

Assessment of vestibulo-spinal reflex function in Multiple sclerosis patients using Computerized Dynamic Posturography

Original
Article

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ABSTRACT

Background: Multiple sclerosis (MS) is a demyelinating autoimmune disease of the central nervous system, with fatigue and impaired upright posture are being important symptoms of the disease. Computerized dynamic posturography (CDP) is an assessment tool for objectively quantifying and distinguishing probable sensory, motor, and cerebral adaptive balance control deficits.

Objective: This study aims at evaluation of findings of computerized dynamic posturography in multiple sclerosis patients with dizziness.

Patients and Methods: This study included 70 participants, 40 who were MS patients and 30 healthy adult volunteers as controls. All participants were subjected to history taking, otological examination, basic audiological evaluation, bedside examination of the dizzy patient, and computerized dynamic posturography (CDP).

Results: Of the 40 Multiple sclerosis patients 80% had abnormal Equilibrium (EQ) pattern and 72.5% had abnormal Sensory Analyses (SA) ratios. (*p-values*= 0.012 and 0.049 respectively) with the abnormalities were mainly vestibular dysfunction.

Conclusion: Multiple sclerosis patients showed a smaller equilibrium scores in all conditions and composite scores, visual ratio, vestibular ratio and preference ratio than those of the control group and the abnormalities were mainly vestibular dysfunction. And we recommend the use of computerized dynamic posturography in the assessment of functional disability in MS patients.

Key Words: Equilibrium, Multiple sclerosis, Posturography, Vertigo.

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INTRODUCTION

Multiple sclerosis is the most frequent non-traumatic debilitating disease that affects young people^[18]. Multiple sclerosis is becoming more common and prevalent in both developed and developing countries^[6], the root cause of which is still unknown. Multiple sclerosis is a complex disease in which multiple genes, as well as several environmental factors, such as vitamin D or ultraviolet B light (UVB) exposure, Epstein–Barr virus (EBV) infection, smoking and obesity, all contribute to disease vulnerability^[3].

It has long been thought of as a two-stage disease, with early inflammation causing relapsing–remitting MS (RRMS) and delayed neurodegenerative stage causing non relapsing progression, it is known as secondary and primary progressive MS^[8,21]. So there are three types of multiple sclerosis: 1) relapsing–remitting MS (RRMS), 2) primary progressive MS (PPMS), and 3) secondary progressive MS (SPMS).

Females are more likely to get MS, and the ratio of females to male in most developed countries is currently close to 3:1 (Female: Male)^[26]. Smoking increases the risk of MS by nearly 50%^[27].

MS is distinguished pathologically by perivenular inflammatory lesions that lead to demyelinating plaques^[16]. Inflammation causes oligodendrocyte damage and demyelination. In the early stages of the disease, axons are relatively preserved; nevertheless, as the disease advances, irreversible axonal damage develops^[31]. In RRMS, the 'classical active lesion' with profound lymphocytic inflammation predominates. It is less common in progressive disease, where lesions have an inactive core of the lesion surrounded by a narrow rim of activated microglia and macrophages^[28].

Remyelination occurs at all stages of the disease, but is most common in progressive disease^[20]. Secondary progressive MS patients have higher levels of demyelination and a decrease in axonal density in the

normal appearing white matter in the cervical spinal cord in primary progressive MS patients (PPMS)^[30]. When a person presents with a clinically isolated syndrome (CIS), MS is usually suspected. Depending on the location of the significant lesion (s), this can be monosymptomatic or polysymptomatic. Optic neuritis, brainstem and spinal cord syndromes are the most common presentations; nevertheless, there are numerous other less common presentations, including cortical presentations such as dominant parietal lobe syndromes^[9].

