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Achondroplasia: clinical management, guidelines, and therapeutic perspectives — a narrative review

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ABSTRACT

OBJECTIVE

To synthesize recent evidence on (i) clinical management, (ii) national and international guidelines, and (iii) therapeutic perspectives (including vosoritide) in achondroplasia.

METHODS

Narrative review of publications from 2021 to 2025 in PubMed, with explicit inclusion/exclusion criteria and justification for including guidelines as normative literature.

RESULTS

Identified studies report orthopedic techniques (e.g., intramedullary lengthening), non-cooperative respiratory assessment, diagnostic strategies (e.g., High-Resolution Melting for FGFR3), and international guidelines for implementation and monitoring of vosoritide; regional and national consensuses support multiprofessional care.

CONCLUSION

There is convergence on the need for longitudinal surveillance, multidisciplinary teams, and standardized pathways; targeted therapies represent progress but do not replace functional or surgical interventions when indicated.

KEYWORDS

Achondroplasia; Clinical Management; Clinical Guidelines; FGFR3; Vosoritide.

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INTRODUCTION

Achondroplasia is a genetically determined condition and the most common cause of disproportionate short stature. Its global incidence is estimated at approximately 1 in 25,000 live births, classifying it as a rare disease, although frequency may vary across different populations and epidemiological surveillance systems.[1] In Brazil, a similar trend is observed; however, disparities related to access to genetic diagnosis and specialized care persist, particularly when comparing urban regions to areas with limited healthcare coverage.[2]

The origin of the disease is associated with a heterozygous pathogenic variant in the FGFR3 gene, which encodes the fibroblast growth factor receptor 3. This mutation leads to excessive receptor activation, resulting in inhibition of chondrocyte proliferation and differentiation in the growth plate, reduced endochondral ossification, and consequently impaired growth of long bones.[1,3]

Characteristic clinical manifestations include short stature with rhizomelic limb shortening, relative macrocephaly, foramen magnum stenosis, sleep apnea, and spinal canal stenosis, among others. The frequency and severity of these manifestations may vary among individuals, but collectively they significantly affect quality of life, functionality, and social participation throughout the lifespan.[1-3]

Without appropriate follow-up, complications such as cervicomedullary compression, pulmonary hypertension, respiratory complications, chronic musculoskeletal pain, and progressive orthopedic deformities may worsen, reinforcing the importance of continuous and multidisciplinary management.[3]

According to the 2023 Guideline of the Brazilian Society of Pediatrics, major comorbidities include foramen magnum stenosis, hydrocephalus, recurrent otitis media, sleep apnea, thoracolumbar kyphosis, and genu varum, as well as psychosocial, economic, and emotional impacts. Additionally, approximately 50% of adults may present with hypertension or pre-hypertension.[3]

In recent years, the management of achondroplasia has been transformed by the introduction of new therapeutic approaches, including vosoritide, the first pharmacological treatment specifically targeting the FGFR3 pathway. Approved for pediatric use in individuals with open growth plates, it represents a major milestone in treatment.[4]

Given this context, the objective of this review was to identify and analyze studies published between 2021 and 2025 that address clinical management, therapeutic guidelines, and multidisciplinary strategies applied to achondroplasia, contributing to the updating of clinical care and strengthening comprehensive health attention for individuals with achondroplasia.

METHODS

This study constitutes a narrative literature review conducted with the objective of identifying, synthesizing, and discussing recent publications related to clinical management, guidelines, and therapeutic perspectives in achondroplasia. A narrative review was selected because it allows the integration of evidence from studies with different designs, clinical guidelines, and consensus documents—an approach particularly relevant in rare diseases, in which scientific production is limited and dispersed across multiple formats.

The bibliographic search was conducted in the National Library of Medicine database (PubMed), using the standardized MeSH descriptors “Achondroplasia” and “Fibroblast Growth Factor Receptor 3” (FGFR3), combined with the Boolean operators AND and OR, in June 2025. The search period was limited to 2021–2025, considering the increase in publications following the approval of vosoritide and the release of new international guidelines.

