NEURO-OPHTHALMOLOGY
2022, VOL. 46, NO. 2, 80–84
https://doi.org/10.1080/01658107.2021.1984540

Course and Predictors of Visual Outcome of Idiopathic Intracranial Hypertension

Raed Behbehani, Abdullah Ali, and Ashraf Al-Moosa

Al-Bahar Ophthalmology Center, Ibn Sina Hospital, Kuwait

ABSTRACT

Idiopathic intracranial hypertension (IIH) is a clinical syndrome characterised by headache and papilloedema that can lead to significant visual morbidity. There are few studies in the literature about the visual outcome of IIH. We have reviewed the record of 76 patients with IIH according to the modified Dandy criteria. There was a significant improvement in the Humphrey 24-2 mean deviation (MD) in the study eyes (worse affected eye at presentation) in both the medically treated group (+2.0 dB; from −5.60 dB at baseline to −3.60 dB at final follow-up, $p < .01$) and in the fellow eyes in the medically treated group (+1.70 dB, from −4.40 dB at baseline to −2.74 dB at final follow-up, $p < .01$). Higher papilloedema grade (beta −0.66, $p < .001$) and age ($p < .02$) were inversely correlated with the final visual field MD in the study eye. The visual outcome for the IIH patients in our study was predominantly favourable, but patients with high-grade papilloedema had a worse visual prognosis and required more aggressive treatment.

ARTICLE HISTORY
Received 12 July 2021
Revised 18 August 2021
Accepted 18 September 2021

KEYWORDS
Idiopathic intracranial hypertension; Pseudotumor cerebri; visual outcome

Introduction

Idiopathic intracranial hypertension (IIH) is a syndrome diagnosed by the modified Dandy criteria, which include normal neuroimaging and cerebrospinal fluid (CSF) composition, high CSF opening pressure (OP) and no other neurological signs except those related to high intracranial pressure.[1] IIH is typically associated with obesity and the female gender at their young reproductive age. The reported annual incidence of IIH in Middle-Eastern populations by some studies is around 2.02–2.2 per 100,000, which is slightly higher than that in Western populations of around 1.6 per 100,000.[2,3] The incidence is thought to be increasing due to the rising obesity levels in many of these countries.[4]

There are limited data in the literature available focusing on predictors of visual outcome in IIH.[5,6] The IIH Treatment Trial (IIHTT) has shown that the visual outcome for patients with IIH treated with acetazolamide alongside weight loss and salt restriction was better than placebo combined with weight loss and salt restriction in cases of mild-to-moderate visual field loss at presentation.[5] Severe obesity and recent weight gain have been associated with a worse visual outcome of IIH.[7] Other reported risk factors for worse visual outcome are male gender, high-grade papilloedema and worse visual acuity at presentation.[8] IIH can lead to a significant visual deficit, and intervention may be required through optic nerve sheath fenestration (ONSF), CSF diversion procedures or venous sinus stenting.[9] We have examined the visual outcome for IIH in patients referred to the large tertiary neurology and neuro-ophthalmology referral centre in Kuwait.

Methods

We have retrospectively reviewed the medical records of patients diagnosed with IIH based on the modified Dandy criteria and who were examined by two neuro-ophthalmologists (RB and AM). Patients with any ocular condition or a disease of the retina or optic nerve or any intervening procedure during the follow-up that could have altered their visual outcome and patients who were on tetracycline medication at the time of diagnosis were excluded. All patients had magnetic resonance imaging and magnetic resonance venography of the brain and a lumbar puncture in the lateral decubitus position with measurement of the CSF OP. A neuro-ophthalmological examination

CONTACT Raed Behbehani rsbehbehani@gmail.com Al-Bahar Ophthalmology Center, Kuwait

was performed for all subjects, including visual acuity measurement, fundus examination and Humphrey automated perimetry (Carl Zeiss Meditec Inc., Dublin, CA, USA) using the 24-2 fast Swedish interactive threshold algorithm strategy at both baseline and the last follow-up assessment to measure the mean deviation (MD). Peripapillary retinal nerve fibre layer thickness (PRNFLT) of the optic nerve was obtained at the final follow-up using spectral-domain (SD) optical coherence tomography (OCT) (SD-OCT 3000, Topcon, Tokyo, Japan). Patients' demographic and clinical variables including age, sex, comorbid conditions, weight and height to calculate the body mass index (BMI) were obtained. Papilloedema was graded at presentation and final assessment as mild, moderate or severe, where mild papilloedema corresponded to Frisén grades 1 and 2, moderate papilloedema corresponded to Frisén grade 3 and severe papilloedema corresponded to Frisén grades 4 and 5.[10] The more affected eye (worse MD) at baseline was designated as the study eye. The final MD was recorded at the final assessment when patients had at least two consecutive visits following the resolution of papilloedema or the appearance of a flat pale optic disc. Snellen visual acuity was converted into a Snellen decimal visual acuity to aid statistical analysis.

