Clinical profile and ophthalmological manifestations of idiopathic intracranial hypertension in adults at a tertiary care center in India: A cross-sectional study

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**Purpose:** Our aim was to describe the clinical profile of patients with idiopathic intracranial hypertension (IIH), assess ophthalmological manifestations, and correlate grade of papilledema with optic nerve sheath diameter (ONSD) and cerebrospinal fluid (CSF) opening pressure. **Methods:** This was a prospective cross-sectional study. Patients between 18 and 60 years, diagnosed with IIH using modified Dandy criteria were included. Demographic details, ocular symptoms and signs were noted and papilledema graded. Ocular investigations such as B-scan ONSD and perimetry findings were noted for analysis. **Results:** The study included 32 patients of mean age 35.25±9.57 years with a predominantly female population (96.9%). Mean BMI was 28.12±5.32 kg/m². Common presenting complaint was headache (87.5%). The most common gynecological disorder was dysmenorrhea (15.6%). Vitamin D deficiency (46.9%) was a biochemical abnormality seen. Most patients had BCVA 6/6 (62.5%). Lateral rectus palsy was present in 12.5%. Papilledema was present in 81.3% eyes with 31.3% Grade I. There was visual field loss in 53.1%, with 20.3% Grade I. Mean CSF opening pressure was 376.3±191.51 mmH₂O. MRI showed empty sella (34.4%) and tortuous optic nerve (18.8%). MRV showed transverse sinus stenosis (52.4%) as common abnormality. There was significant correlation between grade of papilledema and B-scan ONSD. No correlation was seen between CSF opening pressure and ONSD, grade of papilledema and grade of visual field defect and CSF opening pressure with BMI. **Conclusion:** Clinical profile of patients with IIH was an overweight female of child-bearing age with headache. Visual field examinations are essential in management and follow-up. B-scan ONSD is useful to quantify raised ICP.

**Key words:** Headache, IIH, overweight, papilledema

Idiopathic intracranial hypertension (IIH) is of unknown etiology, affecting obese women of childbearing age. Intracranial pressure (ICP) is elevated with neurological manifestation of papilledema, leading to optic atrophy.[1,2]

The diagnosis of IIH is based on the modified Dandy criteria.[3,4] The estimated annual incidence is 0.9 per 100,000 in the general population with a female-to-male ratio of 8.1.[5,6]

Literature[7–8] shows correlation between optic nerve sheath diameter (ONSD) and Cerebrospinal fluid (CSF) opening pressure.

Our aim was to describe the clinical profile of IIH, ophthalmological manifestations and correlate ONSD with CSF opening pressure to help in early diagnosis, treatment and improvement of visual prognosis.

**Methods**

A prospective, cross-sectional, descriptive study was carried out between September 2018 and September 2020. All consecutive patients diagnosed with IIH according to the modified Dandy criteria between ages 18 and 60 years were included. Patients with other concurrent ocular pathology, other neurological symptoms and who were unable to perform automated perimetry were excluded.

The following details were recorded: demographic details of age and gender, a detailed history determining the duration of symptoms, past medical and surgical history, history of medications and family history. Symptoms of headache, tinnitus, vision loss, diplopia, TVO, photophobia and phonophobia were recorded.

Body mass index (BMI) was calculated after height and weight measurements. Ophthalmic examination included visual acuity with Snellen’s chart, near vision with Times New Roman chart and color vision with Ishihara’s pseudo-isochromatic test plates. Anterior segment examination with a slit-lamp biomicroscope, pupillary reactions and extraocular motility were assessed. Fundoscopy was done with a direct ophthalmoscope, an indirect ophthalmoscope and +78 D slit-lamp biomicroscopy. Papilledema was graded according to the Frisen grading system.[3]
Perimetry (30-2 Threshold Swedish Interactive Threshold Algorithm (SITA Standard) was done using Zeiss Humphrey field analyzer. Visual fields defects, mean deviation and visual field index were recorded. Visual field defects were graded according to Wall and George criteria, which included grade I consisting of enlarged blind spot with inferior nasal step; grade II, enlarged blind spot with peripheral nasal loss; grade III, arcuate defects; grade IV, double-arcuate defects arcing around central 10 degrees; and grade V, gradual depression of the visual field more pronounced peripherally.

ONSD was measured using B-scan ultrasonography within 24 hours before lumbar puncture. Opening CSF pressure measured on lumbar puncture in lateral decubitus position was recorded with CSF analysis findings.

