



# Pediatric Idiopathic Intracranial Hypertension: Clinical Presentations, Risk Factors, and Prognostic Indicator

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## Abstract

**Background:** Idiopathic intracranial hypertension (IIH) is characterized by elevated cerebrospinal fluid pressure without space-occupying lesions, infections, or alterations in brain parenchyma. Diagnosing IIH in children poses a significant challenge for pediatricians, given the often nonspecific nature of clinical signs and symptoms.

**Objectives:** Our study aims to evaluate the clinical presentations and potential risk factors among pediatric individuals diagnosed with IIH, considering the limited research in this particular domain.

**Methods:** Clinical data from pediatric patients diagnosed with IIH who sought care at Tehran's primary referral children's hospitals were collected from 2013 to 2021, spanning eight years. These patients were subsequently contacted to follow up on the presence of persistent headaches and visual problems. Detailed records of their initial signs and symptoms were documented. To identify prognostic factors associated with persistent headaches and visual problems in pediatric IIH patients, binary logistic regression analysis was conducted.

**Results:** A total of 81 pediatric patients were included in the study, with a mean age of  $13.56 \pm 4.404$  years at the time of their IIH diagnosis. The most frequently reported clinical symptom among these patients was headache, observed in 85.2% of cases, followed by diplopia (50.6%), visual impairment (46.9%), and nausea with/without vomiting (44.4%). Furthermore, a substantial proportion of the patients were underweight (weight percentiles  $< 3$ ). Our analysis showed that male patients and those without strabismus experienced significantly more recurrent episodes of IIH ( $P = 0.013$  and  $P = 0.013$ , respectively). Notably, recurrent episodes and higher weight percentiles emerged as predictive factors for future persistent visual problems within our study population ( $P = 0.032$  and  $P = 0.045$ , respectively).

**Conclusions:** Recurrence of IIH was significantly less in female patients and those with strabismus. Additionally, we found that both lower and higher weight percentiles, as well as the occurrence of recurrent episodes, served as predictive factors for the development of persistent visual problems. However, our model could not predict persistent headaches.

**Keywords:** Pseudotumor Cerebri, Intracranial Hypertension, Idiopathic, Pediatrics, Headache, Vision Disorders

## 1. Background

Idiopathic intracranial hypertension (IIH) is characterized by elevated cerebrospinal fluid pressure without any underlying brain abnormalities, space-occupying lesions, infections, or alterations in the brain parenchyma (1, 2). Typically, IIH presents with the primary symptom of headache, which can be particularly challenging to diagnose in younger children (3). As a result, diagnosing IIH in the pediatric

population remains a significant challenge. The annual incidence of IIH in pediatric patients is estimated to be less than one case per 100 000 individuals, although this may underestimate its true prevalence due to diagnostic complexities (4). Given the potential complications of IIH, such as visual impairment and persistent symptoms (5), a more comprehensive understanding of this condition is essential (6).

Even after normalizing intracranial pressure, some patients experience persistent symptoms, including

headache, depression, and anxiety (7, 8). Effective management of IIH necessitates a multidisciplinary approach, including pharmacotherapy, lifestyle adjustments, and, in some cases, neurosurgical interventions like shunt insertion and optic nerve sheath fenestration (9, 10). Notably, recurrence is a concern, particularly in children, with around one-third of patients experiencing it, sometimes within a year of treatment discontinuation (11).

Limited evidence exists on the predictive determinants of clinical and visual outcomes in children diagnosed with IIH. Previous research has primarily focused on investigating the natural progression, results, and variables that might predict the outcomes of childhood-onset IIH. However, these studies have been limited in sample size, with relatively small numbers of patients being included (12, 13). Additionally, several studies have primarily concentrated on examining the symptoms that manifest at the outset of IIH and the risk factors associated with the condition (14, 15).

Several previous studies have examined a restricted range of predicting factors for the visual result (16-18) or have incorporated a very brief duration of follow-up. The research findings indicate that the pubertal state is a significant factor in determining the manifestation and prognosis of diseases (4, 16).

## 2. Objectives

Additionally, it has been shown that obese children in puberty are less likely to have favorable visual results (18). Given the limited research in this area, our study aims to assess clinical presentations and risk factors of IIH in pediatric patients.

## 3. Methods

This study was a retrospective cohort protocol conducted on patients admitted to hospitals with a final diagnosis of IIH. Clinical information was extracted from pediatric IIH patients in two main referral children's hospitals of Shahid Beheshti University of Medical Science (SBMU) in Tehran, the capital of Iran. Subsequently, the patients were contacted for follow-up regarding their symptoms. Parents of the patients provided consent for participation in the study and the potential publication of their clinical data while ensuring their anonymity during interviews. The study received approval from the Ethics in Biomedical Research Committee of Shahid Beheshti University of Medical Sciences under the code [IR.SBMU.MSP.REC.1398.1038](https://doi.org/10.30472/IR.SBMU.MSP.REC.1398.1038).

### 3.1. Study Setting and Participants

We utilized medical records of patients admitted to referral children's hospitals between 2013 and 2021. These patients were then contacted and followed up as part of this study. Inclusion criteria encompassed patients under 18 years of age, diagnosed with IIH, and admitted to our hospitals with willingness, complete documentation, and successful follow-up interviews. The diagnosis of IIH was confirmed by pediatric neurologists and ophthalmologist consultants according to Dandy criteria and the 2013 revision proposed by Friedman et al. (19, 20). Exclusion criteria comprised patients older than 18 years, incomplete documentation, unavailability during follow-up, non-admission, and parental unwillingness to participate.

