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A Study of Clinical Etiological and Radiological Profile of Idiopathic Intracranial Hypertension at a Tertiary Care Center

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ABSTRACT

Idiopathic intracranial hypertension (IIH) also known as pseudotumor cerebri is characterized by increased intracranial pressure of unknown cause and is usually seen in young obese women. There is rise in incidence of IIH but only a little progression made in determining its pathogenesis and treatment. To study the clinical profile of patients with IIH. To correlate the presenting symptoms with the examination findings and radiological features and to assess the severity based on these clinical, radiological features. Patients who presented to Government General Hospital, Guntur between September 2020 and August 2023 and diagnosed with IIH were extensively studied. 80 cases met Friedman and Jacobson criteria for IIH, of which 72(90%) were females and 8 (10%) were males. Significant association with obesity has been established and a direct correlation observed between cerebrospinal fluid (CSF) opening pressure and body mass index (BMI) and also clinical visual symptoms and magnetic resonance imaging (MRI) findings. IIH is a serious and challenging condition with a significant burden on individual and health care system. A prompt diagnosis and accurate management are required to avoid permanent visual loss for the patient. Idiopathic intracranial hypertension (IIH), headache, Cerebrospinal fluid (CSF) pressure, obesity, papilledema.

INTRODUCTION

Idiopathic intracranial hypertension [IIH] was first described by Dandy as "Pseudotumor cerebri" because of common clinical signs of intracranial hypertension without tumoral causes[1]. Little is known about the pathogenesis of this disorder which demonstrates no ventriculomegaly or mass lesion and with a normal CSF composition[2]. It is characterized by raised intracranial pressure (ICP) of unknown cause, when all other causes of raised ICP have been excluded[3]. It tends to affect young, overweight women of reproductive age, with symptoms of headache, nausea, vomiting, transient visual loss, impaired visual fields, photopsias, diplopia and eye pain[4]. The prognosis of the condition is difficult to ascertain, some patients can suffer permanent visual impairment due to associated papilledema[5]. There is a slow rise in the incidence of IIH. How ever there is a little progress made in determining the pathogenesis, assessing the severity of the illness and treatment of IIH[6].

Aims and objectives:

- To study the clinical profile of patients with idiopathic intracranial hypertension
- To correlate the presenting symptoms with the examination findings and radiological features and to assess the severity based on these clinical, radiological features

MATERIAL AND METHODS

Study area: This study was conducted in the Department of Neurology, Government General Hospital/Guntur Medical College, Guntur. This is a tertiary care referral center in the Guntur district in the state of Andhra Pradesh, India.

Study population: Patients admitted with features of idiopathic intracranial hypertension at Government hospital, Guntur in the study period.

Study period: September-August 2020-2023. 36 months.

Sample size: 80 patients who met Friedman and Jacobson criteria for IIH were included in the study.

Type of study: It is a prospective study to analyse the patients presenting with symptoms suggestive of IIH.

Data collection: Demographic data (sex, age), clinical signs (ophthalmic and neurological symptoms, time to diagnosis, Body mass index (BMI) and CSF opening pressure) and radiological signs on cerebral MRI (Empty sella, enlarged perioptic subarachnoid space, supero-inferior kinking of optic nerve) and therapeutic strategies used will be collected.

BMI categorisation:

- Normal BMI-18.5-24.99 kg m^2
- PRE-obese-25.00-29.99 kg m^2
- Obese class 2-35.00-39.99 kg m^2
- Bese class 3- $\geq$40.00 kg m^2

Inclusion criteria:

- Age 10-50 years
- Clinical and MRI features suggestive of IIH.

Exclusion criteria: Those with secondary causes of intracranial hypertension like intracranial mass lesions, stroke, dural AV fistula, hydrocephalus and especially venous sinus thrombosis.