Magnetic resonance imaging (MRI) and/or magnetic resonance venogram (MRV) in atypical cases were done to assess for abnormalities. ONSD was measured by MRI before lumbar puncture.

Blood investigations like hemoglobin, anemia profile (serum iron levels, serum folic acid levels and vitamin B12 levels) and vitamin D levels were noted in patients who underwent these tests to assess for a likely risk factor for IIH.

Sample size was calculated using nMaster: Proportion in the population taken was 0.9 and sample population of 0.7 with power of the study 80% and alpha error 5%; sample size was calculated as 24.

Analysis

Descriptive statistics were described in percentages and continuous variables as mean with standard deviation (SD) or median. Pearson’s correlation coefficient was used to correlate variables. Statistical significance was considered when P value was < 0.05. Bias was handled by including all consecutive patients diagnosed with IIH. To avoid errors, all of the measurements were objective and repeated with average readings taken.

Being an observational study, only investigations done routinely were recorded and included.

Results

During this study, 32 consecutive patients with IIH fulfilling the inclusion criteria were analyzed. The age range was 20–60 years with a mean(±SD) of 35.25(±9.57) years. Females accounted for a majority of patients (31/32, 96.9%). BMI was in the range of 18.13–42.60 kg/m² (mean(±SD) of 28.12(±5.32) kg/m²).

Headache in 28/32 (87.5%) followed by blurring of vision in 14/32 (43.8%) patients were the most common complaints. Other symptoms were transient visual obscurations (TVO) (31.3%), diplopia (31.3%), nausea (28.1%), photophobia (25%), neck pain (21.9%), tinnitus (12.5%), phonophobia (12.5%) and CSF rhinorrhea (3.1%).

In 3/32 patients (9.4%), there was history of long-term intake of ayurvedic or homeopathic medications. Hormone therapy medications seen were oral contraceptive pills (OCPs) in 6.3%, estrogen in 6.3% and dehydroepiandrosterone (DHEA) in 3.1%. Gynecological disorders seen were dysmenorrhea or amenorrhea (15.6%), polycystic ovarian syndrome (PCOS) (15.6%), endometriosis (3.1%) and fibroid uterus (3.1%).

Vitamin D deficiency was seen in 15/32 patients (46.9%) and anemia in 14/32 patients (43.8%). Hemoglobin levels were determined in 22/32 patients with a range of 6–14 g/dl (mean of 11.6(±2.34) g/dl). Other comorbidities were vitamin B12 deficiency (34.4%) and hypothyroidism (21.9%).

Most patients (40/64 eyes, 62.5%) in the study had 6/6 visual acuity and only 3/64 eyes had visual acuity less than 6/12. Color vision was normal in 57/64 eyes (89.1%), but a few plates were abnormal in 7/64 eyes (10.9%).

Pupillary reaction was normal in 85.9% of eyes, ill-sustained in 12.5%, and there was relative afferent pupillary defect in 1/64 eyes. 10/32 patients (31.3%) complained of diplopia initially with unilateral lateral rectus palsy in 4/32 (12.5%).

Most patients (17/64 eyes, 26.6%) had chronic papilledema on fundus examination. Papilledema was absent in 14.1% of eyes, and in 3/64 eyes, there was optic atrophy. In the remaining 52/64 eyes (81.3%) Frisen grading of papilledema was done. Grades I, II, III, IV and V were seen in 31.3%, 21.9%, 18.8%, 3.1% and 6.3% of eyes, respectively.

Visual field assessment showed a mean deviation in the right eye of the range – 9.84 to +0.29 dB (mean(±SD) of –2.89(±2.48) dB) and in the left eye of the range of –24.38 to +0.2 dB (mean(±SD) of –4.88(±4.96) dB) [Table 1]. Thirty of the sixty four eyes (46.9%) had no visual field loss. The severity of field loss was grade I in 20.3%, grade II in 10.9%, grade III in 12.5%, grade IV in 3.1% and grade V in 6.3% of eyes.

Lumbar puncture was done in 23/32 patients with a CSF opening pressure range of 100–980 mmH₂O (mean(±SD) of 376.3(±191.51) mmH₂O).

The most common findings on MRI were empty sella (11/32, 34.4%), dilated optic sheath or prominent perioptic CSF spaces (4/32, 12.5%), tortuous optic nerve (6/32, 18.8%) and posterior flattening of sclera (3/32, 9.4%). Thirteen of the thirty-two eyes (40.6%) were normal. Of the 21 MRV done, the common abnormal findings were hypoplastic transverse sinus and sigmoid sinus (19.6%) and transverse sinus stenosis (14.3%).

