Original Article

Pattern of Idiopathic Intracranial Hypertension in Indian Population

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Abstract

Objective: To evaluate the clinical and demographic profile, laboratory parameters and outcomes of Idiopathic Intracranial hypertension (IIH) patients from Indian subpopulation. **Materials and method:** We did a prospective study on patients who fulfilled the revised diagnostic criteria for Primary pseudotumor cerebri syndrome in adults and children, proposed by Friedman *et al* in 2013. All patients were examined for BMI, papilloedema, extraocular muscle movement, opening CSF pressure and underwent MRI, MR venography of brain and perimetry. Patients were followed up for a minimum period of 6 months, upto 2 years, with the outcomes monitored being visual acuity, visual field, headache, diplopia and optic disc changes. **Results:** We evaluated 33 patients (31 female and 2 male). 25 patients had BMI less than 25. Commonest clinical presentation was headache. 7 patients showed normal CSF opening pressure. The most common MRI finding was flattening of posterior aspect of globe and was found in 90.90% (30). 25 patients showed either unilateral or bilateral transverse sinus stenosis. Most common finding in perimetry was enlarged blind spot. 4 patients recovered spontaneously and rests were treated with acetazolamide (1gm/day). All showed favorable outcome when followed up. **Conclusion:** Obesity may not be a dominant risk factor for development of IIH in the Indian subcontinent. Non obese IIH have better prognosis and tend to have a good response to medical management alone.

Keywords: Headache, idiopathic intracranial hypertension, obesity, papilledema, transverse sinus stenosis

Introduction

Idiopathic intracranial hypertension (IIH) is a syndrome of raised intracranial pressure, with normal cerebrospinal fluid (CSF) composition and normal brain parenchyma, without any ventriculomegaly or mass lesion. It is associated with obesity and most commonly occurs in women of childbearing age. Previously, this clinical condition was known as benign intracranial hypertension, and the term had gone out of use because of its potential for causing visual loss and poor quality of life. Although IIH may be an appropriate name for a subset of patients with the above-mentioned combination of clinical features who have primary intracranial hypertension of unknown etiology, the term seems inadequate and inappropriate for substantial segments of individuals with the syndrome precipitated by identifiable secondary causes and requires etiology-specific treatment. Hence, an umbrella term pseudotumor cerebri syndrome (PTCS) has been coined which incorporates both the primary and secondary causes, IIH being a subset of primary category and secondary category that includes causes such as venous sinus thrombosis, drugs, and multiple medical conditions. Previous epidemiological studies on IIH, mostly done on Caucasian populations, point out obesity as the major risk factor.[1,2]

Asian studies, on the other hand, show contrasting association of obesity with IIH. It was postulated earlier that the prevalence of obesity in IIH is much lower in Asians, but these studies were mostly done on Korean, Japanese, and Chinese populations,[3,4] where the overall rate of obesity is also low. This statement thus cannot be generalized for the Indian subcontinent, which is not only ethnically different but also has had a significant growth in obesity rates, in the recent years.[5] Literature from the Middle East, which has a high obesity rate, shows a profile quite similar to the Western world.[6] Studies from the Indian subcontinent are, hence, needed to reevaluate their risk factors.

Materials and Methods

The study was planned to be a prospective study on consecutive patients diagnosed as primary PTCS presenting to the neurology services of our institute, between June 2015 and October 2017.

Inclusion criteria

All patients who fulfilled the revised diagnostic criteria for primary PTCS in adults and children, proposed by Friedman *et al*. in 2013,[7] were included in the study. The patients were classified as definite or probable IIH. All patients of PTCS, who gave written informed consent, were made part of the study.

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Exclusion criteria

Patients with features of secondary PTCS, such as cerebral venous sinus thrombosis, history of medications, or systemic disorders associated with raised intracranial pressure (ICP) were excluded from the study.

