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Original Article

Screening for Cochleovestibular Disorders in Multiple Sclerosis: A Study of 100 Patients

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Abstract

Introduction: Multiple sclerosis (MS) stands out as the most prevalent immune-mediated chronic inflammatory ailment affecting the central nervous system. It ranks among the primary causes of non-traumatic disability among the youth. The condition is characterized by the destruction of myelin and the impairment of oligodendrocytes in the brain, cerebellum, brain stem, and spinal cord. Its impact is predominantly observed in young individuals, with a notable prevalence among women. The clinical presentation is diverse and contingent on the affected structures. A definitive diagnosis relies on clinical and paraclinical criteria, assessing dissemination in time and space. Cochleovestibular damage is frequently reported by individuals with MS, either during the disease's course or as an initial presentation. ***Material and methods:*** We conducted a retrospective descriptive and analytical study of 100 patients being followed for multiple sclerosis in the neurology department of the Mohammed VI University Hospital of Marrakech, who underwent screening for cochleovestibular disorders in the otorhinolaryngology and Head and Neck Surgery department of the Mohammed VI University Hospital of Marrakech, over a 2-year period from January 2021 to December 2023. The audiometric evaluation consisted of pure tone audiometry, otoacoustic emissions (OAEs) and auditory brainstem response (ABR). We used videonystagmography (VNG), caloric tests and the Video Head Impulse Test (VHIT) for vestibular assessment. ***Results:*** The mean age of our patients was 32.8 years. Forty-five percent of patients presented with a cerebellar syndrome, 94% with a pyramidal syndrome, 55% with a spinal cord syndrome, 18% with proprioceptive impairment, and 36% with cranial nerve involvement. Among patients with cochleovestibular involvement, 9% had no lesions in the posterior fossa, 36% had lesions in the pontine and cerebellar peduncles, 23% in the cerebellum, 18% in the midbrain, 11% in the medulla, and 3% around the fourth ventricle. Deafness was the predominant symptom in 66% of cases, tinnitus in 46.6% of cases, and rotational vertigo was found in 33.33% of cases. Audiometrically, we performed a pure-tone audiogram for all our patients, showing mild deafness in 40% of cases, moderate in 27%, severe in 6%, and normal in 27% of cases. Acoustic otoemissions were positive in 67% of cases. The results showed that cochleovestibular disorders are common in MS patients and that they are not necessarily associated with lesions of the cochleovestibular nucleus or nerve. ***Conclusion:*** This study represents an innovative initiative in Morocco, carried out by a multidisciplinary team comprising otorhinolaryngologists and neurologists. The findings from this research suggest that multiple sclerosis (MS) may exhibit diverse clinical manifestations throughout its progression, involving various peripheral and central structures, including those linked to cochleovestibular symptoms. The notably high incidence of such disorders observed in this study underscores the necessity for individuals presenting with these symptoms to undergo comprehensive evaluations, encompassing clinical, radiological, and electrophysiological tests, to rule out MS.

Keywords: ***MS, MSVertigo, VertigoTinnitus, Hearing loss.***

Introduction

Multiple sclerosis (MS) stands out as the most prevalent immune-mediated chronic inflammatory ailment affecting the central nervous system. It ranks among the primary causes of non-traumatic disability among the youth. The condition is characterized by the destruction of myelin and the impairment of oligodendrocytes in the brain, cerebellum, brain stem, and spinal cord. Its impact is predominantly observed in young individuals, with a notable prevalence among women [1,2].

The clinical presentation of MS is diverse and contingent on the affected structures. It can manifest as various syndromes, such as unilateral optic neuritis, spinal cord syndrome, pyramidal syndrome, ataxia, sensory impairment, among others. The progression typically involves relapses followed by periods of remission, during which total or partial recovery occurs after a few

weeks. A definitive diagnosis relies on clinical and paraclinical criteria, including magnetic resonance imaging (MRI) and the examination of cerebrospinal fluid, assessing dissemination in both time and space. Moreover, the diagnosis necessitates the exclusion of other potential differential diagnoses. Cochleovestibular damage is frequently reported by individuals with MS, either during the disease's course (49-59% of patients) or as an initial presentation (15% of patients) [3,4]. In 7 to 10% of cases, these symptoms manifest as vertigo (acute vestibular syndrome or paroxysmal positional vertigo), while in 1 to 17% of cases, they present as hearing impairment, specifically of the sudden sensorineural hearing loss (SSNHL) type [5,6]. The impact of these symptoms on quality of life is substantial, with 5% of patients identifying vertigo as the most challenging symptom and 38% reporting a moderate to severe impact based on the dizziness handicap inventory scale [7,8].

