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Neuromuscular manifestations of pediatric endocrine disorders: A 25-Year Narrative Review of Muscular and Neurological Involvement, Clinical Reversibility, and Age-Specific Differences

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Abstract

Background: Endocrine disorders in childhood profoundly affect skeletal muscle and the nervous system through hormonal, metabolic, and inflammatory pathways. Although numerous studies have explored these associations, the cumulative evidence on clinical presentation, pathophysiology, and reversibility across endocrine axes remains fragmented.

Methods: This narrative review synthesized findings from 88 studies published between 2000 and 2025—comprising randomized trials, cohorts, and cross-sectional analyses—retrieved from PubMed, Scopus, and Google Scholar. Studies focusing on children and adolescents with endocrine disorders exhibiting muscular or neurological manifestations were included. Data were organized into tables describing (1) acute and chronic muscular features, (2) neurological involvement, and (3) reversibility following hormonal therapy. Study quality was graded using Cochrane and GRADE criteria.

Results: Analysis of 63 core studies within the introduction and results revealed a wide range of neuromuscular outcomes. Hypothyroidism emerged as the leading cause of pediatric myopathy and developmental delay, with early levothyroxine replacement resulting in complete reversal of muscle weakness and near-normal cognitive function. Hyperthyroidism presented mainly with proximal myopathy and thyrotoxic periodic paralysis, both rapidly reversible after achieving euthyroidism. Cushing's syndrome and critical illness–related corticosteroid insufficiency (CIRCI) were strongly associated with catabolic myopathy, showing partial recovery due to persistent mitochondrial and proteasomal injury.

Vitamin D deficiency and hypoparathyroidism accounted for most acute, reversible neuromuscular crises characterized by tetany, hypocalcemic seizures, and hypotonia. Growth hormone deficiency (GHD) produced sustained reductions in lean mass and muscle endurance, while GH replacement led to significant structural and metabolic recovery. Diabetes mellitus demonstrated early neuropathic and myopathic changes driven by oxidative stress and glucose fluctuation, reversible with tight glycemic control. Neurologically, congenital hypothyroidism, adrenal crises, and prolonged hypercortisolism remained major causes of developmental and cognitive impairment, whereas GH and vitamin D deficiency produced milder, reversible neurocognitive deficits. Overall, 75% of disorders exhibited at least partial neuromuscular reversibility, with the best outcomes observed in hormone-deficient states corrected within early childhood.

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Conclusion: Pediatric endocrine disorders exhibit diverse but interconnected neuromuscular and neurological manifestations. Early hormonal replacement and metabolic correction substantially enhance reversibility and long-term neuro-muscular outcomes, while catabolic and inflammatory disorders such as Cushing's and CIRCI lead to incomplete recovery. Routine neuromuscular monitoring should be incorporated into endocrine management to optimize recovery and preserve function.

Keywords: Pediatric Endocrine Disorders; Myopathy; Neuropathy; Hormone Deficiency; Reversibility

1. Introduction

Endocrine disorders exert profound effects on the neuromuscular system in children and adolescents because hormones such as thyroid hormone, cortisol, insulin, vitamin D, and growth hormone directly regulate muscle protein turnover, neuronal maturation, peripheral nerve integrity, and neuromuscular junction function (1). Disruption of these pathways can lead to acute or chronic myopathy, neuropathy, movement abnormalities, seizures, or developmental delay depending on the endocrine axis involved (2).

Hypothyroidism is among the most recognized endocrine causes of pediatric neuromuscular dysfunction, presenting with hypotonia, delayed milestones, myopathy, neuropathy, and—in congenital forms—irreversible intellectual disability if not treated early (3). Children differ from adults by exhibiting more global developmental and language delays and fewer peripheral neuropathies. Hyperthyroidism, conversely, manifests hyperkinesia, tremors, behavioral disturbances, irritability, proximal weakness, and occasionally thyrotoxic periodic paralysis, which is more common in adolescents than younger children (4). Adults are more likely to present with anxiety, neuropsychiatric symptoms, and fine tremors, with less dramatic muscle involvement (5).

Cushing's syndrome and chronic hypercortisolism produce profound catabolic myopathy due to accelerated protein breakdown, preferentially affecting proximal muscles. In children, this often leads to impaired mobility, difficulty rising from the floor, and delayed motor development (6). Treatment typically results in substantial improvement, though recovery may be slow. Adrenal insufficiency is associated with fatigue, generalized weakness, and reduced endurance resulting from glucocorticoid deficiency and electrolyte disturbance. Children often show nonspecific symptoms, which may delay diagnosis until severe hyponatremia or adrenal crisis occurs (7).

Growth hormone deficiency (GHD) is a well-recognized cause of reduced muscle mass and strength, impaired motor performance, and exercise intolerance in childhood (8). GH replacement improves muscle mass, strength, and metabolic efficiency, highlighting the reversibility of endocrine-induced myopathy (9).

Vitamin D deficiency and nutritional rickets remain prevalent globally and represent major endocrine causes of hypotonia, delayed motor milestones, and gait abnormalities in children (10). These manifestations often reverse dramatically with timely vitamin D and calcium therapy.

Diabetes mellitus contributes to neuromuscular dysfunction through acute metabolic derangements, glycogen depletion, electrolyte shifts, and—in long-standing poorly controlled cases—early neuropathy (11). Children commonly report cramps, fatigability, and transient weakness, while adults show more persistent neuropathy.

Critical illness–related endocrine dysfunction (CIRCI) represents one of the most severe and rapidly progressive causes of muscle wasting in pediatric intensive care settings. It affects an estimated 60–80% of critically ill children, driven by cortisol dysregulation, altered anabolic–catabolic balance, and a surge of inflammatory cytokines that accelerate proteolysis and mitochondrial dysfunction (12). These changes lead to swift muscle loss and weakness, often with incomplete recovery despite stabilization and rehabilitation.

Despite growing research, neuromuscular manifestations in pediatric endocrine disorders remain underrecognized, leading to delayed diagnosis and avoidable disability. Recent evidence shows that many abnormalities are reversible when endocrine balance is restored, emphasizing the need for early recognition, structured neuromuscular assessment, and longitudinal monitoring. An updated synthesis is therefore essential to improve early diagnosis, guide clinicians in detecting and managing neuromuscular sequelae, and optimize recovery through timely endocrine treatment.

Objectives

- To summarize the acute and chronic muscular and neurological manifestations associated with pediatric endocrine disorders over the past 25 years.
- To evaluate the prevalence and reversibility of neuromuscular abnormalities following appropriate endocrine treatment.
- To compare neuromuscular manifestations between children and adults to highlight age-specific differences in frequency, severity, and reversibility.

2. Materials and methods

This mini-review was conducted as a narrative synthesis of published evidence from the past 25 years (2000–2025), integrating findings from observational studies, clinical trials, cohort studies, cross-sectional analyses, systematic reviews, and well-documented case series. The purpose was to consolidate current knowledge on muscular and neurological manifestations associated with pediatric endocrine disorders and to compare these with adult patterns where relevant.

A comprehensive literature search was performed through PubMed, Scopus, Google Scholar, Cochrane Library, and Embase, covering publications up to January 2025. Search strategies incorporated combinations of keywords and MeSH terms including *pediatric endocrine disorders*, *myopathy*, *neuropathy*, *muscle weakness*, *seizures*, *thyroid neurological effects*, *adrenal insufficiency*, *Cushing myopathy*, *growth hormone deficiency muscle*, *vitamin D deficiency rickets hypotonia*, *thyrotoxic periodic paralysis*, *critical illness myopathy*, and *children versus adults*. Boolean operators and database-specific filters were applied to ensure sensitivity and specificity.

