

Associated Arthropathies in Pediatric Endocrine Disorders: A Systematic Review and Narrative Synthesis

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Abstract

Background: Endocrine disorders in children and adolescents frequently involve the musculoskeletal system, producing characteristic arthropathies that may precede the diagnosis of the underlying hormonal disease. These manifestations are often overlooked despite their diagnostic value and potential reversibility with timely treatment. Improved recognition of endocrine-related arthropathy is essential to optimize diagnosis, management, and long-term functional outcomes. The objectives of the study were to summarize the spectrum and prevalence of arthropathy in pediatric endocrine disorders, evaluate their diagnostic and pathophysiological significance, and discuss management strategies and prognosis.

Methods: A systematic search of PubMed and Scopus was conducted from database inception through January 1, 2026 using combinations of endocrine terms (type 1 diabetes, thyroid disorders, growth hormone (GH) disorders, Cushing syndrome, hyperparathyroidism, and pseudohypoparathyroidism) and musculoskeletal terms (arthropathy, limited joint mobility, joint stiffness, slipped capital femoral epiphysis (SCFE), bone pain, and fractures). Titles, abstracts, and full texts were screened independently by two reviewers according to predefined criteria, and the study-selection pathway was summarized in a PRISMA-style flow diagram. Pediatric studies were prioritized; selected mixed-age cohorts were retained only when they included adolescents or informed rare pediatric phenotypes. Methodological quality was assessed using Cochrane risk-of-bias principles adapted for mixed study designs, supplemented by the Newcastle–Ottawa Scale for observational studies. Because of substantial heterogeneity, a narrative synthesis was performed.

Results: Fifteen studies were included. Diabetic arthropathy, usually presenting as limited joint mobility (cheiroarthropathy), was the most common finding, affecting up to 30% of children in earlier cohorts

but generally < 10% in contemporary populations with improved glycemic control; it correlated with disease duration and microvascular complications. Thyroid disorders showed variable joint involvement: hypothyroidism was associated with arthralgia, non-inflammatory effusions, epiphyseal dysgenesis, and atypical SCFE, whereas Graves disease rarely caused thyroid acropachy or antithyroid drug-related arthritis. GH excess was associated with acromegalic arthropathy involving the hands, spine, and large joints, although prevalence estimates of 70–75% derive mainly from mixed-age cohorts that included adolescents rather than pediatric-only series. In contrast, GH deficiency and hypothyroidism were overrepresented among children with atypical or early-onset SCFE. Pediatric Cushing syndrome was characterized mainly by bone fragility, vertebral fractures, and reduced mobility rather than inflammatory arthritis. Primary hyperparathyroidism caused bone and joint pain with fractures, while pseudohypoparathyroidism was associated with growth-plate abnormalities and occasional SCFE. Across disorders, early endocrine treatment usually stabilized or improved musculoskeletal manifestations.

Conclusions: Arthropathy in pediatric endocrine disorders encompasses a broad, disorder-specific spectrum with important diagnostic and prognostic implications. Early recognition and treatment of the underlying endocrinopathy can prevent or reverse many joint complications, whereas delayed diagnosis may lead to permanent musculoskeletal disability. Multidisciplinary management is essential to optimize long-term outcomes.

Keywords: Pediatric endocrinology; Arthropathy; Limited joint mobility; Slipped capital femoral epiphysis; Growth hormone disorders; Systematic review

Introduction

Musculoskeletal complaints, including arthralgia, joint stiffness, reduced range of motion, and structural joint abnormalities, are increasingly recognized as relevant comorbidities in children and adolescents with endocrine disorders [1, 2]. Although traditionally considered secondary or minor manifestations, arthropathy in pediatric endocrinology has important clinical implications, as it may affect mobility, physical activity, growth-related function, and quality of life during critical developmental periods [1–3]. In some cases, joint manifestations precede the diagnosis of the underlying endocrine disorder.

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der, making them valuable early clinical indicators [2, 4].

The reported prevalence of endocrine-related arthropathy varies widely across conditions and populations. Among pediatric endocrine disorders, type 1 diabetes mellitus represents the most extensively studied model. Limited joint mobility (LJM) of the hands was historically reported in up to 30–40% of children and adolescents with diabetes [5–7]. More recent cohorts, however, demonstrate substantially lower prevalence—often below 10%—likely reflecting improvements in long-term glycemic control, earlier diagnosis, and advances in diabetes management [8, 9]. These observations highlight the dynamic nature of endocrine arthropathy and its sensitivity to disease duration and metabolic control.

Beyond diabetes, musculoskeletal involvement has been described across a broad spectrum of endocrine disorders in children, including conditions affecting thyroid function, growth hormone (GH) secretion, and mineral metabolism. While the specific patterns and mechanisms differ, shared pathways—such as altered collagen metabolism, glycation of connective tissue, hormonal effects on cartilage and bone turnover, and impaired microvascular supply—appear to underlie joint vulnerability in endocrine disease [1, 2, 10]. Importantly, endocrine disorders are overrepresented among children presenting with atypical orthopedic conditions, including slipped capital femoral epiphysis (SCFE) occurring outside the typical age or weight range, reinforcing the link between hormonal imbalance and joint pathology [10].

