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Epidemiology of uveitis in a referral hospital in Turkey

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Aim: To investigate the causes and clinical characteristics of uveitis in patients presenting to a specialized eye hospital in Turkey.

Materials and methods: The clinical records of 1028 uveitis patients admitted between 1990 and 2010 were retrospectively reviewed. Age at first presentation, sex, laterality, etiology, associated systemic disease, clinical presentation, and course of the disease were noted.

Results: The mean age at presentation was 36.23 ± 14.9 years. Males constituted 58.2% of patients. Anatomically, anterior uveitis (42%) was most common, followed by posterior uveitis (24.9%), panuveitis (24.7%), and intermediate uveitis (8.4%). The course of the disease was mostly chronic (65.7%). The cases were idiopathic at 25.7% and Behçet's disease (BD) was the most common cause of uveitis (32.2%), followed by ocular toxoplasmosis (7.2%) and herpetic uveitis (6.8%).

Conclusion: Uveitis tends to affect patients between 20 and 40 years old. BD is the most common cause, leading to male predominance and a higher frequency of a chronic course.

Key words: Epidemiology, etiology, uveitis, Behçet's disease, iridocyclitis

1. Introduction

Uveitis includes a large group of intraocular inflammatory conditions that may occur at any age but affecting mostly people of working age (1). It is an important cause of visual impairment throughout the world, accounting for about 10% of all legally blind individuals and leading to a significant personal and population burden (2,3). Uveitis has various clinical patterns and characteristics influenced by multiple factors like genetic, geographic, and environmental factors and diagnostic criteria (4). Various epidemiological studies have been performed in different regions and ethnic populations (5–12). Furthermore, changing patterns of intraocular inflammatory diseases have been reported (12–16). Knowledge about the different types and etiology of uveitis in various populations is of importance in order to aid the clinician to make an appropriate investigation, differential diagnosis, and treatment. Turkey, situated at the intersection of Asia, Europe, and the Middle East, on the route of ancient Silk Road and in the Mediterranean region, has a unique geographical position and ethnic diversity. Therefore, the causes, characteristics, and course of uveitis in the Turkish population may differ from those of other populations, and these patterns may also change over the years. This study aimed to investigate the characteristics and causes of uveitis in patients presenting to a referral eye hospital in Turkey and to review the literature on the epidemiology of uveitis.

2. Materials and methods

Institutional review board and ethics committee approval was obtained prior to this study.

Clinical records of 1028 patients (1542 eyes) followed in the uveitis division of a referral eye hospital in Ankara, Turkey, between January 1990 and September 2010 with a minimum of a 6 months of follow-up were retrospectively reviewed. Patients diagnosed with endophthalmitis and scleritis were excluded. The data, including age at first presentation, sex, laterality, etiology, associated systemic disease, clinical presentation, course of the disease, and laboratory findings, were analyzed. Detailed ophthalmological examinations, including best corrected visual acuity, tonometry, slit-lamp biomicroscopy, and indirect ophthalmoscopy, were performed for each patient. Based on the clinical findings, laboratory and ancillary tests were performed when needed. Intraocular inflammation that was not associated with a specific underlying disease or ocular entity was termed as

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idiopathic uveitis. Anatomically, uveitis was classified as anterior, intermediate, posterior, and panuveitis according to the Standardization of Uveitis Nomenclature Working Group criteria (17). As suggested by that group, idiopathic intermediate uveitis accompanied by snowball and/or snowbank formation without any systemic disease or infection was classified as pars planitis. The diagnostic criteria of the International Study Group for Behçet's Disease were used for the diagnosis of Behçet's disease (BD) (18). Inflammation lasting less than 3 months was defined as acute uveitis, whereas inflammation lasting longer than 3 months was defined as chronic uveitis. Uveitis was classified as granulomatous if at least one of the findings of large mutton-fat keratic precipitates, iris nodules, optic disk, or choroidal granulomas was present. The study adhered to the tenets of the Declaration of Helsinki.

3. Results

The study included 598 (58.2%) male and 430 (41.8%) female patients. The mean age at presentation was 36.23 ± 14.9 (range: 1–83) years. Most of the patients (42.9%) presented between the ages of 20 and 40 years. The pediatric group (≤16 years) made up 8.7% and the elderly group (≥60 years) 7.6% of patients. The mean follow-up period was 51.0 ± 42.2 months.

Anatomically, anterior uveitis (42%) was most common, followed by posterior uveitis (24.9%), panuveitis (24.7%), and intermediate uveitis (8.4%). The inflammation was bilateral in half (50%) of the cases. The course of the disease was mostly chronic (65.7%) and nongranulomatous (85%). Infectious etiology was responsible for 14% of patients. Clinical characteristics of uveitis are summarized in Table 1.