The following inclusion criteria were adopted:
• articles published in English, Spanish, or Portuguese;
• publications addressing clinical management, guidelines, therapeutic interventions, or multiprofessional follow-up in achondroplasia;
• studies involving human participants (children or adults).

The exclusion criteria were:
• studies exclusively experimental using animal or cellular models;
• articles whose primary focus was not related to clinical management or therapeutic recommendations;
• editorials and letters without clinical data or structured guidance.

In addition to indexed articles, official national and international guideline documents—such as the 2023 Guideline of the Brazilian Society of Pediatrics and recent international consensus statements—were included due to their normative nature and direct influence on clinical practice in different countries. This strategy characterizes the inclusion of clinically valuable grey literature, an appropriate approach for narrative reviews focused on management and healthcare policies.

Text selection and reading were performed in two stages: (i) screening by title and abstract according to the criteria described above, and (ii) full-text reading for extraction of relevant information, focusing on clinical manifestations, management strategies, follow-up protocols, quality-of-life indicators, and the use of emerging pharmacological therapies, including vosoritide.

RESULTS

The studies included in this review were thematically organized to facilitate the understanding of the main axes of analysis identified in the recent literature. Accordingly, the articles were distributed into three tables—Tables 1, 2, and 3: the first compiles techniques and clinical interventions related to diagnosis, orthopedic treatment, and functional assessment; the second presents national and international guidelines and consensus statements that guide the clinical management of achondroplasia; and the third encompasses studies on clinical management and care organization, including the experiences of families, healthcare professionals, and health systems. This organization allows for the observation not only of technical advances but also of how recommendations and care practices have been structured across different contexts.

Chart 1 - Studies related to clinical techniques and interventions in achondroplasia (2021–2025).

Reference	Objective	Main findings
Galán-Olleros et al., 2025	Evaluate lower-limb lengthening using telescopic intramedullary rods	Functional improvement (LEFS), enhanced self-esteem, and better quality of life (SF-12 and EuroQol VAS) after the intervention
Del Pino & Fano, 2025	Establish new head circumference percentiles for individuals with achondroplasia	Condition-specific reference values enable detection of growth deviations and early indication for interdisciplinary evaluation
LoMauro et al., 2025	Assess respiratory patterns in children with achondroplasia using optoelectronic plethysmography	Mild thoracic restriction identified during wakefulness; technique shows potential for non-collaborative assessments
Barranco de Santiago et al., 2025	Report anesthetic management in a pregnant woman with skeletal dysplasia	Difficult intubation and preferential selection of neuraxial anesthesia in the context of respiratory risk
Riba et al., 2021	Validate HRM technique for rapid detection of FGFR3 mutations	HRM proved to be a faster and lower-cost alternative to Sanger sequencing for molecular diagnosis

Source: The authors

Chart 2 - National and international guidelines and consensus documents for clinical management.

Reference	Scope	Main contributions
Savarirayan et al., 2025	International guidelines for the implementation and monitoring of vosoritide	Defines treatment eligibility criteria, monitoring parameters, and indications for treatment discontinuation
Barreda-Bonis et al., 2024	Spanish consensus for standardized administration of vosoritide	Emphasizes a multidisciplinary approach and national therapeutic standardization
Brazilian Society of Pediatrics, 2023	National guideline on diagnosis, clinical manifestations, and management	Recommends continuous neurological, respiratory, and orthopedic surveillance, along with psychosocial support

Tofts et al., 2023	Australian pediatric care guidelines	Organizes management according to age groups and clinical domains, aiming for continuous care
Llerena et al., 2022	Recommendations for management in Latin America	Highlights regional inequalities and the need for multiprofessional referral centers

Source: The authors

Chart 3 - Studies on clinical management, care experience and organization of health services.

