

Course of Pregnancy in Patients with Idiopathic Intracranial Hypertension: Retrospective Analysis of Cases

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Abstract

Background: Idiopathic Intracranial Hypertension (IIH) is a disease of unknown aetiology which predominantly affects obese women of childbearing age. It can present as a medical and obstetrical challenge to clinicians unfamiliar with the management in context of pregnancy. Its course can mimic obstetric complications like imminent eclampsia. Despite being an obstetrical challenge, only about 50 pregnancies have been reported in literature so far.

Methods: This is a retrospective analysis of cases taken from a tertiary care institute attending a special multidisciplinary clinic run by experienced obstetricians, neurologists and neonatologists. Clinical profile, course of pregnancy and outcome of seven patients selected in our case series will be discussed.

Results: Patients were in the age group of 25-32 years. Out of 7 patients, 4 underwent caesarean section; 2 of these were for obstetric indication (transverse lie and Meconium). Out of 4 caesareans, only 1 was done under spinal anesthesia. Out of 7 deliveries, 6 were at term and 1 was a preterm caesarean done in view of premature prelabour rupture of membranes with meconium stained liquor. Neonatal outcome was favorable in all 7 cases with a good Apgar score.

Conclusion: Normal vaginal delivery can be allowed in patients with IIH. IIH doesn't alter the course of pregnancy nor does the course of disease change due to pregnancy. Medical management or lumbar punctures can be safely done without altering the course of pregnancy. Neonatal outcome is also favourable. Adequate labour analgesia is important.

Keywords: Idiopathic Intracranial Hypertension; Labour analgesia; Headache; Papilledema; Acetazolamide; Lumbar puncture; Visual loss

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Introduction

Idiopathic Intracranial Hypertension is a disease of unknown etiology which predominantly affects obese women of childbearing age [1]. There is increased intracranial pressure, but without hydrocephalus or mass lesion, and a normal cerebrospinal fluid composition [2]. When left untreated it can result in severe irreversible visual loss. The pathophysiology is unclear. Theories include increased brain water content, excess CSF production, reduced CSF absorption, and increased cerebral venous pressure. Underlying endocrine dysfunction related to sex hormones and adipose tissue as an actively secreting endocrine organ has also

been proposed [3].

Since this disease affects reproductive age group females, it is an important cause of morbidity in pregnant women. It can present as a medical and obstetrical challenge. Symptoms may overlap with various causes of secondary headache syndromes, benign headaches, and serious medical conditions like stroke, meningitis etc. Its course can mimic obstetric complications like imminent eclampsia. Its management should involve a multidisciplinary team including the obstetrician, neurologist and anaesthesiologist. Despite being an obstetrical challenge, very few cases have been reported in literature citing the course and

outcome of pregnancies associated with IIH. This is a case series of seven patients with Idiopathic intracranial hypertension in a tertiary care institute is reported.

Case Series

This is a retrospective analysis of cases seen in the years 2017 to 2019 from a special multidisciplinary clinic run by experienced obstetricians, neurologists and neonatologists in a tertiary institute. The disease was suspected based on visual symptoms associated with bothersome headache and other symptoms later confirmed by neurologist. When pregnant women reported with headache, non-obstetrical causes of headache like tension headache, migraine, hydrocephalus, space occupying lesion, thrombosis, haemorrhage, meningitis, psychiatric causes etc. were ruled out by thorough clinical examination, laboratory tests and neuroimaging. Typically, MRI findings were normal in our patients. However a few signs like empty sella, flattening of posterior aspect of globe, distension of perioptic subarachnoid space, tortuous optic nerve and transverse venous sinus stenosis pointed towards the disease. Preeclampsia was ruled out in the presence of hypertension and its typical complications. After ruling out the above mentioned causes, inconclusive neuroimaging studies and presence of papilledema on fundoscopy, lumbar puncture was done to demonstrate opening CSF pressure. Opening lumbar pressure is elevated to more than 250 mm H₂O in IIH, with a normal CSF composition (unlike meningitis). Obstetric management was done according to the protocol of the institute. Medical management of the disease was by the neurology team. During the period of 2017 to 2019, we came across 7 cases if IIH. Clinical profile, course of pregnancy and outcome of 7 patients selected in our case series has been shown in **Table 1**.