Materials & Methods

We conducted a retrospective descriptive and analytical study of 100 patients being followed for multiple sclerosis in the neurology department of the Mohammed VI University Hospital of Marrakech, who underwent screening for cochleovestibular disorders in the otorhinolaryngology and Head and Neck Surgery department of the Mohammed VI University Hospital of Marrakech, over a 2-year period from January 2021 to December 2023. The audiometric evaluation consisted of pure tone audiometry, otoacoustic emissions (OAEs) and Auditory Brainstem Response (ABR). We used videonystagmography (VNG), caloric tests and the Video Head Impulse Test (VHIT) for vestibular assessment.

Inclusion criteria: All patients being monitored for multiple sclerosis (MS) who have provided their consent, regardless of the duration of the disease, clinical form, and type of background treatment.

Exclusion criteria: Patients under the age of 20, those who do not meet the criteria for dissemination in time and space, and patients with cognitive impairment, oculomotor paralysis, or severe visual loss.

Results

The average age of our patients was 32.8 years, ranging from 20 to 62 years. Seventy percent of the patients were female, and 30% were male, with a male-to-female ratio of 3.1. The average disease duration was 27.42 months, ranging from 6 to 264 months. Regarding neurological manifestations, 45% of patients had a cerebellar syndrome, 94% had a pyramidal syndrome, 55% had a spinal cord syndrome, 18% had proprioceptive impairment, and 36% had cranial nerve involvement.

In terms of cochleovestibular symptoms, 55% of patients were symptomatic and 45% asymptomatic (**Figure 1**). Hearing loss was the main symptom in 60% of cases. It was unilateral in 46% of cases and bilateral in 54% (**Table 1**), followed by tinnitus in 46.6% of cases. Rotatory vertigo was present in 34% of cases (**Figure 2**).

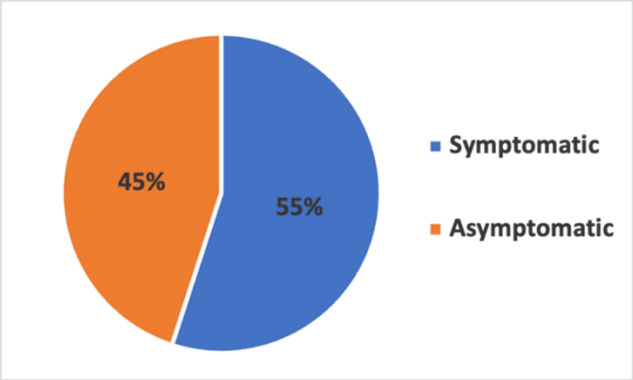

Figure 1: Distribution of patients by symptoms

Table 1: Characteristics of hearing loss

Hearing loss	%
Unilateral	40%
Bilateral	60%

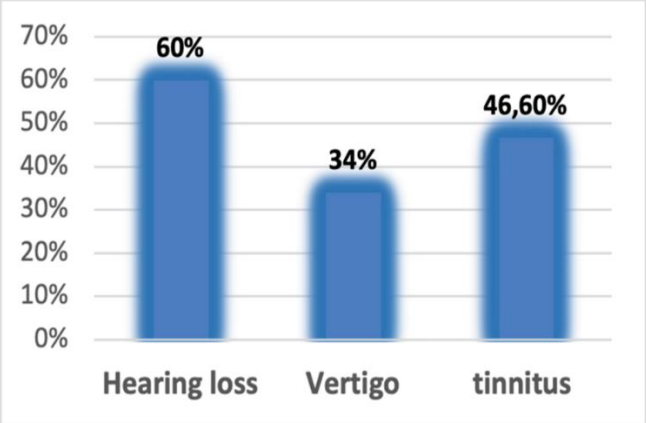

Figure 2: Cochleovestibular manifestations

Vestibular examination showed a positive Romberg in 40% of cases. It was lateropulsion in 70% of cases, multidirectional in 20% of cases and retropulsion in 10% of cases. Nystagmus was found in 42% of cases. It was rotary in 35% of cases, horizontal in 55% of cases and vertical in 10% of cases. Fukuda's test was positive in 20% of cases. Halmaghi's test was positive in 38% of cases.

