Child's Nervous System (2019) 35:991–998
https://doi.org/10.1007/s00381-019-04150-y

ORIGINAL ARTICLE

Demographics, clinical features, and response to conventional treatments in pediatric Pseudotumor Cerebri syndrome: a single-center experience

Sonam Bhalla[1] · Noura Estephane Nickel[2] · Ian Mutchnick[3] · Craig Ziegler[4] · Michael Sowell[5]

Received: 10 December 2018 / Accepted: 3 April 2019 / Published online: 25 April 2019

Abstract

Objective The goal of this study was to better understand pediatric Pseudotumor Cerebri syndrome, and its relationship to age, obesity, and other medical conditions; and to evaluate response to conventional treatments.

Methods A retrospective chart review was performed on consecutive patients who were diagnosed with PTCS between January 1, 2007, and July 31, 2014. A total of 78 patients were included in this study: 54 female (69.3%) and 24 male (30.7%). Variables including age, sex, body mass index, concomitant medical conditions, secondary causes, associated symptoms, physical exam findings, imaging results, recurrence of symptoms, and treatment modalities were analyzed. Patients were grouped into "pre-kindergarten," "elementary," and "adolescent" based on their age; and weight categories of underweight, normal weight, overweight, moderately, and severely obese.

Results Mean age of symptom onset was 11.92 ± 4.09 years. Elementary and adolescent age patients were more likely to be overweight, moderately obese, and severely obese, while this finding was not found for patients in pre-kindergarten group. Headache (83.3%) and visual disturbances (48.7%) were the most common presenting complaints. Asthma (16.6%) was the most common associated concomitant medical condition. Medical management resulted in resolution in 84% of population, 15% required surgical interventions, and the recurrence rate was found to be 20.5%. There was a statistically significant trend in success with medical management in younger patients ($p = 0.04$), while medically refractory PTCS was seen in adolescent females. Recurrence of PTCS had a linear trend with increased occurrence in adolescent age group with higher BMI. Asthma was observed to be frequently associated with PTCS in our cohort. Obesity is strongly associated with PTCS, not only in the adolescent group but also in the younger elementary age group. Treatment remains similar to management in the adults with a good response (84%) to medical management and a low relapse rate.

Keywords Pediatric Pseudotumor Cerebri syndrome · Pre-kindergarten · Elementary and adolescent age groups · Obesity · Concomitant medical conditions

Study was presented as poster at the American Headache Society Meeting.

✉ Sonam Bhalla
sonamb12@gmail.com

Noura Estephane Nickel
noura.estephane@gmail.com

Ian Mutchnick
ianmutchnick@gmail.com

Michael Sowell
michael.sowell@louisville.edu

[1] Division of Child Neurology, Department of Neurology, Columbia University Medical Center, New York, NY, USA

[2] Department of Pediatrics, Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA

[3] Division of Pediatric Neurosurgery, Norton Neuroscience Institute, Norton Children's Hospital and University of Louisville School of Medicine, Louisville, KY, USA

[4] University of Louisville Office of Graduate Medical Education, Louisville, KY, USA

[5] Division of Child Neurology, Department of Neurology, University of Louisville School of Medicine, Louisville, KY, USA

Abbreviations

IIH	Idiopathic intracranial hypertension
PTCS	Pseudotumor Cerebri syndrome
ICP	Intracranial pressure
CSF	Cerebrospinal fluid
BMI	Body mass index
MRI	Magnetic resonance imaging
MRV	Magnetic resonance venography
LPS	Lumboperitoneal shunt
VPS	Ventriculoperitoneal shunt

Introduction

Pseudotumor Cerebri Syndrome (PTCS) is a clinical syndrome defined by elevated intracranial pressure (ICP) without evidence of a structural lesion or ventriculomegaly on neuroimaging with a normal cerebrospinal fluid (CSF) composition [1]. The incidence of PTCS is about 1 in 100,000 in the general adult population and is classically described in obese females of childbearing age, with an incidence as high as 19 in 100,000 [2]. Recent literature in the pediatric population reports the incidence of primary intracranial hypertension at about two-thirds (0.63 per 100,000) of the adult population [3]. Similar to adult demographics, pediatric PTCS is overrepresented in obese post-pubertal children. However, in prepubertal PTCS, there is more age-dependent variability in presentation and a higher incidence of secondary causes for increased ICP. Both asymptomatic papilledema discovered on routine ophthalmologic examination as well as symptomatic PTSC without papilledema occur with greater frequency, which can limit a more prompt diagnosis [1, 4, 5], thereby justifying the need for greater scrutiny in this population. The most common presenting symptom across different pediatric age groups is headache, seen in 85.5–96.5% with associated nausea and vomiting (12.7–52%). Headache characteristics vary, the most commonly diagnosed one being the migrainous type (52%), followed by tension type and medication over-use headache (37%) [6, 7]. Visual symptoms include blurry vision with transient visual obscurations (68%), visual field deficits (90%), and diplopia (16–42.3%) [8, 9]. Other less common symptoms include pulsatile tinnitus (10%) [10]. Papilledema, which can be bilateral, unilateral, or asymmetrical, is the most common sign, but it is not always present [11, 12]. Abducens nerve palsy is the most common (12%) associated cranial neuropathy [13], and less commonly seen are third and fourth cranial nerve palsy [14].