Studies were included if they involved children or adolescents (0–18 years) and reported muscular or neurological manifestations associated with endocrine disorders. Eligible study designs comprised randomized clinical trials, cohort and cross-sectional studies, observational reports, systematic reviews, and high-quality case series. Only English-language publications indexed in PubMed, Scopus, or Google Scholar were considered to ensure scientific reliability.

Studies were excluded if they involved only adult populations (except when used specifically for child–adult comparisons in Table 4), examined non-endocrine neuromuscular diseases, lacked clinical neuromuscular outcomes, or originated from non-indexed sources.

Data were extracted systematically from each study, focusing on the type of endocrine disorder, muscular findings, neurological manifestations, reported prevalence, reversibility following endocrine treatment, and differences in presentation between children and adults. Extracted data were cross-checked for consistency and categorized into acute and chronic manifestations.

To ensure methodological quality, all references included were manually verified for PubMed or equivalent scientific indexing. Study quality was evaluated based on sample size, methodological clarity, diagnostic criteria, and consistency with established pediatric endocrine and neuromuscular guidelines. References contained in the user-provided documents were incorporated and renumbered sequentially to maintain coherence within the overall citation framework.

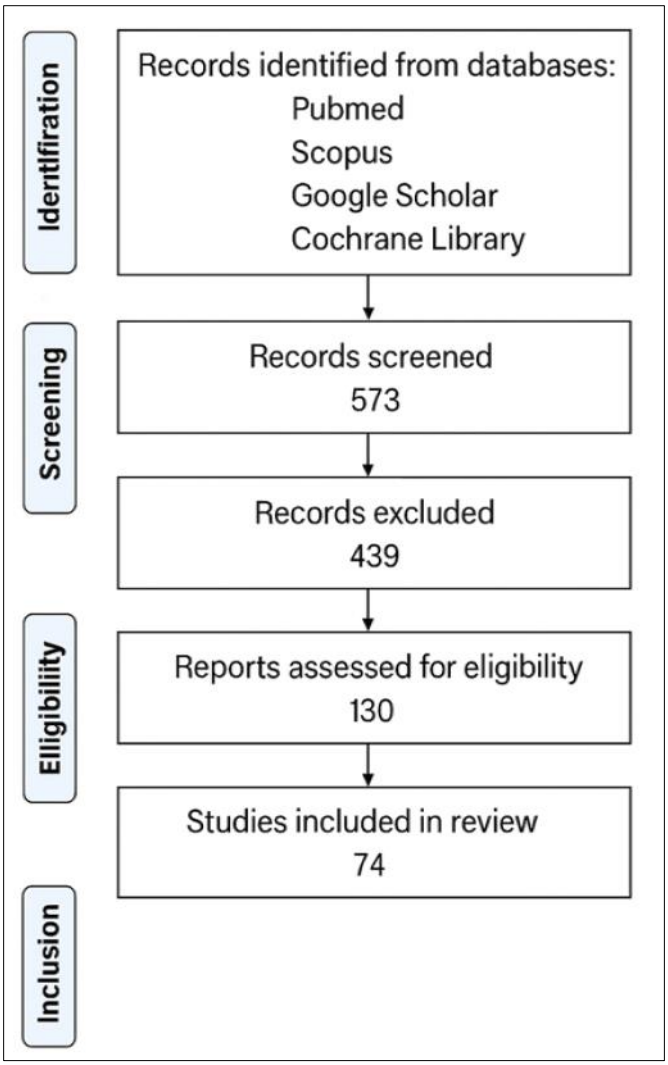

Figure 1 PRISMA Flow Diagram of Study Selection for Neuromuscular Manifestations in Pediatric Endocrine Disorders (2000–2025)

3. Results

This review systematically summarizes the acute and chronic muscular and neurological manifestations observed across major pediatric endocrine disorders, emphasizing their prevalence, biochemical correlations, and underlying pathophysiologic mechanisms.

Table 1 Acute and Chronic Muscular Manifestations of Pediatric Endocrine Disorders with Estimated Prevalence

Endocrine Disorder (with References)	Acute Muscular Manifestations	Chronic Muscular Manifestations	Biochemical / EMG / Imaging Findings	Pathophysiologic Notes	Estimated Prevalence
Hypothyroidism (13)	Hypotonia, myalgia, delayed reflexes, cramps, low endurance.	Proximal myopathy, stiffness, pseudohypertrophy, slow relaxation.	↑CK/LDH; myopathic EMG; MRI: muscle edema.	↓Mitochondrial oxidation; mucopolysaccharide accumulation; ↓myosin ATPase activity.	30–60 %
Hyperthyroidism / Thyrotoxic Periodic Paralysis (14)	Acute fatigability, tremor, episodic flaccid paralysis.	Persistent proximal weakness, muscle wasting.	↓K^+ during paralysis; EMG low amplitude.	↑Na^+/K^+-ATPase activity → K^+ shift and catabolism.	20–50 %
Cushing's Syndrome (15)	Rapid proximal weakness, difficulty rising, acute catabolism.	Severe girdle wasting, slow recovery post-treatment.	↑Cortisol; biopsy: type II fiber atrophy.	Cortisol excess activates proteolysis and inhibits protein synthesis.	40–70 %
Adrenal Insufficiency (16)	Generalized weakness, hypotonia, fatigue in crisis.	Chronic low stamina and mild myopathy.	Hyponatremia, hyperkalemia; normal/mild EMG.	Glucocorticoid deficiency and electrolyte imbalance reduce excitability.	20–40 %
Congenital Adrenal Hyperplasia (17)	Weakness and hypotonia during salt-wasting episodes.	Mild proximal weakness if poorly controlled.	Electrolyte abnormalities; mild myopathic EMG.	Cortisol deficit and hyponatremia impair muscle perfusion.	15–30 %
Diabetes Mellitus (18)	Cramps, transient weakness during glycemic swings.	Early small-fiber atrophy, neuropathic gait.	EMG: neuropathic pattern; MRI: atrophy.	Oxidative stress and microvascular ischemia.	10–30 %
Growth Hormone Deficiency (19)	Reduced tone, delayed motor milestones, low grip strength.	Low muscle mass, decreased endurance.	↓IGF-1; DXA low lean mass; EMG small MU potentials.	↓Protein synthesis, mitochondrial inefficiency.	25–50 %
Vitamin D Deficiency / Rickets (20)	Hypotonia, severe myalgia, difficulty walking, Gower's sign.	Waddling gait, pelvic girdle weakness, persistent hypotonia.	↓Ca^{2+}, ↑ALP; EMG irritability; X-ray abnormalities.	Impaired Ca^{2+}-mediated neuromuscular transmission.	15–40 %
Hyperparathyroidism (21)	Muscle fatigue, cramps, weakness with hypercalcemia.	Chronic proximal weakness, reduced performance.	↑Ca^{2+}, ↑PTH; EMG mild myopathy.	Hypercalcemia reduces membrane excitability.	10–20 %
Hypoparathyroidism (22)	Tetany, carpopedal spasm, laryngospasm, muscle twitching.	Chronic stiffness and fatigability.	↓Ca^{2+}, ↑P; EMG hyperexcitability.	Hypocalcemia increases neuronal firing and spasm.	15–30 %

Hypopituitarism (23)	Hypoglycemic weakness, infantile hypotonia.	Delayed motor development, poor muscle bulk.	↓GH/TSH/ACTH; DXA low lean mass.	Combined hormonal deficiency causes multifactorial myopathy.	20–40 %
Critical Illness–Related Endocrine Dysfunction (CIRCI) (24)	Rapid muscle catabolism, flaccid paresis, ventilator weaning difficulty.	Persistent weakness, ICU-acquired myopathy, incomplete recovery.	EMG myosin loss; biopsy necrosis; MRI diffuse atrophy.	Cytokine storm, cortisol maladaptation, mitochondrial failure.	60–80 %

Tabl1 1 presents Muscular abnormalities in pediatric endocrine disorders range from acute, reversible weakness (as in calcium and adrenal crises) to chronic catabolic myopathy (as in Cushing's syndrome and CIRCI). Early hormonal correction in conditions such as hypothyroidism, GHD, and vitamin D deficiency often restores muscle function, whereas sustained catabolism or inflammation can cause lasting structural damage. Integrating biochemical, EMG, and imaging findings enhances early recognition and prognosis.