- Visual assessment of the cases
- Visual acuity was done in all the patients using "Snellens chart"
- Visual field analysis was done in all the patients by perimetry charting using "Humphreys visual field analyser"
- Grading of papilledema was done on the basis of Modified "Frisens Grading"

CSF analysis: Lumbar puncture was performed in all the patients, in lateral decubitus position, on a surface level. A standard spinal needle 22G was used. The opening pressure was recorded with a manometer positioned at 90° angle to the spinal canal with the patients knees and hip in an extended position and neck straightened. CSF pressure was recorded when the patient was relaxed and the pressure values were stabilized.

Statistical analysis: Categorial variables are reported as frequency and percentage. Continuous variables are reported as median (range) or Mean±Standard deviation. p-values were calculated for relevant variable using SPSS software.

ANALYSIS AND RESULTS

Sex distribution: In our study, 72 (90%) patients were females 8 (10%) were males

Age distribution: Out of 80 patients the youngest was 16 years old and the oldest was 45 years old. Most of the patients were in the age group of 26-30 years (27.5%). Mean age distribution was 28.48±7.43 years. Range is 16-45 years.

Body mass index: In our study, the range of BMI was 19.94±43.56 kg m^{-2}

Mean BMI = 29.39±5.33 kg m^{-2}. 18 (22.5%) patients had normal BMI (18.5±24.99 kg m^{-2}) and 62 (77.5%) patients were obese.

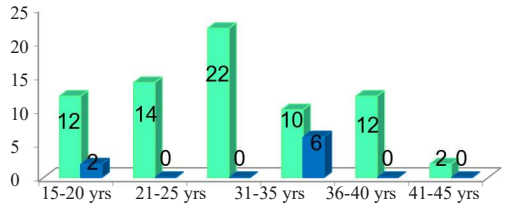

Fig. 1: Age distribution

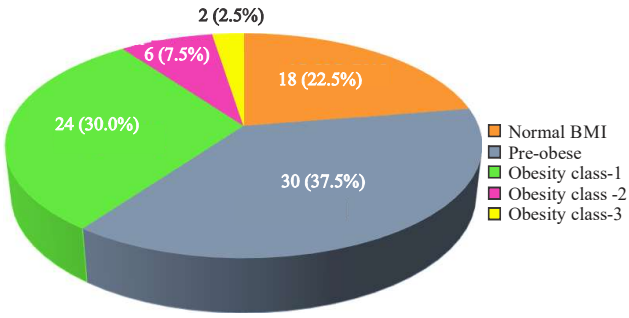

Fig. 2: Body mass index

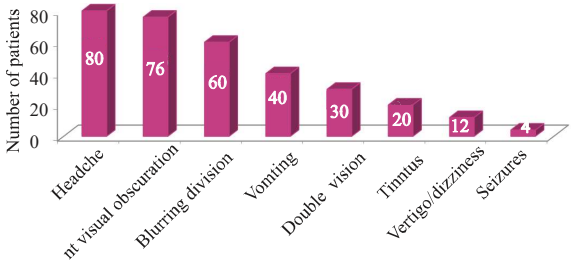

Fig 3: Symptomatology

Comorbidities: Four patients had type-2 diabetes mellitus for more than 1 year, 2 had diabetes for 2 years and bronchial asthma since childhood, 4 had PCOD for 4-5 years duration, 2 had hypothyroidism with PCOD for 2 years, 2 had Hypertension for 6 years with DUB for 3 months, 6 had h/o infertility and 6 had hypothyroidism, 2 had MCTD of 2 years duration, 2 had SLE of 1 year duration, 2 had chronic osteoarthritis of both knees of 2 years duration, 48 cases did not have any co-morbidities.

Addiction to smoking and alcoholism: Six out of 8 males were addicted to smoking. Four out of 8 males were addicted to alcoholism. None of the females had any addiction.