The mean(±SD) of the ONSD on B-scan ultrasonography was 4.21(±0.90) mm and 4.58(±0.77) mm in the right and left eyes, respectively. There was a statistically significant correlation between the grades of papilledema and B-scan ONSD with a Pearson correlation coefficient of 0.428 (P = 0.016) in the right eye and of 0.548 (P = 0.002) in the left eye [Table 2]. No statistically significant correlation was observed between the grades of visual field defect and the B-scan ONSD. Similarly, there was no statistically significant correlation between the B-scan ONSD and the CSF opening pressure in our study.

Although no statistically significant correlation was found between the grade of papilledema and mean deviation of visual fields in the right eye (P = 0.689), it was statistically significant in the left eye (P = 0.022). There was no significant correlation between CSF opening pressure and BMI.

Discussion

Age in our study population was 20–60 years with a mean of 35 years. In the idiopathic intracranial hypertension treatment trial (IIHTT), mean age of the study population was 29 years.
Studies by Ambika et al.,[3] Ayush Dubey et al.,[4] and Claire Chagot et al.[11] had a study population with a mean age of 32 years, 30 years and 33 years, respectively.

Gender distribution in our study showed female preponderance with 96.9% being females. This was similar to the IIHTT trial (97.6% females),[10] and the studies by Ambika et al.,[3] (80% females) and Claire Chagot et al.,[11] (92.4% females). Ayush Dubey et al.[4] had all female patients in their study.

Most patients in our study were overweight with a mean BMI of 28.12 kg/m². In the IIHTT,[10] the mean BMI was 39.9 kg/m², and 35 kg/m² in the Claire Chagot et al.[11] study.

Only 3.1% reported a family history of IIH in our study, while in the IIHTT,[10] it was 5%. The similar demographic data between studies indicate IIH is a disease of adult overweight-to-obese females of child-bearing age with no genetic inheritance.

The most common symptom at presentation was headache (87.5%) followed by blurring of vision (43.8%). Other symptoms were transient visual obscurations (31.3%), diplopia (31.3%), nausea (28.1%), photophobia (25%), neck pain (21.9%), tinnitus (12.5%) and phonophobia (12.5%). Two of the thirty-two patients complained of facial twitching, 1/32 patient had drooping of upper eyelid and 1/32 had CSF rhinorrhea. In the 10/32 patients who complained of binocular diplopia, 4 were found to have lateral rectus palsy. The other 6 patients stated their diplopia had resolved when they presented to us. This indicates that the diplopia is likely transient and was similarly found in the IIHTT,[10] where out of the 18% of patients reporting binocular diplopia, only 3% had esotropia on examination.

Headache was the most common presentation in the IIHT trial,[10] Ambika et al.,[3] Ayush Dubey et al.[4] and Claire Chagot et al.[11] studies with the incidence of headache being 84%, 94%, 92.9%, 82.3% respectively. The IIHTT study,[10] reported a higher incidence of transient visual obscurations (68%), pulse synchronous tinnitus (52%), non-pulsatile tinnitus (23%). There was a lower incidence of diplopia (18%). Back pain occurred in 53% of patients in the IIHTT.[10] In our study, neck pain was the reported complaint. In the study by Ambika et al.,[3] occurrence of TVO and tinnitus was 68% and 58%, respectively. This was higher when compared to our study population. The other complaints were sustained visual loss (26%), photopsia (54%), diplopia (38%) and retrobulbar pain (44%).[3]

The study by Ayush Dubey et al.[4] reported blurring of vision (78.6%), diplopia (57.1%) and tinnitus (50%). Lateral rectus palsy was found in 42.8% of cases with an equal number having bilateral and unilateral lateral rectus palsy. As in our study, the second most common complaint was sustained blurring of vision followed by diplopia and tinnitus.[4] Claire Chagot et al.[11] reported TVO (17.7%), eye tracking impairment (15.2%), tinnitus (12.7%) and dizziness (11.4%). Here, the incidence of transient visual obscurations and diplopia was lower while occurrence of tinnitus was similar to our study.[11] The complaints of phonophobia, facial twitching, drooping of upper eyelid and CSF rhinorrhea were not reported in the other studies.

