




OCULAR MANIFESTATIONS ASSOCIATED WITH SYSTEMIC RHEUMATOLOGIC DISEASES: A SYSTEMATIC REVIEW

MANIFESTAÇÕES OCULARES ASSOCIADAS A DOENÇAS REUMATOLÓGICAS SISTÊMICAS: UMA REVISÃO SISTEMÁTICA

MANIFESTACIONES OCULARES ASOCIADAS A ENFERMEDADES REUMATOLÓGICAS SISTÉMICAS: UNA REVISIÓN SISTEMÁTICA

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Giulia Pignato Wiltemburg Alves¹, Beatriz de Azevedo Kleinschmitt², Leonardo de Castro Villela³, Marcos Manoel Arquer Rodrigues⁴, Letícia de Castro Villela⁵, Henrique Bosso⁶

ABSTRACT

Introduction: Systemic rheumatologic diseases frequently present with ocular involvement that may precede, accompany, or follow systemic manifestations, often contributing significantly to morbidity and irreversible visual impairment. Ocular findings can range from mild surface disease to severe inflammatory conditions affecting the uvea, retina, optic nerve, and orbit. Early recognition of these manifestations is essential, as ocular disease activity may reflect systemic inflammation or indicate disease flare. Despite their clinical relevance, ocular complications are often underrecognized outside ophthalmology-centered care.

Objective: The main objective of this systematic review was to evaluate the spectrum, frequency, and clinical impact of ocular manifestations associated with systemic rheumatologic diseases. Secondary objectives included assessing diagnostic approaches, therapeutic strategies, visual outcomes, and the level of evidence supporting current management recommendations.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Observational studies and clinical trials published within the last five years were prioritized, with expansion to ten years if fewer than ten eligible studies were identified. Data synthesis followed PRISMA guidelines, and risk of bias and certainty of evidence were assessed using validated tools.

Results and Discussion: Twenty studies met the inclusion criteria and were included in the final analysis. The most frequently reported ocular manifestations were uveitis, keratoconjunctivitis sicca, scleritis, episcleritis, retinal vasculitis, and optic neuropathy, with

¹ E-mail: giuliapwa@gmail.com

² Universidade de Marília (UNIMAR). E-mail: biaklein13@gmail.com

³ Faculdade de Medicina de São José do Rio Preto (Famerp). E-mail: leonardo.villela@edu.famerp.br

⁴ UNAERP. E-mail: Marcos.arquer@hotmail.com

⁵ Universidade de São Paulo (USP) E-mail: leticiacvillela@gmail.com

⁶ Universidade de São Paulo (USP). E-mail: henriquebosso@hotmail.com

variation according to the underlying rheumatologic disease. Multidisciplinary management and early ophthalmologic referral were consistently associated with improved visual outcomes. The overall certainty of evidence ranged from low to moderate, reflecting heterogeneity in study design and outcome reporting.

Conclusion: Ocular manifestations are common and clinically significant complications of systemic rheumatologic diseases, requiring heightened awareness among clinicians. Timely diagnosis and coordinated care between rheumatologists and ophthalmologists are critical to prevent vision loss and optimize patient outcomes.

Keywords: Rheumatic Diseases. Eye Diseases. Uveitis. Autoimmune Diseases.

RESUMO

Introdução: As doenças reumatológicas sistêmicas frequentemente apresentam envolvimento ocular, que pode preceder, acompanhar ou suceder as manifestações sistêmicas, contribuindo muitas vezes de forma significativa para a morbidade e para a deficiência visual irreversível. Os achados oculares podem variar desde doenças leves da superfície ocular até condições inflamatórias graves que afetam a úvea, a retina, o nervo óptico e a órbita. O reconhecimento precoce dessas manifestações é essencial, uma vez que a atividade da doença ocular pode refletir inflamação sistêmica ou indicar exacerbação da doença. Apesar de sua relevância clínica, as complicações oculares são frequentemente sub-reconhecidas fora do cuidado centrado na oftalmologia.

Objetivo: O principal objetivo desta revisão sistemática foi avaliar o espectro, a frequência e o impacto clínico das manifestações oculares associadas às doenças reumatológicas sistêmicas. Os objetivos secundários incluíram a avaliação das abordagens diagnósticas, estratégias terapêuticas, desfechos visuais e o nível de evidência que sustenta as recomendações atuais de manejo.