Table 1. Clinical characteristics of uveitis compared with previous studies.

	No. of patients	% of total cases	% of previous studies (8,12,19)
Anatomic			
Anterior	432	42.0	29.6–60.6
Posterior	256	24.9	6.8–31.2
Panuveitis	254	24.7	9.4–41.5
Intermediate	86	8.4	6.1–17.6
Course			
Acute	353	34.3	32.8–83.4
Chronic	675	65.7	26.2–67.2
Laterality			
Unilateral	514	50.0	47–75.9
Bilateral	514	50.0	24.1–53
Type of inflammation			
Granulomatous	154	15.0	11–49
Nongranulomatous	874	85.0	51–89
Infectious vs. noninfectious			
Infectious	144	14.0	5.2–55
Noninfectious	884	86.0	45–94.8
Age at presentation			
≤16 years	90	8.7	7–16
20–40 years	441	42.9	46.4 (8)
≥60 years	78	7.6	7.3–10.4

In 264 of patients (25.7%), an underlying cause or a specific uveitic entity was not present, and the uveitis was considered idiopathic. The most commonly encountered systemic disease was BD, observed in 331 (32.2%) patients. Ocular toxoplasmosis (74 patients, 7.2%) and herpes (70 patients, 6.8%) were the second and third leading causes, respectively. Ocular toxoplasmosis was the most frequent reason for infectious uveitis. The etiological classification of our patients and some other epidemiological studies are listed in Table 2.

The etiologic distribution of uveitis differed according to anatomical location. Among 432 anterior uveitis cases, 31.5% were idiopathic. The 2 leading causes were herpes (15.5%) and Fuchs' uveitis (11.6%). Of the 86 intermediate uveitis patients, 63 (73.2%) were idiopathic. Of them, 31 (36.0%) patients were diagnosed with pars planitis with typical snowbank and/or snowball formations. The other most common causes of intermediate uveitis were BD (18.6%) and masquerading uveitis (6.9%). BD was the most common cause of both posterior uveitis (46.1%) and panuveitis (61.0%). Toxoplasmosis (27.0%) was the second foremost cause of the posterior segment inflammation. Of the panuveitis cases, 27.6% were idiopathic, constituting the second most common clinical diagnosis. The distribution of uveitis etiologies according to anatomical location is shown in Table 3.

4. Discussion

Epidemiological studies, giving extremely important clues about the commonly faced specific underlying causes, enable clinicians to better understand, diagnose, and treat uveitis (4,5,8,12). Furthermore, as in Japan, where the incidence and severity of ocular BD is decreasing, changes in environment and lifestyle may also lead to changes in incidence, prevalence, and causes of uveitis over time (11–13). Thus, updating the data on the epidemiology of uveitis would seem to be important for a population.

Uveitis affects mostly the 20–40-year-old working population (5,8,11,12). The mean age in our study was 36.23 ± 14.9 years and 42.9% of patients were in the 20–40-year group, in accordance with previous reports indicating that uveitis is most common in the third decade (7,10,12). Pediatric and elderly uveitis cases are less frequent and have been reported in 5%–16% and 6%–21.8% of patients, respectively (12). Our rates for pediatric (8.7%) and elderly (7.6%) uveitis were consistent with the literature.

There was a male predominance in our patient population with a rate of 58.2% versus 41.8% and a male-to-female ratio of 1.4:1. Most of the previous studies reported equal sex distribution (3,4,10,12,20,21). There are, however, studies stating a female (6,13,16,22) or male (9,23–25) predominance. Female predominance has been explained by the greater proportion of chronic disease

Table 2. Most common causes of uveitis (%) in our series and a summary of previously published series.

	Şengün (9) 2005	Rathinam (12) 2007	Goto (11) 2007	Khairallah (8) 2007	Kazokoğlu (10) 2008	Current study
Idiopathic	28.3	40.5	38.9	35.2	43.2	25.7
Behçet's disease	26	0.6	6.2	12.3	32.1	32.2
Toxoplasmosis	7.3	2.5	1.1	10.1	4.7	7.2
Herpetic uveitis	3.0	4.9	3.6	11.9	2.8	6.8
Fuchs' uveitis	2.7	4.8	0.5	3	5.1	5.0
HLA- B27 (+) uveitis	1.7	NA	1.5	NA	2.4	4.6
A. spondylitis/other spondylarthropathies	9.0	4.1	NA	3.8	2.1	4.7
Pars planitis	5.7	4.1	NA	NA	3.4	3.0
JIA[a]	1.7	0.2	0.5	0.6	1.0	0.9
VKH[b]	1	1.4	6.7	4.4	1.1	0.4
Other causes[c]	13.4	0.3	11.1	18.7	3.2	9.6

[a] JIA: Juvenile idiopathic arthritis.

