European Journal of Neurology

european journal of neurology
the official journal of the european academy of neurology

REVIEW ARTICLE OPEN ACCESS

Idiopathic Intracranial Hypertension in Pregnancy. A Systematic Review on Clinical Course, Treatments, Delivery and Maternal-Fetal Outcome

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Received: 5 March 2025 | **Revised:** 3 April 2025 | **Accepted:** 27 April 2025

Funding: The authors received no specific funding for this work.

Keywords: Idiopathic intracranial hypertension | intracranial pressure | lumbar puncture | pregnancy | shunt

ABSTRACT

Background: Idiopathic intracranial hypertension (IIH) during pregnancy presents significant challenges due to the physiological gestational changes, which can exacerbate its symptoms.

Methods: We conducted a systematic review on studies reporting maternal-fetal outcomes of IIH during pregnancy, selecting 49 papers reporting on clinical course, management strategies, and mode of delivery.

Results: We retrieved 165 patients with 178 pregnancies affected by IIH. Obesity represented a common risk factor (69.1%), but the association with other cardiovascular and metabolic risk factors was poorly discussed. Overall, 62.9% presented worsening of the headache and 66.8% impairing visual disturbances, but these data were extrapolated from single cases or small series comporting a selection bias potentially overestimating the real risk.

First-line treatment is currently represented by acetazolamide (52 cases) or other diuretics (4 cases) associated with weight control. Serial lumbar punctures (LP) were reported in 26.9% of cases of ineffective pharmacological treatment. Shunt (3.9%) and optic nerve sheath fenestration (1.1%) were overall performed in a minority of cases.

Second-line management was characterized by serial LP in patients initially treated only with diuretics and shunt placement (4.5%) or optic nerve sheath fenestration (1.7%) for patients requiring continuous CSF subtractions.

Conclusions: Although pregnancy-related physiological changes may exacerbate the IIH and the actual risk remains difficult to quantify, this appears overall low in terms of re-exacerbation of the disease or de-novo onset. Diuretics, in particular acetazolamide, that did not show a causal relationship with congenital malformations, and serial lumbar punctures represent safe and effective first-line managements, whereas shunt procedures should be reserved for fulminant cases. A pre-gestational symptoms relief seems to reduce the probability of a severe worsening in pregnancy.

Abbreviations: CSF, cerebrospinal fluid; ICP, intracranial pressure; IIH, Idiopathic intracranial hypertension; LPS, lumbo-peritoneal shunt; ONSF, optic nerves sheath fenestration; VFC, visual field cut; VPS, ventriculo-peritoneal shunt.

1 | Introduction

Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri, is a neurological disorder characterized by elevated intracranial pressure (ICP) manifesting with refractory headache (94%), pulsatile tinnitus (58%), papilledema, progressive visual field cut (VFC) and acuity impairment (68%) [1, 2].

The pathophysiology of IIH is complex, and despite being believed to be primarily associated with impaired cerebrospinal fluid drainage and increased venous pressure, may encompass other factors including hormonal changes i.e., altered testosterone or androsterone levels [3].

IIH mainly affects overweight women in reproductive life.

Although IIH is considered an idiopathic condition without a known cause, recurrent findings such as chronic stenosis or thrombosis of intracranial (e.g., the transverse-sigmoid sinuses) and extracranial venous structures (e.g., the jugular veins) are often identifiable.

Historically speaking, the Dandy criteria represented the gold standard for diagnosing and were based on a triad including specific typical neuroradiological signs, cerebrospinal fluid (CSF) opening pressures > 250 mmHg, and exclusion of other potential causes [4]. Since 2024, the Friedman criteria were introduced to refine the diagnosis of IIH, leading to a quintad of the former criteria: symptoms of increased ICP; papilledema; CSF pressure > 250 mmHg; normal neuroimaging; exclusion of secondary causes [4, 5].

First line management is based on weight reduction for mild cases, whereas severe conditions presenting with significant headaches and visual impairment may require a pharmacological approach with diuretic drugs and steroids. Refractory cases or those presenting with rapid visual deterioration may require surgical interventions of CSF diversion such as ventriculoperitoneal shunt (VPS) or lumbo-peritoneal shunt (LPS) and in some selected cases an optic nerve sheath fenestration (ONSF).

The concomitant presence of venous sinus stenosis can be managed with angiographic pressure gradient measurements and eventual stenting [5].

Management of IIH during pregnancy is a unique challenge due to the lack of a protocol and the necessity of a tailored approach. Additionally, the efficacy and safety of drugs and surgical maneuvers need to be carefully considered to preserve both fetal and mother's health.

This paper is a systematic review of the literature focusing on this topic, which aims to collect and discuss all the retrievable findings in order to illustrate the commonly agreed treatment strategies for IIH during pregnancy.

2 | Materials and Methods

This review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines [6]. The PICO framework (Population: pregnant women with IIH; Intervention: medical and surgical treatment; Comparison: management strategies and mode of delivery; Outcome: maternal and fetal safety) was used to formulate the research question.

2.1 | Search Strategy

Two Authors (GT and MP) performed a comprehensive search on PubMed/MEDLINE and Scopus databases to identify relevant studies comparing treatment methodologies for women with IIH using the search terms: "(idiopathic OR benign) AND (intracranial hypertension OR psedotumor cerebri) AND (pregnant OR pregnancy)".

The search was updated to February 2nd, 2025, with no time limit. A forward search on references of the retrieved articles was also performed to increase the search power.

2.2 | Study Selection

The search was limited to peer-reviewed studies published in English.

Other inclusion criteria were papers reporting case reports and series illustrating clinical management and procedural interventions for patients affected by IIH during pregnancy. Review papers and studies not presenting explicit data were excluded. Two authors (CLS and MP) independently screened titles and abstracts of the articles retrieved by the search algorithm and selected studies according to the inclusion or exclusion criteria.

After the exclusion of ineligible articles, full texts of the remaining studies were assessed for eligibility according to the same criteria. Disagreements were resolved in a consensus meeting through a new reading of the article and collegial re-evaluation of the extracted data.

2.3 | Data Extraction

We categorized the selected studies into two main groups as it is shown in tables.

Table 1 shows case reports and series including data regarding the progression of the IIH during pregnancy with particular emphasis on visual outcome. Maternal risk factors and fetal complications were also extracted.

Table 2 collects larger series focusing on occurrence or worsening of IIH during pregnancy, which does not specifically report on the progression of visual disturbances and other maternal symptoms, but exclusively focused on other maternal risk factors and fetal outcome.

For each eligible study in Table 1, we extracted: author, year of publication, data on headache and visual field impairment during pregnancy, first- and second-line treatment strategies,

TABLE 1 | Summary of the included studies (small-sample-size).