The clinical expression of endocrine-related arthropathy in children differs fundamentally from that in adults due to ongoing growth, open physes, and rapid changes in body composition during childhood and adolescence [1, 2]. These developmental factors influence not only susceptibility to joint involvement but also the potential for reversibility following timely treatment. While some joint manifestations improve with optimal endocrine control, others may persist or progress, particularly when diagnosis is delayed or exposure to hormonal imbalance is prolonged [3, 9].

Despite its clinical relevance, arthropathy remains under-recognized in routine pediatric endocrine practice. Clinical evaluations often prioritize auxological parameters, pubertal staging, and biochemical targets, with less systematic attention to joint examination and functional assessment [1, 3]. This may result in delayed recognition, missed opportunities for early intervention, and underestimation of disease burden, especially in children with subtle or painless joint involvement.

Accordingly, a focused review of arthropathy in endocrine disorders among children and adolescents is warranted. By summarizing prevalence patterns and clinical presentations using validated evidence, this review aims to improve awareness and early recognition of musculoskeletal involvement in pediatric endocrinology. Condition-specific mechanisms, diagnostic considerations, and management strategies are addressed in detail in subsequent sections, with the goal of optimizing multidisciplinary care and improving long-term musculoskeletal outcomes.

Objectives

The objectives were: 1) to summarize the prevalence and clinical

patterns of arthropathy associated with major endocrine disorders in children and adolescents; 2) to identify endocrine conditions in which joint manifestations serve as early diagnostic or prognostic indicators; and 3) to synthesize current evidence on outcomes following endocrine-specific management, with emphasis on reversibility and long-term musculoskeletal impact.

Methods

Literature search and study selection

A structured literature search was performed in PubMed (MEDLINE) and Scopus from database inception through January 1, 2026 to identify reports of arthropathy or joint-related musculoskeletal manifestations in children and adolescents with endocrine disorders. The core search strategy combined endocrine terms (“type 1 diabetes”, “hypothyroidism”, “hyperthyroidism”, “Graves disease”, “growth hormone excess”, “pituitary gigantism”, “acromegaly”, “growth hormone deficiency”, “Cushing syndrome”, “hyperparathyroidism”, and “pseudohypoparathyroidism”) with musculoskeletal terms (“arthropathy”, “arthritis”, “arthralgia”, “limited joint mobility”, “cheiroarthropathy”, “joint stiffness”, “slipped capital femoral epiphysis”, “bone pain”, “fracture”, and “musculoskeletal”). Boolean operators AND/OR were used, and the reference lists of relevant review articles were hand-searched for additional eligible reports.

Searches were restricted to human studies and English-language publications. Pediatric studies (0–18 years) were prioritized. Because several endocrine arthropathies are rare in childhood, selected mixed-age cohorts were also retained when they included adolescents or when pediatric-specific evidence was limited but the study directly informed mechanisms, phenotype, or management relevant to pediatric disease.

Eligible studies included original research articles of any design (randomized trials, cohort studies, case-control studies, cross-sectional studies, case series, and single-case reports) that described joint or skeletal manifestations in the context of a clearly defined endocrine disorder in pediatric patients. Review articles, editorials, and textbook chapters were excluded as primary evidence but were used for background context. Studies focused on primary rheumatologic disorders or non-endocrine metabolic bone diseases were excluded.

After duplicate removal, titles and abstracts were independently screened by two reviewers using predefined inclusion and exclusion criteria. Potentially eligible full texts were assessed independently, and disagreements were resolved by consensus or by consultation with a third reviewer when required. The study-selection pathway is summarized in a PRISMA-style flow diagram (Fig. 1).

