International Journal of Medical Science and Public Health Research
ISSN : 2767-3774
SJIF: 2021: 5.456, 2022: 5.681, 2023: 6.591

TYPE Original Research
PAGE NO. 01-08

Check for updates

A Comprehensive Review Of Ocular Manifestations In Rheumatoid Arthritis: From Pathophysiology To Clinical Management

Dr. Eleanor Vance

Department of Rheumatology, King's College Hospital, London, United Kingdom

Dr. Aisha Khan

Faculty of Autoimmune Research, National University of Singapore, Singapore

OPEN ACCESS

SUBMITTED 03 August 2025
ACCEPTED 02 September 2025
PUBLISHED 01 October 2025
VOLUME Vol.06 Issue10 2025

Abstract: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that frequently presents with extra-articular manifestations. Ocular involvement is common and can range from mild discomfort to sight-threatening conditions. This review provides a comprehensive overview of the visual complaints and ocular manifestations in patients with RA.

Methods: A literature review was conducted using a systematic approach to identify relevant articles on the ocular manifestations of RA. The search included peer-reviewed articles, clinical trials, and case reports. The focus was on the pathophysiology, clinical presentation, diagnosis, and management of these conditions.

Results: The most common ocular manifestation of RA is keratoconjunctivitis sicca (dry eye syndrome). Other significant anterior segment complications include episcleritis, scleritis, and peripheral ulcerative keratitis. Posterior segment involvement, such as uveitis and retinal vasculitis, is less common but can be more severe. A critical aspect of management is monitoring for drug-induced toxicities, particularly hydroxychloroquine retinopathy, which can cause irreversible vision loss (1). The risk of QT interval prolongation with hydroxychloroquine use, especially with concomitant medications, also warrants consideration (2). Recent clinical trials have provided further insights into the implications of these ocular manifestations (3).

Conclusion: Ocular manifestations in RA are diverse and require a high index of suspicion for early diagnosis and

treatment. A multidisciplinary approach involving rheumatologists and ophthalmologists is essential for optimal patient care. Regular ophthalmic screening is recommended for all RA patients, especially those on long-term hydroxychloroquine therapy, to prevent irreversible vision loss and improve quality of life.

Keywords: Rheumatoid Arthritis, Ocular Manifestations, Visual Complaints, Hydroxychloroquine Retinopathy, Scleritis, Keratoconjunctivitis Sicca, Uveitis.

Introduction:

1.1 Background of Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized primarily by inflammation of the synovial joints, leading to progressive joint damage, deformity, and functional disability. While its articular manifestations are the most recognized feature, RA is fundamentally a systemic disease, capable of affecting a wide array of organ systems throughout the body. The underlying pathophysiology involves a complex interplay of genetic predisposition, environmental triggers, and a dysregulated immune response. This leads to the production of autoantibodies, such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), and the activation of various immune cells, including T-cells, B-cells, and macrophages. These elements orchestrate a sustained inflammatory cascade, releasing pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which not only attack the synovium but also contribute to systemic inflammation. Consequently, extra-articular manifestations (EAMs) are a key feature of the disease, occurring in a significant portion of patients and contributing substantially to both morbidity and mortality. These EAMs can involve the skin, lungs, heart, nervous system, and, critically, the eyes.

1.2 Ocular Complications in RA: An Overview

The ocular system is a frequent target of the systemic inflammation associated with RA. Visual complaints from patients with RA are common and should never be dismissed, as they can range from the discomfort of dry eyes to the profound, irreversible vision loss associated with severe inflammatory events or medication toxicity. The prevalence of ocular complications in the RA population underscores the need for vigilant monitoring and a high degree of clinical suspicion. The spectrum of ocular diseases linked to RA is broad, reflecting the various tissues within the eye that can be affected by autoimmune processes. The most common complication is keratoconjunctivitis sicca (KCS), or dry eye syndrome, which results from inflammation of the lacrimal glands. However, more severe, sight-threatening conditions also occur, including scleritis (inflammation of the sclera), episcleritis, peripheral ulcerative keratitis (PUK), and uveitis. These conditions often mirror the severity and activity of the underlying systemic disease. Furthermore, the very medications used to control RA, particularly disease-modifying antirheumatic drugs (DMARDs) like hydroxychloroquine, can induce significant ocular toxicity, creating a complex clinical challenge (3).

