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Glaucoma and Cataract in Multiple Sclerosis

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Dear Editor,

Multiple sclerosis (MS) is a chronic inflammatory disorder characterized by gradual central nervous system demyelination and subsequent degeneration (1). Several ophthalmological manifestations, such as uveitis, ocular motor involvement, nystagmus, and optic neuritis, have been reported due to MS. Moreover, other ophthalmological disorders, such as glaucoma and cataract, have been investigated in MS patients, and different prevalence rates were reported (2, 3).

Glaucoma is a type of optic neuropathy that leads to the degeneration of retinal nerve fibers and irreversible visual loss. The global prevalence of glaucoma has been estimated to be 3.5% in people aged 40 - 80 years (4). The risk of glaucoma may increase in MS patients due to reduced macular thickness in these people (5). A cataract is a significant cause of visual impairment worldwide, characterized by the opacification of the crystalline intraocular lens. Cataract has been reported in 2.5% of people aged 40 - 49 and 6.8% of those aged 50 - 59 years in the USA (6). Similar to glaucoma, the risk of cataract may augment in patients with MS as a result of glucocorticoid use or shared disease mechanisms (7).

Previous studies had controversial results regarding the prevalence of glaucoma and cataract in MS cases. Therefore, we aimed to perform a systematic review and meta-analysis to investigate the prevalence of glaucoma and cataract in patients with MS. The study was conducted according to the PRISMA statement. We searched PubMed, Scopus, Embase, and Web of Science in October 2021. Original studies (except case reports) which reported cataract or glaucoma in MS cases without any other comorbidities were considered eligible. Two independent investigators performed article selection and data extraction, and a third researcher was consulted in case of disagreements. Study characteristics, sample size, mean age, number of MS cases, glaucoma and cataract, and definition of disorders were extracted from the included studies. The mean point of glaucoma and cataract prevalence was measured using the random-effect model with a 95% confidence interval (CI) by the Stata 11.0 (College Station, TX). I-squared (I^2) statistics were used to evaluate heterogeneity among the included studies.

A total of 1934 studies were identified by literature search, of which five articles with 57,418 MS cases were entered into our study (Table 1). The point prevalence of glaucoma in people with MS had a range of 1.1%-3.5%, with an overall meta-analysis prevalence of 2.3% and high heterogeneity (I^2: 96%, P = 0) (Figure 1). Furthermore, the point prevalence of cataract ranged between 1.7% and 12.5%, with an overall meta-analysis prevalence of 7.1% and high heterogeneity (I^2: 96%, P = 0) in MS patients (Figure 1).

The risk of cataract in patients with MS seems to be higher based on our findings (7.1%). In addition, epidemiological studies on the general population reported that cataract affects 2.5% of those aged 40 - 49 and 6.8% of those aged 50 - 59 years in the USA (6). However, the prevalence of glaucoma in patients with MS was lower than the previously reported results (3.55%) in the general population of North America (4). Research by Bazelier et al. revealed that the risk of cataract and glaucoma increases in MS cases younger than 50 years compared to healthy individuals (2). In their study, the prevalence of cataract and glaucoma was almost similar between people with MS and controls, while after adjusting for covariates, they found a higher risk in MS cases.

The shared mechanism between MS and cataract may be explained by calpains (proteolytic enzymes) which are