While several risk factors for PTCS have been identified, its pathogenesis is not clearly understood. Obesity and female gender in reproductive age patients have been historically associated with idiopathic intracranial hypertension (IIH) suggesting a strong steroid hormonal influence in development of PTCS [15]. Additionally, PTCS can also develop in prepubertal patients without this hormonal context. PTCS can be categorized into primary, where the etiology is idiopathic and secondary, where the cause is known [1]. The goal of this study was to review our experience with pediatric PTCS to better understand the demographics, clinical features, associated co-morbidities, and response to conventional treatments.

Methods

A retrospective chart review was performed of patients who presented to our center and were diagnosed with pediatric PTCS between January 1, 2007, and July 31, 2015. Records from the departments of pediatric neurology, pediatric ophthalmology, and pediatric neurosurgery were extracted based on the International Classification of Diseases, 9th Edition (ICD-9) diagnostic code for IIH or benign intracranial hypertension or PTCS (348.2) and papilledema (377.0).

Inclusion criteria was as follows: (1) patients aged 1 day to 18 years at the time of diagnosis seen at the Norton Childrens Hospital and University of Louisville and (2) with a primary diagnosis of PTCS or IIH with or without papilledema. The diagnosis of PTCS or IIH was only made after recording a CSF opening pressure (OP) at our center. Exclusion criteria was as follows: (1) patients who did not have a recorded CSF OP and (2) patients not fulfilling the diagnostic criteria for PTCS.

Multiple variables were extracted from the patient charts and were logged into a spreadsheet in a de-identified manner to preserve patient confidentiality. Data on the following variables was included: age, sex, height, weight, concomitant medical conditions, home medications, presenting symptoms (including headache, eye pain, visual disturbances, scotoma, diplopia, tinnitus, facial pain, neck pain, back pain, dizziness, nausea, vomiting, photophobia), physical examination findings (including best corrected visual acuity, fundoscopic examination, detailed neurological examination including cranial nerve examination), imaging findings, lumbar puncture opening pressure, cerebrospinal fluid (CSF) analysis (cell count, protein and glucose count), treatment modality, follow-up, and recurrence of symptoms.

Body Mass Index (BMI) for each patient was determined from the recorded weight and height at the time of diagnosis. Patients were then categorized into weight classes based on sex-specific BMI-for-age growth charts. The weight classes were as follows: underweight (BMI-for-age < 5th percentile), normal weight (BMI-for-age ≥ 5th percentile and < 85th percentile), overweight (BMI-for-age ≥ 85th percentile), moderately obese (BMI-for-age ≥ 95th percentile), and severely obese (BMI-for-age ≥ 1.2× 95th percentile). Patients were also categorized by age at which the diagnosis of PTCS was made.

Patients 2–5 years of age were denoted as "pre-kindergarten," patients 6–12 years of age were denoted as "elementary," and patients 13–18 years of age were denoted as "adolescent." Because secondary sexual trait examination was not recorded in all study patients, adolescence was determined by an age of 13 and beyond rather than by objective characteristics of puberty. Patients were categorized into their respective age groups, sex groups, and weight groups. The diagnosis of PTCS was made based on modified Dandy's Criteria [1]. Lumbar punctures were performed under sedation for pre-kindergarten and elementary age groups, and for adolescent age group, it was mostly performed without sedation. CSF opening pressure was measured in lateral decubitus position with knees extended or in prone position, when performed under radiographic guidance. Adult or child neurology residents or pediatric residents under supervision or intervention radiologist performed lumbar puncture. Conventional treatment methods were used which included medical management with carbonic anhydrase inhibitors like acetazolamide and topiramate, diuretic-like furosemide and gabapentin for pain relief and headache prophylaxis. Standard adult doses were used for obese adolescent patients (acetazolamide at 1–4 g divided two or three times in a day and topiramate at 100–200 mg divided two times a day). For pre-adolescent age group, 15–25 mg/kg/day of acetazolamide, divided into two or three doses, and 2–4 mg/kg/day of topiramate, divided into two doses, were used. Surgical management included placement of ventriculo-peritoneal (VP) shunt, lumbo-peritoneal shunt, and optic nerve sheet fenestration.

