

Epidemiology and Prevalence of Uveitis: Review of Literature

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Abstract

Purpose: To review epidemiological aspects of uveitis in Asia and compare it with few major reports from outside of this continent

Methods: We have reviewed 522 articles concerning the causes and patterns of uveitis and 22 major epidemiology reviews, registered from 1962 to 2009 in Medline-Database. We have selected 7 major reviews from Asia and compared it with five major articles from Africa, France, East and West USA and Argentina. We have also used 59 reviews and reports to show some local and regional aspects of uveitis in developed and underdeveloped countries and to indicate the changes in trends of uveitis in recent years.

Results: In these collected data from 12 countries, 14.0% to 51.2% no cause has been found for the uveitis (idiopathic). In almost all these reports noninfectious uveitis (45.0% to 94.8%) dominated the infectious causes. Infectious uveitis such as tuberculosis, leptospirosis ... are present more frequently in the developing countries with exception of herpes simplex which is dominated in the western world. Toxoplasmosis remains the predominant etiology of posterior uveitis in most reports, excluding cytomegalovirus (CMV) retinopathy which has dominated all causes of posterior uveitis during the last 30 years due to the global extension of AIDS.

Conclusion: Despite all the new progresses in laboratory techniques, imaging technology and finding new causes for uveitis such as HTLV1 and HLA dependent diseases, the number of uveitis with unknown etiology (idiopathic) is increasing. That could indicate the uprise of new immunological phenomena. The prevalence of uveitis which was estimated to be around 17.4 per 100,000 population in 1960's, in a more recent investigation has been reported to be 52.4 per 100,000 people and the incidence seems upraising.

Keywords: Epidemiology, Uveitis, Global Variation

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Introduction

Uveitis as an inflammatory disease of inner eyeball can be found all over the world.¹ According to previous studies, performed in the last decades, the prevalence of uveitis was estimated to be 17.5 to 22 per 100,000 population,²⁻⁸ however in recent reports, its prevalence is increased up to three times.⁹ The upward trend might be due to more accurate and controlled studies performed recently; indeed, more incidence of new immunologic diseases also lead to an increase in prevalence of uveitis. In addition, much more spread of new laboratorial techniques are used in our investigations. However, the number of patients with the complaint of primary uveitis (Idiopathic) becomes more, not less.¹⁰⁻¹²

Uveitis can be presented in patients following a huge spectrum of diseases. Genetic, infectious, environmental, systemic and immunologic diseases are some of the predisposing factors their association with uveitis has been proven. Infectious diseases such as leprosy,¹³ leptospirosis¹⁴ or onchocerciasis¹⁵ are found most likely in underdeveloped countries, thereby, the infection related uveitis is estimated to be more prevalent in such regions. There are also some specific HLA dependent inflammatory diseases which can lead to uveitis; Behçet's disease^{16,17} (a HLA-B51 associated disease), acute anterior uveitis (AAU) (a HLA-B27 associated disease)^{18,19} and also Birdshot (a disease which is in association with HLA-A29) are some of the HLA dependent diseases their predisposing role in leading to uveitis has been verified.²⁰ Besides, in the past three decades some new diseases like AIDS and cytomegalovirus (CMV) infection were presented as the major cause of uveitis in underdeveloped and also developed countries.²¹⁻²⁴

Epidemiologic studies conducted through recruitment of great number of patients not only can present the condition of the whole population in a more reliable way, but also the obtained results can be applied in health policies of treatment and prevention of uveitis.

The authors of this manuscript have intended to review the accomplished epidemiologic studies in the matter of uveitis to note and categorize the predisposing factors of this inflammatory disease.

Methods

In this vast study, 522 articles concerning the causes, patterns of uveitis and 22 major articles on epidemiology of uveitis in the world, from 1962 to 2009 in Medline Database have been reviewed. We have selected 7 major epidemiological presentations from Asia and five from Africa, Europe, East and West USA, and one from Argentina. We have used 59 other publications concerning local and regional causes of uveitis in different ages, ethnics, and the prevalence of this affection. In this regard, we tried to use from new and more reliable studies. Although some subtypes of uveitis were not evaluated in 12 major preferred studies, in the present study, we also reviewed the unmentioned above aspects of uveitis such as senile and pediatric uveitis, and also some special diseases like onchocerciasis.

