). A male predominance was observed in epilepsy (55%) and gastroenterological diseases (66%). In cases of thyroid pathology associated with hypertension, we noticed that women were much more affected, whereas in cases of epilepsy or gastroenterological disease, the difference was much less noticeable.

The majority of patients had a relapsing-remitting form (73%), 10% had a secondarily progressive form and 17% a primary progressive form.

The frequency of the relapsing-remitting form also differed according to the associated comorbidity, being very marked in associations with autoimmune diseases (80.76%), psychiatric illnesses (90%) and epilepsy (70%), and less marked in associations with diabetes (60%), cancer (1/3 of cases) and cardiovascular disease (50%).

Diagnosis time averaged 45.46 months for all cases and comorbidities, with extremes ranging from 5 months for autoimmune pathologies to 75 months for diabetes.

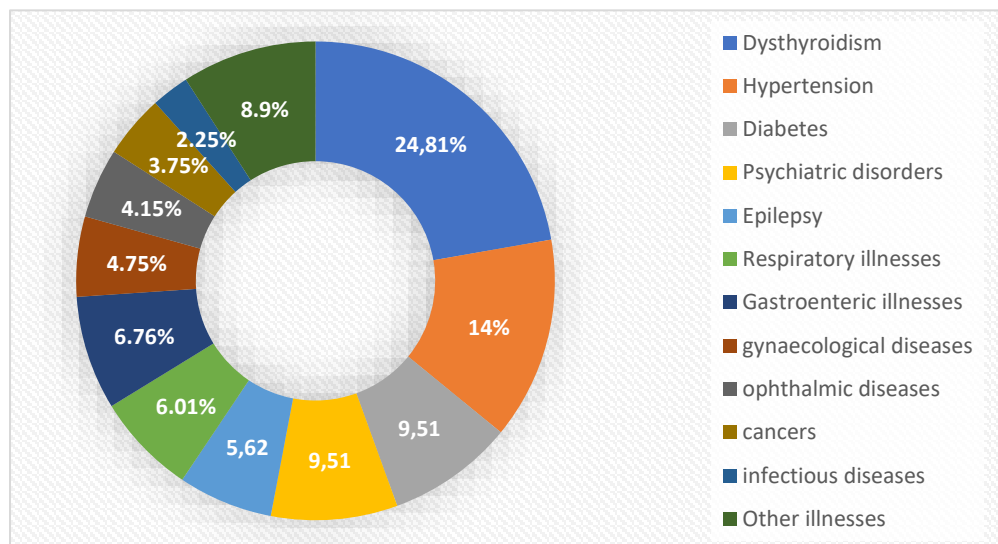


Fig 1: Proportion of different comorbidities

In terms of comorbidities, MS was associated primarily with autoimmune pathologies (24.81%), with a clear predominance of dysthyroidism (19.54%). In second place were cardiovascular pathologies such as hypertension (14%), diabetes and psychiatric disorders in third place (9%). Epilepsy, gastroenteric diseases and respiratory illnesses are less frequent.

The median age at diagnosis is 39.9 years.

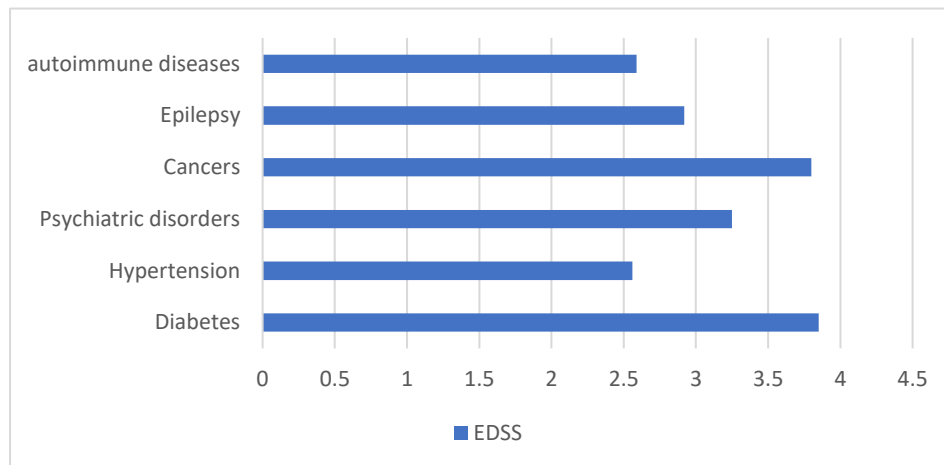


Fig 2: EDSS score for each comorbidity

Disability in the disease is estimated by the average EDSS clinical score at diagnosis, and is highest in diabetes (EDSS= 3.85), psychiatric disorders (EDSS = 3.25) and cancer (EDSS =3.8), and lowest in autoimmune disorders (2.59), hypertension (2.56) and epilepsy (2.92).

Discussion

Comorbidities are common in the multiple sclerosis population, and play an important role in delaying diagnosis, clinical presentation, disability progression and the rate of medical referral. The relationship between multiple sclerosis and comorbidities is complex, and may be due to a direct causal relationship, common risk factors or a secondary and fortuitous association. The study of comorbidities may lead to a better understanding of the common etiological factors of these coexisting pathologies as well as the pathophysiological mechanisms, which could provide us with indications of protective factors against multiple sclerosis.

