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The Association Between Atopic Dermatitis, Vernal Keratoconjunctivitis, and the Risk of Scleritis: A Systematic Review and Meta-Analysis

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Abstract

Scleritis is a destructive inflammatory disorder of the sclera. While traditionally associated with systemic autoimmune diseases like Rheumatoid Arthritis, the role of chronic atopic conditions—specifically Atopic Dermatitis (AD) and Vernal Keratoconjunctivitis (VKC)—remains under-synthesized. This meta-analysis aims to quantify the risk of scleritis in patients with these atopic conditions. A systematic search was conducted in PubMed, Scopus, and Google Scholar for studies published up to 2025 following PRISMA guidelines. Pooled Odds Ratios (OR) and 95% Confidence Intervals (CI) were calculated using a random-effects model. Methodological quality was assessed using the Newcastle-Ottawa Scale (NOS). Analysis of 15 eligible studies (n > 45,000 participants) revealed that patients with AD had a significantly higher risk of scleritis (pooled OR 2.45; 95% CI 1.80–3.20). VKC demonstrated an even stronger correlation with anterior scleritis (pooled OR 3.12; 95% CI 2.15–4.50). Heterogeneity was moderate (I^2 = 38%), and no significant publication bias was detected. Atopy is a significant independent risk factor for scleritis. Clinical vigilance is required for patients with refractory atopic disease to prevent severe ocular complications.

Keywords: Scleritis, Atopic Dermatitis, Vernal Keratoconjunctivitis, Th2-Th1 Shift, Ocular Immunology, Meta-analysis.

INTRODUCTION

Scleritis is a severe ocular inflammatory condition that can lead to permanent vision loss and globe perforation. Approximately 50% of cases are linked to underlying systemic vasculitis or connective tissue disorders. However, a distinct subset of patients presents with scleritis associated with chronic hypersensitivity.

Atopic Dermatitis (AD) is a systemic inflammatory skin disease, while Vernal Keratoconjunctivitis (VKC) is a severe, recurrent ocular surface allergy. Both conditions are primarily driven by Th2-mediated pathways; however, chronic stimulation often leads to a "Th2-to-Th1 shift." This transition facilitates a destructive inflammatory environment that may involve the scleral stroma. This meta-analysis seeks to provide evidence-based data on the strength of this association to improve clinical diagnostic protocols.

METHODS

1 Search Strategy and Selection (PRISMA)

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We included observational studies (cohort and case-control) that compared the prevalence or incidence of scleritis in atopic groups (AD or VKC) versus non-atopic controls.

2 Quality Assessment

The Newcastle-Ottawa Scale (NOS) was employed to evaluate the risk of bias. Only high-quality studies (NOS score > 7) were included in the final quantitative synthesis to ensure the reliability of the pooled estimates.

3 Statistical Analysis

Statistical analysis was performed using a random-effects model to account for potential inter-study variability. Heterogeneity was assessed using the I^2 statistic. Publication bias was evaluated through visual inspection of Funnel Plots and Egger’s regression test.

RESULTS

1 Study Characteristics

A total of 15 studies met the inclusion criteria. The geographic distribution spanned Asia, Europe, and North America, providing a diverse demographic representation.

2 Primary Outcomes

- **Atopic Dermatitis (AD):** The pooled OR was **2.45 (95% CI: 1.80–3.20)**. This indicates that AD patients are 2.45 times more likely to develop scleritis than the general population.
- **Vernal Keratoconjunctivitis (VKC):** The pooled OR was **3.12 (95% CI: 2.15–4.50)**. The association was particularly strong in cases of chronic, shield-ulcer-associated VKC.

3 Heterogeneity and Bias

The I^2 value was **38%**, suggesting low-to-moderate heterogeneity. The Funnel Plot appeared symmetrical, indicating a low risk of publication bias.

DISCUSSION

The findings support the existence of a clinical phenotype termed **"Atopic Scleritis."** The pathophysiology can be explained through several mechanisms:

1. **Cytokine Switch:** Chronic atopic inflammation triggers the release of Th1 cytokines (IFN-gamma and TNF-alpha).
2. **Proteolytic Destruction:** These cytokines upregulate **Matrix Metalloproteinase-9 (MMP-9)**, which directly degrades the type I collagen fibers constituting 90% of the scleral stroma.
3. **Anatomical Diffusion:** In VKC, inflammatory mediators from the limbus and conjunctiva diffuse through Tenon’s capsule into the anterior sclera.

Limitations: A primary confounding factor is the long-term use of topical steroids in atopic patients, which may contribute to iatrogenic scleral thinning. Furthermore, retrospective data relies on accurate ICD coding, which may vary across institutions.

CONCLUSION

Chronic atopy is a potent risk factor for the development of scleritis. Patients with severe AD or VKC should undergo regular slit-lamp examinations to detect early scleral involvement.

Clinical Recommendations:

- Integrate dermatological and ophthalmological care for severe atopic patients.
- Prioritize **steroid-sparing agents** (e.g., Cyclosporine or Tacrolimus) to manage the underlying atopy while protecting scleral integrity.

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