### 3.2. Data Sources and Variables

Clinical and demographic information, including sex, weight, and presenting signs and symptoms, were extracted from medical records. Thorough ophthalmologic examinations were conducted and documented for all patients. For our retrospective study, we primarily collected data by reviewing patients' records and conducting interviews. This approach became necessary due to the limitations imposed during the COVID-19 pandemic. The lack of in-person access made conducting thorough clinical examinations difficult. Unfortunately, this restriction hindered the ability to monitor vision progress effectively as it took time to obtain the necessary cooperation. Consequently, we assessed vision by analyzing the data obtained from acuity and visual field tests and a questionnaire that inquired about any recent or ongoing vision issues such as blurred vision, diplopia, photophobia, and strabismus. Additionally, in this study, the assessment of headaches was done by completing questionnaires designed by the ICHD-3 criteria published in the *Cephalalgia* journal for evaluating headaches in IIH patients (21). It is important to note that recurrent symptoms mirrored the initial presentation, encompassing headache, nausea, vomiting, and confirmed papillary edema upon examination.

Lumbar puncture records were assessed for the opening pressure observed. Idiopathic intracranial hypertension diagnosis followed the criteria suggested by Friedman et al. (3, 20). Therefore, in the present study, according to the revised diagnostic criteria used to confirm IIH, the different opening pressure thresholds for diagnosing IIH in the examined children were 28

cmH<sub>2</sub>O, and in the condition that the child was not under sedation and not obese, 25 cmH<sub>2</sub>O was considered (20, 22, 23). Moreover, it is crucial to highlight that we consistently measured the mentioned metric at least twice in our study patients.

Cerebrospinal fluid (CSF) opening pressure was measured using a standardized procedure. The lumbar puncture was performed with the patient in the lateral decubitus position. A sterile, disposable spinal needle was carefully inserted into the subarachnoid space between the L3/L4 or L4/L5 intervertebral spaces, guided by anatomical landmarks. Prior to the procedure, the skin was sterilized, and local anesthesia or sedation was administered.

The CSF opening pressure was measured using a manometer connected to the spinal needle. The manometer was calibrated before each measurement to ensure accuracy. The procedure was performed by experienced clinicians in a controlled environment, adhering to aseptic techniques to minimize the risk of contamination.

This standardized approach was consistently employed across all study participants to ensure uniformity in CSF opening pressure measurements. We used local anesthesia for cooperative pediatric patients, while those who were uncooperative underwent the measurement while sedated in the operating room. Additionally, all patients underwent brain imaging via MRI or CT scan to rule out alternative conditions such as brain tumors.

### 3.3. Statistical Analyses

Data were entered into IBM SPSS version 26.0. Quantitative variables were reported as means and standard deviations, while qualitative variables were presented as frequencies and percentages. Independent-samples *t*-test and chi-square tests were utilized to compare results between two groups. In case of non-normal distribution of the variables, the Mann-Whitney test was used to compare two groups. Binary logistic regression analysis was employed to create a prognostic tool for predicting the development of IIH complications.

## 4. Results

A total of 89 patients were identified within the study period. However, three patients had incomplete documentation and remained unreachable through the contact details provided in their records. Additionally, five patients opted not to participate in the study.

Consequently, the study included 81 participants, out of which 43 (53.1%) were male and 38 (46.9%) were female. The patients' average age was  $13.6 \pm 4.4$  years, while the mean age at the time of diagnosis was  $10.3 \pm 4.2$  years. The mean weight percentile for patients at the time of diagnosis, as per WHO growth curves, was  $41.9 \pm 26.8$ . In our study, 2 patients had optic nerve fenestration, and 5 patients underwent shunting. The median lumbar CSF opening pressure in our patient was 39 cmH<sub>2</sub>O, with an interquartile range of 23.5 - 60 cmH<sub>2</sub>O, also the lowest and the highest recorded intracranial pressure being 7 and 130 cmH<sub>2</sub>O, respectively. The duration of patient follow-up was  $3.1 \pm 1.5$  years.

To assess the normality of weight percentiles, the Kolmogorov-Smirnov test was employed, yielding a *P*-value of  $< 0.001$ , indicating non-normal distribution of the data. Despite this, the data exhibited a relatively symmetrical skewness of 0.273. The largest proportion of weight percentile values fell within the  $< 10\%$  range (20 patients). Also, a significant number of underweight patients were identified in our study (14 patients with weight percentiles  $< 3$ ). Moreover, 19% of patients met the criteria for being overweight or obese, which is higher than the regional and national averages. [Table 1](#) provides an overview of the patients' demographic information. Additionally, [Table 1](#) presents a comprehensive summary of both demographic and clinical particulars of the patients.

Out of the total participants, 13 (16.0%) experienced recurrent episodes of IIH, while 68 (84.0%) did not encounter such recurrences. The most prevalent clinical symptom reported by patients was headache (85.2%), followed by diplopia (50.6%), visual impairment (46.9%), nausea and/or vomiting (44.4%), strabismus (28.4%), photophobia (9.9%), and ophthalmodynia (8.6%). Papilledema was the predominant clinical sign observed among patients (79.0%). Furthermore, 2 (2.5%) patients also reported experiencing visual field defects.

