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Idiopathic Intracranial Hypertension: Relation Between Obesity and Visual Outcomes

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Abstract

Background—Increased body mass index (BMI) has been associated with increased risk of idiopathic intracranial hypertension (IIH), but the relationship of BMI to visual outcomes in IIH is unclear.

Methods—A retrospective chart review of all adult cases of IIH satisfying the modified Dandy criteria seen at our institution between 1989 and 2010 was performed. Demographics, diagnostic evaluations, baseline visit and last follow-up examination data, treatment and visual outcome data were collected in a standardized fashion. Groups were compared and logistic regression was used to evaluate the relationship of BMI to severe visual loss, evaluating for interaction and controlling for potential confounders.

Results—Among 414 consecutive IIH patients, 158 had BMI ≥ 40 (WHO Obese Class III), and 172 had BMI 30–39.9. Patients with BMI ≥ 40 were more likely to have severe papilledema at first neuro-ophthalmology encounter than those with a lower BMI ($p=0.02$). There was a trend toward more severe visual loss in one or both eyes at last follow up among those patients with BMI ≥ 40 (18 vs. 11%, $p=0.067$). Logistic regression modelling found that ten unit (kg/m^2) increases in BMI increased the odds of severe visual loss by 1.4 times (95%CI: 1.03–1.91, $p=0.03$), after controlling for sex, race, diagnosed hypertension, and diagnosed sleep apnea.

Conclusion—Our finding of a trend for severe papilledema and visual loss associated with increasing BMI suggests that very obese IIH patients should be closely monitored for progression of visual field loss.

Keywords

Idiopathic Intracranial Hypertension; Body Mass Index; Obesity; Visual Outcomes; Severe Vision Loss; Risk Factors

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Introduction

Idiopathic intracranial hypertension (IIH) is a syndrome characterized by increased intracranial pressure of unknown cause, occurring most commonly in obese women of childbearing age (1). Multiple studies have found an association between IIH and obesity (2–4), but it is unclear whether obesity is also a risk factor for poor visual outcomes in IIH. We hypothesized that higher BMI at diagnosis was a risk factor for worse visual outcomes in IIH.

Methods

The study was approved by our Institutional Review Board. All consecutive post-pubertal patients with definite IIH, according to the modified Dandy criteria (5), seen by our neuro-ophthalmology service from 1989 to 2010 were included.

Although the study was a retrospective chart review, all patients had been evaluated in a standardized fashion by experienced neuro-ophthalmologists (N.N., V.B., B.B.), including documentation of height, weight, blood pressure, and complete neuro-ophthalmic examination with formal visual fields, fundus photography, and review of neuroimaging tests. Demographic information regarding age, gender, and race were collected. Symptoms, medication use (particularly antibiotics, immunosuppressant agents, oral contraceptives, and vitamin A preparations), associated factors (recent weight gain, known sleep apnea, anemia [hemoglobin <12 g/dL], systemic hypertension, pregnancy, and endocrine disorders [polycystic ovarian syndrome, diabetes mellitus, and thyroid dysfunction]) were recorded (6). Pre-diagnosis duration of symptoms, CSF opening pressure, medical and surgical treatments, follow-up duration, and visual outcomes were also recorded. MRIs were all reviewed at the time of diagnosis and MR venography or CT venography was obtained when there was a doubt regarding possible cerebral venous thrombosis. Those patients who could not have a MRI had a head CT with contrast, often accompanied by CT venography. Body mass index (BMI) was routinely documented on all IIH patients and where it was not available, it was calculated from documented height and weight. BMI was divided into categories corresponding to World Health Organization BMI cutoff points (7–8): normal (18.5–24.9), overweight (25–29.9), class I/II obesity (30–39.9), and class III obesity (≥40).

Snellen visual acuity was converted to logMAR for analysis. Visual fields (Goldmann or Humphrey) were systematically reviewed and graded on a 1 to 4 scale as 1) normal; 2) enlargement of the blind spot; 3) nasal or temporal defect; or 4) diffusely constricted. Papilledema was graded with the Frisén staging scheme (9) by systematic review of fundus photography: stage 0 defines a normal optic nerve head and stage 5, severe papilledema. Severe visual loss in an eye was defined by the US criteria for legal blindness (best-corrected visual acuity ≥20/200 or total central visual field <20°) and assessed at the last available visit.