Vertigo, balance problems, and the presence of nystagmus are frequently observed as early presentations of multiple sclerosis^[1]. Different types of positional nystagmus (rotatory and vertical), spontaneous, and caloric hyperreflexia may also be seen in MS patients^[12]. Dizziness, including postural intolerance, has been found to affect 49–59% MS patients^[22], and 75–82 percent of mild to moderately disabled subjects have balance problems^[7]. These symptoms have been related to sensory deficits in the visual, vestibular, and proprioceptive pathways^[7]. Moreover, poor integration of these sensory cues along the subcortical and/or cortical areas has been associated with impaired balance performance^[10].

CDP is a balance test that assesses the person's ability to maintain balance by using visual, vestibular, and somatosensory inputs independently, as well as suppressing or compensating for inaccurate or challenging sensory information. This necessitates the integration of accurate sensory input as well as the proper execution of motor control. When the body is displaced, automatic postural responses (that are not under volitional control) control the immediate motor control of balance. Ankle, hip, stiffening, counterbalance, step, and grab responses are the postural responses^[23,25]. The CDP is divided into two sections: sensory organization tests (SOTs) and motor coordination tests. The method is based on a sensory and motor balance control model which includes: (a) orientation inputs from the visual, vestibular, and somatosensory systems; (b) central integrating mechanisms for selecting functionally appropriate orientation sense(s); (c) functionally appropriate movement strategy(s) under a variety of task conditions; and (d) motor output mechanisms for generating timely and correct postural movements^[5,24].

It is most useful in situations where quantitative balance is required to determine whether a disorder is improving or worsening, or the response to treatment^[14]. CDP is recommended for use in the assessment of patients complaining of disequilibrium or vertigo based on patient population publications.

As MS affects balance and postural control and this may be due to delayed somatosensory conduction, we aimed in our study at evaluating the findings of computerized dynamic posturography in multiple sclerosis patients with dizziness.

PATIENTS AND METHODS:

2.1. Subjects

The present study comprised 70 adult subjects of both genders, aged 20–45 years. Subjects were divided into two groups. The study group included 40 multiple sclerosis (MS) patients whose Expanded Disability Status Scale (EDSS) score^[19] was 4 or less and not in relapse, and who had dizziness with or without vertigo. They were age and sex matched to 30 healthy individuals with normal hearing as a control group. The study group was compared to the control group. The study was approved by the Research Ethical Committee and Otolaryngology department council of Faculty of Medicine, Cairo University, registration number 1-530315. Written informed consent was given by all subjects for participation in the study, and tests were performed in the audiology unit of the ENT department, Kasr Al-Ainy hospital, Cairo university. The study took place from March 2016 to March 2020. Exclusion criteria were patients with peripheral vestibular disorders including benign paroxysmal positional vertigo (BPPV), postural hypotension, general diseases causing peripheral neuropathy such as diabetes, critically ill patients, patients with impaired cognitive function and/or psychiatric disorder, or if the MS patient was in relapse.

The patients were all on disease modifying therapy and none of them was on steroid therapy as no one of them was taken during an attack.

2.2. Methods

This investigation was a cross-sectional, case-control study. All participants were subjected to 1) History taking, including a full assessment of the dizziness/vertigo complaint. 2) Full general and neurological examination and EDSS scoring^[19]. MS patients in the current study were fully ambulatory without aid according to EDSS score. 3) Otologic examination, including otoscopy and tuning fork tests. 4) Bedside examination of the dizzy patient to confirm the central origin of the complaint and to exclude peripheral vestibulopathy, including Romberg test and sharpened Romberg test. Fukuda stepping test. Gait examination and tandem walking. Test for spontaneous nystagmus to detect unidirectional horizontal nystagmus to exclude peripheral vestibulopathy, and to detect any rotatory or vertical nystagmus or direction changing nystagmus suggestive of central lesion. Head thrust test. Head shaking test to detect any post head shaking nystagmus (HSN) to exclude chronic unilateral peripheral vestibulopathy and detect any abnormal HSN result reflecting central vestibulopathy. Cover test of skew deviation to detect any vertical misalignment of the eyes. Gaze testing to detect any gaze-evoked nystagmus, suggestive of central