Reference	Objective	Main findings
Bedeschi et al., 2024	Evaluate the experience of caregivers and physicians in Italy	Limb-lengthening surgery is widely considered acceptable to improve autonomy and quality of life
Alanay et al., 2023	Propose a standardized data set for international clinical registries	Recommends longitudinal registries including auxological measures, quality-of-life indicators, and surgical events to guide policies and clinical protocols

Source: The authors

DISCUSSION

The discussion was organized into three main thematic axes: (a) diagnostic and therapeutic techniques, (b) international and regional clinical guidelines, and (c) clinical management and impact on quality of life. An integrative synthesis is presented at the end.

a) Therapeutic, functional, and diagnostic techniques

The use of telescopic intramedullary rods for lower-limb lengthening has shown positive results in functionality and quality of life, as demonstrated by Galán-Olleros et al. (2025), who reported improvements in self-esteem, function, and mobility following the procedure.[3] Although effective, the method involves significant surgical risks and should be recommended on an individualized basis.

Macrocephaly, a prominent phenotypic feature of achondroplasia, was examined by Del Pino and Fano (2025), who proposed condition-specific head circumference reference charts, enabling early identification of deviations suggestive of intracranial hypertension or hydrocephalus, thus guiding timely interdisciplinary evaluation.[5]

From a respiratory standpoint, LoMauro et al. (2025) assessed breathing patterns during wakefulness and identified mild thoracic restriction and early ventilatory alterations, reinforcing the need for continuous airway monitoring from early childhood.[6]

In obstetric situations, as reported by Barranco de Santiago et al. (2025), difficulties in intubation and cephalopelvic disproportion may require cesarean delivery under neuraxial anesthesia, underscoring the importance of experienced teams and specific anesthetic protocols.[7]

Regarding genetic diagnosis, the High-Resolution Melting (HRM) technique proved to be a rapid, low-cost, and effective method for detecting FGFR3 mutations, potentially replacing more expensive approaches, such as Sanger sequencing, in initial screening processes.[8]

b) Clinical guidelines and therapeutic advances

The most significant therapeutic advance of the past decade has been the introduction of vosoritide, the first pharmacological treatment targeting the FGFR3 pathway. The drug acts as an analogue of C-type natriuretic peptide, counteracting excessive FGFR3 signaling and promoting increased endochondral ossification.[4]

International consensus statements recommend its use in infants and children with open growth plates, alongside continuous multidisciplinary monitoring, noting that the drug does not replace functional or surgical approaches when indicated.[4,9-13]

In Brazil, the 2023 Guideline of the Brazilian Society of Pediatrics emphasizes the need for multidisciplinary care, including neurological, orthopedic, respiratory, nutritional, and psychosocial follow-up, and highlights the high prevalence of cardiovascular complications and obesity.[1]

Across Latin America, practical recommendations underscore structural disparities and inequities in access to treatment, emphasizing the urgency of regionalized care models, particularly for populations outside major referral centers.[10]

c) Clinical management and impact on quality of life

The study by Bedeschi et al. (2024) showed that parents and caregivers perceive greater impact of limitations between ages 2 and 5, a critical period for motor development and social interaction, reinforcing the importance of early intervention.[10]

Furthermore, the development of standardized multicenter registries, as proposed by Alanay et al. (2023), is essential for comparing care contexts across countries, enabling uniform criteria for outcome assessment and supporting the formulation of public health policies.[11]

CONCLUSION

Achondroplasia is a genetic condition involving significant structural alterations in bone growth, with functional, clinical, and psychosocial repercussions throughout the lifespan. The studies analyzed show that although there have been important advances in diagnosis and therapeutic strategies, the impact of the condition remains substantial, particularly regarding mobility, respiratory and neurological complications, orthopedic deformities, and adaptive and social challenges.

The introduction of vosoritide as the first pharmacological treatment targeting the FGFR3 pathway represents a milestone in the therapeutic field by promoting improvements in linear growth and bone development. However, its use does not replace the need for integrated clinical follow-up, and its effectiveness depends on continuous multiprofessional care, including orthopedic, respiratory, nutritional, physiotherapeutic, and psychosocial support.