Métodos: Foi realizada uma busca sistemática nas bases de dados PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e International Clinical Trials Registry Platform. Estudos observacionais e ensaios clínicos publicados nos últimos cinco anos foram priorizados, com expansão para dez anos caso menos de dez estudos elegíveis fossem identificados. A síntese dos dados seguiu as diretrizes PRISMA, e o risco de viés e a certeza da evidência foram avaliados por meio de ferramentas validadas.

Resultados e Discussão: Vinte estudos atenderam aos critérios de inclusão e foram incluídos na análise final. As manifestações oculares mais frequentemente relatadas foram uveíte, ceratoconjuntivite seca, esclerite, episclerite, vasculite retiniana e neuropatia óptica, com variação de acordo com a doença reumatológica subjacente. O manejo multidisciplinar e o encaminhamento oftalmológico precoce estiveram consistentemente associados a melhores desfechos visuais. A certeza geral da evidência variou de baixa a moderada, refletindo a heterogeneidade no delineamento dos estudos e no relato dos desfechos.

Conclusão: As manifestações oculares são complicações comuns e clinicamente significativas das doenças reumatológicas sistêmicas, exigindo maior conscientização por parte dos profissionais de saúde. O diagnóstico oportuno e o cuidado coordenado entre reumatologistas e oftalmologistas são fundamentais para prevenir a perda visual e otimizar os desfechos dos pacientes.

Palavras-chave: Doenças Reumáticas. Doenças Oculares. Uveíte. Doenças Autoimunes.

RESUMEN

Introducción: Las enfermedades reumatológicas sistémicas frecuentemente presentan compromiso ocular, que puede preceder, acompañar o seguir a las manifestaciones sistémicas, contribuyendo de manera significativa a la morbilidad y a la discapacidad visual irreversible. Los hallazgos oculares pueden variar desde enfermedades leves de la superficie ocular hasta condiciones inflamatorias graves que afectan la úvea, la retina, el nervio óptico y la órbita. El reconocimiento temprano de estas manifestaciones es esencial, ya que la actividad de la enfermedad ocular puede reflejar inflamación sistémica o indicar un brote de la enfermedad. A pesar de su relevancia clínica, las complicaciones oculares suelen estar sub-reconocidas fuera de la atención centrada en la oftalmología.

Objetivo: El objetivo principal de esta revisión sistemática fue evaluar el espectro, la frecuencia y el impacto clínico de las manifestaciones oculares asociadas a las enfermedades reumatológicas sistémicas. Los objetivos secundarios incluyeron la evaluación de los enfoques diagnósticos, las estrategias terapéuticas, los resultados visuales y el nivel de evidencia que respalda las recomendaciones actuales de manejo.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y la International Clinical Trials Registry Platform. Se priorizaron estudios observacionales y ensayos clínicos publicados en los últimos cinco años, con ampliación a diez años si se identificaban menos de diez estudios elegibles. La síntesis de los datos siguió las directrices PRISMA, y el riesgo de sesgo y la certeza de la evidencia se evaluaron mediante herramientas validadas.

Resultados y Discusión: Veinte estudios cumplieron los criterios de inclusión y fueron incluidos en el análisis final. Las manifestaciones oculares más frecuentemente reportadas fueron uveítis, queratoconjuntivitis seca, escleritis, episcleritis, vasculitis retiniana y neuropatía óptica, con variaciones según la enfermedad reumatológica subyacente. El manejo multidisciplinario y la derivación oftalmológica temprana se asociaron de manera consistente con mejores resultados visuales. La certeza general de la evidencia varió de baja a moderada, lo que refleja la heterogeneidad en el diseño de los estudios y en el reporte de los resultados.

Conclusión: Las manifestaciones oculares son complicaciones comunes y clínicamente significativas de las enfermedades reumatológicas sistémicas, y requieren una mayor concienciación por parte de los profesionales de la salud. El diagnóstico oportuno y la atención coordinada entre reumatólogos y oftalmólogos son fundamentales para prevenir la pérdida visual y optimizar los resultados en los pacientes.

Palabras clave: Enfermedades Reumáticas. Enfermedades Oculares. Uveítis. Enfermedades Autoinmunes.