lesion. Dix-Hallpike and Roll positioning tests to exclude BPPV. 5) Video-nystagmography (VNG) using VNG equipment (Micromedical Corp, USA) to exclude peripheral vestibular lesions and detect any oculomotor tests or gaze abnormalities, including spontaneous or gaze-evoked nystagmus. Oculomotor testing (saccade, smooth pursuit, and optokinetic (OPK) tests). Positional testing, to exclude BPPV. Caloric test to exclude peripheral vestibulopathy. 6) Sensory organization test (SOT) of the computerized dynamic Posturography (CDP) testing using "Balance Master NeuroCom Equitest": to assess vestibulo-spinal reflex function: The SOT procedure requires the subjects to stand (with bare feet) on a pressure-sensitive, dynamic tilted force plate facing a sway-referenced visual surround while strapped into a safety harness to prevent injury in the event of a loss of balance. Before each section of the trial, the patients were given instructions detailing what would follow. Each test comprised 3 trials for each of the 6 conditions representing different aspects of balance. For condition 1, the subject's eyes were open, and the force plate remained in a fixed position. This condition assessed baseline postural stability under normal circumstances. For condition 2, the subject's eyes were closed, and the force plate remained in a fixed position. For condition 3, the subject's eyes were open, the force plate remained in a fixed position, and the visual surround was tilted. For condition 4, the subject's eyes were open, the force plate tilted, and the visual surround remained upright. For condition 5, the subject's eyes were closed, and the force plate tilted. For condition 6, the subject's eyes were open, the force plate tilted, and the visual surround tilted. For each condition, an equilibrium score (ES): 1-6 was calculated that quantifies the center of gravity sway or postural stability under each of the 3 trials of the 6 sensory conditions. The scores were based on the amount of anterior-posterior sway compared to the maximal theoretical sway limits of stability (8.5° anterior and 4° posterior). The score was calculated by the following formula: $ES = \{12.5^\circ - (\theta_{\max} - \theta_{\min})\} / 12.5^\circ \times 100\%$. In this formula, θ_{\max} indicated the greatest anterior-posterior sway displayed by the subject and θ_{\min} indicated the least anterior-posterior sway. A score of 100 represented perfect balance (no sway), and a score of 0 represents a potential fall (sway exceeded limits of stability). If at any time during the test, the subject took a step or required the assistance of the safety harness, the subject scored a 0 for that test. An average score was calculated for each of the 6 conditions and a composite equilibrium score was calculated as a weighted average of all 6 individual scores with each of the first 2 conditions carrying a weight of 1/14 and each of the other 4 conditions carrying a weight of 3/14. These weights were specified by the manufacture to reflect the difficulty levels of the 6 tasks. Sensory analysis ratios were also used to identify possible impairments of individual sensory systems: a) The somato-sensory ratio (condition 2/condition 1), b) The visual ratio (condition 4/condition 1), c) The vestibular ratio (condition 5/condition 1) assessed the ability to use input from each sensory

system to control balance and d) The visual preference ratio (condition 3 + 6/condition 2 + 5) assessed the extent upon which a subject relies on visual input to control balance, even when the visual information was incorrect.

2.3. Statistical measures

Data collected from the control group and the cases was coded, entered, and analyzed using Microsoft Excel 2010 software and then imported into SPSS (Statistical Package for Social Science) version 19.0 for analysis. Description of variables was presented as follows. Quantitative variables were in the form of mean and standard deviation (SD); qualitative variables were in the form of numbers and percent. According to the type of data, a Mann–Whitney U-test and Chi-square test with least significance difference were performed to test for significant differences. Pearson's correlation test was used to determine correlations between individual results. Differences were considered statistically significant at $p < 0.05$.

