Int Ophthalmol (2021) 41:2225–2234
https://doi.org/10.1007/s10792-021-01783-4

ORIGINAL PAPER

Aetiology and clinical characteristics of uveitic glaucoma in Turkish patients

Cigdem Altan · Berna Basarir

Received: 23 November 2020 / Accepted: 6 March 2021 / Published online: 17 March 2021

Abstract

Purpose To investigate the types, frequency and clinical profiles of uveitic glaucoma seen at a tertiary care center and also to have an idea about the distribution of uveitic glaucoma types in Turkish population.

Methods Consecutive case notes of all patients attending a specialized uveitis clinic over a 3-month period were reviewed retrospectively.

Results One hundred and seven eyes of 96 patients were included. Sixty-five of the eyes had anterior, one intermediate, nine posterior uveitis while 32 of them had panuveitis. Twenty-three eyes had acute, 52 chronic and 32 recurrent uveitis. Herpes virus associated iridocyclitis was the leading cause of anterior uveitis-associated uveitic glaucoma followed by cytomegalovirus (CMV) associated anterior uveitis; while steroid-induced glaucoma accounted for the majority of chronic uveitis with glaucoma followed by Fuchs' uveitis syndrome (FUS).The most common causes of glaucoma among the cases were steroid-induced in 30 eyes (28%), Herpes virus anterior uveitis in 24 eyes (22%), CMV anterior uveitis in 20 eyes (18%), FUS in 15 eyes (14%), ocular toxoplasmosis in 5 eyes (4%). Behçet's uveitis was the most common (n = 11, 36%) cause of steroid-induced glaucoma.The need for surgical intervention was 23.32% (n = 25; 12 of them were FUS, 8 steroid-dependent, 1 HSV and 3 CMV anterior uveitis and 1 angle closure glaucoma with idiopathic uveitis) in our cases.

Conclusion Uveitic glaucoma is a common complication in a tertiary clinic. The most common causes are steroid-induced, FUS, viral anterior uveitis. The most common disease causing steroid induced glaucoma was Behçet's disease. Glaucoma surgery is required in a significant number of cases.

Keywords Aetiology of uveitic glaucoma · Glaucoma · Uveitis · Uveitic glaucoma

C. Altan (✉) · B. Basarir
University of Health Sciences Turkey, Beyoglu Eye Training and Research Hospital, Bereketzade Street Number: 2, Beyoglu, Istanbul, Turkey
e-mail: cigdem_altan@yahoo.com

B. Basarir
e-mail: bdemirel@hotmail.com

Introduction

Uveitic glaucoma, which is the intersection of two potential causes of blindness, uveitis and glaucoma, is one of the most serious complications of intraocular inflammation.

The prevalence of uveitis-related glaucoma in the literature varies greatly because of the undefined diagnostic criteria of uveitic glaucoma, the characteristics of the clinics in which the studies are conducted and the etiology of uveitis may differ regionally [1, 2].

The frequency of intraocular pressure (IOP) increases in uveitis patients is 20–40%; the incidence of secondary glaucoma development is between 4 and 40%, and in studies covering all types of uveitis, this rate is frequently reported to be between 10 and 20% [1–12].

Uveitic glaucoma has been associated with a wide spectrum of inflammatory diseases. It appears that the type of inflammation, the steroid-response and the anatomical alterations of the anterior chamber play a main role in pathogenesis [5]. The incidence, clinical features and the mechanism of high IOP vary depending upon the clinical entity of the uveitis [3]. Many different types of uveitis have been associated with glaucoma, but in certain types of uveitis are characterized by elevated IOP more common, such as Posner–Schlossman Syndrome (PSS), Fuch's uveitic syndrome (FUS) and varicella zoster virus (VZV)-associated iridocyclitis [4, 7]. Corticosteroids used for the treatment of uveitis also contribute to elevation of IOP [13].

The aim of the treatment of uveitic glaucoma is to control inflammation firstly and lower IOP; thus, to prevent permanent structural changes in the iridocorneal angle and optic nerve damage. Once the structural changes developed, it is challenge to manage and maintain long-term control of uveitic glaucoma. In eyes with uveitic glaucoma, surgical intervention is required in 25–30% of the cases [5].

The aim of this study to investigate the types, frequency and clinical profiles of uveitic glaucoma seen at a tertiary care center and also to have an idea about the distribution of uveitic glaucoma types in Turkish population.

