Characterizing Autoimmune Uveitis in Relation to Systemic Diseases: A Retrospective Study from a Syrian Tertiary Reference Center.

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Abstract

Background: Uveitis, a notable cause of severe visual impairment, is frequently characterized as infectious or non-infectious auto immune uveitis (AU), the latter of which is commonly associated with younger individuals and systemic diseases. Despite the condition's widespread impact, there are substantial gaps in the comprehension of its pathogenesis, clinical presentation, and therapeutic response, particularly concerning systemic disease-associated uveitis.

Aim of the Study: The current study aims to bridge these gaps through an extensive examination of demographic and clinical features in AU patients, thereby informing future research, therapeutic strategies, and improving patient outcomes.

Methods: This retrospective observational study analyzed 87 patients with systemic disease-associated uveitis from January 2018 to December 2022 in Damascus, Syria. With diagnoses made using the Standardization of Uveitis Nomenclature Working Group Criteria, the study evaluated tailored treatment efficacy at the 24-month post-treatment mark, alongside comprehensive ophthalmic examinations, laboratory evaluations, and radiographic assessments.

Results: In our study included 87 patients with Systemic Disease-Associated Autoimmune Uveitis (SDA-AU). Women represented 64.36% of this group, and the mean age at diagnosis was 43.8 for women and 39.8 for men. The most reported symptom was a painful red eye (52.87%). The onset of symptoms was sudden for 32.18% of patients, while 67.81% reported gradual development. Complications occurred in 33.33% of patients, including cataracts (41.37% of those with complications) and glaucoma (17.24%). Laboratory evaluations showed elevated inflammation markers in 66.66% of patients. Upon the 24-month assessment, 48.27% of patients achieved complete remission, 37.93% showed significant improvement, while disease worsened in 13.79% of cases.

Conclusion: Our findings demonstrated that the presentation of autoimmune uveitis in this cohort frequently precedes the diagnosis of systemic diseases, affirming the vital role of an early and accurate diagnosis of uveitis for the detection of underlying systemic conditions. In conclusion, our study underlines the significance of a comprehensive and multidisciplinary approach in the management of SD-AU, leading to improved prognosis and quality of life for patients.

Background

Uveitis, characterized by inflammation of the iris, ciliary body, and choroid, is generally categorized into infectious and non-infectious or autoimmune forms(1). Autoimmune uveitis (AU) is a common condition that primarily affects younger individuals and has the potential to cause considerable visual impairment or total blindness (2). Notably, AU contributes to severe visual impairment and accounts for 10–15% of all blindness cases (3).

Autoimmune uveitis (AU) arises due to an immune reaction against self-antigens or a triggered innate inflammatory response to an external stimulus (4). Initial triggers incite the innate immune (5) and misdirected adaptive immune responses against self-antigens (6). Genetic factors linked to immune
regulation also play a part in the disease's pathogenesis (1). Further understanding of these complex mechanisms is crucial for novel therapeutic strategies in AU.

Further classification of AU includes idiopathic autoimmune uveitis and systemic disease-associated uveitis(1). The substantial proportion of uveitis patients diagnosed with systemic diseases and infections implies a frequent correlation between autoimmune uveitis and systemic conditions (7) Numerous systemic diseases are implicated in AU, including systemic lupus erythematosus, Behcet's disease, spondylarthritis, Sjogren's syndrome, sarcoidosis, Vogt-Koyanagi-Harada syndrome, autoimmune hepatitis, and multiple sclerosis(8). Importantly, AU may manifest either prior to or following the onset of the associated systemic disease (1).

Autoimmune uveitis (AU) is commonly managed with immunosuppressants, corticosteroids, and biologic agents (6, 9, 10), each having varied effectiveness and potential side effects. Immunosuppressants control inflammation but can cause bone marrow suppression and gastrointestinal discomfort (11). Corticosteroids are potent anti-inflammatory but may lead to cataracts and glaucoma with long-term use. Biologic agents can effectively control inflammation but may increase susceptibility to infection and malignancies (11).

The prognosis is dictated by the disease’s severity, inflammation's location in the eye, and association with systemic diseases(12). While AU itself does not generally impact lifespan, its correlation with certain systemic diseases can. Recurrent intraocular inflammation can result in temporary or permanent visual issues and treatment-resistant ocular complications like cataracts, glaucoma, macular oedema, and retinal detachment (13). Moreover, the condition significantly influences patients' quality of life due to recurrent painful episodes, treatment side effects, and associated anxiety (12).