Statistical analysis was performed with R: A language and environment for statistical computing (R Foundation for Statistical Computing, <http://www.R-project.org>). Continuous and ordinal variables were compared using the Mann–Whitney U test. Pearson chi square with Yates continuity correction or Fisher exact test, as appropriate, were used to compare categorical variables. A test for linear trend of proportions was performed using the median of each BMI category. Tests were two tailed, and significance was set at 5%. With severe visual loss in at least one eye as the outcome, the effect of BMI as primary exposure of interest was assessed with logistic regression. Race, gender, sleep apnea, hypertension, the patient's grade of papilledema at first visit (calculated as the mean of the two eyes), and

diagnosed endocrine disease, were the variables studied as potential confounders/effect modifiers based on their significance in univariate analyses of BMI and severe visual loss. The final model was determined by the method described by Kleinbaum and Klein (10).

Results

We included 414 patients with IHH. There were 383 (93%) women. The median age at diagnosis was 28 years (range: 13–62). Overall, 44% of our study population were black, with the non-black population including whites (Hispanic and non-Hispanic) and Asians.

The characteristics of our patients with BMI<40 and BMI ≥40 are summarized in Table 1. There was a higher percentage of black patients in the BMI ≥40 group (48.7%) compared with BMI<40 group (40.6%). Patients with BMI ≥40 had higher rates of several medical conditions: diagnosed sleep apnea (16.5% vs 5.1%, $p<0.001$), endocrine disorders (18.4% vs 8.6%, $p=0.003$) and hypertension (25.3 vs 13.7%, $p=0.003$). Except for possibly fewer patients with transient visual obscurations as the first sign of disease in the BMI ≥40 group (7.6% vs 13.3%, $p=0.07$), there were no other differences in presenting symptoms. Patients with BMI ≥40 seemed less likely to be symptomatic at presentation (0.8% vs 3.8%, $p=0.06$). There was no difference in pre-diagnosis duration of symptoms, frequency of recent weight gain, medication use, CSF shunting procedures, or optic nerve sheath fenestration between groups (Table 1). Mean recent weight gain was higher among patients with BMI ≥40 (6.0 vs. 3.6 kg, $p=0.04$, independent sample t-test), but there was no difference in the mean recent weight gain between patients with severe visual loss and those without (3.9 vs. 4.6 kg, $p=0.61$).

There was a trend toward worse visual acuity and visual field grade among patients with BMI ≥40 compared with patients with a lower BMI (Table 2), but no difference in the mean deviation of Humphrey visual field testing. Median stage of papilledema was equal between the two groups, but there was an over-representation of stage 4 and 5 papilledema seen in patients with BMI ≥40 at both first and last examinations. Severe visual loss occurred more frequently at last follow up (in one or both eyes) among those with BMI ≥40 compared with those with a lower BMI (18 vs. 11%, $p=0.067$).

There was an unadjusted linear trend of an increasing proportion of patients with visual loss with increasing obesity class (Table 3, $p<0.05$). In multivariable logistic regression analysis, black race (OR 2.21, 95% CI 1.22 to 4.07) and male gender (OR 2.91, 95% CI 1.09–7.20) were independent risk factors for visual loss. Hypertension and sleep apnea were not found to have a significant effect on severe visual loss, nor did their exclusion from the model change the magnitude of effect attributed to BMI by more than 10%, but they were retained in the final model based on their potential confounding effects suspected from previous studies (6,11). Diagnosed endocrine disorder and papilledema grade were excluded from the model because they did not change the magnitude of effect attributed to BMI by more than 10% and led to reduced precision of the estimates. In addition, papilledema grade was excluded from the model, because controlling for intermediates (i.e., papilledema grade) in the causal pathway between the exposure of interest (i.e., BMI) and the outcome (i.e., severe visual loss) could lead to bias in the exposure's estimate of effect (10). The logistic model shows that there is a 1.4 times greater odds (95%CI: 1.03–1.91, $p=0.03$) of severe vision loss for every 10 unit increase in BMI and a 2.0 times greater odds of severe visual loss for every 20 unit increase in BMI, after controlling for sex, race, diagnosed hypertension, and diagnosed sleep apnea (Table 4).