Patients and methods

Among the patients attended in the uveitis department of University of Health Science Turkey Beyoglu Eye Training and Research Hospital between December 16, 2019 and March 16, 2020, consecutive patients who were being followed up or newly diagnosed for uveitic glaucoma were included in this study. The records of 107 eyes of 96 patients were reviewed retrospectively. Informed consent was obtained from each subject before enrollment. The protocol of the study was approved by the local Committee with the decision number 42/I-1 on 26.08.2020 and it also adhered to the ethical principles stated in the 'Declaration of Helsinki'.

The patients were considered to be uveitic glaucoma if IOP was above 21 mmHg with or without glaucomatous optic neuropathy and/or visual field defects on more than one examination at our hospital, or if the patient was started antiglaucoma therapy at an examination in our hospital and had a well documented increase in IOP concurrent with intraocular inflammation previously or firstly at the current examination [4, 6, 7]. Patients with history of glaucoma prior to the diagnosis of uveitis; cases of transient postoperative uveitis and patients with 'masquerade syndromes' were excluded. Steroid-induced glaucoma was defined as IOP of > 6 mmHg from baseline, or elevated IOP requiring treatment or two measurements higher than 21 mmHg after the start of steroid administration, accompanied by IOP decrease after discontinuation or dose reduction of corticosteroids with or without medical therapy to control IOP [14].

All examinations were done by 2 experienced uveitis and glaucoma specialists (CA, BB). Routine ophthalmological examination, including visual acuity test with Snellen chart, slit-lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry and fundus examination with + 90 Diopter lens, was performed for each participant before laboratory and imaging tests as required. The patients' ages at the study visit, gender, complaints at the examination, systemic diseases were recorded. Each patient was examined for anatomical classification of uveitis, disease chronicity and frequency of IOP increase: Cases were classified as anterior, intermediate, posterior or panuveitis depending on the site of intraocular inflammation with more specific aetiology of uveitis where appropriate. Uveitis was classified using the International Uveitis Study Group Classification System [15]. Patients were further classified as acute uveitis if they lasted less than 3 months, and were classified as chronic uveitis otherwise; recurrent uveitis was described repeated episodes of uveitis separated by periods of inactivity without treatment of ≥ 3 months in duration [15]. Intraocular pressure raised was coded in the analysis as "first elevation attack", "elevated intermittently (no treatment)'', "elevated intermittently (requiring treatment)'' and "sustained elevation requiring treatment''. IOP raised requiring treatment refers to eyes with IOP greater

than 28 mmHg with or without optic disc and field changes, or IOP greater than 21 mmHg with glaucomatous optic disk damage [10].

The diagnosis of FUS was based on the presence of several of the following clinical features: Absence of acute symptoms, such as photophobia, pain or ciliary injection; small to medium-sized diffuse distributed stellate keratic precipitates (KP); diffuse iris stromal atrophy with or without heterochromia; a chronic low-grade anterior chamber reaction; lack of posterior synechiae and absence of cystoid macular edema, snowbanks, retinal vasculitis or chorioretinal infiltrates despite the presence of vitreous cells and debris [16]. In this cases, steroid treatment was not given, only antiglaucomatous treatment was used.

When present, active or a past episode of herpes zoster ophthalmicus or herpetic corneal disease was considered diagnostic of herpetic anterior uveitis. In patients without corneal involvement, the diagnosis was based on the presence of at least three of the following features: recurrent unilateral inflammatory attacks in the same eye, an acute elevation of the IOP during inflammatory episodes, granulomatous KPs that were not confined to the inferior cornea, patchy or sectorial iris atrophy with or without transillumination defects, posterior synechiae, and a pupil distortion or spiraling of the iris [17]. In herpetic uveitis, all patients received oral antiviral therapy (oral acyclovir or valacyclovir) during active inflammatory episodes. Anti-inflammatory treatment consisted of frequent instillations of prednisolone acetate drops in all patients. After the resolution of inflammatory episodes, topical corticosteroid treatment was tapered very slowly. Topical mydriatic agents were used to prevent posterior synechiae. Anti-glaucomatous therapy included topical beta-blockers, alpha-adrenergic agonists, and topical or oral carbonic anhydrase inhibitors. Prostaglandin analogues and miotic agents were avoided in all patients.

Cytomegalovirus (CMV)-associated anterior uveitis (AU) was considered in patients with unilateral recurrent episodes of mild iridocyclitis with a few fine keratic precipitates and elevated IOP in the range of 40–60 mmHg during episodes [18]. Other clinical findings in the patient diagnosed with CMV anterior uveitis were as follows: corneal endothelitis with corneal edema; keratic precipitates, usually granulomatous, are usually located in the middle or inferior half of the cornea. They may be diffuse, linear or show a ring pattern or may appear as a coin-like lesions. White, medium-sized, nodular lesions surrounded by a translucent halo are also possible. In 14 (70%) patients, aqueous samples were tested with polymerase chain reaction (PCR) analysis in order to confirm the diagnosis. The patients with CMV anterior uveitis were treated with topical steroids, topical antiglaucoma medications and topical (ganciclovir gel) or if needed, oral valganciclovir [19].