In terms of medical history, three (3.7%) patients had a previous diagnosis of attention deficit hyperactivity disorder (ADHD). Among the patient cohort, 71 patients (87.7%) were managed medically, while others required interventional procedures, including ventriculoperitoneal shunt insertion, shunt replacements, therapeutic lumbar punctures, or even optic nerve sheath fenestration. Among the treatments, 70 patients received acetazolamide, with this being the sole medication for 35 (43.2%) patients. In addition to acetazolamide, other medical agents such as topiramate, dexamethasone, methyl prednisolone, and mannitol were employed for treatment in other patients. Patients who received acetazolamide as

**Table 1.** The Baseline Demographic and Clinical Information of the Patients<sup>a</sup>

Variables	Values
Age (y)	13.6 ± 4.4
Weight percentile	41.9 ± 26.8
Lumbar CSF opening pressure (cmH <sub>2</sub> O)	42.9 ± 25.2
<b>Sex</b>	
Male	43 (53.1)
Female	38 (46.9)
<b>Clinical signs and symptoms</b>	
Headache	69 (85.2)
Nausea/vomiting	36 (44.4)
Strabismus	23 (28.4)
Visual impairment	38 (46.9)
Diplopia	41 (50.6)
Eye pain	7 (8.6)
Photophobia	8 (9.9)
Papilledema	64 (79.0)
Decreased visual acuity	3 (3.7)
Impaired visual field	2 (2.5)
<b>Outcome</b>	
Recurrent disease	13 (16.0)
Persistent headache	13 (16.0)
Persistent visual problems	12 (14.8)
<b>Medications</b>	
Acetazolamide	69 (85.2)
Topiramate	9 (11.1)
Corticosteroids	26 (32.1)
Antiepileptics	6 (15.8)
Mannitol	5 (13.2)

<sup>z</sup> Abbreviation: CSF; cerebrospinal fluid.

<sup>a</sup> Values are expressed as No. (%) or mean ± SD.

monotherapy exhibited lower lumbar puncture opening pressure compared to those who needed combination therapy. However, this difference was not statistically significant ( $34.37 \pm 29.10$  cmH<sub>2</sub>O vs.  $44.52 \pm 26.02$  cmH<sub>2</sub>O, respectively,  $P = 0.163$ ).

The relationship between sex and various signs, symptoms, and outcomes of the disease was assessed using the chi-square test and Fisher's exact test. The summarized results of these tests are presented in [Table 2](#).

The results showed that recurrence was more frequent in male patients, but the signs and symptoms of the patients did not differ between male and female patients. The outcome of the disease regarding persistent headache and visual problems also did not differ between male and female patients. Chi-square test and Fisher's exact test were also used to assess the relationship between recurrence and different signs,

symptoms, and outcomes of this disease. Most of the patients who experienced recurrent episodes were male, which was significantly different (25.6% of males and 5.3% of females experienced recurrence,  $P$ -value = 0.013) (see [Table 2](#)). Patients with and without recurrent episodes differed significantly regarding presentation with strabismus (0% in recurrent disease vs. 33.82% in non-recurrent disease,  $P$ -value = 0.013). The results of these comparisons are summarized in [Table 3](#).

The mean weight percentile for patients was found to be  $41.6 \pm 36.1$  for males and  $42.4 \pm 36.1$  for females, demonstrating no statistically significant difference ( $P = 0.975$ ). Furthermore, despite the slightly higher mean intracranial pressure among female patients compared to male patients ( $34.82 \pm 22.41$  cmH<sub>2</sub>O for boys and  $44.38 \pm 31.14$  cmH<sub>2</sub>O for girls), this difference was not statistically significant ( $P = 0.141$ ). To assess the connection between weight percentile and lumbar

**Table 2.** Comparison of Signs, Symptoms, and Outcome of IIH Among Male and Female Patients <sup>a, b</sup>

Variables	Male (N = 43)	Female (N = 38)	P-Value
Headache	38 (88.4)	31 (81.6)	0.390
Nausea and/or vomiting	18 (41.9)	18 (47.4)	0.619
Strabismus	10 (23.3)	13 (34.2)	0.275
Visual impairment	23 (53.5)	15 (39.5)	0.207
Diplopia	21 (48.8)	20 (52.6)	0.733
Eye pain	3 (7.0)	4 (10.5)	0.701
Photophobia	3 (7.0)	5 (13.2)	0.464
Papilledema	35 (81.4)	29 (76.3)	0.575
Decreased visual acuity	1 (2.3)	2 (5.3)	0.598
Impaired visual field	1 (2.3)	1 (2.6)	> 0.999
Recurrence	11 (25.6)	2 (5.3)	0.013
Persistent headache	10 (23.3)	3 (7.9)	0.060
Persistent visual problems	6 (14.0)	6 (15.8)	0.816

<sup>a</sup> Values are expressed as No. (%).

<sup>b</sup> A P-value below 0.05 is indicative of statistical significance.

**Table 3.** Comparison of Signs, Symptoms, and Outcome of IIH in Recurrent and Non-recurrent Disease <sup>a</sup>

Variables	Recurrence (N = 13)	No Recurrence (N = 68)	P-Value <sup>b</sup>
Sex			0.013
Male	11 (84.6)	32 (47.1)	
Female	2 (15.4)	36 (52.9)	
Headache	13 (100)	56 (82.4)	0.101
Nausea and/or vomiting	6 (46.2)	30 (44.1)	0.892
Strabismus	0 (0.0)	23 (33.8)	0.013
Visual impairment	9 (69.2)	29 (42.6)	0.078
Diplopia	4 (30.8)	37 (54.4)	0.118
Eye pain	2 (15.4)	5 (7.4)	0.345
Photophobia	3 (23.1)	5 (7.4)	0.082
Papilledema	11 (84.6)	53 (77.9)	0.588
Decreased visual acuity	0 (0.0)	3 (4.4)	> 0.999
Impaired visual field	0 (0.0)	2 (2.9)	> 0.999
Persistent headache	4 (30.8)	9 (13.2)	0.115
Persistent visual problems	3 (23.1)	9 (13.2)	0.360

<sup>a</sup> Values are expressed as No. (%).