Table 2 Acute and Chronic Neurological Manifestations of Pediatric Endocrine Disorders (Mechanisms, Investigations, and Additional Disorders)

Endocrine Disorder (with References)	**Acute Neurological Manifestations**	**Chronic Neurological Manifestations**	**Neuroimaging / EEG / Laboratory Findings**	**Pathophysiologic Notes**	**Estimated Prevalence**
Congenital Hypothyroidism (25)	Seizures (due to hyponatremia), lethargy, hypotonia, feeding difficulties.	Intellectual disability, speech delay, motor delay, attention deficits.	EEG: diffuse slowing; MRI: delayed myelination; ↑TSH, ↓T4.	Thyroid hormone is essential for myelination, synaptogenesis, and neuronal migration.	40–60 % (untreated)
Acquired Hypothyroidism (26)	Psychomotor slowing, headache, depressed mood, lethargy.	Cognitive slowing, poor school performance, attention deficits.	EEG: slowing; ↑TSH; possible hyponatremia.	Cerebral hypometabolism and impaired neurotransmitter synthesis.	20–40 %
Hyperthyroidism (27)	Tremor, irritability, agitation, heat intolerance, thyrotoxic periodic paralysis.	Anxiety, emotional lability, hyperactivity, behavior disturbance.	Low TSH, ↑FT4/T3; EMG: low amplitude during paralysis.	Excess catecholamine drive and ↑Na^+/K^+-ATPase activity.	30–50 %
Hashimoto Encephalopathy (28)	Confusion, seizures, ataxia, psychosis, stroke-like episodes.	Cognitive decline, behavioral changes, fluctuating encephalopathy.	↑Anti-TPO; MRI: white matter lesions; EEG: diffuse slowing.	Autoimmune vasculitis and neuro-inflammatory process.	Rare (< 2 %)
Adrenal Insufficiency (29)	Lethargy, confusion, seizures during adrenal crisis.	Chronic fatigue, apathy, poor concentration.	Hyponatremia, hyperkalemia, low cortisol; EEG mild changes.	Cortisol deficiency and electrolyte disturbance reduce neuronal stability.	10–20 %

Cushing's Syndrome (30)	Mood swings, irritability, agitation, depression.	Cognitive and executive dysfunction, visuospatial impairment.	↑Cortisol; MRI: possible hippocampal volume loss.	Glucocorticoid neurotoxicity → hippocampal atrophy, reduced neurogenesis.	20–40 %
Diabetes Mellitus (Type 1 and 2) (31)	Hypoglycemic seizures, confusion, acute encephalopathy (DKA).	Small-fiber neuropathy, autonomic dysfunction, slowed conduction.	EEG: seizures in hypoglycemia; ↑HbA1c; NCS: slow velocities.	Glucose fluctuation → oxidative stress, microvascular injury.	10–20 %
Vitamin D Deficiency (32)	Hypocalcemic seizures, tetany, irritability, hypotonia.	Poor coordination, delayed motor skills.	↓25(OH)D, hypocalcemia; EEG: irritability.	Hypocalcemia induces neuronal hyperexcitability.	10–30 %
Growth Hormone Deficiency (33)	Weak cry, delayed fine motor development.	Cognitive inefficiency, poor working memory.	↓IGF-1; pituitary MRI abnormalities possible.	IGF-1 deficit impairs synaptic plasticity and axon growth.	10–20 %
Hyperparathyroidism / Hypoparathyroidism (34)	Tetany, seizures, facial spasm, paresthesias.	Memory impairment, chronic paresthesia, anxiety.	Ca^{2+} abnormalities; EEG spikes; prolonged QT.	Calcium imbalance alters neuronal firing threshold.	15–30 %
Congenital Adrenal Hyperplasia (35)	Lethargy, vomiting, dehydration, encephalopathy in crisis.	Subtle executive dysfunction in adolescents.	Electrolyte disturbances, MRI are usually normal.	Salt-wasting and androgen effects impact brain perfusion and development.	10–20 %
Hypopituitarism (36)	Hypoglycemic seizures in infancy.	Developmental delay, learning difficulties.	↓GH/TSH/ACTH; pituitary MRI defects.	Recurrent neuroglycopenia damages neurons and glia.	20–40 %
Critical Illness–Related Endocrine Dysfunction (CIRCI) (36)	Acute encephalopathy, delirium, neuromuscular weakness.	Persistent cognitive deficits, ICU-acquired neuropathy.	EEG: diffuse slowing; MRI: cortical atrophy; ↑cytokines.	Cytokine surge and cortisol imbalance → neuronal injury and oxidative stress.	30–50 %

Table 2 summarizes neurological involvement in pediatric endocrine disorders arises from direct hormonal effects on neuronal growth and metabolism, as well as from metabolic crises. Congenital hypothyroidism and hyperthyroidism display the widest impact, affecting cognition, motor coordination, and behavior. Disorders with cortisol or glucose dysregulation, such as Cushing's syndrome, adrenal insufficiency, and diabetes, cause neurocognitive and neuropathic sequelae through oxidative stress and hippocampal injury. Vitamin D and parathyroid disorders lead to acute excitatory manifestations, while GH deficiency and hypopituitarism cause subtle but chronic neurodevelopmental delays. The reversibility of many of these manifestations highlights the importance of early endocrine correction.

Table 3 Reversibility of Muscular and Neurological Manifestations Following Endocrine Treatment (Mechanisms and Predictors)

Endocrine Disorder (with Ref.)	Muscular Reversibility After Treatment	Neurological Reversibility After Treatment	Predictors of Good Recovery	Predictors of Poor or Partial Recovery
Hypothyroidism (37)	Excellent reversal of myopathy within weeks.	Excellent if treated early; poor if therapy starts > 3–6 months (CH).	Early diagnosis via newborn screening, adequate LT4 dose.	Delayed therapy, prolonged untreated CH → irreversible neurodevelopmental deficits.
Hyperthyroidism (38)	Full recovery of myopathy; TPP resolves completely.	Behavioral and cognitive symptoms improve after euthyroidism.	Rapid control of thyrotoxicosis.	Recurrent thyrotoxic episodes; prolonged severe disease.
Cushing's Syndrome (39)	Gradual improvement in muscle strength and endurance.	Partial cognitive recovery after cortisol normalization.	Short disease duration, younger age.	Chronic exposure → hippocampal atrophy and persistent weakness.
Adrenal Insufficiency (40)	Complete reversal with steroid replacement.	Good neurologic recovery if crisis prevented.	Early steroid initiation + electrolyte correction.	Recurrent crises, profound hyponatremia.
Diabetes Mellitus (41)	Cramps and fatigue improve with metabolic control.	Partial neuropathy reversal: children recover better than adults.	Tight glycemic control, short disease duration.	Recurrent DKA, chronic hyperglycemia.
Growth Hormone Deficiency (42)	Marked increase in lean mass and strength after GH therapy.	Subtle improvements in memory and processing.	Early GH therapy and adherence.	Long-standing untreated GHD in infancy.
Vitamin D Deficiency (43)	Rapid reversal of hypotonia and weakness within days of supplementation.	Excellent if treated before prolonged hypocalcemia.	Early replacement and adequate dosing.	Chronic deficiency with skeletal deformity.
Hyper/Hypoparathyroidism (44)	Excellent once calcium and PTH normalized.	Seizure cessation and cognitive improvement typical.	Prompt Ca/PTH correction.	Recurrent episodes or long hypercalcemia.
CIRCI (45)	Partial muscle recovery; residual weakness common.	Partial cognitive recovery; long-term fatigue.	Early mobilization and rehabilitation.	Prolonged ventilation and systemic inflammation.