Discussion

Our study shows that higher BMI at diagnosis is associated with increased risk of severe visual loss in IHH, independent of other known risk factors, providing another variable to consider when evaluating IHH patients. This is especially important information in light of the growing epidemic of obesity throughout the world (12,13). Few studies have addressed the role of the degree of obesity in vision loss in IHH. One multicenter retrospective review of 107 patients found that weight alone was not significantly different between groups with no visual dysfunction, definite visual function deterioration, and severe visual loss (14). A case-control study of 34 IHH patients reported an increased risk of IHH with increasing BMI but found no association between visual outcomes and increasing BMI when using vision-specific quality-of-life surveys (3). Another study showed no association between visual field deficits at time of diagnosis and BMI, weight gain or percent change in ideal body weight, but did not specifically consider severe visual loss (15). In one case control study of 50 patients (2), the amount of recent weight gain, but not the degree of obesity, was significantly higher among the five patients who experienced visual deterioration. We did not find a similar association in our study, although the severely obese patients reported a higher amount of recent weight gain, as might be expected. In a recent report of 18 IHH patients with normal BMI, none of the patients had severe visual loss (7). To our knowledge, no prior study has demonstrated a relationship between obesity and vision loss. The size of these older studies likely limited their power to detect such a difference and most failed to control for confounding effects such as gender and race. In addition, because visual outcomes in IHH are usually good, particularly central visual acuity, summary measures (e.g., means and medians) are unsurprisingly similar and may mask the substantial differences in the risk of severe visual loss as body mass index increases. Our failure to demonstrate a difference in mean deviation on automated visual field testing while finding a trend toward a worse visual field grade at the last visit in more obese patients, likely reflects our practice to obtain Goldmann visual fields when patients cannot reliably perform automated testing (e.g., those with severe visual loss).

Previous reports have found an association between papilledema grade and visual loss, especially in cases of severe papilledema (1). In our study, although there was no obvious difference in median papilledema grades between the groups, there was an over-representation of grades 4-5 papilledema among more obese patients. Since severely obese patients were also more likely to be asymptomatic, they may have been exposed to the deleterious effects of papilledema for a longer period of time before presentation, and this could explain their higher risk for visual loss.

Limitations of our study include its retrospective nature. However, all patients were systematically evaluated in a standardized fashion in a single neuro-ophthalmic center. Because most of our patients are requested consultations from ophthalmologists or neurologists, they may manifest a more severe clinical presentation, resulting in referral bias. Additionally, this referral pattern makes it likely that in some cases, treatment may have begun prior to our first documented neuro-ophthalmic examination. Finally, we measured visual acuity using Snellen charts as a part of routine clinical practice, rather than in a standardized research setting using ETDRS charts, but we appropriately converted our measurements to the logMAR scale for analysis.

Our finding of a trend for severe papilledema and visual loss associated with increasing BMI suggests that very obese IHH patients should be closely monitored for progression of visual field loss. If progression is seen, early consideration for definitive surgical intervention may be especially important in IHH patients with multiple risk factors for severe vision loss, including black race, male sex, anemia, hypertension, and very high BMI. While it has been

definitively shown that aggressive efforts at weight loss often lead to remission of the disease, whether these efforts also reduce the risk of severe visual loss in very obese IIIH patients remains to be determined.

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Demographics, risk factors, opening pressure and treatment of patients with idiopathic intracranial hypertension with BMI<40 and BMI 40

Table 1

	BMI <40 (n=256)		BMI 40 (n=158)		pValue
Demographics/risk factors	N or median	% or range	N or median	% or range	
Age, y	29.5	[13–62]	28	[13–59]	0.37
Gender [M/F]	15/241	[5.9%/94.1%]	16/142	[10.1%/89.9%]	0.10
Race					0.10
Black	104	[40.6%]	77	[48.7%]	
Non-black	152	[59.4%]	81	[51.3%]	
Contributing medications *	21	[8.2%]	13	[8.2%]	0.99
Sleep Apnea	13	[5.1%]	26	[16.5%]	<0.001
Anemia	14	[5.5%]	13	[8.2%]	0.26
Endocrine disorder	22	[8.6%]	29	[18.4%]	0.003
Hypertension	35	[13.7%]	40	[25.3%]	0.003
Symptoms					
Headache	231	[90.2%]	138	[87.3%]	0.36
Pulsatile tinnitus	104	[40.6%]	58	[36.7%]	0.43
Diplopia	52	[20.3%]	27	[17.1%]	0.42
Transient visual obscurations	97	[37.9%]	66	[41.8%]	0.43
None	2	[0.8%]	6	[3.8%]	0.06
Pre-diagnosis duration of symptoms (wk, n=369)	5.5	[0–500]	5.0	[0–250]	0.35
Follow-up duration (wk, n=376)	23.5	[0–368]	15.0	[0–279]	0.09
CSF opening pressure (cm CSF, n=339)	37	[20–60]	36	[20–75]	0.85
Recent weight gain present (self-reported), n=396)	68	[26.6%]	44	[27.8%]	0.77
Treatment					
Medication **	239	[93.4%]	145	[91.8%]	0.54
Diet Modification	102	[39.8%]	71	[44.9%]	0.31
Number of lumbar punctures	1	[1–18]	1	[1–20]	0.30
CSF Shunt	65	[25.4%]	30	[19%]	0.13