If any, systemic drugs and the number of glaucoma drugs used during the study visit, was recorded. Anterior and posterior segment examination findings of the patients and the presence of remission of uveitis at the visit were recorded. Retinal nerve fiber layer (RNFL) thickness via spectral-domain optical coherence tomography (SD-OCT) and VF findings were recorded, if any. The highest IOP in the notes at follow-up exams, total follow-up time, recommended treatment at the study visit and whether glaucoma surgery is needed were recorded. Glaucoma surgery was carried out or recommended in patients with uncontrolled IOPs, deteriorating visual fields or progressive optic nerve head cupping despite the use of maximal medical treatment.

Statistical Package for the Social Sciences (SPSS) software (version 10.1, SPSS Inc., Chicago, IL) was used for statistical analysis. Descriptive analysis was done, where categorical variables were presented as frequencies and percentages while continuous variables as mean (± SD). Student's t-test was used for comparison of mean continuous variables. The chi-square test was used to investigate potential association between two categorical variables.

Results

The mean age of the patients (30 females, 66 males) was 42.2 ± 15.5 years. The mean visual acuity of the patients at the time of the study visit was 0.56 ± 0.37. The symptoms of the patients at study visit were shown in Table 1.

Sixty-five of the eyes had anterior (60%), one intermediate (0,9%), nine posterior (8%) and 32 panuveitis (30%). Twenty-three eyes had acute (21%), 52 chronic (48%) and 32 (30%) recurrent uveitis. The patients' anterior segment signs at visit were shown in Table 1. The distribution of uveitis type was shown in Table 2. Thirty-three of the cases were in

Table 1 The patients' symptoms and anterior segment signs at study visit

Symptoms: The number of patients	Anterior segment signs: The number of eyes
Routine control: 51	Keratic precipitate: 62
Pain and redness: 13	Granulomatous: 58
Blurred vision: 11	Non-granulomatous: 4
Pain: 7	Endothelitis: 21
Blurred vision, pain and redness: 6	Corneal involvement (active or sequel): 17
Blurred vision and pain: 3	Iris atrophy: diffuse: 16, sectoral: 8
Pain and photophobia: 1	Heterochromia: 4
Redness and photophobia: 1	Iris nodule: 7
Glaucoma surgery was recommended in another center, she/he came to get an idea: 3	Lens: 59 clear, 21 cataract, 27 Pseudophakic
	Anterior chamber cell
	Trace: 27
	1(+): 10
	2(+): 8
	3(+): 4
	4(+): 3

Table 2 The distribution of uveitis type in patients (*FE* First elevation attack, *EİN* Elevated intermittently (no treatment), *EİT* Elevated intermittently (requiring treatment), *SE* Sustained elevation requiring treatment)

Anatomic classification	Total number of eyes	Presentation	Increase in IOP pattern
Anterior	65	Acute: 19	FE: 13
		Chronic: 16	EİN: 17
		Recurrent: 30	EİT: 12
			SE: 23
Intermediate	1	Chronic	SE
Posterior	9	Acute: 1	FE: 1
		Chronic: 7	EİN: 1
		Recurrent: 1	EİT: 7
Panuveitis	32	Acute: 3	FE: 6
		Chronic: 28	EİN: 3
		Recurrent: 1	EİT: 5
			SE: 18

remission at visit. There were signs of posterior segment involvement in 42 eyes on examination and/or OCT or fundus fluorescein angiography.

Herpes virus associated iridocyclitis ($n = 24$) was the leading cause of anterior uveitis-associated uveitic glaucoma followed by CMV associated anterior uveitis ($n = 20$), while steroid-induced glaucoma ($n = 27$) accounted for the majority of chronic uveitis with glaucoma followed by FUS ($n = 15$). Eight of 14 PCR samples were found CMV positive.

It was the first attack in 20 of the eyes during the study visit; 20 had intermittent IOP increase that did not require treatment, 18 had intermittent IOP increase requiring treatment, and 49 had a sustained IOP increase requiring treatment (Table 2).

