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Review Article

The Early Clues of Infantile Hemangiomas: Identifying Subtle Signs and Avoiding Diagnostic Delay

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Abstract

Purpose of the Study: Infantile Hemangiomas (IHs) are the most common benign vascular tumors of infancy, affecting 2-10% of children. Although many lesions regress spontaneously, 10-15% develop complications such as ulceration, airway obstruction, visual impairment or cardiac failure. Because most growth occurs before three months of age, early recognition and referral are critical; however, delays in diagnosis remain common. This review aimed to identify early clinical signs of IHs, summarize diagnostic challenges and evaluate tools that support timely recognition and referral.

Methodology: A PRISMA-guided scoping review was conducted using PubMed on August 17, 2025. Primary studies published between 2015 and 2025 involving infants or children with IHs were eligible for inclusion. Of 1,279 records identified, 24 studies met inclusion criteria following screening and exclusion of irrelevant articles.

Key Findings: Infantine hemangiomas were most commonly recognized within the first days to three months of life. Early indicators included red or bluish lesions and premonitory signs such as pale macules, telangiectasia and bruise-like patches. In select cases, presenting symptoms included feeding difficulties, respiratory distress, hepatomegaly or neurologic deficits. Imaging modalities were primarily utilized for complex or atypical lesions. Several studies emphasized the importance of distinguishing IHs from vascular and nonvascular mimickers. High-risk IHs often required treatment, with oral propranolol identified as the first-line therapy. Emerging referral tools and artificial intelligence-based diagnostic approaches demonstrated potential to improve.

Conclusion: Recognition of subtle early findings, particularly premonitory cutaneous changes, is essential for timely diagnosis of IHs. Increased provider and caregiver education, implementation of standardized screening and referral tools and continued research into novel diagnostic technologies may help reduce delays in care and improve patient outcomes.

Keywords: Infantile Hemangiomas; Early Detection; Treatment; Pediatric Dermatology; Diagnostic Accuracy

Abbreviations

IH: Infantile Hemangiomas; IHReS: Infantile Hemangioma Referral Score; AI: Artificial intelligence

Introduction

Infantile Hemangiomas (IHs) are benign vascular tumors with a reported incidence of 2-10%, though rates appear to be rising [1]. While typically benign and self-limited, 10-15% of IHs are associated with complications such as cutaneous expansion, ulceration, necrosis, high-output cardiac failure and consumptive hypothyroidism, all of which can cause significant morbidity [2]. Because of this, understanding the growth phases of IHs is critical to halting or reducing proliferation.

Infantile hemangiomas generally present between two and seven weeks of age and undergo gradual involution between three and nine years [3]. Most cases are diagnosed clinically and early recognition is essential for timely treatment. The most rapid growth occurs between one and two months of age [4]. Early referral and treatment is a determining factor for treatment success. In a prospective cohort study, 80% of the final hemangioma size was reached by 3 months, yet the mean age at first specialist evaluation was 5 months [5]. Delays in referral are often related to primary care access, diagnostic uncertainty and variable provider approaches. Some primary care physicians adopt a "watchful waiting" strategy, given the natural tendency of IHs to regress [6]. However, this can postpone treatment in patients who might otherwise benefit from early intervention. High-risk infantile hemangiomas, particularly those located near the eyes, nose, lips, airway or anogenital region, warrant early recognition and referral because of their increased potential for functional impairment and complications [7]. There is a paucity of studies examining factors for delayed referral for IHs. The reason for delayed treatment initiation may be multifactorial, including diagnostic uncertainty and provider education about IHs and treatment. Referral guidelines remain inconsistent. A European consensus panel recommends referral from three and five weeks of age, whereas American guidelines recommend evaluation at one month [2]. No universally accepted early diagnostic framework exists. One validated triage tool, the Infantile Hemangioma Referral Score, incorporates lesion location, size and patient age to help primary care physicians determine when referral to a specialist is warranted [8]. There remains a need to better define the earliest clinical signs of IHs to guide frontline providers. The objective of this review is to synthesize existing literature and case data to identify the earliest visible and clinical indicators of IHs and to develop a practical framework to support early and accurate diagnosis.

Methodology

Study Design

This study was conducted as a PRISMA-guided scoping review to evaluate the early clinical signs, presentation, diagnosis and management of Infantile Hemangiomas (IHs). Primary research studies published between 2015 and 2025 were systematically identified and assessed.