1.3 Rationale and Objectives

While the association between RA and various ocular diseases is well-established, there remains a need for a comprehensive clinical review that synthesizes the current understanding of these manifestations, connects them to diagnostic challenges, and outlines contemporary management strategies. Clinicians, including rheumatologists, ophthalmologists, and general practitioners, require a clear framework for identifying, evaluating, and treating these complex conditions. The primary objective of this article is to provide a detailed and extensive overview of the ocular manifestations of rheumatoid arthritis. We aim to explore the pathophysiology behind each major condition, describe their clinical presentations, discuss the critical role of diagnostic evaluation, and review current and emerging treatment options. A significant portion of this review is dedicated to the iatrogenic effects of RA therapies, with a particular focus on the retinal toxicity of hydroxychloroquine, a cornerstone of RA management (1). By integrating information on both disease-related and treatment-related ocular pathology, this review seeks to equip clinicians with the knowledge necessary to mitigate vision loss and improve the quality of life for patients living with rheumatoid arthritis.

METHODS

2.1 Literature Search Strategy

This review is based on a structured search of the existing medical literature to identify seminal and contemporary research on the topic of ocular manifestations in rheumatoid arthritis. A comprehensive search was conducted using prominent electronic databases, including PubMed/MEDLINE and Google Scholar, to ensure a broad capture of relevant publications. The search strategy employed a combination of medical subject headings (MeSH) and free-text keywords. Key search terms included, but were not limited to: "rheumatoid arthritis," "ocular

manifestations," "visual complaints," "keratoconjunctivitis sicca," "scleritis," "episcleritis," "peripheral ulcerative keratitis," "uveitis," "hydroxychloroquine," "retinal toxicity," and "DMARDs." The search was further refined by combining these terms to focus on specific areas of interest, such as the association between systemic disease activity and ocular inflammation, and the guidelines for screening for medication-induced eye disease.

2.2 Inclusion and Exclusion Criteria

The selection process for articles to be included in this comprehensive review was guided by a predefined set of criteria to ensure relevance and quality. The primary inclusion criteria were: (1) peer-reviewed publications, including original research articles, systematic reviews, meta-analyses, and major clinical guidelines; (2) studies focusing directly on the diagnosis, pathophysiology, or management of ocular conditions in patients with a confirmed diagnosis of rheumatoid arthritis; and (3) articles discussing the ocular side effects of medications commonly used to treat RA. Seminal articles providing foundational knowledge and recent publications reflecting the latest clinical trials and management paradigms were prioritized (3). Articles were excluded if they were not published in the English language, existed only as abstracts without a full-text version, or focused on ocular diseases in other autoimmune conditions without a specific RA cohort.

2.3 Data Extraction and Synthesis

Data from the selected articles were systematically extracted and organized to facilitate a comprehensive synthesis. Information was categorized according to the primary sub-topics of this review, as outlined in the introduction. This included data on the epidemiology and pathophysiology of specific ocular conditions, their clinical features and diagnostic criteria, and evidence-based management strategies. A thematic analysis approach was employed to synthesize the findings. This involved identifying recurring themes and patterns across the literature, such as the classification of anterior versus posterior segment diseases, the mechanisms of drug toxicity (1), and the importance of interdisciplinary collaboration. This method allowed for the construction of a coherent narrative, integrating diverse sources of information into a structured and clinically useful overview of the topic. The synthesis focuses on translating research findings into practical implications for clinical practice.

RESULTS

3.1 Spectrum of Ocular Manifestations

The ocular complications of rheumatoid arthritis are varied, affecting nearly every structure of the eye. They can be broadly categorized based on the anatomical location of involvement: the anterior segment and the posterior segment. The prevalence and severity of these manifestations often correlate with the overall activity and duration of the systemic RA.

3.1.1 Anterior Segment Manifestations

The anterior segment of the eye is the most frequent site of RA-related pathology. These conditions are often the first to present and can cause significant discomfort and, in some cases, severe visual impairment.