Medical treatment for patients consisted of acetazolamide in a dose ranging from 1 to 4 g/day as tolerated in conjunction with recommendations for weight loss and salt restriction.

ONSF was performed as required using a transeyelid approach. The decision to perform ONSF was made clinically and was indicated for patients who presented with significant visual field deficit at presentation with severe high-grade papilloedema (fulminant IIH). In some of these patients, a short trial of medical treatment was attempted, but ONSF was performed with a few weeks if the visual function deteriorated. The study was approved by the Institutional Review Board.

Statistical analysis

Continuous and ordinal variables were reported as mean ± standard deviation. Categorical variables were reported as frequency and percentage. Comparison between the baseline and the final assessment visual field MD and between the baseline and final average Snellen decimal visual acuity was performed using the non-parametric Wilcoxon signed-rank test. Multivariable regression analysis was performed to determine if there was an independent effect of the clinical variables and predictors on the final visual field MD in the study or on attaining a favourable visual outcome defined as a final MD better than −3 decibels (dB) in the study eye. Statistical analysis was done using SPSS statistical package (IBM Corp., IBM SPSS, Version 27.0).

Results

We reviewed 76 patients with IIH in this study, and the clinical characteristics are shown in Table 1. Most of the patients (89.5%) were managed successfully with medical treatment (weight loss, diuretics and salt restriction), but 10.5% had a more severe and progressive visual loss at onset and required ONSF. Patients who required ONSF had more severe loss of visual acuity at presentation in the study eye compared with the medically

Table 1. Baseline clinical characteristics of the study subjects.

Patients (n = 76)		Mean ± SD or N (%)
Age (years)		29.6 ± 8.36
Duration of follow-up (months)		16.3 ± 11.3
Snellen decimal visual acuity	Baseline	0.82 ± 0.23
	Final follow-up	0.86 ± 0.40
OCT PRNFLT (μm) at final follow-up	Study eye	105.35 ± 15.31
	Fellow eye	109.04 ± 16.65
Gender	Female	66 (87%)
	Male	10 (13%)
BMI (kg/m^2)		33.8 ± 5.8
BMI categories (N = 70)	(20–25)	3 (3.9%)
	(25–30)	14 (18.5%)
	(30–40)	46 (60%)
	(>40)	5 (6.5%)
Lumbar puncture opening pressure (mmCSF)		388.5 ± 63.5
Presenting symptoms	Headache	57 (75%)
	Diplopia	17 (22.4%)
	Transient visual obscurations	25 (33%)
	Tinnitus	23 (30.3%)
Comorbid conditions	Anaemia	4 (5.3%)
	Migraine	9 (11.8%)
	Hypothyroidism	7 (9.2%)
	Diabetes	9 (11.4%)
	Hypertension	17 (22.4%)
	Recent weight gain	13 (17.1%)
Papilloedema grade	Mild	42 (55.3%)
	Moderate	22 (28.9%)
	Severe	12 (15.8%)
Treatment	Medical (weight loss, diuretics)	68 (89.5%)
	ONSF	8 (10.5%)

BMI: body mass index; CSF: cerebrospinal fluid; OCT: optical coherence tomography; ONSF: optic nerve sheath fenestration; PRNFLT: peripapillary retinal nerve fibre layer thickness; SD: standard deviation.

treated group (Snellen decimal visual acuity 0.45 ± 0.4 versus 0.86 ± 0.78, p = .03), worse MD in the study eye (−10.80 ± 4.15 dB versus −5.61 ± 2.92 dB, p < .001) and more severe thinning of the OCT PRNFLT in the study eye at the final assessment (88.25 ± 9.96 µm versus 106.90 ± 14.60 µm, p < .001). In addition, they were more obese (39.0 kg/m^2 versus 33.2 kg/m^2, p = .05) and had higher CSF OP (446.2 mmCSF versus 381.6 mmCSF, p = .01). Four of the subjects underwent bariatric surgery for weight loss as part of their treatment for IIH.