Drug usage

Chronic steroid usage for >1 year: 6 patients (OA, MCTD, BA)

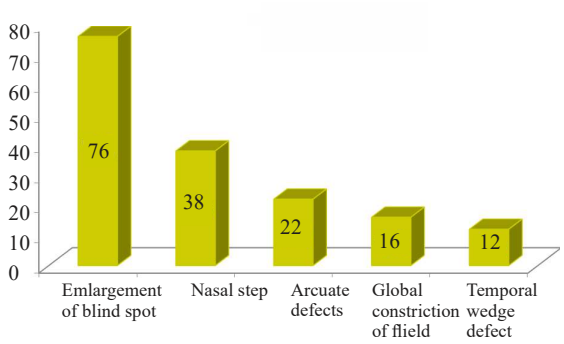

Fig. 4: Visual field defects

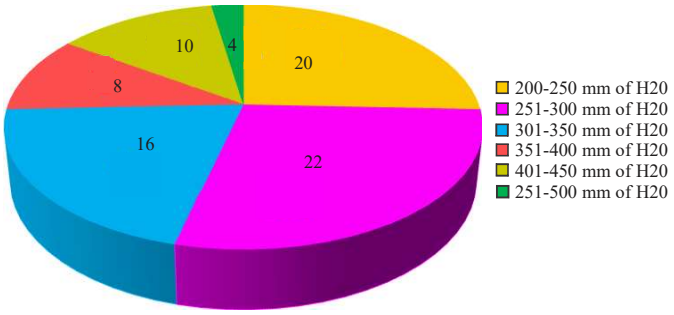

Fig. 5: CSF opening pressure

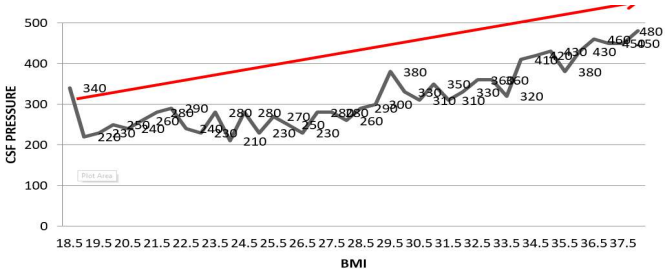

Fig. 6: Association between BMI and CSF opening pressure

OCPs for >6 months: Fourteen patients (3 Infertility, 3 PCOD, 1 DUB)

OCPs + Steroids >3 months: Two patients (SLE)

Minocycline for 2 months: Two patients (Acne vulgaris)

Minocycline + retinoic acid for 3 months: Two patients (Acne vulgaris)

Clinical symptomatology: Headache was the most common presenting symptom present in all the patients (100%). Transient visual obscurations in 76 (95%), Blurring of vision seen in 60 (75%), Nausea and

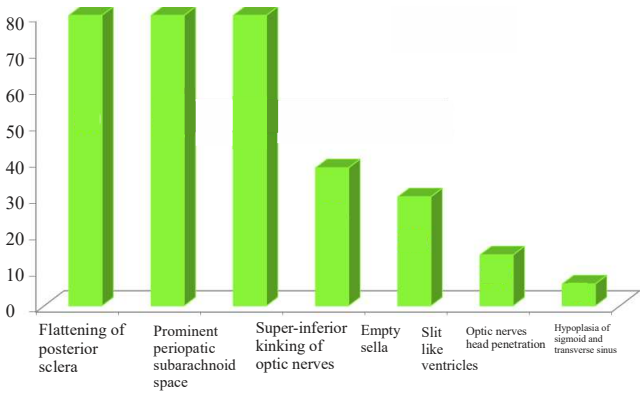

Fig. 7: MRI findings

Table 1: Association between duration of headache and blurring of vision

	Blurring of vision		
Headache	Yes	No	Total
0-3months	38	12	50
3-6months	12	6	18
6-12months	8	2	10
12-24 months	2	0	2
Total	60	20	80

Table 2: Association between CSF opening pressure and blurring of vision

	Blurring of vision		
CSF opening pressure	Yes	No	Total
200-300mm of H_2O	22	20	42
301-400 mm of H_2O	24	0	24
401-500 mm of H_2O	14	0	14
Total	60	20	80

Chi square value is 12.063, p-value= 0.002 → Significant.