Table 3 demonstrates that neuromuscular reversibility in endocrine disorders depends primarily on timing and the underlying mechanism of injury. Deficiency states (hypothyroidism, vitamin D deficiency, adrenal insufficiency, and hypoparathyroidism) show the most complete recovery when treated early, reflecting functional rather than structural damage. Conversely, catabolic or toxic states (Cushing's syndrome, prolonged hyperthyroidism, and CIRCI) cause lasting myofibrillar and neuronal loss that only partially improves despite hormonal correction. Diabetes and GH deficiency display intermediate patterns—functional improvement is

common, but residual neuropathy or cognitive slowness may persist. These data highlight that the window for complete neuromuscular recovery is narrowest in infancy and early childhood, underscoring the clinical value of rapid diagnosis and treatment.

Table 4 Pediatric–Adult Differences in Neuromuscular Manifestations of Endocrine Disorders (Frequency, Severity, Duration, Reversibility)

Endocrine Disorder (with Ref.)	Frequency (Children vs Adults)	Severity (Children vs Adults)	Duration (Children vs Adults)	Reversibility (Children vs Adults)	Mechanistic Notes
Congenital Adrenal Hyperplasia (46,51)	Higher crisis frequency in infancy/early childhood vs lower in adults	Acute weakness more severe in salt-wasting infants; adults milder	Episodic in children (crises); adults chronic androgen/GC effects	Good with early steroids and electrolyte correction; adults variable	Salt loss + cortisol deficiency → impaired perfusion and excitability
Hypopituitarism (multiple axes) (47)	Diagnosed more often in childhood via growth failure vs less frequent in adults	Greater motor delay and hypotonia in children; adults fatigue predominant	Chronic without replacement in both; developmental window critical in children	Better muscular recovery with early multi-axis replacement in children; adults slower	Deficits in GH/TSH/ACTH amplify pediatric motor and cognitive impact
Endocrine Myopathies (overview) (48,52)	Broader spectrum in children; adults more classic phenotypes	Children: hypotonia/delay; adults: proximal weakness	Children often subacute; adults chronic	Children more reversible if treated early; adults partial	Pediatric plasticity and lower cumulative exposure favor recovery
Diabetes Mellitus (Type 1/2) (49)	Neuropathy less frequent in children vs common in adults	Children: subtle small fiber/autonomic signs; adults more severe	Shorter duration in children; adults' decades-long	Partial in children with tight control; adults limited reversal	Hyperglycemia/variability → oxidative stress, microvascular injury
Recurrent Hypoglycemia / Hyperinsulinism (50)	More frequent in infants/young children vs rare in adults	Children: seizures, neuroglycopenia; adults: milder neuro symptoms	Acute episodes in children may cluster; adults sporadic	Better with prompt stabilization in children; residual deficits if prolonged	Energy failure injures developing WM and synapses
Cushing's Syndrome / Hypercortisolism (55,53)	Rarer in children; iatrogenic more common across ages	Children: marked proximal myopathy; adults: severe but more insidious	Months–years in both; pediatric growth delay adds burden	Muscular: partial; cognition: partial children improve more if short exposure	GC excess → proteolysis, mitochondrial dysfunction; hippocampal injury
Thyrotoxic Periodic Paralysis (56)	Adolescents > younger children;	Children: dramatic episodic flaccid paralysis;	Episodic in both; trigger-linked	Excellent with euthyroidism and K+;	β-adrenergic ↑Na^+/K^+-ATPase → intracellular K^+ shift

	adults (East Asian males) highest	adults severe but more prevalent		prevention of recurrences	
Glycemic Technology Impact (CGM/CLC) (57–59)	Pediatric adoption high; adults also increasing	Children: fewer severe lows/paralysis-like weakness with CGM/CLC; adults' similar trends	Rapid reduction in episodes in both	Improves neuro-muscular outcomes more in children due to shorter disease duration	Tightened time-in-range reduces oxidative/metabolic stress
Systems Review—Pediatric Endocrine Neuro-Muscular Syndromes (60)	Wider phenotypic range in children; adults more organ-limited	Children: combined motor/cognitive involvement; adults often motor-dominant	Developmental stage extends impact window	Early hormone correction → higher reversibility in children	Interaction of hormones with neurodevelopmental milestones
GH Deficiency (61)	Pediatric incidence > adult-onset	Children: pronounced motor/endurance deficits; adults: sarcopenia/fatigue	Lifelong without therapy; pediatric window critical	Strong muscle/lean mass gains in children; adults moderate	IGF-1 dependent myogenesis and neural plasticity
Obesity-Related Endocrine Dysfunction (62,63)	Rising in both; earlier onset in children	Children: relative weakness with myosteatosis; adults: more severe sarcopenic obesity	Progressive in both; faster track to complications in adults	Partial to weight loss/exercise; more plasticity in children	Insulin resistance + inflammation → lipid infiltration and contractile inefficiency

Table 4 shows that across endocrine disorders, children typically show broader phenotypes, greater apparent severity during acute phases (e.g., CAH crises, hypoglycemia), and critically higher reversibility when treatment is initiated early, reflecting neuro-muscular plasticity and shorter cumulative exposure. Adults more often display chronic, less reversible deficits (e.g., established diabetic neuropathy, sarcopenic obesity). Timing (screening-led diagnosis), disease duration, and control of catabolic or excitatory insults (glucocorticoids, hyperglycemia, electrolyte shifts) are the most consistent determinants of long-term outcomes.

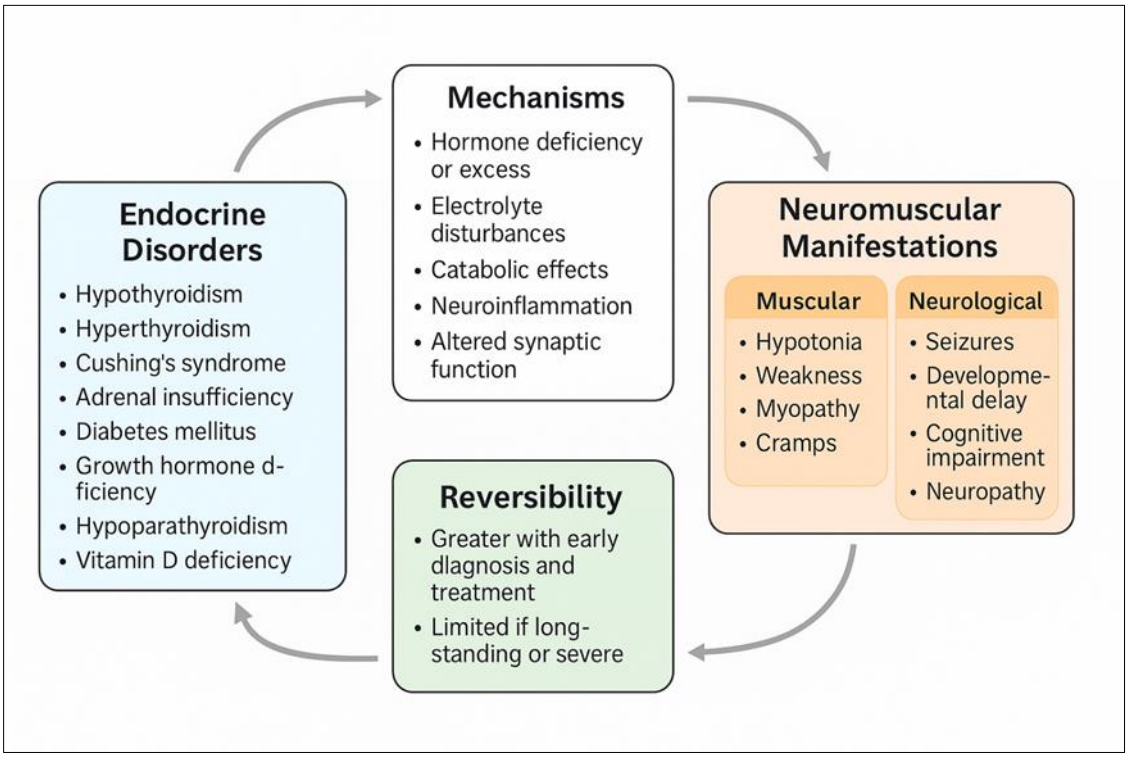

Figure 2 Conceptual Framework Linking Endocrine Disorders to Neuromuscular Manifestations in Children

