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ORIGINAL ARTICLE

Digital subtraction angiography as an additional modality in idiopathic intracranial hypertension and its comparison with magnetic resonance venography: A prospective study

Kishor Kumar Paikara[1], Chandradev Sahu[1], Arpit Agrawal[2], Abhijeet Kumar Kohat[2], Anam Fatima[1]

[1]Department of Radiology, Pandit Jawaharlal Nehru Memorial Medical College, Raipur, India
[2]Department of Neurology, Dau Kalyan Singh Post Graduate Institute and Research Centre (DKSPGI & RC) Raipur, India

ABSTRACT

Objectives: This study aimed to compare the diagnostic accuracy of brain magnetic resonance venography (MRV) with digital subtraction angiography (DSA) in the evaluation of idiopathic intracranial hypertension (IIH).

Patients and methods: This cross-sectional, hospital-based, prospective observational study included 15 patients (8 males, 7 females; mean age: 34.3±13.6 years; range, 18 to 60 years) with suspected IIH who met modified Dandy's criteria for a period of two years (January 2021 to January 2023). We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of the MRV and DSA to diagnose IIH.

Results: The female participants had a mean age of 30±10.23 years, and the male participants had a mean age of 37±13.46 years. Out of seven female participants, three (42.8%) were obese, two (28.6%) were overweight, and two (28.6%) had normal body mass index (BMI). Of eight male participants, tree (37.5%) were obese, three (37.5%) were overweight, and two (25%) had normal BMI. All patients had headache, 60% had diminished vision, 20% had tinnitus, 20% had diplopia, 46.67% had dizziness, and 80% had papilledema. All the patients underwent lumbar puncture, and cerebrospinal fluid opening pressure was more than 25 cm of water in all patients. Digital subtraction angiography revealed that, two (13.3%) patients had cerebral venous sinus thrombosis, and two (13.3%) patients had dural arteriovenous fistula. The diagnostic accuracy measures of MRV in the diagnosis of IIH showed a sensitivity of 45%, a specificity of 75%, a PPV of 83%, and a NPV of 33%.

Conclusion: In patients with suspected IIH, DSA can rule out cerebrovascular alterations, venous sinus pressure can be measured, and venous sinus stenting can be done in the same sitting, which can be an excellent additional modality for selected patients.

Keywords: Digital subtraction angiography, idiopathic intracranial hypertension, magnetic resonance venography, venous sinus stenting, transverse sinus stenosis.

Idiopathic intracranial hypertension (IIH) is characterized by headache, pulsatile tinnitus, transient visual obscurations, and visual impairment associated with elevated intracranial pressure without an intracranial mass or cerebral venous sinus thrombosis.[1-3] The incidence of IIH is increasing in parallel with the epidemic of obesity and due to increased recognition of this disorder.[4-6] Visual loss is the most significant morbidity in IIH.[7] Brain imaging is used to rule out secondary or emergent causes of increased intracranial pressure, including tumors, infection, hydrocephalus, or venous thrombosis. Brain magnetic resonance imaging (MRI) with gadolinium enhancement and magnetic resonance venography (MRV) are the most appropriate imaging methods in patients

Correspondence: Arpit Agrawal, MD. 2Department of Neurology, Dau Kalyan Singh Postgraduate Institute and Research Centre, 492001 Raipur, India
E-mail: arpdoc@gmail.com

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with IIH.[8] Additionally, MRI and MRV can serve as valuable imaging tools to rule out causes for secondary intracranial hypertension, detect indirect signs of IIH resultant from increased intracranial pressure, and demonstrate potentially treatable sinus venous stenosis. Flattening of the globes, an empty sella, distended optic nerve sheaths, and slit-like ventricles are common neuroradiological findings in IIH.[2,9] Magnetic resonance venography is the standard of practice in IIH to rule out a dural venous sinus thrombosis. Although there is no evidence of deformity or obstruction of the ventricular system, the presence of venous sinus stenosis as a radiological finding in the majority of IIH patients has led to an increased understanding of the pathophysiological mechanism of this disorder.[10] Many researchers have proposed that increased intracranial venous pressure is the primary mechanism of raised intracranial pressure in IIH.[11,12] Digital subtraction angiography (DSA) is the gold standard in vascular imaging. It can be used to rule out cerebrovascular alterations, measure venous sinus pressure, and perform venous sinus stenting (VSS) in the same sitting. However, DSA is an invasive procedure associated with a risk of complications, a 1% overall incidence of neurologic deficit, and a 0.5% incidence of persistent deficit.[13] We conducted the present study to explore cerebral DSA's utility in diagnosing and further managing IIH by comparing it with MRV.