The change in vision scores according to the treatment group is shown in Table 2. A multivariable linear regression analysis model (R^2 = 0.58, p < .001) showed that severe papilloedema was inversely correlated with the final visual field MD in the study eye (beta = −0.66, p < .001) compared with mild papilloedema. Similarly, moderate papilloedema was inversely correlated (beta = −0.23, p < .01) with the final MD compared with mild papilloedema. There was a trend for BMI > 40 kg/m^2 to be inversely correlated with the final MD in the study eye (beta = −1.85, p = .07). None of the other clinical predictors (CSF OP, sex, recent weight gain, anaemia or transient visual obscurations) were independently associated with the final visual field MD in the study eye. Using a final MD ≥−3.0 dB in the study eye as a cut-off-point for a favourable visual outcome, binary logistic regression showed that increasing age by 1 year was associated with a 12% reduced probability of a favourable visual outcome (p < .02).

Discussion

We have found that the clinical course of IIH is generally favourable with medical treatment as the MD improved from baseline to final follow-up visit in both the study eyes (+2.0 ± 1.90 dB) and the fellow eyes (+1.70 ± 1.69 dB, p < .01). This is similar to the improvement in MD reported in the IIHTT and other studies in medically treated patients.[5,11] The IIHTT examined the therapeutic benefit of acetazolamide with a low-sodium weight-reduction diet for patients with mild-to-moderate visual loss and found that there was a mean improvement in MD with acetazolamide (+1.43 dB) at 6 months compared with placebo (+0.71 dB) with a treatment effect of +0.71 dB.[9] Only seven cases in the IIHTT met the criteria of treatment failure defined as worsening of >2 dB in MD in patients with baseline MD −2 to −3.5 dB or >3 dB worsening in MD in patients with baseline MD −3.5 to −7 dB. Risk factors for treatment failure in the IIHTT were male gender, high-grade papilloedema and worse visual acuity at baseline.[8] None of our study subjects met the criteria for treatment

Table 2. Baseline and final visual field mean deviation and acuity in the study eye (worse affected eye) and the fellow eyes (better eye) and baseline and final mean Snellen decimal visual acuity in both the medically treated group and the optic nerve sheath fenestration group.

Treatment group		Mean ± SD	Change from baseline to final	p-Value
Medical treatment	Baseline Snellen decimal visual acuity	0.85 ± 0.78	0.03 ± 0.77	<0.01
	Final Snellen decimal visual acuity	0.88 ± 0.20		
	Baseline MD study eye (dB)	−5.60 ± 2.92	+2.0 ± 1.90	<0.01
	Final MD study eye (dB)	−3.61 ± 2.66		
	Baseline MD fellow eye (dB)	−4.40 ± 2.40	+1.67 ± 1.69	<0.01
	Final MD fellow eye (dB)	−2.73 ± 2.27		
	Final OCT PRNFLT study Eye (µm)	107 ± 14.60		
ONSF	Baseline Snellen decimal visual acuity	0.45 ± 0.40	0.19 ± 0.24	<0.03
	Final Snellen decimal visual acuity	0.65 ± 0.36		
	Baseline MD study eye (dB)	−10.70 ± 4.15	+1.80 ± 1.88	<0.03
	Final MD study eye (dB)	−8.96 ± 5.27		
	Baseline MD fellow eye (dB)	−9.0 ± 3.90	+1.93 ± 1.83	<0.02
	Final MD fellow eye (dB)	−7.00 ± 3.82		
	Final OCT PRNFLT study eye (µm)	88.25 ± 9.96		

p-Value <0.05 was considered significant (Wilcoxon signed-rank test).
dB: decibel; OCT: optical coherence tomography; ONSF: optical coherence tomography; PRNFLT: peripapillary retinal nerve fibre layer thickness; SD: standard deviation.

failure as defined by the IIHTT, although our study included patients with more variable visual impairment at onset as some of our patients had severe visual loss at onset and required surgical intervention.

