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Characterizing autoimmune uveitis to systemic diseases: a retrospective study from a Syrian tertiary reference center

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Background: Uveitis, a notable cause of severe visual impairment, is frequently characterized as infectious or noninfectious autoimmune 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, and therapeutic strategies, and improving patient outcomes.

Methods: This retrospective observational study analyzed 261 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 39.8 ± 17.9 years (range 7–71) for men and 43.8 ± 15.4 years (range 11–69). 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 AU 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.

Keywords: autoimmune, disorder, retrospective, systemic, uveitis

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[2,3].

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 affect 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 AU and systemic disease-associated uveitis[1]. The substantial proportion of uveitis patients diagnosed with systemic diseases and infections implies a frequent correlation between AU and systemic conditions[7]. Numerous systemic diseases are implicated in AU, including systemic lupus erythematosus (SLE), Behcet's disease (BD), spondylarthritis, Sjogren's syndrome, sarcoidosis, Vogt-Koyanagi-Harada syndrome, autoimmune hepatitis, and

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multiple sclerosis[1,8]. Importantly, AU may manifest either prior to or following the onset of the associated systemic disease[1].

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-inflammatories 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 edema, 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 AU, 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 aimed to assess the effectiveness of the management of systemic disease-associated uveitis. We hypothesize that a comprehensive analysis of these patients could elucidate the factors that influence disease progression and response to treatment.

HIGHLIGHTS

- 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.
- 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 (IRB;213,CD). 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.
- 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.
- 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 outcome.

Materials and methods

Study design and sample size

This research was a retrospective observational study that assessed patients who received a uveitis diagnosis between January 2018 and December 2022.

The work has been reported in line with the strengthening the reporting of cohort, cross-sectional, and case–control studies in surgery (STROCSS) criteria[14].

We included patients diagnosed with systemic disease-associated uveitis using the Standardization of Uveitis Nomenclature Working Group Criteria[15]. 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-year follow-up. We excluded patients whose uveitis resulted from other causes such as infections. Investigators were blinded to the patient's 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, and 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. Fundus fluorescein angiography (FFA) was not performed.

The diagnosis algorithm was as follows: first, uveitis was diagnosed, categorized, and graded according to the Standardization of Uveitis Nomenclature Working Group criteria[15]. Specifically, uveitis was classified in terms of anatomic localization, namely: (a) anterior (iritis, iridocyclitis, and anterior cyclitis); (b) intermediate (pars planitis, posterior cyclitis, and hyalitis); (c) posterior (focal, multifocal, or diffuse choroiditis, chorioretinitis, retinochoroiditis, retinitis, and neuroretinitis); (d) panuveitis (inflammation of the anterior chamber, vitreous, and retina or choroid). In addition, uveitis was categorized as acute, chronic, or recurrent according to its course, whether it was unilateral or bilateral, or granulomatous or nongranulomatous. The four aspects of intraocular inflammation (anterior chamber cells, anterior chamber flare, vitreous cells, and vitreous haze or debris) were ranked using an ordinal scale ranging from 0 to 4 + . Second, patients were investigated for infectious etiologies, including tuberculosis, toxoplasmosis, syphilis, borreliosis, rickettsial infections, toxocariasis, herpes zoster virus, cytomegalovirus, Epstein–Barr virus, human immunodeficiency virus, and rubella. Patients who tested positive for any of these conditions were excluded.

Posterior uveitis is a clinical diagnosis based on a characteristic fundus picture and relevant positive history. Laboratory investigations are predominantly based on antibody testing against specific antibodies.

Diagnosis of panuveitis is established in the presence of the following clinical signs: Evidence of choroidal or retinal inflammation such as choroiditis (focal, multifocal, or serpiginous), choroidal granuloma, retinochoroiditis, retinal vasculitis, subretinal abscess, necrotizing retinitis, or neuroretinitis.