RESULTS:

3.1. Posturography results

The study included 40 patients with MS, 29 (72.5%) females, and 11 (27.5%) males with a mean age of 29.9 ± 7.2 , ranging from 23.0 to 45.0 years. The control group included 30 healthy participants, 15 (50%) female and 15 (50%) males, with a mean age of 29.8 ± 5.4 , ranging from 24.0 to 44.0 years. Groups were matched regarding age and gender ($p = 0.945$; $p = 0.080$) respectively. The mean MS duration was 5.3 ± 3 years, ranging from 1 to 15 years; 39 (97.5%) of patients were under treatment. The mean EDSS score was 1.9 ± 2 , ranging from 0 to 4 with a median of 1.6.

Regarding the clinical symptoms: 40 (100%) had dizziness, 22 (55%) had vertigo, and 8 (20%) had dysarthria. MS patients with brainstem symptoms only: 5/40 (12.5%); those with cerebellar symptoms only: 14/40 (35%); those with combined cerebellar and brainstem symptoms: 15/40 (37.5%); and those without any cerebellar or brainstem symptoms: 6/40 (15%).

Regarding MRI findings: MS patients with brainstem only MRI lesions were 10 (25%), those with cerebellar only MRI lesions were 9 (22.5%), those with brainstem and cerebellar lesions were 9 (22.5%), while other MRI lesions (juxtacortical, periventricular, and pericallosal) were found in 12 (30%).

There were statistically significant differences (P -value < 0.05) between MS group and control group regarding EQC1, EQC2, EQC3, EQC4, EQC5, EQC6, visual ratio, vestibular ratio, preference ratio and composite score (Table 1).

The majority of MS patients had abnormal EQ (80%) and SA ratios (72.5%). SOM ratio was abnormal in 5%, VIS ratio was abnormal in 30%, VEST ratio was abnormal in 65% and VIS PREF Ratio was abnormal in 17.5%. The composite score was abnormal in 77.5% in MS patients. Figure 1 and table 2 show EQ deficits and affected sensory analyses.

An example of posturography of a case of MS in our study is shown in Figure 2.

Our study showed that there was no statistically significant difference ($P\text{-value} > 0.05$) among MS patients with different lesions on MRI regarding posturography findings. Also, there were no statistically significant differences ($p\text{-value} > 0.05$) between MS patients with and without vertigo, and between MS patients with and without brainstem symptoms, and between MS patients with and without cerebellar symptoms, as well as between MS patients with and without brainstem and cerebellar symptoms regarding posturography findings

Table 1: Comparison between MS patients and their controls according to equilibrium scores, composite scores and sensory analysis ratios.

		Control (n = 30)	MS (n = 40)	U	p
EQC1	Mean ± SD	95.24 ± 2.40	88.47 ± 8.62	124.50*	<0.001*
	(Min-Max)	(90.30 – 98.60)	(42.50 – 96.0)		
EQC2	Mean ± SD	92.76 ± 3.26	82.14 ± 15.79	135.50*	<0.001*
	(Min-Max)	(82.30 – 97.60)	(0.0 – 94.50)		
EQC3	Mean ± SD	90.21 ± 4.47	79.35 ± 16.50	226.50*	<0.001*
	(Min-Max)	(81.30 – 98.60)	(0.0 – 94.0)		
EQC4	Mean ± SD	85.69 ± 5.26	68.11 ± 18.94	118.00*	<0.001*
	(Min-Max)	(77.30 – 98.40)	(0.0 – 92.0)		
EQC5	Mean ± SD	68.06 ± 14.76	37.76 ± 26.27	128.50*	<0.001*
	(Min-Max)	(0.0 – 92.40)	(0.0 – 74.0)		
EQC6	Mean ± SD	69.71 ± 8.79	29.33 ± 24.05	44.00*	<0.001*
	(Min-Max)	(55.30 – 90.10)	(0.0 – 71.66)		
SOM ratio	Mean ± SD	97.45 ± 3.13	93.02 ± 16.85	474.00	0.135
	(Min-Max)	(84.67 – 101.1)	(0.0 – 118.42)		
VIS ratio	Mean ± SD	89.75 ± 5.49	76.06 ± 20.78	268.50*	<0.001*
	(Min-Max)	(80.30 – 102.1)	(0.0 – 97.71)		
VEST ratio	Mean ± SD	71.19 ± 15.40	41.98 ± 29.23	220.50*	<0.001*
	(Min-Max)	(0.0 – 97.80)	(0.0 – 82.45)		
PREF ratio	Mean ± SD	94.65 ± 19.03	90.72 ± 26.92	400.00*	0.018*
	(Min-Max)	(0.0 – 114.0)	(0.0 – 184.76)		
composite score	Mean ± SD	79.17 ± 5.82	57.43 ± 14.96	64.50*	<0.001*
	(Min-Max)	(71.0 – 92.0)	(13.0 – 79.0)		