Similar to medical literature, we found that patients had a history of taking alternative medicine, oral contraceptive pills, estrogen hormone replacement and DHEA. Literature states that history of corticosteroid withdrawal and hormone replacement therapy can trigger IIH.[1] In our study population, the patients gave a history of gynecological disorders like dysmenorrhea, PCOS, endometriosis and fibroid uterus. Studies have shown a link between incidence of PCOS and IIH.[1]

Other common comorbidities found were vitamin D deficiency (46.9%), anemia (43.8%), vitamin B12 deficiency (34.4%) and hypothyroidism (21.9%). The mean hemoglobin level was 11.6 g/dl, mean vitamin B12 344.33 pg/ml and mean vitamin D 13.51 ng/dl.

T Van Gelder et al.[12] presented a case of IIH in a patient with megaloblastic anemia. How vitamin B12 or iron deficiency can trigger IIH is unknown, but it may be that the presence of anemia itself can trigger IIH. Vitamin D deficiency was not reported in other studies. Hypothyroidism could be linked to the intake of thyroid hormone drugs which medical literature states could trigger IIH.[1]

Our study found that most eyes had a visual acuity of 6/6 (62.5%) which was similar to that found in the IIHTT (70.9% in study eyes and 77.0% in fellow eyes)[10] and Ambika et al.[3] (55%). Ambika et al.[3] also reported 6/9–6/18 visual acuity in 20%, 6/24–6/60 in 7% and <6/60 in 18%. Our study showed that 32.9% eyes had visual acuity between 6/9 and 6/18, 3.2% eyes between 6/24 and 6/60 and 1.6% less than 6/60. The visual acuity did not correlate with the degree of visual field loss in our study. Some amount of visual field loss was seen in 53.1% of eyes. The IIHTT[10] reported that the most common perimetric finding was a partial arcuate scotoma with enlarged blind spot. However, the IIHTT[10] inclusion criterion was that the study eye should have a mild degree of visual field loss. Therefore, their perimetric results might not be representative of visual loss of IIH in general. In Ambika et al.[3] normal visual field was seen in 12% of cases, nasal and arcuate defects in 7% and advanced generalized constricted fields in 11%. Claire Chagot et al.[11] reported visual field defects in 50%.

### Table 1: Visual fields

|                | Right Eye | Left Eye |
|----------------|-----------|----------|
| Range          | Mean ±SD  | Range    | Mean ±SD  |
| Mean Deviation (dB) | −9.84 ±2.89 | −24.38 ±4.96 |
| Visual Field Index (%) | 83 to 97.16 | 30 to 92.56 |

### Table 2: Grade of papilledema and optic nerve sheath diameter (ONSD)

|                | Right Eye | Left Eye |
|----------------|-----------|----------|
| Grade of papilledema | 0-5 | 0-5 |
| B-scan ONSD (mm) | 2.54-6.85 | 3.60-5.90 |
| MRI ONSD (mm)    | 3.60-5.90 | 3.10-5.10 |
The mean deviation on perimetry in right eye was a mean of $-2.89$ dB and left eye was a mean of $-4.88$ dB. The visual field index of the right eye was a mean of 97.16% and in left eye was 92.56%. The average mean deviation in the study eyes was $-3.5$ dB and in the fellow eye was $-2.3$ dB in the IHTT.\textsuperscript{[10]} Our study, like other studies, had eyes with a visual field loss even though visual acuity was good, indicating that visual field rather than visual acuity is a better indicator of visual loss in IIH.

Another clinical sign assessed in our study was pupillary reaction. It was brisk in 85.9%, ill-sustained in 12.5% and relative afferent pupillary defect in 1.6%. The IHTT\textsuperscript{[10]} reported 5.4% eyes had relative afferent pupillary defect. The above findings indicate that progression to optic atrophy in IIH is a late occurrence and occurs due to a delay in diagnosis and treatment.

Papilledema was present in a majority of our study eyes (81.4%): grade I in 31.3%, grade II in 21.9%, grade III in 18.8%, grade IV in 3.1% and grade V in 6.3%. There was no papilledema in 14.1%, and 4.7% had progressed to optic atrophy. In our study, the most common grade of papilledema was grade I. This differed from the IHTT\textsuperscript{[10]} where it was grade II. Similarly, Ayush Dubey et al\textsuperscript{[14]} reported grade II papilledema was most common (28.6%), followed by grades I, III, IV, each present in 21.4%, and grade V in 7.1%. No statistically significant correlation was found between the grades of papilledema and grade of visual field defect.