Audiometrically, we performed a pure tone audiometry for all our patients, it showed mild deafness in 40% of cases, moderate in 27% of cases, severe in 6% of cases and normal in 27% of cases (Figure 3). Otoacoustic emissions were positive in 67% of cases (Figure 4).

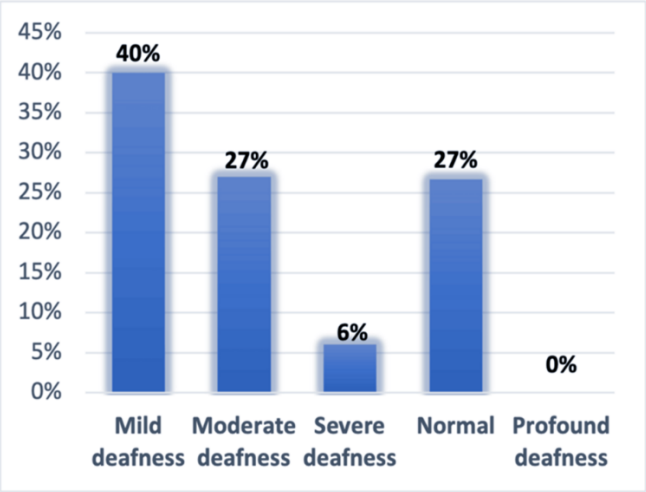

Figure 3: Pure Tone Audiometry Results

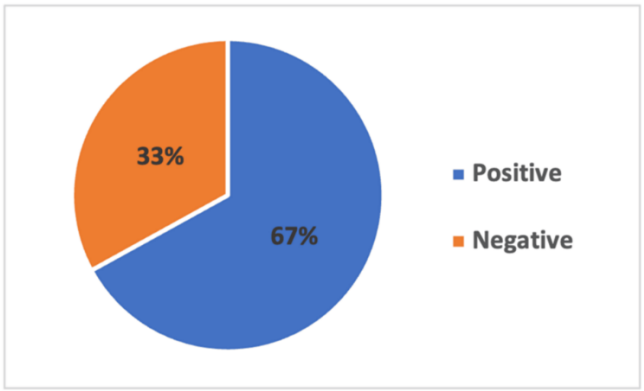

Figure 4: OAEs Results

Brainstem auditory evoked potentials showed an absence of the V wave in 34% of cases, a prolongation of the I-V interpeak interval in 40% of cases and were normal in 26% of cases (Figure 5).

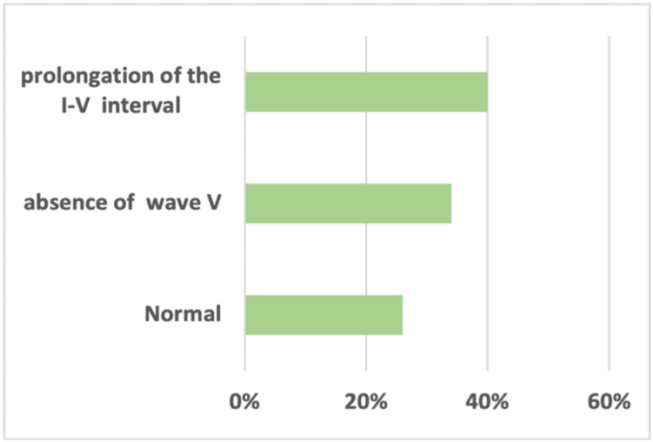

Figure 5: ABR Results

All of our patients have had a videonystagmography. Eye movements were normal in 73%. Square waves were found in 17% of cases and eye flattering in 10% of cases. Slow eye mouvment tracking were steady in 71% of cases and jerky in 29% of cases (Figure 6). Spontaneous nystagmus was found in 36% of cases with suppression on visual fixation in 16 patients. Saccades were present in 60% of cases: hypermetric in 40% of cases, hypometric in 20% of cases.