*p-value is statistically significant

Table 2: Equilibrium deficits findings affected sensory analyses ratios, and abnormalities in MS patients.

	MS patients (n=40)	
	No.	%
Equilibrium deficit		
Normal (no deficit)	8	20
Visual preference/vestibular dysfunction pattern	2	5
Visual /vestibular dysfunction pattern	11	27.5
Severe dysfunction pattern	5	12.5
Vestibular dysfunction pattern	11	27.5
Visual preference pattern	3	7.5
Sensory analysis (affected sensory ratios)	No.	%
Normal SA ratios	11	27.5
Abnormalities	No.	%

VEST	14	35.0
VIS	1	2.5
PREF	1	2.5
VEST / SOM	0	0.0
VEST /VIS	7	17.5
VIS / PREF	1	2.5
SOM / VEST/ PREF	2	5.0
VIS / VEST/ PREF	3	7.5
Abnormalities	No.	%
SOM ratio	2	5
VIS ratio	12	30
VEST ratio	26	65
PREF ratio	7	17.5

NB. Numbers are not mutually exclusive as a patient in the group can have multiple abnormalities (i.e. numbers are not representing the total group numbers in either group).

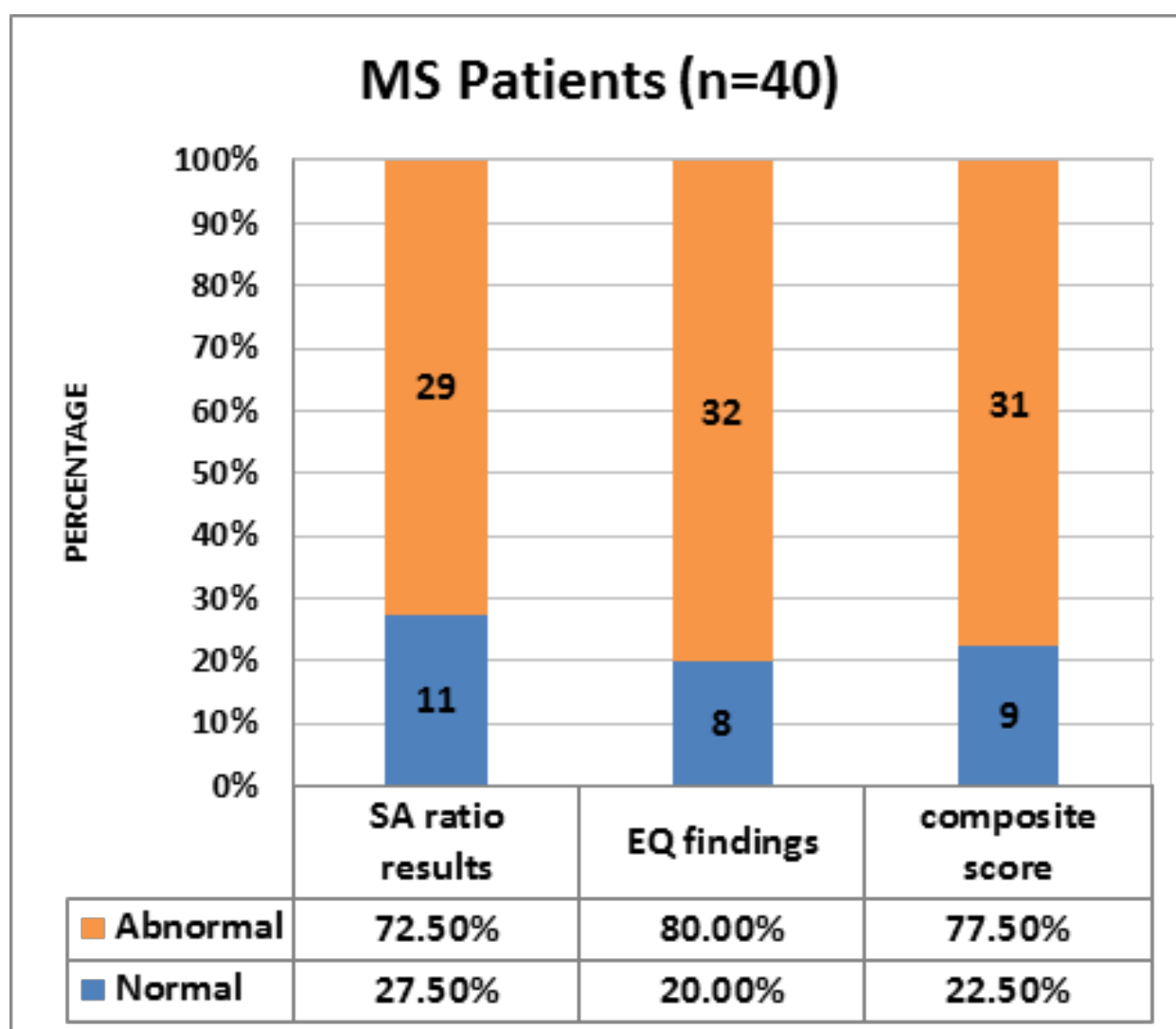


Fig. 1: The Distribution of the percentage of abnormalities in equilibrium (EQ) and sensory analyses (SA) findings and of composite score abnormalities in MS patients