Table 3: Association between CSF opening pressure and presence of double vision

	Double vision		
CSF opening pressure	Present	Absent	Total
200-300 mm of H_2O	8	34	42
301-400 mm of H_2O	8	16	24
401-500 mm of H_2O	14	0	14
Total	30	50	80

Chi square value= 14.806, p-value= 0.001→ Significant

vomiting in 40 (50%), Double vision in 30 (37.5%) Tinnitus in 20 (25%), Vertigo/ dizziness in 12 (15%), Seizures in 4 (5%).

Headache duration: 62.5% presented with headache duration of <3 months. In 22.5% cases the duration was 3-6 months. In 12.5% it was 6-12 months. 2 cases presented with slow progressive headache of 2 years duration. Mean duration 4.35±4 months.

Association between duration of headache And blurring of vision: No association was found between the headache duration and the presence or absence/severity of symptoms of blurring of vision or double vision. p-value is 0.862 (Not significant). It's the rate progression of headache rather than the duration that is important in assessing the severity of the disease.

Table 4: Association between CSF opening pressure and grade of papilledema.

	Pailledema grade				
CSF opening pressure	Grade 1	Grade 2	Grade 3	Grade 4	Total
200-300 mm of H_2O	14	20	6	2	42
301-400 mm of H_2O	0	2	14	8	24
401-500 mm of H_2O	0	0	0	14	14
Total	14	22	20	24	80

Chi square value= 36.937, p-value= 0.000021 → Significant

Table 5: Correlation between CSF opening pressure and presence of finding of empty sella on MRI

	Empty sella on MRI		
CSF opening pressure	Absent	Present	Total
200-300mm of H_2O	38	4	42
301-400mm of H_2O	4	20	24
401-500mm of H_2O	0	14	14
Total 42	38	80	

Chi square value= 26.060, p-value= 0.000032 à Significant

Table 6: Correlation between CSF opening pressure and finding of optic nerve head protrusion on MRI

	Optic nerve head protrusion on MRI		
CSF opening pressure	Absent	Present	Total
200-300mm of H_2O	42	0	42
301-400mm of H_2O	24	0	24
401-500mm of H_2O	0	14	14
Total 66	14	80	

Chi square value= 40.080, p-value= 0.000017 à Significant

Table 7: Correlation between CSF opening pressure and presence of finding of slit like ventricles on MRI

	Slit like ventricles on MRI		
CSF opening pressure	Absent	Present	Total
200-300 mm of H_2O	34	8	42
301-400 mm of H_2O	14	10	24
401-500 mm of H_2O	2	12	14
Total	50	30	80

Chi square value= 10.083, p- value= 0.006 à Significant

Bilateral abducens palsy: Bilateral abducens palsy was present in 22 cases (27.5%). The presence of bilateral abducens palsy has correlated with the severity of visual loss and double vision.

Papilledema:

- Papilledema was present in all the cases in our study
- Grade 1 papilledema in both eyes in 14 cases (17.5%)
- Grade 2 papilledema in both eyes in 22 cases (27.5%)
- Grade 3 papilledema in both eyes in 20 cases (25%)
- Grade 4 papilledema in both eyes in 20 cases (5%)

Two patients had Grade 4 papilledema in right eye and grade 3 in left eye. One patient had grade 5 papilledema in left eye and grade 4 in right eye. One patient had grade 5 papilledema in right eye and grade 4 in left eye

Visual acuity: Assessed by Snellens chart. Normal visual acuity (VA) of 6/6 was present in 12 cases (15%).