Participants/Subjects

Eligible studies included human subjects consisting of newborns, infants and children diagnosed with IHs. Inclusion criteria were: (1) publication between 2015 and 2025, (2) English language, (3) primary research involving pediatric patients with IHs and (4) human-subject studies. Review articles, studies published before 2015, non-English publications, non-free full-text articles and studies not specifically focused on IHs were excluded. Study selection was performed independently by 2 reviewers at both the title/abstract and full-text screening stages, with disagreements resolved through discussion and consensus.

Data Collection

A literature search was performed in PubMed on August 17, 2025, using the search terms: ((infantile hemangioma) OR (vascular lesion in infants)) AND ((early signs) OR (early presentation)). Titles, abstracts and full texts were screened according to predefined eligibility criteria. Data extracted from eligible studies included study title, publication year, study design, inclusion and exclusion criteria, sample size, participant age, geographic location, diagnostic findings and treatment approaches. Extracted data were organized in a standardized spreadsheet for review.

Data Analysis

A descriptive analysis of the included studies was performed. Following the initial search, 1,279 records were identified. After removal of 1,072 articles that were outside the specified publication period or unavailable as free full-text articles, 109 secondary sources were excluded. Title screening yielded 50 potentially relevant studies and abstract screening resulted in 24 studies meeting eligibility criteria for full-text review. Findings from the included studies were synthesized to identify common early clinical signs, diagnostic approaches, referral considerations and treatment strategies for IHs.

Results

After data extraction, which was summarized in Fig. 1, a total of 24 papers were reviewed and key information is outlined in Table 1 [9-32]. Studies reviewed included clinical trials, retrospective cohorts, multicenter studies and case reports. Sample sizes ranged from individual patient case reports to larger studies with 138 patients. The average age at presentation varied, but most IHs were first noticed between the first days of life and three months of age. Early clinical signs most often included superficial red or bluish cutaneous lesions. Specific site symptoms were also reported, such as feeding difficulties, respiratory distress, hepatomegaly and neurological deficits. Imaging was not routinely employed but was selectively used in more complex or atypical presentations, such as ultrasound or MRI for hepatic, airway and neurological involvement. Collectively, these studies emphasized that while most IHs are recognized in early life, delays in referral remain common and site-specific complications often prompt earlier diagnosis with imaging and appropriate intervention.