Author and year	N. of pts (preg)	Maternal risk factors			Clinical impairments during preg		FLT during pregnancy (No. of cases)	SLT during pregnancy (No. of cases)	Foetal morbidities	Mode of delivery	Anesthesia (GEN or SP)	Post-partum treatment	Post-partum follow-up
		HBP	Obesity	Diabetes	H	VFC							
Greer, 1963	8	N/A	2	N/A	8	8	SUBT-D (3); Serial LP (1)	N/A	Abortions (2)	N/A	N/A	N/A	Symptom-free (8)
Nickerson, 1965	1	N/A	N/A	N/A	N/A	1	SUBT-D	N/A	N/A	N/A	N/A	N/A	N/A
Elian, 1968	1	N/A	N/A	N/A	1	1	A	N/A	Abortion	N/A	N/A	N/A	N/A
Traviesa, 1976	1	N/A	1	N/A	1	1	Serial LP + A	N/A	N/A	N/A	N/A	N/A	Symptom-free
Caroscio, 1978	1	N/A	N/A	N/A	N/A	N/A	Serial LP	N/A	N/A	N/A	N/A	N/A	N/A
Keltner, 1979	1	N/A	N/A	N/A	N/A	1	Shunt	N/A	N/A	N/A	N/A	N/A	VFC persistence
Henry, 1979	1	N/A	N/A	N/A	1	1	Serial LP + Steroids	N/A	N/A	N/A	N/A	N/A	N/A
Palop, 1979	2	N/A	2	N/A	2	2	Serial LP (2); A (2); Steroids (2)	N/A	N/A	V (1); C (1)	SP (2)	N/A	Symptom-free (1)
Shekelton, 1980	1	N/A	N/A	N/A	1	1	Serial LP + Steroids + OD	N/A	N/A	C (1)	N/A	N/A	VFC persistence (1)
Kassam, 1983	4	1	2	N/A	4	4	Serial LP (3); OD (1); A (2); Steroids (2)	Shunt (1)	N/A	V (1); C (3)	N/A	N/A	Symptom-free (3); 1 HBP
Digre, 1984	5	N/A	N/A	N/A	N/A	N/A	SUBT-D (1): A (1); Serial LP (2); ONSF (1); WC (2); Shunt (1)	N/A	N/A	N/A	N/A	N/A	VFC persistence (3)
Abouleish, 1985	3	N/A	3	1	3	3	Serial LP (2); Shunt (1)	N/A	Abortion (1); Preterm (1)	C (3)	G (2); SP	N/A	Symptom-free (2)
Thomas, 1986	2	N/A	N/A	N/A	2	2	Serial LP (2) + Steroids (2)	N/A	N/A	V (2)	SP	Steroids (1)	N/A
Wheatley, 1986	1	N/A	N/A	1	N/A	1	Steroids + OD	N/A	N/A	V	N/A	N/A	N/A
Douglas, 1991	1	1	1	1	1	1	Steroids + A	ONSF	N/A	V	SP	N/A	Symptom-free

(Continues)

TABLE 1 | (Continued)

Author and year	N. of pts (preg)	Maternal risk factors			Clinical impairments during preg		FLT during pregnancy (No. of cases)	SLT during pregnancy (No. of cases)	Foetal morbidities	Mode of delivery	Anesthesia (GEN or SP)	Post-partum treatment	Post-partum follow-up
		HBP	Obesity	Diabetes	H	VFC							
Shapiro, 1995	4	N/A	N/A	N/A	N/A	N/A	A (4); Serial LP (4); Steroids (3)	Shunt (3); ONSF (1)	N/A	N/A	N/A	N/A	VFC persistence (4)
Lesny, 1999	1	N/A	N/A	N/A	1	1	Serial LP + F	N/A	N/A	V	SP	N/A	N/A
Kim, 2000	1	N/A	N/A	N/A	N/A	N/A	Shunt	N/A	N/A	N/A	N/A	N/A	VFC persistence
Baron, 2002	12 (16)	N/A	16	N/A	10	11	A (2); Serial LP (2); Steroids (1); WC (11)	Shunt (1); ONSF (1)	Abortion (3)	V (15); C (1)	N/A	N/A	VFC persistence (1)
Bagga, 2005	3	1	3		3	2	Serial LP (1)	Steroids (2)	Abortion (1)	V (1)	SP (2)	A (1)	N/A
Lee, 2005	12	N/A	N/A	N/A	12	12	A (12)	N/A	Preterm (1)	V (11); C (1)	N/A	N/A	N/A
Zamecki, 2007	1	N/A	1	N/A	1	1	Serial LP + Steroids	N/A	N/A	N/A	N/A	Steroids	Symptom-free
Worrell, 2007	1	N/A	N/A	N/A	1	1	Serial LP	N/A	N/A	V	SP	N/A	Symptom-free
Aly, 2007	1	N/A	1	N/A	1	1	Serial LP	N/A	N/A	V	SP	A	Symptom-free
Heckatron, 2009	2	N/A	1	N/A	1	N/A	Serial LP (2); A (2); Steroids (2)	N/A	Preterm (2)	C (2)	SP	N/A	N/A
Evans, 2010	1	N/A	1	N/A	1	1	Serial LP	N/A	N/A	N/A	N/A	N/A	N/A
Month, 2011	2	N/A	2	N/A	2	2	Serial LP (2)	Shunt (1)	Congenital abnormality (1)	C (1); V (1)	SP (2)	N/A	H persistence (2)
Varea, 2012	1	N/A	1	1	1	1	A + WC	Serial LP + A	N/A	C	N/A	Shunt	VFC persistence
Butala, 2013	1	1	1	N/A	1	1	Serial LP + A	N/A	N/A	C	G	N/A	Symptom-free
Moore, 2014	1	N/A	1	N/A	1	1	Serial LP + A	N/A	N/A	V	SP	A	H persistence
Salem, 2016	1	N/A	N/A	N/A	1	1	A	N/A	Congenital abnormalities	V	N/A	A	N/A
Gragasin, 2016	1	N/A	N/A	N/A	1	1	Serial LP	N/A	N/A	C	SP	WC + Steroids	Symptom-free
Dogan,2018	1	N/A	N/A	N/A	1	1	Serial LP	Shunt	Abortion	N/A	N/A	N/A	Symptom-free

(Continues)

TABLE 1 | (Continued)

