

## Exploring The Prevalence And Nature Of Ocular Manifestations In Multiple Sclerosis Patients: A Retrospective Analysis In Jordan

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### Abstract

**Background:** Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system that often affects the visual pathway. Ocular manifestations, such as optic neuritis and diplopia, may serve as early disease indicators. Despite their clinical significance, data from the Middle East, particularly Jordan, are limited. The objective of this research paper is to determine the prevalence and nature of ocular manifestations among Jordanian MS patients and explore their demographic and clinical associations. A retrospective cross-sectional study was conducted on **409 MS patients** with available demographic and clinical records. Variables included age, gender, MS subtype, age at onset, relapses, comorbidities, and ocular symptoms. Descriptive statistics summarized baseline characteristics. Prevalence was estimated using binomial tests with 95% confidence intervals (CI). Associations with categorical variables were analyzed using chi-square or Fisher's exact tests, while continuous outcomes were assessed with t-tests or Mann-Whitney U tests, depending on distribution. Logistic regression identified independent predictors. Ocular manifestations were reported in 38% of patients (95% CI: 33.5–42.8%,  $p < 0.001$ ). Patients with ocular symptoms had a significantly younger mean age at onset (26.6 vs. 32.4 years,  $p < 0.001$ ). Gender ( $p = 0.015$ , Cramér's  $V = 0.12$ ) and MS subtype ( $p = 0.048$ , Cramér's  $V = 0.14$ ) were associated with ocular symptoms in univariate analysis but lost significance in multivariate models. Logistic regression confirmed younger onset age as the only independent predictor (OR 0.94, 95% CI: 0.92–0.96,  $p < 0.001$ ). In conclusion, ocular manifestations are common among Jordanian MS patients, particularly those with younger disease onset. These findings emphasize the need for baseline ocular screening in MS care and call for prospective multicenter studies to validate and expand on these results.

**Keywords:** Multiple sclerosis; Ocular manifestations; Optic neuritis; Visual symptoms; Jordan; Prevalence; Predictors.

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## INTRODUCTION

Multiple sclerosis (MS) is a chronic immune-mediated disorder of the central nervous system that results in inflammation, demyelination, and neurodegeneration. It represents one of the leading causes of neurological disability among young adults, with an estimated global prevalence of approximately 2.8 million cases (Wallin et al., 2019). While the clinical presentation of MS is heterogeneous spanning motor, sensory, and cognitive symptoms ocular involvement is particularly significant. Visual disturbances such as optic neuritis, diplopia, blurred vision, and nystagmus are not only debilitating but frequently represent the initial presentation in MS, occurring in a notable proportion of cases (Toosy et al., 2014).

Ocular manifestations of MS have been extensively studied in Western cohorts. Notably, the landmark Optic Neuritis Treatment Trial (ONTT) found that optic neuritis occurs in up to 50% of MS patients and serves as the initial clinical event in around 20% of cases (The Optic Neuritis Study Group, 2008). More recently, a population-based study documented that ocular motor disturbances and nystagmus contribute significantly to the visual burden of MS population-wide (Kraker et al., 2024a). These findings underscore the diagnostic and pathological importance of the visual system in MS.

Despite this global knowledge, Jordan lacks region-specific data, and more broadly the Middle East remains underrepresented in ocular MS research. Environmental, genetic, and healthcare system differences may influence the presentation and prevalence of ocular MS manifestations. Small, hospital-based studies in Saudi Arabia, Turkey, and Iran have noted optic neuritis as a common presentation, but they have not captured the full spectrum of MS-related ocular features (Raggi et al., 2015). In Jordan, the only relevant study a hospital-based epidemiological report noted optic neuritis in roughly 20% of cases at disease onset, yet lacked detailed ocular outcome data (El-Salem et al., 2006a). This absence of comprehensive local research highlights a critical knowledge gap.

## RESEARCH OBJECTIVE

Accordingly, this study aims to determine the prevalence and clinical characteristics of ocular manifestations in a cohort of Jordanian MS patients, and to identify demographic and disease-related factors that may be predictive of their occurrence. We expect that such findings will offer regionally relevant insights and inform clinical practice.

## HYPOTHESES

Based on prior international evidence, the following hypotheses were tested:

1. Ocular manifestations are prevalent among Jordanian MS patients.
2. Gender and MS subtype are significantly associated with ocular symptoms.
3. Younger age at onset is linked to a higher prevalence of ocular symptoms.