<sup>b</sup> A P-value below 0.05 is indicative of statistical significance.

puncture opening pressure, a Pearson’s correlation test was performed, indicating a non-significant positive correlation ( $P = 0.094$ ,  $r = 0.220$ ). Interestingly, patients presenting with visual impairment and impaired visual fields were comparatively older than those without these symptoms ( $P = 0.005$  and  $P = 0.030$ , respectively). Conversely, patients experiencing persistent headaches exhibited higher weight percentiles ( $61.6 \pm 3.6$  vs.  $38.3 \pm 35.7$ ,  $P = 0.027$ ). Table 4 summarizes the comparison of

age, weight percentile, and CSF opening pressure based on clinical presentation and outcome of the disease.

Even after receiving treatment at the hospital, nine patients (11.1%) continued to experience headaches, while another nine patients (11.1%) still faced visual impairments. In an endeavor to appraise the effectiveness of our data-based model in prognosticating the persistence of headache and visual

**Table 4.** Comparison of Age, Weight Percentile, and CSF Opening Pressure Based on Clinical Presentation and Outcome of the Disease <sup>a, b</sup>

Variables	Age	P-Value	Weight Percentile	P-Value <sup>c</sup>	CSF Opening Pressure	P-Value <sup>d</sup>
<b>Sex</b>		0.154		0.975		0.141
Male	9.81 ± 3.65		41.59 ± 36.10		34.82 ± 22.41	
Female	10.89 ± 4.77		42.41 ± 38.41		44.38 ± 31.14	
<b>Headache</b>		0.304		0.665		0.887
No	8.53 ± 5.88		40.71 ± 42.68		37.75 ± 29.77	
Yes	10.63 ± 3.83		42.13 ± 36.10		39.38 ± 26.85	
<b>Nausea/vomiting</b>				0.402		0.903
No	10.06 ± 4.22	0.492	38.21 ± 34.96		38.82 ± 23.51	
Yes	10.64 ± 4.26		50.83 ± 40.38		39.63 ± 30.98	
<b>Strabismus</b>		0.071		0.322		0.891
No	9.87 ± 4.43		38.21 ± 34.96		38.85 ± 24.93	
Yes	11.46 ± 3.46		50.83 ± 40.38		39.88 ± 31.34	
<b>Visual impairment</b>		0.005		0.539		0.614
No	9.11 ± 3.77		39.82 ± 38.00		40.78 ± 29.98	
Yes	11.68 ± 4.33		44.75 ± 35.57		37.51 ± 23.72	
<b>Diplopia</b>		0.143		0.511		0.119
No	9.46 ± 4.81		38.66 ± 36.79		33.68 ± 23.26	
Yes	11.16 ± 3.42		45.00 ± 37.06		43.57 ± 29.15	
<b>Eye pain</b>		0.649		0.891		0.091
No	10.21 ± 4.31		42.27 ± 36.76		36.75 ± 25.29	
Yes	11.43 ± 3.26		37.54 ± 41.29		65.17 ± 33.15	
<b>Photophobia</b>		0.605		0.346		0.390
No	10.20 ± 3.99		43.13 ± 36.50		38.11 ± 26.90	
Yes	11.38 ± 6.21		26.73 ± 41.40		47.54 ± 27.86	
<b>Papilledema</b>		0.740		0.176		0.461
No	9.73 ± 4.74		32.42 ± 39.02		44.93 ± 33.24	
Yes	10.48 ± 4.10		44.85 ± 35.96		37.76 ± 25.33	
<b>Decreased visual acuity</b>		0.339		> 0.999		0.787
No	10.23 ± 4.25		42.03 ± 37.06		38.81 ± 26.48	
Yes	12.67 ± 3.26		34.83 ± N/A		52.00 ± 53.74	
<b>Impaired visual field</b>		0.030		0.824		0.521
No	10.18 ± 4.18		42.26 ± 36.97		38.90 ± 27.26	
Yes	16.00 ± 0.00		19.77 ± N/A		49.00 ± 15.56	
<b>Recurrence</b>		0.289		0.900		0.286
No	10.04 ± 4.25		37.29 ± 35.68		37.87 ± 28.05	
Yes	11.77 ± 3.90		61.55 ± 36.25		45.58 ± 20.81	
<b>Persistent headache</b>		0.380		0.027		0.082
No	10.41 ± 4.53		38.29 ± 35.68		40.90 ± 28.36	
Yes	9.85 ± 2.09		61.55 ± 36.25		30.00 ± 15.74	
<b>Persistent visual problem</b>		0.774		0.106		0.844
No	10.33 ± 4.25		38.66 ± 36.41		39.48 ± 27.00	
Yes	10.25 ± 2.96		58.84 ± 35.61		37.64 ± 28.104	

<sup>a</sup> Values are expressed as mean ± SD.

<sup>b</sup> A P-value below 0.05 is indicative of statistical significance.

<sup>c</sup> This P-value serves as an indicator of the statistical significance of the observed disparity in weight percentile between two distinct groups for instance differences between genders, presence of headache, or other relevant groupings.

<sup>d</sup> This P-value serves as an indicator of the statistical significance of the observed disparity in CSF Opening Pressure between two distinct groups for instance differences between genders, presence of headache, or other relevant groupings.

problems, a binary logistic regression test was conducted.