The Institutional Review Boards at the University of Louisville School of Medicine and Norton Healthcare each approved this study. Informed consent was not obtained since this study was a chart review and no patient contact was made.

Statistical analysis was performed using SAS version 9.2. Pearsons χ^2 test or the binomial test of proportions were used to compare occurrence of PTCS in the different genders, age groups, and weight groups. Treatment response was assessed based on clinical improvement. Treatment response and recurrence rate was compared among different age and weight groups using the χ^2 test for linear trend. Exact methods were used where appropriate, i.e., when the sample size for cells was too small. For this study, $p < 0.05$ was used to determine statistical significance.

Results

We identified 86 patients between the ages of 1 day old and 18 years, who were diagnosed with PTCS between January 1, 2007, and July 31, 2015. Eight patients did not have a recorded lumbar puncture opening pressure and were excluded, leaving 78 study patients. Twenty-four patients were male (30.7%) and 54 were female (69.3%). Figure 1 summarizes the gender distribution among age groups. The mean age at diagnosis was 11.92 years with a standard deviation of 4.09. Table 1 summarizes the age and weight distributions of PTSC patients. Patients in the underweight and normal weight groups were combined and compared to patients in the overweight, moderately obese, and severely obese weight groups. We found no difference of weight distribution in the rate of PTCS in pre-kindergarten age patients ($p = 1.000$), while a significant difference for elementary age ($p = 0.003$) and adolescent patients ($p < 0.001$) did exist, as being overweight or obese was more prevalent with these age groups.

Table 2 summarizes concomitant medical conditions seen in PTSC patients. Thirteen patients had asthma (16.6%), 10 patients with attention deficit hyperactivity disorder (12.8%), eight patients with acne (10.2%), eight patients with diabetes or pre-diabetes (9.0%), three patients with irritable bowel syndrome (3.8%), three patients with autism (3.8%), two patients

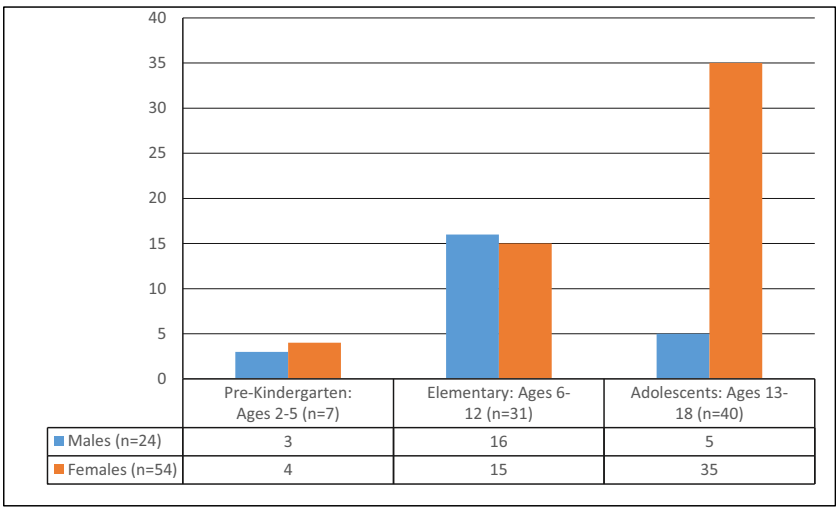

Fig. 1 Gender distribution among age groups

Table 1 Distribution and association of weight among different age groups

	Pre-kindergarten $n = 7$ $p = 1.000^{\Omega}$	Elementary $n = 31$ $p = 0.003^{\Omega}$	Adolescents $N = 40$ $p < 0.001^{\Omega}$
Underweight	1	1	0
Normal weight	3	6	6
Overweight	3	4	5
Moderately obese	0	3	9
Severely obese	0	17	20

$^{\Omega}p$ value reflects Binomial Test of Equal Proportions where BMI categories were grouped into underweight and normal weight versus overweight, moderately obese, and severely obese for each age classification

with polycystic kidney disease (2.6%), two patients with seizure disorder (2.6%), and two patients with polycystic ovarian syndrome (2.6%).