In this study, of the 706 patients diagnosed with MS, 137 (18.8%) already had at least one comorbidity at the time of diagnosis, which is lower than the data found in the main studies which describe an average prevalence of 50% of comorbidities in MS patients. This may be explained by the inclusion of much more frequent and less objective parameters such as fatigue, anxiety and constipation [17]. The time interval between the onset of comorbidities and the diagnosis of multiple sclerosis is difficult to determine, but it has been shown that the presence of comorbidities delays the diagnosis of MS and consequently increases the degree of disability at that time [5].

The median age at diagnosis is 39.9 years, which is slightly older than the average age described in the majority of studies (38.2 years) [3].

A higher median age is associated with cardiovascular comorbidities such as hypertension (45 years), diabetes (36 years), and autoimmune diseases (39 years). On the other hand, a younger age is more frequently associated with comorbidities such as epilepsy (30 years) and psychiatric diseases (30 years).

The delay of diagnosis in cases with 1 or more comorbidities is 46 months (4 years on average), which is relatively close to the literature with an average delay of diagnosis of 6.03 years [5]. In our series, this latency is more marked in diabetes (74.8 months), which could be explained by confusion over sensory disorders linked to diabetic neuropathy. It is followed by autoimmune diseases (49 months) and cancer (38 months), which could also be explained by the side effects of cancer chemotherapy, which sometimes overshadow MS symptoms.

Comorbidity present at the onset of MS may be associated with the clinical phenotype of the disease, and may affect therapeutic decisions and disease prognosis. Muscular weakness of one or more extremities is seen mainly in autoimmune disease and hypertension in our series, optic neuritis is found most often in psychiatric illnesses; while as regards sensory disorders, they are seen most in diabetes.

In terms of comorbidities, MS is associated primarily with autoimmune pathologies (24.81%), with a clear predominance of dysthyroidism (19.54%). This is not consistent with the literature, where psoriasis (7.74%) is in the foreground, followed by dysthyroidism (6.44%) [1]. Our results are probably compatible with an environmental factor specific to the Mediterranean region.

Psychiatric disorders (depression, anxiety, psychosis, etc.) and epilepsy are also frequently associated. In some cases, these pathologies are considered a complication directly linked to MS, or even present as a form of early disease presentation [16]. In addition to patients with epilepsy at the time of MS diagnosis, 4.25% of patients develop epilepsy, usually of the focal type, during their lifetime, which is much more frequent than the general prevalence in the non-MS population of 0.5% [11, 12].

A 2016 Canadian study of 1,6803 patients reported depression as the main comorbidity in 19.1% of MS patients, followed by hypertension at 15.2%, chronic lung disease (12.1%) and anxiety (11.1%) [6]. This study not only demonstrated the significant prevalence of comorbidities in MS patients, but also the absence of these comorbidities in 116638 non-MS control subjects who were matched in age, sex and geographic location with the MS patients studied.

Another 2016 Danish study revealed that anxiety and depression were more prevalent in MS patients than in controls 2 years before diagnosis. [7] Several studies have reported high rates of depression in MS, with around 50% of patients experiencing depression at some point during the course of their disease [13]. This may be secondary to the CNS lesions encountered during MS, in reaction to the chronic course of the disease, or a possible side effect of certain MS treatments [15]. Depression is also a major aggravating factor in fatigue and cognitive impairment, underscoring the vital importance of its management. [14].

The prevalence of comorbidities seems to increase significantly with age compared with the non-MS population, and their impact is particularly felt in elderly patients, in whom the presence of comorbidities is associated with modified disease activity, worsened disability (EDSS score), increased mortality and, above all, a deterioration in quality of life. [5]

In the North American Research Committee on Multiple Sclerosis (NARCOMS) registry, 8983 participants self-reported their comorbidities in the year of diagnosis [8]. At diagnosis, 24% reported a medical comorbidity (hypertension, hyperlipidemia, pulmonary disease) and 8.9% a psychiatric comorbidity. After 7 years, 35% had a medical comorbidity and 18% a psychiatric comorbidity. This underlines the increasing frequency of comorbidities as the disease progresses [9].

In this study, none of the pediatric MS patients had a comorbidity at diagnosis or in the 2 years following diagnosis. It has been described that the childhood form may be associated with increased fatigue, cognitive decline, and psychiatric disorders such as depression, attention deficit disorder and hyperactivity, leading to significant difficulties at school [10].

Conclusion

Comorbidities complicate the long-term care and treatment of patients with multiple sclerosis, and have a real impact on their health, as well as on the social and economic aspects of their lives. As a result, a multidisciplinary approach to this pathology and improved medical monitoring are essential. These comorbidities should be a clinical priority, to be detected and evaluated at the patient's first consultation.

Nevertheless, more needs to be done to understand the prevalence and incidence of these comorbidities, and to extend the field of research to a larger population in order to better address the issue, reduce delays in diagnosis, and optimize therapeutic management.

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