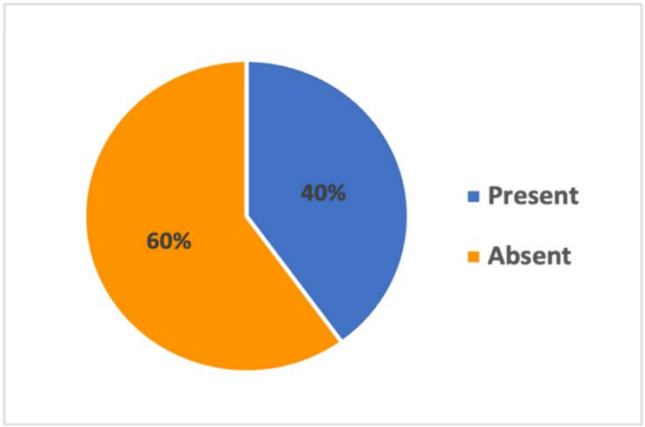

Figure 6: Results of saccades

The optokinetic reflex was abnormal in 66% of cases (Figure 7) with low gain in 50% of cases. Caloric tests had found right- hyporeflexia in 27% of cases, left hyporeflexia in 20% of cases, bilateral hyporeflexia in 13% of cases, right areflexia in 7% of cases and were normal in 33% of cases (figure 8).

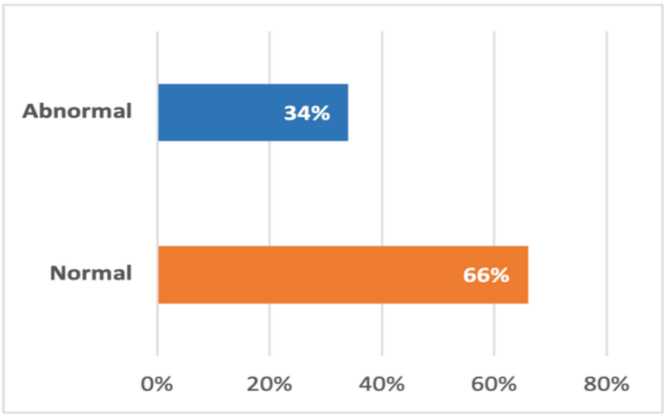

Figure 7: Optokinetic reflex results

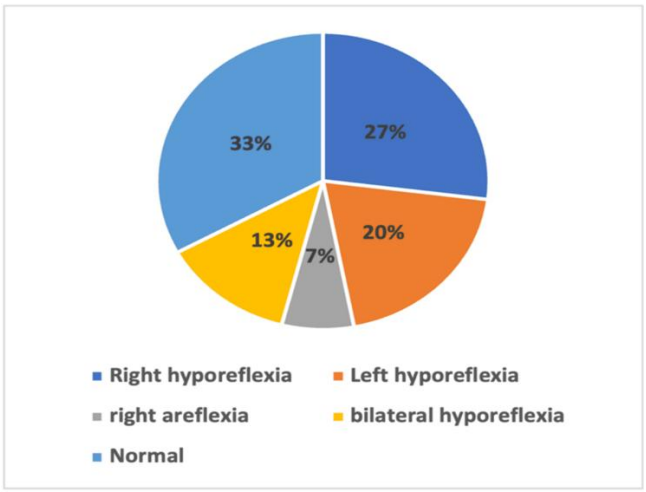

Figure 8: Results of Caloric Tests

VHIT was performed in all of our patients. We found overt-saccades in 32% of cases, covert-saccades in 28% of cases with a low gain in 61% of patients. (Table 2)

Table 2: VHIT Results

Results	Percentage (%)
Overt-saccades	32 %
Covert-Saccades	28%
Low gain	61%
Normal	30%

All patients underwent brain and spinal cord MRI, with 86% of patients having at least one lesion in the posterior fossa, 45% having at least one lesion in the spinal cord, and all patients having multiple lesions in the brain. Among patients with cochleovestibular involvement, 9% had no lesions in the posterior fossa, 36% had lesions in the pontine and cerebellar peduncles, 23% in the cerebellum, 18% in the midbrain, 11% in the medulla, and 3% around the fourth ventricle.

