



Clinical Course of Uveitis in Children in a Tertiary Ophthalmology Center in Northwest Iran

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Abstract

Objective: In the present research, the clinical course of pediatric uveitis was studied by examining the demographic characteristics of afflicted children, the results of clinical examinations, and uveitis complications.

Materials and Methods: The present research was a retrospective study in which the medical records of 243 children who had been visited and diagnosed as uveitis in the uveitis clinic of Nikookari Eye hospital of Tabriz in 2003-2015, were reviewed. The data were statistically analyzed by descriptive statistics and mean comparison tests in IBM-SPSS 23 and the significance level of $P < 0.05$.

Results: According to the results, 73 (30%), 146 (60.1%), 12 (4.9%), and 12 (4.9%) eyes diagnosed with uveitis had anterior, intermediate, posterior, and panuveitis type, respectively. In addition, 73 cases of uveitis (30%) were acute and 170 cases (70%) were chronic. Based on the LogMAR chart, the mean visual acuity before and after treatment was 0.39 and 0.15 for the right eye and 0.4 and 0.09 for the left eye, which suggests a significant difference. The most common complications observed in this study were macular edema (32.5%) and cataract (22.6%).

Conclusion: This study indicates that intermediate uveitis is the most common type of pediatric uveitis, while anterior uveitis is the second. Posterior and panuveitis are less common in our study. The prevalence of chronic uveitis is significantly high in pediatric group which could justify the higher rate of complications in this age group.

Keywords: Uveitis, pediatric, Iran

Introduction

Uvea is the pigmented and vascular part of the eye which is divided into 3 anatomical parts of iris, ciliary body, and choroid (1,2). Uveitis may be caused by an infectious process or dysfunction of the immune system (2). Uveitis is the third leading cause of blindness in the United States which accounts for 10% of blindness cases in the whole population and 5% of cases in children. The incidence of blindness from uveitis in children is higher than adults (3).

Studies have shown that the prevalence of uveitis in individuals aged 16 and younger is lower than adults, as 2%-14% of uveitis cases are related to children (4-7), with an incidence of 4-5 cases per 100 000 people (8). According to different studies, the incidence of blindness due to uveitis is higher in children than in adults (3).

Several differential diagnosis, numerous clinical symptoms, difficulty in early diagnosis, limited therapeutic protocols, risk of vision loss and even complete loss of vision have increased the importance of pediatric uveitis (4,9). Etiologies for uveitis in children include trauma, inflammation, infections, masquerade syndromes and idiopathic (4,10,11).

There are many geographical and racial differences between infectious and noninfectious causes of uveitis in

children which show the heterogeneity and mismatch in different populations. This can be attributed to different geographical, genetic, demographic, and sociocultural factors (8). In developing countries, tuberculosis is an important cause of pediatric uveitis. Other microbial factors such as cysticercosis are also involved in the occurrence of intermediate uveitis (6). Other infectious agents associated with uveitis in children such as leprosy, leptospirosis, and onchocerciasis are abundantly found in developing countries (3). Drug reaction is another cause of uveitis. For instance, rifabutin can cause anterior uveitis (1).

It seems that demographic features have an important role on the incidence of uveitis in different communities. As a result, this study aims to evaluate the epidemiology of pediatric uveitis in the north west of Iran.

Materials and Methods

In this descriptive study, children at the age of 18 or lower diagnosed with uveitis at Nikookari eye hospital of Tabriz, Iran during 2004-2016 were evaluated prospectively. The data in the medical records of patients were gathered by considering the epidemiologic variables (age, gender), visual acuity before and after treatment, type of uveitis,



results of clinical examination and laboratory tests, response to treatment and complications. Patients with a follow-up period of less than 8 weeks and inability to undergo follow-up examinations were excluded from the study. In this study, different types of uveitis were classified according to the anatomical location as anterior, intermediate, posterior and panuveitis and also according to the disease duration as an acute (duration less than 12 weeks) or chronic (duration more than 12 weeks).