Data extraction

From each included study, the following data were extracted

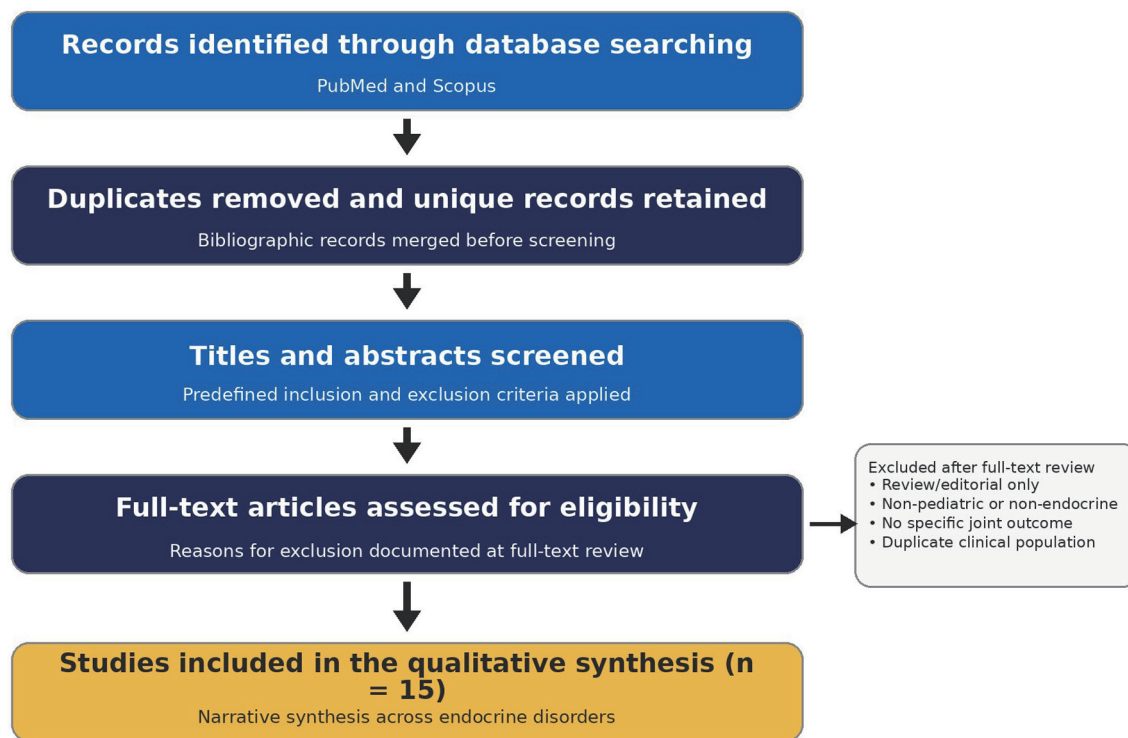


Figure 1. PRISMA-style study-selection pathway for the systematic review. This PRISMA-style figure summarizes database searching, duplicate removal, screening, full-text eligibility assessment, and final inclusion of 15 studies in the qualitative synthesis.

using a standardized form: study design, sample size, age range, endocrine diagnosis, type of arthropathy or joint involvement, reported prevalence or frequency, diagnostic methods, and clinical outcomes following endocrine treatment.

For observational studies, reported associations between arthropathy and clinical variables (e.g., disease duration, metabolic control) were recorded. For interventional or longitudinal studies, changes in joint manifestations after endocrine therapy were documented. Case reports and case series were included to capture rare but clinically relevant presentations. Extracted data were organized by endocrine disorder and summarized in thematic tables.

Quality assessment

Methodological quality and risk of bias were assessed using an adapted Cochrane risk-of-bias framework, appropriate for mixed study designs.

For cohort and case-control studies, the Newcastle–Ottawa Scale was used as a supplementary guide. Case series and case reports were recognized as having inherent high risk of bias but were retained for descriptive purposes due to the rarity of several endocrine arthropathies. Two reviewers independently rated each study as having low, moderate, or high risk of bias, with disagreements resolved by consensus. A summary quality assessment table is provided.

Given the heterogeneity of endocrine disorders, study designs, and outcome definitions, a narrative synthesis was un-

dertaken. Results were grouped by endocrine condition and type of arthropathy. Prevalence data are presented as ranges where applicable. Descriptive statistics reported in the original studies (percentages, means, confidence intervals) are cited directly.

Formal meta-analysis was not performed due to methodological heterogeneity and limited availability of comparable quantitative data. No additional statistical analyses were conducted beyond those reported in the original studies.

Reporting standards

This systematic review was conducted and reported in accordance with PRISMA 2020 principles. Because the included evidence was clinically heterogeneous and frequently descriptive, the results are presented as a narrative synthesis. As this review was based exclusively on published literature, institutional review board approval and informed consent were not required.

Results

The results synthesize evidence from observational cohorts, registry analyses, and selected case-based reports to characterize the prevalence, clinical patterns, and risk profiles of arthropathy across pediatric endocrine disorders. To reduce overlap, Table 1 [4, 9, 11–22] focuses on study characteristics and

Table 1. Study Characteristics and Key Clinical Messages of Arthropathy in Pediatric Endocrine Disorders