PATIENTS AND METHODS

This cross-sectional prospective observational study was conducted at the Pandit Jawaharlal Memorial Medical College & Hospital, Department of Radiodiagnosis located in Central India with the collaboration of the Department of Radiodiagnosis and Department of Neurology at Pandit Jawaharlal Memorial Medical College and Dau Kalyan Singh Postgraduate Institute and Research Center for a period of two years (January 2021 to January 2023). The study enrolled 15 consecutive patients (8 males, 7 females; mean age: 34.3±13.6 years; range, 18 to 60 years) diagnosed with IIH according to the modified Dandy criteria.[14,15] Pregnant women, patients with secondary pseudotumor cerebri syndrome features, such as cerebral venous sinus thrombosis, history of medications, or systemic disorders associated with raised intracranial pressure, were excluded. We conducted a complete general and neurological assessment, lumbar puncture, complete ophthalmologic evaluation, including visual acuity measurement using a Snellen chart, ophthalmoscopic fundus examination to assess and grade papilledema, and automated perimetry for all patients. Written informed consent was obtained from the participants. The study protocol was approved by the Pt. J.N.M. Medical College Ethics Committee (Date 14.03.2022, No: 101). The study was conducted following the Declaration of Helsinki and the principles of Good Clinical Practice.

A Magnetom Skyra 3 Tesla MRI system (serial no. 45445; Siemens Healthineers AG, Erlangen, Germany), computed tomography (128 slices), and a GE HealthCare Innova 4100 Angio harmony DSA system (GE HealthCare, Kemnath, Germany) were used. We gave local anesthesia at the intended puncture site (usually lidocaine hydrochloride 1% or 2% w/v). In some patients, we performed moderate analgesia. Under ultrasound guidance, the Seldinger technique was used to access a blood vessel. Local complications included thrombus formation, local tissue damage, pseudoaneurysms, and arteriovenous fistula. Systemic complications included the risks of air embolism, thromboembolism, dissection, and contrast-mediated nephrotoxicity. We explained the procedure's risks, benefits, and alternatives to the patient and the family, after which we took written informed consent. We performed a timeout before the procedure to confirm the patient's identity and the appropriate method. The patient was positioned supine on the angiographic table, and the right or left groin was prepped and draped using sterile technique. Afterward, the right common femoral artery and vein were punctured and cannulated using an 18-gauge single puncture needle set. We placed A 6F sheath over a guidewire. Systemic heparinization with 70 IU/kg heparin was administered. A 5F diagnostic catheter was used to perform a cerebral arteriogram to evaluate venous outflow pathways. Next, we advanced a 5F diagnostic catheter into the internal jugular vein microcatheter and navigated it over a microwire to the superior sagittal sinus. A diagnostic cerebral venogram was performed, followed by serial venous manometry measurement in the superior sagittal sinus, torcula, bilateral transverse sinuses, sigmoid sinus, and ipsilateral jugular veins (Figure 1). Pressure gradients of 8 mmHg were considered diagnostic for venous stenosis.[16] The pressure was stabilized across all locations before recordings. When possible, bilateral transverse-sigmoid pathways were assessed, and manometry recording was

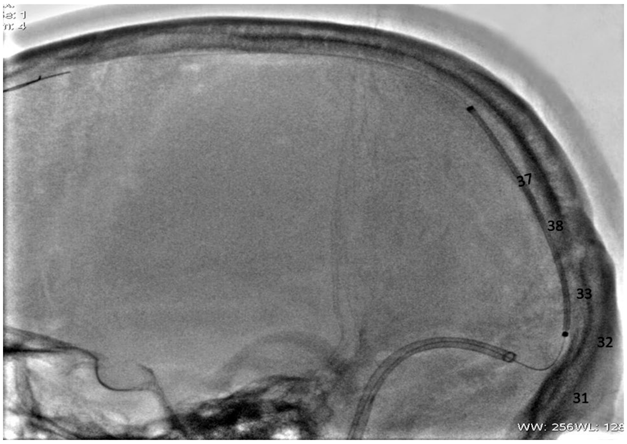

Figure 1. Venous manometry by cerebral digital subtraction angiography (venous phase). There is increased venous pressure in left side of cerebral venous system with significant difference: *(i)* 13 mmHg between left transverse sinus and superior sagittal sinus; *(ii)* 14 mmHg between left transverse sinus and sigmoid sinus. Above features are suggestive of stenosis of superior sagittal sinus, left transverse sinus, and sigmoid sinus, with significantly increased cerebral venous pressure.