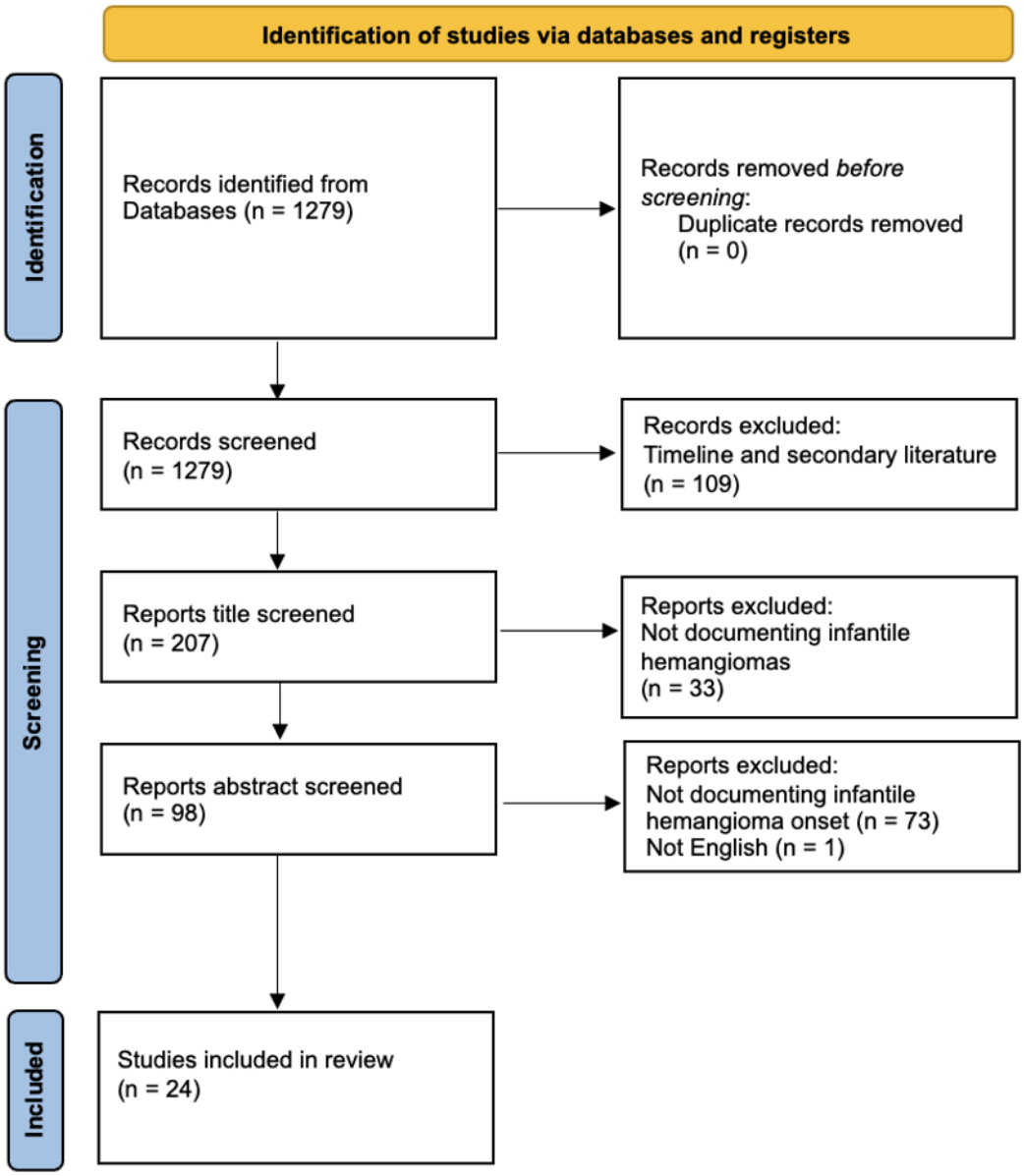

Figure 1: PRISMA 2020 Flow Diagram for Scoping Literature Review. PRISMA flow diagram demonstrating identification, screening, eligibility and inclusion of studies in this scoping review. Of 1,279 records identified through database searching, studies were screened by title and abstract, followed by full-text review for eligibility. After exclusions based on predefined criteria, 24 studies were included in the final analysis.

First Author	Year	Journal/Book	Study type	Number of Patients (n)	Age at first presentation	Key early clinical signs	Imaging utilized
Muñoz-Garza [9]	2021	JAMA Dermatology	Randomized clinical trial	69	10-60 days	Not applicable, treatment study	None
Nazemian [10]	2023	Int J Environ Res Public Health	Case report	1	2 weeks	Superficial red or deep bluish lesion	None
Giachetti [11]	2023	An Bras Dermatol	Retrospective observational study	138	~3 months	Not applicable, treatment study	None
Hadrawi [12]	2022	Am J Ophthalmol Case Rep	Case report	1	Not specified	Not specified	None
Sakai [13]	2023	Plast Reconstr Surg Glob Open	Case report	1	2 years	Involuting lesion, early signs not described	Ultrasound (US)
Diociaiuti [14]	2020	Acta Derm Venereol	Retrospective cohort study	24	2.7 months	Red or bluish cutaneous lesions; neurologic deficits	US and Magnetic Resonance Imaging (MRI)
Del Frari [15]	2018	Pharmacol Res Perspect	Multicenter study	22	Not specified	Not applicable	None
Bleve [16]	2022	Pediatr Med Chir	Case report	1	30 months	Not specified	None
Bakalli [17]	2019	BMC Pediatr	Case report	1	13 months	Not specified	None
Demie [18]	2021	HCA Healthc J Med	Case report	1	<6 months	Multiple cutaneous hemangiomas	US
Zhu [19]	2015	Medicine (Baltimore)	Case report	1	Birth	Large scalp hemangioma with necrosis	None
Sandru [20]	2024	Reports (MDPI)	Case report	1	10 days	Frontal hemangioma at hairline	None
Baniya [21]	2024	JNMA J Nepal Med Assoc	Case report	1	4 months	Cough, noisy breathing, vascular airway lesion	Bronchoscopy
Lam [22]	2024	Cureus	Case report	1	1 week	Epistaxis from nasal septum hemangioma	MRI