Author and year	N. of pts (preg)	Maternal risk factors			Clinical impairments during preg		FLT during pregnancy (No. of cases)	SLT during pregnancy (No. of cases)	Foetal morbidities	Mode of delivery	Anesthesia (GEN or SP)	Post-partum treatment	Post-partum follow-up
		HBP	Obesity	Diabetes	H	VFC							
Hasoon, 2020	1	N/A	1	N/A	1	1	Serial LP	N/A	N/A	C	SP	N/A	N/A
Harrison, 2020	1	N/A	1	1	1	1	shunt	N/A	N/A	C	G	N/A	Pelvic pain
Huo, 2020	1	N/A	N/A	N/A	1	1	Serial LP + A	N/A	N/A	N/A	N/A	N/A	N/A
Morenas-Inglesias, 2021	1	N/A	N/A	N/A	N/A	1	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Tyndel, 2022	1	1	1	N/A	1	1	Serial LP + A	Shunt	N/A	C	N/A	N/A	N/A
Mafrici, 2022	2	1	N/A	N/A	2	2	Serial LP (2)	N/A	N/A	N/A	N/A	N/A	Symptom-free (2)
Bell, 2022	1 (2)	N/A	N/A	N/A	2	2	Shunt (2); ONSF (1)	N/A	N/A	C (2)	G (2)	N/A	Persistence H (2)
Byth,2022	1	N/A	1	N/A	1	1	Serial LP + A + WC	Shunt	Preterm	V	SP	WC	H persistence
Alves, 2022	3	N/A	3	N/A	2	3	A + WC (3)	Serial LP (3); Steroids (1)	N/A	C (3)	SP (3)	A (1); Serial LP (1)	H persistence (2); VFC persistence (2)
Michelle, 2023	1	N/A	1	N/A	1	N/A	N/A	N/A	N/A	C	SP	N/A	Symptom-free
Knoche, 2023	16 (19)	N/A	14	N/A	18	19	Serial LP (5); A (3); WC (11)	N/A	Abortion (2)	V (1); C (3)	N/A	N/A	Symptom-free (12)
Subedi, 2023	1	N/A	1	N/A	1	1	Serial LP + A	N/A	N/A	C	SP	A	Symptom-free
Lamberty-Cheatham, 2024	13	N/A	Y (13)	N/A	N/A	13	N/A	N/A	N/A	N/A	N/A	A (1); WC (3)	VFC persistence (3)
Cvetkovic, 2024	42 (47)	N/A	47	N/A	17	8	A (8)	Serial LP (1)	Preterm (8); Abortion (2)	C (20); V (25)	N/A	N/A	N/A
Revuelta, 2025	1	1	1	1	1	1	Serial LP + A	EVD + Steroids	Preterm	C	SP	WC	Symptom-free

(Continues)

TABLE 1 | (Continued)

Author and year	N. of pts (preg)	Maternal risk factors			Clinical impairments during preg		FLT during pregnancy (No. of cases)	SLT during pregnancy (No. of cases)	Foetal morbidities	Mode of delivery	Anesthesia (GEN or SP)	Post-partum treatment	Post-partum follow-up
		HBP	Obesity	Diabetes	H	VFC							
Total	166 (178)	7	123	6	112	119	Serial LP (48); A (52); WC (29); Shunt (7); Steroids (17); ONSF (2); SUBT-D (5); OD (4)	Serial LP (5); A (1); EVD (1); Steroids (3); ONSF (3); Shunts (8)	Abortion (13); Preterm (14); Cong abnorm (2)	V (66) C (50)	SP (23); G (6)	A (7); Serial LP (1); WC (6); Shunt (1); Steroids (3)	VFC persistence (17); Symptom-free (39); HBP (1); H persistence (8); VFC persistence (14)

Abbreviations: A, acetazolamide; C, caesarean; EVD, external ventricular drain; FLT, first line treatment; G, general anaesthesia; H, Headache; HBP, High Blood Pressure; OD, other diuretics; ONSF, optic nerve sheath fenestration; Preg diab, Pregestational diabetes; preg, pregnancies; Pts, patients; Serial LP, serial lumbar punctures; SLT, second line treatment; SP, spinal anaesthesia; SUBT-D, sub-temporal decompression; V, vaginal; VFC, Visual field cut; WC, weight control.

fetal morbidities, mode of delivery, anesthesia, and postpartum follow-up.

For each eligible study in Table 2, we extracted: maternal risk factors, maternal complications, treatment during pregnancy, and fetal complications.

2.4 | Risk of Bias and Limitations

According to the ROBINS-I tool, several older studies showed a high risk of bias in multiple domains due to confounding, deviation from intended interventions, and participant selection. Conversely, most recent studies demonstrated a low risk of bias across all domains. Missing data and measurement of outcomes were less frequent sources of high risk but contributed to moderate concerns in several cases.

3 | Results

The search algorithm retrieved 157 results. The initial screening process excluded irrelevant articles based on predefined inclusion and exclusion criteria. Specifically, 19 were not in English, 27 were reviews, and 57 were not pertinent to the research question. Upon second selection, 5 studies were discarded because of a lack of data. Lastly, we included 49 studies in the final analysis, whose quality was assessed using the ROBINS-I V2 tool for risk of bias evaluation (Figure 1).

The study selection process was documented using the PRISMA 2020 flowchart, outlining the stages of identification, screening, eligibility assessment, and final inclusion (Figure 2).

3.1 | Systematic Review

The comprehensive review of all case reports and series retrieved a total of 165 patients affected by IIH with overall 178 pregnancies (Table 1).

As regards maternal risk factors, pregnant women demonstrated a higher percentage of obesity, which was reported in 123 pregnancies (69.1%), but a low rate of high blood pressure and diabetes. However, the association with these cardiovascular and metabolic risk factors was poorly discussed among the papers, and the relative percentages could be underestimated [4, 7–30]. Concerning the progression of the maternal neurological symptoms during pregnancy, we found that 112 patients (62.9%) presented worsening of the headache [4, 7–10, 12–38], whereas 119 (66.8%) new occurrences or impairments of visual disturbances [4, 7–10, 12–20, 22–39].

First line treatment strategy was analyzed among all the included papers covering a timespan of about 60 years (from 1963 to 2025).

Basically, acetazolamide (52 cases) or other diuretics (4 cases) administration represented the most frequent first-line pharmacological approach (31.4%) for symptomatic patients during the gestational period [2, 4, 9, 10, 12, 16–18, 20, 22–25, 27, 28, 33, 34, 40–42].

TABLE 2 | Summary of the included studies (large-sample-size).

Author and year	Study design	N. of pts w/ IIH vs. ctrl	Maternal risk factors (%)				Maternal complications (%)			Maternal treatment during pregnancy (%)				Fetal complications (%)			
			Pre-gest or gest diab	Obesity	PCOS	HBP	H	VFC	Coag disord	mortality	Anesthesia (G/SP)	Shunt	FLT	SLT	Abortion	Preterm	Fetal morbidities	Cesarean section delivery
Thaller, 2023	P	377	N/A	100	N/A	N/A	N/A	N/A	N/A	N/A	N/A	15	N/A	N/A	N/A	N/A	N/A	N/A
Falardeau, 2013	R	101 (158)	3.8	N/A	N/A	3.8	N/A	N/A	N/A	N/A	N/A	N/A	31.6 A	N/A	23.4	N/A	N/A	42.4
Hallan, 2022	R C-C w/PSM	6069 vs. 6069	6.3 vs. 5.7	31.9 vs. 30.9	N/A	17.9 vs. 16.7	28.4 vs. 27.8	N/A	5.0 vs. 4.6	1.1 vs. 0.2	N/A	N/A	N/A	N/A	8.8 vs. 11.2	8.2 vs. 11.0	N/A	12.9 vs. 14.5
Amikam, 2024	R C-C w/o PSM	1454 vs. 29,080	3.1 vs. 1.3	25.1 vs. 7.1	N/A	18.3 vs. 2.6	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	12.9 vs. 6.2	1.7 vs. 0.7 congenital anomalies	55.4 vs. 31.2

Abbreviations: A, acetazolamide; Coag disord, Coagulation disorder; FLT, first line treatment; G, general anesthesia; H, Headache; HBP, High Blood Pressure; P, Prospective; PCOS, polycystic-ovarian syndrome; Preg diab, Pregestational diabetes; R C-C w/PSM, retrospective case–control with propensity score matching; R C-C w/o PSM, retrospective case–control without propensity score matching; R, retrospective; SLT, second line treatment; SP, spinal anesthesia; VD, Visual deficits.