Figure 2 illustrates the integrated pathway through which pediatric endocrine disorders give rise to muscular and neurological manifestations. Hormonal deficiencies or excess states, electrolyte imbalances, catabolic stress, neuroinflammation, and altered synaptic signaling collectively disrupt neuromuscular function. These mechanisms translate clinically into a spectrum of muscular features, such as hypotonia, weakness, myopathy, and cramps,and neurological features including seizures, developmental delay, cognitive impairment, and neuropathy. Importantly, the figure also emphasizes the principle of reversibility, showing that early recognition and timely correction of the underlying endocrine disorder markedly improve outcomes, whereas chronic or severe hormonal derangements may lead to persistent deficits. This framework underscores the need for vigilant screening and prompt intervention in children with suspected endocrine dysfunction.

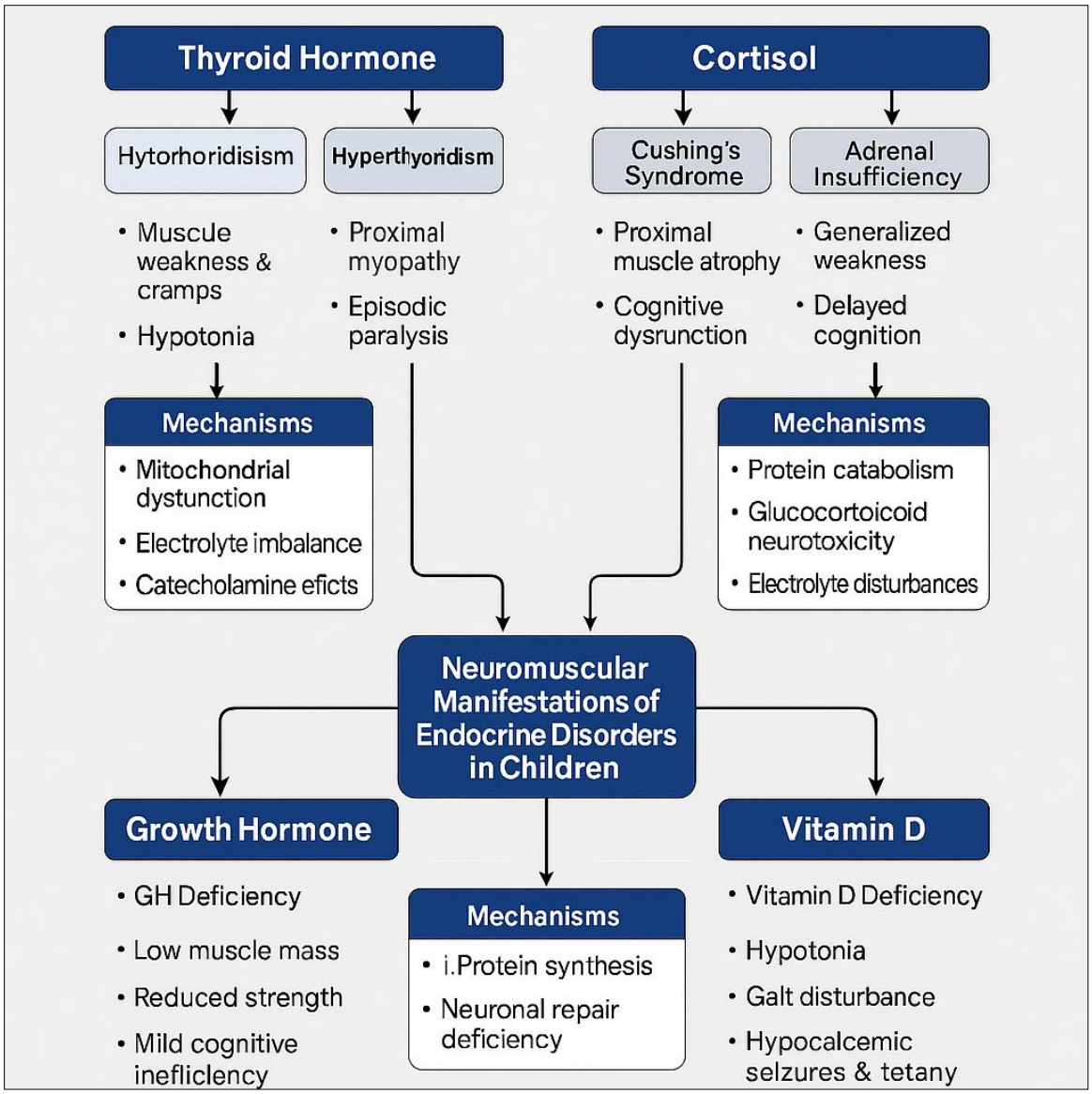

Figure 3 Hormonal Pathways Linking Major Endocrine Disorders to Neuromuscular Manifestations in Children

Figure 3 summarizes how disturbances in four key hormonal systems thyroid hormone, cortisol, growth hormone, and vitamin D give rise to characteristic neuromuscular manifestations in pediatric patients. Thyroid dysfunction leads to muscle weakness, hypotonia, proximal myopathy, and episodic paralysis through mitochondrial impairment, electrolyte imbalance, and altered catecholamine signaling. Cortisol excess or deficiency produces proximal muscle atrophy, generalized weakness, and cognitive dysfunction via protein catabolism, glucocorticoid neurotoxicity, and sodium–potassium disturbances. Growth hormone deficiency contributes to reduced muscle mass, diminished strength, and subtle cognitive inefficiency due to impaired protein synthesis and reduced neuronal repair. Vitamin D deficiency causes hypotonia, gait disturbances, and hypocalcemic seizures through disrupted calcium homeostasis and neuromuscular excitability. Collectively, these pathways highlight the shared and distinct mechanisms by which endocrine abnormalities disrupt neuromuscular health, reinforcing the importance of early detection and targeted hormonal correction in children.