The most common presenting symptoms for PTCS were headache (83.3%, $n = 65$), blurred vision (48.7%, $n = 38$), nausea (41.0%, $n = 32$), photophobia (38.5%, $n = 30$), vomiting (25.6%, $n = 20$), and diplopia (24.4%, $n = 19$). Four patients (5.1%) were asymptomatic where PTCS was diagnosed by discovery of incidental papilledema on routine fundoscopic exam. Physical exam findings in study patients included papilledema (91.0%, $n = 71$), abducens nerve palsy (9.0%, $n = 7$), and visual field abnormalities (7.7%, $n = 6$) (Table 3). Seven patients (9%) had no papilledema on physical examination and were diagnosed with IIH without papilledema.

All study patients underwent magnetic resonance imaging/venogram (MRI/MRV) of the brain, lumbar puncture with recording of the opening pressure, and CSF analysis. Per imaging reports, three patients were found to have an empty sella (3.8%), and five patients had peri-optic subarachnoid space distention with flattening of globe and tortuosity of optic nerves (6.4%). Other imaging findings that were not pertinent to PTCS included two patients with mildly low lying cerebellar tonsils, two patients with pineal cysts, one patient with a neuroepithelial cyst, and one patient with ethmoid sinus disease. The average lumbar puncture opening pressure was 310.5 mm of H_2O, and CSF composition was within normal limits for all patients.

Weight loss with a referral to a dietician was recommend to all overweight and obese patients. Standard medical management with acetazolamide was begun for all patients after the diagnosis of PTCS was made. Topiramate and furosemide were added or substituted for the patients who were refractory or could not tolerate acetazolamide. Resolution of symptoms was achieved with acetazolamide in 40 patients (51.3%); acetazolamide and topiramate in 11 patients (14.1%); acetazolamide and furosemide in seven patients (9.0%); topiramate in two patients (2.6%); and acetazolamide, topiramate, and furosemide in two patients (2.6%); two patients (2.6%) had resolution of headaches with therapeutic lumbar punctures and did not require medications. Their papilledema had also resolved after a few weeks. Medications were tapered to off 4 to 6 months or sometimes longer after resolution of all signs and symptoms (Fig. 2). Most common reported side effect was gastritis or abdominal discomfort from acetazolamide. Twelve patients (15.0%) had symptoms that were refractory to all medical management and required neurosurgical interventions. Table 4 summarizes these neurosurgical

Table 2 List of concomitant medical conditions seen in the cohort population

Medical condition	*n* (%)
Asthma	13 (16.6)
Attention deficit hyperactive disorder (ADHD)	10 (12.8)
Acne	8 (10.2)
Diabetes mellitus/pre-diabetes mellitus	8 (9.0)
Irritable bowel syndrome	3 (3.8)
Autism	3 (3.8)
Polycystic kidney disease	2 (2.6)
Polycystic ovarian syndrome	2 (2.6)
Seizure disorder	2 (2.6)
Scoliosis	1 (1.3)
Hypertension	1 (1.3)
Hodgkin's lymphoma	1 (1.3)
Precocious puberty	1 (1.3)
Growth deficiency	1 (1.3)
Renal artery stenosis	1 (1.3)
Tethered cord syndrome	1 (1.3)
Bipolar disorder	1 (1.3)
Celiac disease	1 (1.3)
Down syndrome	1 (1.3)

Table 3 Common signs and symptoms with PTCS

Signs and symptoms	*n* (%)
Headache	65 (83.3)
Blurred vision	38 (48.7)
Nausea	32 (41)
Photophobia	30 (38.5)
Vomiting	20 (25.6)
Diplopia	19 (24.4)
Visual field abnormalities	6 (7.7)
Papilledema	71 (91)
Abducens nerve palsy	7 (9)
Asymptomatic with papilledema	4 (5.1)