[b] VKH: Vogt–Kayanagi–Harada syndrome.

[c] Other causes included multifocal choroiditis [11 patients (11.1%)], diabetic iritis [10 patients (10.1%)], serpiginous choroiditis [8 patients (8.1%)], tuberculosis [6 patients (6.1%)], toxocariasis [6 patients (6.1%)], traumatic iritis [6 patients (6.1%)], masquerading uveitis [6 patients (6.1%)], sarcoidosis [4 patients (4.0%)], familial Mediterranean fever [2 patients (2.0%)], and phacogenic uveitis [2 patients (2.0%)].

Table 3. Etiology of uveitis according to anatomical location.

Etiology of uveitis	%
Anterior uveitis	
Idiopathic uveitis	31.5
Herpetic uveitis	15.5
Fuchs' uveitis	11.6
Spondylarthropathies	11.1
HLA B27+ uveitis	10.9
Behçet's disease	9.7
Diabetic iritis	1.6
Traumatic iritis	1.4
JIA	1.2
Intermediate uveitis	
Idiopathic uveitis[a]	73.2
Behçet's disease	18.6
Masquerading uveitis	6.0
Herpetic uveitis	1.1
Tuberculosis	1.1
Posterior uveitis	
Behçet's disease	46.1
Toxoplasmosis	27.0
Idiopathic uveitis	10.2
Multifocal choroiditis	5.1
Toxocariasis	2.1
Serpiginous choroiditis	1.7
Panuveitis	
Behçet's disease	61.0
Idiopathic uveitis	27.6
Tuberculosis	4.6
JIA	1.6
Vogt–Koyanagi–Harada	1.5
Toxoplasmosis	1.2

[a] Including pars planitis, which constitutes 31% of total intermediate uveitis cases.

in women (6). Rathinam and Namperumalsamy (12) emphasized no sex predilection of uveitis in the developed world, in contrast to the male predominance in developing countries. They stated that certain socioeconomic habits put males at greater risk for certain types of uveitis. Consul et al. (26) suggested that men tend to seek medical attention more often than women in agricultural societies, and this might explain the reported male predominance. BD is the leading cause of uveitis in series from Turkey (9,19), Saudi Arabia (27), Israel (4), China (7,28), Iran (29), and Japan (13). BD cases constituted nearly one-third of our patient population and there was a 3-fold male predilection in this subgroup, accounting for nearly 20% of the whole population. In the study by Şengün et al. (9) from Turkey, BD was also the leading cause of uveitis (26%) and the male-to-female ratio was 1.17:1. We think that the reason for the male predominance in our series is the male predilection of BD.

The course of the uveitis was chronic in most (65.7%) of the patients. This might be related with the referral pattern of our patients and also the high frequency of BD. As reported previously, acute uveitis tends to predominate in community-based studies, whereas chronic uveitis tends to be more common in tertiary referral practices (12,23).

As stated before, BD was the leading cause of uveitis, accounting for 32.2% of our cases. This rate is similar to that of a multicenter study from Turkey reporting BD in 32.1% of their cases (10). BD was mostly encountered in countries located on the ancient Silk Road, and in the Mediterranean and Middle East regions (30). The reasons for the higher frequency in these countries are various, including genetic, geographical, environmental, and social factors (31). Alterations of these factors may result in changes in uveitis patterns, as reported by Wakabayashi et al. (13) and Goto et al. (11). They stated a decrease in the frequency of BD in Japan compared to previous epidemiological studies. Of the 3 most common causes of uveitis in Japan, the prevalence of sarcoidosis and Vogt–Koyanagi–Harada (VKH) syndrome remained stable over the past few decades, whereas BD has steadily decreased due to unclear presumptive factors. Although the study period covered both the 1990s and 2000s, almost 80% of the data were obtained from patients presenting during the 2000s, due to lost follow-up or medical records. For that reason, we could not compare patients who presented in the 1990s and 2000s. Behçet's uveitis presents mostly in the form of posterior uveitis or panuveitis, and isolated anterior or intermediate uveitis is rare (32). Consistently, the disease was the leading cause of posterior uveitis (46.1%) and panuveitis (61.0%), and a less common cause of anterior uveitis (9.7%) in our study. Patients presenting with vitritis only, without any accompanying anterior or posterior segment involvement and angiographic leakage,

were considered to have intermediate uveitis. These cases made up 18.6% of all intermediate uveitis. BD was found to be the leading cause of panuveitis in different studies performed in China, Tunisia, and Turkey (7–9). Similar to our study, Kazokoglu et al. (10) found BD to be the most frequently associated systemic disease in both posterior uveitis and panuveitis. On the other hand, toxoplasmosis, observed in 7.2% of our patients, was the leading cause of posterior segment inflammation in most of the epidemiological studies (3,7–9,12). It was the second most common cause of posterior uveitis, with a rate of 27%, and the leading cause of infectious uveitis in our series. The disease is especially more prevalent in South America and Africa due to poor hygienic and dietary habits (25,33). The consumption of a popular Turkish meal made with raw meat might be an important factor for the high frequency of toxoplasmosis in Turkey.

