

Prevalence of Inflammatory Back Pain in a Cohort of Patients With Anterior Uveitis

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- **PURPOSE:** To determine the prevalence of inflammatory back pain in an anterior uveitis cohort.
- **DESIGN:** Retrospective cohort study.
- **METHODS:** Patients with anterior uveitis were recruited from the clinic of an ophthalmologist to complete a survey between March and December 2008. Patients were classified with inflammatory back pain if they had ≥ 2 positive responses to 4 validated inflammatory back pain questions: presence of morning stiffness > 30 minutes in duration; improvement in back pain with exercise but not with rest; awakening from back pain during the second half of the night only; and presence of alternating buttock pain. Disease activity was assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The impact of disease on quality of life was measured using the EuroQOL (EQ-5D) questionnaire. Twenty-five patients underwent further rheumatologic examination.
- **RESULTS:** One hundred forty-one of 167 patients (84.4%) completed the survey. Sixty-six of 141 patients (46.8%) were classified to have inflammatory back pain. Mean BASDAI (4.2, SD 2.41) and EQ-5D scores (0.73, SD 0.21) were lower than patients with no inflammatory back pain (0.82, SD 0.16, $P = .0048$). In the subgroup that underwent rheumatologic assessment, a classification of inflammatory back pain was 92% sensitive and 67% specific for a diagnosis of inflammatory back pain.
- **CONCLUSIONS:** The prevalence of inflammatory back pain in a cohort of anterior uveitis patients was found to be 46.8%. Patients with inflammatory back pain had worse quality of life than those without. Ophthalmologists may use these questions on back pain to select patients classified to have inflammatory back pain to refer for early rheumatologic assessment. (Am J Ophthalmol 2012;153:1025–1030. © 2012 by Elsevier Inc. All rights reserved.)

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DEPENDING ON THE PREDOMINANT LOCATION OF the inflammation in the eye, uveitis may be divided into anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis. Uveitis can occur as a manifestation of many diseases including infections, malignancy, and several systemic diseases. Thirty-seven percent to 50% of patients with anterior uveitis have no identifiable etiology to their inflammation and their uveitis is considered idiopathic.^{1,2}

The spondyloarthropathies are also known as seronegative or HLA-B27-associated arthropathies, a group of diseases that share common characteristics and preferentially involve the axial skeleton. Subcategories include ankylosing spondylitis, reactive arthritis (formerly known as Reiter syndrome), psoriatic arthritis, enteropathic spondylitis (or arthritis associated with inflammatory bowel disease), and undifferentiated spondyloarthropathies.^{3,4} Spondyloarthropathies overall are associated with 33% of anterior uveitis. Up to 40% of patients with ankylosing spondylitis, 26% with reactive arthritis, 25% with psoriatic arthritis, 37% with enteropathic spondylitis, and 13% of patients with undifferentiated spondyloarthropathy will develop acute anterior uveitis.^{5–7} Conversely, 50% of patients with anterior uveitis are HLA-B27 positive.⁸ Currently, there are limited data on the prevalence of spondyloarthropathies in an anterior uveitis population in Canada.^{9,10}

Spondyloarthropathy patients may develop restricted mobility and severe spinal deformity. Spinal stiffness and pain in spondyloarthropathies results in work disability being 3 times higher than the healthy population.¹¹ Unfortunately, the diagnosis of spondyloarthropathies is often made late¹² as symptoms may be overlooked or go undiagnosed until an extraspinal manifestation is identified.¹³ Uveitis, in particular anterior uveitis, is often a presenting feature of a spondyloarthropathy;¹⁴ so the ophthalmologist may be these patients' earliest medical encounter. In a report of 175 consecutive patients with HLA-B27-associated uveitis, 65% of patients had uveitis prior to diagnosis of an extraocular disease.¹⁵

Inflammatory back pain is defined as back pain attributable to a spondyloarthropathy. Thus, recognition that a patient's back pain is inflammatory in nature can lead to earlier diagnosis of spondyloarthropathies. Early diagnosis is important as 1 study demonstrated that ankylosing spondylitis patients with uveitis tend to have more severe

functional and radiologic outcomes than those without uveitis.¹⁶ Inflammatory back pain in patients with ankylosing spondylitis can be identified using validated criteria such as those defined by Rudwaleit.¹⁷ These criteria include positive responses to 2 out of 4 questions asked of the patient: presence of morning stiffness of more than 30 minutes in duration; improvement in back pain with exercise but not with rest; awakening because of back pain during the second half of the night only; and presence of alternating buttock pain.