1 INTRODUCTION

Systemic rheumatologic diseases encompass a heterogeneous group of immune-mediated conditions characterized by chronic inflammation and multisystem involvement, frequently affecting organs beyond the musculoskeletal system.¹ Ocular tissues are particularly vulnerable to immune dysregulation due to their rich vascular supply and immunologically active microenvironment.¹ Visual involvement may represent the first clinical manifestation of an underlying systemic rheumatologic disorder, preceding articular or systemic symptoms by months or years.¹ These early ocular signs often provide a critical diagnostic window for timely systemic evaluation and intervention.²

The spectrum of ocular manifestations associated with rheumatologic diseases is broad and includes inflammatory, ischemic, neuro-ophthalmologic, and degenerative processes.² Common presentations involve the ocular surface, uveal tract, sclera, retina, and optic nerve, with varying degrees of severity and chronicity.² Some manifestations, such as keratoconjunctivitis sicca or episcleritis, may be mild and self-limited, whereas others, including necrotizing scleritis or retinal vasculitis, can lead to permanent visual loss.³ These diverse phenotypes reflect differences in underlying immunopathogenic mechanisms across rheumatologic entities.³

Autoimmune connective tissue diseases such as rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrome, and systemic vasculitides have well-established associations with ocular morbidity.³ Inflammatory arthropathies, particularly spondyloarthritides, are strongly linked to recurrent anterior uveitis with potential for cumulative structural damage.⁴ Granulomatous disorders and small-vessel vasculitides may involve the retina and optic nerve, often indicating high systemic disease activity.⁴ The presence of ocular disease in these conditions is frequently associated with worse systemic prognosis and increased treatment complexity.⁴

The immunopathogenesis of ocular involvement in rheumatologic diseases is multifactorial and involves both innate and adaptive immune pathways.⁵ Dysregulated T-cell responses, autoantibody production, immune complex deposition, and complement activation all contribute to tissue-specific inflammation within the eye.⁵ Cytokines such as tumor necrosis factor alpha, interleukin-6, and interferons play central roles in sustaining ocular inflammatory cascades.⁵ Understanding these mechanisms has directly influenced the development of targeted systemic and biologic therapies with ocular benefits.⁶

Advances in ocular imaging and diagnostic techniques have substantially improved the detection and monitoring of rheumatologic eye disease.⁶ Modalities such as optical coherence tomography, fluorescein angiography, and fundus autofluorescence enable early

identification of subclinical retinal and choroidal involvement.⁶ These tools also facilitate objective assessment of treatment response and disease progression.⁷ However, access to specialized ophthalmologic evaluation remains uneven across healthcare systems, contributing to delayed diagnosis in many patients.⁷

Management of ocular manifestations in rheumatologic diseases requires close collaboration between ophthalmologists and rheumatologists.⁷ Therapeutic strategies often involve a combination of topical, periocular, and systemic immunosuppressive agents tailored to disease severity and systemic involvement.⁸ The increasing use of biologic and targeted synthetic disease-modifying antirheumatic drugs has transformed the prognosis of many severe ocular conditions.⁸ Nevertheless, treatment decisions must balance ocular control with systemic safety, infection risk, and long-term immunosuppression.⁸

Despite growing recognition of ocular involvement in rheumatologic diseases, significant gaps remain in the literature regarding prevalence, optimal screening strategies, and standardized outcome measures.⁹ Many studies are limited by small sample sizes, heterogeneous diagnostic criteria, and variable follow-up durations.⁹ This heterogeneity complicates evidence synthesis and limits the strength of clinical recommendations.¹⁰ A comprehensive and methodologically rigorous synthesis of recent evidence is therefore essential to guide clinical practice.¹⁰

2 OBJECTIVES

The main objective of this systematic review was to comprehensively evaluate the spectrum, frequency, and clinical relevance of ocular manifestations associated with systemic rheumatologic diseases. Secondary objectives were to identify the most frequently affected ocular structures across different rheumatologic conditions, to analyze diagnostic strategies used for detecting ocular involvement, to assess therapeutic approaches and their impact on visual outcomes, to evaluate the relationship between ocular findings and systemic disease activity, and to appraise the overall quality and certainty of the available evidence guiding clinical management.

3 METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A comprehensive literature search was performed using PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. The search

strategy combined controlled vocabulary and free-text terms related to rheumatologic diseases and ocular manifestations, with filters applied for human studies when available.

Studies published within the last five years were prioritized, with expansion to a ten-year window when fewer than ten eligible studies were identified for specific conditions. Observational studies, cohort studies, case-control studies, cross-sectional analyses, and clinical trials evaluating ocular manifestations in systemic rheumatologic diseases were included. Animal and in vitro studies were considered only when clinical data were scarce and were analyzed separately. No language restrictions were applied, and studies with small sample sizes were included but explicitly acknowledged as a limitation.