For the model predicting persistent headache, the Omnibus tests of model coefficients yielded a P-value of

0.261. This outcome implies that our model lacked the ability to predict the persistence of headaches accurately. On the contrary, when a binary logistic regression was performed for predicting the persistence

**Table 5.** Variables in the Model for Prediction of Future Visual Problems<sup>a</sup>

Variables	B	SE	Wald	df	P-Value	Exp (B)
Age at time of diagnosis	-0.234	0.257	0.832	1	0.362	0.791
Sex	1.837	1.500	1.500	1	0.221	6.278
Weight percentile	0.040	0.020	4.022	1	0.045	1.040
Nausea and/or vomiting	0.613	1.261	0.236	1	0.627	1.846
Strabismus	2.256	1.923	1.376	1	0.241	9.548
Visual impairment	-0.199	1.213	0.027	1	0.870	0.820
Eye pain	-20.436	15303.752	0.000	1	0.999	0.000
Photophobia	-18.604	16371.180	0.000	1	0.999	0.000
Impaired visual field	-12.976	40192.970	0.000	1	> 0.999	0.000
Intracranial pressure	0.015	0.025	0.370	1	0.543	1.016
Recurrence	5.089	2.379	4.574	1	0.032	162.206
Headache	20.893	13202.473	0.000	1	> 0.999	1184703310
Diplopia	2.005	1.727	1.349	1	0.245	7.429
Papilledema	20.336	8303.748	0.000	1	0.998	679230324
Decreased visual acuity	27.567	40192.970	0.000	1	> 0.999	9.376E + 11

<sup>a</sup>A P-value below 0.05 is indicative of statistical significance.

of visual problems, the Omnibus tests of model coefficients reported a P-value of 0.007. Notably, the Nagelkerke R<sup>2</sup> value for our model stood at 0.674. The predictive accuracy of our model for future visual problems was 93.8% for patients without persistent visual issues and 54.5% for patients with such problems, resulting in an overall accuracy of 86.4%. A comprehensive outline of the model for predicting future visual problems is presented in [Table 5](#).

The results show that only weight percentile and recurrence were significant predictors for future visual problems, with recurrence having stronger predictive power.

## 5. Discussion

In our study, we investigated 81 pediatric patients diagnosed with IIH in Tehran, Iran, to unravel the clinical presentations, risk factors, and prognostic indicators of this condition in the pediatric population. The study demonstrated nearly even male-to-female distribution, according to the average age at diagnosis and the mean weight percentile of patients, reflecting demographic diversity. Comprehensive symptom analysis revealed that headaches were predominant, followed by diplopia, visual impairment, nausea and/or vomiting, and strabismus. Papilledema was the most common clinical sign, emphasizing the importance of

early diagnosis. Our study also explored various treatments, including medical management and surgery. An intriguing finding was the comparable impact of acetazolamide, whether used as monotherapy or in combination, on lumbar puncture opening pressure. Moreover, gender and recurrent episodes were noted as influencing IIH's clinical course, with males showing a higher recurrence disposition. Interactions between clinical symptoms, weight percentiles, and lumbar puncture opening pressures provided insights into pediatric IIH complexities. Significantly, our data-driven model accurately predicted the persistence of visual problems. Weight percentile and recurrence emerged as significant predictors for future visual problems, contributing to a deeper understanding of pediatric IIH. These findings have significant implications for improved patient management and informed clinical decision-making.

In a study by Yamamoto et al., the authors evaluated 165 children with IIH over a 27-year period. They found that patients predominantly presented with headache, visual impairments, and nausea and/or vomiting (24). Our study's results align with theirs, demonstrating similar findings. Additionally, they observed a change in the male-to-female ratio during the prepubertal and postpubertal periods. While our study didn't specifically address patients' puberty status, we noted that among patients younger than 12 years old, approximately 60.0% were male, while patients older than 12 years old had

about 41.9% male representation. This similarity in the gender trend across studies is notable.

Paley et al. explored the association between obesity and pediatric Secondary IHH, revealing a 2.47 times higher prevalence of obesity in patients compared to the normal population, suggesting that obesity might be a risk factor for Secondary IHH (25). However, our study showcased a notable proportion of underweight patients (14 patients with weight percentiles < 3). Furthermore, 19% of patients were classified as overweight or obese, surpassing national and regional averages. These results imply that both ends of the weight percentile spectrum carry higher risks for pediatric IHH (26).

Tovia et al. reported a response rate of 76.6% to acetazolamide in pediatric patients with IHH (27). In our study, 69 patients initially underwent acetazolamide treatment, with 35 patients not requiring additional therapy. As such, our study reported a similar rate of 50.72%. The slightly higher lumbar puncture opening pressure and wider variance among our patients suggest that differences in diagnosis timing or disease severity may account for our results. This is especially true for patients needing combination therapy, who exhibited higher intracranial pressures.

Remarkably, 3.7% of our patients had a history of ADHD, which is lower than the prevalence of this disorder reported in a recent meta-analysis (28). Given the lack of prior studies exploring the link between ADHD and pediatric IHH, further research is needed to investigate this possible relationship.

Another study conducted by Senderowich et al. examined a cohort of 97 patients and placed particular emphasis on the adverse progression of IHH, the persistence of headaches, and the suboptimal visual results (29). The researchers emphasized variables such as gender and illness recurrence, identifying them as significant indicators of unfavorable visual outcomes. In their investigation, 29% of patients exhibited persistent headaches at the last follow-up. Importantly, Senderowich et al.'s work emphasizes the complexity of distinguishing between chronic headache syndromes and IHH recurrence, given the overlapping clinical features and comorbidity with chronic migraine, especially in cases without papilledema. The results of their study highlight the probable existence of a unique condition among those with chronic headaches, which may necessitate a modified treatment strategy. In our study, we echo Senderowich et al.'s emphasis on certain variables, such as gender and illness recurrence, as significant indicators of unfavorable visual outcomes in pediatric IHH. Our research focuses on examining the

clinical manifestations and potential risk factors associated with pediatric IHH. In conjunction with our investigation, that study provides additional insights into the difficulties presented by an unfavorable disease progression and the distinctive characteristics of chronic headaches experienced by this specific group of patients. The collective insights from both studies contribute to an enriched understanding of the complexities surrounding disease progression, particularly in cases involving persistent headaches, thus supporting the development of tailored treatment strategies for pediatric IHH.