Results and Discussion

Patients were in the age group of 25-32 years. Out of 7 patients, 4 underwent caesarean section; 2 were for obstetric indication (transverse lie and meconium). Two caesarean sections were done in view of the disease itself, however a trial of vaginal delivery could have been considered as the first line mode of delivery. Out of 4 caesareans, only 1 was done under spinal anesthesia. Out of 7 deliveries, 6 were at term and only 1 was a preterm caesarean done in view of premature prelabour rupture of membranes with meconium stained liquor. Neonatal outcome was favorable in all 7 cases with a good Apgar score.

Idiopathic Intracranial Hypertension (IIH) is a headache syndrome characterized by raised cerebrospinal fluid (CSF) pressure in the absence of an intracranial mass lesion or ventricular dilatation, a normal spinal fluid composition, absence of other causes of increased intracranial hypertension on neuroimaging and examination and a normal level of consciousness.

It carries significant morbidity, including permanent visual loss in up to 25% cases [4]. Peak age of onset is between 20 and 40 years [5]. In our case series, patients were in the age group of 25-32 years. It has a striking female predominance (8:1). Its incidence is 1 – 3/100 000/year in the general population and 12–28/ 100 000/year in obese women of reproductive age group.

Interestingly, while this appears to be a disorder that occurs in obese women, only 1/7 patients in this series had a BMI above 30. In women of childbearing age, it is 0.9/100 000 [6]. The prevalence in pregnant women is between 2% and 12% [7]. The prevalence of PCOS in women with IIH is reported to be as high. It is also associated with metabolic syndrome [8]. In our institute 2 /7(28.6%) women had PCOS.

This disease usually presents with symptoms of headache, pulsatile tinnitus, transient visual obscurations (due to disc edema) and diplopia (in 1/3rd – 2/3rd cases). Other associated symptoms include mood disturbances and impairment in memory and concentration. In our institute, out of 7 cases, 6 had headache as the presenting symptom, 6 had blurring of vision including 1 patient who presented with loss of vision, and 3 patients had vomiting associated with headache. Since moderate to severe headache can be chief complaint in a variety of medical and obstetrical diseases, a systematic approach to rule out all the possible causes of headache syndromes should be followed.

Once the diagnosis is made, treatment is aimed at alleviating pain and preventing visual loss, as blindness may develop in 10% pregnant women with IIH [9]. Interestingly, grade of papilledema is not related to the severity of visual symptoms. Weight reduction is an effective non pharmacological management strategy. Reduction of body weight is associated with improved visual function and papilledema grade in IIH, but this cannot be tightly followed in pregnancy. Pregnant women with IIH are allowed 20lbs weight gain throughout pregnancy [10]. Pharmacological therapy is the mainstay of management in pregnancy. Acetazolamide is often started as the first line drug, the dose being titrated based on severity of visual symptoms. When no visual symptoms are present, a dose of 1-1.5 g/day is appropriate. When light to moderate visual field defects are present, it can be used in a dose of 1.5-4g/ day with or without additional therapeutic agents like topiramate and diuretics [11]. When severe or rapidly progressive visual field defects are present, spinal tap or neurosurgical assessment is done. Second line drugs like topiramate and diuretics are used when acetazolamide is contraindicated or not tolerated [12]. Topiramate is FDA category D drug. It is suspected to cause oral clefts [13]. It is not a first line treatment for the condition; the drug may be an acceptable alternative if first line therapy fails when balanced against the risk of no treatment.

Serial lumbar punctures can be done in any trimester. Surgical management in the form of Optic Nerve Sheath Fenestration (ONSF), neurosurgery employing shunts or stenting of transverse venous sinuses is undertaken if vision is deteriorating rapidly despite rigorous medical therapy [12]. Speaking trimester wise, if the onset of visual compromise is in the first trimester, serial lumbar punctures can be done. If needed, CSF diversion can be done during their second trimester. If onset is in 2nd and 3rd trimester-Medical therapy/ Lumbar punctures/ surgical management is undertaken depending on severity of visual field loss.

Monitoring the response to treatment is done by periodic visual fields assessment. If the patient's visual symptoms are stable, visual field testing may be done every 2-3 months.

Table 1 Patient profile and course of pregnancy of patients with IIH.

