

# Profile of idiopathic intracranial hypertension in indian population – A prospective study

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## ABSTRACT

**Background.** Idiopathic intracranial hypertension (IIH) also termed pseudotumor cerebri syndrome (PTCS). It mainly affects young overweight women of the reproductive age group. There is a scarcity of literature on IIH among the Indian population.

**Objective.** To evaluate the clinical, demographic profile, laboratory parameters and outcomes of Idiopathic Intracranial hypertension (IIH) patients.

**Materials and method.** The current study was a prospective observational study on 43 patients who were diagnosed as primary PTCS presenting to the neurology department of Sri Ramachandra Medical College and Research Institute from December 2019 to August 2021. Patients were assessed for BMI, papilledema, CSF manometry, MRI brain with MR venography was done. Co-guide software, V.1.03, was used for statistical analysis.

**Results.** The mean age was  $33.12 \pm 12.29$  years (ranged 14 to 55) in the study population. There were 5(11.63%) males and 38(88.37%) females. The mean BMI was  $26.72 \pm 3.56$  kg/m<sup>2</sup> (ranged from 17.40 to 34.20). The mean duration of headache was  $28.41 \pm 26.23$  days (ranged 3 to 120) in the study population, and 39(90.69%) had papilledema. The mean CSF manometry was  $29.6 \pm 5.88$ (ranged from 16 to 42) cmH<sub>2</sub>O.

**Conclusion.** In the Indian subcontinent, obesity may not be considered as a major risk factor in the causation of IIH.

**Keywords:** Headache, idiopathic intracranial hypertension, obesity, papilledema, Indian population

## INTRODUCTION

Idiopathic intracranial hypertension (IIH) is also termed pseudotumor cerebri syndrome (PTCS) [1]. Foley first introduced the term “benign intracranial hypertension” [BIH] [2]. After many decades in 1989, Corbett and Thompson changed the name of BIH to “idiopathic intracranial hypertension (IIH)” after recognizing the “not so benign” nature of the entity [3]. It is a disease of unknown aetiology that causes increased intracranial pressure (ICP) without any identifiable cause. It's seen affecting young, overweight females of reproductive age, with symptoms of headache, transient vision loss, pulsatile tinnitus, vomiting, nausea, impaired visual fields, photopsia, diplopia, and eye pain. It is rarely seen among the male population [4,5].

Among the visual complications in IIH, Visual loss from papilledema is considered to be the most dangerous visual complication. It is caused when the optic disc swells because of increased intracranial pressure (ICP) [6]. Over 30% of patients are reported to suffer from permanent vision loss [4]. Headache is one of the most recurrent symptoms seen in IIH patients, which has varying severity. Headache due to increased intracranial pressure is commonly identified as throbbing or bursting and is triggered by factors that increase ICP, such as migraine, coughing, bending, sneezing, or exertion. Studies conducted in the past suggest that the pattern of the headache changes over some time and also is associated with the stage of IIH [7,8].

Along with high obesity rates, the incidence of idiopathic intracranial hypertension is also showing

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a rise [9]. The incidence in the UK general population is approximately 4.7 per 100,000, which has recently increased in connection with obesity [10]. More than 93% of people with idiopathic intracranial hypertension fall under the obese category [11]. Jan Hannerz et al. study results presented that obesity may secondarily elevate the pre-existent IIH [12]. Previous epidemiological studies on IIH, majorly conducted on Caucasian populations, suggest obesity as the crucial risk factor [13,14]. However, this association between obesity and IIH cannot be generalized for the Indian population due to ethnic and cultural variations [15]. There is a cavity in the literature on IIH among the India population. Hence, we conducted this research to evaluate the clinical and demographic profile, laboratory parameters, and outcomes of Idiopathic Intracranial hypertension (IIH) patients from an Indian subpopulation.

## MATERIALS AND METHODS

This study was a prospective observational study on consecutive patients diagnosed as primary PTCS presenting to the neurology department of Sri Ramachandra Medical College and Research Institute from December 2019 to August 2021. This study was performed in compliance with the ethical principles of the assigned institutional board. Written informed consent was obtained from the patients.

