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Frequency of ocular manifestations in multiple sclerosis patients admitted in tertiary care hospital in Saudi Arabia

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Abstract. – OBJECTIVE: Multiple Sclerosis (MS) is one of the most destructive demyelinating diseases of the nervous system, and it manifests through broad involvement of the visual system. The present study was aimed to evaluate the frequency of ocular symptoms among MS patients admitted to the Kingdom Hospital in Saudi Arabia

PATIENTS AND METHODS: This is a cross-sectional study aiming at investigating the prevalence of eye disease among MS patients referred to Hawtat Sudair Hospital, Zulfi General Hospital, Majmaah General Hospital, and Kingdom Hospital in Riyadh (Saudi Arabia) from January 2020 to December 2020. The sample size was made of 100 MS patients including 50 males and 50 females, all presented with eye disorders. The data were analyzed with SPSS 25, Chi-square test, and descriptive statistics.

RESULTS: The examined patients included 100 patients with MS symptoms aged 35 years, ranging from 20 to 70 years. The results showed a considerable lack of sharpness of vision among patients (80%), and the rate of double vision was reported to be about 49% among them which was the most prevalent vision problem from the onset of the disease until the examination time.

CONCLUSIONS: The achieved data from this study demonstrated that multiple sclerosis could cause eye diseases. Initial recognition of this syndrome provides the possibility of having an appropriate evaluation of patients to clinicians. Moreover, after the prevalence of MS, other ocular symptoms may occur consequently.

Key Words:
Multiple sclerosis (MS), Neurologic manifestations, Double vision.

Introduction

Multiple sclerosis (MS) is a common disease of the central nervous system in youth, during which ocular problems are common. By inflaming the grey and white matters of the central nervous system, this chronic disease can disrupt the myelin, a fatty substance that provides insulations and protection for nerve cell fibers in the optic nerve, spinal cord, and the brain[1]. This inflammation is due to the intravascular penetration of lymphocytes and monocytes, which causes multiple ulcers (sclerosis). Although ocular problems are frequently seen throughout the MS course, they are more common in the early stages of the disease. Clinical diagnosis of MS consists of two episodes: central nervous system involvement in two or more regions over time and clinical proof of existing two or more lesions in distinct sites inside the myelin-coated regions of the central nervous system[2].

MS pathogenesis remains unknown. It has complex pathophysiology consisting of environmental factors, genetic susceptibility, and developing an immune-mediated pathologic response and causes focal inflammatory infiltrations, axonal loss, and focal myelin destruction[2]. Ethnic origin and geographic location are two important factors influencing the prevalence of MS. Recent research has reported high rates of MS worldwide[3]. However, the underlying factors of this increase in incidence are still unknown. Some of the main neurological signs and symptoms of MS include urinary disorders, blurred vision, ataxia, increased tendon reflexes, motor and/or sensory dysfunction, and brain stem symptoms (impaired speech, double vision, dizziness). This study aimed to investigate the prevalence of initial clinical symptoms in patients with MS [4]. MS causes various signs and symptoms in patients, including psychiatric, neuro-ophthalmologic, and neurologic manifestations either alone or in combination. These signs and symptoms can be seen similarly in both familial and sporadic MS.

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Table I. Age group and sex distribution of patients and their living place in this study.

Age group	Female	Male	Total
20-30	8	4	12
30-40	23	6	29
40-50	21	13	34
50-60	14	6	20
60-70	3	2	5
Total	69	31	100

Two main categories of neuro-ophthalmologic manifestations of multiple sclerosis can be distinguished: those affecting the ocular motor system and the visual sensory system[5].

Patients and Methods

This cross-sectional study evaluated the prevalence of ocular symptoms in patients with MS from January 2020 to December 2020. The participants in this study were 100 patients with confirmed MS disease who were admitted at the Hawtat Sudair Hospital, Zulfi General Hospital, Majmaah General Hospital, and Kingdom Hospital in Riyadh (Saudi Arabi). The information collected was performed using questionnaires as study tools. Before the study, written informed consents were obtained from the patients.

