

# HLA-B27-associated acute anterior uveitis in the University Referral Centre in North Thailand: clinical presentation and visual prognosis

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**Background:** Acute anterior uveitis (AAU) is the most frequent type of uveitis encountered in the west. Although human leucocyte antigen (HLA)-B27-associated ankylosing spondylitis was reported in South East Asia, it is not known whether HLA-B27-associated ocular disease is prevalent in Thailand.

**Methods:** A prospective study of 100 unrelated blood donors and 121 consecutive patients with AAU was carried out. All people underwent HLA-B27 typing and full ocular examination. Radiological examination of the sacroiliac joints was conducted in patients with low back pain or arthralgias.

**Results:** The prevalence of HLA-B27 was 10% among the blood donors in contrast with 44% in the AAU group ( $p < 0.001$ ). The clinical characteristics of HLA-B27-associated AAU were similar to those published throughout the world (unilaterality in 74%, hypopyon in 31%, recurrent AAU in 64%). However, the increased intraocular pressure (IOP) was more common in the HLA-B-27-negative group ( $p = 0.03$ ) than in their HLA-B27-positive counterparts. At least 15% of the HLA B27-positive group had radiological signs of ankylosing spondylitis.

**Conclusion:** The prevalence of HLA-B27 in the population without uveitis in Thailand is about 10% and clinical characteristics of HLA-B27-positive AAU are similar to those reported in the west. In contrast with earlier reports, HLA-B27-negative AAU in Thailand was associated with increased IOP and should be further studied.

Acute anterior uveitis (AAU) is the most frequent type of uveitis encountered in western Europe and the US, accounting for about 50% of all cases of uveitis.<sup>1,2</sup> In Asia, similar findings were reported for the Indian sub-continent, but by contrast, in Japan the frequency of AAU was reported to be low.<sup>3,4</sup> In most uveitis series, the prevalence of HLA-B27 in patients with AAU was about 50%, ranging from 19% to 82% across the different racial groups.<sup>1,3,5,6</sup>

In Thailand, the presence and role, if any, of HLA-B27-associated AAU in patients with uveitis is not known. The purpose of this study was to assess the frequency of HLA-B27 in healthy people without AAU and in patients with AAU in northern Thailand and to describe the clinical features of HLA-B27-positive AAU in this particular population.

## METHODS

We studied 100 unrelated Thai blood donors without history and clinical presentation of anterior uveitis, and 121 consecutive Thai patients with AAU who were examined at the ophthalmologic department of the University Maharaj Nakorn Hospital, Chiang Mai, Thailand, from January 2004 to December 2005. AAU was defined as anterior chamber inflammation of any cause that completely healed within 3 months. Patients in whom anterior uveitis was initially diagnosed, but which later become chronic, were not included in the study. Increased intraocular pressure (IOP) was considered in cases with measurements  $>21$  mm Hg. The complete ophthalmological examination was carried out in all blood donors and patients with AAU, and all patients were questioned about systemic complaints indicating the presence of human leucocyte antigen (HLA)-B27-associated systemic diseases. During the course of follow-up, all ocular

complications were recorded, including the development of cataract, ocular hypertension or glaucoma, and posterior segment abnormalities. Clinical data including sex, age, clinical features at onset, management, follow-up time, ocular complications and visual outcomes were also registered, as well as results of HLA-B27 typing. HLA-B27 allele typing was carried out in all patients by a standard genotyping of DNA extracted from peripheral blood.<sup>7</sup> Radiological examination of sacroiliac joints was carried out in all patients with AAU with low back pain or arthralgias. The mean (range) follow-up duration was 20 (0–108) months.

The data were analysed by calculating the descriptive statistics for the prevalence of HLA-B27 in blood donors without a history or presence of uveitis, and in the HLA-B27-positive and HLA-B27-negative AAU groups. The differences were assessed using  $\chi^2$  test and Student's *t* test where appropriate, and *p* values  $<0.05$  were considered significant.

