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REVIEW

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Idiopathic scoliosis in subjects with eye diseases: A systematic review with meta-analysis

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Abstract

Our aim was to find the best evidence on the prevalence of idiopathic scoliosis (IS) in subjects with eye diseases (EDs) and to determine the most common visual alterations that are present. Following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a bibliographic search up to June 2023 in the PubMed, PsycINFO, SCOPUS, and CINAHL Complete databases was performed. Observational studies were selected and the results were analyzed with prevalence odds ratio (OR). A total of six studies, including 18,396 subjects, were selected. The group of subjects with EDs was made up of 6048 individuals, of whom 655 (10.83%) had IS. The group of subjects without EDs was made up of 12,348 individuals of whom 444 (3.60%) presented with IS with an OR = 2.91, CI (95%) = [1.75, 4.83]. Blindness was assessed in a single study with an OR = 7.83, CI (95%) = [1.66, 36.90]; all three studies in the refractive error subgroup yielded an OR = 2.24, CI (95%) = [1.10, 4.58]; and the two studies that included subjects with strabismus showed an OR = 3.09, CI (95%) = [1.38, 7.00]. EDs were associated with an almost three times greater odds of having IS. We recommend the inclusion of vision testing in children with IS.

KEYWORDS
blindness, eye diseases, refractive errors, scoliosis, strabismus

INTRODUCTION

Idiopathic scoliosis (IS) is a three-dimensional and progressive spinal malformation that usually appears in childhood or adolescence.[1] It produces a twisting of the spine that affects the normal alignment of the vertebrae, which will adapt to lateral shift and rotation, resulting in the appearance of spinal lateral curves.[2] According to the Cobb method used to measure these curves, a coronal plane deviation over 10° is considered pathological.[3] Data from countries all around the world show a wide prevalence of between 0.96% and 13.6% in children and adolescents[4–6]—making it the most frequent pediatric malformation.[7]

There is no consensus concerning its etiology; hence, treatment is focused on stopping the progression of the curvature by the use of braces and/or therapeutic exercises, although sometimes when the curve passes 40°, surgery is required for aesthetic and functional reasons.[1] A better understanding of what causes this spinal malformation would facilitate improvement of the approaches to reduce sequelae.[8] To date, authors have found relationships between IS and several conditions: structural alterations during growth,[9] geographical

latitude and its influence in menarche,[10,11] plagiocephaly,[12] melatonin receptor polymorphism,[13] alterations in calcium–phosphorus balance,[14] morphological[8] or functional alterations in the vestibular system,[15] neurological findings (presumably harmless),[16] and orthodontic abnormalities.[17] Most authors consider IS to be multifactorial, involving genetic, tissular, hormonal, biomechanical, and neurosensorial factors.[18]

Recent studies have focused on the analysis of visual function and eye morphology of IS patients. Grivas et al. found an unusually high prevalence (42.3%) of IS in visually impaired women.[19] In another study, a high prevalence of scoliosis was found both in subjects blind from birth (59%) and with acquired blindness (42.9%).[20] Thus, these authors speculate about the possible relationship between visual and somatosensory alteration in the genesis of spinal curvature.[19,20] Another study found statistically significant differences in choroidal thickness between subjects with and without IS.[21] This may be relevant because the thinness of the choroid can cause anisometropic amblyopia,[22] inducing a distortion of how the subject visually perceives the environment.

Although studies linking IS with vision loss,[20] visual impairment,[19] or choroidal thinness[21] have been published, nothing is known about the nature of the possible visual problems that might be present in subjects with IS, and no review of the scientific literature has been performed on this topic. For this reason, this review aimed to find evidence of the prevalence of IS in subjects with eye diseases (EDs) and, secondarily, to identify the most common visual alterations related to lateral deviations of the spine.

MATERIALS AND METHODS

Study design

This systematic review was conducted in line with the recommendations of the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) group guidelines,[23] the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[24] and the Cochrane Handbook for Systematic Reviews.[25] The protocol of this work was previously registered in PROSPERO (code CRD42023420041).