Other reported risk factors associated with poor IIH visual outcome include BMI, frequent transient visual obscurations and the absence of headache.[7,12–14] Szewka et al. found that patients with BMI ≥40 kg/m^2 were more likely to have severe papilloedema at presentation than those with a lower BMI, with a trend towards more severe visual loss in one or both eyes at the last follow-up.[7] Skau et al. followed 17 IIH patients over a 3-month period using OCT, visual field testing and CSF OP measurements, and they found that in patients with weight loss >3.5% of BMI, measured CSF OP decreased significantly (p = .0003).[15]

Kuwait ranks the first among Middle Eastern countries in obesity prevalence in women (55.2%), which is slightly higher than obesity in European countries and is comparable to the US obesity prevalence of 48.3%.[4] There was a relatively high prevalence of diabetes (11.4%) and hypertension (22.8%) in our study, which are common comorbidities associated with obesity. Four of our subjects (5%) underwent bariatric surgery for weight loss as part of treatment for IIH.

Almost 45% of our subjects had either moderate or severe papilloedema, and we have found that higher baseline papilloedema grade was associated with a worse visual field MD in the study eye at presentation.[16]

Five patients had a final OCT PRNFLT of <81 μm (less than 5th percentile) in their study eyes at the final follow-up in assessment. They were all females, with BMI range from 37 to 50 kg/m^2 and CSF OP ranging from 350 to 550 mmCSF. Two of these subjects had moderate and three had severe papilloedema at baseline. Two were treated medically, while three were treated with ONSF. In the IHTT, 10 study eyes and nine fellow eyes had PRNFLT at less than the 5th percentile at 6 months, but this was not associated with worse MD or final visual acuity. One explanation for this discrepancy is that the associated visual morbidity is not only due to optic atrophy but other mechanisms such as outer retinal changes, subretinal fluid and peripapillary retinal neovascularisation, all of which have also been shown to determine the final visual outcome.[17] Chen et al. found that measuring the ganglion-cell inner plexiform layer (GCIPL) is probably a more robust OCT predictor of visual outcome in IIH than RNFLT as diminished GCIPL thickness in the early stages of papilloedema correlated with a poor visual outcome.[17]

Our study is limited by its retrospective nature and the referral bias to a tertiary care centre; nevertheless, they were from the main tertiary care centre for neuro-ophthalmology and neurology, and thus, they should reflect the clinical profile of IIH in the general population. There are eight patients whose weight and height data were missing, and thus, their BMI could not be calculated; however, they were generally described as either overweight or obese. Some of the variables we obtained, such as recent weight gain, relied on self-reporting, and weight loss was not determined objectively in the follow-up. The study subjects generally had good visual outcome with medical treatment, which precluded identifying more risk factors for a poor visual outcome or treatment failure. In determining the OCT outcome, we have only used the PRNFLT, and we have not used the GCIPL thickness, which would probably be more accurate and less affected by disc swelling. Finally, there may have been a preference and selection bias for the procedure performed (ONSF) for patients with progressive loss of vision at onset and those who did not respond to initial medical treatment. Other procedures such as ventriculo-peritoneal shunting or venous sinus stenting were not performed on any patients in this study, but they may be the preferred procedures in different centres and settings. However, our aim in this study was not to compare the visual outcome for various modalities of treatment for IIH but rather to demonstrate the visual outcome based on a set of independent clinical factors related to patients.

In summary, we have found that IIH patients in our study had predominantly a good visual outcome with medical treatment. However, patients with high-grade papilloedema at presentation were at a higher risk for a worse visual outcome and therefore required more aggressive treatment.

Declaration of interest statement

We declare that we have no financial conflict to disclose.

Funding

The author(s) reported that there is no funding associated with the work featured in this article.

ORCID

Raed Behbehani http://orcid.org/0000-0002-6633-3567
Abdullah Ali http://orcid.org/0000-0001-8963-5931