Table 8: Categorisation of treatment

Category	BMI (kg m^2)	No. Of cases	Treatment given
Category 1	18.5-24.99	18 (22.5%)	acetazolamide alone (250 mg qid)
Category 2	25.00-29.99	30 (37.5%)	acetazolamide (250 mg qid) + Topiramate (25 mg od)
Category 3	30.00-39.99	30 (37.5%)	acetazolamide (250 mg 4^{th} hrly) + Topiramate 50 mg od + weight reduction
Category 4	≥40.00	2 (2.5%)	Acetazolamide (250 mg 4^{th} Hrly) + Topiramate 50 mg BID + weight reduction referred to neurosurgeon

Table 9: Sex distribution comparison with previous studies

	Claire Chagot *et al.*[7]	SrdjanLjubisavjevic *et al.*[8]	Radhakrishnan *et al.*[9]	Durcan *et al.*[10]	Our study
No. of cases	79	18	18	48	40
F:M ratio	9.2:1	5:1	8:1	4.3:1	9:1

Table 10: Age distribution comparison with previous studies

	Claire Chagot *et al.*[7]	SrdjanLjubisavjevic *et al.*[8]	Devin Binder *et al*[11]	Hingwala *et al.*[12]	Our study
Mean age	33 years	29 years	28 years	27 years	29 years
Range	16-63 years	18-52 years	18-44 years	7-44 years	9:1

Table 11: Body mass index comparison with previous studies

	Claire Chagot *et al.*[7]	SrdjanLjubisavjevic *et al.*[8]	Radhakrishnan *et al*[9]	Durcan *et al*[10]	Our study
Percentage with obesity	69%	84%	70%	67%	77.5%
Range of BMI	17-68 kg m^2	24-39 kg m^2	18-40 kg m^2	17-38 kg m^2	19-43 kg m^2
Mean BMI	35±9.7 kg m^2	30.2±3.1 kg m^2	32.3 kg m^2	29.6 kg m^2	29.39±5.33 kg m^2

VA between 6/12-6/60 was seen in 48 cases (60%). VA beyond 6/60 i.e. Counting fingers, Hand movements and Perception of light is considered blinding. Seen in 20 cases (25%). CF + in 6 cases (7.5%), HM+ in 12 cases (15%), PL+ in 2 cases (2.5%). Worsening of visual acuity was corresponding to the degree of papilledema.

Visual field defects: The visual field defects in idiopathic intracranial hypertension are a direct expression of the pathological changes in the optic nerve and optic nerve head. Done with Humphreys visual field analyser. The most common visual field defect observed in our cases is enlargement of blind spot (95%).

Csf opening presure: The mean CSF opening pressure in our case series is 313.25 mm of H_2O with a SD of 73.21 mm of H_2O. Range was 210-480 mm of H_2O. CSF cellularity and chemistry was normal in all the patients.

Association between bmi and csf opening pressure: We observed a positive correlation between the body mass index and CSF opening pressure. ($p<0.00004$) Association between CSF opening pressure and blurring of vision. Association between CSF opening pressure and presence of double vision. Association between CSF opening pressure and grade of papilledema.

MRI findings: Correlation between CSF opening pressure and presence of finding of Empty Sella on MRI. Correlation between CSF opening pressure and the finding of Optic Nerve head protrusion on MRI. Correlation between CSF opening pressure and presence of finding of slit like ventricles on MRI.

CSF analysis: All the parameters of CSF analysis were within normal limits in all the patients.

- Mean Total count per cumm = 3.4±1.17.
- Mean sugar levels in mg dL = 69.90±13.0.
- Mean protein levels in mg dL = 30.24±6.56.

Treatment given: We have categorized patients based on their BMI and severity of symptoms. All the patients were advised to stop prior offending drugs. Patients with normal BMI and mild symptoms were started on Acetazolamide 1 g day. Two patients with impending visual loss at diagnosis were started on acetazolamide and topiramate and were referred to neurosurgeon but they were lost to follow up.

Follow up after 3 months: All the patients were assessed for visual symptoms and signs at a 3month follow up after discharge. 20 patients did not turn up for follow up assessment. Out of 58 cases, all the patients of normal BMI category showed a significant improvement in symptoms and resolving papilledema on fundus examination.

In the high BMI category, 6 cases presented with worsening symptoms and were referred to neurosurgeon. 6 cases showed persistence of visual symptoms and signs and their BMI assessed showed no change when compared to previous values. Remaining cases of high BMI category showed a significant improvement in symptoms and a resolving papilledema on fundus examination. However visual fields did not show a drastic improvement at 3month follow up.