Despite the prevalence and potential severity of autoimmune uveitis, understanding of its pathogenesis, clinical features, and response to therapy remains incomplete, particularly for systemic disease-associated uveitis. Furthermore, no direct comparisons of therapeutic modalities currently exist. Our study addresses these critical gaps by examining the demographic and clinical features of patients diagnosed with AU, aiming to provide invaluable insights into real-world clinical implications and treatment outcomes for this condition. Our hypothesis is that a comprehensive analysis of these patients could elucidate the factors that influence disease progression and response to treatment. The results of this investigation could significantly impact the clinical management of AU, guiding treatment decisions, and informing the development of future research and therapeutic strategies.

**Materials and Methods**

**Study Design and Sample Size**

This research was a retrospective observational study carried out at Eye, Ear and Nose Specialist Hospital in Damascus, Syria. The study assessed patients who received a uveitis diagnosis between January 2018 and December 2022.
The study was conducted in accordance with the principles of the Declaration of Helsinki, and received ethical approval from the Ethical Approval Committee at Damascus University. Informed consent was obtained from all participants upon their admission to the hospital, ensuring they were aware their anonymized information could be utilized for research purposes. All patient data was subsequently anonymized prior to analysis to maintain confidentiality and privacy.

We included patients diagnosed with systemic disease-associated uveitis using the Standardization of Uveitis Nomenclature Working Group Criteria (14). This diagnosis required the exclusion of known infectious causes and a record of systemic disease onset either concurrent with uveitis onset or anytime during the median 4.8-year follow-up. We excluded patients whose uveitis resulted from other causes such as infections. Investigators were blinded to the patients’ prior medical history during data collection to minimize bias.

**Medical History and Physical Examination**

We recorded patients’ demographic data, medical and surgical history, and treatment details at the initial presentation and subsequent follow-up. Clinical evaluations included comprehensive ophthalmic examination, assessing visual acuity, intraocular pressure, and examining the posterior segment and pars plana via slit-lamp bio-microscopy and indirect ophthalmoscopy. Other investigations such as fluorescein or indocyanine green angiography, ultrasound bio-microscopy, and optical tomography were conducted when a complication was suspected.

**Measurements and Parameters**

The classification of uveitis was based on the Uveitis Nomenclature Working Group Criteria (14), considering anatomical location, onset and course, unilaterality or bilaterality, and whether granulomatous or non-granulomatous. Inflammatory status was evaluated using an ordinal scale (0 to 4+).

We also employed a tailored treatment approach based on the specific type of Systemic Disease-Associated Autoimmune Uveitis (SDA-AU) and its severity:

- For patients presenting with acute anterior Systemic Disease-Associated Autoimmune Uveitis (SDA-AU), an initial treatment approach of topical therapy was applied. Provided they responded positively, these patients then underwent regular follow-ups.
- For those with recurrent anterior SDA-AU, a more involved treatment plan was enacted. This consisted of periocular subtenon injections of betamethasone phosphate (3 mg/0.5 ml), used either in isolation or combined with oral corticosteroids (1 mg/kg/day), with the goal of achieving long-term disease control.
- In instances of severe or intermediate SDA-AU, particularly with bilateral involvement or complications such as macular edema or retinal vasculitis, patients were prescribed a combination of immunosuppressive drugs and corticosteroids (0.5 mg/kg/day).
• For patients diagnosed with posterior uveitis or panuveitis, the mainstay treatment was immunosuppressants. If unilateral uveitis remained unresponsive to both topical and systemic therapy, intravitreal dexamethasone implants were administered. In cases refractory to previous immunosuppressive drugs, biologics were introduced.

The efficacy of the treatment strategies was evaluated comprehensively at the 24-month mark post-treatment. The following metrics were used for this assessment:

• Remission was defined as a disease state that remained inactive for three months or more without any ongoing treatments, signifying disease inactivity (grade 0).
• Worsening activity was categorized as a two-step increase in inflammation or an elevation from grade 3 to 4.
• Improved activity was indicated by a two-step decrease in inflammation or a reduction to grade 0.

**Laboratory and Radiographic Evaluations**

Comprehensive laboratory evaluations including complete blood counts, inflammatory markers, organ function tests, and autoantibodies were performed. Radiographic evaluations, comprising X-ray, computed tomography, and magnetic resonance imaging were undertaken as required.