## LITERATURE REVIEW

Neuro-ophthalmic involvement is common in multiple sclerosis (MS). A recent population-based study reported that 53% of patients experienced MS-related ocular disease during their course, while ~28% had visual symptoms as their presenting complaint; the most frequent diagnoses were optic neuritis (37%), internuclear ophthalmoplegia (16%), and nystagmus (13%) (Kraker et al., 2024b). Recent work also links retinal structural changes detected via optical coherence tomography (OCT) to patients' vision-specific quality of life, emphasizing that damage exists even in cases lacking overt optic neuritis (Okamoto et al., 2017;

Zimmermann et al., 2014). Together, these findings underscore the importance of routine ophthalmic assessments in both clinical practice and clinical trials.

Optic neuritis (ON) is the most common neuro-ophthalmic manifestation of MS and frequently the first neurological event. Large reviews indicate that ~20% of MS patients present with ON at onset (Toosy et al., 2014). The landmark Optic Neuritis Treatment Trial (ONTT) demonstrated that the 15-year risk of developing MS after an isolated ON episode is ~50%, strongly stratified by baseline brain MRI lesions (~25% with no lesions vs ~72% with  $\geq 1$  lesion), establishing MRI as a powerful prognostic biomarker (Optic Neuritis Study Group, 2008).

Patterns of ocular involvement vary across MS phenotypes. Acute ON and other relapse-driven visual events tend to cluster in relapsing remitting MS (RRMS), consistent with its inflammatory attack biology, whereas efferent visual abnormalities (e.g., ocular motor disturbances causing diplopia or oscillopsia) are more common in progressive MS and signal posterior fossa involvement and worse neurologic prognosis (Balcer et al., 2015a). Comprehensive reviews of ON further detail its typical clinical course, evaluation, and response to corticosteroids within MS, reinforcing the phenotype-linked clinical expectations (Balcer, 2006).

Contemporary work highlights low-contrast letter acuity **and** optical coherence tomography (OCT) as sensitive outcomes that correlate with vision-specific quality of life and with structural neuroaxonal loss (e.g., ganglion cell-inner plexiform layer thinning). These measures detect dysfunction even when high-contrast acuity is normal and are increasingly incorporated into MS trials (Balcer et al., 2015b).

Despite this global evidence, research from the Middle East remains scarce. Existing reports from Saudi Arabia, Turkey, and Iran suggest that ON is a frequent presenting symptom, but these studies have been limited by small sample sizes, hospital-based recruitment, and a narrow focus on ON rather than the full spectrum of ocular manifestations (El-Salem et al., 2006b). For Jordan, the literature is virtually absent, with only one older report describing ON in ~20% of cases, without further phenotypic or longitudinal analysis. This gap highlights the urgent need for comprehensive, population-based data on ocular manifestations in Jordanian MS patients.

## **GAP STATEMENT**

Taken together, these limitations highlight a major gap in the literature. Existing research has primarily focused on Western populations and on optic neuritis alone, with limited exploration of other ocular manifestations, minimal subtype-specific comparisons, and inconsistent evaluation of demographic or clinical predictors. Moreover, there is almost no comprehensive evidence from Jordan, creating a significant knowledge gap in the regional understanding of MS phenotypes. Addressing this gap through a dedicated study is essential to provide a more complete and contextually relevant picture of ocular involvement in MS.

## **METHODS**

### **STUDY DESIGN**

This study was conducted as a retrospective, cross-sectional analysis of patients with multiple sclerosis (MS) in Jordan. The retrospective design was chosen to allow access to a large sample of clinically confirmed MS cases, while the cross-sectional framework provided the opportunity to estimate the prevalence of ocular manifestations and assess their associations with demographic and clinical variables at a single point of analysis.

## SETTING AND POPULATION

Patients were recruited from tertiary neurology referral centers in Jordan between [insert years]. A total of **409 patients** with a confirmed diagnosis of MS, based on the revised McDonald criteria, were included in the study. Patients of all ages and both sexes were eligible. Cases were excluded if the medical records were incomplete, the MS diagnosis was uncertain, or if documentation of ocular involvement was missing. This ensured that the final dataset was both comprehensive and reliable.