DISCUSSION

Sex distribution: In our study, F:M = 9:1.

Age distribution: In our study of 40 patients, the mean age at presentation is 28.48±7.43 years. Range is 16-45 years.

Body mass index (BMI): In our study, the range of BMI was 19.94±43.56 kg m^2, Mean BMI= 29.39±5.33 kg m^2. 9 (22.5%) patients had normal BMI (18.5±24.99 kg m^2) and 31 (77.5%0 patients were obese. In the present study, the obtained results support the fact that obesity can predispose a patient to IIH. On the other hand, in our study 22.5% patients were not obese. Obesity plays a possible role, but it is purely hemodynamic because the pressure in the venous system is increased due to increased intraabdominal and intrathoracic pressure resulting in decreased CSF reabsorption and increased ICP[13,14].

Clinical symptomatology: Although IIH is considered to be a disease whose causes are only assumed, IIH symptoms and signs are anyway defined. The presentation of IIH was not asymptomatic in any of the patients in our study. Headache was the most common presenting symptom present in all the patients.

Papilledema: Papilledema was present in all the cases in our study. Papilledema is the cardinal sign of IIH. Optic disc edema either directly or indirectly is the cause of visual loss of IIH. The higher the grade of the papilledema the worse the visual loss[15] however, in the individual patient the severity of visual loss cannot accurately be predicted from the severity of the papilledema. A partial explanation for this is that when papilledema causes axonal death the amount of papilledema decreases.

Visual field charting: The visual field defects in idiopathic intracranial hypertension are a direct expression of the pathological changes in the optic nerve and optic nerve head. Visual field loss is ubiquitous in IIH. The most common defects are enlargement of the physiologic blind spot and loss of inferonasal portions of the visual field, along with constriction of isopters. Central defects are distinctly uncommon and warrant a search for another diagnosis unless there is a large serous retinal detachment from high-grade optic disc edema spreading toward the macula. The loss of visual field may be progressive and severe, leading to blindness.

CSF opening pressure: The mean CSF opening pressure in our case series is 313.25 mm of H_2O with a SD of 73.21 mm of H_2O. CSF cellularity and chemistry was normal in all the patients. We observed a positive correlation between the body mass index and CSF opening pressure ($p<0.00004$). This is in contrary to some of the previous studies where they found no such correlation[16]. And there was also a positive correlation between CSF opening pressure and severity of symptoms like blurring of vision, double vision and the grade of papilledema, visual acuity and visual field defects on examination irrespective of the duration of the symptoms.

MRI findings: Many articles have described imaging signs of IIH on MRI. Most reports regarding this subject conclude that in the appropriate clinical setting, there are several neuro imaging signs that, although not specific, can assist in establishing the diagnosis of IIH. Findings of flattening of posterior sclera, tortuosity with supero-inferior kinking of both the optic nerves and enlarged perioptic subarachnoid space were found in all the cases. In our study we found out that presence of findings of optic nerve head protrusion and slit like ventricles correlated positively with increasing CSF opening pressures.

Treatment: Carbonic anhydrase inhibitors (acetazolamide) are the only effective medications for the treatment of papilledema. Acetazolamide was originally demonstrated by Rubin *et al*.[17] to variably decrease CSF production by 6-57% among human subjects. We have categorized patients based on their BMI and severity of symptoms. All the patients were advised to stop prior offending drugs.

CONCLUSION

IIH represents an increasing burden to public health as well as clinical practice especially in countries experiencing epidemic obesity. It is a diagnosis of exclusion. The etiology of increased intracranial pressure in IIH is unclear and remains a topic of much interest and continued research. Obesity is an important risk factor associated with IIH occurrence and recurrence.

IIH requires a multi-disciplinary approach by a Neurologist, an Ophthalmologist and a Neurosurgeon. Patients presenting with papilledema need careful evaluation and timely investigations. A systematic approach to the patient is of utmost importance. Once the diagnosis of IIH is confirmed, acute management depends on the immediate risk to vision. Disease modifying therapy is weight loss.

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