The data were statistically analyzed with descriptive statistics (frequency, percentage, mean, and standard deviation), mean comparison tests in SPSS software for Windows (SPSS Inc., Chicago, IL, USA) and the significance level of $P < 0.05$.

Results

The study population consisted of 243 children diagnosed with uveitis and aged 1 to 18 years. The data showed that 113 patients (46.5%) were male and 130 (53.5%) of them were female. The mean age of the population was 12.3 ± 4.53 with a minimum and maximum of 1 and 18 years, respectively. According to the results, 73 (30%), 146 (60.1%), 12 (4.9%), and 12 (4.9%) eyes diagnosed with uveitis had anterior, intermediate, posterior, and panuveitis type, respectively. In addition, the most common form of intermediate uveitis was the idiopathic type or pars planitis (80%). Considering the duration of illness, 73 cases of uveitis (30%) were acute and 170 cases (70%) were chronic. Etiologic evaluation has revealed that 215 cases (88.48%) had noninfectious etiologies and 28 cases (11.52%) had infectious etiologies. The most common etiology of infectious uveitis was toxoplasmosis (46.42% of infectious cases). Forty cases (16.5%) detected to have granulomatous form of disease and 23 cases (83.5%) nongranulomatous form. A total of 105 cases (43.2%) had unilateral involvement while 138 cases (56.8%) had bilateral involvement.

The study results showed that the mean visual acuity based on LogMAR (Logarithm of the minimum angle of

resolution) was significantly reduced in both eyes after treatment which caused considerable improvement in the vision of patients (Table 1).

According to the data from this study, the most common complications observed in patients included macular edema (32.5%), cataract (22.6%), and posterior synechia (19.3%), while band keratopathy (3.7%) and disc inflammation (3.7%) were the least prevalent complications (Table 2). Moreover, 19 children presented 2 or more of the above-mentioned complications and there was not any record of complication in 37 children (15.2%).

Noninfectious uveitis was totally treated with topical cycloplegics, nonsteroidal anti-inflammatory drugs, topical or systemic corticosteroids, and immunomodulators. To treat macular edema, the underlying inflammation, topical, systemic or periocular corticosteroids and immunomodulatory agents were used such as methotrexate (MTX), CellCept (mycophenolate mofetil) and azathioprine. In the case of persistent macular edema, periocular or intraocular injection of corticosteroids and ultimately 23-gauge pars plana deep vitrectomy were prescribed.

Depending on the probable causes, treatment of high IOP included medications to control inflammation or reduction of corticosteroid dose and prescription of pressure-lowering drugs. Patients with glaucoma underwent surgery with implantation of glaucoma valve. In 10% of cases, cataract surgery was performed. In patients with retinal neovascularization, intravitreal anti-inflammatory and anti-VEGF drugs and pan-retinal photocoagulation were administered.

In summary, because of uncontrolled glaucoma, 3 patients underwent glaucoma surgery (Ahmed valve implantation) 2 of whom with cataract extraction (phacoemulsification). In addition, 5 patients underwent pars plana vitrectomy for vitreoretinal complications 2 of whom had cataract extraction (phacoemulsification) and 1 with glaucoma surgery (Ahmed valve implantation).

Table 1. The Mean Visual Acuity Based on LogMAR Chart, Before and After Treatment

	Right Eye			Left Eye		
	Before treatment	After Treatment	Significance	Before Treatment	After Treatment	Significance
Mean visual acuity (LogMAR)	0.39	0.15	$P=0.00$, SD =1.64	0.4	0.09	$P=0.00$, SD = 2.06
Minimum visual acuity (LogMAR)	2	1		2	2	
Maximum visual acuity (LogMAR)	0	0		0	0	
Standard deviation	3.04	2.56		3.1	3.24	

Table 2. Complications of Uveitis in the Study Population

Complication	Macular Edema	Cataract	Posterior Synechia	Increased Intraocular Pressure	Neovascularization	Glaucoma Resulting in Surgery	Band Keratopathy	Disc Inflammation	Two or More Complications	No Complication
Number	79	55	47	21	19	14	9	9	19	37
Percent	5.32	6.22	3.19	.68	8.7	7.5	7.3	.73	7.8	15.2

Discussion

Uveitis may be caused by an infectious process, dysfunction of the immune system or other mechanisms. It is less common among children aged fewer than 16 than adults and only 2%-14% of uveitis cases are related to children (12-14).