27 patients (37 eyes) were receiving systemic therapy during the visit: Seven patient (11 eyes) were using metilprednisolone and azathioprine, 4 patients (4 eyes) prophylactic dose acyclovir, 1 patient (1 eye) oral acyclovir + ganciclovir gel, 1 patient (1 eye) fingolimod, 6 patient (9 eyes) azathioprin, 1 patient (1 eye) interferon beta 1a, 1 patient (1 eye) metilprednisolon and anti-tuberculosis therapy, 1 patient (1 eye) cyclosporine and azathioprine, 1 patient (2 eyes)

interferon-alpha-2a, 1 patient (1 eye) cyclosporine and azathioprine and prednisolone, 1 patient (1 eye) methotrexate, 1 patient (2 eyes) metilprednisolone 4 mg and colchicine and 1 patient (2 eyes) adalimumab.

The most common causes of glaucoma among the cases were steroid-induced in 30 eyes (28%), Herpes virus AU in 24 eyes (22%), cytomegalovirus AU in 20 eyes (18%), FUS in 15 eyes (14%), ocular toxoplasmosis in 5 eyes (4%). Three of the cases were angle-closure glaucoma (One idiopathic, one ankylosing spondilitis and the other MS) (Table 3).

The mean age was 36.4 ± 12.8 in steroid-induced group, 52.3 ± 16.6 in herpetic uveitis group, 32.9 ± 10.5 in anterior CMV uveitis, 42.3 ± 10.0 in FUS group (ANOVA, $p < 0.001$).

Behçet's uveitis was the most common ($n = 11$, 36%) cause of steroid-induced glaucoma. The other causes were idiopathic ($n = 7$), tuberculosis ($n = 5$), sarcoidosis ($n = 2$), FUS ($n = 1$, a patient who received intravitreal dexamethasone implant in another hospital), psoriasis and ampiginous choroiditis ($n = 1$), multiple sclerosis (MS; $n = 2$), ancylosing spondylitis (AS; $n = 1$) (Table 3).

Mean IOP at the study visit was 24.3 ± 10.4 mmHg; the highest mean IOP in the follow-up was 35.9 ± 8.8 mmHg. While 59 of the cases did not use antiglaucomatous drugs during the study visit, 48 (5 of them used 1 drug, 17 of them 2 drugs, 23 of them 3 drugs and 3 of them 4 drugs) were using antiglaucomatous drugs. Antiglaucomatous medication was added to 47 eyes at the visit. At the

Table 3 The Specific aetiology of uveitic glaucomas and accompanying systemic disease of the patients according to anatomic localization (*FUS* Fuchs' uveitis syndrome, *CMV* Cytomegalovirus anterior uveitis, *HSV* Herpes simplex virus anterior uveitis, *AS* Ankylosing spondylitis, *ACG* Angle closure glaucoma, *MS* Multiple sclerosis)

Uveitis category	The specific aetiology of uveitic glaucomas	Accompanying systemic disease
Anterior	FUS: 15 (1 of 15 steroid-induced)	Behçet's disease: 1
	CMV: 20	AS: 4
	HSV/VZV: 24	Diabetes mellitus: 3
	Idiopatic: 3	Burger disease: 1
	Steroid-induced: 2	
	AS + ACG	
	AS:1 (Steroid induced)	
Intermediate	FUS + MS	MS
Posterior	Steroid-induced: 8 Behcet's disease: 2 (Steroid-induced)	Behçet's disease: 2
	Tuberculosis: 4 (Steroid-induced)	Tuberculosis: 4
	Idiopathic: 1 (Steroid-induced)	Psoriasis: 1
	Ampiginous choroiditis: 1 (Steroid induced)	
	Toxoplasmosis: 1	
	Ampiginous choroiditis: 1	
Panuveitis	FUS + Toxoplasmosis: 1	Behçet's disease: 11
	MS: 2 (Steroid-induced)	MS: 2
	Tuberculosis: 1 (Steroid-induced)	Sarcoidosis: 4
	Toxoplasmosis: 4	Tuberculosis: 1
	Behçet's disease: 11 (9 of 11 Steroid induced)	
	ACG (One MS, one idiopathic)	
	Sarcoidosis: 3 (2 of 3 Steroid-induced)	
	Idiopathic: 7 (6 of 7 Steroid induced)	

end of the data analysis, 69 of the patients were using at least one glaucoma medication.

The mean total follow-up period of the patients in our clinic was 38.7 ± 44.2 months. Mean IOP was 16 ± 6.6 mmHg at the last control visit. The mean visual acuity was 0.60 ± 0.36 at the end of the data analysis.