Literature search and bibliographical sources

Two authors (J.R.G.-S. and M.J.S.-F.) independently performed a literature search up to June 2023 in the PubMed, PsycINFO, SCOPUS, and CINAHL Complete databases. The searches were accompanied by additional searches of other sources, such as previously published articles, abstracts and conference proceedings, expert articles, and gray literature. For the search strategy, we identified two search domains: scoliosis and EDs. In accordance with the Medical Subject Headings (MeSH) for MEDLINE, the keywords employed were "scoliosis," "eye diseases," and "vision disorders" (Table 1). A third expert author (R.L.-V.) reviewed the bibliographic search and resolved any doubts.

TABLE 1 Search strategy.

PUBMED	(eye diseases [mh] OR eye diseases [tiab] OR eye disorders [tiab] OR strabismus [mh] OR squint [tiab] OR vision disorders [mh] OR vision disorders [tiab] OR amblyopia [mh] OR amblyopia [tiab]) AND (scoliosis [mh] OR scoliosis [tiab] OR idiopathic scoliosis [tiab] OR adolescent idiopathic scoliosis [tiab] OR scoliosis juvenile [tiab])
SCOPUS	(TITLE-ABS-KEY ("eye diseases" OR "eye disorders" OR "strabismus" OR "squint" OR "vision disorders" OR "amblyopia") AND TITLE-ABS-KEY ("scoliosis" OR "idiopathic scoliosis" OR "adolescent idiopathic scoliosis" OR "scoliosis juvenile")
CINAHL	(eye diseases OR eye disorders OR strabismus OR squint OR amblyopia OR vision disorders) AND (scoliosis OR idiopathic scoliosis OR adolescent idiopathic scoliosis OR scoliosis juvenile)
PsycINFO	(eye diseases OR eye disorders OR strabismus OR squint OR amblyopia OR vision disorders) AND (scoliosis OR idiopathic scoliosis OR adolescent idiopathic scoliosis OR scoliosis juvenile)

Study selection: Inclusion and exclusion criteria

Two blinded reviewers (I.C.-P. and A.J.I.-V.) independently screened the titles and abstracts of all references retrieved from each database and additional sources. When one of the searchers identified a work with the potential for inclusion in the qualitative synthesis, this article was examined in detail by the two authors. All disagreements were resolved by a third researcher (E.O.-G.).

The inclusion criteria in the present review were the following: (1) observational studies, such as cross-sectional, case–control, and cohort studies; (2) including patients with EDs; (3) comparison with healthy subjects or subjects with conditions other than EDs; and (4) studies analyzing the prevalence of IS in patients with EDs compared to visually healthy subjects. The exclusion criteria were as follows: (1) studies carried out in animals; (2) observational studies without a comparison group; and (3) a comparison group including miscellaneous samples with subjects with and without scoliosis.

Data extraction

Two authors (J.R.G.-S. and M.J.S.-F.) independently extracted data from the included articles in a standardized Microsoft Excel data-collection form. Disagreements were resolved by a third author (R.L.-V.). The researchers extracted the following data: authorship, publication date, country, total sample size, number of participants in each group (cases and controls or healthy subjects), age, and sex. We collected data on the variable of interest and the main findings reported by each study.

Outcomes

The main variable was the count of subjects with or without IS in each group of subjects with vision disorders. Taking into account the previous literature, these anomalies could range from severe visual impairment to mild amblyopia; the presence of abnormalities in the parallelism of the ocular axes (strabismus); or refractive status such as myopia, hyperopia, astigmatism, or difference in refractive status between the eyes (anisometropia).