Variables	Age and parity	BMI	Duration	Symptoms at diagnosis	CSF Pressure/ Finding	Treatment	Obstetric Complication	Period of gestation	Type of delivery/ Anaesthesia	Indication	Neonatal outcomes
1	28 years PGR	33.2	3 months	Blurring of vision in Right eye, tinnitus with mild Right orbital pain at 25 weeks	Pressure-29 cm Grade 4 papilledema	Acetazolamide Methylprednisolone Lumbar Punctures	None	39+4 weeks	LSCS under General anaesthesia	IIH	APGAR 8, 9 Birth weight-3.03 kg
2	26 years G3P1011	24.6	3 years	Throbbing headache, vomiting Diagnosed IIH in 2015	Pressure- 30 cm	Acetazolamide	None	37+2weeks	LSCS under General anaesthesia	IIH	APGAR 8, 9 Birth weight 2.6 kg
3	25 years G2P1001	23.4	9 months	Throbbing headache, vomiting Diagnosed with IIH just before conception	Pressure-27 cm Fundus- Bilateral Papilledema	Topiramate Acetazolamide	None	37+5 weeks	LSCS under General anaesthesia	Transverse lie	APGAR 8, 9 Birth weight-2.39 kg
4	30 years G5P4002	29.2	2 years	Headache, vomiting loss of vision in bilateral eyes in 2016	Fundus- optic atrophy	Optic nerve fenestration Acetazolamide for 1 year Propranolol (not on drugs since 3rd month Period of gestation)	Gestational hypertension hypothyroid	39+5 weeks	Augmented with oxytocin Normal vaginal delivery	In view of gestational hypertension	APGAR 7, 9 Birth weight 3.115 kg
5	32 years G2P1001	27.3	1 year	Headache Blurring of vision in 2017	Pressure- 460mmHg	Diagnosed with IIH in 2017 when her CSF pressure was raised and MRI brain normal. Took acetazolamide 500 mg thrice a day for 1 month, then stopped treatment herself Known case of Chronic Kidney Disease stage 4 since 1.5 years and chronic hypertension since 3 years (was on telmisartan, amlodipine, torsemide before conception)	A known case of IIH, also developed Preeclampsia, started on labetalol 100 mg thrice a day Developed eclampsia on Day 2 post op Received Levetiracetam MRI done on day 2 postop suggestive of Posterior reversible encephalopathy Preterm premature rupture of membranes with Meconium	33+5 weeks	LSCS Under Spinal anaesthesia	Meconium	APGAR 7, 8 Birth weight- 1.9 kg
6	29 yrs G5P2022	25.7	8 months (diagnosed in 1st trimester)	Blurring of vision at 12 weeks	Fundus- Bilateral Papilledema	Acetazolamide	Intrahepatic cholestasis of pregnancy	Induced with dinoprostone followed by oxytocin for ICP at 37+3 weeks	Forceps delivery (to cut short second stage of labour)	-	APGAR-8, 9 Birth weight- 2.5 kg
7	30 years G3P1011	25	9 months (diagnosed in first trimester)	Rapidly progressive bilateral blurring of vision for 1 month, Headache in bilateral temporal area associated with nausea, vomiting	Fundus-Grade 4 papilledema Pressure- 25 cm Glaucoma hemifield testing- fluctuating during pregnancy	Acetazolamide	None	Spontaneous onset of labour at 37 weeks	Normal Vaginal Delivery	-	APGAR-8, 9 Birth weight-2.4 kg

In our series of 7 patients, all had received acetazolamide, one received topiramate, one had to receive pulse doses of methylprednisolone, one underwent optic nerve sheath fenestration and one underwent serial lumbar punctures. None of the patients required shunt surgery. The subsequent course of disease seems to be unaffected by pregnancy, neither does the disease add to pregnancy complications. Pregnancy is not associated with exacerbation or recurrence [7]. There is no further increase in visual loss due to pregnancy. There is no increase in maternal, fetal, or neonatal mortality or morbidity in pregnant women diagnosed with IIH. There are no additional antenatal complications reported. Outcome of the disease is same as in non-pregnant patients. Subsequent pregnancies also do not increase the risk of recurrence. Therapeutic abortion to limit the progression of disease is not indicated.