- Keratoconjunctivitis Sicca (Dry Eye Syndrome): KCS is the single most common ocular manifestation in patients with RA, affecting a substantial portion of this population. It is a feature of secondary Sjögren's syndrome, an autoimmune condition that often coexists with RA. The underlying pathophysiology involves lymphocytic infiltration of the lacrimal and accessory lacrimal glands. This autoimmune-mediated inflammation disrupts the normal function of the glands, leading to a significant reduction in aqueous tear production. The resulting tear film instability and hyperosmolarity cause desiccation of the ocular surface, leading to a cascade of inflammatory events on the cornea and conjunctiva. Clinically, patients present with a range of persistent and bothersome symptoms, including a gritty or foreign body sensation, burning, itching, redness, light sensitivity (photophobia), and paradoxically, reflexive tearing. Visual acuity can be affected due to ocular surface irregularities, with patients often reporting fluctuating or blurry vision that may temporarily improve with blinking. Diagnosis is supported by clinical examination and several specific tests. Schirmer's test measures the rate of tear production and is often abnormal in these patients. Tear film breakup time (TBUT) assesses the stability of the tear film, which is typically reduced. Staining of the cornea and conjunctiva with vital dyes like fluorescein, lissamine green, or rose bengal can reveal areas of epithelial cell damage and devitalization, confirming ocular surface disease.
- Episcleritis and Scleritis: Inflammation of the sclera (scleritis) and the overlying episcleral tissue (episcleritis) are serious complications of RA. It is crucial to differentiate between them, as their prognosis and management differ significantly.
  - Episcleritis is a relatively benign, self-limiting inflammation of the vascularized tissue between the conjunctiva and the sclera. It often presents with acute onset of sectoral or diffuse redness and mild to moderate discomfort or irritation. Vision is typically

unaffected. The inflammation is superficial, and the deeper scleral tissue is not involved. On examination, the injected vessels are larger, straighter, and will blanch with the topical application of a vasoconstrictor like phenylephrine, a key diagnostic feature that distinguishes it from true scleritis.

- Scleritis, in contrast, is a much more severe, potentially destructive inflammation of the sclera itself. It is considered a strong indicator of systemic vasculitis and is associated with increased mortality in RA patients. The presentation is characterized by the insidious onset of severe, deep, boring eye pain that may radiate to the jaw, temple, or brow and characteristically awakens the patient at night. The eye exhibits a deep, violaceous hue, and the inflamed vessels do not blanch with phenylephrine. Scleritis is classified based on its location and appearance. Anterior scleritis can be diffuse, nodular, or necrotizing. Necrotizing scleritis is the most feared form; it is often associated with severe pain (though it can be painless in a variant called scleromalacia perforans) and can lead to thinning and perforation of the globe, resulting in catastrophic vision loss (3). Posterior scleritis is less common and more difficult to diagnose, presenting with decreased vision, pain with eye movement, and signs such as choroidal folds, optic disc swelling, or exudative retinal detachment.

- Peripheral Ulcerative Keratitis (PUK): PUK is a rare but aggressive and sight-threatening condition characterized by inflammation and ulcerative destruction of the peripheral cornea. It represents a localized corneal vasculitis. The pathophysiology is thought to involve the deposition of immune complexes in the peripheral corneal vessels, triggering a complement-mediated inflammatory cascade that leads to enzymatic degradation of the corneal stroma. Patients typically present with pain, redness, photophobia, and decreased vision. Clinically, a crescent-shaped infiltrate is seen at the corneal limbus, which progresses to stromal thinning, ulceration, and potentially perforation. PUK is strongly associated with active systemic RA and the presence of vasculitis in other organs.

3.1.2 Posterior Segment Manifestations

While less common than anterior segment disease, posterior segment manifestations of RA can have devastating consequences for vision.

- Uveitis: Uveitis, the inflammation of the uveal tract (iris, ciliary body, and choroid), is an uncommon but recognized complication of RA in adults. It is more classically associated with juvenile idiopathic arthritis. When it does occur in adults with RA, it is typically anterior uveitis (iritis), presenting with pain, redness, photophobia, and blurred vision. However, posterior uveitis and panuveitis can also occur, particularly in patients with severe, long-standing disease. These forms can lead to complications such as cystoid macular edema, cataracts, and glaucoma.

- Retinal Vasculitis: This is a rare but very serious manifestation of systemic RA-associated vasculitis. It involves inflammation of the retinal blood vessels, which can lead to vessel occlusion, retinal ischemia, neovascularization, vitreous hemorrhage, and tractional retinal detachment. Patients may present with floaters, decreased vision, or scotomas (blind spots). Funduscopic examination may reveal signs such as cotton-wool spots, retinal hemorrhages, and vascular sheathing. Retinal vasculitis is a marker of severe systemic disease and requires aggressive systemic immunosuppression to preserve vision and control the underlying RA.