Methodological quality assessment

The methodological quality of the studies included in this review was evaluated by the Newcastle-Ottawa Scale (NOS).[26] This scale explored the domains "selection of study groups" (maximum, 4 stars), "comparability of groups" (maximum, 2 stars), and "ascertainment of exposure/outcome" (maximum, 3 stars). The quality of the included studies according to the NOS score was considered either low (score 1–3), medium (score 4–6), or high quality (score 7–9).[27] Quality scores ranged from 0 (lowest) to 9 stars (highest).[28] The quality of evidence in each meta-analysis was evaluated using Grading of Recommendations Assessment, Development, and Evaluation (GRADE).[29]

Statistical analysis

Two researchers were in charge of the statistical analysis (R.L.-V. and E.O.-G.). Due to the heterogeneity and characteristics of the pathologies analyzed in this work as well as following the recommendations of Cooper et al.,[30] we chose the DerSimonian and Laird random effects model to estimate the overall pooled effect and its 95% confidence interval (CI) to improve the generalizability of the findings.[31] To analyze the prevalence of scoliosis in patients with and without visual disorders, we calculated the prevalence odds ratio (OR) together with its 95% confidence interval. The findings were displayed graphically using a forest plot resulting from each analysis.[32] Heterogeneity analysis was performed by calculating the Higgins *Q*-test and degree of inconsistency (I^2), which classifies heterogeneity as low (<25%), medium (25%–50%), or large (>50%), as well as by calculating its *p*-value.[33] Risk of publication bias was assessed using funnel plot asymmetry[34] and Egger's test ($p < 0.1$ indicates possible risk of publication bias).[35] Data analysis was performed using Comprehensive Meta-Analysis version 3.0 (Biostat) with a 95% confidence level.

RESULTS

A total of six studies[36–41] met the eligibility criteria and were included in the review (Figure 1). Table 2 shows the main characteristics of the included studies. The methodological quality of the studies included in this review, as evaluated with the NOS, was moderate (NOS mean score of 6.2 ± 0.8). Four studies[36,39–41] (67% of included studies) showed moderate quality, and two studies[37,38] showed high quality (33% of the total). Table 3 summarizes the NOS rating for selection, comparability, and exposure/outcome of the selected studies.

The group of subjects with visual disturbances was made up of 6048 individuals, of whom 655 (10.83%) had scoliosis. The group of subjects without visual disturbances was made up of 12,348 individuals, of whom 444 (3.60%) presented with scoliosis (OR = 2.91, CI (95%) = [1.75, 4.83], $p < 0.001$) (Figure 2 and Table 4). In the subgroup analysis, blindness was assessed in a single study with an OR = 7.83, CI (95%) = [1.66, 36.90]; all three studies in the refractive error subgroup yielded an OR = 2.24, CI (95%) = [1.10—4.58]; and the two studies that included subjects with strabismus showed an OR = 3.09, CI (95%) = [1.38, 7.00].

In the subgroup meta-analysis, heterogeneity was virtually nil. The quality of the evidence was moderate for the overall analysis, low for the meta-analysis of the refractive error subgroup, and very low for the rest of the analyses (Table 4).

DISCUSSION

Our study set out to identify the available evidence on the relationship between EDs and IS. In our work, we have found six cross-sectional studies that analyzed this relationship, having found that various alterations such as strabismus, refractive errors, or visual impairment are associated with an increase in the prevalence of scoliosis. The odds of suffering from IS could be almost three times higher in subjects with impaired vision and the quality of evidence of this finding was moderate. To the best of our knowledge, this is the first review to focus on this topic.

The relationship between vision impairment and the presence of IS has previously been analyzed, specifically the association of *ROBO3* gene polymorphisms and horizontal gaze palsy.[42] More recently, a significant association has been found between the gene variant (rs74787566) of *ROBO3* and the development of adolescent idiopathic scoliosis (AIS).[43] The fact that some *ROBO3* gene polymorphisms have been related to lateral gaze disorders is compatible with our finding of a higher prevalence of IS in subjects with strabismus, especially concomitant exotropia.[38,40]