Patients were evaluated by following parameters:

A. Detailed history was taken including
   i. Demographic features of age, gender, body mass index (BMI), and ethnicity
   ii. Detailed clinical symptoms with special emphasis on duration of symptoms, presenting symptoms (headache type and site, nausea, vomiting, and ocular symptoms such as transient visual obscuration, double-vision, and visual field defects)

B. General systemic examination
C. Detailed neurological examination with special emphasis on fundus examination, visual acuity, extraocular movements, confrontation test for visual field defects
D. Investigation including perimetry (Humphrey automated perimetry by Humphrey field analyzer II-I series, manufacturer-Zeiss), magnetic resonance imaging (MRI) brain, and magnetic resonance venography (MRV) brain (by 1.5 Tesla GE Voyager, manufacturer-GE Electronics), CSF manometry, and routine examination of CSF.

The patients were categorized into groups of normal BMI (18.5–24.9), overweight (25–29.9), and obese (≥30) patients as per the World Health Organization criteria.[8] For simplifying data, we compared the clinical and follow-up features between the two groups of normal and overweight patients.

All patients were treated medically with oral acetazolamide at a dose of 1 g/day.

Patients were followed up for a minimum period of 6 months, up to 2 years, with the outcomes monitored being visual acuity, presence of headache and diplopia, optic disc changes, and visual field by automated perimetry. All patients underwent a minimum of two follow-up perimetry, at 2 and 6 months after diagnosis.

The patients are divided into two groups, one being of normal BMI (<25) and the other being overweight (>25). The two groups are compared with respect to their baseline clinical features, including visual blurring, and follow-up recordings of visual acuity, fundus picture, and perimetry. An attempt is made to determine the correlation, if any, of BMI with diminution of vision as well as response to therapy in the form of normalization of optic disc and perimetry. Results were analyzed by IBM SPSS Statistics version 21.0 Armonk, New York: IBM Corp (mean, Mann–Whitney U-test, independent *t*-test).

Results

We evaluated 33 patients who met the revised diagnostic criteria for PTCS proposed by Friedman *et al*. Out of them, nine were classified probable and 24 were definite IIH. All patients were ethnically Eastern Indian. Table 1 shows the age and sex distribution of the patients. Table 2 shows the BMI distribution of the patients.

Clinical features

All patients except two presented with headache, which was dull aching in nature. Seventy-six percent had holocranial and 24% had bifrontal headache. The remaining two acephalgic patients had transient visual obscuration and diplopia as their presenting symptoms [Figure 1]. Papilledema was present in all, ranging Frisen[9] Grades 2–4. The duration of symptoms before presentation to our clinic ranged from 1 week to 3 months. There was no significant difference in occurrence of visual diminution at onset, between the normal BMI and overweight groups. Other variables including age at onset and duration of symptoms also had no significant correlation with visual blurring.

Investigations

CSF opening pressure ranged from 160 mm to 380 mm of H_2O [Figure 2]. The most common MRI finding was flattening of posterior part of the eye ball [Figure 3].

MRV showed unilateral transverse sinus (TS) stenosis in 13 (39.39%), bilateral stenosis in 15 (45.45%), and normal study in 5 (15%) patients. Among those with bilateral TS stenosis, all had a CSF opening pressure of >300 mm and papilledema Grades 3 or 4. No correlation of bilateral TS stenosis was found with higher BMI in our cohort.

The most common findings on perimetry were enlarged blind spot in 19 (63.33%), additional nasal field restriction in 3 (10%), peripheral field restriction in 4 (13.33%), and normal in 4 (13.33%). Perimetry could not be done in three patients. None of these patients, however, reported any field restriction on clinical confrontation testing.