Additionally, 29 patients (16.3%) were on weight control (WC) as an initial approach [4, 17, 26, 30, 33], followed by serial LP in 48 cases (26.9%) as stand-alone or in combination [2, 8–10, 12, 13, 16–19, 22–25, 27, 29, 30, 33, 35, 36, 41–43] due to ineffective pharmacological and conservative treatment [18, 44].

Although a certain emphasis was common on WC as part of the first-line treatment, it rarely represented the only measure during the following gestational weeks.

Steroids as first-line treatment was reported in a minority of pregnancies (17 cases, 9.5%) [4, 8, 22–24] while invasive treatments, such as shunt (7 cases, 3.9%) and ONSF (2 cases, 1.1%), were overall performed in 11 cases [10, 16, 18, 22, 43].

Craniotomic approaches were used only in 5 cases until 1984, generally through a limited subtemporal decompression [11, 15].

Second-line management was mainly characterized by invasive maneuvers such as serial LP in patients initially treated only with pharmacological approaches, as well as definitive shunt placement (8 cases, 4.5%) and ONSF (3 cases, 1.7%) for patients requiring continuous CSF subtractions [10, 12, 16, 22, 27].

As concerning fetal morbidities, we found that 14 children (8.5%) were born prematurely [10, 16, 18, 23, 28, 34]; 2 (1.2%) showed congenital abnormalities [22, 40], while abortion was reported in 13 cases (7.3%) [2, 8, 16, 17, 28, 37, 43]. None of the children with congenital malformation was exposed to acetazolamide during the gestational period.

Mode of delivery was described in 116 out of 165 pregnancies (excluding aborts, 70.3%), with a similar rate of vaginal (66 cases, 56.9%) [7, 8, 10, 12, 16–18, 22, 23, 29, 34, 35, 38–40] and cesarean (50 cases, 43.1%) [4, 8, 9, 14, 16, 17, 21, 22, 24, 25, 27, 28, 31, 32, 34, 36, 38].

The anaesthesiologic regimen was reported only in 21 out of 48 studies, with 23 patients receiving spinal or epidural anesthesia, while 6 patients received general anesthesia.

Postpartum treatment was anecdotally reported, with some patients receiving medical management with diuretics or steroids. Additionally, one patient who underwent serial LP during pregnancy ultimately required definitive shunt placement.

Also post-operative maternal outcome was reported in a minority of patients, with 39 of them described as symptoms-free and 2 needing definitive shunt placement [7, 9, 12, 14, 15, 17, 19, 21, 24–26, 29, 30, 43]. Conversely, a permanent VFC hesitated in 17 patients (9.5%), although 13 of them had undergone CSF drainage during the gestation [4, 16, 18, 20, 36, 45, 46].

4 | Discussion

IIH management in pregnancy represents a unique challenge due to the need of balancing both maternal ICP and fetal safety.

The prevalence of pregnant women with a diagnosis of IIH is reported around 16/100.000 [1].

The risk of disease progression is associated with a rapid visual deterioration and refractory headache, which constitute a medical emergency for the mother.

Additionally, both the clinical status of the mother and the pharmacological treatments required to control the disease progression may pose a significant risk to the fetus. Therefore, a multidisciplinary approach involving neurologists, obstetricians, ophthalmologists, and neurosurgeons is required to optimize the outcomes.

This systematic review of the literature underscored the lack of detailed prospective observational studies that simultaneously monitor the impact of pregnancy on the clinical progression of IIH in the mother and associated risks for the fetus. Most of the information regarding the evolution of the maternal clinical symptoms comes from case reports and small clinical series, which tend to focus on patients experiencing disease worsening, thus overestimating the real risk.

On the other hand, larger series and registers analysis reassumed in Table 2 only focuses on the association of IIH during pregnancy and maternal risk factors, but fails to capture individual clinical characteristics and outcomes, thus limiting the possibility of retrieving patient-specific data on the worsening of the clinical picture during pregnancy [1, 41, 47, 48].

4.1 | Maternal Risk Factors

The evidence suggests that a multifactorial pathophysiology, including obesity, metabolic dysregulation, hormonal oscillations, and coagulation abnormalities, may increase the risk of IIH during pregnancy [49, 50].

Obesity is commonly identified as a main risk factor by all the studies. In fact, obesity leads to the elevation of intra-abdominal and intrathoracic pressures, thus increasing the venous pressure in the caval veins. It is believed that the increase in caval pressure is transmitted to the jugular veins and consequently to the intracranial venous system, thus impairing the efficiency of the CSF outflow and enhancing intracranial pressure (ICP) (Figure 3). However, within certain boundaries, obesity may represent a partially confounding factor in pregnant women, as the intra-abdominal pressure physiologically increases independently (but proportionally) from the amount of deposited visceral fat, but symptoms re-exacerbation occur only in a part of them.

Additionally, it is also supposed that a high level of leptin synthesized by the abundant adipose tissue may lead to CSF overproduction and reduced reabsorption. It seems, in fact, that leptin stresses the choroid plexus to become hyperactive, although the precise mechanism behind this process is not yet clear.

Furthermore, plasma volume expansion and fluid retention commonly occur in pregnancy may enhance this condition.