	BMI <40 (n=256)	BMI 40 (n=158)	
Optic nerve sheath fenestration			0.41
Unilateral	15 [5.9%]	11 [7%]	
Bilateral	7 [2.7%]	8 [5.1%]	

BMI (body mass index), y (years), CSF (cerebrospinal fluid), wk (weeks)

* Contributing medications include vitamin A preparations, minocycline, doxycycline, tetracycline, depot progestins, oral contraceptives, cyclosporine, tacrolimus and recent discontinuation of steroids.

** With acetazolamide, furosemide or topiramate

Table 2

Clinical Examination Results of IIH patients with BMI <40 and BMI ≥ 40.

	BMI <40 (n=256)	BMI ≥ 40 (n=158)	
Demographics/risk factors	N or median (% or range)	N or median (% or range)	pValue
Visual acuity, first visit (logMAR, n=409)	0.1 (−0.3,6.9)	0.1 (−0.3,5.3)	0.12
Visual acuity, last visit (logMAR, n=363)	0.0 (−0.3,6.9)	0.1 (−0.3,6.9)	0.06
Visual field grade, first visit (n=381)	2.5 (1.0,4.5)	2.5 (1.0,4.0)	0.74
Visual field grade, last visit (n=356)	2.0 (1.0,4.0)	2.0 (1.0,4.0)	0.08
HVF MD, first visit (n=284)	−4.5 (0.2,−33.5)	−4.6 (0.3, −33.4)	0.32
HVFMD, last visit (n=289)	−3.3 (0.1,−29.3)	−3.6 (0.3,−33.1)	0.36
Severe visual loss (n=414)	29 (11.3%)	28 (17.7%)	0.07
Papilledema, first exam(n=385)			0.02
0	10 (4%)	4 (2%)	
1	23 (10%)	15 (10%)	
2	59 (25%)	23 (16%)	
3	81 (34%)	51 (34%)	
4	41 (17%)	36 (24%)	
5	23 (10%)	19 (13%)	
Papilledema, last exam(n=361)			0.08
0	98 (45%)	56 (39%)	
1	61 (28%)	38 (26%)	
2	42 (19%)	28 (19%)	
3	15 (7%)	11 (8%)	
4	1 (<1%)	7 (5%)	
5	0 (0%)	4 (3%)	

Severe visual loss = corrected visual acuity less than or equal to 20/200 or total visual field less than 20°.

HVF MD = Humphrey visual field mean deviation (dB).

Table 3

Risk of severe visual loss by obesity category

Obesity Class (BMI)	Severe visual loss	Total	%*
Not obese (<25)	0	23	0.0
Overweight (25–29.9)	4	61	6.5
Grade I/II obese (30–39.9)	25	172	14.5
Grade III obese (≥ 40)	28	158	17.7

*
p for linear trend < 0.05

Table 4

Odds ratios for Severe Visual Loss as Outcome (Final Logistic Model)

Variable	Odds Ratio	95% Confidence Interval	p Value
BMI per 10 kg/m²	1.40	1.03–1.91	0.03
Male gender	2.91	1.09–7.20	0.02
Black race	2.21	1.22–4.07	0.01
HTN	1.54	0.75–3.04	0.23
Sleep Apnea	0.54	0.17–1.46	0.26

BMI: body mass index, HTN: hypertension; Intercept: −3.69; Deviance: 311.96; Homer-Lemeshow test, p=0.29