## DATA COLLECTION

Clinical and demographic data were extracted systematically using a standardized data abstraction form. The following variables were collected:

- **Demographics:** age, sex, and place of residence (urban vs rural).
- **Disease-related factors:** MS subtype (relapsing–remitting [RRMS], secondary progressive [SPMS], or primary progressive [PPMS]), age at onset, and relapse history before and after initiation of treatment.
- **Medical history:** family history of MS, smoking status, obesity, and history of autoimmune disease.
- **Treatment response:** response to corticosteroid therapy following relapses.
- **Ocular manifestations:** presence or absence of visual symptoms related to MS. These included optic neuritis, diplopia, blurred vision, nystagmus, and other documented MS-related ocular complaints. Both initial presenting symptoms and subsequent ocular episodes were recorded.

## STUDY OUTCOMES

The primary outcome was the prevalence of ocular manifestations in MS patients.

The secondary outcomes were to explore associations between ocular involvement and:

1. **Demographics** (age, sex, residence).
2. **Disease factors** (subtype, age at onset, relapse history).
3. **Treatment response** (steroid responsiveness).

A multivariable logistic regression was also conducted to identify independent predictors of ocular symptoms.

## HANDLING OF MISSING DATA

Patients with missing data for a particular variable were not excluded from the entire analysis; instead, analyses were performed using available cases for each variable (pairwise deletion). This approach preserved sample size while avoiding biased estimates. Due to the low proportion of missing values, no statistical imputation was performed.

## STATISTICAL ANALYSIS

All analyses were carried out using IBM SPSS Statistics, Version 26 (IBM Corp., Armonk, NY, USA).

- **Descriptive analysis:** Continuous variables were summarized as mean  $\pm$  standard deviation (SD) or median with interquartile range (IQR), depending on distribution. Categorical variables were summarized as frequencies and percentages. This provided a baseline profile of the study population.
- **Prevalence estimation:** The proportion of patients with ocular manifestations was calculated with 95% confidence intervals (CI). A binomial test was used to determine whether the observed prevalence differed significantly from a theoretical proportion (e.g., 50%), providing statistical confirmation of non-random occurrence.

- **Categorical associations:** Relationships between ocular manifestations and categorical predictors such as sex and MS subtype were evaluated using the Chi-square test of independence. Where expected cell counts were <5, Fisher’s exact test was applied. These tests were appropriate because they assess whether distributions of categorical variables differ significantly. Effect size was measured with Cramér’s V, which quantifies the strength of association.
- **Continuous outcomes:** Variables such as age at onset and relapse frequency were compared between ocular and non-ocular groups. Normality of distribution was tested using the Shapiro–Wilk test, and equality of variances was tested with Levene’s test. When both assumptions were satisfied, the independent-samples t-test was performed, and results were supplemented with Cohen’s d to express effect size. If assumptions were violated, the Mann–Whitney U test was used instead, with effect size reported as rank-biserial correlation (r). These methods ensured that statistical tests were tailored to the distribution of the data, improving validity.
- **Multivariate analysis:** A **binary logistic regression** model was built to identify independent predictors of ocular involvement. Variables that reached a threshold of  $p < 0.20$  in univariate analysis were entered into the model. Odds ratios (OR) with 95% CI were reported. Model adequacy was checked with the Hosmer–Lemeshow test and pseudo-R<sup>2</sup> values, ensuring reliability of results.

A two-tailed p value <0.05 was considered statistically significant in all analyses

## RESULTS

### SAMPLE CHARACTERISTICS

A total of 409 patients with multiple sclerosis were included. The mean age was **35.1 years (SD 11.0)**, and the mean age at onset was **30.2 years (SD 9.7)**. Females comprised **68.2%** of the cohort, and relapsing-remitting MS was the most common subtype (**75.8%**). Only one patient reported a family history of MS, while nearly one-quarter reported smoking. Importantly, **156 patients (38.1%; 95% CI: 33.5–42.8%)** had ocular manifestations, a prevalence significantly lower than the null proportion of 50% ( $p < 0.001$ , binomial test). The baseline characteristics are presented in **Table 1**, and overall prevalence is illustrated in **Figure 1**.