Study (first author, year)	Study type	Population (endocrine disorder)	Key findings related to arthropathy
Rosenbloom, 2013 [9]	Historical cohort analysis (1970s vs. 1990s)	476 children with type 1 diabetes (USA)	Prevalence of limited joint mobility (LJM) declined from ~30% to ~7% over two decades; LJM associated with poor metabolic control and ~4-fold increased risk of microvascular complications.
Clarke, 1990 [11]	Cross-sectional	70 children with type 1 diabetes (UK)	LJM prevalence 31% by prayer sign; 7% using strict criteria. More frequent with older age and longer diabetes duration; no significant HbA1c correlation in this small cohort.
Montana, 1995 [12]	Cross-sectional	89 adolescents with type 1 diabetes (Spain)	LJM present in ~42%; moderate–severe in 14%. Strong association with microalbuminuria, suggesting linkage with early diabetic microangiopathy.
Arkkila, 2003 [13]	Narrative review (pediatric data included)	Children and adults with diabetes mellitus	Summarized musculoskeletal complications of diabetes, including LJM and cheiroarthropathy; highlighted higher prevalence with longer disease duration and poor glycemic control.
McLean, 1995 [4]	Literature review and case series	Pediatric and adult hypothyroid patients	Hypothyroidism is associated with arthralgia, non-inflammatory joint effusions, and in children, epiphyseal dysgenesis and SCFE; synovial fluid typically viscous and acellular.
Gutch, 2013 [14]	Prospective cohort (6-month follow-up)	29 children with juvenile hypothyroidism (India)	Delayed bone age and metaphyseal thickening in all patients; short stature improved with therapy, but epiphyseal abnormalities persisted in >50% after 6 months; one SCFE case identified.
Lehmann 2006 [15]	Retrospective cohort	85 children with SCFE and endocrine disorders (USA)	Endocrine-related SCFE frequently bilateral and atypical; hypothyroidism and GH deficiency most common associations; recommended routine endocrine screening in atypical SCFE.
Karthikeyan, 2012 [16]	Case report	8-year-old girl with pseudohypoparathyroidism type 1b (UK)	Bilateral SCFE as presenting feature; associated with physeal widening and genu valgum; orthopedic fixation plus calcitriol led to physeal healing over 2 years.
Lindgren, 2023 [17]	Review with case series	90 patients with acromegaly (mostly adults; adolescents included, but pediatric subgroup not separately reported)	Highlighted endocrine etiologies (hypothyroidism, GH deficiency, hyperparathyroidism); endocrine-related SCFE occurred outside typical age/weight range and was frequently bilateral.
Dons, 1988 [18]	Retrospective cohort (long-term follow-up)	31 patients with long-term controlled acromegaly (mixed-age cohort; pediatric subgroup not separately reported)	Universal radiographic osteoarthritis at baseline; continued progression of hand and spine arthropathy despite biochemical remission in >80%; findings derive from a mixed-age cohort rather than a pediatric-only series.
Pelsma, 2021 [19]	Prospective cohort (9-year follow-up)	1 adolescent with Graves disease (Brazil)	Universal radiographic osteoarthritis at baseline; continued progression of hand and spine arthropathy despite biochemical remission in >80%.
Perini, 2019 [20]	Case report	16-year-old boy with Graves disease (Brazil)	Thyroid acropachy developed 2 years after radioiodine therapy; periosteal new bone formation and digital clubbing; rare pediatric manifestation.
Benina, 2023 [21]	Case series	Three children with primary hyperparathyroidism (Korea)	Presentations included bone pain, gait disturbance, and fractures; all due to parathyroid adenoma; musculoskeletal symptoms improved after surgery.
Lodish, 2018 [22]	Retrospective cohort	Children with endogenous Cushing syndrome (USA)	Vertebral fractures and musculoskeletal pain are common at diagnosis; bone density improved after cure, but some skeletal morbidity persisted.

GH: growth hormone; LJM: limited joint mobility; SCFE: slipped capital femoral epiphysis; UK: United Kingdom; USA: United States of America.

the principal clinical message of each included study, whereas Table 2 [4, 11–14, 16–24] summarizes disorder-specific manifestations and reported prevalence. Findings are organized by disorder and mechanism, with emphasis on population-level trends when available and on distinctive clinical phenotypes

that inform diagnosis and management.

Table 1 summarizes the foundational clinical evidence linking endocrine disorders to pediatric arthropathy, highlighting diabetes as the most extensively studied model and illustrating how improvements in disease management have altered

Table 2. Disorder-Specific Clinical Manifestations and Reported Prevalence of Arthropathy in Pediatric Endocrine Disorders

Endocrine disorder	Type of arthropathy/musculoskeletal involvement	Reported prevalence in children/adolescents	Key references (serial order)
Type 1 diabetes mellitus	Limited joint mobility (cheiroarthropathy), predominantly hands; may extend to wrists and elbows	7–42% (historical cohorts up to 30–42%; contemporary cohorts ~5–10%)	[11–13]
Juvenile hypothyroidism	Arthralgia, non-inflammatory joint effusions, epiphyseal dysgenesis; SCFE (rare but characteristic)	Arthralgia/effusions 10–30%; SCFE < 5% (largely case-based)	[4, 14, 16]
Hyperthyroidism (Graves disease)	Arthralgia, periosteal reaction; thyroid acropachy (very rare)	Arthralgia < 10%; acropachy < 1%	[20, 23]
Growth hormone excess (gigantism/acromegaly)	Degenerative arthropathy involving hands, spine, knees, and hips	70–80% in mixed-age cohorts including adolescents; pediatric-only prevalence unavailable	[18, 19]
Growth hormone deficiency	No primary inflammatory arthritis; increased risk of atypical SCFE and reduced bone strength	SCFE in GHD < 5% (overrepresented in atypical SCFE series)	[17]
Cushing syndrome (endogenous)	Bone pain, vertebral fractures, reduced mobility	Vertebral fractures 20–35%; musculoskeletal pain > 50%	[22, 24]
Primary hyperparathyroidism	Bone pain, gait disturbance, fractures; chondrocalcinosis (rare)	40–60% in small pediatric series	[21]
Pseudohypoparathyroidism	Skeletal dysplasia, occasional SCFE, functional joint limitation	Arthropathy uncommon; SCFE sporadic (case-based)	[16]

GH: growth hormone; GHD: growth hormone deficiency; SCFE: slipped capital femoral epiphysis.

musculoskeletal risk over time. It establishes the heterogeneity of joint involvement across endocrine conditions and underscores the influence of disease duration and metabolic control on arthropathy prevalence.