performed on both sides. Mean venous pressures and pressure gradients, integral parameters for diagnostic components for VSS, provided baseline information for endovascular therapeutic decisions potentially benefiting the patients. Pullback pressures were measured in the central nervous system, torcular Herophili, proximal and distal transverse sinus, sigmoid sinuses, and jugular bulbs on each side with a standard blood pressure transducer connected to a monitor. The pressure monitor was set to 0 using standard techniques to determine the position of the right atrium. Hemostasis was applied to the puncture site upon the completion of the procedure. The patient was instructed to be immobilized for 4 to 6 h and was kept supine after the procedure.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Data were entered into a pre-designed proforma and organized in Microsoft Excel. Demographic, clinical, and imaging data were recorded. Continuous variables were summarized as means ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. Sensitivity, specificity, and positive and negative predictive values were calculated where appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

The female participants had a mean age of 30±10.23 years, and the male participants had a mean age of 37±13.46 years. Out of 15 patients, seven (46.67%) were between 18 and 30 years, four (26.67%) were between 31 and 40 years, three (20%) were 41 to 60 years of age, and one (6.67%) was over 61 years. In the Consensus Statement for Diagnosis of Obesity, Abdominal Obesity, and Metabolic Syndrome for Asian Indians,[17,18] normal body mass index (BMI) was defined as 18.0 to 22.9 kg/m^2, overweight as 23.0 to 24.9 kg/m^2, and obesity as >25 kg/m^2. In our study, the mean BMI for males was 23.96±4.23 kg/m^2 and 27.13±5.64 kg/m^2 for females. Out of seven female participants, three (42.8%) were obese, two (28.6%) were overweight, and two (28.6%) had normal BMI. Of eight male participants, tree (37.5%) were obese, three (37.5%) were overweight, and two (25%) had normal BMI. All 15 (100%) participants had a headache, nine (60%) patients had diminished vision, three (20%) had

TABLE 1
Neuroimaging findings on magnetic resonance venography

No.	Findings	Frequency	Percentage (%)
1	Stenosis of superior sagittal sinus and left transverse sinus.	1	6.7
2	Sluggish flow noted in post one-third of superior sagittal sinus	1	6.7
3	Normal	9	60.0
4	Bilateral transverse sinus stenosis	1	6.7
5	Perineural cerebrospinal fluid (CSF) space along bilateral optic nerve with the mild posterior concavity of optic disc, partial empty Sella, attenuation flow-related signal from right transverse and sigmoid sinus.	2	13.3
6	Partial empty Sella	1	6.7
	Total	15	100

TABLE 2
Final diagnosis after DSA

No.	Diagnosis after DSA	Frequency	Percentage (%)
1.	Cerebral venous sinus thrombosis	2	13.33
2.	Dural arteriovenous fistula	2	13.33
3.	Idiopathic intracranial hypertension	8	53.33
4.	Normal	3	20
	Total	15	100

DSA: Digital subtraction angiography.

tinnitus, three (20%) had diplopia, seven (46.67%) had dizziness, and 13 (80%) had papilledema. Among the subjects, the neuroimaging finding was significant in 40% of cases on MRV (Table 1). After DSA, we reported IIH in 53.33% of cases and cerebral venous sinus thrombosis (CVT) and dural fistula in 13.33% each (Table 2). In the present study, we found that an MRV for the diagnosis of IIH showed a sensitivity of 45%, specificity of 75%, positive predictive value (PPV) of 83%, and negative predictive value (NPV) of 33%.

DISCUSSION

The present study compared MRV with DSA in the diagnosis of IIH and explored the utility of DSA in diagnosing and managing IIH. Interestingly, two out of 15 patients had dural arteriovenous fistula, and two patients had CVT, which was not suspected in the MRV studies. Therefore, these patients were not “idiopathic,” as there was a known cause for raised intracranial pressure. In the present study, the neuroimaging finding was significant in 40% of cases. The final diagnoses after DSA among study subjects were IIH in 53.33%, CVT in 13.33% and dural fistula in 13.33%.