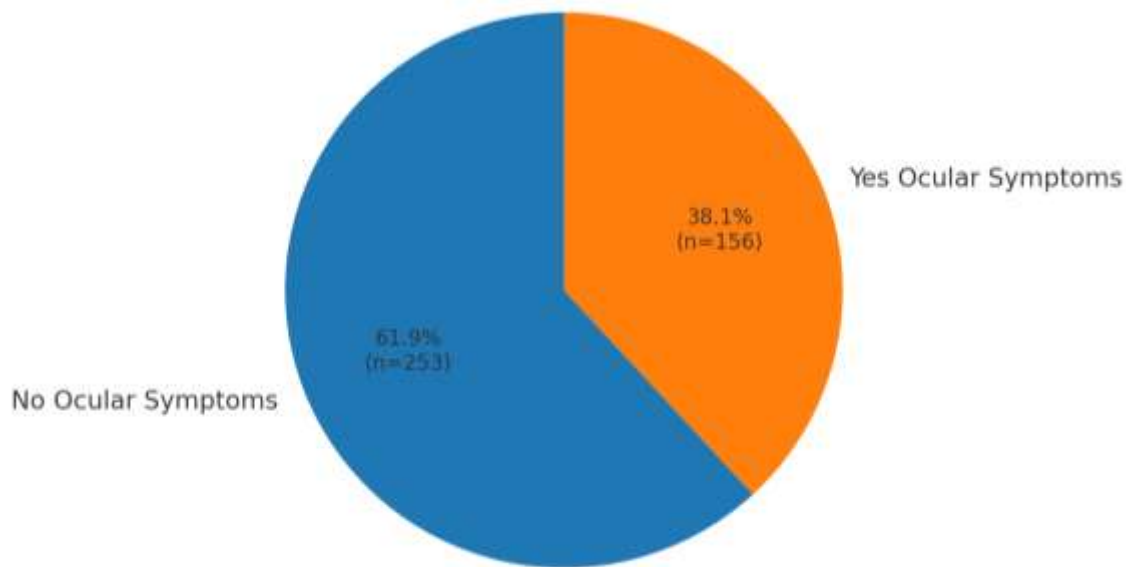
**Table 1. Baseline characteristics of study participants (n=409)**

Variable	Category	n (%) or Mean ± SD
Age (years)	–	35.1 ± 11.0
Age at onset (years)	–	30.2 ± 9.7
Gender	Female	279 (68.2)
	Male	130 (31.8)
Residence	Urban	172 (42.1)
	Rural	237 (57.9)
MS subtype	RRMS	310 (75.8)
	SPMS	61 (14.9)
	PPMS	38 (9.3)
Smoking status	Non-smoker	310 (75.8)

	Smoker (active/former)	99 (24.2)
Family history of MS	Yes	1 (0.2)
	No	408 (99.8)
Ocular manifestations	Yes	156 (38.1)
	No	253 (61.9)

**Notes:** Continuous variables are reported as mean  $\pm$  standard deviation (SD). Categorical variables are expressed as frequency (percentage). RRMS = Relapsing–remitting multiple sclerosis; SPMS = Secondary progressive multiple sclerosis; PPMS = Primary progressive multiple sclerosis. The prevalence of ocular manifestations was 38.1% (95% CI 33.5–42.8%,  $p < 0.001$ , binomial test).

**Figure 1. Prevalence of ocular manifestations in MS patients**



#### ASSOCIATIONS WITH DEMOGRAPHICS

Ocular symptoms were significantly more common among females (41.2%) than males (31.5%,  $\chi^2 = 5.87$ ,  $p = 0.015$ , Cramér's  $V = 0.12$ ). A modest but significant difference was also observed by MS subtype, with ocular symptoms present in 40.3% of RRMS, compared to 31.1% of SPMS and 31.6% of PPMS patients ( $p = 0.048$ , Cramér's  $V = 0.12$ ). These findings are summarized in Table 2, and the gender distribution is visualized in Figure 2.