Outcomes

All patients, excepting four, were managed with optimal medical management, with oral acetazolamide 1 g/day. At 2-month follow-up, 22 (66.6%) had normal fundus, while 11 (33.3%) still had a lower grade of papilledema. Four patients recovered spontaneously without treatment with improvement of clinical symptoms and resolution of papilledema. Perimetry revealed a persistent enlarged blind spot in 8 (24.2%) at

Table 1: Age and sex distribution

Total	Age (years)		Gender		Ratio
	Range	Mean	Female	Male	Female:male
33	13-40	24.30	31	2	15.5:1

Table 2: Body mass index (WHO International Classification) distribution

Total	Normal (<25)		Overweight (25-29.9)		Obese (>30)	
	Male	Female	Male	Female	Male	Female
33	2	23	0	6	0	2
	25		6		2	

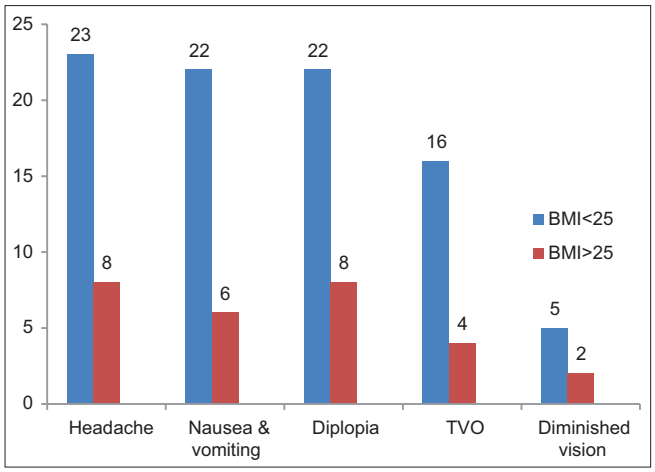

Figure 1: Clinical features - body mass index distribution

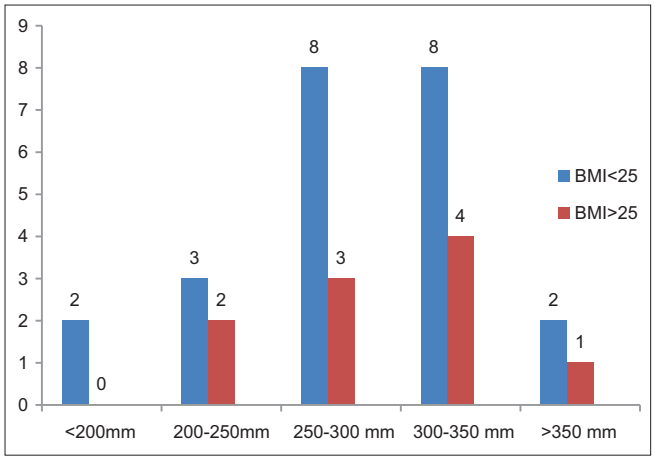

Figure 2: Cerebrospinal fluid opening pressure - body mass index distribution

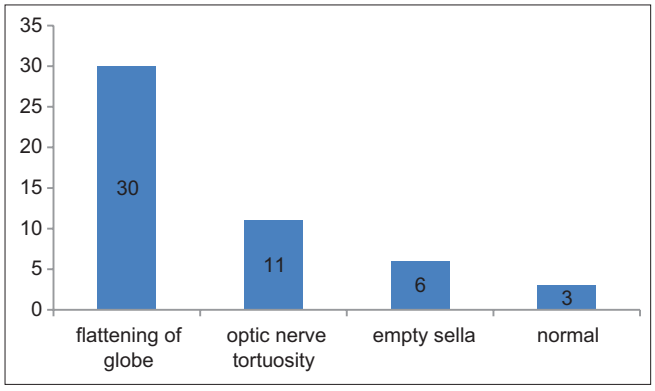

Figure 3: Magnetic resonance imaging findings

2 months and 3 (9%) patients at 6 months. The fundus had normalized (Frisen Grade 0) in all patients, by 6 months of follow-up. Clinically, all patients became asymptomatic, including normalized vision, at 2 months of follow-up. None of the patients had any long-term visual diminution and new-onset worsening or required surgical intervention [Table 3].