In most of studies carried out in the matter of uveitis, only the idiopathic type of disease is reported in a poor way of evaluation; therefore, the results of these uncontrolled and less generalizable studies were not included in findings respecting the epidemiology of idiopathic uveitis debated in the present study. As it is demonstrated in tables 1 and 2, only rare causes of uveitis were not mentioned in our study.

Table 1. Characteristics of patients and etiology of uveitis from 12 referral centers

First author	Wakabayashi	Yang	Singh	Rathinam	Soheilian	Islam	Kazokoglu	Khairallah	Bodaghi	Rodriguez	McCannel	Couto
Reference	62	63	64	37	65	12	66	67	59	58	24	68
Published	2003	2005	2004	2007	2004	2002	2008	2007	2001	1996	1996	1993
Country	Japan	China	North India	South India	Iran	Saudi	Turkey	Tunisia	France	USA	USA	Argentina
City	Tokyo	Zhongshay	Chandigarh	Madurai	Tehran	Riyadh		Monaster	Paris	Massachussets	Los Angeles	Buenos Aires
Years of Study	1999-2001	1996-2003	1996-2001	1996-2001	1997-2001	1995-2000	2004	1992-2003	1991-1996	1982-1992	1996	1986-1991
Number	189	1752	1233	8759	544	200	761	472	927	1237	213	311
Male/Female	0.82/1	1.06/1	1.08/1	1.6/1	1/1.27	1.5/1	1.04/1	1/1.1	1/1.05	1/1.4	1.01/1	1/1.27
Mean-age	45	34	33	36.5	32	35	35.5	32	37	37	45	NS
Ant.Uveitis %	29.6	45.6	49.2	57.4	38.4	59.5	52.5	35.2	28.5	51.6	60.6	34.4
Intermed. Uveitis %	6.9	6.1	16.1	9.5	17.6	6.5	6.7	15.5	15	13	12.2	9
Post.Uveitis %	31.2	6.8	20.2	10.6	18.6	13.5	12.7	28.2	21.6	19.4	14.6	19.3
Panuveitis %	30.7	41.5	14.7	22.4	25.4	20.5	28.2	21.2	35	16	9.4	37.3
Infectious N %	21 (19.3)	50 (5.2)	179 (29.7)	2670 (55.0)	90 (30.6)	NS	64 (14.8)	137 (44.8)	297 (48.5)	209 (26)	44 (35.8)	127 (47.7)
Noninfectious N %	88 (80.7)	917 (94.8)	423 (70.3)	2180 (45.0)	204 (69.4)	NS	368 (85.2)	169 (55.2)	315 (51.5)	596 (74)	79 (64.2)	137 (52.3)
Unknown etiology	80 (42.3)	785 (44.8)	631 (51.2)	3909 (44.6)	250 (45.5)	28 (14.0)	329 (43.2)	166 (35.2)	315 (34)	432 (34.9)	90 (42.2)	47 (15.1)