However, in our work, the range of vision disorders associated with IS was diverse, ranging from severe visual impairment[44] to the presence of myopia[37,39] and anisometropia[41] (the difference in refractive error between both eyes). The work by Ulusoy et al.[21] has already found that a thinning of the choroid layer of the eye could be the basis for the development of anisometropic amblyopia.[22] All of these visual problems, such as amblyopia, refractive errors, and strabismus, can be concomitant. In animal models, it has been observed that early onset strabismus disrupted the emmetropization process, thus producing anisometropia. Early hyperopic anisometropia is a significant risk factor for amblyopia, and early esotropia can trigger the onset of both anisometropia and amblyopia.[45] All these disorders originate at the neurological level, producing changes in the anatomy and functioning of the central nervous system. In fact, a pseudo-right lateralization of the corpus callosum and a reduced fractional anisotropy

TABLE 2 Main characteristics of the included studies.

Studies	Country	Cases pathology	Scoliosis diagnosis	Controls	Age (years)[a]	Female/total	Scoliotic curve
Catanzariti et al.[37]	France	Visual deficiency	FBT/Moire topography	Healthy	11.5	292/803	Miscellaneous
Egorova et al.[38]	Russia	Myopia	Moire topography	Healthy	7–18	–/104	Miscellaneous
Pan et al.[39]	China	Strabismus	Radiograph: Cobb method	Respiratory patients	8.55	1822/3870	Thoracic scoliosis
Cai et al.[40]	China	Myopia	Radiograph: Cobb method	Healthy	8.75	2479/2547	Not reported
Zhu et al.[41]	China	Strabismus	Radiograph: Cobb method	Eye trauma	16.53	398/1571	Not reported
Zhou et al.[42]	China	Anisometropia	FBT/Moire topography	Healthy	13.32	4447/9501	Not reported

Note: Filters related to language, publication date, and free full-text access were not selected.
Abbreviation: FBT, Forward Bending Test.
[a]Age data are expressed as means except for Egorova et al.,[38] in which it is a range.

TABLE 3 Newcastle-Ottawa Scale (NOS) score for the methodological quality assessment of included studies.

Author and year	S1	S2	S3	S4	C	E1	E2	E3	Total	Quality
Cai et al. 2021[40]	*	*	*	*	*	*	–	–	6	Moderate
Catanzariti et al. 2001[37]	*	*	*	*	*	*	–	–	6	Moderate
Egorova et al. 2016[38]	*	*	*	–	**	*	*	–	7	High
Pan et al. 2020[39]	*	*	*	–	**	*	*	–	7	High
Zhou et al. 2023[42]	*	*	*	*	*	*	–	–	6	Moderate
Zhu et al. 2022[41]	*	*	–	–	*	*	*	–	5	Moderate

Note: Each study can be given a maximum of one star for each numbered item within the Selection (S) and Exposure (E) categories. A maximum of two stars can be given for Comparability (C). S1 = adequate case definition; S2 = representativeness of the cases; S3 = selection of controls; S4 = definition of controls; C1 = comparability of cases and controls; E1 = ascertainment of exposure; E2 = same method of ascertainment for cases and controls; E3 = nonresponse rate.

TABLE 4 Main findings in meta-analysis.

	Summary of findings															Quality of evidence (GRADE)					
	Effect size								Heterogeneity			Publication bias									
													Trim and fill								
	K	Cases with ED	Cases with IS	Controls	Controls with IS	OR	95% CI	p	Q (df)	I^2	p	Funnel plot (Egger p)	Adj SMD	% var	Risk of bias	Incons	Indirect	Imprec	Pub bias	Quality evidence
Overall	6	6048	655	12,348	444	2.91	1.75–4.83	<0.001	4.7 (5)	0%	0.45	Sym (0.38)	2.72	6%	Medium	No	No	No	No	Moderate
Blindness	1	75	6	728	8	7.83	1.66–36.90	0.009	0 (0)	0%	NP	NP	NP		Medium	No	No	Yes	Probable	Very low
Refractive errors	3	3133	248	9019	326	2.24	1.10–4.58	0.027	0.4 (2)	0%	0.81	Sym (0.12)	2.11	7%	Medium	No	No	Probable	No	Low
Strabismus	2	2840	401	2601	110	3.09	1.38–7.00	0.006	2.2 (1)	19%	0.13	NP	NP	NP	Medium	Low	No	Yes	Probable	Very low