### Inclusion criteria:

1. Age >14 years and < 60 years.
2. Patients fulfilling the diagnostic criteria for primary PTCS in adults, proposed by Friedman et al. in 2013 [1], were included in this study. They were divided into definite or probable IIH as per this classification.

### Exclusion criteria:

1. Patients with features of secondary PTCS, those on chronic medications, or other disorders causing raised intracranial pressure (ICP) were excluded from the study.
2. Patients not willing to be included in the study.

The patients were categorized into groups of normal BMI (18.5-24.9), overweight (25-29.9), and obese ( $\geq 30$ ) patients as per the World Health Organization criteria [16].

A complete history was noted, including age, gender, body mass index (BMI). Symptomatology was studied by questions on duration of symptoms, presenting symptoms (headache type, site, and ocular symptoms such as transient visual obscuration, double-vision, and visual field defects). Neurological evaluation was done by fundus examination, visual acuity testing, extraocular movements testing, and test for visual field defects. Magnetic resonance imaging (MRI) brain and magnetic resonance venogra-

phy (MRV) brain, CSF manometry, and routine examination of CSF were also done.

## SAMPLE SIZE

The sample size was calculated assuming the proportion of Idiopathic Intracranial hypertension as 72.7% as per the study by Asutosh Pal et al [17]. The other parameters considered for sample size calculation were 14% absolute precision and 95% confidence level. The formula used for sample size was as per the study by Daniel WW et al [18]. The required sample size as per the above-mentioned calculation was 39. To account for a non-participation rate of about 10%, another 4, subjects were added to the sample size. Hence the final required sample size was 43.

## STATISTICAL METHODS

Examination findings, MRI findings etc., were considered as outcome variables. BMI was considered as explanatory variable. Risk factors and other symptoms were considered as study relevant variables. Mean and standard deviation was calculated for quantitative variables, frequency and proportion for categorical variables. Chi square test was used for categorical variable comparison. P value < 0.05 was considered statistically significant. Data was analysed by using Co-guide software, V.1.03 [19].

## RESULTS

A total of 43 subjects were included in the final analysis

The mean age was  $33.12 \pm 12.29$  years (ranged 14 to 55) in the study population. There were 5 (11.63%) males and 38(88.37%) females. The mean BMI was  $26.72 \pm 3.56$  kg/m<sup>2</sup> (ranged from 17.40 to 34.20). As risk factors, 5(11.63%)patients had anaemia, 3(6.98%) patients had PCOD, 2 (4.65%) patients had hypothyroidism and 1 (2.33%) patient is a known case of CKD, 1 (2.33%) patient received hormonal RX for amenorrhoea, 1 (2.33%) patient had Imatinib intake, 1 (2.33%) had oral contraceptive intake, 1 (2.33%) patient is a known case of SLE, 1 (2.33%) patient had steroid withdrawal history and 1(2.33%) patient had history of significant weight loss. 1 (2.33%) had history of old CVT and 4 (9.30%) had seizure as other associated neurological comorbidities. Out of 29 participants, 22 (75.86%) women had regular menstrual cycles, 6 (20.69%) had irregular menstrual cycles and 1(3.45%) was post-menopausal. The mean duration of headache was  $28.41 \pm 26.23$  days (ranged 3 to 120) in the study population (Table 1).

**TABLE 1.** Summary of baseline parameter (n=43)

Parameter	Summary
Age (in years)	33.12 ± 12.29 (Ranged 14 to 55)
<b>Gender</b>	
Male	5(11.63%)
Female	38(88.37%)
<b>BMI (in Kg/M2)</b>	26.72 ± 3.56 (Ranged 17.40 to 34.20)
<b>Risk Factors</b>	
Anaemia	5(11.63%)
PCOD	3(6.98%)
Hypothyroidism	2(4.65%)
CKD	1(2.33%)
Hormonal RX for amenorrhoea	1(2.33%)
Imatinib	1(2.33%)
Oral contraceptive	1(2.33%)
SLE	1(2.33%)
Steroid withdrawal	1(2.33%)
Loss of weight	1(2.33%)
<b>Associated Neurological Disorder</b>	
OLD CVT	1(2.33%)
Seizure disorder	4(9.30%)
<b>Menstrual History(n=29)</b>	
Regular	22(75.86%)
Irregular	6(20.69%)
Post-menopausal	1(3.45%)
<b>Duration of headache (in days) (n=39)</b>	28.41 ± 26.23 (ranged 3 to 120)