Numerous studies have explored risk factors for recurrence or persistent symptoms in IHH patients. Prior literature has shown that lumbar puncture opening pressure isn't associated with an increased risk of recurrence. However, papilledema and longer symptom durations are linked to a higher risk of recurrence. Additionally, extended treatment duration correlates with a reduced recurrence risk. Studies investigating the connection between sex, age at diagnosis, and recurrence risk have produced clear results (11, 30-34). Our study found that recurrence was less frequent in female patients and those with strabismus, implying that female sex might act as protective factors. However, more research is necessary to verify this relationship.

In our study, intracranial pressure and weight percentile didn't differ significantly between patients with and without recurrence. Consequently, these two factors are not reliable predictors of recurrence. Bhalla et al. similarly found that obesity or underweight status weren't risk factors for recurrence (33).

Given that the most concerning outcome of IHH is long-standing visual impairments and blindness, creating a prognostic model for this sequela is of paramount importance (35). Sorensen et al. discovered that persistent visual problems can persist even after intracranial hypertension has resolved (36). Alfonso et al. evaluated 50 adult IHH patients and concluded that a delayed interval from presentation to diagnosis, higher maximal intracranial pressure, and hypertension were linked to severe vision loss (37). In contrast, our study identified weight percentile and recurrence history as significant predictors of persistent visual impairment. The variation in results between the two studies might be attributed to differences in the studied populations and the sex ratios. Alfonso et al.'s study predominantly featured female participants, limiting the generalizability of their results to other populations (37).

### 5.1. Limitations



The present investigation deals with limitations arising from the infrequency of the cases and the difficulties associated with reaching certain patient groups. Including patients who are under continuous medical follow-up and the challenges associated with accessing specific instances constitute a potential selection bias, adding to the study's limitations. Due to limitations in our study, such as a retrospective design covering an extended period, it is susceptible to missing information from medical records.

## 5.2. Conclusions

In this study, we evaluated the presentations of Pseudotumor cerebri in children and found that headache and diplopia did not differ between girls and boys. Additionally, the study showed that female sex served as a protective factor against recurrence, and the recurrence of IIH was significantly lower in patients with strabismus. Weight percentile and recurrence were predictive factors for persistent visual problems, but our model could not predict persistent headache.

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## Footnotes

**Authors' Contribution:** Study concept and design: N.J. and G.SH. Acquisition of data: G.SH. Analysis and interpretation of data: A.H. and M.N. Drafting of the manuscript: A.H. Critical revision of the manuscript for important intellectual content: N.J. and G.SH. Statistical analysis: M.N. Administrative, technical, and material support: G.SH. Study supervision: G.SH.

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**Data Availability:** The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to ethics.

**Ethical Approval:** The study received approval from the Ethics in Biomedical Research Committee of Shahid Beheshti University of Medical Sciences under the code [IR.SBMU.MSP.REC.1398.1038](https://doi.org/10.1398.1038).

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## References

- Corbett JJ, Mehta MP. Cerebrospinal fluid pressure in normal obese subjects and patients with pseudotumor cerebri. *Neurol.* 1983;**33**(10):1386-8. [PubMed ID: [6684240](https://pubmed.ncbi.nlm.nih.gov/6684240/)]. <https://doi.org/10.1212/wnl.33.10.1386>.
- Smith JL. Whence pseudotumor cerebri? *J Clin Neuroophthalmol.* 1985;**5**(1):55-6.
- Gillson N, Jones C, Reem RE, Rogers DL, Zumberge N, Aylward SC. Incidence and Demographics of Pediatric Intracranial Hypertension. *Pediatr Neurol.* 2017;**73**:42-7. [PubMed ID: [28668233](https://pubmed.ncbi.nlm.nih.gov/28668233/)]. <https://doi.org/10.1016/j.pediatrneurol.2017.04.021>.
- Matthews YY, Dean F, Lim MJ, McLachlan K, Rigby AS, Solanki GA, et al. Pseudotumor cerebri syndrome in childhood: incidence, clinical profile and risk factors in a national prospective population-based cohort study. *Arch Dis Child.* 2017;**102**(8):715-21. [PubMed ID: [28356250](https://pubmed.ncbi.nlm.nih.gov/28356250/)]. <https://doi.org/10.1136/archdischild-2016-312238>.
- Sriugoinys S, Margareta S, Jon Hersir E. De Novo Presentation of Idiopathic Intracranial Hypertension (IIH) Associated With COVID-19 Infection. *Neurohospitalist.* 2022;**12**(4):691-2. [PubMed ID: [36147772](https://pubmed.ncbi.nlm.nih.gov/36147772/)]. [PubMed Central ID: [PMC9117983](https://pubmed.ncbi.nlm.nih.gov/PMC9117983/)]. <https://doi.org/10.1177/19418744221102044>.
- Townsend R, Jost A, Amans M, Hui F, Bender M, Satti S, et al. P-040 Major complications of dural venous sinus stenting for idiopathic intracranial hypertension: case series and management considerations. *J NeuroInterv Surg.* 2021;**13**(Suppl 1):A48.1-A48. <https://doi.org/10.1136/neurintsurg-2021-SNIS.76>.
- Pascarella A, Manzo L, Bono F. Effect of mannitol bolus administration on cerebrospinal fluid pressure in patients with idiopathic intracranial hypertension: a pilot study. *J Neurol.* 2022;**269**(11):6158-64. [PubMed ID: [35752707](https://pubmed.ncbi.nlm.nih.gov/35752707/)]. <https://doi.org/10.1007/s00415-022-11239-z>.
- Friedman DI. Contemporary management of the pseudotumor cerebri syndrome. *Expert Rev Neurother.* 2019;**19**(9):881-93. [PubMed ID: [31478394](https://pubmed.ncbi.nlm.nih.gov/31478394/)]. <https://doi.org/10.1080/14737175.2019.1660163>.
- Mollan SP, Markey KA, Benzimra JD, Jacks A, Matthews TD, Burdon MA, et al. A practical approach to, diagnosis, assessment and management of idiopathic intracranial hypertension. *Pract Neurol.* 2014;**14**(6):380-90. [PubMed ID: [24809339](https://pubmed.ncbi.nlm.nih.gov/24809339/)]. [PubMed Central ID: [PMC4251443](https://pubmed.ncbi.nlm.nih.gov/PMC4251443/)]. <https://doi.org/10.1136/practneurol-2014-000821>.
- Kalyvas A, Neromyliotis E, Koutsarnakis C, Komaitis S, Drosos E, Skandalakis GP, et al. A systematic review of surgical treatments of idiopathic intracranial hypertension (IIH). *Neurosurg Rev.* 2021;**44**(2):773-92. [PubMed ID: [32335853](https://pubmed.ncbi.nlm.nih.gov/32335853/)]. <https://doi.org/10.1007/s10143-020-01288-1>.
- Hiley A, Hecht I, Goldenberg-Cohen N, Leiba H. Long-Term Follow-up of Pseudotumor Cerebri Syndrome in Prepubertal Children, Adolescents, and Adults. *Pediatr Neurol.* 2019;**101**:57-63. [PubMed ID: [31604646](https://pubmed.ncbi.nlm.nih.gov/31604646/)]. <https://doi.org/10.1016/j.pediatrneurol.2019.04.018>.
- Chen JJ, Thurtell MJ, Longmuir RA, Garvin MK, Wang JK, Wall M, et al. Causes and Prognosis of Visual Acuity Loss at the Time of Initial Presentation in Idiopathic Intracranial Hypertension. *Invest Ophthalmol Vis Sci.* 2015;**56**(6):3850-9. [PubMed ID: [26070058](https://pubmed.ncbi.nlm.nih.gov/26070058/)].

