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Research Paper

Ocular Hypertension and Glaucoma in Vogt Koyanagi Harada Syndrome

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ABSTRACT:

BACKGROUND:

Vogt-Koyanagi-Harada syndrome is a multisystem disease of autoimmune etiology, affecting melanocyte-containing tissue such as the uvea, ear, skin, and meninges.

OBJECTIVE:

is to determine the incidence of glaucoma and ocular hypertension in patients with Vogt-Koyanagi-Harada syndrome at a referral center in Iraq.

PATIENTS AND METHODS:

A prospective case series study, included patients diagnosed with Vogt Koyanagi Harada syndrome which was performed at the uveitis clinic in Ibn AL-Haitham teaching eye Hospital in Baghdad, Iraq from April 2021 to February 2022 (10 months). Detailed general and ophthalmic history was obtained and detailed ocular examination including best corrected visual acuity, intraocular pressure, and slit lamp examination as well as gonioscopy using three mirror lens were performed on the patients.

RESULTS:

Among 68 eyes of 36 patients with VKH, 44 eyes (64.7%) of 23 patients developed IOP elevation, Of these, 21 eyes (30.9%) of 11 patients had ocular hypertension and 23 eyes (33.8%) of 12 patients had glaucoma. The mechanisms of glaucoma were open angle in 20 eyes (87%) and angle closure in 3 eyes (13%). 18 eyes(78.3%) with glaucoma required surgical intervention consisting of trabeculectomy with Mitomycin C or Ahmed glaucoma valve, the latter was the procedure of choice which was done for 13 eyes(56.5%).

CONCLUSION:

According to this study the incidence of ocular hypertension was 30.9%, while the incidence of glaucoma was 33.8% in eyes with VKH disease. Open angle glaucoma according to gonioscopic finding was the most common mechanism of IOP elevation.

KEY WORDS: Glaucoma ,Ocular hypertension,Vogt koyanagi harada syndrome, Uveitis.

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Iraqi Postgraduate Medical Journal, 2025; Vol. 24(4): 531-536

DOI: 10.52573/ipmj.2024.154325 Received: September 12, 2024 Accepted: January 12, 2024

INTRODUCTION:

The idiopathic multisystem autoimmune disorder known as Vogt-Koyanagi-Harada (VKH) syndrome is characterized by inflammation of tissues that contain melanocytes, including the meninges, ear, and uvea. (1)

Clinical features and manifestations :

VKH syndrome manifestation occur in four stages;

1. The prodromal stage: is marked by flulike symptoms. patients present with headache, nausea, meningismus, tinnitus, fever, and hypersensitivity of the skin to touch. A Few days preceding the onset of ocular symptoms.(2)
2. Bilateral granulomatous anterior uveitis, varying degrees of vitritis, thickening of the posterior choroid, edema of the optic nerve, and multiple serous retinal detachments are the hallmarks of the acute uveitic stage, which is signaled by the onset of blurring of vision in both eyes 1-2 days after the onset of CNS signs.(3) The ciliary body and iris also be affected, and the anterior chamber may be shallow because of forward displacement of the lens–iris diaphragm as the result of ciliary body edema or annular choroidal detachment.(2)
3. Several weeks later, the convalescent stage is characterized by the resolution of the exudative retinal detachments and the gradual depigmentation of the choroid. In pigmented patients, particularly Japanese ones, this stage

results in the classic orange-red discoloration, sunset-glow fundus, and depigmented limbal lesions (Sugiura sign). [1]

4. Repeated episodes of granulomatous anterior uveitis (mutton fat keratic precipitates, anterior chamber response, iris nodules, iris stromal atrophy, and posterior synechiae)2 are indicative of the chronic recurrent stage [2]

OBJECTIVE:

This study aims to is to determine the incidence of glaucoma in patients with Vogt-Koyanagi-Harada syndrome at a referral center in Iraq.