The mean CSF opening pressure was 376.3 mmH$_{2}$O. This was similar with the IHTT\textsuperscript{[10]} where the mean was 343.5 mmH$_{2}$O. In the study by Claire Chagot et al\textsuperscript{[11]}, median CSF opening pressure was 285 mmH$_{2}$O (range 150–540 mmH$_{2}$O), and in 33%, the pressure was below 250 mmH$_{2}$O. CSF opening pressure is essential for the diagnosis of IIH. In our study, there was no statistically significant correlation between CSF opening pressure and mean deviation. No correlation was also found between BMI and CSF opening pressure as well.

MRI findings in our study were normal in 40.6%. MRI findings were found to be associated with IIH in medical literature\textsuperscript{[1,3,13,14]} and the findings present in our study population were empty sella in 34.4% of cases, dilated optic sheath in 12.5%, tortuous optic nerve in 18.8%, posterior flattening of sclera in 9.4% and all of the above in 3.1%. In the study by Ambika et al\textsuperscript{[11]}, MRI was done in 42/50 patients and was normal in 25, periopic space widening in 14 and empty sella in 3 patients. Ayush Dubey et al\textsuperscript{[14]} reported normal MRI scans in 85.7%, empty sella in 7.1% and distended optic nerve sheath in 7.1%. In the study by Chagot et al\textsuperscript{[11]}, MRI scans showed empty sella in 57% of cases and distension of periopic subarachnoid space in 65%. Of all the MRI findings, empty sella and dilated optic sheath or periopic space widening is seen to be the most common.

Twenty-one patients in our study population underwent MRV. MRV was normal in 38.1%. In the scans with abnormalities, the most common findings were hypoplastic transverse sinus with a hypoplastic sigmoid sinus in 19.0% and transverse sinus stenosis in 14.3%. MRV findings in our study population differed from that in the studies by Ambika et al\textsuperscript{[11]} and Ayush Dubey et al\textsuperscript{[14]} in which all were normal. Abnormal neuroimaging was the exclusion criteria in Ayush Dubey et al\textsuperscript{[14]} In the study by Chagot et al\textsuperscript{[11]}, they found unilateral transverse sinus stenosis or hypoplasia in 17% and bilateral transverse sinus stenosis (bilateral stenosis or unilateral stenosis and hypoplasia) in 74% of cases. However, in the study by Chagot et al\textsuperscript{[11]}, transverse sinus stenosis (TSS) detected on time resolved imaging of contrast kinetics (TRICKS) was part of the inclusion criteria. They hypothesized that raised intracranial pressure causes collapse of transverse sinus with the resultant increase in venous pressure and impaired CSF absorption. They felt TSS plays a role in pathogenesis of IIH. But our findings may indicate that cerebral venous sinus stenosis or hypoplasia may not play a role in the pathogenesis of IIH, and transverse sinus stenosis stenting proposed by Chagot et al\textsuperscript{[11]} as a second line treatment for IIH may not be useful.

Unlike other studies, we measured the ONSD using B-scan ultrasonography at presentation. The mean diameter in the right eye was 4.21 mm (range 2.54–6.85 mm) and in the left eye was 4.58 mm (range 3.49–6.22 mm). We found a statistically significant positive correlation between grade of papilledema and ONSD. No statistically significant correlation was found between grade of visual defect and ONSD, and between ONSD and CSF opening pressure.

**Conclusion**

IIH, if misdiagnosed and inappropriately treated, can lead to loss of vision. Our study findings suggest that IIH is a disease in overweight females of childbearing age. Most common symptom is headache. We must include IIH as a differential diagnosis in female patients with headache and disc edema who give history of intake of corticosteroids, hormone replacement therapy and gynecological disorders. Patients having vitamin D deficiency and anemia should be investigated for IIH, if symptoms are suggestive.

Visual field analysis is a better indicator of the compromise of function of the optic nerve and prognosis because it detects visual field loss before deterioration in visual acuity. This helps start early intervention and more aggressive management. Grading papilledema and noting chronicity is a reliable indicator of visual prognosis and follow-up.

Since ONSD and grade of papilledema are directly proportional, it may be an alternative to determine presence and severity of papilledema and raised ICP even in the presence of optic atrophy. They may be considered as an alternative to the diagnosis of elevated intracranial pressure if lumbar puncture and CSF opening pressure measurement are not feasible.

**Ethical clearance**

Approval was obtained from the Institutional Ethics Committee, St. John’s Medical College Hospital, Bengaluru, Karnataka, India.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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