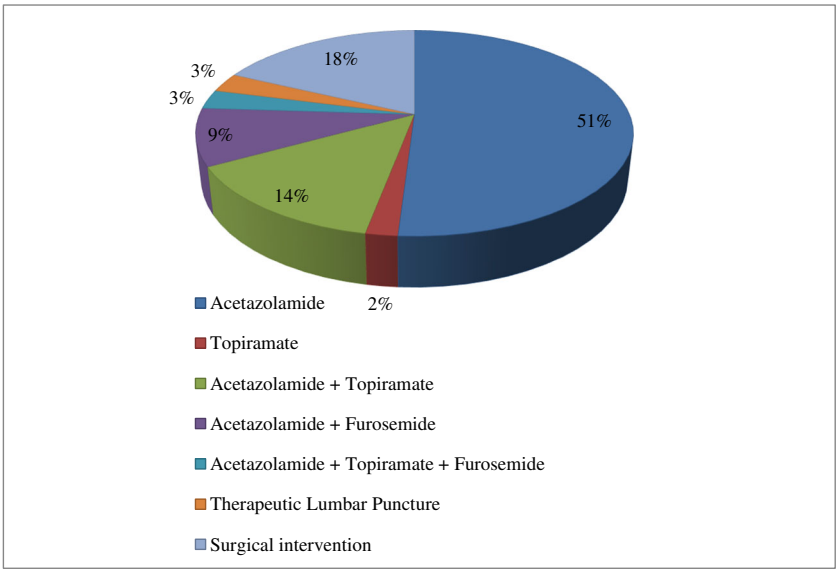

Fig. 2 Summary of overall response rate to different treatment modalities

interventions: lumboperitoneal shunt (LPS) placement (7.6%, $n = 6$), ventriculoperitoneal shunt (VPS) placement (2.5%, $n = 2$), LPS placement with optic nerve sheath fenestration (1.2%, $n = 1$), VPS placement with optic nerve sheath fenestration (1.2%, $n = 1$), LPS placement followed by VPS placement (1.2%, $n = 1$), and VPS placement followed by LPS placement (1.2%, $n = 1$). Patients were followed monthly until stable and then every 3 months until remission was achieved. No significant complications from surgical interventions were reported except for need for shunt revisions.

We defined recurrence of PTCS as return of signs and symptoms with a new lumbar puncture showing elevated opening pressure following treatment that had resulted in resolution of symptoms and papilledema. In our series, recurrence was seen in 16 patients (20.5%). Relationship between age and therapeutic success with medical management and with recurrence was analyzed and is summarized in Table 5. A statistically significant trend was found with age and success with medical management, $p = 0.043$. The younger the child, the more likely to have success. Medically refractory PTCS was seen mostly in adolescent age group. No statistically significant association was found between age and recurrence. Similarly, we also looked at the relationship between BMI and treatment response with medical management and with recurrence (Table 6). A trend was found with BMI and recurrence showing that, in general, children with higher BMIs had a higher recurrence rate. However, this finding was not significant, $p = 0.080$. No association was found between BMI and success with medical management.

Discussion

In our retrospective study, we describe clinical features of PTCS in a large pediatric population across different age groups. Demographic and clinical features of pediatric PTCS vary considerably by age.

Among pre-kindergardeners, pseudotumor is rare. We found no association between gender or obesity and PTCS in pre-kindergarden children, consistent with published data. Papilledema was seen in 100% of the cases, suggesting that this may be an effective screening tool to aid the diagnosis in this age group. MRI findings were normal in all except one.

Table 4 Surgical interventions seen in the patients whose symptoms were refractory to medical management

Surgical interventions	Number of patients (%) ($n = 12$)
Lumboperitoneal shunt placement	7.6% (6)
Ventriculoperitoneal shunt placement	2.5% (2)
Lumboperitoneal shunt placement with optic nerve sheath fenestration	1.2% (1)
Ventriculoperitoneal shunt placement with optic nerve sheath fenestration	1.2% (1)
Ventriculoperitoneal shunt placement followed by lumboperitoneal shunt placement	1.2% (1)
Lumboperitoneal shunt placement followed by ventriculoperioneal shunt placement	1.2% (1)

Table 5 Relationship between age and therapeutic success with medical management with risk for recurrence

		Pre-kindergarten: ages 2–5 *n* (%)	Elementary: ages 6–12 *n* (%)	Adolescents: ages 13–18 *n* (%)	*p* value*
Success with medical management	Yes	7 (100%)	29 (94%)	30 (75%)	0.043
	No	0 (0%)	2 (6%)	10 (25%)	
Recurrence	Yes	1 (14%)	3 (10%)	12 (31%)	0.085
	No	6 (86%)	28 (90%)	27 (69%)	

**p* value reflects chi-square test of linear trend

In elementary aged patients, we found characteristics of PTCS at variance with established literature. We found that obesity is significantly overrepresented ($p = 0.003$) with PTCS in this age group, a correlation not well described with previously presented series [7, 16–18]. This is in line with the Center of Disease Control (CDC) statistics of increasing incidence of childhood obesity (one in five school age children and young people) in the USA. Sheldon et al. also identified a similar correlation between BMI and PTCS in the early adolescent group of children. However, their definition of the early adolescent period was different for boys (8.5 to 12.5 years of age) and girls (7 to 12.5 years of age) making it slightly more difficult to risk stratify BMI for this middle age group in the context of available literature [19]. We also found a higher incidence of papilledema without headache (17%) in this group, supporting the high yield of screening fundus exams for a prompt diagnosis.