Table 2 provides a comparative overview of musculoskeletal involvement across major pediatric endocrine disorders, demonstrating wide variability in prevalence and phenotype. The data emphasize that while some conditions (e.g., type 1 diabetes, GH excess) show relatively frequent joint involvement,

others are characterized by rare but diagnostically important manifestations, reinforcing the need for disorder-specific clinical vigilance.

Table 3 [5, 6, 9, 11, 25, 26] highlights the temporal decline in LJM prevalence in pediatric diabetes cohorts, paralleling advances in glycemic management. It reinforces the strong association between LJM, disease duration, and microvascular complications, supporting its role as a marker of cumulative metabolic burden rather than an isolated musculoskeletal dis-

Table 3. Prevalence and Features of Diabetic Arthropathy (Limited Joint Mobility) in Children With Type 1 Diabetes

Study	Year	No. of diabetic patients (age)	Prevalence of LJM	Notable associations
Rosenbloom et al [9] (historical cohort/era comparison)	1976–1998	182 (7–18 years) in 1976–1978; 294 in 1998	~30% (1970s) → ~7% (1998)	LJM associated with about four-fold increased long-term risk of microvascular complications; higher cumulative glycemic exposure markedly increased LJM risk.
Clarke et al [11] (cross-sectional)	1990	70 (8–17 years)	31% (prayer sign); 7% (strict criteria)	Higher prevalence with older age and longer diabetes duration; ~12% of controls showed mild limitation, highlighting the need for standardized assessment.
Rosenbloom et al [5, 6, 9] (prospective natural history)	1981, 1982, 2013	309 (children and young adults, 1–28 years)	~30% overall	LJM clustered in early-onset and pubertal-onset diabetes; associated with reduced linear growth in early cohorts; many cases asymptomatic on routine care.
Traisman et al [25] (screening study including siblings/controls)	1978	310 children with diabetes plus siblings/controls	8.4% (contractures)	Contractures also observed in siblings and controls, suggesting background susceptibility and reinforcing the importance of uniform diagnostic thresholds.
Campbell et al [26] (cross-sectional)	1985	Young patients with type 1 diabetes	Variable (criteria-dependent)	LJM associated with microvascular complications, supporting its role as a marker of cumulative metabolic burden rather than isolated joint disease.

HbA1c: glycated hemoglobin; LJM: limited joint mobility.

Table 4. Thyroid-Related Arthropathy and Musculoskeletal Manifestations in Children and Adolescents

Study	Year	Population (age)	Thyroid disorder	Arthropathy/musculoskeletal phenotype	Reported prevalence	Notable associations/clinical implications
McLean & Podell [4]	1995	Pediatric and adult cases (narrative review)	Hypothyroidism	Non-inflammatory arthralgia, high-viscosity joint effusions, epiphyseal dysgenesis; hip involvement more prominent in children	Not pooled	Pediatric hypothyroidism may present with joint limitation and physcal disease rather than classic adult patterns; emphasizes endocrine testing in unexplained effusions.
Gutch et al [14]	2013	29 children (juvenile onset)	Hypothyroidism	Delayed bone age, metaphyseal thickening, epiphyseal abnormalities; occasional SCFE	Joint-specific prevalence not quantified	Growth improves with levothyroxine, but skeletal abnormalities may persist early after treatment, highlighting the importance of early diagnosis.
Moyer et al [27]	2016	2 children + literature review	Hypothyroidism	Atypical slipped capital femoral epiphysis	Rare (case-based)	Recommends thyroid screening in SCFE presenting outside the typical age or weight range or with delayed healing.
Ploegstra et al [23]	2011	15-year-old girl	Graves disease (on antithyroid drugs)	Antithyroid drug-induced arthritis	Very rare	Rapid resolution after drug withdrawal; important to distinguish from primary inflammatory arthritis.
Nihei et al [28]	2013	2 children (11 and 15 y)	Graves disease	Acute polyarthritis during methimazole therapy	Very rare	Supports early cessation of thionamides when severe arthritis develops.
Pereira et al [20]	2019	16-year-old boy	Graves disease	Thyroid acropachy (periosteal reaction, digital clubbing)	< 1%	Prolonged untreated hypothyroidism can cause severe locomotor disability, largely reversible with thyroid hormone replacement.
Tullu et al [29]	2003	2 children (7 y; 15 months)	Long-standing hypothyroidism	Kocher–Debré–Semelaigne syndrome with functional musculoskeletal limitation	Rare	Prolonged untreated hypothyroidism can cause severe locomotor disability, largely reversible with thyroid hormone.

SCFE: slipped capital femoral epiphysis.

order.