3.2 Drug-Induced Ocular Toxicities

The management of RA relies heavily on medications that can have significant ocular side effects. Therefore, a key part of the clinical picture is iatrogenic disease, which must be carefully monitored.

3.2.1 Hydroxychloroquine Retinopathy

Hydroxychloroquine (HCQ) is a cornerstone of RA therapy, valued for its efficacy and relative safety compared to other DMARDs. However, its potential for irreversible retinal toxicity is its most significant adverse effect.

- Mechanism of Toxicity: The exact mechanism of HCQ toxicity is not fully understood, but it is believed to involve the drug binding to melanin in the retinal pigment epithelium (RPE). This leads to accumulation of the drug within the RPE and photoreceptor cells, disrupting their metabolic function, leading to cellular damage and apoptosis over time. This damage is progressive and, critically, irreversible once it becomes clinically apparent.

- Clinical Presentation and Diagnosis: In the early stages, HCQ retinopathy is asymptomatic. As it progresses, patients may notice a paracentral scotoma (a blind spot near the center of vision), difficulties with reading, or diminished color vision. In advanced stages, the classic sign of "bull's-eye maculopathy" may be visible on fundus examination. This consists of a ring of RPE depigmentation in the macula, surrounding a foveal center that remains relatively preserved. This pattern gives the macula the appearance of a target or bull's-eye (1).

3.2.1.1. Modern Screening Protocols for Hydroxychloroquine Retinopathy: A Practical Guide

The primary goal of screening for hydroxychloroquine

(HCQ) retinopathy is to detect toxic changes at a preclinical stage, before the patient becomes symptomatic and before irreversible central vision is lost. Historically, screening relied on insensitive methods such as color vision testing, Amsler grid evaluation, and fundus photography. These methods are now considered obsolete for primary screening because they only detect retinopathy at a late, advanced stage, often after the classic "bull's-eye maculopathy" has already formed (1). The contemporary standard of care, endorsed by major ophthalmological societies, is a multimodal imaging approach that utilizes objective, high-resolution structural tests supplemented by subjective functional testing. This strategy allows for the identification of subtle, early damage to the photoreceptors and retinal pigment epithelium (RPE), enabling timely cessation of the drug.

The cornerstone of modern screening rests on two primary objective tests: Spectral-Domain Optical Coherence Tomography (SD-OCT) and Fundus Autofluorescence (FAF). These are complemented by a crucial subjective test: automated visual field perimetry.

- Spectral-Domain Optical Coherence Tomography (SD-OCT): SD-OCT is arguably the most important and sensitive tool for detecting early HCQ toxicity. This non-invasive imaging technology uses low-coherence interferometry to generate micrometer-resolution, cross-sectional images of the retina, providing a virtual histological view. For HCQ screening, high-resolution macular cube scans are performed. The clinician meticulously examines the integrity of the outer retinal layers in the parafoveal region, which is the area most susceptible to initial damage in most populations. The earliest and most specific sign of HCQ toxicity on SD-OCT is the attenuation or loss of the photoreceptor integrity line, specifically the ellipsoid zone (EZ), in the parafoveal region. The EZ is a hyperreflective band that represents the metabolic powerhouse of the photoreceptors (the inner segments' mitochondria) and its disruption is a direct indicator of cellular stress and damage. This structural change often precedes any detectable functional loss on visual field testing or any visible changes on funduscopic examination. As the toxicity progresses, this focal loss of the EZ is often accompanied by thinning of the outer nuclear layer (ONL), which contains the photoreceptor cell bodies. A characteristic finding in established, though still early, toxicity is the "flying saucer" sign. This describes the appearance on the foveal OCT scan where the central foveal pit remains preserved, but the surrounding parafoveal outer retinal layers (EZ and RPE) become thinned and depressed, creating a shape reminiscent of a saucer. This morphology directly corresponds to the eventual development of the bull's-eye pattern of RPE atrophy (1). It is critical to recognize that the topographical pattern of toxicity can vary, particularly with ethnicity. While the classic pattern involves the parafoveal region, a significant proportion of patients, particularly those of Asian descent, may exhibit a more peripheral, pericentral pattern of damage. In these cases, the damage begins in a more extramacular location, typically 7-10 degrees from the fovea. Standard macular OCT scans may miss this initial damage. Therefore, in these patients, it is imperative to perform wider-field OCT scans (e.g., 12mm scans) that extend beyond the central macula to the pericentral and near-peripheral regions to ensure these early changes are not overlooked.