PATIENTS AND METHODS:

This study is a prospective case series study, which was conducted at the uveitis clinic in Ibn AL-Haitham teaching eye Hospital. Approval has been obtained from the Iraqi board of medical specializations. This study included patients diagnosed with VKH syndrome who were attending the hospital from April 2021 to February 2022 (10 months). Included patients had the complete criteria of VKH disease (either at presentation or during the period of the study) based on the Revised International Diagnostic Criteria.[1] General and Ophthalmic history were taken from the patients. Any history of ocular trauma had been excluded. Gonioscopy using the Goldmann three mirror lens were performed that provided a detailed 360° view of the ACA. Although the diagnosis of VKH syndrome was mainly clinical, OCT imaging and fluorescein angiography were performed in required cases. Intraocular pressure measurements at the initial visit were recorded as (baseline IOP). Elevated IOP was defined as any measurement above 21 mmHg and it was measured using noncontact air puff tonometry (NT-530, NIDEK) and was corrected for central corneal thickness using Ehler formula; a nomogram that is used to correct the IOP measured for the errors induced due to variation in CCT. IOP rise occurring at least twice and separated by at least two weeks during the research period without any alterations to the optic disc was considered ocular hypertension (OHT).[5] While elevated IOP with the presence of characteristic disc changes (generalized/focal enlargement of the cup, the presence of parapapillary atrophy and splinter hemorrhage) or cup disc ratio asymmetry of > 0.2 between the two eyes associated with focal or diffuse thinning of the neuroretinal and retinal nerve fiber layer was categorized as glaucoma.[7] If more than 180 degrees of the posterior trabecular meshwork were not visible at gonioscopy without indentation, the iridocorneal angle was considered closed.[8] Visual field results were affected by the presence of cataract, posterior synechiae and retinal pigmentary changes and thus could not be used to diagnose glaucoma in our patients. All the patients underwent an IOP measurement at each visit. Treatments were given according to the stage and activity of the disease. YAG laser peripheral iridotomies were performed for cases with seclusio pupillae and iris bombe. While cases with glaucoma and persistent high IOP not responding to medical treatment were referred to glaucoma sub-specialties at Ibn Al Haitham teaching eye hospital for surgical management. Type of surgeries performed for glaucomatous eyes included trabeculectomies and Ahmed glaucoma valve implantations. Subgroup analysis was performed for 3 groups: group A consisted of eyes with neither OHT nor glaucoma, group B consisted of the ocular hypertensive eyes, and group C consisted of the glaucomatous eyes.

Statistical analysis:

Data input was done using Microsoft Excel 2019 ®. Data tabulation and management was done using International Business Machines Corporation® Statistical Package for the Social Sciences (SPSS®) version 23. Frequencies and percentages were used for descriptive statistics. When necessary, Fisher's Exact Test was modified to employ the chi-square test to evaluate the relationship between categorical variables. Independent samples T-test and Analysis of Variances (ANOVA) were used to compare means of normally distributed numerical variables, while Kruskal Wallis Test was used to compare numerical data that did not follow the normal distribution. Any P-value less than 0.05 was considered statistically significant throughout the study period.

RESULTS:

During the study period (from April 2021 to February 2022), there were 36 patients with VKH disease and 68 eyes met the inclusion criteria of this study. Four patients had lost one of their eyes due to complications of uveitis.

Demographics characteristics of the patients:

Forty-four eyes of 23 patients showed a rise in IOP. Of these, 21 eyes of 11 patients who had elevated IOP without optic disc changes or thinning of the neuro-retinal nerve fiber layer were included in group B as OHT patients. Twenty-three eyes of 12 patients showed sustained elevation in IOP with glaucomatous changes of optic discs and nerve fiber layer were included in group C. The remaining 24 eyes who had normal IOP and the optic disc throughout the study period were included in group A as shown in Table 1.

Table 1: Distribution of patients and eyes according to study group.

Variables	Group A	Group B	Group C	Total
	No. (%)	No. (%)	No. (%)	No. (%)
Number of patients	13 (36.1)	11 (30.6)	12 (33.3)	36 (100.0)
Number of eyes	24 (35.3)	21 (30.9)	23 (33.8)	68 (100.0)

Group A: patients with non-glaucomatous, non-ocular hypertensive eyes.
Group B: patients with ocular hypertensive eyes.
Group C: patients with glaucomatous eyes.

The mean age in group A was 32.31± 13.22 years and the mean age in group B was 35± 11.22 years and the mean age in group C was 31±13.2 years as shown in Table 2.

Table 2: Distribution of age according to study groups.

Age groups	Group A	Group B	Group C	Total
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**
10-19	2(15.4)	0(0)	3(25)	5(13.9)
20-29	3(23.1)	4(36.4)	2(16.7)	9(25)
30-39	5(38.5)	3(27.3)	3(25)	11(30.6)
40-49	1(7.7)	2(18.2)	4(33.3)	7(19.4)
50-59	2(15.4)	2(18.2)	0(0)	4(11.1)
Total	13(100)	11(100)	12(100)	36(100)

There was no statistically significant difference in the distribution of gender according to study groups, the female to male ratios were 1.17:1 in group A, 2.6:1 in group B and 0.7:1 in group C. As shown as shown in Table 3.