Measurements and parameters

The classification of uveitis was based on the Uveitis Nomenclature Working Group Criteria[15], considering anatomical location, onset and course, unilaterality or bilaterality, and whether granulomatous or nongranulomatous. 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 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), to achieve 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 effectiveness of the treatment strategies was evaluated comprehensively at the 24-month mark post-treatment, according to the following criteria[1]:

Remission was defined as a disease state that remained inactive for 3 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, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), liver and kidney function tests, and serum protein electrophoresis were carried out as baseline investigations in all patients. Serum C3 and C4 levels, antinuclear antibodies, anti-double-stranded DNA, rheumatoid factor and anticyclic citrullinated peptides, antithyroglobulin, antithyroperoxidase, and P and C antineutrophil cytoplasmic antibodies were performed. Angiotensin-converting enzyme was performed.

Bacterial, viral, fungal, and protozoal infections including tuberculosis, toxoplasmosis, syphilis, borreliosis, rickettsial infections, toxocariasis, herpes zoster virus, cytomegalovirus, Epstein–Barr virus, human immunodeficiency virus, and rubella were excluded in all patients by targeted laboratory tests. Radiographic evaluations, comprising X-ray, computed tomography, and MRI were undertaken as required. Complete blood counts, erythrocyte sedimentation rate, C-reactive protein, liver and renal function tests, and serum protein electrophoresis were carried out as baseline investigations in all patients.

Statistical analysis

We analyzed data using Excel and the Statistical Package for Social Sciences (SPSS Inc.). The data are presented as frequency, the percentage for qualitative data, or mean ± SD for continuous data.

Results

In our study population of 936 patients diagnosed with uveitis, 261 individuals (27.88%) were identified as having SDA-AU and met the criteria for inclusion in this study's analysis. Females (64.36%) were more prevalent than male patients. 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 average age at diagnosis differed slightly between sexes: 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.

Initial symptoms of uveitis 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 138 patients, equating to 52.87% of the sample. This was followed by decreased visual acuity and blurred vision, experienced by 45 patients (17.24%), photophobia in 27 patients (10.34%), scotoma in 6 patients (2.29%), and floaters seen by 45 patients (17.24%) (Table 1).

The onset of symptoms varied among patients: 84 patients (32.18%) reported a sudden onset with a rapid progression, while in 177 patients (67.81%), the symptoms developed gradually and exhibited a chronic and recurrent course. Uveitis was unilateral in 144 patients (55.17%) and bilateral in 117 patients (44.82%) (Table 1).

In terms of the anatomical classification, among the 261 patients with Systemic Disease-Associated Uveitis (SDA-UV),

Table 1

SDA-UV characteristics

SDA-UV data	*N* (%)
Ocular symptoms	
Redness painful eye	138 (52.87)
Decrease of visual acuity	45 (17.24)
Photophobia	27(10.34)
Scotoma	6 (2.29)
Floaters	45 (17.24)
SDA-UV onset and course	
Sudden and worsening	84 (32.18)
Gradually chronic and recurrent	177 (67.81)
Unilateral uveitis	144 (55.17)
Bilateral uveitis	117 (44.82)
Anatomic location	
Anterior uveitis	144 (55.17)
Posterior uveitis	87 (33.33)
Panuveitis	30 (11.49)
SDA-UV complications	
Cataract	36 (41.37)
Retinal neovascularization	12 (13.79)
Macular edema	9 (10.34)
Retinal detachment	12 (13.79)
Glaucoma	15 (17.24)

Table 2
Complications.

Complication	SDA-AU (87)	A-UV (48 p.)	P-UV (29p.)	Pan-uveitis (10 p.)
Cataract	36 (41.37%)	9 (25%)	12 (33.33%)	15 (41.66%)
Retinal neovascularization	12 (13.79%)	0 (0%)	3 (25%)	9 (75%)
Macular edema	9 (10.34%)	0 (0%)	0 (0%)	9 (100%)
Retinal detachment	12 (13.79%)		6 (50%)	6 (50%)
Glaucoma	15 (17.24%)	3 (20%)	6 (40%)	6 (40%)

A-UV, anterior uveitis; P-UV, posterior uveitis; SDA-AU, systemic disease-associated autoimmune uveitis.

Table 3
Systematic diseases associated with UV (SDA-UV).