Twenty of the cases (9 of them were FUS, 8 steroid-induced, 2 CMV anterior uveitis and 1 angle closure glaucoma with idiopathic uveitis) had undergone glaucoma surgery during their follow-up before the study visit. Glaucoma surgery was recommended for 5 cases (3 FUS (One of them had also MS), 1 CMV, 1 HSV anterior uveitis) at the study visit (Table 4). Of the 25 patients requiring glaucoma surgery, 21 were chronic uveitis; 15 were anterior uveitis, 1 was intermediate uveitis, 2 were posterior uveitis and 7 were panuveitis (Chi-square, $p < 0.001$ and $p = 0.35$).

There was no significant difference between the ages of patients with (40.7 ± 10.9) and without (42.7 ± 16.7) glaucoma surgery ($p = 0.57$). The highest IOP measured at follow-up was significantly higher in cases requiring glaucoma surgery (42.9 ± 9.3 vs 33.7 ± 7.4; $p < 0.001$); BCVA was also significantly lower in cases requiring glaucoma surgery (0.34 ± 0.38 vs 0.62 ± 0.34, $p = 0.001$).

Table 4 The patients requiring glaucoma surgery, ages, etiology of uveitic glaucoma and glaucoma surgeries performed

Case number	Age	Etiology	Glaucoma surgery
1	40	Steroid-induced, BD	Trabeculectomy with MMC
2	40	Steroid-induced, FUS	AGV implantation
3	20	Steroid-induced, BD	Trabeculectomy with MMC
4	20	Steroid-induced, BD	Trabeculectomy with MMC
5	38	Steroid-induced, BD	Trabeculectomy with MMC
6	38	Steroid-induced, BD	Trabeculectomy with MMC
7	44	Steroid-induced, BD	Trabeculectomy with MMC
8	39	Steroid-induced, tuberculosis	Trabeculectomy with MMC
9	38	CMV anterior uveitis	Trabeculectomy with MMC
10	55	Idiopathic, ACG	Trabeculectomy with MMC
11	39	FUS	2 Trabeculectomies with MMC
12	30	FUS	Trabeculectomy with MMC, bleb needling
13	60	FUS	Diod laser cyclophotocoagulation
14	35	CMV anterior uveitis	Trabeculectomy with MMC, bleb needling
15	41	FUS	2 Trabeculectomies with MMC, bleb needling
16	37	FUS	2 Trabeculectomies with MMC, AGV
17	37	FUS	Trabeculectomy with MMC, bleb needling, AGV
18	49	FUS	Trabeculectomy with MMC, AGV
19	61	FUS	Trabeculectomy with MMC, diod laser cyclophotocoagulation
20	45	FUS	Trabeculectomy with MMC, diod laser cyclophotocoagulation
21	41	CMV anterior uveitis	Trabeculectomy with MMC recommended at visit
22	23	FUS + MS	Trabeculectomy with MMC recommended at visit
23	56	HSV/VZV anterior uveitis	Trabeculectomy with MMC recommended at visit
24	39	FUS	Trabeculectomy with MMC recommended at visit
25	54	FUS	Trabeculectomy with MMC recommended at visit

FUS Fuchs' uveitis syndrome, *BD* Behçet's disease, *CMV* Cytomegalovirus anterior uveitis, *HSV* Herpes simplex virus anterior uveitis, *ACG* Angle closure glaucoma, *MS* Multiple sclerosis

Discussion

Secondary glaucoma is still an important sight-threatening complication in uveitis. It is known that the etiology of uveitis also varies between different countries, regions, ethnic groups and even among regions of the same country [1–3, 5, 12]. Racial, genetic, geographic, social, and environmental factors influence distribution of the types, clinical associations, and causes of uveitis in different populations [2]. The present study which evaluates the profile of consecutive patients with secondary glaucoma in uveitis admitted or referred within 3 months was performed in a university-based tertiary referral center in Istanbul, Turkey. In our study, steroid-induced glaucoma was the most prevalent clinical entity of the defined etiologies followed by Herpes virus anterior uveitis, CMV anterior uveitis, FUS and ocular toxoplasmosis.

Takahashi et al. disclosed that secondary glaucoma was found in 217 of 1099 patients (19.7%) or 293 of 1604 eyes (18.3%) with uveitis in their retrospective study in the southern part of Japan where human T-lymphotropic virus type 1 (HTLV-1) is known to be endemic [3]. Secondary glaucoma patients were defined as patients whose IOP was higher than 21 mmHg at two consecutive visits and who were treated with medication to control the high IOP in that study. HTLV-1 uveitis was the most common cause, followed by Vogt-Koyanagi-Harada's (VKH) disease, ocular toxoplasmosis, sarcoidosis, Behçet's disease. The proportion of steroid-induced glaucoma was 26 of 293 eyes (8.9%) with secondary glaucoma in their study [3].