In this research, the medical records of 243 children referred to our clinic from 2004 to 2016 and diagnosed as uveitis were evaluated. In terms of gender, 113 children were male (46.5%) and 130 of them were female (53.5%). The mean age of the population was 12.3 ± 4.53 . The sex ratio (female predominance) in this study was similar to most studies conducted on pediatric uveitis (8,15). In a study by Chams and colleagues, the epidemiology and prevalence of uveitis were evaluated. They have concluded that sex difference is observable in children with pediatric uveitis. The mean age was 8-9 years and bilateral involvement was observed in 75% of cases (4). In this study, 60.1% of cases were intermediate uveitis and 30% anterior. Posterior and panuveitis were less common. American pathology and strabismus has announced the prevalence of different types of uveitis as 30%-50%, 5%-30%, 12%-28%, 13%-21% for anterior, posterior, intermediate and panuveitis respectively.

This study has been performed in a tertiary referral center that could be an explanation for the higher rate of intermediate uveitis. In addition to our study, Rahimi and colleagues evaluated 54 children diagnosed with uveitis in a tertiary referral center and concluded that female to male involvement ratio is 1.25 and anterior uveitis is the most common form of uveitis (with a prevalence of 40.7%), the next intermediate uveitis (33.3%), then posterior uveitis (18.5%) and the last pan uveitis (7.5%). Moreover 74% of children had chronic form of pediatric uveitis in this study (16).

Lonngi et al evaluated 310 children diagnosed with pediatric uveitis in Colombia. There was a female predominance in their study (51.9% of cases) and the prevalence of different types of uveitis is 58.7%, 16.5%, 14.2%, 10.6% for posterior uveitis, intermediate uveitis, anterior uveitis and pan uveitis respectively. Posterior uveitis was the most prevalent type (17).

In a study by Gautam and colleagues, 369 children were evaluated in a tertiary referral center in Northern India. In this study the prevalence was higher in male gender (54.2% of cases) and anterior uveitis with a prevalence of 42.81% was the most common type of pediatric uveitis followed by posterior uveitis (prevalence of 27.64%), pan uveitis (20.32%) and intermediate uveitis (9.21%) (18). In another study, which was conducted by Ganesh et al in a tertiary referral center in central India, 190 children were included in the study in which 64.2% of cases were male. The prevalence of anterior, intermediate, posterior and pan uveitis were 52%, 26%, 14% and 7.9% respectively (19).

Clarke et al evaluated 79 children diagnosed with uveitis of which 37 cases were female (20.1%). Anterior uveitis was the most common form (39.2%) followed by

intermediate (32.9%), posterior (22.8%) and pan uveitis (5.1%) (20).

In a study conducted by Päivönsalo-Hietanen et al, the most common types of uveitis included acute uveitis associated with juvenile rheumatoid arthritis (JRA), idiopathic acute anterior uveitis, and idiopathic chronic anterior uveitis (9). In addition, toxoplasma is known as the most common leading cause of posterior uveitis. In a reported case, a diagnosed pan-uveitis which had led to microphthalmos was found to be caused by toxoplasma (21). Herpes simplex, toxocara, hereditary Lowe syndrome, and retinoblastoma in infants and toxocariasis, toxoplasmosis, leukemia, and juvenile rheumatoid arthritis in school-age children and toddlers have been reported as the causes of uveitis. In another study conducted by Alizadeh Ghavidel et al, in a tertiary ophthalmic care center in north west of Iran, records of 220 anterior uveitis patients were investigated, 47.3% of which were male and 52.7% were female. Causes of uveitis in 65.45% were idiopathic, whereas 26.82% and 7.73% of cases preceded autoimmune and infectious causes, respectively. The most common causes were Behcet disease (13.2%), herpes (6.4%), multiple sclerosis (4.1%), rheumatoid arthritis (3.6%) and ankylosing spondylitis (2.3%) (22).