NS: Not stated, Ant.: Anterior, Intermed.: Intermediate, Post.: Posterior

Table 2. Epidemiology of uveitis from 12 referral centers

First author	Wakabayashi	Yang	Singh	Rathinam	Soheilian	Islam	Kazokoglu	Khairallah	Bodaghi	Rodriguez	McCannel	Couto
Reference	62	63	64	37	65	12	66	67	59	58	24	68
Published	2003	2005	2004	2007	2004	2002	2008	2007	2001	1996	1996	1993
Country	Japan	China	North India	South India	Iran	Saudi	Turkey	Tunisia	France	West USA	East USA	Argentina
Known etiology N %	109 (57.7)	967 (55.2)	602 (48.8)	4850 (55.4)	294 (54.5)	172 (86)	432 (56.8)	306 (64.8)	612 (66)	805 (65.1)	123 (57.8)	264 (84.9)
Leptospirosis	NS	NS	NS	850 (17.5)	NS	NS	NS	NS	NS	NS	NS	NS
Tuberculosis	3 (2.7)	13 (1.3)	125 (20.8)	488 (10.1)	8 (2.7)	21 (12.2)	3 (0.7)	5 (1.6)	38 (6.2)	8 (1.0)	NS	18 (6.8)
Toxoplasmosis	7 (6.4)	2 (0.2)	21 (3.5)	219 (4.5)	55 (18.4)	13 (7.6)	36 (8.3)	51 (16.6)	110 (17.9)	59 (7.3)	11 (8.9)	63 (23.9)
Herpes family	3 (2.7)	26 (2.7)	19 (3.2)	541 (11.1)	8 (2.7)	32 (18.6)	30 (6.9)	61 (19.7)	96 (15.7)	90 (11.2)	30 (24.4)	23 (8.7)
Syphilis	NS	NS	3 (0.5)	NS	NS	NS	1 (0.2)	3 (0.98)	6 (0.98)	21 (2.6)	1 (0.8)	3 (1.1)
Trematode	NS	NS	NS	218 (4.5)	NS	NS	NS	NS	NS	NS	NS	NS
HLA-27 & Rheumatoid	12 (11.0)	136 (14.3)	88 (14.6)	NS	14 (4.8)	61 (35.5)	19 (4.4)	5 (1.6)	46 (7.5)	247 (30.7)	23 (18.7)	NS
JIA, JRA	NS	NCS	20 (3.3)	14 (0.3)	10 (3.4)	NS	8 (1.8)	3 (0.98)	25 (4.1)	59 (7.3)	5 (4.1)	2 (0.7)
Sarcoidosis	18 (16.5)	3 (0.3)	56 (9.3)	351 (7.3)	19 (6.5)	6 (3.5)	7 (1.6)	8 (2.6)	59 (99.6)	119 (14.8)	1 (0.8)	3 (1.1)
BD	11 (10.1)	289 (29.9)	23 (3.8)	50 (1.0)	47 (15.9)	13 (7.6)	245 (56.7)	58 (18.9)	57 (9.3)	31 (3.8)	2 (1.6)	6 (2.3)
VKH	19 (17.4)	278 (28.7)	44 (7.3)	124 (2.4)	21 (7.1)	5 (2.9)	9 (2.1)	21 (6.8)	19 (3.1)	11 (1.4)	5 (4.1)	44 (16.7)
Fuchs'	1 (0.9)	100 (10.3)	31 (5.1)	423 (8.3)	36 (12.2)	7 (4.1)	39 (9.0)	14 (4.6)	25 (4.1)	NS	4 (3.2)	8 (3.0)
Birdshot	NS	NS	NS	NS	1 (0.34)	NS	1 (0.2)	1 (0.3)	41 (6.7)	NS	2 (1.6)	3 (1.1)
Serpiginous	2 (1.8)	NS	62 (10.3)	102 (2.0)	4 (1.4)	NS	3 (0.7)	7 (2.3)	NS	NS	1 (0.8)	1 (0.37)
Sympathetic	4 (3.7)	28 (2.9)	26 (4.3)	67 (1.4)	7 (2.4)	NS	1 (0.21)	5 (1.6)	11 (1.8)	NS	1 (0.8)	1 (0.37)
AS	NS	57 (5.9)	88 (14.6)	358 (7.4)	11 (3.7)	3 (1.7)	11 (2.5)	8 (2.6)	46 (7.5)	47 (5.8)	NS	11 (4.2)

AS: Ankylosing spondylitis, NCS: Not clearly stated, JIA: Juvenile idiopathic arthritis, BD: Behçet's disease, VKH: Vogt Koyanagi Harada, Sympathetic: Sympathetic ophthalmia, 0: Absent or not mentioned

Epidemiology of uveitis in the world and history of its detection

Uveitis is the inflammatory disease of inner eyeball, which can be categorized according to the site of involvement in following 4 groups: 1) Uveitis which involves the anterior part of eye (Anterior uveitis), 2) Uveitis which involves the mid part of eye and vitreous body (Intermediate uveitis), 3) Uveitis which presents with involvement of posterior part of eye which consist of retina, choroid, retinal and choroid vessels and also optic nerve (posterior uveitis), and finally 4) Uveitis which presents with involvement of the whole eyeball (Panuveitis).

Uveitis is found all over the world with different etiologies including infections, systemic diseases, trauma, immunologic diseases, drugs and cancers. Meeting the possible etiologies and epidemiologic findings of uveitis were mostly occurred in the recent half of the last century, and these successes might be due to the development of laboratory technologies used in diagnosis of uveitis, like PCR.²⁵ The inflammatory ocular complications following AIDS²¹ and Human T lymphotropic virus 1 (HTLV1) disease²⁶ are two particular prevalent clinical problems leading to uveitis that their association with uveitis has been verified.