Abbreviations: % var, percentage of variation; 95% CI, 95% confidence interval; Adj SMD, adjusted standard mean difference; df, degree of freedom; ED, eye disease; I^2, degree of inconsistency; Imprec, imprecision; Incons, inconsistency; Indirect, indirectness; IS, idiopathic scoliosis; K, number of comparisons; NP, not possible to calculate; OR, odds ratio; Q, *Q*-test; Sym, symmetric.

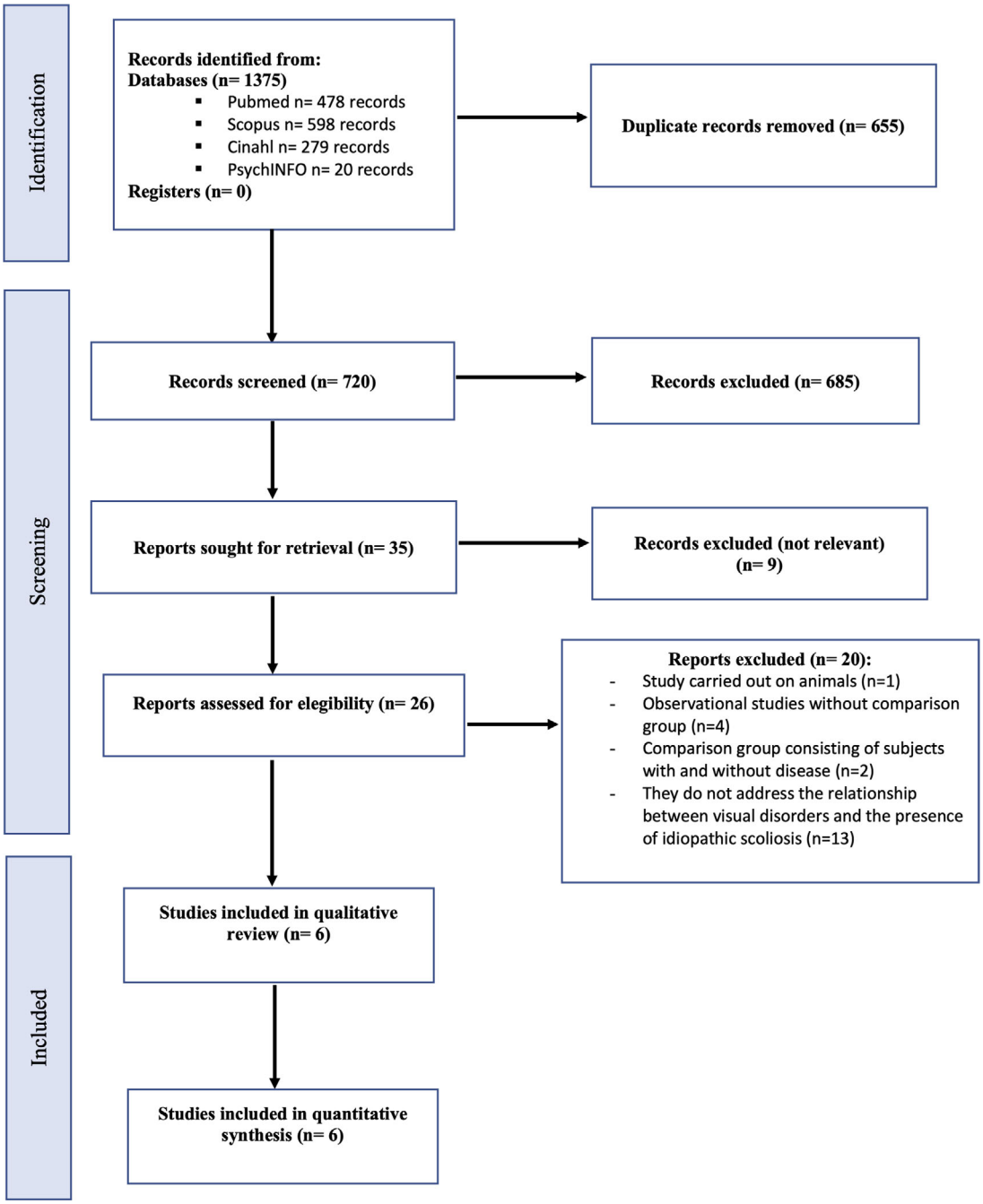

FIGURE 1 Flow diagram.

of the interhemispheric fibers which, through the splenium, interconnects Brodmann's areas 17 and 18 (corresponding to the primary and secondary visual cortices), have been found in subjects with AIS.[46]

Indirectly, geographical latitude seems to play a relevant role in scoliosis due to melatonin production, which is mediated by sunlight, and its relation to menarche. The lack of light increases melatonin production, so people living in countries with reduced quantity of sunlight hours during the day produce more melatonin. This influences menarche because melatonin overproduction is related with late menarche so people exposed to reduced sunlight hours could suffer a late sexual maturation.