Conventional hearing aid was proposed for 15 patients, 6 of whom had severe hearing loss and 9 of whom had moderate hearing loss. Vestibular rehabilitation has been proposed for 20% of our patients with a good clinical course. In terms of therapeutic management, 45% of patients were treated with azathioprine or cycles of double bolus solumedrol-endoxan, 10% with teriflunomide, 35% with fingolimod, 7% with natalizumab, 2% with rituximab, and 1% with ocrelizumab. 87% of our patients reported an improvement in their cochleovestibular symptoms after therapeutic rehabilitation. 13% of patients had stabilisation of their cochlear sequelae and continued to use their hearing aids with good

evolution. No cases of worsening of symptoms were noted in our study.

Discussion

Multiple sclerosis (MS) is a persistent inflammatory and demyelinating condition marked by focal lesions and widespread neurodegeneration in the brain's white matter. The clinical manifestation of MS is diverse and influenced by the location and course (relapsing or progressive) of lesions within the central nervous system (CNS) [9].

Numerous studies have documented a heightened prevalence of cochleovestibular abnormalities in both symptomatic and asymptomatic individuals with multiple sclerosis (MS), in comparison to healthy controls. While dizziness and vertigo are prevalent symptoms in MS, demyelination is an infrequent instigator of acute vertigo, which is more commonly attributed to peripheral cochleovestibular disorders or stroke. Cochleovestibular disorders can manifest through various symptoms, including vertigo, tinnitus, and sudden hearing loss [10].

Although hearing loss is often linked to central nervous system demyelination, vertigo is typically associated with demyelination of the vestibular nuclei, musculoskeletal weakness, and ocular diseases, rather than issues within the labyrinth or vestibular nerve. Nevertheless, a mounting body of pathophysiological evidence suggests the involvement of the inner ear and vestibulocochlear nerve in hearing loss and vertigo among MS patients. The presence of macrophages in the temporal bones of individuals with autoimmune diseases, even in early disease stages, supports the hypothesis that autoimmune mechanisms in MS may impact the inner ear. Lymphocytes may target hair cells, auditory and vestibular spiral ganglion neurons, resulting in damage that manifests as hearing loss and vertigo. Temporal bone studies have identified M1 phenotype microglia in the cochlea, demonstrating their migration into the internal auditory canal and the inner ear. M1 microglia could potentially demyelinate cochlear and vestibular structures, leading to hearing loss and vertigo. In patients with cochleovestibular symptoms associated with multiple sclerosis (MS), MRI scans typically reveal demyelinating plaques predominantly located in and around the eighth nerve fascicle, medulla, cerebellar peduncles, posterior tegmentum, midbrain, and around the fourth ventricle. These plaques may potentially disrupt the central otolithic connections between deep cerebellar structures and vestibular nuclei [11].

Audiometrically, six published studies have examined pure-tone thresholds in both individuals with multiple sclerosis (MS) and control subjects. The findings have been inconsistent, and the reliability of the data has been questioned. Half of these studies assert that MS has a chronic and negative impact on auditory sensitivity, while the remaining half report no significant adverse effects of MS on this sensitivity. One of the largest case-control studies in this field, indicate that multiple sclerosis (MS) does not exert a chronic influence on pure-tone auditory thresholds. Furthermore, the study corroborates the idea that lesions related to MS in the lower auditory pathways are infrequent, and lesions in higher brain regions are typically not connected to deficits in pure-tone thresholds. This underscores the importance of rigorously controlling basic variables such as sex and age before making inferences about the causal associations between MS and hearing deficits [12].

OAEs assess the activity of outer hair cells in the cochlea and are capable of detecting cochlear damage that may go unnoticed with ABR testing. The examination of outer hair cell function in the context of multiple sclerosis has been a topic of recent discussion, as highlighted by Di Stadio & Ralli [13]. In three studies involving a total of 218 participants (120 individuals with MS and 98 controls), the comparison of OAEs was conducted. Two of the studies reported no significant differences between MS and controls. However, the third study observed weaker responses in MS when compared to healthy controls. ABR are widely used in multiple sclerosis (MS) to assess auditory dysfunction, which is observed in over 50% of patients across both pediatric and adult populations. Thirteen series, investigated ABR involving a total of 881 participants. In 12 out of the 13 studies, Abnormal ABR were reported, including: Prolonged latencies of wave I, III, and V, prolonged interpeak intervals of I-V, absent waves III and V and reduced wave V amplitude. However, brainstem ABR may yield normal results in 30-50% of multiple sclerosis (MS) patients with brainstem-related symptoms or signs [14].