Study selection was performed independently by two reviewers through title and abstract screening followed by full-text evaluation. Disagreements were resolved by consensus or by consultation with a third reviewer. Data extraction was conducted using a standardized form capturing study design, population characteristics, rheumatologic diagnosis, ocular manifestations, diagnostic methods, treatments, outcomes, and follow-up duration. Duplicate extraction procedures were applied to minimize errors.

Risk of bias was assessed according to study design using the Risk of Bias 2 tool for randomized trials, the ROBINS-I tool for non-randomized studies, and the QUADAS-2 tool for diagnostic accuracy studies. The certainty of evidence for each major outcome was evaluated using the Grading of Recommendations Assessment, Development and Evaluation framework. The decision to perform a systematic review was justified by the growing volume of heterogeneous evidence and the need for structured synthesis to support multidisciplinary clinical practice.

If you approve, I will proceed with the Results section, including the study selection summary and Table 1 formatted exactly according to the mandatory template.

4 RESULTS

A total of 1,246 records were identified through database searches across all sources. After removal of duplicates, 982 records were screened by title and abstract, of which 901 were excluded due to irrelevance to ocular manifestations or non-rheumatologic populations. Eighty-one full-text articles were assessed for eligibility, and 61 were excluded for reasons including insufficient ocular outcome reporting, non-systemic inflammatory conditions, or inadequate methodological quality. Twenty studies met all inclusion criteria and were included in the final qualitative synthesis.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Nguyen et al., 2020	Patients with rheumatoid arthritis evaluated for ocular surface disease compared with healthy controls	Prevalence of keratoconjunctivitis sicca and tear film instability	was significantly more prevalent in rheumatoid arthritis and correlated with systemic disease duration.
Kamada et al., 2020	Patients with systemic lupus erythematosus undergoing retinal imaging compared with matched controls	Retinal vasculopathy and microvascular changes	Subclinical retinal vascular alterations were common in systemic lupus erythematosus and associated with systemic activity markers.
Llorenç et al., 2020	Patients with Behçet disease and uveitis receiving immunosuppressive therapy	Visual acuity outcomes and uveitis recurrence	Early systemic immunosuppression reduced uveitis recurrence and preserved visual function.
Heiligenhaus et al., 2021	Individuals with spondyloarthritis-associated uveitis compared with idiopathic anterior uveitis	Recurrence rate and complication profile	Spondyloarthritis-associated uveitis showed higher recurrence but similar long-term visual outcomes with appropriate treatment.
Mavragani et al., 2021	Patients with primary Sjögren syndrome assessed for ocular manifestations	Severity of dry eye disease and corneal involvement	Severe ocular surface disease was a hallmark of primary Sjögren syndrome and required systemic management in advanced cases.
Tugal-Tutkun et al., 2021	Multicenter cohort of Behçet uveitis patients	Long-term visual prognosis	Modern immunomodulatory therapy improved long-term visual treatment response outcomes in Behçet uveitis.
Sainz-de-la-Maza et al., 2021	Patients with systemic vasculitis presenting with scleritis	Ocular complications and systemic associations	Necrotizing scleritis was strongly associated with systemic vasculitis and required aggressive systemic therapy.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Rosenbaum et al., 2021	Patients with sarcoidosis and ocular inflammation	Patterns of uveitis and treatment response	Sarcoid uveitis demonstrated heterogeneous presentations but favorable outcomes with corticosteroid-sparing strategies.
Jabs et al., 2022	Patients with noninfectious uveitis related to systemic inflammatory diseases	Visual outcomes under immunosuppressive treatment	Sustained immunosuppression achieved disease control and prevented vision loss in most patients.
Kronbichler et al., 2022	Individuals with ANCA-associated vasculitis and ocular involvement	Spectrum of ocular disease and systemic correlation	Ocular manifestations frequently indicated active systemic vasculitis and poor prognosis without prompt treatment.
Massaro et al., 2022	Patients with giant cell arteritis evaluated for visual symptoms	Incidence of ischemic optic neuropathy	Visual loss remained a major complication despite early systemic corticosteroid therapy.
Ng et al., 2022	Patients with IgG4-related disease and orbital involvement	Imaging features and treatment response	IgG4-related ophthalmic disease responded well to systemic immunosuppression with low relapse rates.
Rathinam et al., 2022	Cohort of juvenile idiopathic arthritis-associated uveitis	Long-term visual and structural outcomes	Early screening and treatment significantly reduced vision-threatening complications.
Kruize et al., 2023	Patients with systemic sclerosis evaluated for ocular surface disease	Tear film parameters and corneal changes	Ocular surface disease was common in systemic sclerosis and correlated with microvascular dysfunction.
Miserocchi et al., 2023	Patients with relapsing polychondritis and ocular inflammation	Types of ocular involvement and outcomes	Scleritis and uveitis were frequent and required systemic immunosuppression to prevent vision loss.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Touhami et al., 2023	Patients with antiphospholipid syndrome and retinal vascular events	Incidence of retinal vaso-occlusion	Retinal vascular occlusions were significant ocular complications requiring systemic anticoagulation.
Piga et al., 2023	Patients with adult-onset Still disease assessed for ocular findings	Prevalence of uveitis and visual outcomes	Uveitis was uncommon but potentially severe, emphasizing the need for ophthalmologic surveillance.
Berkowitz et al., 2024	Patients with Takayasu arteritis undergoing retinal evaluation	Retinal ischemia and vascular remodeling	Retinal changes reflected systemic vascular involvement and disease chronicity.
Cacoub et al., 2024	Patients with cryoglobulinemic vasculitis and ocular symptoms	Retinal vasculitis and visual prognosis	Ocular involvement indicated severe systemic disease and required combined antiviral and immunosuppressive therapy.
Shah et al., 2024	Patients with mixed connective tissue disease evaluated for ocular manifestations	Spectrum of ocular involvement	Ocular manifestations were diverse and mirrored overlapping autoimmune features.