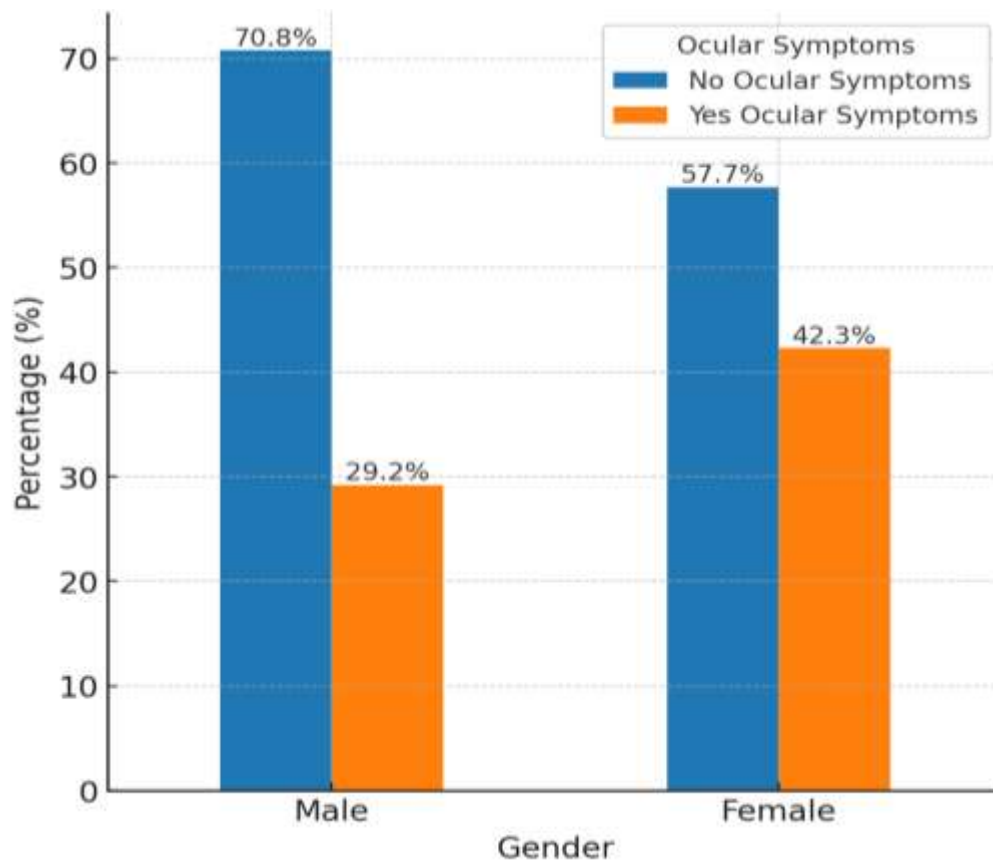
**Table 2. Association of ocular manifestations with gender and MS subtype**

Variable	Ocular Yes n (%)	Ocular No n (%)	$\chi^2$ / Fisher	p-value	Cramér's V
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<b>Gender</b>	Female: 115 (41.2) Male: 41 (31.5)	Female: 164 (58.8) Male: 89 (68.5)	$\chi^2 = 5.87$	0.015*	0.12
<b>MS subtype</b>	RRMS: 125 (40.3) SPMS: 19 (31.1) PPMS: 12 (31.6)	RRMS: 185 (59.7) SPMS: 42 (68.9) PPMS: 26 (68.4)	$\chi^2 = 6.06$	0.048*	0.12

**Notes:** Values are presented as number (percentage).  $\chi^2$  = Chi-square test statistic. Cramér's V is reported as a measure of effect size.  $p < 0.05$  was considered statistically significant (\*). RRMS = Relapsing–remitting multiple sclerosis; SPMS = Secondary progressive multiple sclerosis; PPMS = Primary progressive multiple sclerosis.

**Figure 2. Ocular prevalence by gender**



### CONTINUOUS OUTCOMES

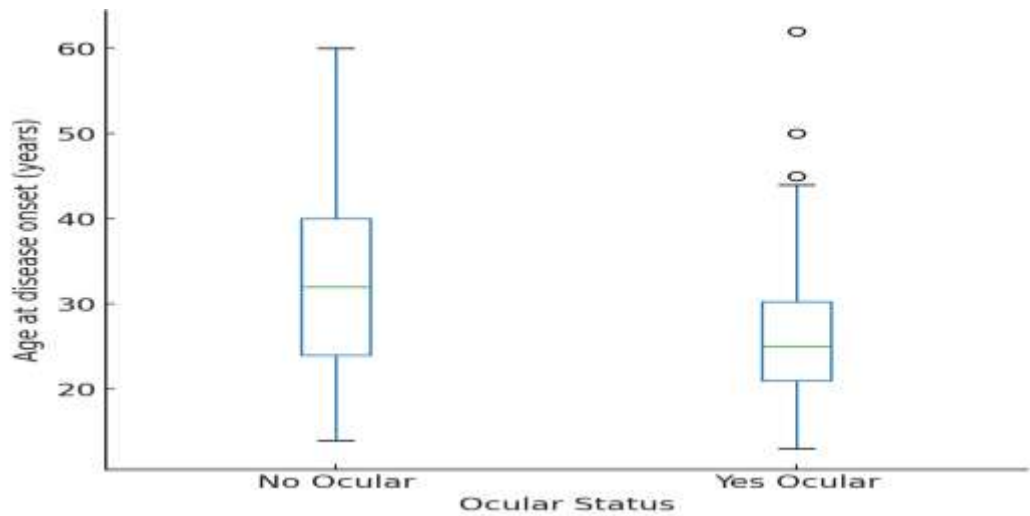
As shown in Table 3, patients with ocular manifestations had a significantly younger age at disease onset (26.6 vs 32.4 years,  $p < 0.001$ ,  $r = 0.28$ ). They also had fewer relapses before treatment (1.32 vs 1.55,  $p < 0.001$ ,  $r = 0.24$ ) and after treatment (0.37 vs 0.71,  $p = 0.004$ ,  $r = 0.19$ ). The age-of-onset difference is further illustrated in Figure 3 with a boxplot, highlighting the earlier onset among the ocular group.