References

1. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the Pseudotumor cerebri syndrome in adults and children. *Neurology*. 2013 Sep 24;81(13):1159–1165. PubMed PMID: 23966248. doi:10.1212/WNL.0b013e3182a55f17.
2. Kesler A, Stolovic N, Bluednikov Y, et al. The incidence of idiopathic intracranial hypertension in Israel from 2005 to 2007: results of a nationwide survey. *Eur J Neurol*. Aug 2014;21(8):1055–1059. PubMed PMID: 24698554. doi:10.1111/ene.12442.
3. Almarzouqi SJ, Morgan ML, Lee AG. Idiopathic intracranial hypertension in the Middle East: a growing concern. *Saudi J Ophthalmol*. 2015 Jan-Mar;29(1):26–31. PubMed PMID: 25859136; PubMed Central PMCID: PMCPMC4314590. doi:10.1016/j.sjopt.2014.09.013.
4. Karageorgi S, Alsmadi O, Behbehani K. A review of adult obesity prevalence, trends, risk factors, and epidemiologic methods in Kuwait. *J Obes*. 2013;2013:378650. doi:10.1155/2013/378650.
5. Wall M, Johnson CA, Cello KE, et al. Visual field outcomes for the idiopathic intracranial hypertension treatment trial (IIHTT). *Invest Ophthalmol Vis Sci*. Mar 2016;57(3):805–812. PubMed PMID: 26934136; PubMed Central PMCID: PMCPMC4777274. doi:10.1167/iovs.15-18626.
6. Takkar A, Goyal MK, Bansal R, et al. Clinical and neuro-ophthalmologic predictors of visual outcome in idiopathic intracranial hypertension. *Neuroophthalmology*. Aug 2018;42(4):201–208. PubMed PMID: 30042789; PubMed Central PMCID: PMCPMC6056212. doi:10.1080/01658107.2017.1400570.
7. Szewka AJ, Bruce BB, Newman NJ, et al. Idiopathic intracranial hypertension: relation between obesity and visual outcomes. *J Neuroophthalmol*. Mar 2013;33(1):4–8. PubMed PMID: 22217456; PubMed Central PMCID: PMCPMC3323689. doi:10.1097/WNO.0b013e31823f852d.
8. Wall M, Falardeau J, Fletcher WA, et al. Risk factors for poor visual outcome in patients with idiopathic intracranial hypertension. *Neurology*. 2015 Sep 1;85(9):799–805. PubMed PMID: 26245929; PubMed Central PMCID: PMCPMC4553022. doi:10.1212/WNL.0000000000001896.
9. Friedman DI, McDermott MP, Kieburtz K, et al. The idiopathic intracranial hypertension treatment trial: design considerations and methods. *J Neuroophthalmol*. Jun 2014;34(2):107–117. PubMed PMID: 24739993. doi:10.1097/WNO.0000000000000114.
10. Sinclair AJ, Burdon MA, Nightingale PG, et al. Rating papilloedema: an evaluation of the Frisen classification in idiopathic intracranial hypertension. *J Neurol*. Jul 2012;259(7):1406–1412. PubMed PMID: 22237821. doi:10.1007/s00415-011-6365-6.
11. D'Amico D, Curone M, Erbetta A, et al. Intracranial idiopathic hypertension: 1-year follow-up study. *Neurol Sci*. May 2014;35(Suppl 1):177–179. PubMed PMID: 24867861. doi:10.1007/s10072-014-1765-x.
12. Orcutt JC, Page NG, Sanders MD. Factors affecting visual loss in benign intracranial hypertension. *Ophthalmology*. 1984 Nov;91(11):1303–1312. PubMed PMID: 6514295. doi:10.1016/s0161-6420(84)34149-5.
13. Digre KB, Corbett JJ. Pseudotumor cerebri in men. *Arch Neurol*. 1988 Aug;45(8):866–872. PubMed PMID: 3395260. doi:10.1001/archneur.1988.00520320056015.
14. Wall M, George D. Idiopathic intracranial hypertension. A prospective study of 50 patients. *Brain*. 1991 Feb;114(Pt 1A):155–180. PubMed PMID: 1998880.
15. Skau M, Sander B, Milea D, et al. Disease activity in idiopathic intracranial hypertension: a 3-month follow-up study. *J Neurol*. Feb 2011;258(2):277–283. PubMed PMID: 20853113. doi:10.1007/s00415-010-5750-x.
16. Micieli JA, Bruce BB, Vasseneix C, et al. Optic nerve appearance as a predictor of visual outcome in patients with idiopathic intracranial hypertension. *Br J Ophthalmol*. Oct 2019;103(10):1429–1435. PubMed PMID: 30530819. doi:10.1136/bjophthalmol-2018-313329.
17. Chen JJ, Thurtell MJ, Longmuir RA, et al. Causes and prognosis of visual acuity loss at the time of initial presentation in idiopathic intracranial hypertension. *Invest Ophthalmol Vis Sci*. Jun 2015;56(6):3850–3859. PubMed PMID: 26070058; PubMed Central PMCID: PMCPMC4697859. doi:10.1167/iovs.15-16450.