Among the other symptoms, 1(2.33%) had CSF rhinorrhoea, 8(18.60%) had associated nausea and vomiting. 39(90.69%) patients in our study had papilledema. The mean CSF manometry was 29.6 ± 5.88(ranged from 16 to 42) in the study population. Among MRI findings, the majority 24(55.81%) had optic nerve findings, followed by 21 (48.84%) with empty Sella. On MR Venogram, majority 27 (64.29%) were normal, 6 (13.95%) had Left transverse sinus stenosis and 5 (11.63%) had bilateral transverse sinus stenosis. Out of 43 participants, 39 (90.70%) were treated with medication and 4 (9.30%) were treated with thecal shunt (Table 2).

Normal eye symptoms were reported by 26 (60.47%) patients, 10 (23.26%) patients had blurring of vision, 4 (9.30%) had vision loss, and 3(6.98%) had diplopia. On examination, 34 (79.07%) had normal extraocular eye movements, 6 (13.95%) patients had 6<sup>th</sup> nerve palsy, 2 (4.65%) had vision loss and 1 (2.33%) had left eye visual field defect (Table 3).

The difference in the proportion of gender across BMI (in kg/m<sup>2</sup>) was found to be insignificant with a p-value of 0.584, since majority-15 (93.75%) participants were female among overweight. Out of 17 participants in normal BMI, 3 (17.65%) had nausea and vomiting. Out of 16 participants in overweight, 1 (6.25%) had CSF rhinorrhoea and 3 (18.75%) had nausea and vomiting. Out of 10 participants in

**TABLE 2.** Summary of MRI findings and other parameters (n=43)

Parameter	Summary
<b>Other Symptoms</b>	
CSF Rhinorrhoea	1(2.33%)
Nausea and vomiting's	8(18.60%)
Nil	34(79.1%)
<b>Papilledema</b>	39(90.69%)
<b>CSF manometry cm H<sub>2</sub>O</b>	29.6 ± 5.88 (ranged 16 to 42)
<b>MRI Findings</b>	
Empty Sella	21(48.84%)
Optic nerve findings	24(55.81%)
Optic bulb flattening	9(20.93%)
Normal	12(27.91%)
<b>MR Venogram</b>	
Normal	27(64.29%)
Right transverse sinus stenosis	2(4.76%)
Left transverse sinus stenosis	6(13.95%)
Bilateral transverse sinus stenosis	5(11.63%)
Left transverse sinus & sigmoid sinus stenosis	2(4.76%)
<b>Treatment</b>	
Medication	39(90.70%)
Thecal shunt	4(9.30%)

**TABLE 3.** Descriptive analysis of other parameter in the study population (n=43)

Parameter	Summary
<b>Eye Symptoms</b>	
Normal	26(60.47%)
Blurring of vision	10(23.26%)
Vision loss	4(9.30%)
Diplopia	3(6.98%)
<b>Examination Findings</b>	
6 <sup>th</sup> Nerve palsy	6(13.95%)
Left eye visual field defect	1(2.33%)
Vision loss	2(4.65%)
Normal extraocular eye movements	34(79.07%)

obese, 2 (20%) had nausea and vomiting. There was no statistically significant difference found across BMI with respect to MRI findings like Empty Sella (p value 0.349), Optic nerve findings (p value 0.454), Optic bulb flattening (p value 0.941) and normal MRI findings (p value 0.620).

## DISCUSSION

This study showed that the mean BMI was 26.72 ± 3.56 kg/m<sup>2</sup> among study population indicating that obesity may not be the dominant risk factor of IIH. MRI findings showed 55.81% had optic nerve findings and 64.29% had normal MR venogram. Thecal shunting was done in 9.30% of the patients, while majority of patients responded to medical management.