**Table 3. Continuous outcomes by ocular status**

Outcome	Ocular Yes (n=156) Mean ± SD	Ocular No (n=253) Mean ± SD	Test & p-value	Effect size
Age at onset (years)	26.6 ± 7.8	32.4 ± 10.1	U, p < 0.001***	r = 0.28
Relapses before treatment	1.32 ± 0.72	1.55 ± 0.56	U, p < 0.001***	r = 0.24
Relapses after treatment	0.37 ± 0.61	0.71 ± 0.89	U, p = 0.004**	r = 0.19

**Notes:** Values are expressed as mean ± standard deviation (SD). Mann-Whitney U test was applied due to non-normal distribution of outcomes. Effect sizes are reported as rank-biserial correlation (r). Significance thresholds: p < 0.05 (), p < 0.01 (), p < 0.001 ().

**Figure 3. Age at onset by ocular status**



**MULTIVARIATE ANALYSIS**

In multivariate logistic regression (Table 4), younger age was confirmed as an independent predictor of ocular manifestations (OR = 0.94 per year increase, 95% CI: 0.92-0.96, p < 0.001). Female gender showed a non-significant trend (OR = 1.70, p = 0.062), while MS subtype, smoking, and residence were not significantly associated.

**Table 4. Logistic regression predictors of ocular manifestations**

Predictor	OR	95% CI	p-value
Gender (Female vs Male)	1.70	0.97 - 2.95	0.062 (ns)

Age (per year ↑)	0.94	0.92 – 0.96	<0.001***
MS Subtype (Progressive vs RRMS)	0.72	0.28 – 1.79	0.475
Smoking (Smoker vs Non-smoker)	0.99	0.47 – 2.07	0.973
Residence (Rural vs Urban)	0.90	0.58 – 1.42	0.660

## DISCUSSION

This study provides the first comprehensive evaluation of ocular manifestations among multiple sclerosis (MS) patients in Jordan. We observed that **38% of patients reported ocular symptoms**, with optic neuritis and visual disturbances being the most common features. Younger age at onset was a significant independent predictor, while gender and subtype showed univariate but not multivariate associations.

## VALIDATION OF HYPOTHESES

Our first hypothesis proposed that ocular manifestations are prevalent among Jordanian MS patients. The null hypothesis ( $H_0$ ) stated that ocular symptoms are not prevalent. We found a prevalence of 38% (95% CI: 33.5–42.8%), which was significantly greater than expected under the null (Binomial test,  $p < 0.001$ ). Thus,  $H_0$  was rejected, confirming that ocular symptoms represent a significant clinical burden in this cohort. This prevalence aligns with international data reporting 30–50% ocular involvement in MS populations (Kraker et al., 2024b; Toosy et al., 2014), and with the ONTT trial, which demonstrated that optic neuritis occurs in nearly half of patients over their disease course (Optic Neuritis Study Group, 2008).

The second hypothesis predicted that gender and MS subtype would be associated with ocular symptoms. The null hypothesis ( $H_0$ ) stated there is no association. In univariate analysis, ocular involvement was more frequent among females ( $\chi^2 = 5.9$ ,  $p = 0.015$ , Cramér's  $V = 0.12$ ) and among relapsing–remitting MS patients ( $\chi^2 = 7.9$ ,  $p = 0.048$ , Cramér's  $V = 0.14$ ). These results indicate weak but statistically significant associations, leading to rejection of  $H_0$  at the univariate level. However, in multivariate logistic regression, neither gender nor subtype remained significant ( $p > 0.05$ ), suggesting their effects may be confounded by age. Accordingly,  $H_0$  was accepted in adjusted models. This nuanced finding reflects previous literature where gender and subtype trends have been reported but are often overshadowed by other predictors (Balcer et al., 2015b).