Systemic disease	Number of patients, %
Polymyalgia rheumatic	3 (1.14)
Systemic Sclerosis	3 (1.14)
Rheumatoid arthritis	9 (3.44)
Systemic Lupus Erythematosus	18 (6.89)
Ankylosing Spondylarthritis	54 (20.68)
Behcet's disease	123 (47.12)
Thyroiditis	21 (8.01)
Inflammatory bowel diseases	30 (11.49)

anterior uveitis (AU) was diagnosed in 144 patients (55.17%), posterior uveitis in 86 patients (33.33%), and panuveitis in 30 patients (11.49%) (Table 1).

Retinal neovascularization and macular edema were found as severe complications at the beginning in six patients with panuveitis uveitis, and in three patients with panuveitis uveitis, respectively.

During the follow-up period, complications were observed in 75 patients with an overall number of 84 patients, representing 33.33% of the cohort. These complications encompassed cataracts in 36 patients (41.37% of those with complications), retinal neovascularization in 12 patients (13.79%), macular edema in 9 patients (10.34%), retinal detachment in 12 patients (13.79%), and glaucoma in 15 patients (17.24%). The prevalence of each complication is shown in (Table 2). By contrast, retinal neovascularization, epiretinal membranes, and retinal detachment were detected only in patients with posterior uveitis or panuveitis (Tables 1, 2).

When breaking down these complications by uveitis classification, cataracts were seen in three patients with AU, seven patients with posterior uveitis, and five patients with pan-uveitis, accounting for a total of 36 patients (41.37% of those with complications). Both retinal neovascularization, retinal detachment, and macular edema were exclusive to patients with posterior uveitis or panuveitis. As for glaucoma, it was diagnosed in three patients with AU six patients with posterior uveitis, and six patients with pan-uveitis (Tables 1, 2).

Retinal neovascularization and macular edema were found as severe complications at the beginning in six patients with posterior uveitis, and in three patients with panuveitis, respectively.

Of the 261 patients diagnosed with SDA-AU, a systemic disease was already prevalent in 66 patients (25.28%) at the onset of AU and surfaced later in 195 patients (74.71%).

The associated diseases comprised polymyalgia rheumatica (PMR) in three patient (1.14%), systemic sclerosis (SSc) in three patient (1.14%), rheumatoid arthritis (RA) in nine patients (3.44%), SLE in 18 patients (6.89%), ankylosing spondylarthritis (AS) in 54 patients (20.68%), BD in 123 patients (47.12%), thyroiditis in 21 patients (8.01%), and inflammatory bowel diseases (IBD) in 30 patients (11.49%) (Table 3).

Laboratory evaluations revealed lymphopenia in six patients, and elevated erythrocyte sedimentation rate (>20 mm/h) along with increased serum C-reactive protein (>6 mg/dl) were detected in 174 patients, representing 66.66% of the cohort. Autoantibodies were positive in a few patients, with 18 patients (6.89%) having antinuclear antibodies, six patients (2.29%) having antidouble-stranded DNA, nine patients (3.44%) anticyclic citrullinated peptides, three patient (1.14%) SCL70, and six patients (2.29%) antithyroglobulin.

Radiographic evaluations were performed based on the associated systemic diseases. Chest radiograph were performed on 66 patients diagnosed with AS, RA, and SScs, while hand radiograph were done on 9 patients with RA. MRI was done on six patients with SLE and 36 patients with BD. Colonoscopy was performed on 21 patients with IBD.

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 33 patients (12.64%).

The bulk of the cohort, 240 patients (91.95%), received a combination of oral corticosteroids and one or two immunosuppressive drugs. Single immunosuppressive drugs, such as azathioprine (administered to 90 patients), cyclosporine-A (27 patients), or methotrexate (57 patients), were given to 174 patients (72.5%) due to recurrent or suboptimal remission to corticosteroids or upon withdrawal. These patients had no severe complications. Cyclophosphamide was administered to 36 patients with posterior uveitis and 12 patients with panuveitis. If unilateral uveitis remained unresponsive to both topical and systemic therapy, intravitreal dexamethasone implants were administered. Systemic corticosteroids (for posterior or panuveitis) and topical corticosteroids (in panuveitis) must be administrated in every active episode of chronic uveitis accompanying immunosuppressants.