Table 4 [4, 14, 20, 23, 27–29] clearly shows that thyroid-related arthropathy in children is usually non-inflammatory and often reflects growth-plate and skeletal maturation effects rather than primary synovitis. Hypothyroidism is linked to arthralgia, viscous effusions, epiphyseal dysgenesis, and atypical SCFE, emphasizing the diagnostic value of thyroid testing in unexplained effusions or SCFE outside the usual age/weight range [4, 14, 27]. In contrast, musculoskeletal problems in Graves disease are rare and typically iatrogenic or periosteal—most often thionamide-related arthritis or very rare thyroid acropachy—so recognizing these patterns helps avoid mislabeling as rheumatologic disease and supports prompt medication adjustment when appropriate [20, 23, 28].

Table 5 [30–36] highlights two distinct GH-related musculoskeletal patterns: degenerative arthropathy in GH excess and growth-plate vulnerability (SCFE) in GH deficiency or GH therapy. Pediatric-onset GH excess is associated with periarticular overgrowth and osteoarthritis (OA)-like joint

changes that may persist despite biochemical control, whereas GH deficiency and GH treatment primarily increase the risk of SCFE, particularly in children with underlying endocrinopathies, supporting the need for early recognition and orthopedic vigilance.

Table 6 [1–36] provides a structured appraisal of methodological quality across the evidence base, demonstrating that most data derive from moderate-quality observational studies, with fewer low-bias population cohorts and necessary reliance on high-bias case reports for rare phenotypes. This assessment contextualizes prevalence estimates and supports cautious interpretation while highlighting areas where prospective pediatric data are most needed.

Overall, the evidence base for pediatric endocrine arthropathy is dominated by observational studies (moderate risk) with stronger epidemiologic inference available for SCFE in endocrinopathy from large population datasets (low-to-moderate risk). Rare thyroid and parathyroid phenotypes rely largely on case-based evidence (high risk), which is informative clini-

Table 5. Growth Hormone (GH) Excess– and Deficiency–Related Arthropathy in Children and Adolescents: Key Clinical Patterns and Representative Evidence

Study	Year	Study type	Population (GH disorder)	Arthropathy/musculoskeletal phenotype	Key findings relevant to arthropathy
Rostomyan et al [31]	2015	Multicenter cohort	Pituitary gigantism (pediatric-onset GH excess)	Arthralgia and early degenerative joint changes accompanying rapid linear growth and soft-tissue overgrowth	Large international cohort describing the clinical burden of pediatric-onset GH excess; musculoskeletal complaints, including joint pain, are frequent and often prompt evaluation alongside accelerated growth.
Beckers et al [32]	2018	Evidence synthesis/ review	Pituitary gigantism (pediatric-onset GH excess)	Overgrowth-related joint pain; propensity to early osteoarthropathy in longstanding GH excess	Demonstrated that prolonged GH/IGF-1 excess drives cartilage and periarticular tissue hypertrophy, predisposing to early degenerative arthropathy and supporting proactive musculoskeletal assessment.
Claessen et al [33]	2017	Comparative MRI study	Active vs. controlled acromegaly (mixed-age cohort; disease biology relevant to adolescent-onset GH excess)	“Acromegalic arthropathy” with knee cartilage thickening, osteophytosis, and OA-like changes	Showed high prevalence of structural joint abnormalities; some cartilage features improved with biochemical control, whereas structural damage often persisted, informing mechanisms relevant to pediatric-onset disease.
Colao et al [34]	2017	Narrative review with clinical synthesis	Acromegaly (mixed-age clinical synthesis)	Progressive degenerative arthropathy affecting hands, spine, hips, and knees	Highlighted that GH excess–related arthropathy may progress despite biochemical remission, supporting the concept of partially irreversible joint disease once established.
Blethen et al [35]	1996	Registry safety analysis	16,514 children receiving recombinant GH (NCGS)	Slipped capital femoral epiphysis (SCFE) as GH therapy–associated hip arthropathy	Identified SCFE as a rare but clinically important orthopedic complication during GH therapy, emphasizing the need for vigilance for hip or knee symptoms in growing children.
Darendeliler et al [36]	2007	Nationwide population-based cohort	80,769 children with endocrinopathy and 191,004 without endocrinopathy	SCFE as an endocrinopathy-associated growth-plate complication	SCFE incidence was approximately fourfold higher in children with endocrinopathy than in children without endocrinopathy (37.1 vs. 9.0 per 100,000). Among endocrinopathies, growth hormone deficiency had the highest SCFE incidence (583.8 per 100,000), supporting risk stratification and early hip evaluation.
Hwang et al [30]	2024	Children with endocrinopathy: 80,769	Endocrinopathy-associated SCFE: 30/191 (16%)	SCFE incidence was ~4× higher in children with endocrinopathy vs without: 37.1 vs. 9.0 per 100,000	Among endocrinopathies, growth hormone deficiency (GHD) had the highest SCFE incidence: 583.8 per 100,000

GH: growth hormone; GHD: growth hormone deficiency; IGF-1: insulin-like growth factor-1; OA: osteoarthritis; SCFE: slipped capital femoral epiphysis.

cally but should not be used to generate population prevalence estimates (Fig. 2).