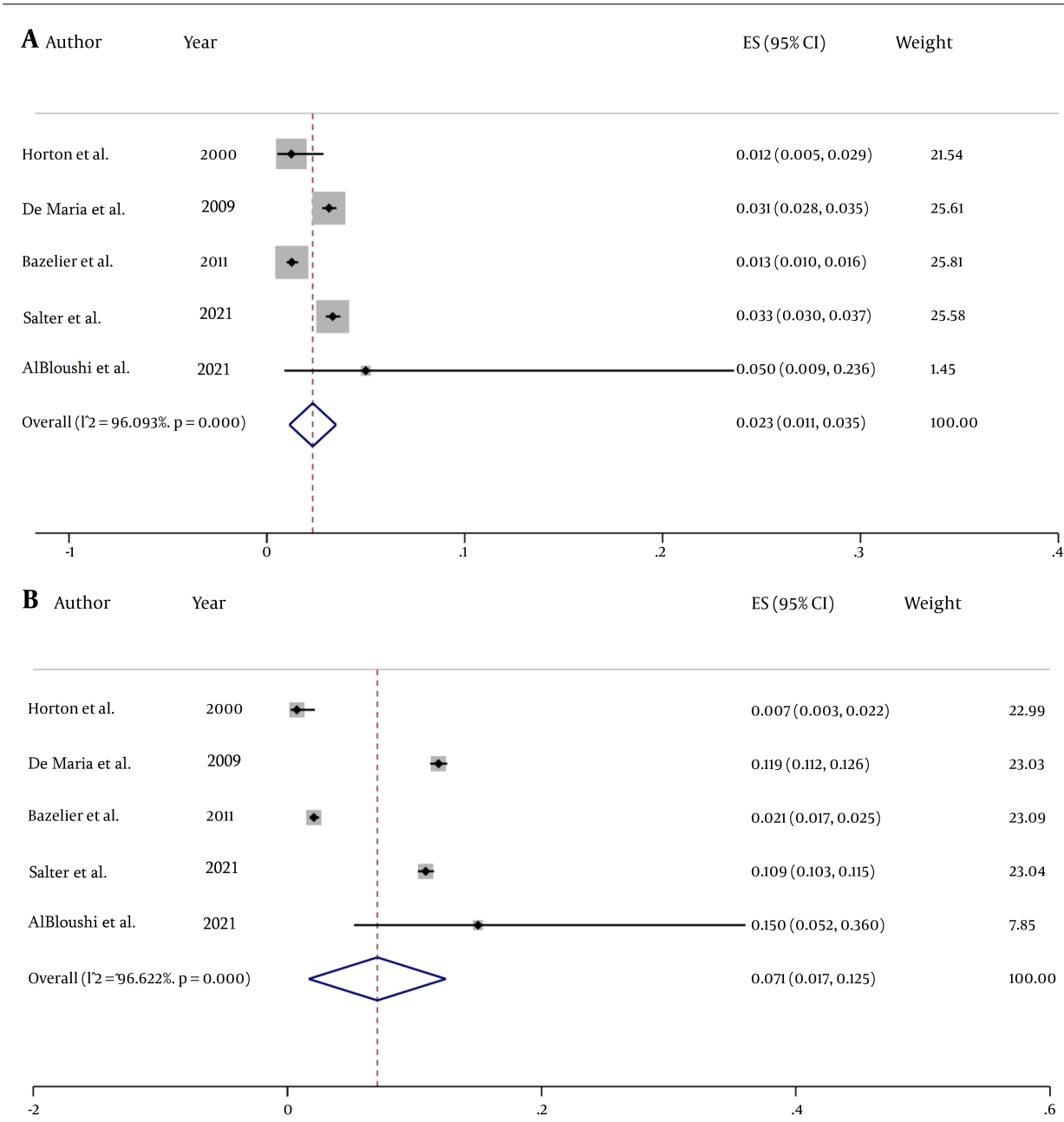

Figure 1. Prevalence of glaucoma (A) and cataract (B) in MS cases

active in the lens and also rise in MS relapses. The overactivation of calpains is thought to cause lens degeneration and cytoskeleton changes (11). The use of GC in patients with MS can be another explanation for the increased risk of cataract based on previous studies (12).

Retinal nerve fiber layer loss is observed in MS and glaucoma (13). However, there is no clear pathophysiological link between these two disorders. Moreover, as we discussed, comparing our results to epidemiological studies revealed no elevated risk of glaucoma in patients with MS. However, further studies are necessary to confirm our findings.

In summary, the risk of cataract seems to be higher in MS cases (7.1%) compared to global prevalence, highlighting the importance of considering cataract development in patients with MS. Furthermore, based on our findings, the prevalence of glaucoma is 2.3% which is even lower than the global prevalence (3.5%). However, our data were limited, and further studies are necessary to investigate the risk of cataract and glaucoma in patients with MS to confirm our findings.

Footnotes

Authors' Contribution: Study concept and design: F.N.; analysis and interpretation of data: F.N.; drafting of the manuscript: F.N.; statistical analysis: F.N.; extracting the data: A.S., and M.A.

Conflict of Interests: We declare that one of our authors (Fardin Nabizadeh, reviewer) is a member of the editorial board. The journal confirmed that the mentioned author with CoI was completely excluded from all review processes. We also introduced this author with CoI during the submission as an opposed reviewer.

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Table 1. Characteristics of Included Studies

Author	Year of Publication	Country	Study Design	Follow-up Duration (Mean), y	Sample Size	Number of MS Patients	Age of MS Patients (Mean), y	Number of controls	Age of Controls (Mean), y	Number of Glaucoma Cases in MS Patients	Number of Glaucoma Cases in Controls	Number of Cataract Cases in MS Patients	Number of Cataract Cases in Controls	MS Definition	Glaucoma Definition	Cataract Definition
AlBloushi et al. (8)	2021	Saudi Arabia	Observational retrospective	3.5 years	1000	20	29.5	NR	NR	1	NR	3	NR	Modified McDonald criteria	NR	NR
Salter et al. (9)	2021	USA	Observational (questionnaire-based data collection)	NR	9107	9107	53.4	NR	NR	303	NR	991	NR	The NARCOMS registry consists of participants who have self-reported their diagnoses of MS	NR	NR
Horton et al. (3)	2000	USA and Canada	Retrospective observational + questionnaire (self-report and medical records)	NR	404	404	46.5	NR	NR	5	NR	3	NR	NR	NR	NR
Bazelier et al. (2)	2011	UK	Retrospective population-based cohort	6.1 years	38904	5483	44.5	33421	44.6	69	479	114	747	NR	Glaucoma was classified according to the International Classification of Diseases (ICD-10)	Cataract was classified according to the International Classification of Diseases (ICD-10)
De Maria et al. (10)	2009	USA	Self-report registry	2 years	8983	8983	52.7	NR	NR	282	NR	1068	NR	NR	NR	NR

Abbreviations: MS, multiple sclerosis, NR, not reported.