Generally, in the first half of the twentieth century, regarding the causes of uveitis, there were limited findings, and no etiology was found for most of the patients. Haut et al²⁷ performed an epidemiologic study in 6th decades of the twentieth century; according to their report, of 850 patients with uveitis only 32% had positive diagnostic criteria; involvement of teeth, sinuses of head and face and also local infections were considered as possible causes and diagnostic criteria of uveitis in the mentioned study. Noting another study performed by Ducass et al,²⁸ uveitis in 27 of 200 patients was associated to the above criteria described previously by Haut et al.²⁷ According to the aforementioned criteria, Vassileva et al²⁹ found involvement of teeth and local infections as the causes of Uveitis in 18.5% and 10.2% of 315 recruited patients, respectively.

In addition, in the past three decades, respecting the lack of reliable epidemiologic data from the underdeveloped countries, finding the prevalence and distribution of

uveitis in the world was impossible and most studies were executed in developed countries and referral centers.

Distribution of endemic diseases in the world implies that endemic diseases are found mostly in underdeveloped countries. Some of these diseases have been advocated as the etiology of uveitis in recent reports. Following described diseases are some of them:

Onchocerciasis is prevalent in central Africa and Latin America. Blindness is one of the major complications of this disease even though it is preventable. According to WHO reports, among the diseases leading to preventable blindness, onchocerciasis presents the highest rate of prevalence.¹⁵ In north of Nigeria³⁰ its prevalence among adults older than 20 years is estimated to be 72%. This disease is also reported from western Africa, Mexico, Ecuador, Colombia, Venezuela and Yemen.³¹⁻³⁴

HTLV-1 which can be followed by intermediate uveitis has been reported from all over the world, however recommended as the cause of an endemic disease in Japan.²⁶ The disease is also reported from Martinique³⁵ and Brazil.³⁶

Leptospirosis as the most prevalent febrile disease in the world was reported as cause of uveitis in 73 patients (106 eyes) in south of India. According to study performed by Rathinam et al¹⁴ 95.5% of stricken eyes had panuveitis, 51.4% had periphlebitis and 12.6% of eyes had hypopyon. In another study conducted by Rathinam et al³⁷ among 8759 patients with uveitis in south of India, leptospirosis was found as the cause of uveitis in 9.7% of the patients. According to the reports of the same author³⁸ Spirochetes via degeneration of endothelial cells of vessels, can bring about pulmonary vessel involvement, pericarditis and nephritis; uveitis is one of the late complications of this aggressive procedure. Hemorrhage of eye and icterus due to leptospirosis (ictero-hemorrhagic leptospirosis) has been reported from Vietnam,³⁹ Korea⁴⁰ and Brazil.⁴¹

The cause of Rift valley fever (RVF) which is followed by fever, sometimes meningoencephalitis and even death is a kind of Phlebovirus. The transmission of the disease to human is proven to be through

domestic animals. Rift valley fever is found as an endemic disease in Africa and the peak incidence of the disease occurs after heavy raining.⁴²

Of total 15-16 million people registered with Leprosy, 10% were became blind. According to the health policies applied by WHO,¹³ the trend of leprosy prevalence is decreasing in the world. Regarding an epidemiologic study conducted in 1980 in Baba Baghi village and its surroundings, western Azarbayejan, Iran, of 326 patients with the history of leprosy, 21.8% had active uveitis and 61.1% had active or inactive uveitis.

A new kind of uveitis disease has been reported among children with an average age of 11 years old in southern India. This sort of uveitis was estimated to be associated with trematode infection. Patient presented with anterior uveitis and granulomatous nodules in anterior chamber of the eyeball.⁴³ Of 417 children with uveitis who were recruited in the study, 113 patients developed this new kind of uveitis.