In a study from the United States, Merayo-Lloves et al. reported the prevalence of secondary glaucoma was 9.6% and also they evaluated forms of uveitis more frequently associated with secondary glaucoma and found that herpes virus associated uveitis (22%), FUS (19%), VKH disease (18%), juvenile idiopathic arthritis (16%), syphilis (14%), and sarcoidosis (12%) were the leading causes of secondary glaucoma in uveitis patients [7].

Kanda et al. diagnosed ocular hypertension (OHT) as if an IOP of 21 mmHg or higher was recorded in at least two consecutive visits within 2–14 days and OHT was found in 93 of 304 (30.6%) uveitis patients in Japan [1]. In their case series the most common uveitis with OHT was sarcoidosis (15.4%), followed by Behçet's disease (14.6%), VKH disease (12.2%), VZV iridocyclitis (8.1%), scleritis (7.3%), PSS (6.5%). In that study, 56 eyes (34.6%) of 43 patients (35.2%) with anterior uveitis, and 67 eyes (23.3%) of 50 patients (31.4%) with panuveitis had OHT, but none of the eyes with posterior uveitis had OHT [1].

In Al-Rubaie et al. study from Riyadh, Saudi Arabia, the forms of uveitis most commonly associated with glaucoma were: HLA-B27-positive anterior uveitis (27.6%), Fuchs uveitis (23.3%), juvenile idiopathic arthritis (23.1%), herpetic uveitis (20.3%), and VKH disease (16.3%). They found that elevated IOP at presentation, secondary glaucoma, and need for glaucoma surgery were most frequent in eyes with anterior uveitis [2].

In a recent study published from our country, Tekeli et al. included uveitis patients who presented or were referred to the glaucoma units in Ankara for 2 months in their multicenter study. They found that uveitic glaucoma comprised 4.1% of all patients with glaucoma. In their study the most common diagnosis of uveitis were idiopathic uveitis (n = 54), Behçet's disease (n = 26), FUS (n = 21), and Herpes Simplex virus infectious uveitis (n = 14) [12].

Panek et al. reviewed retrospectively the records of 161 eyes of 100 consecutive patients with uveitis referred to and examined by one author in Los Angeles, California, USA and they found that 31 eyes (23 patients) had secondary uveitic glaucoma; three patients (three eyes) had acute uveitis and 20 patients (28 eyes) had chronic uveitis. Glaucoma occurred in 12% of patients with acute uveitis and in 26% of patients with chronic uveitis in that study [4]. In our study, we found 65 eyes of 107 had only anterior uveitis, 32 eyes had panuveitis; 23 eyes had acute, 52 had chronic and 32 had recurrent uveitis, however, we did not aim to determine the incidence of uveitic glaucoma.

Disease chronicity and primary anterior segment inflammation are the most commonly factors associated with glaucoma [4]. According to the anatomical classification, secondary glaucoma is most commonly associated with anterior uveitis [1, 3, 7, 10]. The risk of IOP increase in posterior uveitis is lower, because the aqueous outflow pathways are less affected. Secondary glaucoma in pars planitis has not been reported as an important problem [11]. Our anatomical distribution was also consistent with previous studies. The predominant clinical type was anterior (65 eyes, 60%),

chronic uveitis (52 eyes, 48%). Herpes virus associated iridocyclitis was the leading cause of anterior uveitis-associated uveitic glaucoma followed by CMV associated anterior uveitis, while steroid-induced glaucoma accounted for the majority of chronic uveitis with glaucoma followed by FUS.

Increasing prevalence of glaucoma with chronicity reflects the cumulative detrimental effect of inflammation and probably the consequence of chronic corticosteroid therapy [2, 11]. Uveitic patients have a high risk of developing glaucoma, which is attributed not only to the uveitis itself but also to the corticosteroids used for the treatment of uveitis [5]. The reason for the increase in IOP due to corticosteroids is the increased resistance of the aqueous outflow [3]. In our case series, the largest group consisted of steroid-induced glaucoma (28%). Behçet's patients made up 36% of patients with steroid glaucoma. The data recorded here indicate that the majority of secondary glaucoma cases in Behçet's disease were steroid-induced glaucoma (11 of 13 eyes). In Takahashi's study, while sarcoidosis was the most common cause of steroid-induced glaucoma, Behçet's disease ranked fourth place [3]. Kanda et al. investigated the prevalence of steroid-induced OHT in uveitic eyes [1]. The frequency of Behçet's disease-associated OHT was the second highest among all cases of uveitis with OHT. In their study also the prevalence of steroid-induced OHT among uveitic eyes with OHT was the highest in Behçet's disease (94.4%), followed by VKH disease and scleritis [1]. Should be alert for steroid-induced glaucoma, especially in chronic uveitis.