With regard to sex, our data is consistent with previously reported data, associating females with a higher prevalence of PTCS in the adolescent age group. However, this sex association was not true with children of elementary or pre-kindergarten age. Obesity continues to be a significant risk factor ($p < 0.001$) for PTCS in adolescents which is consistent with previous literature [18, 20, 21]. Headache (83.3%) and visual symptoms (73.1%) were found to be most common clinical features among patients of all age groups. IIH without papilledema was found in 8.9% of our group, which is consistent with previously published rate [4, 19]. Patients without papilledema most often presented with headaches and transient visual field abnormalities.

Few studies of PTCS have described associations with other medical conditions beyond obesity in the pediatric population. To our knowledge, the higher prevalence of asthma in PTCS patients is a novel finding. According to the 2016 census from CDC, the estimated prevalence of asthma in pediatric population is 9%, while in our study, 16.6% of patients with PTCS had comorbid asthma. These patients were distributed in the elementary and adolescent age groups. We speculate that the increased risk for PTCS in patients with asthma is multifactorial. Overweight and obese children also have increased asthma severity and poorer disease control [22, 23]. These children have a reduced response to inhaled corticosteroids, leading to increased prednisone courses and moderate-to-severe exacerbations [24]. Chronic glucocorticoid use or withdrawal, or hemodynamic changes from transient hypercapnea, could potentially cause elevated ICP [25, 26]. Inflammation might also contribute to increased ICP. There is evidence of a generalized inflammatory state in obesity with elevated levels of systemic cytokines, chemokines, and leptin that reduce the effectiveness of inhaled steroids. Adipocytes also secrete a number of substances that may influence airway inflammation and reactivity [24]. Elevated cytokines and chemokines have also been reported in the CSF of patients with IIH [27, 28], suggesting that inflammation may be a common etiology for PTCS and asthma. Future prospective studies with detailed steroid medication exposure with asthma and assessing occurrence of PTCS might help us understand the pathophysiology of this association better. ADHD was seen in 12.8% patients, of which two had significant weight gain secondary to risperidone use (2.5%). Other concomitant medical conditions are listed in Table 2.

Table 6 Relationship between BMI and therapeutic success with medical management and risk for recurrence

		Underweight		Normal weight		Overweight		Moderately obese		Severely obese		
		n	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*p* value*
Success with medical management	Yes	2 (100%)		12 (80%)		12 (100%)		8 (73%)		32 (86%)		0.902
	No	0 (0%)		3 (20%)		0 (0%)		3 (27%)		5 (14%)		
Recurrence	Yes	0 (0%)		2 (13%)		1 (8%)		2 (18%)		11 (30%)		0.080
	No	2 (100%)		13 (87%)		11 (92%)		9 (82%)		26 (70%)		

**p* value reflects chi-square test of linear trend

Known causes of secondary PTCS include use of certain supplements like vitamin A and retinoic acid compounds, use of antibiotics (like minocycline, tetracycline), endocrine causes (including growth hormone, thyroxine, chronic glucocorticoid use or withdrawal), use of lithium, medical conditions (like anemia, renal failure, Addison's disease, polycystic ovarian disease, sleep apnea), Turner syndrome, Down syndrome and cerebral venous abnormalities (including sinus stenosis or thrombosis, arteriovenous fistulas), and decreased CSF absorption from previous intracranial infection [7, 19]. In our cohort, prior to their diagnosis of PTCS, eight patients (10.2%) were on isotretinoin and minocycline, and five patients (6.4%) were on oral contraceptive pills, causing secondary PTCS.

Treatment for PTCS is aimed towards symptomatic relief and prevention of visual loss. Various therapies—alone or in combination—have been used [4, 7, 29, 30]. However, there are no pediatric randomized trials to guide treatment. There is only limited data on medication doses, duration of treatment, and follow-up evaluations for management of PTCS from several case studies. At our institution, a multidisciplinary approach is used to evaluate and treat our patients with PTCS, including pediatric neurologists, pediatric neurosurgeons, and pediatric ophthalmologists. Once the diagnosis of PTCS is made, medical management is initiated with a carbonic anhydrase inhibitor such as acetazolamide. Topiramate, furosemide, and other headache prophylactic agents such as gabapentin are also used depending on the treatment outcome with monotherapy and tolerance to acetazolamide. Common side effects seen from acetazolamide were gastritis, paresthesia, fatigue, hypokalemia, hyponatremia, and metabolic acidosis requiring discontinuation of treatment.