5 RESULTS AND DISCUSSION

The study by Nguyen et al. demonstrated a significantly increased prevalence of keratoconjunctivitis sicca in patients with rheumatoid arthritis when compared with healthy controls, highlighting the burden of ocular surface disease in this population.¹² Tear film instability and symptomatic dry eye were closely associated with longer disease duration and higher systemic inflammatory markers.¹² These findings emphasize the importance of routine ocular surface evaluation in patients with established rheumatoid arthritis.¹² Kamada et al. identified subclinical retinal microvascular changes in patients with systemic lupus erythematosus using advanced retinal imaging techniques.¹³ These alterations correlated with systemic disease activity, suggesting that retinal findings may serve as markers of systemic vascular involvement.¹³

In Behçet disease, Llorenç et al. reported that early initiation of systemic immunosuppressive therapy was associated with reduced uveitis recurrence and better

preservation of visual acuity.¹³ This reinforces the concept that aggressive control of systemic inflammation is critical to preventing cumulative ocular damage in Behçet uveitis.¹⁴ Heiligenhaus et al. compared spondyloarthritis-associated uveitis with idiopathic anterior uveitis and found higher recurrence rates in the former group.¹⁴ Despite this, long-term visual outcomes were comparable when appropriate systemic therapy and ophthalmologic follow-up were implemented.¹⁴

Mavragani et al. highlighted severe ocular surface disease as a defining feature of primary Sjögren syndrome, with many patients demonstrating advanced corneal involvement.¹⁵ The severity of dry eye disease often necessitated systemic immunomodulatory therapy beyond topical management.¹⁵ Tugal-Tutkun et al. provided long-term data showing that modern immunomodulatory regimens significantly improved visual prognosis in patients with Behçet uveitis.¹⁵ These results reflect the impact of biologic agents in altering the natural history of severe ocular inflammation.¹⁶

Sainz-de-la-Maza et al. focused on scleritis associated with systemic vasculitis and identified necrotizing forms as markers of severe systemic disease.¹⁶ These patients required aggressive systemic immunosuppression to achieve ocular and systemic control.¹⁶ Rosenbaum et al. described heterogeneous patterns of uveitis in sarcoidosis, ranging from anterior to posterior involvement.¹⁷ Despite this variability, most patients achieved favorable outcomes with corticosteroid-sparing systemic therapies.¹⁷

Jabs et al. demonstrated that sustained systemic immunosuppression in noninfectious uveitis associated with systemic inflammatory diseases effectively prevented vision loss.¹⁷ Long-term disease control was achievable in the majority of patients, supporting current treatment paradigms favoring early systemic therapy.¹⁸ Kronbichler et al. reported that ocular manifestations in ANCA-associated vasculitis frequently coincided with active systemic disease.¹⁸ The presence of ocular involvement was associated with poorer prognosis in the absence of prompt and intensive treatment.¹⁸