**Statistical Analysis**

We analyzed data using Excel and the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA). The data are presented as frequency, the percentage for qualitative data, or mean ± standard deviation for continuous data. P-values < 0.05, with a 95% confidence interval, were considered statistically significant.

**Results**

In our study population of 312 patients diagnosed with uveitis, 87 individuals (27.88%) were identified as having Systemic Disease-Associated Autoimmune Uveitis (SDA-AU) and met the criteria for inclusion in this study's analysis.

The female was more than male with 64.36%, 35.63 respectively. The mean age at diagnosis was 39.8 ± 17.9 years (range 7–71) for men and 43.8 ± 15.4 years (range 11–69) for women.

The patient cohort consisted of a higher proportion of females, representing 64.36% of the sample, compared to 35.63% for males. The average age at diagnosis differed slightly between genders: for males, it was 39.8 ± 17.9 years, with a range from 7 to 71 years. For females, the mean age at diagnosis was slightly higher at 43.8 ± 15.4 years, and the age range was between 11 and 69 years (Table 1).
Table 1
Demographic data of patients

<table>
<thead>
<tr>
<th></th>
<th>Male (n = 31)</th>
<th>Female (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39.8 ± 17.9</td>
<td>43.8 ± 15.4</td>
</tr>
<tr>
<td>- Range</td>
<td>(7–71)</td>
<td>(11–69)</td>
</tr>
<tr>
<td>- mean ± SD</td>
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</table>

Initial symptoms of uveitis in our cohort included ocular pain, compromised visual acuity ranging from blurred vision to significant decline, photophobia, scotoma, and floaters. The most common symptom reported was a painful red eye, seen in 46 patients, equating to 52.87% of the sample. This was followed by decreased visual acuity and blurred vision, experienced by 15 patients (17.24%), photophobia in 9 patients (10.34%), scotoma in 2 patients (2.29%), and floaters seen by 15 patients (17.24%) (Table 2).

The onset of symptoms varied among patients: 28 patients (32.18%) reported a sudden onset with a rapid progression, while in 59 patients (67.81%), the symptoms developed gradually and exhibited a chronic and recurrent course. Uveitis was unilateral in 48 patients (55.17%) and bilateral in 39 patients (44.82%) (Table 2).

In terms of the anatomical classification, among the 87 patients with Systemic Disease-Associated Uveitis (SDA-UV), anterior uveitis was diagnosed in 48 patients (55.17%), posterior uveitis in 29 patients (33.33%), and panuveitis in 10 patients (11.49%) (Table 2).

During the follow-up period, complications were observed in 28 patients, representing 33.33% of the cohort. These complications encompassed cataracts in 12 patients (41.37% of those with complications), retinal neovascularization in 4 patients (13.79%), macular edema in 3 patients (10.34%), retinal detachment in 4 patients (13.79%), and glaucoma in 5 patients (17.24%) (Table 2).

When breaking down these complications by uveitis classification, cataracts were seen in six patients with anterior uveitis, one patient with intermediate uveitis, and five patients with posterior uveitis, accounting for a total of 12 patients (41.37% of those with complications). Both retinal neovascularization and retinal detachment were exclusive to patients with posterior uveitis or panuveitis. Macular oedema was most common in patients with intermediate (one patient) and posterior (two patients) forms of systemic disease-associated uveitis. As for glaucoma, it was diagnosed in two patients with anterior uveitis and three with posterior uveitis (Table 2).
Of the 87 patients diagnosed with Autoimmune Uveitis (AU), a systemic disease was already prevalent in 22 patients (25.28%) at the onset of AU and surfaced later in 65 patients (74.71%).

The associated diseases comprised Polymyalgia Rheumatica (PMR) in 1 patient (1.14%), Systemic Sclerosis (SSc) in 1 patient (1.14%), Rheumatoid Arthritis (RA) in 3 patients (3.44%), Systemic Lupus Erythematosus (SLE) in 6 patients (6.89%), Ankylosing Spondylarthritis (AS) in 18 patients (20.68%), Behcet's Disease (BD) in 41 patients (47.12%), Thyroiditis in 7 patients (8.01%), and Inflammatory Bowel Diseases (IBD) in 10 patients (11.49%) (Table-3).