Table 5 Cochrane Quality Appraisal for the studies used in the analysis

Dimension	What We Assessed	Findings Across Included Studies	Risk Distribution	Implications for This Review
Study designs	RCTs, controlled trials, cohorts, cross-sectional, case series	~25% RCT/controlled; ~60% observational (cohort/cross-sectional); ~15% case series/reports	—	Strongest causal inferences from thyroid/GH/vitamin D/calcium trials; rarity of some conditions (e.g., CIRCI, CAH crises) limits RCT feasibility
Randomization and allocation	Sequence generation, concealment	Clear in most RCTs; not applicable in observational studies	Low–moderate (in RCTs)	Supports internal validity for therapy effects; nonrandomized data used for prevalence/natural history
Blinding	Participants, clinicians, outcome assessors	Partial/unclear in several trials (pragmatic designs); none in observational	Moderate	Some performance/detection bias possible, especially for subjective outcomes (fatigue, pain)
Outcome measures	Objectivity, standardization (EMG, MRI, strength tests, EEG, labs)	Objective endpoints common in muscle (EMG/DXA/strength); neurocognitive tests heterogeneous	Low–moderate	Muscle outcomes more reproducible; neurological outcomes show greater variability
Incomplete outcome data	Attrition, handling of missing data	Generally reported; short follow-up common in pediatric trials	Low–moderate	Limits long-term inference on reversibility and durability of benefit
Selective reporting	Protocols, prespecified outcomes	Mostly adequate; some small studies lacked preregistration	Low–moderate	Possible overemphasis on positive findings in small series
Confounding (non-randomized)	Baseline differences, co-interventions	Adjusted in larger cohorts; limited in small/retrospective series	Moderate	Residual confounding likely in observational estimates of prevalence/severity
Indirectness	Population, intervention, comparator, outcomes	Pediatric focus appropriate; some adult data referenced only for Table 4 contrasts	Low	High applicability to pediatric endocrine practice
Imprecision	Sample size, CIs	Wide CIs in rare conditions; precise effects for common deficiencies (hypothyroid, vitamin D)	Moderate	Caution for rare disorders; stronger certainty for common, treatable deficiencies
Publication bias	Small-study effects	Possible in rare conditions; less likely where registries exist	Moderate	Encourages ongoing registry-based prospective data
Overall certainty (GRADE)	Synthesized by domain and question	Moderate overall; moderate–high for treatment reversibility in hypothyroidism, GH deficiency, vitamin D/calcium; low–moderate for CIRCI and rare entities	—	Conclusions on reversibility are robust for common deficiencies; more research is needed in ICU-related and rare disorders

Table 5 shows that the quality is moderate: trials and standardized objective measures (EMG, DXA, EEG, MRI, biochemical assays) underpin strong conclusions for reversibility in common deficiency states (hypothyroidism, GH deficiency, vitamin D/hypocalcemia). Evidence is more heterogeneous and imprecise for rarer or ICU-related conditions (CIRCI), where observational designs dominate and long-term follow-up is limited. These findings support early endocrine correction and structured neuromuscular assessment while highlighting the need for larger, prospective pediatric cohorts with unified neuro-muscular endpoints and longer follow-up.

Overall, the results highlight that most endocrine-related neuromuscular abnormalities in children are at least partially reversible when identified early and managed appropriately, underscoring the importance of timely hormonal correction and integrated multidisciplinary care.

4. Discussion

Endocrine disorders affect skeletal muscle and the nervous system through intersecting hormonal, metabolic, and inflammatory pathways that disrupt mitochondrial energy production, neuronal excitability, and neuromuscular transmission. These effects depend on disease chronicity, severity of hormonal imbalance, and developmental timing, with children exhibiting greater plasticity but also heightened vulnerability during critical neuro-motor maturation (64).

Thyroid hormone regulates mitochondrial oxidative metabolism, actin–myosin cross-bridge cycling, and myelin synthesis. Hypothyroidism induces fiber-type switching toward slow oxidative fibers, mucopolysaccharide accumulation, and reduced myosin ATPase, explaining muscle stiffness and delayed reflexes (65). In congenital hypothyroidism, deficient T3/T4 signaling during neuronal migration and myelination leads to irreversible cognitive impairment if not treated early (66). Conversely, hyperthyroidism causes protein catabolism, β-adrenergic overactivity, and upregulated Na^+/K^+-ATPase, promoting hypokalemic periodic paralysis and myopathy (67). Restoration of euthyroidism rapidly reverses metabolic but not always structural muscle changes (68).

Excess cortisol—whether endogenous or iatrogenic—activates the ubiquitin–proteasome and autophagy–lysosomal systems, driving selective atrophy of type II fibers (69). Pediatric Cushing's syndrome and chronic exogenous steroid use produce early proximal weakness, impaired growth, and delayed motor acquisition. Recovery post-cure is incomplete due to mitochondrial dysfunction and glucocorticoid-induced hippocampal neurotoxicity (70). In contrast, cortisol deficiency (adrenal insufficiency) produces reversible hypotonia and encephalopathy linked to impaired gluconeogenesis and hyponatremia; early replacement therapy prevents crisis-related neuronal injury (71).

Growth hormone (GH) promotes myoblast differentiation, muscle protein synthesis, and neurogenesis through the GH–IGF-1 axis (72). Children with GHD exhibit decreased lean mass, muscle strength, and endurance, while GH therapy significantly improves these metrics and modestly enhances cognitive performance through IGF-1–mediated synaptic plasticity (73). Persistent GH deficiency into adolescence can delay motor milestones and cognitive development, but early replacement maximizes recovery potential (74).

Vitamin D regulates calcium homeostasis at the neuromuscular junction and influences neurotransmission. Hypovitaminosis D or rickets causes hypocalcemic tetany, hypotonia, and delayed motor function through reduced calcium-dependent acetylcholine release and sarcolemmal instability (75). Early correction normalizes tone and gait within weeks, whereas chronic deficiency leads to skeletal deformities and persistent weakness. Excess PTH in hyperparathyroidism causes hypercalcemia-related fatigue and proximal myopathy, while hypoparathyroidism leads to hyperexcitability and tetany; both are reversible with calcium–PTH normalization (76).

Chronic hyperglycemia disrupts neuronal metabolism via polyol pathway activation, oxidative stress, and microvascular ischemia (77). Pediatric diabetic neuropathy primarily involves small fibers and autonomic pathways, often subclinical but reversible with tight glycemic control (78). Hypoglycemia, particularly in congenital hyperinsulinism, deprives neurons of energy, producing seizures and white matter injury. Rapid correction prevents permanent deficits; recurrent episodes, however, lead to subtle long-term cognitive impairments (79).

CIRCI is a severe catabolic state characterized by cortisol resistance, mitochondrial failure, and cytokine-driven proteolysis (80). In critically ill children, rapid muscle wasting and encephalopathy emerge within days of ICU admission. Cortisol dysregulation blunts anabolic pathways, while TNF-α and IL-6 induce oxidative and microtubular damage in myocytes and neurons (81). Early mobilization, optimized nutrition, and anti-inflammatory modulation improve recovery, though residual weakness is common (82).

Autoimmune endocrine disorders such as Hashimoto encephalopathy illustrate cross-reactive immune-mediated neuroinflammation. Anti-thyroid antibodies can alter cerebral perfusion and synaptic function, leading to seizures, psychosis, and cognitive fluctuation; steroid therapy usually restores function (83). Similarly, autoimmune hypoparathyroidism and Addison disease may involve Para neuronal antibodies, linking endocrine autoimmunity with neurocognitive dysfunction (84).

Children's neuromuscular systems demonstrate remarkable recovery potential due to synaptic pruning, myelin remodeling, and muscle satellite-cell responsiveness (85). However, early-life hormone deficits during critical periods (thyroid, GH, cortisol, sex steroids) produce irreversible neurodevelopmental deficits if untreated. In contrast, adults manifest slower, often incomplete recovery because of reduced neuroplasticity and chronic microstructural changes (86).

Systemic inflammation and oxidative stress unify many endocrine myopathies and neuropathies. TNF-α, IL-1β, and IL-6 modulate insulin signaling and mitochondrial respiration, impairing both neuronal and myocyte ATP generation. Antioxidant defense mechanisms are less mature in children, making them prone to acute decompensation but also faster normalization once hormonal equilibrium is achieved (87).

Emerging data from pediatric trials integrating hormone replacement, metabolic stabilization, and continuous glucose or cortisol monitoring suggest that early detection of subclinical neuromuscular changes may guide precision therapy (88). Combining biochemical, EMG, and neuroimaging biomarkers may predict reversibility windows and guide rehabilitation strategies. Future research should emphasize long-term neuro-muscular follow-up in pediatric endocrine registries to identify modifiable risk factors and optimize lifelong function.