In this study, we sought to determine the prevalence of inflammatory back pain using validated criteria in a population of anterior uveitis patients from a mixed community academic practice over 7.5 years (from September 2000 to March 2008). The degree of the patients' inflammatory disease activity and impact of uveitis and back pain on their quality of life was also measured. We aim to determine the role that ophthalmologists can play to increase earlier detection of spondyloarthropathy so that the rheumatologist can intervene earlier in the disease process. We also examine the sensitivity and specificity of the 4-question survey to identify patients with inflammatory back pain in this anterior uveitis population.

METHODS

• **PATIENT SELECTION:** Three hundred and forty-four patients with a diagnosis of anterior uveitis from the clinical uveitis database of a mixed community and academic practicing ophthalmologist (L.D.) were invited to participate in a survey from March to December 2008. This database included all patients who received a diagnosis of anterior uveitis in the ophthalmology practice over a 7.5-year period. Inclusion criteria included being 18 years old or over and patient ability to complete an English-language questionnaire. Patients were mailed an introductory letter from their ophthalmologist and 10 days later were contacted by phone by research staff. If no phone contact had been made by the researchers after 2 weeks of calling at various times (day and evening), or if an automated message indicated the number was no longer in use, a copy of the informed consent form and study survey were mailed to the patient's last known address. Reminder letters were mailed 14 days later if there had been no response. If all these attempts to contact the patients failed, they were considered uncontactable.

Patients were excluded if they could not be reached by mail or phone (up to 20 repeated phone calls per patient were made), declined to participate, claimed to have no uveitis, were deceased, were unable to complete an English-language questionnaire, or were mentally or physically unable to participate. Clinic chart review was performed for the patients who completed the informed consent process and survey. A sample of 25 patients who completed the survey also underwent a complete rheumatologic

examination (by M.S.) to verify their diagnosis of inflammatory back pain, to determine if they had a spondyloarthropathy, and to rule out back pain caused by other sources. Where clinically indicated, patients underwent laboratory and radiographic examination to confirm the presence of sacroiliitis and disease subclassification. This allowed for data analysis to determine the sensitivity and specificity of the 4-question survey to identify patients with inflammatory back pain in this anterior uveitis population. The diagnosis of a spondyloarthropathy was made using the European Spondyloarthropathy Study Group criteria as the Assessment for Ankylosing Spondylitis criteria were not published at the time this study began.

• **SURVEY CONTENT:** Demographic information was collected and previously described and validated questions for inflammatory back pain were used in our questionnaire.¹⁷ As noted above, the back pain questions consisted of 4 items: 1) presence of morning stiffness of more than 30 minutes in duration; 2) improvement in back pain with exercise but not with rest; 3) awakening because of back pain during the second half of the night only; and 4) presence of alternating buttock pain. The author of these criteria has since updated and published new criteria, but at the time of our study design, these were the criteria available.

The degree of inflammatory disease activity was assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).¹⁸ The BASDAI series of questions has been validated to demonstrate sensitivity to changes in treatment in patients with ankylosing spondylitis.¹⁹ According to international guidelines for commencement of biologic agents, one of the criteria for suitability is disease activity greater than 4 on the BASDAI.²⁰

The impact of uveitis and back pain on patients' quality of life was measured using the EuroQOL (EQ-5D utility/health index, a weighted score) questionnaire.²¹ Patients rated the state of their health in 5 categories: mobility; ability with self-care; ability to perform usual activities such as work, study, housework, family, or leisure; amount of pain or discomfort; and presence of anxiety or depression. A score of 0 meant the worst health state and a score of 1 meant the best health state.

• **PATIENT CHART REVIEW:** Patients' ophthalmology charts were retrospectively reviewed for clinical information on results of investigations performed, including human leukocyte antigen (HLA-B27), and etiology of the anterior uveitis.

• **DATA ANALYSIS:** Data analysis was conducted using SAS v9.1 (SAS Institute Inc, Cary, North Carolina, USA). The specificity and sensitivity of having a positive response to 2 of the 4 back pain questions was calculated for the 25 patients who underwent complete rheumatologic examination.