Table 3: Distribution of gender according to study groups.

Gender	Group A	Group B	Group C	Total	P-value between group*		
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**A/B**	**A/C**	**B/C**
Males	6(46.2)	3(27.3)	7(58.3)	16(44.4)	0.423	0.543	0.133
Females	7(53.8)	8(72.7)	5(41.7)	20(55.6)			
Total	13(100)	11(100)	12(100)	36(100)			

Classification of patients according to the stage of the disease at the time of presentation:

In Group A there were two (15.4%) patients presented with convalescent uveitis and one patient (7.7%) presented with acute uveitis, while all patients in group B and C presented with chronic relapsing disease, as shown in Table 4.

Table 4: Distribution of study groups according to the stage of uveitis.

Variables	Group A	Group B	Group C
	No. (%)	**No. (%)**	**No. (%)**
Acute	1(7.7)	0(0)	0(0)
Convalescent	2(15.4)	0(0)	0(0)
Chronic relapsing	10(76.9)	11(100)	12(100)
Total	13(100)	11(100)	12(100)

Intra ocular pressure:

During the study Forty-four eyes (64.7%) showed a rise in IOP. Of these, 21 eyes (30.9%) had elevated IOP without optic disc changes or thinning of the neuro-retinal nerve fiber layer were diagnosed as OHT, and were included in group B. Twenty three eyes (33.8%) of 12 patients showed sustained elevation in IOP with glaucomatous changes of optic discs and nerve

fiber layer were included in group C. The baseline IOP was significantly lower in group A in comparison to both groups B and C (P <0.001), as in group A it was 14.08±2.83 mmHg, in group B it was 27.33±7.03 mmHg, which showed fluctuations in the IOP measurement during the period of this study while in group C it was 31.48±8.8 mmHg as shown in Table-5.

Table 5: Distribution of groups according to baseline IOP.

Variables		Group A	Group B	Group C
Baseline IOP[#]	Mean± SD	14.08±2.83	27.33±7.03	31.48±8.8
	Range	8-21	15-50	21-53

Ocular findings:

Posterior synechiae were seen in only four(16.7%) group A eyes, 15(71.4%) group B eyes and 13 (56.5%) group C eyes, so they were significantly higher in groups B and C in comparison to group A. Iris Bombe was significantly observed more in group B eyes in comparison to group A (P= 0.017), with 5(23.8%) group B eyes in comparison to none in group A and only one eye (4.3%) in group C had iris bombe. On gonioscopy, without indentation Only three eyes had closed angle due to PAS, and all of them were in group C, and due to the small number of this observation it showed no statistically significant association with study groups, (the four lost eyes had hyoptony and severe corneal opacity precluding the visualization of the iris so they are excluded from the following findings) as shown in Table-6.

Table 6: Distribution of eyes according to iris related abnormality and study groups.

Variables		Group A	Group B	Group C	Total	P-value between group		
		No. (%)	No. (%)	No. (%)	No. (%)	A/B	A/C	B/C
Posterior synechiae	Yes	4(16.7)	15(71.4)	13(56.5)	32(47.1)	<0.001*	0.004*	0.305*
	No	20(83.3)	6(28.6)	10(43.5)	36(52.9)			
Iris Bombe	Yes	0(0)	5(23.8)	1(4.3)	6(8.8)	0.017**	0.489**	0.088**
	No	24(100)	16(76.2)	22(95.7)	62(91.2)			
ACA[#]	Open[1]	24(100)	21(100)	20(87)	65(95.6)	-	0.109**	0.234**
	Closed[2] by PAS	0(0)	0(0)	3(13)	3(4.4)			

*: Chi-square test, **: Fisher's Exact Test , [1]Open: defined as < 180 degrees of iridotrabecular contact without indentation.

[2] Closed: defined as > 180 degrees of iridotrabecular contact without indentation, PAS: peripheral anterior synechiae, [#]ACA: anterior chamber angle.

Management of Raised IOP:

All eyes in ocular hypertensive group and in the glaucomatous group received medical anti-glaucoma therapy at some time during follow up periods. And there were 5 eyes (23.8%) in group B that underwent PI in comparison to one eye (4.3%) (P= 0.007) in group C. While 13 eyes (56.5%) in group C underwent AVG and five eyes (21.7%) underwent trabeculectomy with mitomycin C in comparison to none in group B. The eyes that needed surgical intervention (AVG or trabeculectomy with mitomycin C) in group C were 18/23 (78.3%) eyes. As shown in Table 7.