In pre-kindergarten age group, 100% patients responded well to medical management with acetazolamide with recurrence in one which required subsequent surgical intervention. In elementary age group, only two (6%) required surgical intervention and 94% resolved with medical management alone. There was a statistically significant linear trend (p = 0.043) seen for medically refractory PTCS in adolescent age group. Surgical intervention was needed in 10 patients (25%). All 10 patients were females. The urgency for surgical intervention was determined by severity of symptoms, intractable headaches despite maximal medical management, impending or concomitant visual field loss, intolerance to medical therapies, and physician's clinical judgment. No one received stenting of the transverse/sigmoid junction of the dural sinuses. Therapeutic lumbar punctures provided definitive relief of symptoms for 2.6% of our patients. In our population, acetazolamide was effective in 51% of patients. Topiramate was found to be effective in 16.7% of patients at the standard dosing. Treatment of secondary PTCS was aimed towards eliminating the causative factor in addition to the conventional therapies. Weight loss was recommended but was seldom achieved. The average time to resolution of symptoms was found to be around 6 to 8 months for most, but some the symptoms persisted despite treatment for greater than 1 year. Medications were slowly tapered off 6 months after resolution of signs and symptoms for majority of the patients. Patients were followed for up to 1 year after medications were weaned, or post-operatively. The rate of recurrent PTCS after cessation of medication was found to be 20.5%, similar to that reported in literature [17]. Being overweight or obese increases the risk for recurrence.

There was a linear relationship between age and recurrence with increased recurrence in adolescent age group. Similarly, an increased recurrence was seen in overweight and obese patients (p = 0.08). Success with medical management was increasingly seen in younger age groups (p = 0.04). We found a statistically significant incidence of medically refractory PTCS, requiring surgical intervention, in adolescent females. Demographically, 90% of these patients were obese. It may be that high BMI is a contributing factor to the return of PTSC in addition to the post-pubertal hormonal component, in this population [19]. This suggests that weight management in addition to medical treatment with regular follow up is necessary, though these patients tended to return on their own due to discomfort.

Data limitations forced us to define the adolescent age group numerically rather than based on Tanner staging. Additionally, we lacked documentation to precisely report that the exact duration of each medication, frequency of change in medications, time period for resolution of papilledema or for reemergence of symptoms as well as adverse reactions to medical treatment and complications from surgical interventions were not consistently reported. This occurred due to incomplete records or loss of some records during the merging of different medical record systems. The retrospective nature of our study may also result in recall bias as well as limit our ability to effectively assess improvement in relation to the management of concomitant medical conditions. It also limits our analysis to gauge the strength of association of PTCS and asthma, which should be inferred with caution. Incorporating a standardized clinic note might result in more robust data collection for future studies.

Conclusion

Pediatric PTCS imposes a significant burden on quality of life of children causing pain, missed school days, and risk for permanent visual loss. We conclude that the demographics and treatment outcomes for PTCS differ among the different age groups in the pediatric population. The increase in incidence of obesity and PTCS in elementary age group may suggest the importance of early screening measures for this population. Papilledema is a sensitive sign for diagnosis of

PTCS in younger children: We found a very high sensitivity for fundoscopic exams for this age group. There was an increased correlation between asthma and PTCS—a novel and as yet uncorroborated finding. Larger prospective studies may confirm this association and aid in clarifying the pathophysiology of PTCS. Current treatment strategies for PTCS in the pediatric age group are similar to adult population. Eighty-four percent of our cohort showed a good response to medical management with increased refractoriness seen in adolescent females. We emphasize the importance of a coordinated multidisciplinary approach for prompt diagnosis and treatment. Continued follow-up is needed for management of PTCS to prevent headache, visual loss, recurrence of the condition, and improve overall quality of life of children with this disorder.

Acknowledgements Statistical support for this research was underwritten by the University of Louisville Office of Graduate Medical Education.

Funding information No financial supports were used to perform this study.