## RESULTS

The prevalence of HLA-B27 among the blood donors was 10% (10/100). The prevalence of HLA-B27 in the AAU group was 44% (53/121;  $p < 0.001$ ) and the average age at onset of the uveitis was 38 years (median (range) 38 (4–67) years). The male:female ratio was 1.94:1 among the 53 patients with HLA-B27-positive uveitis and 0.94:1 among the 68 patients with HLA-B27-negative uveitis ( $p = 0.05$ ). HLA-B27-positive patients with AAU were slightly younger than HLA-B27-negative patients (average age 37 *v* 39.5 years, not

**Abbreviations:** AAU, acute anterior uveitis; HLA, human leucocyte antigen; IOP, intraocular pressure

**Table 1** Clinical characteristics of HLA-B27-positive versus HLA-B27-negative patients at the onset of acute anterior uveitis

Characteristic at onset	HLA-B27-positive AAU (n = 53) n (%)	HLA-B27-negative AAU (n = 68) n (%)	p Value
Acuity <0.05	8 (15)	10 (15)	0.952
Unilateral AAU	39 (74)	50 (74)	0.995
Hypopyon	17 (32)	5 (7)	<0.001

AAU, acute anterior uveitis.

significant). The number of patients <40 years was similar in both groups (28/53 v 34/68;  $p = 0.75$ ).

Table 1 shows the general and clinical features of HLA-B27-positive and HLA-B27-negative patients with AAU at onset of uveitis. The HLA-B27-positive and HLA-B27-negative patients with AAU did not differ in initial visual acuity and eye involvement. However, the number of patients with severe AAU complicated by hypopyon was higher in HLA-B27-positive patients ( $p = 0.001$ ). Increased IOP (>21 mm Hg) was more common in the HLA-B27-negative patients than in their HLA-B27-positive counterparts (table 2). In our limited follow-up, the recurrent episodes were slightly more frequent in the HLA-B27-positive group ( $p = 0.04$ ). Development of glaucoma was observed in 10 of 53 (19%) HLA-B27-positive patients and in 21 of 68 (31%) HLA-B27-negative patients ( $p = 0.133$ ).

All patients were treated with topical corticosteroids according to the severity of the intraocular inflammation. Periocular corticosteroids were used for patients who developed posterior segment complications. A short course of systemic corticosteroids was given to patients resistant to local treatments (2 in the HLA-B27-negative v 0 in HLA-B27-positive group,  $p = 0.1$ ).

The number of HLA-B27-positive patients with low back pain was 21, and radiological examinations showed signs characteristic of ankylosing spondylitis in 8 patients (8/53, 15% of patients in the HLA B27-positive group; 8/21, 38% of patients with low back pain in whom radiological examination was carried out). The diagnosis of psoriatic uveitis was made in two patients in the HLA-B27-negative group, but none of the HLA B27-negative patients and none of the blood donors had symptoms characteristic of ankylosing spondylitis.

## DISCUSSION

Our study detected the prevalence of HLA-B27 in 10% of the northern Thai population. Further, we found that the HLA-B27-associated AAU group formed about 43% of all patients with AAU, which is compatible with most published surveys on uveitis.<sup>1 4 8-10</sup> In addition, the clinical characteristics of HLA-B27 AAU in Thailand were similar to those published worldwide.<sup>1 8-15</sup>

HLA-B27 exhibits considerable variation in prevalence in different populations, ranging from 1-6% in Japan to 50% among the Haida Indians of North America.<sup>16-18</sup> In Caucasian populations, the prevalence of HLA-B27 is about 8-10%. In northern Thailand, the frequency of HLA-B27 was previously reported to be about 4%, which approximates to our findings of 10%.<sup>7 16</sup> The HLA-B27-associated systemic diseases such as ankylosing spondylitis, reactive arthritis, and other disorders such as Reiter's syndrome and psoriatic arthropathy are prevalent in Thailand; however, their exact prevalence is as yet unidentified. In our study, at least 15% of HLA-B27-positive patients with AAU had ankylosing spondylitis, which is lower than in most previous studies.<sup>1 8-15 19</sup> The low numbers in our study may be (in part) explained by the fact

**Table 2** Complications and visual outcome of HLA-B27-positive and HLA-B27-negative patients with acute anterior uveitis

Characteristic	HLA-B27-positive AAU (n = 53)	HLA-B27-negative AAU (n = 68)	p Value
Average duration of follow-up	19 months	22 months	
Visual outcome <0.05	1/50 (2%)	6/64 (10%)	0.104
Significant visual improvement*	12/50 (24%)	13/64 (20%)	0.637
More than one episode of AAU	23/36 (64%)	24/57 (42%)	0.041
Intraocular pressure >21 mm Hg	11/53 (21%)	27/68 (40%)	0.026
Glaucoma	10/53 (19%)	21/68 (31%)	0.133
Cataract	7/53 (13%)	12/68 (18%)	0.505
Posterior synechiae	5/53 (9%)	5/68 (7%)	0.680
Cystoid macular oedema†	1/53 (5%)	1/68 (3%)	0.859

AAU, acute anterior uveitis.