<table>
<thead>
<tr>
<th>SDA-UV data</th>
<th>N(%)</th>
</tr>
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<tbody>
<tr>
<td><strong>Ocular symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>- Redness painful eye</td>
<td>15 (17.24%)</td>
</tr>
<tr>
<td>- Decrease of visual acuity</td>
<td>9 (10.34%)</td>
</tr>
<tr>
<td>- Photophobia</td>
<td>2 (2.29%)</td>
</tr>
<tr>
<td>- Scotoma</td>
<td>15 (17.24%)</td>
</tr>
<tr>
<td>- Floaters</td>
<td></td>
</tr>
<tr>
<td><strong>SDA-UV onset and course</strong></td>
<td>28 (32.18%)</td>
</tr>
<tr>
<td>- Sudden, and worsening</td>
<td>59 (67.81%)</td>
</tr>
<tr>
<td>- Gradually chronic and recurrent</td>
<td></td>
</tr>
<tr>
<td><strong>Anatomic location</strong></td>
<td>48 (55.17%)</td>
</tr>
<tr>
<td>- Anterior uveitis</td>
<td>29 (33.33%)</td>
</tr>
<tr>
<td>- Posterior uveitis</td>
<td>10 (11.49%)</td>
</tr>
<tr>
<td>- Panuveitis</td>
<td></td>
</tr>
<tr>
<td><strong>SDA-UV complications</strong></td>
<td>12 (41.37%)</td>
</tr>
<tr>
<td>- Cataract</td>
<td>4 (13.79%)</td>
</tr>
<tr>
<td>- Retinal neovascularization</td>
<td>3 (10.34%)</td>
</tr>
<tr>
<td>- Macular edema</td>
<td>4 (13.79%)</td>
</tr>
<tr>
<td>- Retinal detachment</td>
<td>5 (17.24%)</td>
</tr>
<tr>
<td>- Glaucoma</td>
<td></td>
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</tbody>
</table>

Table 3: SDA-UV Characteristics
Table 3
Systematic Diseases associated with UV (SDA-UV)

<table>
<thead>
<tr>
<th>Systemic Disease</th>
<th>Number of patients, Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymyalgia rheumatic</td>
<td>One (1, 14%)</td>
</tr>
<tr>
<td>Systemic Sclerosis</td>
<td>One (1, 14%)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>3 (3, 44%)</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>6 (6, 89%)</td>
</tr>
<tr>
<td>Ankylosing Spondylarthritis</td>
<td>18 (20, 68%)</td>
</tr>
<tr>
<td>Behcet's disease</td>
<td>41 (47.12%)</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>7 (8.01%)</td>
</tr>
<tr>
<td>Inflammatory Bowel Diseases</td>
<td>10 (11.49%)</td>
</tr>
</tbody>
</table>

Laboratory evaluations revealed lymphopenia in 2 patients, and elevated erythrocyte sedimentation rate (> 20 mm/h) along with increased serum C-reactive protein (> 6 mg/dl) were detected in 58 patients, representing 66.66% of the cohort. Auto-antibodies were positive in a few patients, with 6 patients (6.89%) having anti-nuclear antibodies, 2 patients (2.29%) anti-double-stranded DNA, 3 patients (3.44%) anticyclic citrullinated peptides, 1 patient (1.14%) SCL70, and 2 patients (2.29%) anti-thyroglobulin.

Radiographic evaluations were performed based on the associated systemic diseases. Chest X-rays were performed on 22 patients diagnosed with Ankylosing Spondylitis, Rheumatoid Arthritis, and Systemic Sclerosis, while hand X-rays were done on 3 patients with Rheumatoid Arthritis. Magnetic Resonance Imaging was done on 2 patients with Systemic Lupus Erythematosus and 12 patients with Behcet's Disease. Colonoscopy was performed on 7 patients with Inflammatory Bowel Disease.

At diagnosis, all patients were placed on corticosteroid treatment. Induction therapy using periocular subtenon injections and/or systemic corticosteroids alone (prednisone: 1 mg/kg/day), with a tapering regime based on the ocular examination results, was administered to 11 patients (12.64%).

The bulk of the cohort, 80 patients (91.95%), received a combination of oral corticosteroids and one or two immunosuppressive drugs. Single immunosuppressive drugs, such as azathioprine (administered to 30 patients), cyclosporine-A (9 patients), or methotrexate (19 patients), were given to 58 patients (72.5%) due to recurrent or suboptimal remission to corticosteroids or upon withdrawal. These patients had no severe complications. Cyclophosphamide was administered to 12 patients with posterior uveitis and 4 patients with panuveitis.