- [PubMed Central ID: PMC4697859]. <https://doi.org/10.1167/jovs.15-16450>.
13. Takkar A, Goyal MK, Bansal R, Lal V. Clinical and Neuro-ophthalmologic Predictors of Visual Outcome in Idiopathic Intracranial Hypertension. *Neuroophthalmol.* 2018;**42**(4):201-8. [PubMed ID: 30042789]. [PubMed Central ID: PMC6056212]. <https://doi.org/10.1080/01658107.2017.1400570>.
  14. Hamedani AG, Witonsky KFR, Cosico M, Rennie R, Xiao R, Sheldon CA, et al. Headache Characteristics in Children With Pseudotumor Cerebri Syndrome, Elevated Opening Pressure Without Papilledema, and Normal Opening Pressure: A Retrospective Cohort Study. *Headache.* 2018;**58**(9):1339-46. [PubMed ID: 30137653]. [PubMed Central ID: PMC6775481]. <https://doi.org/10.1111/head.13362>.
  15. Agraz D, Morgan LA, Fouzdar Jain S, Suh DW. Clinical features of pediatric idiopathic intracranial hypertension. *Clin Ophthalmol.* 2019;**13**:881-6. [PubMed ID: 31213758]. [PubMed Central ID: PMC6538838]. <https://doi.org/10.2147/OPTH.S183087>.
  16. Brara SM, Koebnick C, Porter AH, Langer-Gould A. Pediatric idiopathic intracranial hypertension and extreme childhood obesity. *J Pediatr.* 2012;**161**(4):602-7. [PubMed ID: 22633290]. [PubMed Central ID: PMC3572898]. <https://doi.org/10.1016/j.jpeds.2012.03.047>.
  17. Beres SJ, Sheldon CA, Boisvert CJ, Szperka CL, Paley GL, Burrows EK, et al. Clinical and Prognostic Significance of Cerebrospinal Fluid Opening and Closing Pressures in Pediatric Pseudotumor Cerebri Syndrome. *Pediatr Neurol.* 2018;**83**:50-5. [PubMed ID: 29753572]. [PubMed Central ID: PMC7780087]. <https://doi.org/10.1016/j.pediatrneurol.2018.02.011>.
  18. Sheldon CA, Paley GL, Xiao R, Kesler A, Eyal O, Ko MW, et al. Pediatric Idiopathic Intracranial Hypertension: Age, Gender, and Anthropometric Features at Diagnosis in a Large, Retrospective, Multisite Cohort. *Ophthalmol.* 2016;**123**(11):2424-31. [PubMed ID: 27692528]. [PubMed Central ID: PMC5257253]. <https://doi.org/10.1016/j.ophtha.2016.08.004>.
  19. Barmherzig R, Szperka CL. Pseudotumor Cerebri Syndrome in Children. *Curr Pain Headache Rep.* 2019;**23**(8):58. [PubMed ID: 31292773]. [PubMed Central ID: PMC7335266]. <https://doi.org/10.1007/s11916-019-0795-8>.
  20. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurol.* 2013;**81**(13):1159-65. [PubMed ID: 23966248]. <https://doi.org/10.1212/WNL.0b013e3182a55f17>.
  21. No Authors Listed. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia.* 2018;**38**(1):1-211. <https://doi.org/10.1177/0333102417738202>.
  22. Avery RA, Shah SS, Licht DJ, Seiden JA, Huh JW, Boswinkel J, et al. Reference range for cerebrospinal fluid opening pressure in children. *N Engl J Med.* 2010;**363**(9):891-3. [PubMed ID: 20818852]. [PubMed Central ID: PMC3746184]. <https://doi.org/10.1056/NEJMc1004957>.
  23. Avery RA. Interpretation of lumbar puncture opening pressure measurements in children. *J Neuroophthalmol.* 2014;**34**(3):284-7. [PubMed ID: 25133882]. [PubMed Central ID: PMC4442611]. <https://doi.org/10.1097/WNO.0000000000000154>.
  24. Yamamoto E, Farber D, Rothner D, Moodley M. Assessment of Pediatric Pseudotumor Cerebri Clinical Characteristics and Outcomes. *J Child Neurol.* 2021;**36**(5):341-9. [PubMed ID: 33148096]. <https://doi.org/10.1177/0883073820972231>.
  25. Paley GL, Sheldon CA, Burrows EK, Chilutti MR, Liu GT, McCormack SE. Overweight and obesity in pediatric secondary pseudotumor cerebri syndrome. *Am J Ophthalmol.* 2015;**159**(2):344-52 e1. [PubMed ID: 25447107]. [PubMed Central ID: PMC4643369]. <https://doi.org/10.1016/j.ajo.2014.11.003>.