AIDS as a pandemic disease in last three decades is observed in 33 million people all over the world.²² AIDS is another cause of uveitis; 30% to 70% of patients with AIDS have eyeball involvement as a complication of the disease. According to the study carried out in Netherlands,²¹ 20 to 25 percent of these patients would get CMV retinopathy. In recent years, CMV and AIDS were entitled as the major causes of posterior uveitis based on published reports by some referral centers of uveitis, and research centers in industrial countries. Regarding recent epidemiologic findings, the leading cause of posterior uveitis in patients with AIDS was CMV which included 31 to 77 percent of cases^{23,24}; hence, many researchers have omitted CMV infection from the inclusion criteria of the probable causes of uveitis to avoid the bias on prevalence of etiologies of uveitis. Although the new expensive drugs prescribed as the treatment of AIDS is not affordable for about 90% of patients, new treatment methods development like HAART (Highly active anti retroviral therapy) has decreased the rate of eyeball complication occurrence for up to 15 times.^{44,45} It should be mentioned that due to the application of HAART on the patients with AIDS, some new kinds of uveitis like immune recovery uveitis has been displayed.⁴⁶

Although most of aforementioned endemic diseases are seen in developing countries, even countries in North American are not completely immune.

Lyme disease (Lyme-Borreliosis), which mostly is caused by *Borrelia Burgdorferi* (a kind of spirochete), is reported as a prevalent disease in United States. The transmission of the disease is by Ixodes ticks. The rate of prevalence of this disease is 1247.5 individuals per 100,000 people in the state of Massachusetts,⁴⁷ and uveitis is one of the possible complications of this disease.

Histoplasmosis (probably is resulted in by a mycosis named *Histoplasma Capsulatum*), as another disease which can induce uveitis is characterized by macular and peripheral retinal scars. The prevalence of this disease is 1.6% and 2.6% in population in the state of Ohio⁴⁸ and Maryland,⁴⁹ respectively.

Risk factors of uveitis

Following factors affect the incidence and prevalence of ocular inflammatory diseases (Uveitis):

- **Age**
 - **Children**

Particularly in developed countries, systemic diseases are an important cause of uveitis⁵⁰ among children younger than 16 years. The most prevalent systemic disease in this age group which can be followed by uveitis is idiopathic juvenile rheumatoid arthritis (JRA). JRA is the cause of 30 to 40 percent of uveitis incidence among children in developed countries.⁵¹ In developing countries infectious and parasitic diseases are mostly declared as the cause of uveitis in children. For example in south of India trematode⁴³ is a common cause of uveitis in children. Benezra et al⁵² reported parasitic infections as the leading cause of uveitis in children and teenagers.
 - **Senile**

In people over 60 years, sarcoidosis, spondyloarthropathies and herpes infection^{37,53} are the common causes of uveitis. According to the study conducted by chatzistefanou et al⁵⁴ between 1978 and 1992 in Massachusetts Eye and Ear Infirmary

(MEEI) in United States, in 10.4% (n=138) of patients recruited in the study, uveitis was diagnosed for the first time after the age of 60. 56.5% of the mentioned elderly patients had anterior uveitis, 1.4% and 25.4% had intermediate and posterior uveitis respectively, and finally panuveitis was diagnosed in 16.7% of those elderly patients. Primary (Idiopathic) uveitis was observed in 31.2% of the total number of patients in the mentioned study. Herpes infection was found as the cause of uveitis in 18.1% of the patients. Sarcoidosis and syphilis were reported as the 5.8% and 4.3% of the leading cause of uveitis respectively. In addition, spondyloarthropathy and birdshot disease were found as the cause of uveitis in 4.3% and 3.6% of the patients, correspondingly.

- **Race**

In black people, sarcoidosis associated uveitis is more prevalent than whites. Merrill et al⁵⁵ who investigated the prevalence of different kinds of uveitis among blacks and whites, finally reported sarcoidosis and primary panuveitis as the more prevalent diseases among black people in comparison to whites.

- **Environmental factors**

Environment and lifestyle are two important factors affect the incidence of eye inflammatory diseases. Toxoplasmosis as one of the most common cause of posterior uveitis in the world is more prevalent among people who have contact with domestic animals⁵⁶ mostly in humid regions and also the places there are animal husbandries.⁵⁶ Besides, according to the evidence obtained from the study established in Brazil, 17.7% of total 1042 evaluated individuals had eye involved toxoplasmosis.⁵⁶ In the mentioned study the prevalence of toxoplasmosis was reported to be 30 times greater than previous reports.