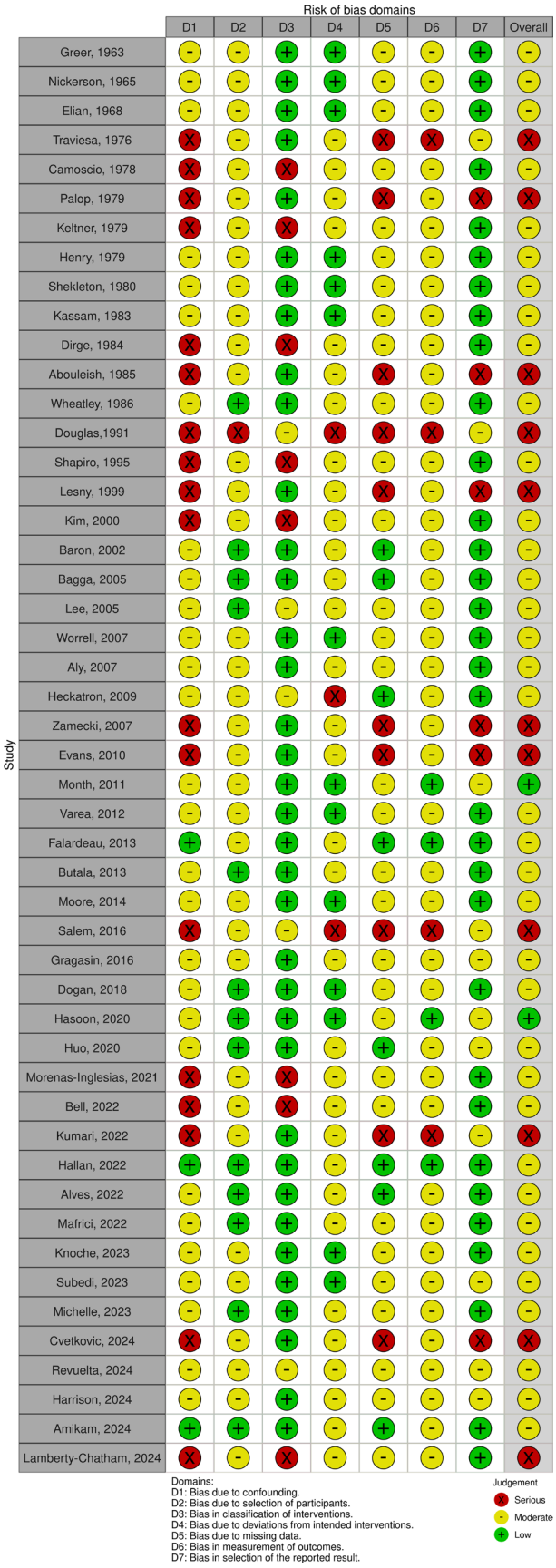

FIGURE 1 | ROBINS-I V2 (Risk Of Bias In Non-randomized Studies – of Interventions, Vers. 2).

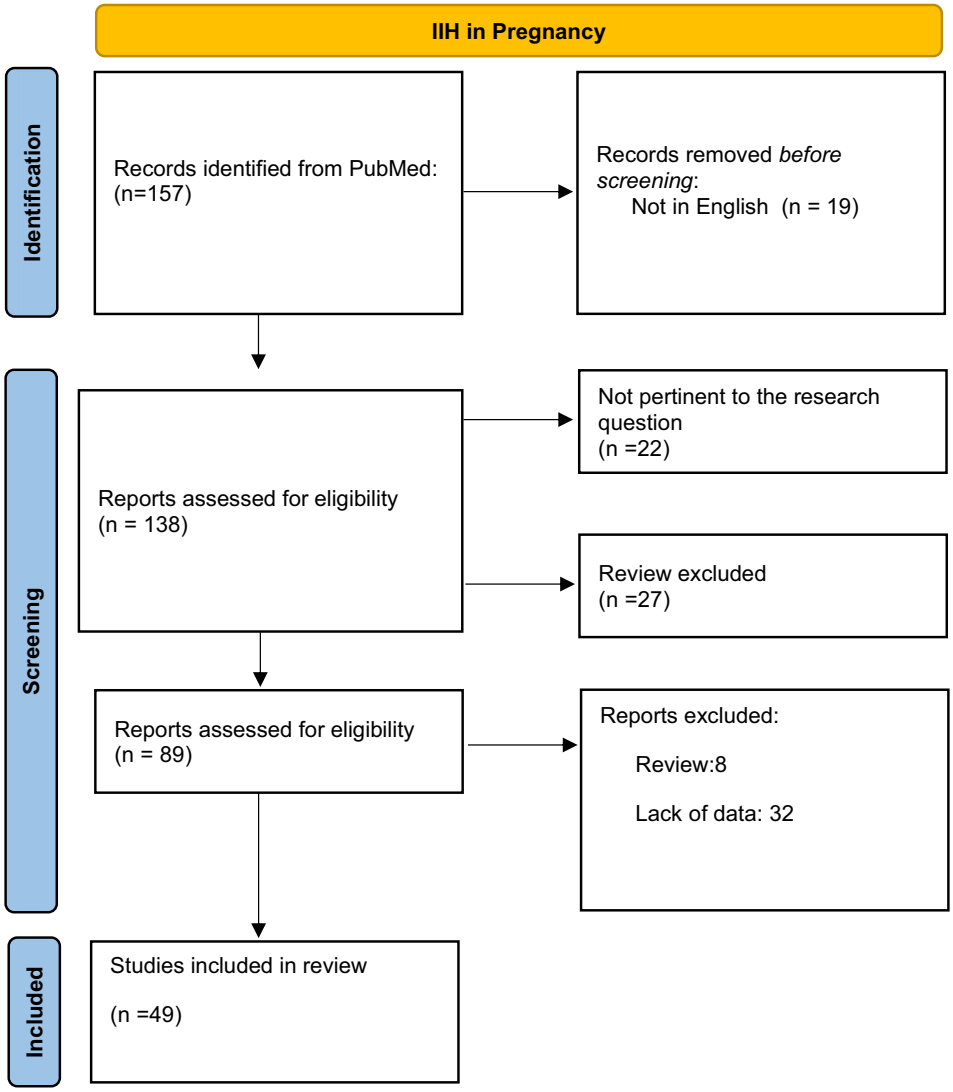

FIGURE 2 | PRISMA 2020 flow diagram for new systematic reviews.

Pregnancy is also related to a prothrombotic state, leading to an increased risk of cerebral venous sinus thrombosis, especially in patients having a focal sinus stenosis, frequently observed in patients with IIH, particularly at the transverse-sigmoidal junction [51, 52].

Hormonal imbalances, especially increased insulin resistance, cortisol, and thyroid hormone abnormalities, may also trigger a latent IIH [1] (Figure 4).

Although they appear underreported in the case series included in this review, a high rate of chronic hypertension (18.3% vs. 2.6%) and pregestational diabetes mellitus (3.1% vs. 1.3%) was found to be significantly higher in the cohort of pregnant women with IIH compared with controls in the large registers analysis by Amikam et al. [1].

In the same study, two additional noteworthy differences in maternal characteristics between IIH patients and controls were higher rates of tobacco smoking and thyroid disorders. However, thyroid disorders and IIH, especially among pregnant women, are still poorly studied, and whether there is a true association or whether this is a coincidental finding remains to be elucidated.

4.2 | Clinical Course of IIH During Pregnancy

This review shows that the worsening of headaches and VFC occurred in approximately 63% and 67% of pregnant women, respectively (Table 1). However, due to the lack of large prospective studies specifically focusing on the clinical course of IIH during pregnancy, most of these data were retrieved from case reports and small series, possibly overestimating risks. In fact, these percentages appear rather high, especially when compared with the larger case–control study by Hallan et al. that showed an incidence of headache (diverse from migraine) of 28.4%. Data on visual field change were instead not reported [47].