[47] Melatonin acts on gonads and reduces gonadotropin secretion, which retards the development of menarche in women and would prolong exposure to scoliosis-causative factors.[48] In the same line, visual impairments such as blindness would also affect menarche as the malfunctioning of the visual system would reduce the quantity of light that the subject would receive and, therefore, increase melatonin production.[48]

Other disorders that have been associated with scoliosis are alterations of the stomatognathic system, mainly Angle Class II malocclusion, which can interfere with the postural balance of children through the trigeminal pathway.[17] In this sense, one study found an association between erroneous posture in children, impaired visual

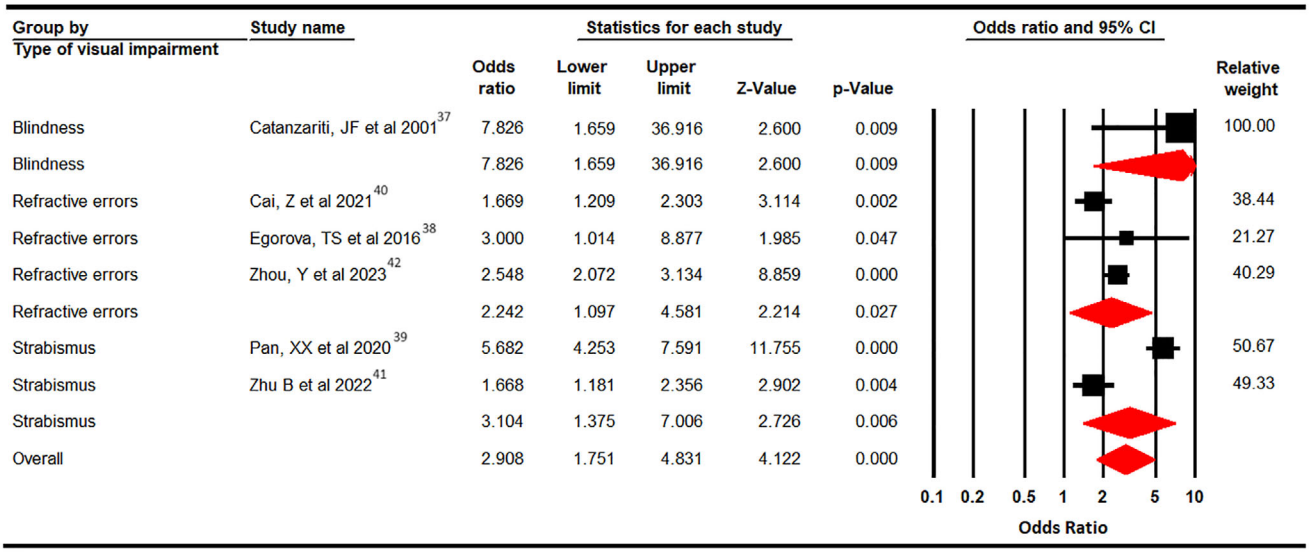

FIGURE 2 Forest plot. *Note*: Analyses of the pooled effects of each type of visual impairment and the overall pooled effect of all visual impairments.