Special precautions should be kept in mind during labour. Adequate labor analgesia is important as uterine contractions can lead to increase in CSF pressure which is exaggerated by pain. Uterine contractions and bearing down efforts are associated with increased BP, cardiac output, Central Venous Pressure which consequently increases CSF pressure. Hence, adequate labor analgesia should be given when vaginal delivery is contemplated. Among various choices for labor analgesia, epidural analgesia is preferred as it minimizes hemodynamic changes during contractions with resultant minimal effect on CSF pressure. Narcotic analgesics are not recommended as they increase $p\text{CO}_2$ via respiratory depression and increased cerebral blood flow. Mode of delivery is decided according to obstetric indications only. While undertaking vaginal delivery, second stage of labor should be cut short by instrumental delivery to minimize increase in CSF pressure by bearing down efforts [14]. If caesarian delivery is undertaken (for obstetric indications), regional anesthesia is preferred in order to have minimum effect on CSF pressure. This is in contrast to rest all other conditions of raised intracranial pressure where regional anesthesia is contraindicated due to risk of coning of intracranial contents. In IIH, risk of coning is not a concern as the pressure is uniformly raised inside the brain. In our hospital out of 7 patients, 4 underwent caesarian section; out of which 2 were for obstetric indication (transverse lie and MSL). Out of 4 caesarians, only 1 was done under spinal anesthesia. Of the 3 vaginal deliveries, one was instrumental delivery (forceps) to cut short second stage of labour. Out of 7 deliveries, 6 were at term and only one was a preterm caesarian which was done in view of premature prelabour rupture of membranes with meconium stained liquor.

Allowing spontaneous vaginal delivery could have been a safe choice for patients who underwent caesarian section without any obstetric indication in our case series. Spinal anesthesia can be preferred in the other three caesarian sections also, as the risk of tonsillar herniation is minimal when ICP is uniformly raised inside the brain (without any space occupying lesion). Remarkably, such patients usually do not suffer from spinal headache. Neonatal outcome was favorable in all 7 cases with a good Apgar score.

In the post-partum period, acetazolamide was continued. Acetazolamide is probably safe for a breastfeeding baby (category C drug). Only 0.06% of the dose of acetazolamide given to the mother is ingested by the child (less than 0.7% of the dose/kg body weight received by the mother). For contraception, OCPs should not be given as IIH is associated with cerebral thrombotic conditions/ predispositions. Limited data show that the effect of progestogens on the risk of venous thrombosis and stroke, if any, is small. POPs should be regarded as category 3.

In a case series reported by Huna Baron et al. published in *J Neurol.* 2002, 240 women with IIH were recruited, 12 had 16 pregnancies [9]. Ten had headaches, five had transient visual obscurations, and three had diplopia. Visual acuity was severely decreased in one and mildly reduced in three women. Six had marked and six had mild bilateral papilledema. Visual field loss occurred in four women. Visual symptoms and loss improved for the duration of the pregnancy after diagnostic lumbar puncture and salt restricted diet in three. Two additional women needed continuous spinal drainage for two days. One woman was treated with acetazolamide and medical abortion. The one woman with severe vision loss had fenestration of one optic nerve sheath and a lumboperitoneal shunt as well as corticosteroids and was the only case with permanent field loss. After intervention, visual acuity improved in all cases with reduced vision. There were 10 full-term normal deliveries, three missed abortions, one therapeutic abortion and two intrauterine fetal deaths. They concluded that IIH presents usually during first two trimesters with typical symptoms and visual outcome is similar as for non-pregnant women. In this case series there were two intrauterine demise, unlike our case series where pregnancy outcome was favorable in all the patients. Similar to our results, patients improved with treatment during the course of pregnancy. There are other case reports where patients are managed either medically or by lumbar punctures or even lumboperitoneal shunt surgery and the pregnancy course was unaffected [15,16].

Conclusion

IIH may first present in pregnancy in otherwise healthy women. In patients with mild to severe visual loss or with deteriorating clinical symptoms, definitive treatment is required. The disease doesn't alter the course of pregnancy nor does pregnancy exacerbate the disease. Normal vaginal delivery can be allowed in patients with IIH. Adequate labour analgesia is important. Our experience confirms the current practice of safe and effective management with the help of medical therapy and/or lumbar punctures. However, a larger case series may be helpful to know the best way to modify or remit the disease in pregnancy. Also the management of acute rapidly deteriorating vision loss and the effect of shunt surgeries in pregnancy is an area of future research with a larger case series.

Conflict of Interest

The authors declare that there is no conflict of interests.

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