- **Genetic factors**

HLA related diseases, particularly the diseases with proven association with HLA-B27 like AAU more often occurs in young people^{18,19} and constitute the major role of

involvement of genetic factors in incidence of uveitis. In spite of HLA-B27 antigen registration in 55% of white people with AAU, this antigen was reported to be present in only 8 to 10 percent of the healthy people of the same society.¹⁸ According to published reports the prevalence of mentioned antigen in population of Nigeria and South Africa is low, following the low prevalence of the AAU in these regions.⁵⁷ In addition, HLA-A29 is found in 70 to 90 percent of patients with birdshot disease,²⁰ The role of HLA-B51 in more prevalence of some inflammatory diseases along the Silk Road including Far East, Middle East and around Mediterranean Sea has been approved.^{16,17}

Prevalence of Uveitis

In most kind of uveitis specially anterior uveitis which would be followed by one or two recurrences during the course of disease, the ophthalmologists are not interested in looking for the cause of the disease. Rodriguez et al⁵⁸ in a study performed in MEEI showed that, finding the obvious diagnosis in the first visit could be obtained in only 17% of patients. Regarding the abovementioned study, after repeated follow-ups and complementary experiments, obvious diagnosis can be achieved in 65% of patients. Most of the existed evidences in the matter of epidemiology of uveitis have been reported from the referral centers of uveitis (tertiary centers). Consequently, we find mostly chronic and complicated cases in these kinds of reports⁵⁹ presenting different algorithm of the prevalence and severity of uveitis in the general population. As stated in an interdisciplinary study performed by researchers in UCLA,²⁴ 213 patients with uveitis who were admitted in Jules Stein Eye Institute were compared with 213 admitted patients in Los Angeles eye clinics in the matter of prevalence of different types of uveitis; according to the published findings of this study, the epidemiologic results achieved in two mentioned groups were totally different and the comparison between them, showed the following significant relations; In non-referral centers, anterior uveitis was diagnosed in 90.6% of the patients with uveitis and posterior, intermediate and panuveitis were diagnosed in 4.7, 1.4 and 1.4 percent of

the mentioned patients. However, in referral health center of UCLA, 60.6% of the patients had anterior Uveitis, 12.2% of the patients had intermediate uveitis, and posterior uveitis and panuveitis were reported in 14.6% and 9.4% of patients respectively. In this study, the difference of prevalence of variable types of uveitis between the referral and non-referral centers was significant $P \leq 0.001$. In spite of the finding which in both groups HLA-B27 related uveitis and toxoplasmosis were the most common causes of uveitis, however in non-referral clinics, cause of uveitis was found in 47.4% of all the cases recruited in the study versus 57.8% of the patients with determined cause of uveitis in UCLA hospital. This difference was statistically significant ($P \leq 0.03$). Generally, there are a few epidemiologic studies performed in large areas concerning uveitis disease. In an evaluation accomplished by Darrel et al² in Olmsted County, Minnesota, during 1945 to 1955, incidence of uveitis was reported to be 17.4 per 100,000 people and according to conducted study by Saari et al³ in Finland, the incidence of uveitis was found to be 22.6 in each 100,000 individuals of population. In other reports from United States and Europe, incidence of uveitis was estimated in a range between two mentioned reports.⁴⁻⁸ Cumulative distribution of uveitis in these studies was reported to be from 38 to 370 in 100,000 individuals. In a study conducted by Gritz et al⁹ during 1998 to 1999 in 6 health centers placed in north of California, the incidence of uveitis was found to be 52.4 per 100,000 people. This result is three times greater than the previous published data. Gritz et al⁹ also found a more cumulative distribution regarding uveitis (115.3 per 100,000 people). According to the evidences obtained by Reeves et al⁶⁰ via evaluation of US health insurance system, among 21,644 patients -all older than 65 years with diagnosis of uveitis for the first time - cumulative distribution of uveitis was 340.9 in 100,000 individuals. 243.6, 76.6, and 41.7 of 100,000 persons had anterior Uveitis, posterior Uveitis, and panuveitis respectively, and 2 cases demonstrated with intermediate Uveitis in each 100,000 persons. By the study carried out to find out the prevalence of uveitis among children in Finland,⁶¹ it was shown that 4 of each 100,000 persons have uveitis and

the cumulative distribution was estimated to be 28 in 100,000.