The development of secondary glaucoma consists the most common complication of herpetic uveitis. [4, 5]. It has been estimated that the prevalence of transient increased IOP in patients with herpetic anterior uveitis varies from 28 to 45%, whereas glaucoma in eyes with viral uveitis is approximately 10–54%. Active iridocyclitis accompanied by an acute increase in IOP are the main features of herpetic infection and in most cases, HSV or VZV are the etiologic factors. Postulated mechanisms include both trabeculitis and blockage of the trabeculum with inflammatory debris [4, 5, 7], similarly to hypertensive episodes of acute CMV anterior uveitis, previously called PSS. This explains why the IOP returns to normal levels while responding to topical corticosteroids [4, 5, 7]. In recent years, the etiological factor CMV has been detected in 22.8–28.6% of hypertensive anterior uveitis cases [20, 21]. Herpes virus associated iridocyclitis ($n = 24$) and CMV associated anterior uveitis ($n = 20$) were the leading causes of anterior uveitis-associated uveitic glaucoma in this study.

Glaucoma is believed to be the major long-term threat to vision in patients with FUS [4]. The incidence of glaucoma may vary from 13 to 59% and usually develops with time. In most of the cases, the glaucoma is persistent, even after the uveitis has subsided, and does not respond to steroids. Antiglaucomatous medication can be effective in the initial glaucoma control and in long-term basis surgical treatment may be necessary [5]. We demonstrated that the need for glaucoma surgery was most frequent in patients with FUS.

Uveitic glaucoma is difficult and challenging to manage. It comprises the treatment of the ocular inflammation, the underlying systemic disease and glaucoma. The inflammation of the eye and glaucoma can be controlled with anti-inflammatory and antiglaucoma agents, respectively [5]. In many cases, like viral anterior uveitis, management of the inflammatory process contributes to the control of IOP as well. But, glaucoma surgery is required in approximately 25–30% of eyes with uveitic glaucoma in cases that anti-glaucoma medications are inadequate [22]. This study also showed that a certain proportion (25/107 eyes, 23.3%) in secondary glaucoma required surgical intervention due to poor control of high IOP despite maximal medical therapy. The majority received or recommended trabeculectomy with mitomycin C.

The prevalence of uveitic glaucoma varies greatly between reports, and these differences are attributed to the great differences in aetiology of uveitis among countries and also the differences in proportion of severe cases seen in individual clinics [1]. This study was conducted in a single referral center at a certain time interval. However, since this study was conducted in a tertiary hospital, the results cannot be generalized to the whole Turkish population. But, the population in this study is of Caucasian origin, so our results are comparable to other population-based studies of Caucasian or non-Caucasian patients. Additionally, the diagnosis of HSV anterior uveitis and CMV anterior uveitis was mainly by the clinical features, not by PCR. Therefore, some misdiagnoses of HSV and CMV anterior uveitis might be included in this study.

In conclusion, uveitic glaucoma is a common complication in our tertiary clinic. The most common causes are steroid-induced, FUS, viral anterior uveitis. The most common disease causing steroid induced glaucoma was Behçet's disease. The therapeutic approach of uveitic glaucoma should be personalized according to the patient. Glaucoma surgery is required in a significant number of cases.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by CA, BB. The first draft of the manuscript was written by CA and BB commented on previous versions of the manuscript. Two of authors approved the final manuscript.

Funding No financial support was received.

Data availability The data used to support the findings of this study are restricted by the University of Health Science Beyoglu Eye Training and Research Hospital Ethics Committee in order to protect patient privacy. Data are available from Cigdem Altan and Berna Basarir for researchers who meet the criteria for access to confidential data.

Declarations

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was received from the University of Health Sciences Turkey, Beyoglu Eye Training and Research Hospital local Committee.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Patients signed informed consent regarding publishing their data.

Informed consent Informed consent was obtained from all individual participants included in the study. Patients signed informed consent regarding publishing their data.