In this study, the Multiple Sclerosis Knowledge Questionnaire (MSKQ) was used for newly diagnosed MS patients, a self-assessed questionnaire with 25 items on general MS knowledge[6]. The questionnaire had two parts. The first part involved demographic information of patients, including age, sex, living place, the history of patient's family, the age of disease onset, and the history of systemic disease. The second part included particular oculist questions to examine patients' eyes, including examination of the slit lamp, external ocular muscles, fundoscopy, visual acuity evaluation, and Ishihara's color vision test.

Statistical Analysis

The collected data from 100 samples were coded and analyzed in a computer using SPSS V28 software (SPSS Inc., IBM, Armonk, NY, USA).

Results

Based on the collected data, the participant in this study included 100 MS patients aged from 20 to 70 years (with a mean age of 35 years). Fifty percent of the participants (50 people) were female, and the rest (50 people) were male, with 74% (74 people) living in urban areas. According to the data collected from the questionnaires, about 20% of patients had a history of MS in their families. Blurred and double vision were the most common vision complaints reported by MS patients with 75% and 55%, respectively. Moreover, the most prevalent findings in ocular examinations were optic nerve atrophy (ONA) and optic neuritis (ON), both of which with 10% (Table I). On the other hand, the most prevalent neurological complications were paresthesia and hypoesthesia with 80% frequency, followed by weakness with 65% frequency.

According to the results, about 10% of patients were observed with daily cluster headaches as the most prevalent systemic disease (Table II). Eye problems were the first symptoms of the disease in 50% of males and 25% of females, neurological problems were found in one-third of patients, and 15 patients showed both neurologic and eye prob-

Table II. Systemic diseases associated with multiple sclerosis (MS) diseases.

Disease	Percentage by gender		Total percentage
	Female	Male	
Cluster headache	4	5	9
High blood pressure	6	4	10
Binocular vision problem	3	2	5

Table III. Neurological symptoms associated with multiple sclerosis (MS).

Symptoms	Percentage by gender		Total percentage
	Female	Male	
Paresthesia and hypoesthesia	43	41	84
Skin paresthesia	40	30	70
Hypoesthesia	21	24	45
Depression	35	25	60
Problems with urination	18	19	37
Eyestrain or ocular fatigue	35	45	80
Dizziness	26	19	45
Lhermitte's Sign	15	10	25

Table IV. Prevalence and percentage of eye demonstrations in patients with multiple sclerosis (MS).

Symptoms	Percentage by gender		Total percentage
	Female	Male	
Blurred vision	43	35	78
Double vision	26	31	57
Eye Pain	19	17	36
ON	11	10	21
Optic nerve pallor	8	7	15
Anomalous color vision	4	6	10
Oculomotor Dysfunction	2	1	3

lems. Neuropathy with 49% frequency and paresthesia and blurry vision with 47% frequency were the most common symptoms in the early stages of the disease. Although double vision problem was more frequent in the older patients, nystagmus syndrome was less prevalent in patients over 35 years old. Uhthoff syndrome was more common in females, while optic nerve atrophy was observed mainly in males aged 20-25 years. All the differences in the studied syndromes between males and females were statistically significant (Tables III, IV).

Patients between the ages of 20 and 40 showed higher rates of color vision deficiency than other age groups. Inflammation disorders (i.e., oculomotor dysfunction, achromatopsia, and optic neuritis) were more common in patients living in non-urban areas with fewer facilities. In addition, patients with a history of multiple sclerosis in their families were at higher risk of developing internuclear ophthalmoplegia disorders. According to the achieved data, at least 25% of participants in this study showed eye problems, including uvea inflammation, oculomotor dysfunction, optic nerve pallor, ON, and acute ON. Male participants living in non-urban areas were at higher risks of these eye symptoms (Table V).

Table V. Prevalence of eye demonstration and its relationship with age groups of study.