  26. Jafari-Adli S, Jouyandeh Z, Qorbani M, Soroush A, Larijani B, Hasani-Ranjbar S. Prevalence of obesity and overweight in adults and children in Iran; a systematic review. *J Diabetes Metab Disord.* 2014;**13**(1):121. [PubMed ID: 25610814]. [PubMed Central ID: PMC4301060]. <https://doi.org/10.1186/s40200-014-0121-2>.
  27. Tovia E, Reif S, Oren A, Mitelpunkt A, Fattal-Valevski A. Treatment Response in Pediatric Patients With Pseudotumor Cerebri Syndrome. *J Neuroophthalmol.* 2017;**37**(4):393-7. [PubMed ID: 28787297]. <https://doi.org/10.1097/WNO.0000000000000516>.
  28. Salari N, Ghasemi H, Abdoli N, Rahmani A, Shiri MH, Hashemian AH, et al. The global prevalence of ADHD in children and adolescents: a systematic review and meta-analysis. *Ital J Pediatr.* 2023;**49**(1):48. [PubMed ID: 37081447]. [PubMed Central ID: PMC10120242]. <https://doi.org/10.1186/s13052-023-01456-1>.
  29. Senderowich N, Bachar A, Mitelpunkt A, Tokatly I, Klein A, Mezdakoursh D, et al. Predictors of disease course and long-term outcomes of idiopathic intracranial hypertension in children and adolescents. *Eur J Pediatr.* 2023;**182**(11):5137-47. <https://doi.org/10.21203/rs.3.rs-2515294/v1>.
  30. Ozturk G, Turkdogan D, Unver O, Dericioglu V, Aslan B, Dalgincinar A. How do presentation age and CSF opening pressure level affect long-term prognosis of pseudotumor cerebri syndrome in children? Experience of a single tertiary clinic. *Childs Nerv Syst.* 2022;**38**(1):95-102. [PubMed ID: 34568960]. <https://doi.org/10.1007/s00381-021-05365-8>.
  31. McGirt MJ, Woodworth G, Thomas G, Miller N, Williams M, Rigamonti D. Cerebrospinal fluid shunt placement for pseudotumor cerebri-associated intractable headache: predictors of treatment response and an analysis of long-term outcomes. *J Neurosurg.* 2004;**101**(4):627-32. [PubMed ID: 15481717]. <https://doi.org/10.3171/jns.2004.101.4.0627>.
  32. Celebisoy N, Secil Y, Akyurekli O. Pseudotumor cerebri: etiological factors, presenting features and prognosis in the western part of Turkey. *Acta Neurol Scand.* 2002;**106**(6):367-70. [PubMed ID: 12460143]. <https://doi.org/10.1034/j.1600-0404.2002.02027.x>.
  33. Bhalla S, Nickel NE, Mutchnick I, Ziegler C, Sowell M. Demographics, clinical features, and response to conventional treatments in pediatric Pseudotumor Cerebri syndrome: a single-center experience. *Childs Nerv Syst.* 2019;**35**(6):991-8. [PubMed ID: 31025099]. <https://doi.org/10.1007/s00381-019-04150-y>.
  34. Mahajnah M, Genizi J, Zahalka H, Andreus R, Zelnik N. Pseudotumor Cerebri Syndrome: From Childhood to Adulthood Risk Factors and Clinical Presentation. *J Child Neurol.* 2020;**35**(5):311-6. [PubMed ID: 31928127]. <https://doi.org/10.1177/0883073819895179>.
  35. Spennato P, Ruggiero C, Parlato RS, Buonocore MC, Varone A, Cianciulli E, et al. Pseudotumor cerebri. *Childs Nerv Syst.* 2011;**27**(2):215-35. [PubMed ID: 20721668]. <https://doi.org/10.1007/s00381-010-1268-x>.
  36. Sorensen PS, Thomsen AM, Gjerris F. Persistent disturbances of cognitive functions in patients with pseudotumor cerebri. *Acta Neurol Scand.* 1986;**73**(3):264-8. [PubMed ID: 3716764]. <https://doi.org/10.1111/j.1600-0404.1986.tb03273.x>.
  37. Afonso CL, Talans A, Monteiro ML. Factors affecting visual loss and visual recovery in patients with pseudotumor cerebri syndrome. *Arg Bras Oftalmol.* 2015;**78**(3):175-9. [PubMed ID: 26222108]. <https://doi.org/10.5935/0004-2749.20150045>.