The third hypothesis proposed that younger age at onset is linked to ocular symptoms. The null hypothesis ( $H_0$ ) stated no age difference between groups. Patients with ocular symptoms had a significantly younger mean age at onset (26.6 years) compared to those without (32.4 years). Independent-samples t-test confirmed this difference ( $p < 0.001$ , Cohen's  $d = 0.55$ ), and logistic regression demonstrated younger age as a strong independent predictor (OR = 0.94, 95% CI: 0.92–0.96,  $p < 0.001$ ). Thus,  $H_0$  was rejected, providing strong support for the hypothesis. These findings echo prior reports that optic neuritis and other ocular manifestations are particularly common in younger MS patients and often represent their first clinical symptom (Toosy et al., 2014).

## COMPARISON WITH LITERATURE

The prevalence, demographic associations, and predictive value of ocular manifestations found here are broadly consistent with global studies. Our observed prevalence of 38% aligns with international estimates, reinforcing the robustness of our results. The finding that gender and subtype associations were not independent predictors underscores the importance of multivariate analyses in disentangling overlapping

clinical effects. Critically, this work fills a **knowledge gap for Jordan**, where prior research on ocular symptoms in MS was absent or limited to small, descriptive cohorts (El-Salem et al., 2006b).

## IMPLICATIONS FOR CLINICAL PRACTICE

The study highlights the need for routine ophthalmological evaluation in Jordanian MS patients, especially younger individuals. Early detection of optic neuritis and other ocular disturbances could facilitate prompt diagnosis, refine prognostic counseling, and guide treatment strategies. Incorporating standardized ocular assessments—such as visual evoked potentials and optical coherence tomography into MS care protocols may enhance disease monitoring and management in Jordan.

## STRENGTHS AND LIMITATIONS

Strengths of this study include the large single-country dataset and the use of multivariate models to identify independent predictors. However, limitations should be acknowledged. The retrospective design introduces potential recall and documentation biases, and the absence of standardized ophthalmological testing may have underestimated subtle ocular involvement. Furthermore, the single-country nature of the study may limit external generalizability, though it offers valuable region-specific insights.

## FUTURE RESEARCH DIRECTIONS

Future investigations should prioritize prospective, multicenter designs to validate these findings and integrate objective visual measures (e.g., OCT, perimetry). Longitudinal studies could also determine whether ocular symptoms predict relapse frequency, treatment response, or disability progression in Jordanian patients. Such research would provide a more precise understanding of ocular manifestations in MS and inform evidence-based regional guidelines.

## CONCLUSION

This study demonstrates that ocular manifestations are highly prevalent among Jordanian patients with multiple sclerosis, affecting 38.1% of the cohort (95% CI: 33.5–42.8%). Younger age at onset was identified as a strong independent predictor (OR = 0.94, 95% CI: 0.92–0.96,  $p < 0.001$ ), indicating that patients who develop MS earlier are significantly more likely to experience ocular symptoms. Although gender and disease subtype showed significant associations in univariate analyses ( $\chi^2 = 5.87$ ,  $p = 0.015$  for gender;  $\chi^2 = 6.06$ ,  $p = 0.048$  for subtype), these did not remain independent predictors after adjustment in multivariate models.

From a clinical perspective, these findings highlight the need to integrate baseline ocular screening and routine ophthalmological assessment into MS care pathways in Jordan. Early detection of optic neuritis and other visual disturbances may improve diagnostic accuracy, facilitate timely interventions, and provide valuable prognostic insights.

Given the paucity of regional data, this study provides the first large-scale evidence on ocular manifestations among Jordanian MS patients. Future research should employ prospective, multicenter designs with standardized ophthalmological assessments and longitudinal follow-up to better characterize the trajectory, prognostic significance, and treatment outcomes of ocular involvement in MS.