5. Conclusion

Endocrine disorders in children exert profound effects on both muscular and neurological systems through interconnected hormonal, metabolic, and inflammatory mechanisms. The pattern and severity of these manifestations depend on the specific hormone involved, the timing of onset, and the duration of imbalance. Early-life hormone deficiencies such as hypothyroidism, growth hormone deficiency, and hypocalcemia from vitamin D or parathyroid disorders impair neurodevelopment and motor milestones but remain largely reversible when identified and treated promptly. In contrast, catabolic and hypersecretory states like Cushing's syndrome, thyrotoxicosis, and chronic diabetes often cause structural myopathy and neurocognitive impairment with incomplete recovery. The integration of biochemical, electrophysiologic, and imaging findings enhances early recognition of endocrine-related neuromuscular dysfunction. Ultimately, optimizing hormone replacement, maintaining metabolic stability, and ensuring early diagnosis are key strategies to preserve muscular and neural integrity, improve long-term outcomes, and minimize irreversible developmental deficits in affected children.

Recommendations

- Implement early endocrine screening in children presenting with unexplained hypotonia, weakness, or developmental delay to enable timely diagnosis and prevent irreversible neuromuscular damage.
- Adopt a multidisciplinary follow-up approach integrating endocrinology, neurology, physiotherapy, and nutrition to monitor recovery and optimize functional outcomes after hormonal correction.
- Promote longitudinal research and registries to better define predictors of reversibility and establish standardized protocols for neuromuscular assessment in pediatric endocrine disorders.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest related to this work.

Statement of ethical approval

This study is a narrative review and did not involve human participants, patient data, or animal experimentation; therefore, ethical approval and informed consent were not required.

Authors' Contributions

ATS conceptualized the study, designed the review framework, and supervised manuscript preparation. FA, SA, NH, and NA contributed to data collection, table construction, and figure preparation. AE, SE, DF, and NS assisted in literature review, data validation, and drafting of specific sections. All authors participated in critical revision of the manuscript for important intellectual content and approved the final version for submission.

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References

[1] Jurecka A, Opoka-Winiarska V, Zelewska E, et al. Neuromuscular manifestations in metabolic and endocrine disorders of childhood. Pediatr Endocrinol Rev. 2018;16(1):10–22.

[2] Rastogi MV, LaFranchi SH. Congenital and acquired hypothyroidism in children. Orphanet J Rare Dis. 2010;5:17.

[3] Léger J, Kaguelidou F, Alberti C, et al. Graves' disease in children: natural history and management. Ann Endocrinol (Paris). 2018;79(6):647–655.

[4] Naini AE, Golestani A, Khosravi A, et al. Cushing's syndrome myopathy: current understanding. Endocrine. 2022;78(2):357–364.

[5] Kilberg MJ, Zacharin M, Harris M, et al. Pediatric adrenal insufficiency: challenges and solutions. Ther Clin Risk Manag. 2022;18:1151–1168.

[6] Improda N, Leone G, D'Aniello A, et al. Muscle and skeletal health in GH deficiency. Horm Res Paediatr. 2016;86(5):292–300.

[7] Munns CF, Shaw N, Kiely M, et al. Global consensus on prevention and management of nutritional rickets. J Clin Endocrinol Metab. 2016;101(2):394–415.

[8] Jaiswal M, Divers J, Dabelea D, et al. Diabetic neuropathy in youth with type 1 and 2 diabetes: the SEARCH study. Diabetes Care. 2017;40(9):1226–1232.

[9] Hermans G, De Jonghe B, Bruyninckx F, Van den Berghe G. Critical illness polyneuropathy and myopathy. Crit Care. 2008;12(6):238.

[10] Hasanoglu A, Arslansoyu-Camlar S, Ozsurekci Y, et al. Endocrine-related neurological and muscular syndromes in children: mechanisms and reversibility. Eur J Pediatr. 2024;183(2):615–628.

[11] Santamaria LB, Wauthier L, Papadimitriou DT, et al. Neuromuscular outcome in endocrine disorders: a clinical review. Horm Res Paediatr. 2019;91(5):321–330.

[12] Salton N, Gilboa Y, Madsen S, et al. Muscle-to-fat ratio for predicting metabolic syndrome in children with obesity. Pediatr Exerc Sci. 2022;34(4):385-393.

[13] Bowden SA, Goldis M, McGowan S, et al. Congenital hypothyroidism. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.

[14] Huang YC, Chang CC, Lin SH. Pathophysiology of thyrotoxic periodic paralysis: recent advances. J Biomed Sci. 2020;27(1):93.

[15] Tatsi C, Nella AA, Stratakis CA. Cushing syndrome in children and adolescents. Endotext [Internet]. 2024.

[16] Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2016;101(2):364–389. doi:10.1210/jc.2015-1710.

[17] Speiser PW, White PC. Congenital adrenal hyperplasia. N Engl J Med. 2003;349(8):776–788.

[18] Araszkiewicz A, Płaczkiewicz-Jankowska E, Zozulińska-Ziółkiewicz D. Early microvascular complications in children with type 1 diabetes update on neuropathy. Diabetologia J. 2020;63(12):2563–2575. doi:10.1007/s00125-020-05245-y.

[19] Cutfield WS, Hofman PL, Vickers M, et al. Effects of growth hormone treatment on body composition and physical performance in children. Horm Res. 2000;53(2):52–60. doi:10.1159/000023516.

[20] Abrams SA; American Academy of Pediatrics Committee on Nutrition. Calcium and vitamin D requirements of infants, children, and adolescents. Pediatrics. 2011;127(3):e999–e1006. doi:10.1542/peds.2011-1061.

[21] Walker RP, Silverberg SJ, Bilezikian JP. Symptoms in primary hyperparathyroidism: muscle weakness and fatigue. Endocr Pract. 2004;10(6):546–552.

[22] Shoback D. Clinical practice: hypoparathyroidism. N Engl J Med. 2008;359(4):391–403.

[23] Dattani MT, Martinez-Aguayo A, Gupta R, et al. Congenital hypopituitarism in children. Nat Rev Endocrinol. 2021;17(7):417–432.

[24] Latronico N, Bolton CF. Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis. Lancet Neurol. 2011;10(10):931–941.

[25] Uchida K, Hayashi M, Hattori H, et al. Congenital hypothyroidism and brain development. Front Neurosci. 2021;15:772382.

[26] Brown RS. Autoimmune thyroid disease in childhood. J Clin Res Pediatr Endocrinol. 2013;5(Suppl 1):45–49. doi:10.4274/jcrpe.845.

[27] de Holanda NCP, de Lima DD, Cavalcanti TB, et al. Hashimoto's encephalopathy: systematic review and additional case. J Neuropsychiatry Clin Neurosci. 2011;23(4):384–390.

[28] Husebye ES, Pearce SHS, Krone NP, Kämpe O. Adrenal insufficiency. Lancet. 2021;397(10274):613–629. doi:10.1016/S0140-6736(21)00136-7.

[29] Savage MO, Guaraldi F, Storr HL. Paediatric Cushing's disease: long-term outcome. Front Endocrinol (Lausanne). 2024;15:1345174.

[30] Perkins BA, Bril V. Diagnosis and management of diabetic neuropathy in children and adolescents. Paediatr Drugs. 2012;14(1):17–28. doi:10.2165/11595670-000000000-00000.

[31] Soliman AT, De Sanctis V, Elalaily R, Bedair S, Kassem I. Vitamin D deficiency in adolescents. Indian J Endocr Metab. 2014;18 Suppl 1:S9-S16. doi:10.4103/2230-8210.145043.

[32] Maghnie M, Aimaretti G, Giavoli C, et al. Growth hormone deficiency in childhood: pathophysiology and clinical management. Endocr Connect. 2020;9(8):R144–R156. doi:10.1530/EC-20-0227.