Compliance with ethical standards

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

References

1. Friedman DI, Liu GT, Digre KB (2013) Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology. 81(13):1159–1165
2. Per H, Canpolat M, Gumus H et al (2013) Clinical spectrum of the pseudotumor cerebri in children: etiological, clinical features, treatment and prognosis. Brain and Development 35(6):561–568
3. Gillson N, Jones C, Reem RE, Rogers DL, Zumberge N, Aylward SC (2017) Incidence and demographics of pediatric intracranial hypertension. Pediatr Neurol 73:42–47
4. Mallery RM, Friedman DI, Liu GT (2014) Headache and the pseudotumor cerebri syndrome. Curr Pain Headache Rep 18(9):446
5. Rook BS, Phillips PH (2016) Pediatric pseudotumor cerebri. Curr Opin Ophthalmol 27(5):416–419
6. Aylward SC, Waslo CS, Au JN, Tanne E (2016) Manifestations of pediatric intracranial hypertension from the intracranial hypertension registry. Pediatr Neurol 61:76–82
7. Aylward SC, Way AL (2018) Pediatric intracranial hypertension: a current literature review. Curr Pain Headache Rep 22(2):14
8. Cinciripini GS, Donahue S, Borchert MS (1999) Idiopathic intracranial hypertension in prepubertal pediatric patients: characteristics, treatment, and outcome. Am J Ophthalmol 127(2):178–182
9. Smith SV, Friedman DI (2017) The idiopathic intracranial hypertension treatment trial: a review of the outcomes. Headache 57(8): 1303–1310
10. Dessardo NS, Dessardo S, Sasso A, Sarunic AV, Dezulovic MS (2010) Pediatric idiopathic intracranial hypertension: clinical and demographic features. Coll Antropol 34(Suppl 2):217–221
11. Aylward SC, Aronowitz C, Roach ES (2016) Intracranial hypertension without papilledema in children. J Child Neurol 31(2):177–183
12. Faz G, Butler IJ, Koenig MK (2010) Incidence of papilledema and obesity in children diagnosed with idiopathic "benign" intracranial hypertension: case series and review. J Child Neurol 25(11):1389–1392
13. Reid JE, Reem RE, Aylward SC, Rogers DL (2016) Sixth nerve palsy in Paediatric intracranial hypertension. Neuroophthalmology 40(1):23–27
14. Phillips PH, Sheldon CA (2017) Pediatric Pseudotumor Cerebri Syndrome. J Neuroophthalmol 37(Suppl 1):S33–S40
15. Markey KA, Mollan SP, Jensen RH, Sinclair AJ (2016) Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions. Lancet Neurol 15(1):78–91
16. Genizi J, Lahat E, Zelnik N, Mahajnah M, Ravid S, Shahar E (2007) Childhood-onset idiopathic intracranial hypertension: relation of sex and obesity. Pediatr Neurol 36(4):247–249
17. Tibussek D, Schneider DT, Vandemeulebroecke N, Turowski B, Messing-Juenger M, Willems PHGM, Mayatepek E, Distelmaier F (2010) Clinical spectrum of the pseudotumor cerebri complex in children. Childs Nerv Syst 26(3):313–321
18. Balcer LJ, Liu GT, Forman S, Pun K, Volpe NJ, Galetta SL, Maguire MG (1999) Idiopathic intracranial hypertension: relation of age and obesity in children. Neurology. 52(4):870–872
19. Sheldon CA, Paley GL, Xiao R, Kesler A, Eyal O, Ko MW, Boisvert CJ, Avery RA, Salpietro V, Phillips PH, Heidary G, McCormack SE, Liu GT (2016) Pediatric idiopathic intracranial hypertension: age, gender, and anthropometric features at diagnosis in a large, retrospective, multisite cohort. Ophthalmology 123(11): 2424–2431
20. Degerliyurt A, Teber S, Karakaya G et al (2014) Pseudotumor cerebri/idiopathic intracranial hypertension in children: an experience of a tertiary care hospital. Brain and Development 36(8):690–699
21. Brara SM, Koebnick C, Porter AH, Langer-Gould A (2012) Pediatric idiopathic intracranial hypertension and extreme childhood obesity. J Pediatr 161(4):602–607
22. Peters U, Dixon AE, Forno E (2018) Obesity and asthma. J Allergy Clin Immunol 141(4):1169–1179
23. Ahmadizar F, Vijverberg SJ, Arets HG et al (2016) Childhood obesity in relation to poor asthma control and exacerbation: a meta-analysis. Eur Respir J 48(4):1063–1073
24. Forno E, Lescher R, Strunk R, Weiss S, Fuhlbrigge A, Celedón JC (2011) Decreased response to inhaled steroids in overweight and obese asthmatic children. J Allergy Clin Immunol 127(3):741–749
25. Balasubramanian S, Shivbalan S, Ganesh R (2005) Pseudotumor cerebri following oral betamethasone for common cold. Indian J Pediatr 72(11):994
26. Dees SC, Mc KH Jr (1959) Occurrence of pseudotumor cerebri (benign intracranial hypertension) during treatment of children with asthma by adrenal steroids; report of three cases. Pediatrics 23(6): 1143–1151
27. Dhungana S, Sharrack B, Woodroofe N (2009) Cytokines and chemokines in idiopathic intracranial hypertension. Headache. 49(2):282–285
28. Edwards L, Constantinescu C (2010) Cytokines in idiopathic intracranial hypertension CSF. Headache. 50(2):323–325
29. Brodsky MC, Vaphiades M (1998) Magnetic resonance imaging in pseudotumor cerebri. Ophthalmology 105(9):1686–1693
30. Biousse V, Bruce BB, Newman NJ (2012) Update on the pathophysiology and management of idiopathic intracranial hypertension. J Neurol Neurosurg Psychiatry 83(5):488–494