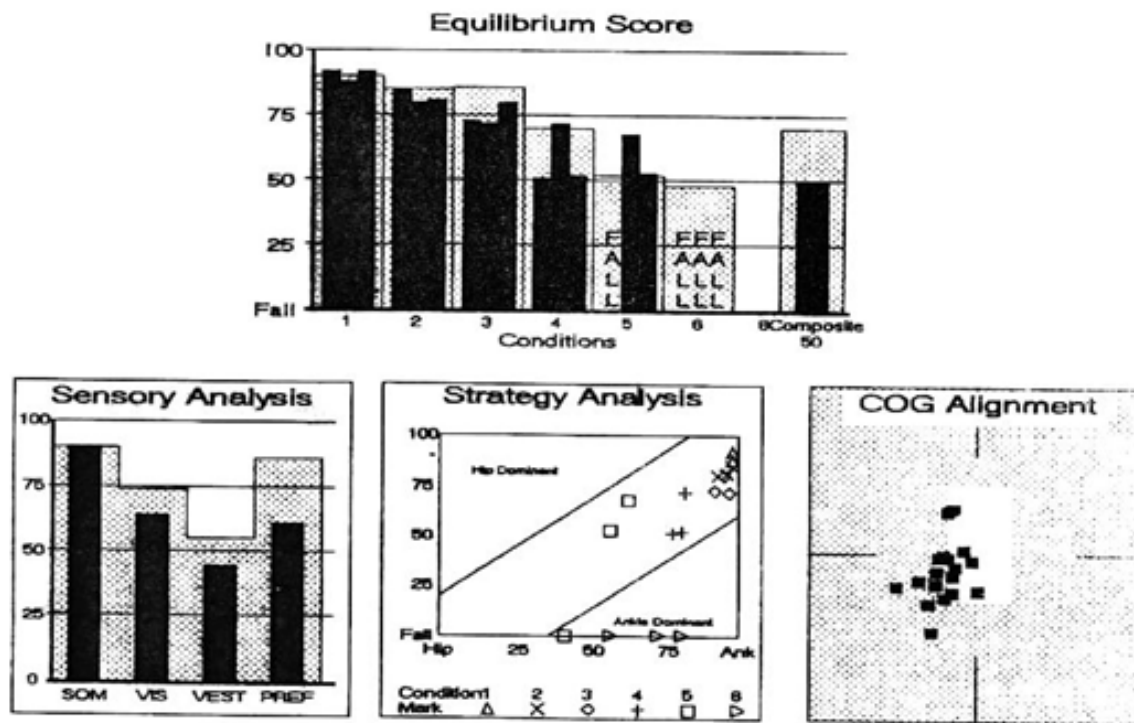


Fig. 2: Posturography of a case of MS

3.2. Correlation between duration of MS and Posturography in MS patients was studied and it was not significant (Table 3).

Table 3: Correlation between duration of MS and Posturography in MS patients (n=40).

Posturography		Equilibrium Conditions scores						SENSORY ANALYSES				
		EQC1	EQC2	EQC3	EQC4	EQC5	EQC6	Composite score	SOM ratio	VIS ratio	VEST ratio	PREF ratio
Duration of MS	r	0.094	-0.029	-0.058	0.201	-0.212	0.082	-0.005	-0.081	0.154	-0.236	0.303
	p	0.562	0.858	0.722	0.213	0.19	0.613	0.977	0.619	0.343	0.143	0.057

3.3. Oculography findings

Oculographic abnormalities were found in all MS patients (Table 4): abnormal saccades in 35 (87.5%), abnormal OPK test results in 31 (77.5%), abnormal smooth pursuit in 26 (65%).

Table 4: Oculographic abnormality in MS patients

Oculographic abnormality	No.	MS (n= 40)
Abnormal	40	100.0
□ Saccades	35	87.5
□ OPK	31	77.5
□ Pursuit	26	65.0

- N.B: OPK: Optokinetic

3.4. Gaze evoked nystagmus, Central Spontaneous nystagmus and Test of skew findings

Gaze evoked nystagmus were found in 6 (15%) of the MS patients, central spontaneous nystagmus in 7 (17.5%), and test of

skew was positive in 3 (7.5%). Gaze evoked nystagmus, Central Spontaneous nystagmus and Test of skew results in MS patients were studied as shown in table 5.

Table 5: Gaze evoked nystagmus, Central Spontaneous nystagmus and Test of skew findings in MS patients (n=40).

	No.	%
Presence of Gaze evoked nystagmus	6	15