Epidemiology of uveitis

The present report is based on evaluation of almost new epidemiologic studies from 12 important uveitis centers (Tables 1, 2) in Asia, Africa, Europe and America.^{12,24,37,58-59,62-68}

From the mentioned reports following information are achieved:

Uveitis has an equal distribution between male and females, excluding few exceptions. In the study performed in MEEI,⁵⁸ due to the higher incidence of arthropathies among women, majority of recruited patients were female (m/f=1/1.4). In the conducted study in south of India³⁷ the ratio of males to females was 1.6/1 which might be related to the more prevalence of leptospirosis among people involved in agriculture and agronomy. Moreover, according to published data from Saudi Arabia¹² the ratio of males to females was 1.5/1 which could be related to lack of public jobs for women in that country.

Mean age of incidence of uveitis in 12 mentioned studies was reported from 32 up to 45 years. Regarding the reports by Rathinam et al,³⁷ 60 to 80 percent of patients with uveitis were between 30 to 60 years old. Their study performed based on collected data from 25 centers with 23,980 recruited patients, 5 to 16 percent of patients were under 16 years old, and 6 to 21.8 percent of patients had over 60 years of age.

Using the data in all 12 studies, anterior uveitis was reported in a range of 28.5% to 60.6% of patients in variable studies (Table 1). In the study ran in UCLA, United States, 60.6% of the patients had anterior uveitis; this rate of anterior uveitis might be related to the high prevalence of HLA-B27 and its related diseases which were observed in 18.7% of patients with known etiology (Table 2). In Saudi Arabia 59.5% of the patients had anterior uveitis with probable relation with the high prevalence of HLA-B27 related diseases (35.5%) and herpes infections (18.6%).

Intermediate uveitis was observed in 6.7% to 16.1% of patients with uveitis. In this matter the highest rate was reported from north of India which might be related to the high prevalence of tuberculosis in that area. Tuberculosis was found as the cause of

uveitis in 20.8% of patients with non-Idiopathic uveitis.

Posterior uveitis was reported in a range of 6.8% to 31.2% of the whole patients with uveitis in all mentioned studies. In Japan, the posterior uveitis was found in 31.2% of the patients, which might be due to the high prevalence of some special diseases in that region. In this matter, Vogt-Koyanagi-Harada⁶² (VKH) was found as the cause of 17.4% of cases with uveitis, sarcoidosis in 16.5% of the patients, and Behçet's disease and toxoplasmosis in 10.1% and 6.4% of the patients, respectively.

The results achieved from the different 12 major centers demonstrated that prevalence of panuveitis was variable from 9.4% to 41.5% of the patients. The highest prevalence of panuveitis was reported from China (41.5%). This finding could be related to the high incidence of Behçet's disease and VKH in China.⁶³

Although infectious diseases were found as the cause of uveitis in 5.2% of patients in developed countries, however, in south of India infectious disease had been led to uveitis in 55% of patients. In this region, appraisal of all patients with a known etiology of disease (non-idiopathic uveitis) shown leptospirosis in 17.5% of patients, tuberculosis in 10.1% of patient, and herpes and trematode in 11.1% and 4.5% of patients were found as the particular causes of uveitis.³⁷

Non-infectious diseases were recommended as the cause of uveitis in 45 to 94.5 percent of patients in the different previously mentioned 12 studies. In this way, the highest rate of uveitis with the etiology of non-infectious disease was reported from China (94.5%).⁶³ In China, of 1,752 patients, 432 patients had AAU which seems to be in association with high rate of rheumatic disease in that area. Respecting the evaluation performed on 253 patients with AAU, positive HLA-B27 antigen was reported in 251 patients.⁶³

Toxoplasmosis not only is known as one of the most prevalent diseases in the world but also is one of the common causes of posterior uveitis.⁵⁶ Due to the importance of nutritional condition, environment and lifestyle in the distribution of different types of uveitis, toxoplasmosis is known as the cause of uveitis in 0.2% of patients in China,⁶³ and

3.5% and 4.5% of patients in north⁶⁴ and south of India,³⁷ respectively.

It should be mentioned that in recent years CMV-AIDS is found as the most common cause of posterior uveitis^{23,24} and in the study carried out in UCLA,²⁴ 103 patients of all 326 recruited patients had CMV who were omitted from the report to impede the probable disturbances in statistical analysis of the data.

Finding tuberculosis as one of the known etiologies of uveitis (20.8% of cases with uveitis),⁶⁴ and serpiginous disease as the etiology of 10.3% of the patients with uveitis in north of India, the probable existence of tuberculosis source in the north of India is suggested. Although tuberculosis infection was also reported in south of India as the possible cause of uveitis in 10.1% of patients with non-idiopathic disease, however in studies performed in other parts of the world, tuberculosis infection is rarely reported as the cause of uveitis.