\*Clinically significant visual improvement was defined as an improvement of more than 2 lines on the Snellen chart.

†The actual number of patients with (slight) CME might actually be higher, as not every patient could be extensively assessed owing to the presence of synechiae or cataract.

that the radiological examinations were carried out only in patients with back pain or arthralgia and were not examined by a rheumatologist, and the real numbers of patients with ankylosing spondylitis might in fact be much higher. This was also the case with the HLA-B27-positive blood donors.

The prevalence of HLA-B27-associated ocular disease in Thailand has so far not been studied. Because the frequency of HLA-B27 found in this study was similar to those in Europe and the US, it is reasonable to expect that the prevalence of HLA-B27-associated diseases might be similar. The prevalence of HLA-B27-associated ocular disease seems indeed to be similar to that of HLA-B27-associated AAU in the Thai population as almost half of all patients with AAU were HLA-B27 positive, a finding that is consistent with the findings from Europe and the US.<sup>1 5 7-15</sup> However, HLA-B27 represents a family of >20 closely related alleles that differ at diverse amino acid positions. The prevalence of various subtypes of HLA-B27 varies in different races, and some subtypes play a stronger disease-predisposing part than other polymorphic positions.<sup>18</sup> The presence of the specific HLA-B27 subtypes that are only weakly associated with ankylosing spondylitis might also have contributed to the low prevalence of ankylosing spondylitis in our patients with HLA-B27 AAU. Other additional various factors such as infections with Gram-negative bacteria and their interaction with HLA antigens might also be involved in the pathogenesis of HLA-B27-associated systemic and ocular diseases.<sup>20-22</sup> It may be important to investigate further whether certain HLA-B27 subtypes show any preferential association with ocular disease, and vary between the various ethnic/racial populations and geographical regions of the world. Further, our patients were not assessed for the existence of additional HLA-B27-related systemic diseases such as reactive arthritis, inflammatory bowel disease and undifferentiated spondyloarthropathy. Financial and organisational causes precluded the addition of extensive rheumatological assessment to this initial study. However, we decided to incorporate the radiological examinations as these objectively show the presence of ankylosing spondylitis. Future studies on the HLA-B27 subtypes and extensive rheumatological analysis could further clarify the pathogenesis of HLA-B27-associated disorders.

The clinical characteristics of HLA-B27-associated AAU have been extensively reviewed in the literature and include mainly unilateral ocular involvement, sudden onset, marked fibrinous reaction and younger age of onset.<sup>1,8-15,23</sup> In addition, some authors indicated a poor visual prognosis, specifically when compared with the HLA-B27-negative patients with AAU.<sup>12,13</sup> For example, legal blindness was observed in HLA-B27-negative patients with AAU in only 2% versus 11% in HLA-B27-positive patients with AAU, and systemic treatment was required more frequently in HLA-B27-positive patients.<sup>12</sup> By contrast, other authors observed different outcomes.<sup>9,24</sup> Undoubtedly, the results of the comparison also depend on the nature and outcome of HLA-B27-negative uveitis. The HLA-B27-negative AAU is an accumulation of known and unknown disorders and seems to be, at least in Europe and the US, associated with a good outcome. In our study from South East Asia, the observed clinical features of HLA-B27-associated AAU accord well with previous findings, including a male predominance and a high number of patients with severe acute features such as hypopyon. The HLA-B27-negative AAU, by contrast, seems to be characterised by more frequent complications, especially by raised IOP. The number of patients with glaucoma in the B27-negative group exceeded slightly that with B27-positive AAU, but the difference was not significant. Definite conclusions concerning the development of glaucoma, however, cannot be made on the basis of this study owing to the limited follow-up, and difficult differentiation between the glaucoma and ocular hypertension because of the frequent presence of cataract or posterior synechiae. Outcomes of visual acuity cannot be exactly compared owing to the different criteria used by various studies. Our findings suggest that HLA-B27-negative patients in Asia might have a pathogenesis different from those in Europe and the US. The aetiology of HLA-B27-negative AAU is essentially undetermined, and may include various viral infections (often associated with increased IOP) and certainly requires further investigation.

In conclusion, we observed that the prevalence of HLA-B27 in a population without uveitis in Thailand, as well as the frequency and clinical characteristics of HLA-B27-positive AAU, is similar to that in populations in the US and Europe. Our findings indicate that the pathogenesis and causes of HLA-B27-negative uveitis in Thailand differ from those in the US and Europe and should be further studied.

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