Anterior uveitis was the most frequent (42%) anatomical type of uveitis in our study, which is compatible with other studies (7–10,22,23,31). About one-third (31.5%) of anterior uveitis cases were idiopathic, followed by herpetic infections (15.5%), Fuchs' uveitis (11.6%), spondylarthropathies (11.1%), and HLA-B27–associated uveitis (10.9%). The striking result for anterior uveitis in our study is the high proportion of herpetic uveitis and the relatively low frequency of spondylarthropathies, reported as the most common cause of anterior uveitis in different studies (9,22,27,34). In previous epidemiologic studies, the frequency of herpetic uveitis varied between 3.2% and 24.4% (9,10,12,13,23,35,36) and made up 1%–33.7% (8,31) of anterior uveitis cases. In concordance with these reports, herpetic uveitis made up 6.8% of our cases and anterior uveitis 15.5%. As in ours, herpetic uveitis was the most prevalent specific cause of anterior uveitis with a rate of 33.7% in Khairallah et al.'s series (8). The discrepancy among the results might be related to the referral or community-based designs of the studies and geographical differences. As the diagnosis is mostly clinical for herpetic uveitis, characteristic findings such as patchy iris atrophy, high intraocular pressure, and keratitis should be closely looked for, and the diagnosis should be confirmed with polymerase chain reaction of humor aqueous in suspected cases. Similarly, the diagnosis of Fuchs' uveitis, which is the second most common cause of anterior uveitis, is based on clinical findings and does not need laboratory confirmation. However, the rate of misdiagnosis is very high for this specific uveitic entity. Data from a tertiary referral center showed that a correct diagnosis had been made in only 8.7% of referral cases and the correct diagnosis could be made in almost 90% of these patients with clinical findings only (37). Thus, compared to the community-based studies, higher frequencies of Fuchs' uveitis are expected from referral centers. Fuchs' uveitis accounted for 5% of our cases, which is similar to the rate of a previous multicenter study from Turkey (10).

Posterior uveitis (24.9%) and panuveitis (24.7%) were the second and third most frequent anatomical types of uveitis, which is not surprising with the high incidence of BD in Turkey. Posterior uveitis has been reported to occur in 6.8%–31.2% and panuveitis in 9.4%–41.5% of patients depending on the country where the study was performed (19). The highest rates are from Japan (13) and China (7), where VKH, BD, and sarcoidosis are frequent.

Similar to previous reports, intermediate uveitis was the least common (8.4%) anatomical type of uveitis and constituted mainly idiopathic cases, including pars planitis (2,7–10,12,13,36).

Increased knowledge of uveitis epidemiology over the past decade and improved diagnostic techniques have helped to better classify certain forms of uveitis. Thus, the frequency of idiopathic cases has significantly decreased. Previous surveys have suggested that the cause of uveitis remains unknown in 28%–45% of patients (8–11,13). Uveitis was idiopathic in only 25.7% of our patients. This relatively low rate might be explained by the fact that the patients were seen in a subspecialty referral practice. Our long follow-up period (51.0 ± 42.2 months) might be another reason for this low frequency of idiopathic cases and the relatively high frequency of BD. Although presenting with ocular findings highly suggestive of BD, some of patients did not fulfill the criteria of the International Study Group for Behçet's Disease at presentation and the definitive diagnosis could be made only during the follow-up period. In general, anterior and intermediate uveitis are more often idiopathic than posterior or diffuse forms of the disease (12). Accordingly, in our series, inflammation was mostly idiopathic in anterior (31.5%) and intermediate (73.2%) uveitis.

In conclusion, the frequency, causes, and clinical characteristics of uveitis are influenced by several factors including genetic, socioeconomic, geographic, and meteorological factors. Because of the ongoing changes in uveitis epidemiology, it is important for ophthalmologists to be aware of the incidence of uveitis subtypes in their geographical area to best serve the needs of the population. Current data representing etiological and clinical features of uveitis in a referral hospital showed that BD is still the most common systemic association of uveitis and that idiopathic uveitis is less common in the Turkish population. Specific uveitic entities, such as Fuchs' uveitis and HLA-B27–associated uveitis, and infectious uveitis, such as toxoplasmosis and herpetic uveitis, are other common causes of uveitis. Uveitis mostly affects the male population aged between 20 and 40 years, and anterior uveitis is the most common anatomical location of the disease.

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