Pensabene [23]	2025	Ital J Pediatr	Case report	1	Birth	Exophytic hard palate lesion causing feeding difficulty	None
Alshalkhaty [24]	2024	Cureus	Case report	1	3 months	Respiratory distress, stridor	Computed Tomography and Bronchoscopy
Tsai [25]	2019	Medicine (Baltimore)	Case report	1	3 months	Hepatomegaly, abdominal distension	US and MRI
Liu [26]	2019	BMJ Case Rep	Case report	1	3 months	Respiratory distress from airway hemangioma	Flexible laryngoscopy
Liu [27]	2021	World J Clin Cases	Case report	2	Not specified	Cutaneous hemangiomas	None
Soares [28]	2025	Cureus	Case report	1	Not specified	Ulcerated sacral hemangioma	MRI
Paulpandian [29]	2025	Cureus	Case report	1	Not specified	Ulcerating lip hemangioma	None
Rais [30]	2018	Case Rep Pediatr	Case report	1	Not specified	Intussusception from hemangioma	None
Strunck [31]	2018	Dermatol Online J	Case report	1	Not specified	Vascular lesion with dermal atrophy	None
Corsello [32]	2025	Ital J Pediatr	Case report	1	Not specified	Hepatomegaly, anemia, hypothyroidism	US and MRI

Table 1: Included studies in scoping review of early infantile hemangioma recognition. Summary of studies included in the scoping review evaluating early clinical presentation, diagnostic evaluation and associated findings of infantile hemangiomas. Data extracted included study type, number of patients, age at presentation, early clinical signs and imaging modalities utilized when reported.

Infantile hemangiomas are the most common benign vascular tumors in infancy [33]. The characteristic growth cycle pattern, combined with clinical presentation, are often diagnostic. However, the presentation of the growth cycle can differ between patients, often influenced by the depth of the lesion [34]. This highlights the importance of distinguishing between early cutaneous findings that may mimic other diagnoses. Infantile hemangiomas can occur anywhere on the skin, but most commonly present on the head and neck. Superficial lesions often present earlier, manifesting as soft, blanchable, bright red flat or bumpy papules [35]. Deeper lesions can have more variation in presentation, ranging from a complete lack of pigmentation to a deep blue or purple hue, depending on the extent of skin epidermal penetration [35]. The premonitory mark of IHs, otherwise described as a solitary, pale, vasoconstricted or translucent patch, a bruise-like telangiectasia, is the earliest presentation of His [36]. These subtle lesions may also appear as an area of pallor with surrounding telangiectasia, a faint bluish or violaceous discoloration or a sharply demarcated erythematous macule that differs from adjacent skin tone [1,36]. In some infants, a reticulated vascular pattern or localized warmth of the skin may be noted before the lesion becomes raised [1]. Such early color changes often precede the proliferative phase and serve as key diagnostic clues for impending hemangioma development.

Recognition of this mark as an early IHs before the lesion may otherwise become more clinically apparent is important, as it also has the potential to be misdiagnosed as a different vascular anomaly. This also facilitates early detection of IHs that may potentially have life-threatening complications, including obstructive airway lesions in subglottic hemangiomas, hepatic hemangiomas associated with high-output congestive heart failure and hypothyroidism and severe hemorrhage from ulcerated lesions [36]. Important differential diagnoses to distinguish include erythema toxicum and even bruising. Erythema toxicum and the IH premonitory mark not only have a similar age of onset, but also share a similar clinical presentation in the appearance of a pale erythematous patch or macule. An important distinction here is the presence of yellow-white pustules and papules in erythema toxicum that may spread to the rest of the face and expand into the chest, trunk and extremities, whereas an IH would not have the presence of pustules or papules and remains localized without diffuse cutaneous dissemination. Equally significant is to distinguish the pre-monitory mark from ecchymosis or bruising, as misinterpretation may raise concerns for a trauma evaluation for an otherwise benign finding. The translucency of the premonitory mark allows for better visualization of the underlying vasculature, mimicking the blue discoloration of a bruise. However, bruises differ in that they are flat, non-blanchable and notably painful to palpation. Additionally, bruises will have a predictable sequence of color change from red-purple to green, yellow and brown before resolving [37]. Location is important when a bruise is on the differential, as accidental bruises are most often found over bony prominences such as the knees or shins, whereas non-accidental bruises occur in atypical sites such as the torso, ears, neck and may appear in a cluster or display the imprint of a hand or object. Most importantly, the premonitory mark of IHs would not be painful. In addition to the most common site being on the head and neck as opposed to other anatomical locations, it would present as a singular patch without clustering or yellow-green discoloration.