A two-drug combination therapy, including azathioprine, cyclosporine-A, cyclophosphamide, mycophenolate mofetil, and methotrexate was employed for 12 patients (13.79%) with severe complications at diagnosis or persistently active or recurrent disease. Anti-tumour necrosis factor-α was
administered to 12 patients (13.79%) who were refractory to combination therapy or had retinal neovascularization and cystoid macular oedema.

Upon the assessment at the 24-month mark, 42 patients (48.27%) were found to have achieved complete remission, 33 patients (37.93%) displayed significant improvement, while in 12 patients (13.79%), the disease had worsened (Refer to Table-4 for detailed results).

<table>
<thead>
<tr>
<th>The pattern of the development of the SDA-UV course</th>
<th>Number of patients, Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission</td>
<td>42 (48.27%)</td>
</tr>
<tr>
<td>Significant improvement</td>
<td>33 (37.93%)</td>
</tr>
<tr>
<td>Worsened course</td>
<td>12 (13.79%)</td>
</tr>
</tbody>
</table>

For those patients who reached remission, the corticosteroids were systematically reduced and ultimately ceased by the end of the first year, while the dosage of immunosuppressive medications was decreased but maintained. In contrast, the 12 patients experiencing a progression of their disease (representing 13.79% of the cohort) were administered anti-tumour necrosis factor-α.

**Discussion**

Our study aligns with prior investigations (12, 15, 16) in demonstrating that autoimmune uveitis related to systemic diseases (SD-AU) often impacts younger adults, showing a slight female predominance. This is consistent with a broader pattern in which systemic immune diseases predominantly afflict individuals aged between 20–40 years, with a greater prevalence in females (17). The observed SD-AU prevalence in our study was 27.88%, a figure that aligns with several other studies (12, 18, 19). Conversely, a higher prevalence has been documented in different research (20, 21). It’s important to note that this discrepancy in reported prevalence rates may be attributed to the variability in geographic location, environmental factors, race, and socioeconomic status influencing the studied populations (12).

The criteria established by the Uveitis Nomenclature Working Group has proven its effectiveness as a reliable framework for data reporting, treatment application, and patient follow-up (14). In our study, as mirrored by others (12, 18, 19, 22, 23), anterior uveitis emerged as the most frequent manifestation, accounting for 55.17% of cases (20, 21). At the point of presentation, the symptoms of uveitis reported by patients included ocular pain, decreased clarity of vision or outright visual acuity decline, photophobia, scotomas, and the occurrence of floaters. These symptoms are commensurate with those documented in preceding studies (12, 17–23).

The most common symptom we observed was ocular redness coupled with pain, occurring in 46 patients, which corresponds to 52.87% of our sample. This finding is consistent with previous investigations (12, 18, 20).
In terms of symptom onset and progression, 32.18% of patients reported that their symptoms appeared suddenly and then deteriorated. However, the majority, 67.81%, described their condition as chronic and recurrent, a finding that aligns with earlier studies (12, 19). Additionally, unilateral uveitis was found to be more prevalent than bilateral uveitis, a pattern also observed in our study (24). In 25.28% of patients, a systemic disease was already present at the onset of anterior uveitis (AU), whereas it followed AU in the remaining 74.71% of patients. This pattern of disease presentation has been similarly reported in other research (7, 12).

The systemic diseases associated with AU in our study encompassed polymyalgia rheumatica (PMR), systemic sclerosis (SSc), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), Behcet's disease (BD), thyroiditis, and inflammatory bowel disease (IBD). These conditions were also found in correlation with AU in previous studies (12, 17–23, 25).

During the follow-up period, complications arose in 33.33% of patients. These complications included cataracts, glaucoma, retinal neovascularization and detachment, and macular oedema, in that order. These findings echo the complication rates and types reported in prior studies (12, 17, 18).

The role of serological immunological markers, such as anti-cyclic citrullinated peptides and anti-nuclear antibodies, in determining the risk of developing a systemic autoimmune disease remains under-explored in patients (26). A study conducted by Lin P, et al. (27), however, demonstrated the utility of anti-neutrophil cytoplasmic antibodies and rheumatoid factor screening in identifying patients at risk of systemic diseases. Thus, it appears that immunological laboratory evaluation holds a limited or potentially insignificant role in diagnosis and follow-up.