Age groups	Eye disorders (%)						
	Blurred vision	Eye pain	Uhthoff syndrome	ON	Double vision	Optic nerve pallor	Anomalous colour vision
20-30	51	18	21	18	18	10	4
30-40	60	31	17	9	38	10	8
40-50	59	34	20	8	33	2	2
50-60	41	19	18	4	25	0	1
60-70	32	27	19	6	17	1	0
p-value	0.724	0.213	0.419	0.112	0.0002	0.065	0.149

Discussion

The general purpose of this study was to determine the frequency of the distribution of ocular and neurological symptoms in MS patients and its relationship with demographic characteristics and disease characteristics. This study is aimed to determine the distribution rate of ocular and neurological symptoms in MS patients and the factors that may affect it. Based on recent studies, the possibility of the development of MS among women is likely to be twice as much as men. In line with the data achieved from the present study, the average age of onset is approximately 34 years[7]. As observed from the present study, about one-fifth of patients had a family history of MS. This result is in line with those reported by Simpson et al[8], who stated that family history of MS is also relevant as there is a genetic predisposition to the disease. Moreover, various viral infections, environmental stressors, and the possibility of connecting with sick individuals should be explored.

In our study, we decided to select the same number of females and males randomly with MS disease while only 20% of them have a family history of MS. For instance, recently, it was reported that the ratio of patients with MS disease varies based on individuals' geographical locations[9]. On the other hand, the ratio of females to males may be 2 to 1 to indicate the influence of genetic and environmental factors. Similarly, it has been reported that common eye problems are relatively common in people with multiple sclerosis and can include blurred sight, double vision, and vision loss[9]. Here we found that one-quarter of MS patients suffer from clinically diagnosed unilateral or bilateral internuclear ophthalmoplegia. The most common symptoms include blurred vision, diplopia, oscillopsia, loss of stereopsis, and reading fatigue, and convergence typically remains intact[10]. Similarly, in our study, more than half of MS patients were detected with blurred sight.

Another prevalent complaint among our study participants was the blurred vision reported by three-fourth of them. In a similar study by Balcer et al[10], it was reported that the vision changes in MS are recognizable when they produce diminished vision or blurred vision. Consequently, there may be a wide variety of visual problems caused by MS, that individuals may also experience some related side effects, such as eye pain and dizziness. In addition, a recent study reported that optic neuritis (ON) is one of the most presenting features in up to one-fifth of MS patients and occurs in up to half of patients with MS[12]. In line with these achievements, our study proved that ON and optic nerve atrophy (ONA) were two of the most prevalent ocular findings in the examination.

The clinical profile for MS needs symptomatic disease activity over time that could be confirmed using an objective neurological examination[13]. In our study, hypoesthesia and paresthesia, and weakness are reported to be among the most prevalent neurological problems among patients. In a similar study by Kataria et al[14], it was reported that subjects with multiple sclerosis may also experience speech impairment, numbness or numbness of limbs, and difficulty walking. Additionally, they reported that the most prevalent symptoms are numbness, numbness or tightness, pain, motor abnormalities, and visual disturbances[13]. Our study revealed that one of the most prevalent systemic diseases was daily cluster headaches. A similar study reported that both headache and MS were associated with the functional or structural alterations of the brainstem and cortex[15]. This suggests a shared anatomical foundation for the comorbid association between MS and headache.

Based on the data achieved from the present study, it was observed that neuropathy and blurry vision were the most prevalent initial symptoms associated with MS. However, patients with double vision symptoms were higher in older patients than in middle-aged ones. This is in line with the results presented by Owsley[16]. A study reported that induced torsional nystagmus and static ocular torsion enhanced significantly from the fourth to the sixth decade and then diminished at the beginning of the seventh decade[17]. Our data showed that in the third and fourth decades' nystagmus syndrome was less prevalent. Based on the data presented by Park et al[18], the happening possibility of Uhthoff's phenomenon among MS patients is higher in comparison with other optic neuropathies or disorders of afferent pathways. Different factors such as fever, exercise, premenstrual period, sauna, hot shower, sun-tanning, psychological and physical stress, and even smoking have been stimulating factors for Uhthoff's phenomenon[19]. In this study, the differences among men and women based on both these syndromes were statistically significant. In line with the results of our study, Bajracharya et al[20] showed that optic atrophy was nearly equal in incidence in both females

and males and common above the fourth decade of life. Moreover, they showed that its most common cause was glaucoma. Additionally, they reported that non-glaucomatous optic atrophy may also be common, and several other causal factors should be considered.