The distinction of IHs from other infantile vascular manifestations is important to ensure timely diagnosis and appropriate treatment (Table 2). Infantile hemangiomas can often be distinguished from nevus flammeus (port-wine stain) by their characteristic postnatal appearance and proliferative growth pattern, whereas nevus flammeus is typically present at birth and grows proportionally with the child [38]. An important distinguishing factor is the typical age of onset, with IHs presenting within two to seven weeks of age, while nevus flammeus will often be present at the time of birth. Recognizing the difference between these two diagnoses is critical because nevus flammeus can be an isolated vascular finding or associated with syndromic presentations such as Sturge-Weber Syndrome or Klippel-Trenaunay Syndrome, both of which require their additional unique interventions and treatment [14]. Also appearing at birth on the face and neck with a similar clinical presentation is nevus simplex, a blanchable pink macule or patch often with irregular 'feathery' borders that may fade around 2 years of age [38]. Unique to nevus simplex is that lesions may become more red with physiologic strain, such as crying, breath holding, straining, vigorous physical activity and changes in temperature, in addition to remaining flat and gradually fading over time as opposed to the raised and proliferative growth pattern of him [37].

Condition	**Age at Onset**	**Clinical Appearance**	**Growth Pattern**	**Key Distinguishing Features**
Infantile Hemangioma [8,9,40]	2-7 weeks	Bright red superficial papules or plaques or deep blue-purple lesions; may begin as subtle premonitory mark	Rapid proliferation at 1-2 months, followed by involution over years (typically 3-9 years)	Often palpable; common on head and neck; GLUT-1 positive
Nevus Flammeus [11,14]	Birth	Flat, well-demarcated red to violaceous patch, often dermatomal	Grows proportionally with child; no involution	Non-compressible, may darken over time; associated with Sturge-Weber and Klippel-Trénaunay syndromes
Ecchymosis [41]	Minutes to hours after trauma	Non-blanchable discoloration, blue-purple evolving to yellow-brown; poorly defined borders	Resolves gradually with predictable color changes	History of trauma; no proliferation; associated edema or inflammation

Nevus Simplex [39,42]	Birth	Blanchable, pale pink macule or patch with irregular, feathery borders	Facial lesions fade by age 2; neck lesions may persist	Midline distribution; accentuated with crying, fever or temperature changes
Erythema Toxicum [43]	First week of life	Yellow-white papules or pustules on erythematous base, "flea-bitten" apparance	Self-limited, resolves within 1-2 weeks	Transient lesions with eosinophils; favors face, trunk and extremities

Table 2: Clinical differentiation of infantile hemangiomas and common mimickers. Summary of distinguishing clinical features of infantile hemangiomas and common mimickers to facilitate early diagnosis and appropriate referral.

Discussion

A patient with an IH may not be referred to a specialist until late childhood [8]. Infantile hemangiomas often present subtly in the first few weeks of life, making early identification challenging for parents and non-specialist providers. At birth, the majority of IHs are not visible. Premonitory marks may be visible weeks to months after birth, appearing as pale macules, a subtle patch of ecchymosis or fine telangiectasia [39,40]. Infantile hemangiomas are commonly encountered in primary care, requiring pediatricians to decide on whether to observe or refer for treatment. Educating primary care providers on these subtle signs is essential to prevent misdiagnosis or delays in referral.

Due to the misconception that all IHs spontaneously regress with time, pediatricians may decide it is appropriate to observe an IH. However, IHs may be located in high-risk areas, requiring close monitoring, initiation of treatment or specialized care. During the proliferative phase, the lesion grows rapidly, with approximately 80% of its final size reached within this period [8]. Deeper lesions may be more difficult to appreciate as they may lack significant overlying skin changes [40]. Rapid growth is followed by gradual involution as the lesion begins to shrink. Complete resolution following involution may not occur as fibrofatty tissue, damaged skin, loss of normal anatomical structures or residual telangiectasias may persist [8]. Reconstructive procedures may be considered after regression to correct these residual changes [8].

Given these challenges, a scoring tool, the Infantile Hemangioma Referral Score (IHReS), was developed to aid primary care physicians in their decision on when a referral is warranted. Age, IH type, size, number, characteristics, locations, anatomical pattern and associated complications are incorporated in this scoring system [41]. A total score of four or higher indicates the need for referral. Baseline photographic documentation at the time of diagnosis and throughout the progression of the lesion provides visual tracking of regression [39]. A study developed an Artificial Intelligence (AI) algorithm that achieved 91.7% overall accuracy in the diagnosis of facial IHs based on clinical images [42]. Emerging technologies such as AI and mobile dermatology applications may further enhance the accuracy and convenience of monitoring lesion evolution.