Compared to similar studies, Sultan et al.[19] found that optic hydrops and empty sella turcica were the most prevalent MRI abnormalities in IIH cases, occurring in 95.8% and 70.8% of cases, respectively. They observed stenosis at the genu junction and transverse sinus in 24% and 20% of cases, respectively. Elmaaty et al.[20] found that MRI suggested IIH in 46% of subjects, and Barkatullah et al.[9] observed significant MRI findings in 35% of IIH cases. Montoya-Casella et al.[21] reported that MRI did not reveal lesions explaining IIH, but MRV followed by DSA identified cerebral venous sinus involvement in 61% of cases, reiterating MRI’s sensitivity of 45%, specificity of 75%, PPV of 83%, and NPV of 33% for diagnosing IIH. Maralani et al.[8] found MRI had a sensitivity of 51%, with significant neuroimaging findings in 40% of subjects. Ibrahim et al.[22] explored the prevalence of venous sinus stenosis in IIH using DSA; MRV had 100% sensitivity and NPV, but it had a specificity of 62% with a PPV of 35%. Cerebral DSA (venous phase) showed nine (30%) patients had stenosis in their dural sinuses. Another study explored the role of DSA as a tool for diagnosing and managing IIH and reported that after an MRI of the brain, none of the cases showed lesions that would explain the IIH.[21] However, upon magnetic resonance angiography followed by DSA, eight (61%) cases of cerebral venous sinus involvement were found. The diagnostic accuracy measures of MRV in the diagnosis of IIH showed a sensitivity of 45%, a specificity of 75%, a PPV of 83%, and a NPV of 33% in our study. Therefore, our study's results are consistent with previous studies, and the possibility of missing data is less in our study due to its prospective design.

Invasive venography leads to superior visualization of the venous system, particularly with detecting focal stenoses that may require stenting. Real-time dynamic assessment more accurately demonstrates venous sinus flow, showing preferential sinus outflow and the proximity of stenosis to cortical veins. A three-dimensional visualization allows superior venous system measurements to select the most appropriate stent size for treatment. The risk of catheter venography and manometry is low. There were no access site or intracranial complications in a series of 164 venograms via the femoral vein for IIH. Another series of 147 venograms via the upper extremity found only two (1.4%) minor complications. Many patients with IIH have stenoses in the cerebral venous sinuses; raised intracranial pressure may cause sinus compression, and VSS may be promising in this scenario.[23-25] One meta-analysis included 136 patients who underwent VSS for refractory IIH, with a mean follow-up time of 22.9±3.2 months.[26] The intervention appeared to be very effective, with improvement in papilledema in 97% of patients (104 out of 108 patients). Headache improvement was reported in 83% (101 out of 121 patients). Complications were observed in 7.4% (n=10) patients, the most significant being related to vessel perforation and acute subdural hemorrhage, stent migration, and thrombosis. Another recent meta-analysis involving 1,066 patients who underwent VSS concluded that VSS appeared to be a safe and effective treatment option for IIH patients who were refractory to medications or had vision loss.[27] In the IIH consensus guidelines,[1] long-term data regarding VSS concerning safety and efficacy is lacking, but in carefully selected patients with clear evidence of an elevated pressure gradient across the stenosis, VSS can be a safe and effective modality.[28] In IIH patients refractory to medical therapy, radiographic evidence of intracranial venous sinus stenosis, and a trans-stenosis pressure gradient of at least 8 to 10 mmHg, VSS can be helpful.[29-31] Further, studies of DSA followed by intracranial VSS have been encouraging.[31,32] Digital subtraction angiography may be added as a diagnostic and therapeutic tool of IIH.[29,30,33]

The main limitation of our study was the small sample size, which was attributed to the rarity of this disease entity and the short study period.

In conclusion, DSA may be helpful in the diagnosis of a selected group of IIH patients along with MRV. Some patients with suspected IIH have a normal cerebrospinal fluid opening pressure, which does not meet the Modified Dandy criteria of IIH. Second, some patients with suspected IIH lack papilledema. Digital subtraction angiography with venous manometry across various venous sinuses may give diagnostic clarity in such a patient population. We explored the utility of cerebral DSA for diagnosing IIH and its comparison to MRV. Increased use of DSA in patients with IIH gives a definite diagnostic advantage. With encouraging studies of intracranial VSS for IIH, DSA can be a diagnostic and therapeutic asset in managing IIH. Furthermore, DSA may give insights into the pathophysiology of a disease that is not fully understood and may present varied presentations.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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