Interestingly, in the prospective study by Thaller et al., which included 377 pregnant women affected by IIH and followed up for 17.5 months, the authors showed that a new diagnosis of the disease during pregnancy was rare. Notwithstanding comparable

visual field and acuity measures, patients diagnosed during pregnancy had a greater risk of developing papilledema compared to those with pre-established IIH. On the other hand, in patients with pre-established IIH before planning a pregnancy, visual field and headache did not adversely worsen over time during gestation.

Due to the specific study design, the percentage of visual field worsening could not be retrieved, but visual outcomes appeared comparable between the groups of patients with a pregestational IIH diagnosis and nulligravids, underlying a non-significant risk variation. Notably, all these patients had shown recovery of papilledema in the 12 months prior to planning pregnancy, either through spontaneous improvement or pharmacological management [53].

Conversely, new diagnoses of IIH during pregnancy were rare; however, visual outcomes were significantly more compromised, particularly with respect to the occurrence of papilledema and VFC. Nevertheless, many patients showed progressive recovery after delivery.

According to Thaller et al., the prognosis of visual outcome was primarily determined by the duration of disease prior to gestation. A longer disease duration was associated with a greater reduction in papilledema. Moreover, in agreement with most of the studies, baseline BMI was also equally important, with higher BMI indicating a poorer prognosis for visual field. Interestingly, however, prognosis did not appear to be affected by weight gain during pregnancy, changes in BMI, or by the opening pressure during diagnostic LP [53].

Despite reassuring, it highlights that pregnancy should not be universally avoided in patients with IIH. However, disease control should be optimized before planned pregnancies whenever possible, particularly with regard to papilledema and the other maternal risk factors [11, 16, 53].

Thus, a scrupulous weight control remains the only disease-modifying risk factor for first-line personalized management, even though challenging in pregnancy due to the peculiar distribution of adipose tissue [53].

Finally, although underreported, IIH in pregnancy may also be associated with mood disturbances such as depression and anxiety, which are in turn predictors of post-partum depression and impairments in memory and concentration. Thus, clinicians should consider the importance of a psychological support to these women during pregnancy and puerperium [50 51].

4.3 | Ophthalmological Surveillance

A regular monitoring of campimetric parameters can play an important role in a timely discovery of a VFC and the unmasking of latent IIH. Although no set guidelines exist for the frequency of visual field and fundoscopic examinations, monitoring should be tailored to the patient's history of IIH, the degree of spontaneous or pharmacological compensation before onset during pregnancy, and current clinical status. If vision remains consistently stable, the visual field test interval can be set monthly or bimonthly; whereas in the case of papilledema or initial VFC, the assessment should be suggested weekly [50].

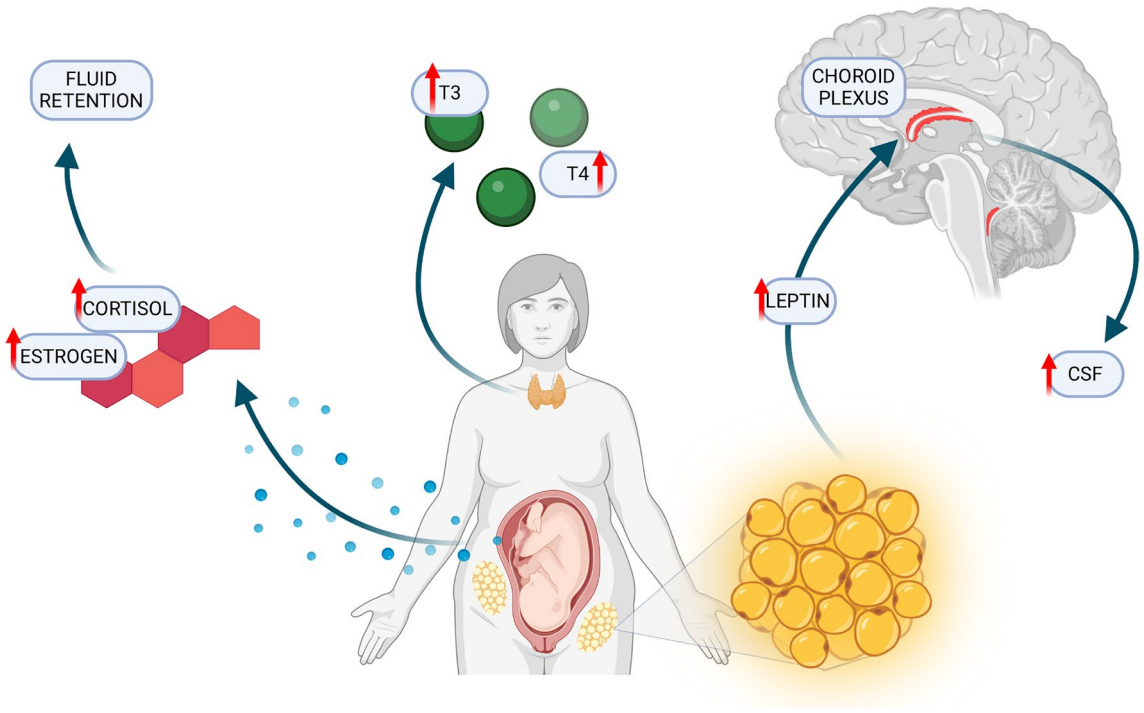

FIGURE 3 | Metabolic changes during pregnancy and mechanisms of ICP raising.

4.4 | Treatment Strategies During Pregnancy

This systematic review shows how the treatment approach of pregnant women with IIH has evolved over the decades. The included papers observed a progressive decline in the use of decompressive craniectomy and shunting as first-line treatments, nowadays largely replaced by serial LP and acetazolamide (Table 1, FLT) (Figure 5).

The optimal timing for initiating medical treatment remains under debate. If on one hand, some authors suggest delivering acetazolamide after the onset of visual deficits [4, 25], others support implementing diuretics in case of headaches persistence, as these usually precede the onset of visual dysfunctions [54]. Acetazolamide is nowadays the first-line treatment in most cases diagnosed with IIH, as it significantly improves papilledema, visual field deficits, and headache severity. Its effectiveness is particularly enhanced when combined with weight control, ultimately improving the patients' quality of life [28]. In studies where IIH was treated with acetazolamide, even in the first trimester at dosages > 1 g/d, the risk of gestational diabetes, preeclampsia, and abortion was similar to the control group [28, 34, 41]. Case reports have described congenital malformations associated with acetazolamide use during pregnancy; however, a causal relationship has not been confirmed. Many authors remain skeptical due to the controversies surrounding FDA guidelines (Table 3) [41]. Furosemide and chlorthalidone may represent second choices, but they need to be accurately evaluated with the obstetricians before substitution.