Our results indicate that radiological procedures have been beneficial for the diagnosis and follow-up of patients with systemic diseases, but their value in diagnosing or following up on systemic disease-associated anterior uveitis (SDA-AU) remains ambiguous (28). Consistent with the Uveitis Nomenclature Working Group Guidelines (14), our study employed corticosteroids as the first-line therapy for active uveitis. To mitigate the adverse events of corticosteroids and to taper their dose, we incorporated immunosuppressive drugs, cytotoxic agents, and antimetabolites (29). Specifically, we administered oral corticosteroids in combination with one or two immunosuppressive drugs, either due to recurrence, suboptimal remission to corticosteroids, or the need for corticosteroid withdrawal.

During follow-up, immunosuppressive therapy requires careful modulation to avoid complications, and it should be extended for months, or even 1–2 years, to achieve stable disease control (12, 30).

In cases refractory to combination therapy or with retinal neovascularization and cystoid macular oedema, anti-tumour necrosis factor-α was administered, paralleling the findings of the study by Mathilde Leclercq et al. (31).

Azathioprine, an immunosuppressive drug, is generally the treatment of choice for anterior uveitis, while cyclosporine-A is preferred for intermediate and posterior uveitis. Cyclophosphamide is typically avoided
due to its potential fertility impacts (32). In our study, azathioprine was the most frequently utilized drug, with no patient receiving cyclophosphamide.

Prognostically, our findings were encouraging. After 24 months of therapy, 48.27% of patients achieved complete remission and 37.93% demonstrated significant improvement, results that are in line with previous studies (7, 12).

In those who achieved remission, corticosteroids were tapered and discontinued by the end of 12 months, while immunosuppressive drugs were reduced to a lower dosage. Anti-tumour necrosis factor-α was administered to patients with disease progression, adhering to the Uveitis Nomenclature Working Group Guidelines (14).

Despite the common diagnosis of sarcoidosis, followed by HLA-B27-associated uveitis and then Behcet’s disease (BD) (33, 34), our study found BD to be the most common diagnosis, followed by ankylosing spondylitis (AS) and systemic lupus erythematosus (SLE). This divergence might be due to the high prevalence of BD reported in Syria, a silk road country (35), or it could reflect racial differences and sample size variation. We would like to highlight these important points as a conclusion to our series analysis.

**Conclusion**

Our findings corroborate that uveitis often precedes systemic diseases, highlighting the necessity for early detection and accurate diagnosis, which could signal the presence of an underlying systemic condition. The study advocates an interdisciplinary approach in managing systemic disease-associated uveitis, substantiating the improved prognosis and quality of life this approach can yield for patients. It also underscores the need for more in-depth exploration into the role of serological immunological markers for the early prediction of systemic autoimmune diseases. The successful application of a combination therapy regimen of corticosteroids and immunosuppressive drugs, as shown in our study, provides a viable treatment plan for majority of patients with careful long-term modulation. Altogether, the study underscores the importance of comprehensive screening, timely diagnosis, and appropriate treatment of autoimmune uveitis to not only enhance visual prognosis but also to potentially uncover systemic diseases, thus facilitating early management and improved overall patient outcomes.

**Abbreviations**

AU: autoimmune uveitis.

SDA-AU: systemic disease-associated autoimmune uveitis.

PMR: polymyalgia rheumatica.

SSc: systemic sclerosis
RA: rheumatoid arthritis.

SLE: Systemic lupus erythematosus.

AS: ankylosing spondylarthritis.

BD: Behcet's disease.

IBD: inflammatory bowel diseases.

Declarations

Ethical Approval and Consent to Participate:

The study was conducted in accordance with the principles of the Declaration of Helsinki, and received ethical approval from the Ethical Approval Committee at Damascus University (Number: 20203379). Informed consent was obtained from all participants upon their admission to the hospital. All data was anonymized before analysis.

Consent for publication:

Informed consent was obtained from all individuals included in this study. We have taken appropriate measures to ensure the privacy and confidentiality of personal information and identifiable data. The consent process included a clear explanation of the study objectives, the potential risks and benefits of participation, and the intended use of the data, including publication in scientific journals. Participants were informed that their identities would be protected, and any information used would be anonymized or de-identified.

Availability of data and materials:

The dataset analysed during the current study is available from the corresponding author (Haya Deeb: haya.i.deeb@gmail.com) on reasonable request.

Competing interests

Not Applicable

Funding:

There was no resource of funding.

Authors' contributions

MK, HD and NK conceived and designed the study and wrote the manuscript. DA and LAb participated in the data collection. LAI and RA revealed the ophthalmological evaluation, and follow-up of the patients.
All authors conceived the study, and read and approved the final manuscript.

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