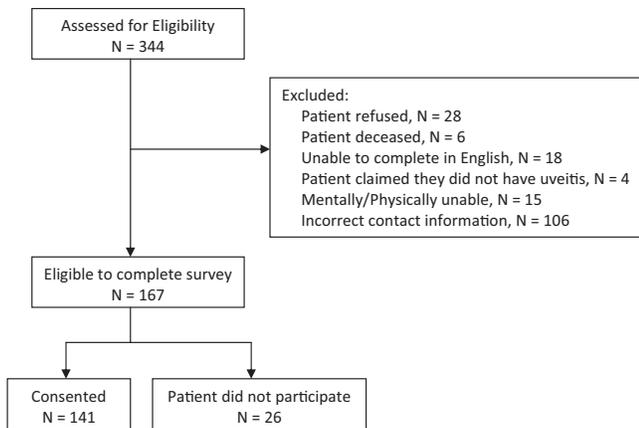


FIGURE. Breakdown of patient recruitment outcomes in this study of inflammatory back pain in patients with anterior uveitis. Of the 167 patients with anterior uveitis who received the survey, 141 patients (84.4%) returned the survey by mail or completed the survey over the phone with an interviewer.

TABLE 1. Distribution of Answers From All Anterior Uveitis Patients Who Responded to the Inflammatory Back Pain Questionnaire

Question	Response		% Yes
	Yes	No	
Do you ever have a “stiff” back in the morning that lasts more than 30 minutes?	54	86	38.3%
Do you ever have back pain that gets better when you exercise and not when you rest?	74	65	52.5%
Does your back pain ever wake you up in the middle of the night (after you have slept for a few hours)?	43	97	30.5%
Do you have buttock pain that moves from side to side?	38	102	27.0%

RESULTS

OF THE 344 PATIENTS WHO HAD A DIAGNOSIS OF ANTERIOR UVEITIS in the clinical database, 177 (51%) were excluded because they could not be reached by multiple phone and mailing attempts (106), declined to participate (28), claimed to have no uveitis (4), were deceased (6), were unable to complete an English-language questionnaire (18), and were mentally or physically unable to participate (15). Patients for whom phone contact was never made received an average of 6.5 calls at various times of the day and evening. The response rate was 84% (141/167) for the remaining 167 patients who

TABLE 2. Patient Demographics, Bath Ankylosing Spondylitis Disease Activity Index Score, EuroQuality of Life 5-D Score, and Human Leukocyte Antigen-B27 Testing Results for Patients With Anterior Uveitis Who Participated in the Study Survey

	Inflammatory Back Pain (N = 66)	No Inflammatory Back Pain (N = 75)
Mean age at survey, years (SD)	45.6 (13.4)	51.4 (16.0)
# Male (%)	22 (33.3)	42 (56)
# Female (%)	44 (66.7)	42 (56)
# White (%)	55 (83.3)	49 (65.3)
Mean BASDAI Score (SD) ^a	4.2 (2.4)	Test does not apply to patients with noninflammatory back pain
Mean EuroQOL-5D Score (SD) ^{b,c}	0.72 (0.21)	0.82 (0.16)
# Patients tested for HLA-B27 (%) ^d	54 (82)	55 (73)
# Patients HLA-B27-positive (%) ^e	28 (42)	17 (23)

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index.
^aBASDAI scores of 4 or more suggest suboptimal control of disease and these patients should be considered for a change in their medical therapy.
^b $P = .005$.
^c0 = worst health state, 1 = best health state.
^dPatients with rheumatologic diagnosis at presentation were not tested.
^e $P = .020$.

were invited to complete the survey. Twenty-six patients (16%) did not return the survey (Figure).

Sixty-six of 141 patients (46.8%) had 2 or more positive responses to the questions about their back pain and were thus classified to have inflammatory back pain. Improvement of back pain with exercise was answered most often positively in 58 of 66 patients (87.9%). The distribution of all patients' responses is shown in Table 1. Patient demographic information and clinical outcomes such as disease activity as measured by BASDAI and health-related quality of life (HRQOL), as measured by EQ-5D and HLA-B27 positivity, are presented in Table 2. Patients with inflammatory back pain had a significantly lower HRQOL with a mean EQ-5D score of 0.72 compared to patients without inflammatory back pain (0.82, $P = .005$). HLA-B27 was positive in 28 of 54 tested patients (52%) with inflammatory back pain compared to 17 of 55 tested patients (31%) without inflammatory back pain ($P = .033$). Overall, an HLA-B27-related association was found in 45 of 141 patients (31.9%), although 33 of 141 patients (23%) did not undergo HLA-B27 testing and other diagnostic investigations by ophthalmology, especially if the patient had a