Table 7: Distribution of study groups according to laser or surgical management of raised IOP.

Variables	Group B	Group C	Total	P-value*
	No. (%)	No. (%)	No. (%)	
Peripheral iridotomy	5(23.8)	1(4.3)	6(8.8)	0.007
Surgical management	No. (%)	No. (%)	No. (%)	
AGV	0(0)	13(56.5)	13(19.1)	
Trabeculectomy	0(0)	5(21.7)	5(7.4)	

AGV: Ahmed Glaucoma Valve, * Fisher's Exact Test

DISCUSSION:

This study describe the incidence of glaucoma and ocular hypertension in group of Iraqi patients who were diagnosed with VKH Syndrome at the time of presentation at referral center during an average follow up of 10 months. Glaucoma is a common complication in patients with chronic intraocular inflammation.[6] Our study demonstrates that glaucoma is a common complication of VKH Syndrome as well with an incidence of 33.8% and ocular hypertension with an incidence of 30.9% in comparison with the incidence that had been reported by other studies which ranging from 2.5 up to 45% .[3,4,5,9] This wide range in the incidence is due to the difference of criteria used to define OHT/glaucoma and different follow up periods.

In this study; female/male ratio in patients with glaucoma was 0.7 to 1, the age of them ranged from 11-49, and the mean age of presentation was 31.

Most studies reported no significant difference in gender distribution between patients with and without glaucoma,[3,4,9] as in our study.

In this study, the baseline IOP was significantly higher in glaucoma eyes compared to eyes without glaucoma in addition that eyes with ocular hypertension and eyes with glaucoma showed high fluctuation of IOP and this results were found in many previous studies.[4,5,10] This is because the attacks of exacerbations of uveitis are accompanied by ocular hypotony due to ciliary shut down. In our study, we found that open angle glaucoma was probably the most common mechanism that developed in 87%, Foster et al and Pandey et al also reported open angle as the most common mechanism with 56% and 69% respectively.[4,5] In our study, we found angle closure due to peripheral anterior synechiae in only 13% of eyes with glaucoma While a study done by Yang et al. in china reported angle closure in 50.6%.[7] This lower percentage in our study because we define angle closure based on the gonioscopic finding of >180 degree of iridotrabecular contact while in that study they include extensive posterior synechiae and pupillary block as part of angle closure disease. Even though indentation gonioscopy can distinguish between permanent and non-permanent appositional angle closure, this investigation used the Goldmann three mirror lens for gonioscopy because indentation gonioscopy was not accessible.In our study we found high prevalence of posterior synechiae 56.5% in eyes with glaucoma during the follow up period which is consistent with a study done by Veerappan et al. who found it in 65%.[9] Yang et al. found it in 55.4%.[7] Since all of our patients in the OHT/glaucoma group are in the chronic relapsing stage of the disease at presentation, the comparatively high prevalence of posterior synechiae in OHT/glaucoma eyes raises the possibility that VKH recurrent episodes of anterior segment inflammation may be a major mechanism in the development of glaucoma. In our study, 4.3% of glaucoma eyes and 23.8% of OHT eyes developed complete iris posterior synechiae and iris bombe configuration requiring immediate peripheral iridotomy, which is consistant with previous studies Yang et al found it in 28.9%, Guzman et al found it in 25.4%,[7,10] this may be because of severe and refractory anterior segment inflammation which is thought to be an important contributor to OHT/glaucoma in our population of VKH. Al-Kharashi et al. showed that the presence of posterior synechiae at initial presentation and a more severe anterior chamber reaction were linked to the development of glaucoma in VKH patients.[12] Regarding management of raised IOP, in our study all eyes with OHT and 5 eyes(21.7%) with glaucoma could be controlled with IOP lowering drugs combined with systemic corticosteroid and immune suppressive agents to control inflammation, while the surgical intervention was needed in 18 eyes(78.3%) with glaucoma which is slightly higher than a study done by Foster et al (68.7%) , Pandey et al. (56.2%),[4,5] While Yang et al. report surgical intervention in (44%). [7] This high prevalence of glaucoma surgery in our patients probably because of late presentation and inadequate treatment at an early stage of the disease.Ahmed glaucoma valve was the surgery of choice in our study which was done for 13 eyes(56.5%) while trabeculectomy with mitomycin C was done for 5 eyes (21.7%). In a study done by Guzman et al. in Mexico, the AGV was placed in 36.2% and trabeculectomy for 14.9%.[10] while Yang et al the AGV in 30.7% and trabeculectomy in 13.7%.[7] Most previous studies support the finding that AGV and trabeculectomy with mitomycin c achieve adequate IOP control in uveitic glaucoma eyes with a success rate higher for the Ahmed glaucoma valve.[4,5,11]