Another factor associated with MS progression is high blood pressure introduced by Hubbard et al[21]. Another study from Israel worked on risk factors for heart disease in MS patients and revealed that patients with high blood pressure symptoms are at greater risk for their disability to get worse. Anyway, individuals with these symptoms will take longer to reach certain disability signs than those who did not have such symptoms. In line with these results, our study showed that one-tenth of patients with MS suffer from the systemic disease of hypertension.

More than four-fifth of MS patients suffer from paresthesia and hypoesthesia as the most prevalent neurological symptoms. This is just according to the results achieved by Ghasemi et al[22], who showed that during MS, inflammatory attacks on myelin and nerve fibers occur. The central nervous system (CNS) lesions caused by activated immune cells could generate visual impairments symptoms, fatigue, numbness, and tingling, disorders of the intestinal and urinary system, muscle stiffness, and amnesia. Nearly 10% of MS patients are diagnosed with primary progressive MS (PPMS) that could affect the spinal nerves. Moreover, the same study reported that the risk of brain lesion among MS patients is lower than others[22]. However, it cannot be ignored that walking problems, weakness, stiffness, and trouble with balance are common in MS.

A similar study found that progressive relapsing, as the least common type of MS, occurred in almost 5% of patients. They further reported some of the main symptoms associated with this disease as double vision, pain in the eyes, depression, dizziness, and intestinal, sexual, and urinary system dysfunction. In general, MS is more common in the age group of 20-40 years old. However, about 2-10% can occur in people over 50 years old and less than 1% in childhood[23]. The present study results are consistent with previous research that reported dizziness in about half of patients with MS.

Lhermitte's sign, a neurological condition related to multiple sclerosis, was observed in 25% of MS patients in our study. Some studies indicated that over one-third of MS patients will show Lhermitte's sign, sometimes as a demonstration sign. However, this disorder is not MS specific and can occur in the case of any abnormalities in the cervical spinal cord, causing impingement on a disc or active inflammation. Lhermitte's sign can also occur in the case of cervical spondylosis, vitamin B12 deficiency, etc. To detect the underlying cause, an MRI may be administered. MS patients usually experience Lhermitte's sign as a form of neuropathic pain[24]. Several studies have reported blurry vision and double vision as two common disorders in MS patients. Nystagmus and diplopia are the most common eye movement problems in MS patients, especially those older than 40 years. The results of our study showed that the prevalence of double vision in MS patients was significantly associated with age, which is in line with the findings of previous studies.

Conclusions

Recent progression in neuro-ophthalmology has led to the development of visual systems that allow better study and evaluation of the pathogenesis and novel therapeutics for multiple sclerosis. Our study showed that ocular disorders are frequent in MS patients and are often considered the initial manifestations of this disease. In line with the results of other studies, our research also found that vision disorders are very common in patients with MS. Vision disorders are affected by several factors, including sex, age, family background, and residence. As a result, the demographic characteristics of these patients should be considered in their initial examinations. Our results showed some differences in the initial clinical manifestations of MS patients in comparison with previous studies. Accurate evaluation of the initial clinical symptoms of MS requires further epidemiological studies in the future. Although optic neuritis was found as the most common manifestation in our study, it should be noted that other ocular manifestations might also be present before or at the same time as this disease. Since vision disorders are well common in MS patients, those with vision complaints such as double vision and blurred vision should be screened for MS disease.

Conflict of Interest

The author declares that he has no conflict of interests.

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