Regarding vestibular symptoms, Vertigo is noted as an initial symptom in 10-20% of multiple sclerosis (MS) patients, as reported in the literature. The frequency of vertigo throughout the disease course is documented at 30%, while non-vertiginous dizziness is reported at a frequency of 60%. Vertigo occurring during the initial relapse of multiple sclerosis (MS) may serve as a potential predictor for the recurrence or persistence of vestibular symptoms throughout the disease's progression. Nonetheless, additional research with more extensive patient cohorts is required to validate this observation [15,16]. In the diagnostic realm, a study involving 16 relapsing-remitting MS (RRMS) patients emphasizes the heightened sensitivity of clinical examination and electronystagmography (ENG) over ultralow-field MRI in assessing brainstem and cerebellar lesions in RRMS patients. Furthermore, the findings underscore the significance of ENG as a more sensitive tool in detecting vestibular system involvement, particularly when neurological examination and MRI results may not fully capture the extent of the pathology in MS patients [17,18].

One of the key purposes in using ENG is to distinguish between peripheral and central vestibular system disorders. In the study of Zeigelboim *et al.* [19], peripheral vestibular disorder was predominantly identified (83.4%) whereas Degirmenci *et al.* primarily observed central vestibular pathology in 83.3% of the cases [20]. These conflicting findings could be attributed to the variations in lesion site within the central nervous system, the severity of impairment, disease development stage, and frequency of relapses. Oculo-vestibular reflex (OVR) abnormalities stand out as among the most common ocular motor irregularities in MS. A diminished OVR gain is frequently associated with bilateral peripheral vestibular lesions or brainstem lesions. However, an unusually high gain of the oculo-vestibular reflex (OVR) is rare and is typically linked to cerebellar lesions. Interestingly, abnormal ENG results can manifest in patients without vestibular symptoms (13.3%), underscoring the high sensitivity of ENG in detecting both symptomatic and asymptomatic cases of MS. Sanders *et al.* reported that ENG can detect 49% of asymptomatic lesions and 84% of symptomatic lesions [21].

The utilization of VHIT in assessing individuals with MS has revealed a higher prevalence of pathological results, as indicated by refixation saccades and reduced VHIT gains, compared to healthy controls. When the VHIT gain value falls below 0.70, it indicates a low VHIT gain, signifying pathology within the vestibular system [22]. Abnormal low VHIT gain was reported in 50% of the cases by Kabel *et al.* [23]. In our study, 61% of the patients had a low VHIT gain. On the other hand, the presence of corrective saccades in VHIT does not necessarily imply vestibular hypofunction. In our study, overt-saccades and covert-saccades were found in 32% and 28% of

the cases respectively. Our results corroborate those of Rambold *et al.* [24] (overt saccades and covert saccades in 34,3% and 13,7% of the cases respectively). In the study of Kabel *et al*. [23], no corrective saccades were reported in MS patients. These findings underscore the potential of VHIT as a valuable tool for detecting vestibular abnormalities in MS patients.

Conclusions

This study represents an innovative initiative in Morocco, carried out by a multidisciplinary team comprising otorhinolaryngologists and neurologists. The findings from this research suggest that multiple sclerosis (MS) may exhibit diverse clinical manifestations throughout its progression, involving various peripheral and central structures, including those linked to cochleovestibular symptoms. The notably high incidence of such disorders observed in this study underscores the necessity for individuals presenting with these symptoms to undergo comprehensive evaluations, encompassing clinical, radiological, and electrophysiological tests, to rule out MS. The limited availability of literature on this topic emphasizes the need for further studies aimed at standardizing the diagnosis, treatment methods, and follow-up procedures for these patients.

Declarations

Author Contributions

The first and second authors contributed equally to this work and share first authorship.

Ethical Considerations

All procedures performed in this study were conducted in accordance with relevant ethical standards and guidelines.

Source of Funding

None

Conflict of Interest

There is no conflict of interest regarding the publication of this paper."

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