Topiramate was used as a secondary pharmacological treatment for pregnant patients who did not respond to acetazolamide in a few reported cases during the 1980s (other diuretics—OD—Table 1). However, it is no longer used because of its known well-documented teratogenic effects (Table 3) [55].

In the past, corticosteroids were often used as FLT strategy for acute vision-threatening situations, but due to risks like gestational diabetes and fetal complications, they should be limited only to severe cases. Steroids like dexamethasone and prednisone have been used in pregnancy with normal neonatal outcomes, though some cases showed a rebound effect after tapering [4, 8, 22–24, 50].

Interventional first-line strategies nowadays mainly include LP drainage, which represents a very effective but temporary measure. Complications of lumbar punctures include post-dural puncture headache, discomfort, and significant anxiety [50]. Serial LPs are often proposed by many authors to postpone the timing of shunt, hoping for a spontaneous regression after delivery [7]. If serial LPs fail to control worsening IIH, patients may undergo surgical treatment or induction of labor if the gestational period is complete [50].

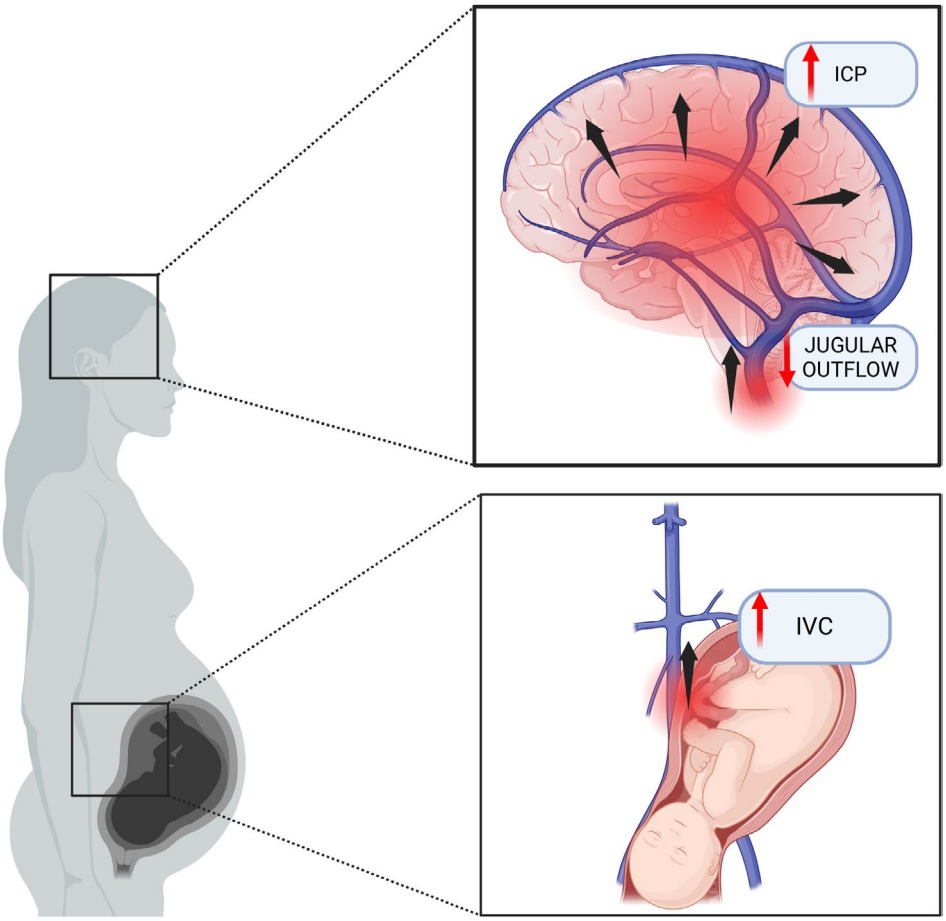

FIGURE 4 | Caval vein compression and jugular outflow reduction during pregnancy.

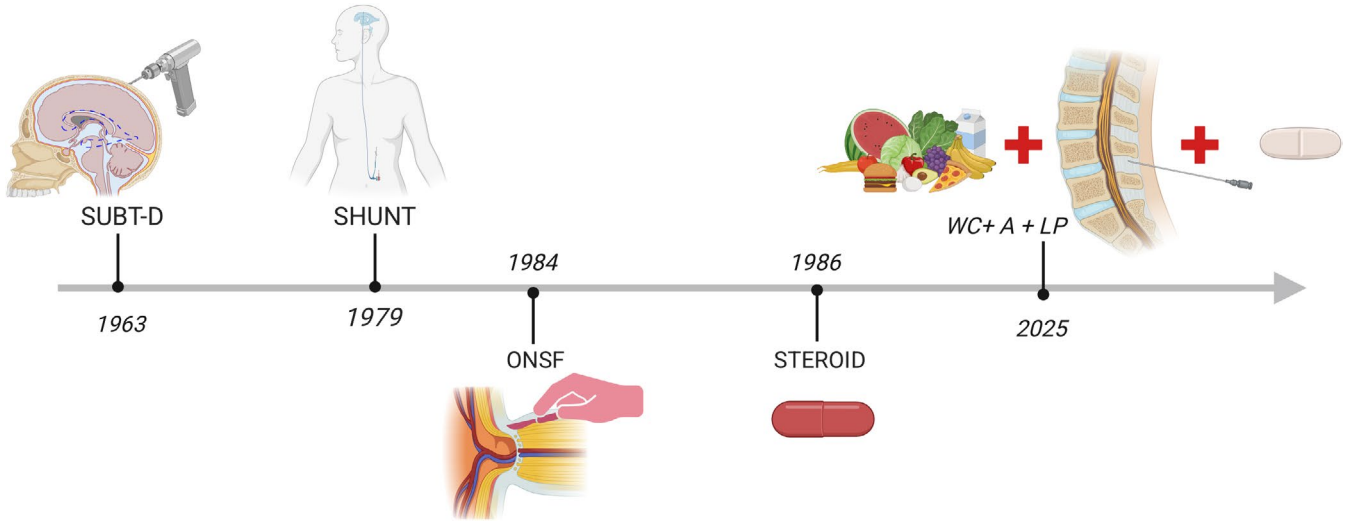

FIGURE 5 | Evolution of the treatment of IIH during pregnancy over time.

TABLE 3 | Summary of pharmacological indications – National Health and Medical Research Council (NHMRC) grades for recommendations and levels of evidence.