**TABLE 4.** Comparison of gender and MRI findings across BMI (n=43)

Parameter	BMI			Chi square	P value
	Normal <25 (n=17)	Over weight 25 to 29.9 (n=16)	Obese >30 (n=10)		
<b>Gender</b>					
Male	3 (17.65%)	1 (6.25%)	1 (10%)	1.075	0.584
Female	14 (82.35%)	15 (93.75%)	9 (90%)		
<b>Other Symptoms</b>					
CSF Rhinorrhoea	0 (0%)	1 (6.25%)	0 (0%)	*	*
Nausea and Vomiting's	3 (17.65%)	3 (18.75%)	2 (20%)		
Nil	14 (82.35%)	12 (75%)	8 (80%)		
<b>MRI Findings</b>					
Empty Sella	10 (58.82%)	8 (50%)	3 (30%)	2.107	0.349
Optic nerve findings	11 (64.71%)	9 (52.94%)	4 (40%)	1.579	0.454
Optic bulb flattening	4 (23.53%)	3 (18.75%)	2 (20%)	0.121	0.941
Normal	4 (23.53%)	4 (25%)	4 (40%)	0.956	0.620

\*No statistical test was applied- due to 0 subjects in the cells

There are many studies and literature available on IIH but, there are very few studies done on Indian population. In the present study, mean age was 33.12 years. Wall M et al. observation was similar to the current study and the mean age was 30 years at time of diagnosis [20]. Similarly Ahmet OK et al. also observed mean age as  $30.25 \pm 13.12$  years [21]. As per the study in UK, estimated incidence in women aged 15-44 years was 3.5/100,000 [22]. The proportions of females were high (88.37%) in the current study as compared to males. Bruce et al. in their study found a 9% prevalence of IIH in male population confirming that IIH is rarely observed in men [23]. Another study results also showed IIH rarely occurs in men when compared with women [24]. An epidemiological study conducted in the United States estimated that women are 8 times more likely to have IIH than men [25].

In the present study, mean BMI was 26.72 kg/m<sup>2</sup> which fell under overweight category. Previous literature supports these findings as it has shown that approximately 70-80% of IIH patients are obese and over 90% are overweight [26-28]. Another study suggests that as many as 90% of patients with IIH are obese [29]. Study done by Daniels et al. concluded that those with (BMI <30) are also at higher risk of IIH [18]. This shows even overweight population is at risk of IIH. Anaemia and PCOD/PCOS were common risk factors in the current study population. Our results were in harmony with results of study done in Kuwait where Anaemia was found in 38.1% of study population [30]. A retrospective cohort study of 607 patients with IIH found an independent association between IIH and anaemia in patients with obesity [31]. Glueck et al. reported that in 38 women with IIH, 15 (39%) were found to have PCOS

[32]. Knochelhauer et al. stated that occurrence of PCOS (39-57%) in women with IIH was observed to be 5 to 8 times higher than the general population, which have only 7% prevalence [33]. Previous literature gives agreement on the statement that the majority of patients with IIH are obese women of child-bearing age [34,35].

Headache is present in 90% of IIH patients and is a major reason for seeking medical advice [36]. Our study also showed headache as a common symptom. Similarly, in a study out of 153 patients, 69 patient's presenting symptoms was headache [37]. Friedman DI et al concluded that headache was observed in 139 (84%) of the 165 participants at baseline [38]. Craig JJ et al and Yri HM et al concluded that headache is present in around 93% of patients at the time of diagnosis [39,40]. In our study, papilledema was commonly observed sign (90.69%). Similarly, another study reported that 71% of study population had papilledema [21]. Outcome of the study was good with majority of patients responding to medical management alone.

The current study has limitations such as relatively small sample size and the generalizability of the present study findings is poor. Hence, large scale multi-centric studies are recommended in future.

## CONCLUSION

As per this study, obesity may not be considered as a major risk factor. Atypical IIH, with unknown risk factors/other risk factors like anaemia, form an important proportion of Indian IIH patients. Outcome of IIH in our study was good with majority of patients responding to medical management alone.

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