Presence of Central Spontaneous nystagmus	7	17.5
Positive Test of skew	3	7.5

DISCUSSION

In the present study, MS patients showed a statistically significant smaller equilibrium scores in all conditions (EQC1, EQC2, EQC3, EQC4, EQC5, EQC6) and composite scores than those of the control group. MS patients also showed a statistically significant smaller visual ratio, vestibular ratio, preference ratio than those of the control group.

Stability was normal in only 8 patients (20%) of the present study. The majority of MS patients had EQ abnormalities (80%), and SA ratios abnormalities (72.5%). EQ abnormalities were mainly Vestibular dysfunction pattern alone (27.5%) and Combined Visual / vestibular dysfunction pattern (27.5%), while combined Visual preference / vestibular dysfunction pattern (5%) , Visual preference pattern only in 7.5% of cases, and Severe dysfunction pattern only in 5% of cases. SA ratios abnormalities were mainly VEST ratio affection alone in 35% of cases, and combined with VIS ratio affection in 17.5%, while combined with VIS and VIS PREF ratios affection in 7.5% of cases and combined with SOM and VIS PREF ratios affection in 5% of cases. However, VIS affection alone VIS PREF alone or combined, each was rare (in 2.5%) of cases.

As MS can affect any area of the central nervous system, when a number of systems affected may contribute to loss of balance control. And the more systems damaged the more balance dysfunction which will give more abnormality in posturography findings.