Discussion

This review synthesizes available evidence on arthropathy in pediatric endocrine disorders, highlighting that joint and peri-articular involvement represents a clinically relevant but frequently underrecognized component of endocrine morbid-

ity in children and adolescents. Across disorders, arthropathy manifests along a spectrum ranging from subclinical limitation of joint mobility to overt structural joint and growth-plate pathology. The findings from Tables 1–5 collectively address the review objectives by defining prevalence patterns, identifying diagnostic signals, and clarifying implications for prognosis and management.

One consistent theme emerging from the data is that arthropathy often reflects cumulative disease exposure rather than acute metabolic status. LJM was most prevalent in ear-

Table 6. Overall Risk of Bias Across Studies Included in the Review

Overall risk of bias	Reference numbers	Main study types represented	Brief quality summary
Low risk	5–7, 19, 22, 24, 30, 31, 33, 35, 36	Large cohorts, population-based studies, prospective longitudinal studies, registry analyses, comparative imaging studies	Strong population definition, clear outcome ascertainment, and consistent exposure assessment. Longitudinal follow-up and population-based designs reduce selection bias; residual confounding possible but generally well controlled.
Moderate risk	8, 11, 12, 14, 15, 17, 18, 21	Retrospective and prospective cohorts, cross-sectional studies, imaging studies, medium-sized clinical series	Non-randomized designs with variable outcome definitions (e.g., LJM criteria, arthropathy phenotypes, SCFE ascertainment) and incomplete adjustment for confounders such as disease duration or severity. Generally robust clinical populations with biologically plausible and clinically anchored outcomes.
High risk	1–4, 9, 10, 13, 16, 20, 23, 25–29, 32, 34	Narrative reviews, expert syntheses, case reports/series, very small uncontrolled cohorts	High susceptibility to selection and reporting bias; limited generalizability; often descriptive without standardized outcome measurement. Particularly valuable for rare phenotypes (e.g., thyroid acropachy, antithyroid drug–induced arthritis, pseudohypoparathyroidism-related SCFE, Kocher–Debré–Semelaigne syndrome) but not suitable for prevalence estimation.

SCFE: slipped capital femoral epiphysis.

lier cohorts with less intensive glycemic management and declined substantially in more recent cohorts [5–7, 11, 12]. Importantly, LJM correlated with microvascular complications such as retinopathy and microalbuminuria, supporting its role

as a clinical surrogate of long-term tissue glycation and micro-angiopathy rather than an isolated musculoskeletal condition [5, 9, 12]. This observation aligns with the first objective of summarizing prevalence and patterns, while also reinforcing the prognostic value of joint examination in routine endocrine follow-up.

Mechanistically, diabetic arthropathy is thought to result from non-enzymatic glycation of collagen, leading to increased cross-linking, reduced tissue elasticity, and impaired remodeling within peri-articular connective tissue [13]. Accumulation of advanced glycation end products may also compromise microvascular perfusion of tendons and joint capsules, explaining the parallel association between LJM and microvascular complications observed across multiple cohorts [5, 9, 11, 12]. Clinically, the prayer sign is elicited by asking the patient to oppose the palmar surfaces of both hands fully; inability to bring the fingers and palms into complete apposition supports LJM. Although often asymptomatic, this process can lead to progressive stiffness and reduced range of motion, particularly in the hands, underscoring the practical value of bedside screening in endocrine clinics.

In contrast to diabetes, thyroid-related arthropathy is less prevalent but often diagnostically pivotal. Hypothyroidism in children rarely causes inflammatory arthritis; instead, joint symptoms arise indirectly through delayed skeletal maturation, epiphyseal dysgenesis, and altered cartilage turnover [4, 14, 29]. These changes predispose to atypical SCFE, particularly in children presenting outside the usual pubertal age or weight profile [15, 27]. In this context, “atypical SCFE” refers to bilateral disease, presentation in a younger child or in a non-obese adolescent, short stature, or the presence of additional endocrine/systemic features that lower the threshold for endocrine testing. The association between hypothyroidism and SCFE therefore emphasizes that joint manifestations may serve as early diagnostic indicators of underlying endocrine disease.

Graves disease–related joint manifestations are rare and



Figure 2. Arthropathy in pediatric endocrine disorders: clinical patterns, diagnostic clues, and management pathways. Infographic summarizing disorder-specific joint manifestations, diagnostic red flags, and management considerations in pediatric endocrine arthropathy. SCFE: slipped capital femoral epiphysis.

mechanistically distinct. When present, they are more often related to antithyroid drug reactions or rare periosteal syndromes such as thyroid acropachy rather than direct effects of thyroid hormone excess [20, 23, 28]. Recognition of these patterns is essential to avoid misdiagnosis as primary rheumatologic disease and to guide appropriate management, such as drug withdrawal rather than immunosuppression.

Evidence summarized in Table 5 demonstrates that GH excess, whether presenting as gigantism or acromegaly, is associated with a high burden of arthropathy. Joint involvement in GH excess is characterized by peri-articular soft-tissue overgrowth, cartilage hypertrophy, and subsequent degenerative changes, which may progress despite biochemical control [18, 19, 31–34]. Importantly, the highest prevalence estimates derive mainly from mixed-age cohorts that included adolescents rather than pediatric-only series. Imaging studies indicate that while some cartilage abnormalities may partially regress with treatment, established structural changes often persist, leading to chronic pain and functional limitation [19, 33]. These findings underscore that early diagnosis and endocrine treatment are critical, but they also support early orthopedic assessment, individualized physical therapy, and range-of-motion preservation strategies to reduce secondary disability once symptoms emerge.