Table 3: Response of clinical and other abnormalities on follow-up

Parameter	Response at 2 months follow-up	Response at 6 months follow-up
Visual dimness	57% (4)	100% (7)
Headache	100% (33)	100% (33)
Diplopia	100% (33)	100% (33)
Fundus	66.6% (22)	100% (33)
Perimetry	75.8% (25)	91% (30)

There was no correlation of delayed improvement in fundus and perimetry at 2 months with the BMI, age, or duration of symptoms.

There was no significant difference in age and BMI distribution and duration of symptoms between the two outcome groups – perimetry findings on follow-up (independent samples *t*-test) and visual diminution. There was no significant correlation between the normal weight and overweight group, with visual acuity, follow-up perimetry, and imaging findings [Table 4].

Discussion

Our study uses the revised diagnostic criteria for PTCS, proposed by Friedman *et al*.,[5] for diagnosis of IIH. Although the modified Dandy criteria[10] is most widely used for diagnosing IIH, Friedman *et al*. in 2013 proposed a revised nomenclature, suggesting the use of the umbrella term PTCS, for all headaches with raised ICT with normal brain parenchyma. PTCS would then comprise primary PTCS of which IIH is a subset and secondary PTCS which would include cerebral venous sinus thrombosis and all patients with an underlying precipitating factor. While the modified Dandy criteria considers a CSF opening pressure >200 mm of H_2O as pathological, the new classification considers patients with clinical and radiological features of raised ICT, patients with CSF opening pressure >250 mm of H_2O as definite IIH, and those <250 mm of H_2O as probable IIH.[6]

The clinical presentation of our patients was similar to those in previously published studies.[3,4,6,11-15] However, most of these data involved Caucasian patients,[1,6,11,13-15] who had high association of IIH with obesity. The two most important risk factors for the development of primary PTCS in Caucasian and population in Middle East Asia included obesity and the female gender.[11,13-19] There have been previous studies on IIH in Asian patients, performed on Chinese, Japanese, and Korean populations.[3,4] Kim *et al*.[3] in their study on 14 Korean patients suffering from IIH found obesity in only one, normal weight in six, and overweight in seven. The mean BMI of all patients was 25.4, and the conclusion of their study was that obesity may not be a risk factor for IIH. In the study done by Liu *et al*.,[4] on 12 Taiwan patients suffering from IIH, obesity was found in only four, and the conclusion of the study was that in IIH in Chinese population, men were more affected

Table 4: Correlation of visual dimness and clinical response with clinical and laboratory parameters

Parameter	Diminution of vision at onset	Delay in response
Age	No difference in distribution of age across categories of decreased vision*	No difference*
Duration of symptoms	No difference*	No difference*
BMI	No difference*	No difference*
CSF opening pressure	Significant correlation (P<0.05)**	No correlation**

*Mann-Whitney U-test, **Independent *t*-test. BMI=Body mass index, CSF=Cerebrospinal fluid

than women and obesity was not as frequent as observed in Western countries.

Our patients, on the other hand, were all from the eastern part of Indian subcontinent, ethnically different from the Caucasians and East Asians. Our cohort had only two patients who were obese (3.3%) and 6 (20%) patients who were overweight. This was in stark contrast with other IIH studies, where all patients are overweight and 88% were obese.[6,11-15] For nonobese patients, a recent weight gain, even 5%–15%, is considered a risk factor.[14] None of our patients had a history of rapid or recent weight gain either.

In our study, there was no difference in clinical features, including the occurrence of visual blurring, between the normal BMI and overweight patients. Other variables such as age at presentation and duration of symptoms also had no correlation with the occurrence of diminution of vision. Diminished vision was noted only among seven patients with CSF pressures >300 mm, but all of them improved without any surgical intervention. None of the patients had any recurrence or worsening of symptoms on follow-up which has been found in some studies.[15,16] CSF opening pressure alone had a significant correlation with the presence of visual diminution at onset in some studies.[17,18] Thus, no particular factor apart from a higher CSF opening pressure was found to be associated with an increased risk for visual blurring in our study.