TABLE 3. Anterior Uveitis Etiology or Association in Anterior Uveitis Patients Who Participated in the Study Survey

Etiology or Association	Number of Patients (%) (N = 141)
Idiopathic	45 (31.9)
HLA-B27	20 (14.2)
Ankylosing spondylitis	15 (10.6)
Infectious ^a	15 (10.6)
Inflammatory bowel disease	7 (5.0)
Fuchs iridocyclitis	7 (5.0)
Lens induced/pseudophakic	6 (4.3)
Sarcoid	5 (3.6)
Juvenile idiopathic arthritis	4 (2.8)
Psoriatic arthritis	4 (2.8)
Rheumatoid arthritis	3 (2.1)
Reactive arthritis (Reiter syndrome)	3 (2.1)
Undifferentiated spondyloarthropathy	2 (1.4)
Other ^b	5 (3.6)

HLA = human leukocyte antigen.

^aLyme, tuberculosis, herpes zoster, herpes simplex, human immunodeficiency virus.

^bBehcet, Possner Schlossman, polyarteritis nodosa, drug-related, masquerade.

previous rheumatologic diagnosis. Seventy-six of 141 patients (54.3%) had bilateral anterior uveitis disease. The most common anterior uveitis etiologies or associations found in our cohort included idiopathic, HLA-B27-positive without a spondyloarthropathy diagnosis, ankylosing spondylitis, and infectious causes (Table 3). Idiopathic means HLA-B27-negative and also negative for other causes of uveitis by review of systems, examination, and lab testing. HLA-B27-positive means HLA-B27-positive serology. In situations where a systemic diagnosis (ankylosing spondylitis, Crohn, psoriasis, sarcoidosis, Reiter syndrome) was already made, HLA-B27 test was not always done.

Of the 25 patients (17.7% of 141 respondents) who participated in a complete rheumatologic assessment, 16 (64%) were classified to be positive for inflammatory back pain (answered positively to 2 or more questions about back pain). The diagnoses in the 16 patients included 9 with ankylosing spondylitis, 3 with undifferentiated spondyloarthropathy, 3 with degenerative disc disease, and 1 with lupus and osteoporosis as well as mechanical back pain. All the patients with ankylosing spondylitis and undifferentiated spondyloarthropathies were HLA-B27 positive. Nine patients (36%) were classified to be negative for inflammatory back pain, of which only 1 had a diagnosis of ankylosing spondylitis. A positive score on 2 or more of the 4 back pain questions was 92% sensitive (12/13) and 67% specific (8/12) for the diagnosis of ankylosing spondylitis or an undifferentiated spondyloarthropathy.

DISCUSSION

THE MAIN PURPOSE OF THIS RETROSPECTIVE STUDY WAS to determine the prevalence of inflammatory back pain in a cohort of patients with anterior uveitis. Based on survey data of 141 respondents from a tertiary care uveitis specialist's practice (L.D.), the prevalence of inflammatory back pain was found to be 46.8%. Patients with 2 or more positive responses to the 4 previously validated questions about their back pain (Figure) were classified to have inflammatory back pain.¹⁷ In a subgroup of 25 patients who underwent a complete rheumatologic assessment to verify their diagnosis, this classification criterion used was 92% sensitive and 67% specific for the diagnosis of ankylosing spondylitis or an undifferentiated spondyloarthropathy. This compares to Rudwaleit's findings of 70.3% sensitivity and 81.2% specificity when using this classification criterion.¹⁷ The simplicity of these 4 questions on back pain is useful for ophthalmologists, who may frequently be the first medical professional these patients encounter,¹⁴ to screen patients with anterior uveitis and to aid in timely referrals to the rheumatologist.

These back pain questions have additional significance as the mean BASDAI score of patients classified with inflammatory back pain in our study was 4.2, signifying that these patients had only moderate disease control.^{18,19} In the same vein, based on their mean EQ-5D score (0 = worst health state; 1 = best health state), patients with inflammatory back pain in our study had significantly worse quality of life than those without inflammatory back pain (0.72 vs 0.82, $P = .005$). While there is no validated minimal clinically important difference for EQ-5D for spondyloarthropathy, a clinician may examine a patient's individual scores to determine which domain is more affected. Complaints for each domain (mobility, ability for self-care, performance of usual activities, pain/discomfort, and anxiety/depression) could then be addressed. Patients with spondyloarthropathies include those with ankylosing spondylitis, psoriatic arthritis, reactive arthritis, enteropathic spondylitis, and undifferentiated spondylitis. Early identification of inflammatory back pain can lead to the earlier diagnosis of a spondyloarthropathy so that appropriate management can be initiated by a rheumatologist. Prevention of spondyloarthropathy disease progression and treatment of symptoms such as spinal stiffness and pain can improve patient outcomes and decrease work disability.¹¹