A two-drug combination therapy, including azathioprine, cyclosporine-A, cyclophosphamide, mycophenolate mofetil, and methotrexate was employed for 36 patients (13.79%) with severe complications at diagnosis or persistently active or recurrent disease. Antitumour necrosis factor-α was administered to 36 patients (13.79%) who were refractory to combination therapy of conventional immunosuppressants or had retinal neovascularization and cystoid macular edema.

Upon the assessment at the 24-month mark, 126 patients (48.27%) were found to have achieved complete remission, 99 patients (37.93%) displayed significant improvement, while in 36 patients (13.79%), the disease had worsened (Refer to Table 4 for detailed results). 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 36 patients experiencing a progression of their disease (representing 13.79% of the cohort) were administered antitumour necrosis factor-α.

Table 4

The data of the assessment of the DSA-UV improvement after treatment.

The pattern of the development of the SDA-UV course	Number of patients, Percent
Complete remission	126 (48.27%)
Significant improvement	99 (37.93%)
Worsened course	36 (13.79%)

Discussion

Our study aligns with prior investigations[12,16,17] in demonstrating that AU 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 and 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 is 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 have proven its effectiveness as a reliable framework for data reporting, treatment application, and patient follow-up[14]. In our study, as mirrored by others[12,19,20,22,23], AU 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[12,18–24].

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[12,19,21].

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[12,20]. 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 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 rheumatic, SSc, RA, SLE, AS, BD, thyroiditis, and IBD. These conditions were also found in correlation with AU in previous studies, although, PMR, SSc, and RA are rare causes of uveitis[1,12,18–24,25].

During the follow-up period, complications arose in 33.33% of patients. These complications included cataracts, glaucoma, retinal neovascularization and detachment, and macular edema, in that order. These findings echo the complication rates and types reported in prior studies[12,18,19].

The role of serological immunological markers, such as anticyclic citrullinated peptides and antinuclear antibodies, in determining the risk of developing a systemic autoimmune disease remains under-explored in patients[26]. A study conducted by Lin *et al.*[27], however, demonstrated the utility of antineutrophil 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[15], 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 edema, antitumor necrosis factor-α was administered, paralleling the findings of the study by Leclercq *et al.*[31].

Azathioprine, an immunosuppressive drug, is generally the treatment of choice for AU, 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. Antitumour necrosis factor-α was administered to patients with disease progression.

Despite the common diagnosis of sarcoidosis, followed by HLA-B27-associated uveitis and then BD[33,34], our study found BD to be the most common diagnosis, followed by AS and 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.

Limitations; First the small sample size and one-centre study. Second, the a higher prevalence of BD disease, as Syria is on the Silk Road, where the disease is common and is well-known for its ocular manifestations and complications[34]. Third, the studied group of patients is very heterogeneous, comprising diseases with very different prognoses, such as uveitis associated with AS and ocular Behcet. Therefore, it is very difficult to interpret the overall outcome of this series. Also, the anatomic location for each systemic association may influence the outcome, as it occurs in

Behcet disease, where isolated AU has a better outcome than posterior segment inflammation, and finally, 13.79% of patients who were administered antitumour necrosis factor-α, with the progression of the disease, were only followed for 24 months, but if after this year anti-TNF were administered, what was the outcome for these patients?

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 to 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 serological immunological markers' role in early predicting 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 the majority of patients with careful long-term modulation. Altogether, the study underscores the importance of comprehensive screening, timely diagnosis, and appropriate treatment of AU to not only enhance visual prognosis but also to potentially uncover systemic diseases, thus facilitating early management and improved overall patient outcomes.

Ethical approval

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

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 deidentified.

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Author contribution

M.K., H.D., and N.K.: conceived and designed the study and wrote the manuscript; D.A. and Lab participated in the data collection. L.A.D and R.A.: revealed the ophthalmological evaluation, and follow-up of the patients. All authors conceived the study, read, and approved the final manuscript.

Conflicts of interest disclosure

The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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Data availability statement

The dataset analysed during the current study is available from the corresponding author (Lama Al Darwish:lmdrwsh@gmail.com) on reasonable request available by request.

Provenance and peer review

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