There was no incidence of visual loss or significant visual impairment in our cohort which is striking in comparison to previous studies. In the study by Almarzouqi *et al*.[6] in a Middle Eastern population suffering from IIH complete visual loss was found in 4% of the 57 patients. In another study done by Baheti *et al*.[20] in Kerala, India, 10% patients had permanent visual loss. A study by Bruce *et al*.[13] in the USA on a total of 450 definite IIH patients (197 Blacks, 253 non-Blacks) reported that the relative risk of severe visual loss for Blacks compared with non-Blacks was 3.5 (95% confidence interval [CI] 2.0–5.8, $P < 0.001$) in at least one eye and 4.8 (95% CI 2.1–10.9, $P < 0.001$) in both eyes.

Follow-up visits of our patients revealed persistent perimetry and fundus abnormalities in 75.8% and 66.6% patients, respectively, at 2 months, while the remaining patients improved. There was, however, no significant correlation of delayed improvement with BMI, age at onset, duration of symptoms, or CSF opening pressure. Our patients, therefore, do not show any correlation of visual diminution or delay in recovery with the BMI. Previous studies, on the other hand, suggest obesity as the most widely known risk factor for IIH and visual loss.[11-15,19] This indirectly highlights the role of obesity in visual loss and therapeutic response and projects a normal BMI, as a good prognostic marker.

Investigations such as imaging and perimetry were similar to previously published data, with the most common findings being flattening of posterior aspect of globe[21,22] and enlarged blind spot;[21,23] seven patients showed normal CSF opening pressure and their symptoms responded to treatment. Although the normal CSF pressure classifies the patients as probable IIH if the patient has typical symptoms of PTCS with papilledema, a low opening pressure measurement should not negate the diagnosis of PTCS and this finding corroborates with the previous studies regarding this.[7,24-26] The low value may have been taken at the nadir of a pressure wave, respectively.

All of our patients responded clinically, to oral acetazolamide therapy alone, with four patients improving spontaneously, without any specific management. There was subsequent normalization of fundus (Frisen Grade 0) and perimetry picture in all patients.

It has been postulated before that the incidence of obesity as well as IIH is much lower in some Asian countries such as China, Japan, and Korea[3,4] than among the Western and the Middle Eastern countries. Our cohort of Indian patients, despite being ethnically different from the East Asian population and having an overall higher rate of obesity, shows a similar low prevalence of obesity in IIH.

There are two important points that are being elucidated in this study. First, it highlights low occurrence of obesity among Indian IIH patients, with our cohort having only two obese and six overweight patients. This is in contrast with Western literature stating a high prevalence of obesity in IIH. This may indicate the presence of other risk factors for pathogenesis of IIH in Indian patients.

Second, it was seen that the clinical presentation and outcome did not vary much with rising BMI. The ultimate clinical response to medical therapy, including headache and visual loss also, did not differ between the normal BMI and overweight categories, with all responding to oral acetazolamide alone and none requiring surgery or bridging steroid therapy. This could indicate a better prognosis for IIH patients in the Indian subcontinent. Whether it is due to the low prevalence of obesity among these patients needs to be determined with larger studies in the future.

There are some limitations to this study. First, the definition of obesity, according to the BMI criteria, may not be universally applicable among all racial populations and especially in an ethnically heterogeneous country like India. It has also been stated that the percentage of body fat is relatively higher in Asians than in their Caucasian counterparts, and the BMI thus does not accurately reflect the body fat content. It is the increased adipose tissue that poses a risk for raised ICP, and not just the body weight per se. Second, the study includes a small sample of patients from Eastern India.

Conclusion

Obesity may not be a dominant risk factor for the development of IIH in the Indian subcontinent. Further studies are required to determine the role of other factors responsible for its pathogenesis. Atypical IIH, in the form of nonobese patients, without other commonly known risk factors, forms an important proportion of Indian IIH patients. It may be proposed that these patients, though similar to their Western counterparts in terms of baseline characteristics, tend to have a good response to medical management alone, without lasting visual loss, needing surgical intervention.

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Conflicts of interest

There are no conflicts of interest.

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