- Fundus Autofluorescence (FAF): FAF is a non-invasive imaging technique that provides information about the health and metabolic state of the RPE. It maps the distribution of lipofuscin, a metabolic byproduct that accumulates in RPE cells. Healthy RPE has a relatively uniform, grayish autofluorescence. Stressed or metabolically compromised RPE may exhibit increased autofluorescence (hyper-AF), while dead or atrophied RPE will show no autofluorescence (hypo-AF). In the context of HCQ screening, FAF can be a valuable adjunct to OCT. Very early signs of toxicity may manifest as a subtle stippling or a mottled pattern of hyper-AF in the parafoveal ring, indicating RPE stress before significant cell death has occurred. As the retinopathy advances, a distinct ring of hyper-AF often develops, which may correspond with the "flying saucer" sign on OCT. In late-stage disease, this ring becomes profoundly hypo-autofluorescent, directly correlating with the area of RPE atrophy seen in bull's-eye maculopathy. The central fovea typically remains iso-autofluorescent until the very end stages. FAF is particularly useful for confirming abnormalities suspected on other tests and for documenting the progression of atrophy over time.

- Automated Visual Field Perimetry: While OCT and FAF assess retinal structure, automated visual field testing assesses retinal function. It is a critical component of screening because it provides the functional correlate to the structural damage seen on imaging. The standard protocol for HCQ screening is a white-on-white 10-2 visual field test. The "10-2" designation means the test assesses the central 10 degrees of the visual field with a dense pattern of test points, making it highly sensitive for detecting the subtle paracentral scotomas characteristic of HCQ toxicity. For patients where a pericentral pattern of damage is suspected (e.g., in Asian patients), a wider field test, such as a 24-2 or 30-2, should be performed in addition

to the 10-2 to ensure the more peripheral defects are not missed. A reliable and repeatable visual field defect that topographically matches an area of structural damage on OCT is strong evidence of definite toxicity. The characteristic defect is a ring or partial ring scotoma located between 2 and 8 degrees from fixation. It is essential to ensure the reliability of the test (e.g., low fixation losses, low false positives/negatives) and to repeat the test to confirm that any detected defect is persistent and not an artifact. It is important to remember that due to the high sensitivity of modern OCT, structural damage is often detected before a clear and repeatable functional defect emerges on visual field testing.

- Synthesizing the Data: A Multimodal Diagnostic Framework: The strength of the modern screening approach lies in synthesizing the information from all tests. A diagnosis of HCQ retinopathy should not be made based on a single test in isolation. Clinicians can categorize findings to guide management:

  - No Toxicity: All objective (OCT, FAF) and subjective (visual field) tests are normal and stable. Screening continues according to the recommended schedule.

  - Indefinite or Suspected Toxicity: A subtle, non-specific, or unrepeatable abnormality is noted on one test but is not confirmed by others. For example, a questionable area of ONL thinning on OCT without a corresponding EZ disruption or visual field defect. In these cases, the drug should not be stopped. Instead, the patient should be monitored more frequently (e.g., in 6 months), and the tests should be repeated to assess for definitive progression.

  - Definite Toxicity: There is a clear, reproducible, and topographically corresponding abnormality on both an objective structural test and a subjective functional test. For example, a clear area of parafoveal EZ loss on OCT that perfectly matches a dense paracentral scotoma on the 10-2 visual field. This finding mandates a conversation with the prescribing rheumatologist about the immediate and permanent cessation of hydroxychloroquine. The ophthalmologist must clearly communicate that the damage is irreversible and may even continue to progress for some time after the drug is stopped.

- Risk Stratification and Recommended Screening Schedule: Effective screening also involves identifying patients at the highest risk. The most significant risk factors for developing HCQ retinopathy are a high daily dose and a long duration of use. The current recommendation is to keep the daily dose at or below 5.0 mg/kg of real body weight. It's crucial that this calculation is based on the patient's actual weight, not an ideal weight, as the drug accumulates in body tissues. Other major risk factors include: duration of use (>5 years), renal disease, concomitant tamoxifen use, and pre-existing macular disease. Based on this risk stratification, the recommended screening schedule is as follows: A baseline examination should be performed within the first year of starting HCQ to rule out any pre-existing confounding macular disease. Following this baseline, annual screening should commence after five years of cumulative drug use. However, if a patient has any of the major risk factors, annual screening should be considered sooner.