Although herpes infections and herpetic diseases were found as the known cause of uveitis in 24.4%, 18.6% and 15.7% of patients in the studies performed in United States,²⁴ Saudi Arabia¹² and France⁵⁹ respectively, this disease was reported rarely as the cause of uveitis in Japan (2.7%), China (2.7%) and Iran (2.7%).^{62-63,65}

Sarcoidosis which is proven to be one of the common causes of uveitis in Japan (16.5%),⁶² is rarely as the etiology of uveitis in China (0.3%).⁶³

VKH disease mostly seen in races with colored skin, is one of the known causes of uveitis in China (28.7% of patients),⁶³ Japan (17.4% of patients)⁶² and Argentina (16.7% of patients).⁶⁸

Conclusion

The trends and prevalence of global uveitis is changing in the last decades. It might be due to the prevention and treatment of some uveogenic diseases such as leprosy, onchocerciasis or whether decline in some particular diseases such as Behçet's disease. However, in many cases the prevalence of some specific uveitis has remained unchanged during decades. According to the consecutive evaluations performed by researchers affiliated to Tokyo University, the prevalence of VKH disease during consecutive years were remained

constant^{10,62}; however in recent years Behçet's disease related uveitis had less prevalence and severity.^{62,71} In accord with the study performed by Izawa et al¹⁰ during 1974 to 1977, 17% of patients with uveitis had Behçet's disease; however in the new report by Wakabayashi et al⁶² which is performed at the same center, only 5.8% of all patients with uveitis had Behçet's disease. In addition, regarding the report by Chavis et al¹¹ during 1983 to 1989 in Saudi Arabia, 26.9% of patients with uveitis had Behçet's disease; however during 1995 to 2000 just 6.5% of all patients with uveitis had Behçet's disease.¹² In spite with the reports signify to the decreasing trend of Behçet's disease related uveitis, an investigation in Turkey,⁶⁶ found Behçet's disease, as the cause of non-idiopathic uveitis in 56.7% of patients with known etiology.

In annual evaluation of Behçet's disease center in Shariati Hospital, Tehran, Iran, incidence of Behçet's disease and its severity was reported to being decreased.^{69,70} According to the study performed by Chams et al,⁷¹ late refer of patients and lack of swift treatment of them in the first visit are the major predisposing factors for ocular inflammation and decreased eyesight of the patient with Behçet's disease; therefore, through awareness of physicians and patients and also swift refer and treatment of patients, the prognosis of patients with Behçet's disease can be improved.

As an important point it was expected that rate of reporting of idiopathic uveitis would be decreased due to the development of technology and finding new methods in ophthalmologic evaluation, but according to published data in recent years, 14%¹² to 51.2%⁶⁴ of the causes of uveitis which mostly were led to anterior and intermediate uveitis remained unknown (Idiopathic uveitis). Although so many studies in the matter of some factors like HTLV1²⁶ which is known to

be cause of intermediate uveitis and also extensive evaluations about HLA-B27^{18,19} which have shown it as the marker of AAU have been performed; to date, lots of patients with uveitis have unknown cause for their disease which is named primary uveitis (Idiopathic). In the uveitis center of Tokyo University, unknown causes of uveitis increased from 29.3% during 1974-77¹⁰ to 42.3% in the study performed during 1999 to 2001.⁶² This upward trend of idiopathic uveitis shows the increase of immunologic related uveitis, a group of disease, the clinicians will encounter more in following years.

The limits of this review are not neglectable:

- Most studies on epidemiology of uveitis are performed at the tertiary uveitis referral centers which includes many severe and complicated cases of uveitis.
- In many cases the study has been achieved at a small area of a community which is not usually representative of that country.
- In many publications the investigators have focussed on a particular disease, such as leprosy, leptospirosis etc., and ignoring the other causes of uveitis at that area.
- The epidemiological datas are more or less similar in most European countries. Therefore, we have selected France as representative of that continent.
- The prevalence of uveitis in all cases has been estimated on a small area such as Olmsted county of Minnesota² or North California⁹, which could not be representative of uveitis in the world.
- As a whole a vast and global exploration on epidemiology and prevalence of uveitis is needed to answer to all these pitfalls.

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