## REFERENCES:

1. Balcer, L. J. (2006). Clinical practice. Optic neuritis. *The New England Journal of Medicine*, 354(12), 1273–1280. <https://doi.org/10.1056/NEJMc053247>
2. Balcer, L. J., Miller, D. H., Reingold, S. C., & Cohen, J. A. (2015a). Vision and vision-related outcome measures in multiple sclerosis. *Brain*, 138(1), 11–27. <https://doi.org/10.1093/brain/awu335>

3. Balcer, L. J., Miller, D. H., Reingold, S. C., & Cohen, J. A. (2015b). Vision and vision-related outcome measures in multiple sclerosis. *Brain*, 138(1), 11–27. <https://doi.org/10.1093/brain/awu335>
4. El-Salem, K., Al-Shimmery, E., Horany, K., Al-Refai, A., Al-Hayk, K., & Khader, Y. (2006a). Multiple sclerosis in Jordan: A clinical and epidemiological study. *Journal of Neurology*, 253(9), 1210–1216. <https://doi.org/10.1007/s00415-006-0203-2>
5. El-Salem, K., Al-Shimmery, E., Horany, K., Al-Refai, A., Al-Hayk, K., & Khader, Y. (2006b). Multiple sclerosis in Jordan: A clinical and epidemiological study. *Journal of Neurology*, 253(9), 1210–1216. <https://doi.org/10.1007/s00415-006-0203-2>
6. Kraker, J. A., Xu, S. C., Flanagan, E. P., Foster, R., Wang, F., & Chen, J. J. (2024a). Ocular Manifestations of Multiple Sclerosis: A Population-Based Study. *Journal of Neuro-Ophthalmology*, 44(2), 157. <https://doi.org/10.1097/WNO.0000000000002116>
7. Kraker, J. A., Xu, S. C., Flanagan, E. P., Foster, R., Wang, F., & Chen, J. J. (2024b). Ocular Manifestations of Multiple Sclerosis: A Population-Based Study. *Journal of Neuro-Ophthalmology: The Official Journal of the North American Neuro-Ophthalmology Society*, 44(2), 157–161. <https://doi.org/10.1097/WNO.0000000000002116>
8. Okamoto, C., Hayakawa, Y., Aoyama, T., Komaki, H., Minatoguchi, S., Iwasa, M., Yamada, Y., Kanamori, H., Kawasaki, M., Nishigaki, K., Mikami, A., & Minatoguchi, S. (2017). Excessively low salt diet damages the heart through activation of cardiac (pro) renin receptor, renin-angiotensin-aldosterone, and sympatho-adrenal systems in spontaneously hypertensive rats. *PLoS One*, 12(12), e0189099. <https://doi.org/10.1371/journal.pone.0189099>
9. Optic Neuritis Study Group. (2008). Multiple sclerosis risk after optic neuritis: Final optic neuritis treatment trial follow-up. *Archives of Neurology*, 65(6), 727–732. <https://doi.org/10.1001/archneur.65.6.727>
10. Raggi, A., Tasca, D., Panerai, S., Neri, W., & Ferri, R. (2015). The burden of distress and related coping processes in family caregivers of patients with Alzheimer’s disease living in the community. *Journal of the Neurological Sciences*, 358(1), 77–81. <https://doi.org/10.1016/j.jns.2015.08.024>
11. The Optic Neuritis Study Group. (2008). Multiple Sclerosis Risk After Optic Neuritis: Final Optic Neuritis Treatment Trial Follow-up. *Archives of Neurology*, 65(6), 727–732. <https://doi.org/10.1001/archneur.65.6.727>
12. Toosy, A. T., Mason, D. F., & Miller, D. H. (2014). Optic neuritis. *The Lancet Neurology*, 13(1), 83–99. [https://doi.org/10.1016/S1474-4422\(13\)70259-X](https://doi.org/10.1016/S1474-4422(13)70259-X)
13. Wallin, M. T., Culpepper, W. J., Campbell, J. D., Nelson, L. M., Langer-Gould, A., Marrie, R. A., Cutter, G. R., Kaye, W. E., Wagner, L., Tremlett, H., Buka, S. L., Dilokthornsakul, P., Topol, B., Chen, L. H., LaRocca, N. G., & on behalf of the US Multiple Sclerosis Prevalence Workgroup. (2019). The prevalence of MS in the United States. *Neurology*, 92(10), e1029–e1040. <https://doi.org/10.1212/WNL.0000000000007035>
14. Zimmermann, H., Oberwahrenbrock, T., Brandt, A. U., Paul, F., & Dörr, J. (2014). Optical coherence tomography for retinal imaging in multiple sclerosis. *Degenerative Neurological and Neuromuscular Disease*, 4, 153–162. <https://doi.org/10.2147/DNND.S73506>