3.2.2 Other Medication-Related Ocular Side Effects

- Corticosteroids: Both systemic and topical corticosteroids are frequently used to control inflammation in RA. Their long-term use is associated with two major ocular side effects: the development of posterior subcapsular cataracts, which cause glare and blurred vision, and elevated intraocular pressure, which can lead to iatrogenic glaucoma and optic nerve damage.

- Methotrexate and Other DMARDs: While less common, other DMARDs can also have ocular side effects. Methotrexate has been rarely associated with a painful conjunctivitis or episcleritis. Biologic agents, particularly TNF-α inhibitors, have been paradoxically implicated in rare cases of new-onset or worsening uveitis or optic neuritis.

3.3 Clinical Evaluation and Diagnosis

The diagnosis of ocular complications in RA requires a comprehensive approach. A strong collaboration between the rheumatologist and the ophthalmologist is paramount for effective patient care. The rheumatologist is responsible for assessing systemic disease activity and managing immunosuppressive therapy, while the ophthalmologist performs the detailed ocular examination required to diagnose and manage the specific eye condition. A thorough patient history should focus on specific visual symptoms. The ophthalmic examination must include a careful assessment of visual acuity, a slit-lamp examination to evaluate the anterior segment structures (cornea, sclera, iris), measurement of intraocular pressure, and a dilated fundus examination to assess the posterior segment (retina, optic nerve). Advanced imaging techniques, such as OCT for HCQ screening or fluorescein angiography for retinal vasculitis, are often indispensable for accurate diagnosis and monitoring.

DISCUSSION

4.1 Synthesis of Findings

This review consolidates the understanding that the

ocular system is a significant site for both the primary manifestations of rheumatoid arthritis and the secondary complications of its treatment. The findings underscore a critical clinical reality: visual symptoms in an RA patient are a red flag that demands immediate and thorough investigation. The spectrum of disease, from the highly prevalent and symptomatic KCS to the rare but devastating necrotizing scleritis and retinal vasculitis, highlights the pleiotropic nature of RA's inflammatory processes (3). A crucial theme emerging from the synthesis of the literature is the strong correlation between ocular inflammation and systemic disease activity. The presence of severe ocular disease, particularly scleritis or PUK, often signals uncontrolled systemic inflammation or vasculitis and may necessitate an escalation of systemic therapy. Conversely, the successful management of systemic RA often leads to the resolution of associated ocular inflammation.

The discussion around iatrogenic disease, particularly HCQ retinopathy, brings another layer of complexity. Here, the clinician's goal is purely preventative. The irreversible nature of the retinal damage caused by HCQ means that management is entirely focused on risk mitigation and early detection through diligent screening (1). The potential for cardiac complications from HCQ, such as QT interval prolongation, further complicates its risk-benefit analysis, especially when used in combination with other medications (2). This duality—managing inflammation caused by the disease while preventing damage from the treatment—is a central challenge in the long-term care of RA patients.

4.2 Management Strategies

The management of RA-related eye disease is multifaceted and tailored to the specific condition and its severity. A stratified approach is typically employed.

4.2.1 Medical Management

- Topical Therapies: For anterior segment conditions, topical treatments are the first line of defense. KCS is managed with preservative-free artificial tears, lubricating ointments, and topical immunomodulators like cyclosporine or lifitegrast to increase tear production. Mild episcleritis can often be managed with topical corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs).

- Systemic Immunosuppressive Therapy: Ocular conditions that are severe, sight-threatening, or unresponsive to topical therapy require systemic treatment. This is particularly true for scleritis, PUK, and retinal vasculitis. High-dose oral corticosteroids are often used for initial control of severe inflammation, but long-term management requires the use of steroid-sparing DMARDs. Methotrexate, mycophenolate mofetil, and azathioprine are commonly used. In refractory cases, biologic agents, such as TNF-α inhibitors (e.g., infliximab, adalimumab) or rituximab, have proven to be highly effective in controlling severe ocular inflammation and are often necessary for necrotizing scleritis (3). The choice of agent is often guided by the rheumatologist, who considers both the ocular and articular disease activity.

- Management of Drug-Induced Toxicities: The management of HCQ retinopathy is straightforward: immediate and permanent discontinuation of the drug upon detection of definite toxicity. Because the damage can progress even after cessation, continued monitoring is required. For corticosteroid-induced cataracts, the definitive treatment is surgical removal. For steroid-induced glaucoma, the first step is to reduce or eliminate the steroid if possible, while managing the elevated intraocular pressure with topical anti-glaucoma medications.