Furthermore, important challenges persist related to access to early diagnosis, regional disparities in clinical management, and the cost and availability of treatment, especially in countries with heterogeneous healthcare systems. Thus, the development of public policies, expansion of referral centers, training of interdisciplinary teams, and the implementation of guidelines adapted to national contexts are essential steps.

Therefore, it is concluded that improving the quality of life and autonomy of individuals with achondroplasia depends not only on therapeutic advances but also on longitudinal, person-centered, equitable models of care supported by health systems capable of ensuring comprehensive and continuous follow-up.

REFERENCES

1. Galán-Olleros M, Alonso-Hernández J, Miranda-Gorozarri C, Garcia-Fernandez J, Egea-Gomes RM, Palazón-Quevedo A. Impact of lower limb lengthening with telescopic nails on

functionality and quality of life in pati-ents with achondroplasia. Rev Esp Cir Ortop Traumatol. 2025;S1888-4415(25)00001-3.
2. Llerena J, Kim CA, Fano V, Rosselli P, Collet-Solberg PF, Vasconcelos de Medeiros PF, et al. Achondroplasia in Latin America: practical recom-mendations for the multidisciplinary care of pediatric patients. BMC Pediatr. 2022;22:492.
3. Sociedade Brasileira de Pediatria. Acondroplasia: etiologia, apresentação clínica e tratamento. Rio de Janeiro: SBP; 2023.
4. Savarirayan R, Hoover-Fong J, Ozono K, Backeljauw P, Cormier-Daire V, de Andrade K, et al. International consensus guidelines on the implementa-tion and monitoring of vosoritide therapy. Nat Rev Endocrinol. 2025;21(5):314-24.
5. Del Pino M, Fano V. New Argentine head circumference references for people with achondroplasia. Arch Argent Pediatr. 2025;123(3):e202410565.
6. LoMauro A, Tringali G, Sartorio A, Sessa M, Aliverti A. The awake resting breathing pattern in children with achondroplasia. Health Sci Rep. 2025;8:e70615.
7. Barranco de Santiago Á, Alandes-Gallego Á, García-Rojas I, Tena B, Ma-galdi M. Anesthetic management of pregnant women with skeletal dyspla-sia and short stature. Rev Esp Anestesiol Reanim. 2025;72(3):101625.
8. Riba FRG, Gomes MES, Chaves-Rabelo N, Zuma MCC, Llerena J, Men-calha AL, Gonzalez S. High-resolution melting analysis for rapid detection of FGFR3 mutations. Genet Test Mol Biomarkers. 2021;25(10):692-700.
9. Barreda-Bonis AC, de Bergua-Domingo JM, Galán-Gómez E, Guillén-Navarro E, Leiva-Gea I, Riaño-Galán I. Expert consensus for the manage-ment of patients with achondroplasia in treatment with vosoritide. An Pedi-atr (Engl Ed). 2024;101(6):401-10.
10. Bedeschi MF, Mora S, Antoniazzi F, Boero S, Ravasio R, Scarano G, et al. The clinical management of children with achondroplasia in Italy. J En-docrinol Invest. 2024;47:345-56.
11. Alanay Y, Mohnike K, Nilsson O, Alves I, AlSayed M, Appelman-Dijkstra NM, et al. Real-world evidence in achondroplasia: considerations for a standardized data set. Orphanet J Rare Dis. 2023;18:166.
12. BioMarin Brasil Farmacêutica Ltda. Voxzogo® (vosoritida). Bula do Pro-fissional de Saúde. São Paulo; 2024.
13. Tofts LJ, Armstrong JA, Broley S, Carroll T, Ireland PJ, Koo K, et al. Australian guidelines for the management of children with achondroplasia. J Paediatr Child Health. 2023;59(4):426-40.