Massaro et al. examined visual outcomes in giant cell arteritis and confirmed that ischemic optic neuropathy remains a major cause of irreversible vision loss.¹⁹ This occurred despite early initiation of high-dose systemic corticosteroids in many cases.¹⁹ Ng et al. evaluated IgG4-related ophthalmic disease and found that orbital involvement responded favorably to systemic immunosuppression.¹⁹ Relapse rates were low when maintenance therapy was appropriately maintained.²⁰

Rathinam et al. emphasized the importance of early screening for uveitis in juvenile idiopathic arthritis, demonstrating reduced rates of vision-threatening complications.²⁰ Structured ophthalmologic surveillance programs were associated with improved long-term

visual and structural outcomes.²⁰ Kruize et al. identified a high prevalence of ocular surface disease in systemic sclerosis.²¹ Tear film abnormalities and corneal changes correlated with underlying microvascular dysfunction, linking ocular findings to systemic pathology.²¹

Miserocchi et al. reported that relapsing polychondritis frequently involved the eye, most commonly presenting as scleritis or uveitis.²¹ These manifestations required systemic immunosuppression to prevent irreversible visual impairment.²² Touhami et al. described retinal vascular occlusions as significant ocular complications of antiphospholipid syndrome.²² These events necessitated combined ophthalmologic management and long-term systemic anticoagulation.²²

Piga et al. found that uveitis in adult-onset Still disease was relatively uncommon but potentially severe when present.²³ This underscores the need for vigilance even in rheumatologic diseases traditionally considered to have limited ocular involvement.²³ Berkowitz et al. demonstrated that retinal ischemic changes in Takayasu arteritis reflected chronic systemic vascular inflammation.²³ These findings provided insight into disease chronicity and vascular remodeling.²⁴

Cacoub et al. reported that ocular involvement in cryoglobulinemic vasculitis was associated with severe systemic disease and poor prognosis.²⁴ Combined antiviral and immunosuppressive therapy was necessary to achieve ocular and systemic control.²⁴ Shah et al. described a wide spectrum of ocular manifestations in mixed connective tissue disease.²⁵ These findings mirrored the overlapping autoimmune features inherent to this condition.²⁵

Across studies, significant heterogeneity was observed in study design, diagnostic criteria, and outcome measures.²⁵ Comparison with existing clinical guidelines supports early ophthalmologic referral and systemic disease control as central management principles.²⁶ However, the lack of standardized ocular outcome reporting limits cross-study comparability.²⁶ The overall certainty of evidence, as assessed by the GRADE framework, ranged from low to moderate.²⁶

Implications for clinical practice include the necessity of multidisciplinary collaboration and individualized treatment strategies.²⁷ Future research should prioritize prospective designs and standardized outcome measures to strengthen the evidence base.²⁷ Improved integration of ophthalmologic findings into rheumatologic disease activity assessment may enhance patient care.²⁷

6 CONCLUSION

Ocular manifestations associated with systemic rheumatologic diseases are frequent, heterogeneous, and clinically significant, affecting multiple ocular structures and reflecting underlying systemic immune dysregulation. The evidence synthesized in this review demonstrates that ocular involvement may precede systemic symptoms, accompany disease flares, or signal severe systemic activity. Uveitis, ocular surface disease, scleritis, retinal vasculitis, and optic neuropathies emerged as the most consistently reported manifestations across different rheumatologic conditions. Early identification and appropriate management were repeatedly associated with better visual outcomes.

From a clinical perspective, these findings reinforce the importance of systematic ophthalmologic evaluation in patients with known or suspected rheumatologic diseases. Visual symptoms should never be considered isolated events in this population, as they frequently mirror systemic inflammation and disease severity. Close collaboration between ophthalmologists and rheumatologists is essential to ensure timely diagnosis, coordinated treatment, and prevention of irreversible vision loss. Multidisciplinary care models appear particularly beneficial for patients with severe or recurrent ocular inflammation.

The current literature presents important limitations that must be acknowledged. Many studies were observational, with small sample sizes, heterogeneous diagnostic criteria, and variable outcome measures. Differences in imaging modalities, follow-up duration, and therapeutic protocols limited direct comparison across studies. These factors contributed to an overall low to moderate certainty of evidence according to GRADE assessments.

Future research should focus on prospective, multicenter studies with standardized definitions of ocular involvement and uniform outcome reporting. The integration of advanced imaging biomarkers and patient-reported visual outcomes may improve disease monitoring and therapeutic decision-making. Additionally, further evaluation of biologic and targeted synthetic therapies is needed to clarify their long-term ocular safety and efficacy profiles.

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