

## **BILATERAL TRANSVERSE SINUS STENOSIS IS A CRITICAL FINDING IN IDIOPATHIC INTRACRANIAL HYPERTENSION SYNDROME (IIH)**

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**INTRODUCTION:** Idiopathic intracranial hypertension (IIH) or pseudotumor cerebri is defined by clinical criteria that include:

- increased intracranial pressure (eg, headache, papilledema, vision loss)
- elevated intracranial pressure
- normal cerebrospinal fluid composition
- no other cause of intracranial hypertension evident on neuroimaging or other evaluations.

Previously it was wrongly called benign intracranial hypertension, to distinguish it from secondary intracranial hypertension from a malignancy. However it is not a benign disorder. It can cause intractable headache and a risk of severe, permanent vision loss.

**EPIDEMIOLOGY:** The incidence of IIH is 1 to 2 per 100,000 population/year. There is a higher incidence in obese women between the ages of 15 and 44 years (4 to 21 per 100,000). With the increasing obesity epidemic in the United States and in other parts of the world, the incidence and prevalence of IIH is rising.

**Risk factors:** IIH affects women of childbearing age who are overweight. In a prospective study of 50 consecutively-diagnosed IIH patients, 92 percent were women with a mean age of 31 years (range 11 to 58 years) and 94 percent were obese. Other case series in different geographic areas and ethnic groups report consistent findings.

IIH can also occur in males, in children as young as four months, in older patients (up to 88 years), and in patients who are not overweight. Risk factors are somewhat different in prepubertal children compared with adults.

**Other conditions:** Although IIH is, by definition, idiopathic, a number of systemic diseases, drugs, vitamin deficiencies and excesses, and hereditary conditions have been reported to be associated with IIH. Most patients with IIH do not have one of these conditions.

The true link between these conditions and IIH is uncertain in many cases. In case-control studies, the prevalence of menstrual irregularities, pregnancy, antibiotic use, iron deficiency anemia, thyroid dysfunction, and oral contraceptive use were no different among cases versus controls.

**Systemic illnesses:** In addition to obesity, systemic illnesses reportedly associated with IIH include:

- Addison disease
- Hypoparathyroidism
- Anemia, usually severe
- Sleep apnea
- Systemic lupus erythematosus (SLE)
- Behcet's syndrome
- Polycystic ovary syndrome
- Coagulation disorders
- Uremia

The pathogenic mechanisms associating these conditions with IIH are uncertain and in some cases the apparent association may be indirect or spurious.

**PATHOGENESIS:** Although many theories for IIH have been proposed, the precise pathogenesis of IIH remains unknown. Any theory must account for the high incidence of IIH in obese women of the childbearing years. Proposed etiologies include cerebral venous outflow abnormalities (eg, venous stenoses and venous hypertension); increased cerebrospinal fluid (CSF) outflow resistance at either the level of the arachnoid granulations or CSF lymphatic drainage sites; obesity-related increased abdominal and intracranial venous pressure; altered sodium and water retention mechanisms; and abnormalities of vitamin A metabolism.

**Intracranial venous hypertension:**

Elevated intracranial venous pressure is postulated both as a primary mechanism and as a "final common pathway" for IIH. This theory is supported by the similar clinical appearances of IIH and secondary intracranial hypertension due to cerebral venous thrombosis and other causes of obstructed venous outflow. Some patients thought to have IIH have been later discovered to have one of these conditions. Although several authors have reported cerebral venous outflow abnormalities on magnetic resonance imaging (MRI) and MR venography (MRV) in patients with IIH, there is some disagreement as to the frequency or the significance of these findings. Clear venous sinus thrombosis has definite clinicopathologic significance, but apparent venous sinus narrowing or stenosis may not. Differentiation of venous stenosis from flow related abnormalities, especially on non-contrast MRV, can be difficult as flow-related artifacts can mimic venous sinus stenoses or even be mistaken for sinus thrombosis. These can sometimes be resolved with post-contrast MRV. Literature that suggests a high frequency of venous sinus abnormalities in patients with IIH must be viewed with caution.

Cerebral venous sinus structural abnormalities were systematically identified in a series of 29 patients with IIH using a specialized MR venography technique, auto-triggered elliptic-centric-ordered three-dimensional gadolinium-enhanced MR venography (ATECO MRV). Blinded readers detected substantial bilateral sinovenous stenoses in 27 of 29 patients compared with 4 of 59 controls, corresponding to a sensitivity and specificity of 93 percent. The investigators speculated that congenital narrowing of the venous sinus might be a primary cause of IIH or instead may be a secondary, but potentially contributing factor. In the latter scenario, increased CSF

pressure compresses the transverse sinus leading to the stenosis, which in turn would exacerbate the increased intracranial pressure (ICP), potentially bringing the patient to clinical presentation.

There is some evidence that the venous abnormalities are secondary to the intracranial hypertension. One study documented high intracranial venous sinus pressures in patients with IIH that was reduced by removal of CSF. This finding implies that increased cerebral venous sinus pressure and apparent stenosis in IIH is caused by the elevated ICP and not the reverse. Other reports have also documented reversal of apparent transverse sinus stenosis after CSF shunting. In contrast, one case series documented persistent transverse sinus stenosis in nine patients with IIH whose CSF pressure normalized over six years with medical treatment.

Other theories: There is some evidence that central obesity increases intra-abdominal pressure, pleural pressure, cardiac filling pressure, and central venous pressure and may lead to increased intracranial venous pressure and IIH. However, this mechanism does not account for the gender difference in IIH, the lack of increased incidence in pregnancy, and the cases of IIH in thin patients.

Cerebral edema was one of the earliest proposed mechanisms for IIH and had pathologic support in one case series. However, subsequent pathologic and MRI studies have not found evidence of cerebral edema in patients with IIH.

Other causes of impaired CSF absorption or increased CSF production have also been postulated as an etiology of IIH. However, most known causes of impaired CSF absorption (after subarachnoid hemorrhage or infectious meningitis) and CSF overproduction (choroid plexus papilloma) produce hydrocephalus, which is not seen in IIH.

Sleep apnea can be a complication of obesity, and may play a role in IIH, perhaps in men in particular. Hypercarbia may produce elevated ICP through vasodilation. One study found that 14 of 37 patients with IIH had a sleep disturbance, and of these, 13 had evidence of sleep apnea or upper airway resistance syndrome. In another report, a patient with IIH underwent ICP monitoring with pulse oximetry to reveal that apneic episodes were associated with marked elevations of ICP.

**SUMMARY** — Idiopathic intracranial hypertension (IIH) is a disorder defined by clinical criteria including symptoms of increased intracranial pressure (eg, headache, papilledema, vision loss), elevated intracranial pressure with normal cerebrospinal fluid composition, and no other cause of intracranial hypertension evident on neuroimaging or other evaluations.

*REFERENCES on request*