In children with GH deficiency or those receiving GH therapy, the dominant arthropathic concern is SCFE rather than intrinsic joint disease [15, 17, 30, 35, 36]. Large registry and population-based cohort studies demonstrate that SCFE risk is elevated in children with endocrinopathies, particularly those with multiple pituitary hormone deficiencies or rapid growth acceleration during therapy [30, 35, 36]. Mechanistically, this vulnerability likely reflects disproportionate physal stress during periods of accelerated linear growth, compounded by underlying skeletal immaturity or hormonal imbalance. These data support proactive orthopedic surveillance and rapid evaluation of hip or knee pain in at-risk patients.

It must be noted that heterogeneity in study design, outcome definitions, and screening intensity substantially influences reported prevalence. Conditions such as diabetic LJM benefit from multiple cohort studies with relatively consistent methodologies, whereas rarer disorders (e.g., pseudohypoparathyroidism, pediatric hyperparathyroidism) rely largely on case reports and small series [16, 21]. As summarized in the quality assessment (Table 6), most evidence falls into the moderate risk-of-bias category, emphasizing the need for cautious interpretation of prevalence figures and avoidance of overgeneralization.

From a diagnostic perspective, the data reinforce that joint findings should prompt consideration of endocrine etiologies, particularly when presentations are atypical for primary rheumatologic disease. Recognizing these musculoskeletal patterns helps distinguish endocrine-related arthropathy from primary inflammatory arthritis and guides targeted hormonal evaluation. Bilateral SCFE, SCFE outside the usual age range, non-inflammatory joint effusions, or progressive stiffness without synovitis should trigger focused endocrine assessment [1, 2, 10, 15]. Incorporating structured musculoskeletal examination into pediatric endocrine clinics may therefore improve early detection and prevent irreversible complications.

Management of endocrine-related arthropathy remains largely etiology-specific. Optimal endocrine control is foundational but not always sufficient to reverse joint pathology, particularly in GH excess and long-standing hypothyroidism [4, 18, 19, 31–34]. Adjunctive strategies, including physical therapy to preserve range of motion, early orthopedic review for symptomatic hip disease or SCFE risk, and longitudinal monitoring for degenerative change, are often required. Recognizing drug-induced arthropathy in Graves disease is equally important because prompt withdrawal or substitution of the offending antithyroid medication may resolve symptoms without unnecessary escalation to immunosuppressive therapy [23, 28].

Prognosis varies widely across disorders and phenotypes. Diabetic LJM often stabilizes or improves with modern care, whereas GH excess-related arthropathy may progress despite remission [19, 33, 34]. SCFE associated with endocrine disorders carries a higher risk of bilaterality and long-term morbidity [17, 30, 35, 36], reinforcing the importance of early recognition and coordinated care. These distinctions highlight the value of disorder-specific counseling for patients and families.

The findings also expose gaps in the literature, including the lack of standardized definitions for pediatric endocrine arthropathy, limited prospective data linking early joint findings to long-term functional outcomes, and sparse pediatric-specific evidence for uncommon disorders. Future studies that integrate imaging, validated functional assessments, and endocrine biomarkers may better define risk trajectories and inform preventive strategies, particularly for mixed-age conditions in which pediatric estimates currently rely on indirect extrapolation.

Conclusion

Arthropathy in children and adolescents with endocrine disorders represents a heterogeneous but clinically significant source of morbidity that extends beyond traditional metabolic and growth outcomes. Evidence from observational cohorts and registry studies demonstrates that joint manifestations may serve as early diagnostic clues, markers of cumulative disease burden, or predictors of long-term functional impairment, depending on the underlying endocrinopathy. While some forms of endocrine-related arthropathy improve with timely hormonal correction, others—particularly those associated with GH excess or growth-plate vulnerability—may persist or progress despite biochemical control. Integrating systematic musculoskeletal assessment into pediatric endocrine care is therefore essential to optimize diagnosis, management, and prognosis.

Recommendations

1. Routine joint assessment, including range of motion, gait evaluation, and screening for SCFE, should be incorporated into the clinical evaluation of children with chronic or complex endocrine disorders.
2. Early endocrine evaluation is recommended in children pre-

senting with atypical or bilateral joint pathology, particularly SCFE or non-inflammatory joint stiffness.

3. Multidisciplinary management, involving pediatric endocrinology, orthopedics, and physiotherapy, should be adopted for children with established endocrine-related arthropathy to reduce long-term functional disability.

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Conflict of Interest

The authors declare that they have no conflict of interest relevant to this work.

Informed Consent

Not applicable because no individual participant data were collected directly by the authors.

Author Contributions

ATS conceived the review; MQ, MA, and KAS contributed to study selection and data organization; FA and NA contributed to manuscript review and administrative support; NH and SA assisted data extraction and table preparation; ATS and MQ interpreted the evidence; all authors revised the manuscript critically and approved the final version.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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