Symptoms of uveitis differ depending on the involvement site, speed of development, duration of the disease, and clinical course (acute or chronic). However, general symptoms include eye redness, pain, photophobia, tearing, and visual disturbances such as blurred vision, spots in the visual field, and flouter (13). Due to stabilization of uveitis in children caused by delayed diagnosis, vision loss among them is more probable than adults (7,23-25). Inflammation and its causes can lead to structural changes in the eye which may affect its function and predispose patients to glaucoma, vision loss or both of them. Pediatric uveitis can cause severe eye diseases and vision loss in 25%-33% of affected children (9,10).

Uveitis in children is often diagnosed at routine eye examinations (10), and the diagnosis is late because of both the inability of children in expressing the symptoms and the asymptomatic nature of this disease in children. Parents are not usually aware of the existence of uveitis until some complications such as band keratopathy, strabismus or leukocoria appear (1,8,10,26). This fact can explain the higher rate of complications in this age group. Acute angle closure glaucoma (more likely in older patients and those with impaired vision), herpetic keratitis, microbial keratitis (caused by the use of contact lenses), episcleritis or scleritis, recurrent corneal erosion or abrasion, and viral conjunctivitis are among the complications of uveitis that should be taken into account.

According to the data obtained from this study, complications of uveitis in children included macular edema (32.5%), cataract (22.6%), posterior synechia (19.3%), increased intraocular pressure (8.6%), neovascularization (7.6%), glaucoma (5.7%), band keratopathy (3.7%), disc inflammation (3.7%), and others (7.8%). As an explanation to the fact that the prevalence of

cataract has been more common than macular edema in other studies, it can be stated that, according to statistics, anterior uveitis is the most common type of uveitis in the world (15). Given that 60.1% of patients, who visited the uveitis clinic in Nikookari Eye Hospital of Tabriz were affected by intermediate uveitis and cases of anterior uveitis and treated without the need for referral, higher prevalence of macular edema is justifiable. The findings of Rosenberg et al indicated that the risk for band keratopathy increased with the occurrence of anterior and intermediate uveitis ($P=0.005$) and posterior and intermediate uveitis were associated with cataract ($P=0.009$) or posterior synechia ($P<0.001$). On the other hand, intermediate uveitis increases the risk of cystoid macular edema ($P=0.002$) (27). In a study conducted by Kump et al on 165 affected eyes diagnosed with uveitis, complications included cataract in 105 cases (64%), increased intraocular pressure in 23 cases (20%), band keratopathy in 76 cases (46%), and posterior synechia in 96 cases (58%) (15). In another study conducted by Shafran and colleagues in the University of Leicester, macular edema was reported to be the most common complication of intermediate uveitis (28).

Finally, we can conclude that the pattern of pediatric uveitis and its complications depend on demographic features of the studied society and epidemiologic studies are imperative in order to determine the prevalence of uveitis in different societies and centers.

Conclusion

According to the results of present study (obtained from the largest uveitis center in the northwest of Iran), the most prevalent type of uveitis among the patients visited in this center was intermediate uveitis, the most common form of which was idiopathic. Then, anterior, posterior, and panuveitis ranked second to fourth. *Toxoplasma* was also found to be the most common infectious pathogen of uveitis. It was also revealed that most children visited and diagnosed with uveitis were affected by the chronic type of this condition. The results of studying the visual acuity before and after treatment showed a significant improvement in acuity of either of eyes. The most prevalent complications of uveitis in children observed in this study included macular edema, cataract, posterior synechia, increased intraocular pressure, neovascularization, glaucoma, band keratopathy, and disc inflammation, respectively. According to the study findings, it seems that identification of more common types of uveitis in children and paying attention to the clinical course and its complications are very decisive in the development of treatment policies and guidelines.

Conflict of Interests

The authors do not have any conflict of interest.

Ethical Issues

This study was approved by the review board ethics committee of the training hospital and Tabriz University of Medical Sciences, Tabriz, Iran.

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