It is interesting that there were more female patients in our cohort of patients classified with inflammatory back pain (66.7%), even though it has been reported there is a sex bias of 2.2 to 1 in favor of men for ankylosing spondylitis.^{15,22} There may be a few reasons for this finding. There are more female patients in the overall practice of the uveitis specialist (L.D.) at the time of this study (59% female patients and 41% male patients, or 1.44 to 1). Out of the 141 patients who completed the survey questions, 61% were female. Also, as a function of the study design, it is possible that female patients

may be more likely to respond and complete extensive surveys. A study by Gritz and Wong reported a 12-month prevalence rate of anterior uveitis in Northern California to be higher in female subjects (58.4%).²³ It also described that relative to men, women may have a higher risk of being diagnosed with recurrent or chronic disease after the initial bout of inflammation. Furthermore, the study postulated that older women may be at higher risk than younger women than for men of the same age group. In this study, the average age of presentation to the uveitis specialist (L.D.) was 45.8 years (range 15 to 77 years). Another paper on HLA-B27-associated uveitis and sex differences²² found that female patients had significantly more bilateral disease after 10 years of follow-up, mean duration of required topical treatment per uveitis episode was significantly longer, and systemic disease usually developed after uveitis onset whereas in male subjects, HLA-B27-associated disease was usually diagnosed prior to the onset of uveitis. The cohort of anterior uveitis patients in this study were recruited from the practice of a tertiary care uveitis specialist where the majority of referrals are from ophthalmologists or optometrists. Therefore, a selection bias of more complex patients in our cohort could also have led to the higher percentage of female patients with inflammatory back pain found in this study.

Etiologies and associations for anterior uveitis were identified in 66.6% (94/141) of this study's population. A total of 33.3% (47/141) were classified as "idiopathic," which is a lower percentage than the findings of previous studies^{1,2}. 31.9% (45/141) of patients in our study population had an HLA-B27-positive test result (although not all patients were tested for their HLA genotype). This is less than the 50% reported in another study⁸ but slightly more than the 23.6% reported by a Canadian study.²⁴ Many patients did not undergo further diagnostic investigations, especially if they already had an established rheumatologic diagnosis of a spondyloarthropathy (Table 2). Patients classified with inflammatory back pain were more likely to test positive for HLA-B27 compared to those without inflammatory back pain. Twenty-two percent of anterior uveitis patients in our study had an associated spondylo-

arthropathy, the most common systemic disease associated with anterior uveitis was ankylosing spondylitis (10.6%), and 14.2% were HLA-B27 positive without an associated rheumatologic diagnosis; these data are comparable to another Canadian study that found rates of 21.4%, 13%, and 6%, respectively.²⁴

Weaknesses of this study include the inherent difficulties with survey-based investigations. Many of the factors for excluding a patient were typical challenges for studies that require patient direct participation, for example, patient refusal, death, language limitations, physical or mental restrictions, incorrect contact information, and patients stating that they did not suffer from uveitis. Of the 167 patients who did receive the survey, the response rate was excellent, with 141 patients (84.4%) returning the survey by mail or completing the survey over the phone with an interviewer. In addition, many patients with established spondyloarthropathy may not have had active inflammatory back pain at the time of the survey as the disease is associated with flares and remissions.²⁵ This may have led to an underreporting of the overall prevalence of inflammatory back pain in this cohort.

Referral bias and patient case-mix bias, as seen in other studies involving practice-based reviews, is another limitation to this study. The cohort of anterior uveitis patients in this study may have been more complex as they were recruited from the practice of a tertiary care uveitis specialist where the majority of referrals are from ophthalmologists or optometrists. The findings therefore may not be appropriately extrapolated to the general community.

In summary, this study has demonstrated the prevalence of inflammatory back pain in a Canadian cohort of anterior uveitis patients to be 46.8%. Anterior uveitis is often a presenting feature of a spondyloarthropathy, especially for women. Ophthalmologists, who may be the first medical professional to encounter these patients, should consider the use of the simple validated questions on back pain used in this study so that early referral to rheumatology can be made for patients classified to have inflammatory back pain.

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Biosketch

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