References

1. Kanda T, Shibata M, Taguchi M et al (2014) Prevalence and aetiology of ocular hypertension in acute and chronic uveitis. Br J Ophthalmol 98(7):932–936. https://doi.org/10.1136/bjophthalmol-2013-304416
2. Al Rubaie K, Al Dhahri H, Al Fawaz A et al (2016) Incidence and risk factors for developing glaucoma among patients with uveitis in a university-based tertiary referral center in Riyadh, Saudi Arabia. Ocul Immunol Inflamm 24(5):571–578
3. Takahashi T, Ohtani S, Miyata K et al (2002) A clinical evaluation of uveitis associated secondary glaucoma. Jpn J Ophthalmol 46(5):556–562
4. Panek WC, Holland GN, Lee DA, Christensen RE (1990) Glaucoma in patients with uveitis. Br J Ophthalmol 74(4):223–227
5. Kalogeropoulos D, Sung VC (2018) Pathogenesis of uveitic glaucoma. J Curr Glaucoma Pract. 12(3):125–138. https://doi.org/10.5005/jp-journals-10028-11257.Review
6. Neri P, Azuara-Blanco A, Forrester JV (2004) Incidence of glaucoma in patients with uveitis. J Glaucoma 13(6):461–465
7. Merayo-Lloves J, Power WJ, Rodriguez A et al (1999) Secondary glaucoma in patients with uveitis. Ophthalmologica 213(5):300–304
8. Nagpal Agnieszka G, Acharya Nisha R (2009) Uveitic Glaucoma. In: Grehn F, Stamper R (eds) Glaucoma (Essentials in Ophthalmology Progress III). Springer-Verlag, Heidelberg, pp 49–58
9. Elgin U, Berker N, Batman A (2004) Incidence of secondary glaucoma in Behçet's disease. J Glaucoma 13:441–444
10. Herbert HM, Viswanathan A, Jackson H et al (2004) Risk factors for elevated intraocular pressure in uveitis. J Glaucoma 13(2):96–99
11. Kok H, Barton K (2002) Uveitic glaucoma. Ophthalmol Clin North Am 15(3):375–387
12. Tekeli O, Elgin U, Takmaz T, Ekşioğlu Ü, Baş Z, Yarangümeli A, Karakurt A, Evren Kemer Ö, Mumcuoğlu T, Aktaş Z, Akman A, Bayer A (2020) Characteristics of uveitic glaucoma in Turkish patients. Eur J Ophthalmol. https://doi.org/10.1177/1120672120950932
13. Lewis JM, Priddy T, Judd J et al (1988) Intraocular pressure response to topical dexamethasone as a predictor for the development of primary open-angle glaucoma. Am J Ophthalmol 106:607–612
14. Nuyen B, Weinreb RN, Robbins SL (2017) Steroid-induced glaucoma in the pediatric population. J AAPOS 21(1):1–6. https://doi.org/10.1016/j.jaapos.2016.09.026.Review
15. Bloch-Michel E, Nussenblatt RB (1987) International uveitis study group recommendations for the evaluation of intraocular inflammatory disease. Am J Ophthalmol 103:234–235
16. Tugal-Tutkun I, Güney-Tefekli E, Kamaci-Duman F, Corum I (2009) A cross-sectional and longitudinal study of Fuchs uveitis syndrome in Turkish patients. Am J Ophthalmol 148(4):510-515.e1. https://doi.org/10.1016/j.ajo.2009.04.007
17. Tugal-Tutkun I, Otük-Yasar B, Altinkurt E (2010) Clinical features and prognosis of herpetic anterior uveitis: a retrospective study of 111 cases. Int Ophthalmol 30(5):559–565. https://doi.org/10.1007/s10792-010-9394-8
18. Muñoz-Negrete FJ, Moreno-Montañés J, Hernández-Martínez P et al (2015) Current approach in the diagnosis and management of uveitic glaucoma. Biomed Res Int 2015:742792. https://doi.org/10.1155/2015/742792

19. Pang CE (2012). Review of cytomegalovirus anterior uveitis, inflammation, chronic diseases and cancer-cell and molecular biology, immunology and clinical bases. Dr Mahin Khatami (ed), InTech, Available from: http://www.intechopen.com/books/inflammation-chronic-diseases-and-cancer-celland-molecular-biology-immunology-and-clinical-bases/review-of-cytomegalovirus-anterior-uveitis
20. Carmichael A (2012) Cytomegalovirus and the eye. Eye (Lond) 26(2):237–240
21. Choi JA, Kim KS, Jung Y, Park HY, Park CK (2016) Cytomegalovirus as a cause of hypertensive anterior uveitis in immunocompetent patients. J Ophthal Inflamm Infection 6(1):32
22. Moorthy RS, Mermoud A, Baervedt G et al (1997) Glaucoma associated with uveitis. Surv Ophthalmol 41:361–394