Our study's limitations include a small sample size, a brief follow-up period, and the fact that neuroretinal rim and retinal nerve fiber defects are difficult to assess due to disc and retinal swelling in VKH eyes. Additionally, the visual field could not be performed, which limits the

ability to detect the presence of glaucomatous visual field defects. Lastly, because our clinical facility is a tertiary referral center and most of our patients were referred after receiving initial care after varying lengths of time, we are unable to provide information about the onset of glaucoma and its timing.

CONCLUSION:

According to this study the incidence of ocular hypertension was 30.9%, while the incidence of glaucoma was 33.8% in eyes with VKH disease. According to gonioscopic finding open angle glaucoma was the most common mechanism of IOP elevation.

Recommendation:

The high incidence and complexity of glaucoma in those patients emphasize the significance of early detection, regular evaluation, and monitoring of intraocular pressure in patients with VKH.

Authorship from

Administrative Approvals

Approval were obtained from the council of Iraqi Board of Medical Specializations and Ibn AL-Haitham teaching eye Hospital.

Ethical Considerations and Official Approvals

Verbal permission was obtained from all patients before collecting data, and all informations were secured and used for research purposes only.

REFERENCES:

1. Kanski JJ, Bowling B. Clinical ophthalmology: a systematic approach. Elsevier Health Sciences; 2011.
2. Sen HN. Uveitis and ocular inflammation. American Academy of Ophthalmology; 2021.
3. Arevalo JF, Lasave AF, Gupta V, Kozak I, Al Harbi MB, Al Rushood AA, Al Dhibi HA. Clinical outcomes of patients with Vogt–Koyanagi–Harada disease over 12 years at a tertiary center. Ocular immunology and inflammation. 2016;24(5):521-29.
4. Forster DJ, Rao NA, Hill RA, Nguyen QH, Baerveldt G. Incidence and management of glaucoma in Vogt-Koyanagi-Harada syndrome. Ophthalmology. 1993;100(5):613-18.
5. Pandey A, Balekudaru S, Venkatramani DV, George AE, Lingam V, Biswas J. Incidence and management of glaucoma in Vogt Koyanagi Harada disease. Journal of glaucoma. 2016 ;25(8):674-80.
6. Panek WC, Holland GN, Lee DA, Christensen RE. Glaucoma in patients with uveitis. British Journal of Ophthalmology. 1990;74(4):223-27.
7. Yang P, Wang C, Su G, Pan S, Qin Y, Zhang J, Cao Q, Zhong Z, Zhou C, Wang Y, Kijlstra A. Prevalence, risk factors and management of ocular hypertension or glaucoma in patients with Vogt-Koyanagi-Harada disease. British Journal of Ophthalmology. 2021;105(12):1678-82.
8. Yang P, Liu X, Zhou H, Guo W, Zhou C, Kijlstra A. Vogt-Koyanagi-Harada disease presenting as acute angle closure glaucoma at onset. Clinical & experimental ophthalmology. 2011;39(7):639-47.
9. Veerappan M, Fleischman D, Ulrich JN, Stinnett SS, Jaffe GJ, Allingham RR. The relationship of vogt–koyanagi–harada syndrome to ocular hypertension and glaucoma. Ocular Immunology and Inflammation. 2017;25(6):748-52.
10. Alvarez-Guzman C, Valdez-Garcia JE, Ruiz-Lozano RE, Rodriguez-Garcia A, Navas-Villar CF, Hartleben-Matkin C, Pedroza-Seres M. Prevalence of Angle Closure Glaucoma in Vogt-Koyanagi-Harada Disease.
11. Bettis DI, Morshedi RG, Chaya C, Goldsmith J, Crandall A, Zabriskie N. Trabeculectomy with mitomycin C or Ahmed valve implantation in eyes with uveitic glaucoma. Journal of glaucoma. 2015;24(8):591-99.
12. Al-Kharashi AS, Aldibhi H, Al-Fraykh H, Kangave D, Abu El-Asrar AM. Prognostic factors in vogt-koyanagi-harada disease. International ophthalmology. 2007;27:201-10.