Treatment	Considerations
Weight management	Gestational weight gain should be limited to levels recommended for overweight and obese women
Treatment of secondary causes	Treatment of anemia and obstructive sleep apnea may be beneficial (grade C, level III-2)
Acetazolamide	Effective treatment outside of pregnancy (grade A, level II). Former FDA category C – may be safe in pregnancy and breastfeeding
Glucocorticoids	Use in fulminant cases supported only by case reports. Former FDA category B – possible increased risk of orofacial clefts with first trimester exposure. Conflicting data regarding risk of prematurity, low birth weight, preeclampsia, and gestational diabetes mellitus
Furosemide	Use in fulminant cases supported only by case reports. Consider need for stress dosing during delivery with prolonged use. Former FDA category C—may be associated with oligohydramnios.
Topiramate	Former FDA category D—contraindicated due to teratogenicity
Serial lumbar puncture	Temporizing measure—safe for mother and fetus (grade D, level IV). Unlikely to have sustained efficacy given rate of CSF formation
Lumbar drain	Temporizing measure—safe for mother and fetus (grade D, level IV). May improve CSF outflow, obviating need for surgery
CSF shunt	Effectively lowers ICP and improves papilloedema and visual field loss. Does not always improve headache. Requires general anesthesia. Compression by gravid uterus can cause shunt dysfunction
Optic nerve sheath fenestration	Effectively improves papilloedema and visual field loss, not headache. Dependent on local expertise. Local anesthesia. Risk of blindness in 1%–2%
Endovascular procedures	Transverse sinus stenting is used in case of bilateral transverse sinus stenosis outside of pregnancy. No reports of use during pregnancy.

Note: Treatment of Idiopathic Intracranial Hypertension in Pregnancy.

Surgical maneuvers include both ONSF and shunting. ONSF is still used in some cases. A recent meta-analysis on the effectiveness of this technique in preserving vision in patients with IIH showed that ONSF may improve visual outcomes, especially in cases of prompt intervention to prevent ischemic damage [56]. Its primary indication is visual impairment due to papilledema; however, it is ineffective in controlling headaches.

Instead, shunting represents the most efficacious treatment for severe cases, but it is rarely performed before delivery unless

uncontrolled symptomatology and rapid progression of VFC [10]. Shunting procedures include lumboperitoneal (LPS), ventriculoperitoneal (VPS) and ventriculoatrial shunts (VAS). LPS is the preferred primary choice in pregnancy, although VPS has shown a lower revision rate per patient. Shunt complications include infection, abdominal and back pain, and intracranial hypotension, necessitating careful consideration [50]. No cases of venous sinus stenting were reported during pregnancy as either first- or second-line approaches.

Although several studies support the idea of a possible thrombotic component associated with the pathophysiology of IIH, which can be physiologically enhanced during gestation, no experience of anticoagulants or antiplatelets prophylaxis is retrievable from the analysis of the literature on this topic.

4.5 | Mode of Delivery and Anesthetic Management

According to the available data (Table 1), the rate of spontaneous delivery and cesarean section were similar, and the choice for a section was more strictly related to obstetric reasons rather than to the IIH symptoms during the gestational period. Accordingly, in the recent series by Cvetkovic et al. accounting for 47 pregnancies, although 8 patients were under acetazolamide and only 1 needed serial LP for symptomatic IIH, a C-section was, however, preferred in 20/47 cases [28]. On the other hand, a significantly higher rate of cesarean sections (55.4%) was reported in the large register analysis by Amikam et al. compared to the control group (31.2%) [47]. Anyway, current practical guidelines on IIH in pregnancy reserve cesarean section only for obstetrical indications not considering vaginal delivery and even a prolonged second stage associated with a higher risk of vision [1].

However, some authors stressed the risk that prolonged labour and vaginal delivery with repeated Valsalva maneuvers may enhance the ICP in these cases, suggesting to opt for a C-section in cases of severe papilledema, neurological deterioration, and other comorbidities such as maternal hypertension, thrombophilia, or obesity [1, 4, 8].

Anesthetic management includes neuraxial anesthesia (epidural or combined spinal-epidural) and general anesthesia.

Epidural analgesia was reported as the preferred technique during labour and in case of C-section [4, 6–8, 10, 14, 15, 23–25, 29, 32, 43, 50, 54]. It is supported by most of the authors as the best approach since it can provide pain relief while maintaining maternal consciousness.

On the hand, some authors expressed concerns about the possible risks of spinal anesthesia [24]. In fact, the administration of large volumes of anesthetics in the subdural space may increase the ICP pressure, while a compensating pre-injection CSF drainage could cause sudden drops in ICP with potential headache exacerbation and visual changes.

A combination of spinal and epidural anesthesia with CSF withdrawal before subdural injection has been suggested to obtain analgesia while stabilizing any ICP changes [22].

There is a common consensus that general anesthesia should not be the first choice for patients with IIH, except in medical emergencies. The risks associated with general anesthesia, particularly during intubation and extubation, may lead to ICP due to airway manipulation and sympathetic stimulation [24].

4.6 | Limitations and Strengths

Our study had several strengths.

First, we employed a broad range of search terms and screened the entire available literature on the subtopic of IIH in pregnancy, including a forward search of the references cited in the included papers. This allowed us to identify and include a larger number of papers compared to a previous review on the same topic [50].

Secondly, we analyzed all recognized maternal and fetal risk factors from the included studies, along with specific data on the clinical course of the disease during pregnancy, which are often underreported in large cohorts from gestational registries.

As regards to limitations, almost all the included studies were single cases or small series reporting on pregnant patients affected by IIH; thus, we cannot exclude that they emphasized the more severe and complicated cases, where IIH progression is more likely to be noticeable or clinically significant. Therefore, it may represent a selection bias, potentially overestimating the real risk of worsening of visual symptoms compared to the general population of pregnant women. On the other hand, larger series and registers analysis mainly focused on risk factors and fetal outcome, failing to provide valid information on the evolution of the maternal visual deficit [1, 47, 53].

5 | Conclusions

In conclusion, while pregnancy-related physiological changes may exacerbate the symptoms of IIH and the actual risk remains difficult to quantify, this appears overall low in terms of recurrence or de-novo onset of the disease. A pre-gestational compensation with symptoms relief obtained with WC or medical treatment seems to reduce the probability of a severe worsening in pregnancy.

Diuretics such as acetazolamide, which did not show a causal relationship with congenital malformations, and serial LP in the case of persistently raised ICP represent safe and effective FLTs during pregnancy, whereas a shunt procedure should be reserved for fulminant cases with rapid and severe VFC occurrence. ONSF may also represent a safe and effective alternative in selected cases.

Mode of delivery and anesthetic regimen should be tailored mainly on the basis of obstetricians' consideration rather than the potential risk of ICP raising during labor.

Author Contributions

Matteo Palermo: conceptualization, investigation, writing – review and editing, software, data curation. **Gianluca Trevisi:**

conceptualization, methodology, software. **Sonia D'Arrigo:** investigation, methodology, validation, writing – review and editing, software, data curation. **Carmelo Lucio Sturiale:** conceptualization, investigation, validation, writing – review and editing, supervision, project administration.

Ethics Statement

IRB approval was not required for the systematic review.

Consent

The authors have nothing to report.

Acknowledgement

Open access funding provided by BIBLIOSAN.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Available upon reasonable request.

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