Alpini *et al.*^[2] studied the characteristics of MS patient stance control disorders, measured by means of posturography and they found that stability was normal in only 7 patients (18.4%). Stability in MS patients was lower with the eyes closed standing on foam pads. And this agreed with our study.

Fritz *et al.*^[11] studied the impact of dynamic balance, static balance, sensation, and strength measures to walking in individuals with MS. They found that all measures were significantly abnormal in MS subjects when compared to age and sex-matched norms ($p < 0.05$ for all). Also, these results agreed with our results.

Grassi *et al.*^[13] assessed balance performances of 17 adults with MS and 13 age-matched healthy controls using both perturbed (PT) and not-perturbed (NPT) postural tests. There were no significant differences between groups for all indices when subjects performed NPTs. Conversely, significant differences in postural indices between MS and their controls emerged during PTs. And these results agreed with ours.

Also, Atteya *et al.*^[4] evaluated 50 ambulatory individuals with MS [42 RRMS and 8 secondary progressive (SPMS)] for balance using quantitative Berg balance scale (BBS) and Biodex stability system (BSS). There was a statistically significant difference between the patient and their 20 healthy controls assessed by BBS. According to BSS, MS group showed more sway in the three limits of stability (mediolateral, antero-posterior, and overall) when compared to the control group, which agree with our results.

We found comparable posturography results between MS patients with and without vertigo, and between MS patients with and without brainstem symptoms, and between MS patients with and without cerebellar symptoms, as well as between MS patients with and without brainstem and cerebellar symptoms.

Alpini *et al.*^[2] observed clinical and/or MRI evidence of brainstem involvement in 21 of 38 (55.3 %) of patients. They found no relationship between general stability or weight distribution index and clinical signs of brainstem involvement. This agreed with our results. Kalron *et al.*^[15] found non-significant differences for all posturography parameters (with eyes open and closed) between MS patients with and without cerebellar symptoms. And this agreed with our results.

In our study MS patients with different MRI lesions showed comparable posturography results. This coincided with the results of Alpini *et al.*^[2] who found no relationship between general stability or weight distribution index and MRI brainstem lesions.

We found that no significant correlation between duration of MS and Posturography in MS patients.

Oculographic abnormalities of MS patients were abnormal saccade in 35 patients (87.5%), abnormal optokinetic in 31 patients (77.5%) and abnormal pursuit in 26 patients (65%). In MS patients, 6 patients (15%) had gaze evoked nystagmus, 7 patients (17.5%) had central spontaneous nystagmus and 3 patients (7.5%) had positive skew deviation.

In comparison, Kenig *et al.*^[17] found that 65% of MS patients had abnormal saccadic test and smooth pursuit test, abnormal optokinetic test was recorded in 60% of patients, presence of vertical nystagmus component in 30 patients (75%) and spontaneous nystagmus in 10% of patients. Servillo *et al.*^[29] found that skew deviation was recorded in (13.5%) of MS patients and gaze evoked nystagmus in (13.5%) of patients.

CONCLUSION

MS patients showed a statistically significant smaller equilibrium scores in all conditions and composite scores and smaller visual ratio, vestibular ratio, preference ratio than those of the control group. Stability was normal in only 20% patients and 27.5% had normal sensory analyses ratios. The abnormalities were mainly vestibular dysfunction. And we recommend the use of computerized dynamic posturography in the assessment of functional disability in MS patients.

CONFLICT OF INTEREST

There are no conflicts of interest.

LIST OF ABBREVIATIONS

BPPV	Benign paroxysmal positional vertigo
COG	Center of gravity
CDP	Computerized dynamic posturography
EBV	Epstein–Barr virus
EQ	Equilibrium
EDSS	Expanded Disability Status Scale
MS	Multiple sclerosis
OPK	Optokinetic
PPMS	Primary progressive MS
RRMS	Relapsing–remitting MS
SPMS	Secondary progressive MS
SA	Sensory Analyses
UVB	Ultraviolet B light
VNG	Video-nystagmography

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