4.2.2 Surgical Interventions

Surgery is generally reserved for the complications of ocular inflammation or drug toxicity. In cases of PUK with impending or actual corneal perforation, surgical intervention, such as the application of a tissue adhesive, a conjunctival flap, or a tectonic keratoplasty (corneal transplant), may be required on an emergency basis to preserve the integrity of the globe. As mentioned, cataract surgery is the standard of care for visually significant cataracts.

4.3 Implications for Clinical Practice

The findings of this review have several important implications for routine clinical practice. Firstly, there is a clear need for increased awareness among all clinicians involved in the care of RA patients about the potential for ocular complications. Patient education is a cornerstone of effective management; patients should be counseled to report any new visual symptoms—such as pain, redness, light sensitivity, or changes in vision—promptly. Secondly, a low threshold for ophthalmologic referral is essential. Any RA patient with a red eye, eye pain, or change in vision should be referred for a comprehensive eye examination. Finally, routine ophthalmic screening should be considered for all RA patients, even in the absence of symptoms. This is particularly critical for patients on HCQ, for whom strict adherence to established screening guidelines is mandatory to prevent irreversible blindness (1). The establishment of clear communication channels between rheumatologists and ophthalmologists is vital for co-managing these complex patients effectively.

4.4 Limitations

It is important to acknowledge the limitations inherent in a review of this nature. The heterogeneity of the studies in the existing literature, with variations in patient populations and diagnostic criteria, can make it challenging to establish precise prevalence rates for some of the rarer ocular manifestations. Furthermore, while the association between RA and these eye conditions is strong, establishing direct causality can be difficult due to the presence of confounding variables, such as medication use and comorbid conditions. The current review is based on a focused selection of the literature and does not represent an exhaustive systematic meta-analysis. As such, its conclusions are intended to provide a broad clinical overview rather than definitive statistical evidence.

4.5 Future Directions

The future of managing ocular disease in RA lies in the advancement of both diagnostic and therapeutic modalities. On the diagnostic front, newer imaging technologies, such as enhanced-depth imaging OCT, may offer improved visualization of the sclera and choroid, aiding in the diagnosis and monitoring of scleritis. In therapeutics, the continued development of more targeted biologic and small-molecule therapies for RA holds promise for better control of both systemic and ocular inflammation with potentially fewer side effects. Further research is needed to better understand the specific molecular pathways that drive ocular inflammation in RA, which could pave the way for novel, locally-delivered therapies that could minimize systemic immunosuppression. Finally, establishing large, prospective registries of RA patients could provide more robust data on the incidence, risk factors, and long-term outcomes of ocular complications, guiding the development of more refined, evidence-based screening and treatment protocols.

CONCLUSION

Ocular manifestations are a frequent and clinically significant component of rheumatoid arthritis, posing a substantial threat to vision and quality of life. The pathogenic scope ranges from tear film deficiency to destructive inflammation of the cornea and sclera, reflecting the systemic nature of the underlying autoimmune disease. Furthermore, the therapies used to control RA carry their own risk of serious ocular toxicity. Therefore, the effective management of these patients hinges on a proactive and collaborative approach. Early detection through vigilant screening, prompt reporting of symptoms by educated patients, and a multidisciplinary care model involving close communication between rheumatologists and ophthalmologists are the pillars of a strategy aimed at preserving vision. By recognizing the eye as a critical window into the systemic activity of rheumatoid arthritis, clinicians can better navigate the complexities of this chronic disease and improve outcomes for their patients.

REFERENCES

1. Au SCL. Hydroxychloroquine retinal toxicity: The bull's eye in the human eye. [Published online ahead of print, 2020 June 25]. Vis J Emerg Med. 2020; 21:100818. doi:10.1016/j.visj.2020.100818
2. Mercuro NJ, Yen CF, Shim DJ, et al. Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease, 2019. (COVID-19) [Published online ahead of print, 2020 May 1]. JAMA Cardiol. 2020; e201834. doi:10.1001/jamacardio.2020.11834
3. Bhamra MS, Gondal I, Amarnani A, et al. Ocular Manifestations of Rheumatoid Arthritis: Implications of Recent Clinical Trials. Int J Clin Res Trials. 2019; 4(2):139. doi:10.15344/2456-8007/2019/139