convergence, and malocclusion.[49] A relationship has also been found between Angle's Class II malocclusion and myopia—one of the disorders that has been associated with scoliosis in our work.[50] It can, therefore, be verified that there is also a relationship between dental occlusion and vision disorders, all of which seem to be related to the presence of IS, possibly through the alteration of postural balance and spinal development in subjects during growth.

The possible alteration of the regulation of posture in children with scoliosis has received other support. Recently, a review found that IS subjects appear to show structural abnormalities of the vestibular apparatus.[8] This could compromise the perception of the subject's gravitational verticality[44] and cause an alteration of self-image.[51] These works have speculated that spinal curvature could develop in response to an inappropriate postural pattern. Although the alteration of the perception of visual verticality in subjects with IS is not completely clear,[15] the distortion of the perception of verticality could cause coronal head tilt,[52] and it does seem that the treatment of a spinal curvature through exercises could destabilize the subject's internal schema, producing a deviation from the subjective visual vertical.[53] We speculate that several visual, somatosensory, or vestibular disorders could cause an inadequate internal perception of verticality that would cause spinal curvature as an adaptation to the erroneous internal perception of gravitational verticality.

A previous study pointed to thoracolumbar curvature as the associated type of curvature developed by women with visual deficiencies.[48] Although the studies included in our review do not clarify a specific type of curvature or imply a causal relationship between EDs and the presence of IS, they do show a fairly probable relationship that has important implications for clinical practice. In the first place, and in light of our results, the integrity of the visual system should be investigated in subjects with scoliosis, and the presence of vision alterations should be screened for. Due to the concomitance with dental malocclusion, screening for vision disorders would also be advised. Future investigations should also determine if the treatment of vision disorders produces appreciable postural improvements, as already suggested in some classic studies.[54] It should also be investigated whether the treatment of any of these concomitant alterations generates changes in the others,[55] and if these changes could have substantial therapeutic implications for the management of IS patients.

This work has several limitations. First of all, there are few studies that have evaluated the relationship of EDs and IS, and the cross-sectional methodology of the studies included in our reviews precludes the drawing of any conclusions about causation. Second, there is great variability in the pathologies whose relationship with scoliosis has been evaluated. Although the reference bibliography indicates that thoracolumbar curves are more frequently developed in visual deficiency patients,[48] the included studies in this review did not always state the type of curvature displayed by the patients or whether there were differences in the type and severity of the curvature between subjects with and without EDs, so no conclusion can be reached about the type of curvature that is associated with visual disturbances. Despite the foregoing limitations, this is the first review to focus on the relationship between EDs and IS, and the number of patients included for each study is significant.

CONCLUSIONS

There was moderate evidence for a relationship between EDs and IS. The prevalence of IS was almost three times higher in subjects with EDs than in controls without EDs. The conditions that showed the greatest prevalence of IS were a severe decrease in visual acuity, followed by strabismus, and lastly refractive errors, such as myopia and anisometropia. In light of these results, we recommend the inclusion of vision testing (visual acuity, refraction, and trophies) in children with scoliosis.

AUTHOR CONTRIBUTIONS

J.R.G.-S., A.J.I.-V., and I.C.-P. were responsible for data curation. J.R.G.-S., A.J.I.-V., I.C.-P., and E.O.-G. were responsible for writing the original draft. M.J.S.-F., E.O.-G., and R.L.-V. were responsible for the conceptualization of the study. E.O.-G. and R.L.-V. were responsible for data analysis. M.J.S.-F. and R.L.-V. supervised the study. R.L.-V. provided resources and wrote the final version.

COMPETING INTERESTS

The authors declare no competing interests.

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