Most IHs undergo spontaneous involution and do not require treatment. However, intervention is indicated for lesions at risk of functional impairment (e.g., periorbital, airway or genital involvement), those prone to ulceration, bleeding or scarring and cases that may lead to significant cosmetic disfigurement or psychosocial impact [1]. Early identification of high-risk IH is crucial to prevent complications and optimize therapeutic outcomes. It is essential to look out for the early, subtle signs of IHs such as areas of pallor with surrounding telangiectasia, faint bluish discoloration or sharply demarcated erythematous macules in order to diagnose and treat in a timely fashion. Oral propranolol is the established first-line therapy for problematic IHs and has largely replaced systemic corticosteroids due to superior efficacy and safety. The recommended dosing is 2 to 3 mg/kg/day, divided into two or three daily doses, ideally initiated during the proliferative phase, preferably before 5 months of age [2]. Propranolol's therapeutic mechanism involves vasoconstriction, inhibition of angiogenesis and promotion of apoptosis in capillary endothelial cells [4]. Clinical studies demonstrate response rates exceeding 80%, with visible improvement often occurring within days of treatment initiation [3]. Although generally well tolerated, propranolol carries a risk of bradycardia, hypotension and hypoglycemia, particularly in preterm infants or those with cardiac comorbidities. Baseline cardiovascular assessment and close monitoring during dose escalation are recommended [5].

Alternative and adjunctive therapies are available for cases unsuitable for propranolol or requiring additional cosmetic improvement. Topical timolol, typically applied as a 0.5% gel or solution, is effective for small, superficial lesions and offers minimal systemic absorption with a favorable safety profile [6]. Systemic corticosteroids are now reserved for patients in whom beta blockers are contraindicated or ineffective [1]. Laser therapy, particularly pulsed dye laser, can be used to accelerate healing of ulcerated lesions and treat residual telangiectasias after involution [1]. Finally, surgical excision is considered in select post-involution cases to address scarring, fibrofatty tissue or persistent bulk, but is rarely used during the proliferative phase unless other modalities fail [1].

The timing of diagnosis and treatment initiation is critical. Beginning therapy early, during the proliferative window, significantly improves response rates, reduces long-term complications and enhances both functional and cosmetic outcomes [2]. Prompt referral to a pediatric dermatologist is therefore strongly recommended to ensure optimal management.

A limitation of this review is that much of the available literature specifically describing the earliest clinical manifestations of infantile hemangiomas consists of case reports and small retrospective studies. Although larger cohort studies were identified, many focused primarily on treatment outcomes, referral patterns or disease progression rather than documenting premonitory signs and diagnostic timelines. Consequently, the evidence synthesized in this review is disproportionately derived from isolated clinical observations, which may overrepresent atypical presentations and limit the generalizability of findings. Therefore, the early clinical signs described in this review should be interpreted as potential diagnostic clues rather than definitive predictors of infantile hemangioma development. Larger prospective studies are needed to better characterize the frequency, timing and predictive value of these early manifestations.

The lack of standardized diagnostic tools and imaging protocols further complicates early identification. While the IHRes provides a useful clinical framework, it is not yet universally adopted. Future research should aim to standardize early diagnostic criteria and standardized referral guidelines to reduce delays and ensure timely care and treatment for IHs. The integration of AI into clinical practice presents a promising avenue for image-based diagnosis and longitudinal lesion tracking. Further validation of these technologies is necessary before implementation.

Conclusion

Infantile hemangiomas are common vascular tumors of infancy that often present with subtle early clinical signs, making prompt recognition and referral a persistent challenge for physicians. Clinical signs that are essential to look out for include areas of pallor surrounded by telangiectasias or subtle blue discoloration. While most IHs involute spontaneously, those located in high-risk sites or with rapid proliferation can lead to functional impairment, disfigurement and psychosocial consequences if not treated early. Current management is highly effective when initiated during the proliferative phase, with propranolol established as first-line therapy and adjunctive modalities available for specific indications. Tools such as the IHReS scoring system and baseline photographic documentation can aid in decision-making, but standardized diagnostic criteria remain limited. Emerging technologies, including artificial intelligence and mobile dermatology applications, hold significant promise for improving accuracy and accessibility of early IH diagnosis. Future large-scale, prospective studies are needed to better define early clinical predictors, optimize referral pathways and validate novel diagnostic approaches. Ultimately, improving recognition of subtle early signs and ensuring timely treatment are critical to minimizing complications and optimizing outcomes for children with IHs.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The project did not meet the definition of human subject research under the preview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

This does not apply as no personal information or photographs were used in this manuscript.

Authors' Contributions

All authors have contributed equally to this work and have reviewed and approved the final manuscript for publication.

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