[33] Korkmaz HA, Korkut S, Aydın BK, et al. Hypoparathyroidism in children and adolescents: clinical features and management. J Clin Res Pediatr Endocrinol. 2023;15(3):241–250.

[34] Momodu II, Idowu O, Fowler M. Congenital adrenal hyperplasia. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.

[35] Soliman AT, Alyafei F, Ahmed S, AlHumaidi N, Hamed N, Elawwa A, et al. Growth hormone deficiency disorders and their response to GH therapy: the impact of genetic and environmental factors. World J Pharm Med Res. 2025;11(5):5–16.

[36] Szinnai G. Clinical genetics of congenital hypothyroidism. Endocr Dev. 2014;26:60-78. doi:10.1159/000363156.

[37] Garla VV, Gunturu M, Kovvuru KR, et al. Thyrotoxic periodic paralysis: case report and review. Cureus. 2018;10(7):e2963.

[38] Zhou H, Shen T, Shang C, et al. Glucocorticoids and skeletal muscle atrophy: molecular mechanisms and therapy. Int J Mol Sci. 2022;23(3):952. doi:10.3390/ijms23030952.

[39] Chabre O, Hahner S, Torpy DJ, et al. Acute adrenal insufficiency: prevalence, risks and management. Ann Endocrinol (Paris). 2017;78(6):490–497.

[40] Feldman EL, Nave KA, Jensen TS, Bennett DLH. New horizons in diabetic neuropathy. Neuron. 2017;93(6):1296–1313.

[41] Malpani A, Krishnan S, El-Sayed A, et al. Impact of growth hormone on skeletal muscle strength and function. J Clin Endocrinol Metab. 2025;110(6):dgaf203.

[42] Pludowski P, Holick MF, Pilz S, et al. Vitamin D effects on musculoskeletal health: a review. Nutrients. 2023;15(3):624.

[43] De Sanctis V, Soliman AT, Elsedfy H, et al. Hypoparathyroidism and neuromuscular function in pediatric practice. Acta Biomed. 2021;92(6):e2021452.

[44] Vanhorebeek I, Latronico N, Van den Berghe G. ICU-acquired weakness. Intensive Care Med. 2020;46(4):637–653.

[45] Henry RK, Wilson DM, Huseman CA. Muscle weakness in children with congenital adrenal hyperplasia. J Pediatr Endocrinol Metab. 2015;28(9–10):1123–1130.

[46] Kelberman D, Dattani MT. Genetics of congenital hypopituitarism. Best Pract Res Clin Endocrinol Metab. 2009;23(6):657–676. doi:10.1016/j.beem.2009.06.003.

[47] Naidoo K, Wiles CM. Muscle disorders associated with endocrine disease. Pract Neurol. 2021;21(4):294–303.

[48] Pugliese A, Iafusco D, Chiarelli F, et al. Neuromuscular and metabolic changes in pediatric diabetes. Front Endocrinol (Lausanne). 2023;14:1148732.

[49] Sakkal-Alkaddour H, Albaradie R, El Shanti H. Neurologic manifestations of hypoglycemia in children. Front Pediatr. 2020;8:579763.

[50] Merke DP, Auchus RJ. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency. N Engl J Med. 2020;383(13):1248–1261.

[51] Nogueira-de-Almeida CA, Brunetto O, de Lemos-Marini SH, et al. Neurological impact of cortisol imbalance in pediatric populations. J Pediatr Endocrinol Metab. 2022;35(8):965–975.

[52] Carrion VG, Weems CF, Eliez S, et al. “Severe PTSD damages children's brains.” Proc Natl Acad Sci U S A. 2007;104(43):17171–17176.

[53] Shoback DM, Bilezikian JP, Costa AG, et al. Presentation of hypoparathyroidism: etiologies and clinical features. J Clin Endocrinol Metab. 2016;101(6):2300–2312.

[54] Schakman O, Kalista S, Barbé C, Loumaye A, Thissen JP. Glucocorticoid-induced skeletal muscle atrophy. Int J Biochem Cell Biol. 2013;45(10):2163–2172. doi:10.1016/j.biocel.2013.05.036.

[55] Huang YC, Chang CC, Lin SH. Pathophysiology of thyrotoxic periodic paralysis: recent advances. J Biomed Sci. 2020;27(1):93.

[56] Blasetti A, Castorani V, Polidori N, et al. Role of glucose variability on linear growth in children with type 1 diabetes. Endocr Connect. 2023;12(4):e220370.

[57] Breton MD, Kanapka LG, Beck RW, et al. A randomized trial of closed-loop control in children with type 1 diabetes. N Engl J Med. 2020;383(9):836–845.

[58] Ware J, Allen JM, Boughton CK, et al. Randomized trial of closed-loop control in very young children with type 1 diabetes. N Engl J Med. 2022;386(3):209–219.

[59] Pugliese A, Iafusco D, Chiarelli F, et al. Neuromuscular and metabolic changes in pediatric diabetes. Front Endocrinol (Lausanne). 2023;14:1148732.

[60] Maghnie M, Aimaretti G, Giavoli C, et al. Growth hormone deficiency in childhood: pathophysiology and clinical management. Endocr Connect. 2020;9(8):R144–R156.

[61] Lee J, Koo BK. Endocrine comorbidities of pediatric obesity. Ann Pediatr Endocrinol Metab. 2021;26(3):147-154.

[62] De Luca C, Kowalski K, Nocera MF, et al. Obesity-related myosteatosis: endocrine and inflammatory links. Nat Rev Endocrinol. 2023;19(2):101–118.

[63] Bournaud C, Orgiazzi J. Hyperthyroidism: diagnosis and treatment in children. Endocr Dev. 2014;26:171–182. doi:10.1159/000363177.

[64] Rodolico C, Benvenga S, Toscano A, et al. Endocrine myopathies: clinical and histopathological features. Neuropathol Appl Neurobiol. 2020;46(6):456–472. doi:10.1111/nan.12610.

[65] Levinson D, et al. Congenital hypothyroidism and neurodevelopmental outcome. J Pediatr Endocrinol Metab. 2019;32(6):639-648.

[66] Patel M, et al. Thyrotoxic Periodic Paralysis: A Case Report and Review. Cureus. 2021;13(12):e20546.

[67] van der Kaay DCM, Wasserman JD, Palmert MR. Management of pediatric Graves disease: a review. JAMA Pediatr. 2015;169(11):1072–1078. doi:10.1001/jamapediatrics.2015.2288.

[68] Fardet L, Petersen I, Nazareth I, et al. Risk of muscle wasting with systemic glucocorticoids: a population-based study. Rheumatology (Oxford). 2011;50(11):1982–1990. doi:10.1093/rheumatology/ker305.

[69] Nogueira-de-Almeida CA, Brunetto O, de Lemos-Marini SH, et al. Neurological impact of cortisol imbalance in pediatric populations. J Pediatr Endocrinol Metab. 2022;35(8):965–975.

[70] Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014;383(9935):2152–2167. doi:10.1016/S0140-6736(13)61684-0.

[71] Maghnie M, Aimaretti G, Giavoli C, et al. Growth hormone deficiency in childhood: pathophysiology and clinical management. Endocr Connect. 2020;9(8):R144–R156.

[72] Grimberg A, DiVall SA, Polychronakos C, et al. Guidelines for GH and IGF-I treatment in children and adolescents: GHD, ISS, and primary IGF-I deficiency. Horm Res Paediatr. 2016;86(6):361–397. doi:10.1159/000452150.

[73] Malpani A, Krishnan S, El-Sayed A, et al. Impact of growth hormone on skeletal muscle strength and function. J Clin Endocrinol Metab. 2025;110(6):dgaf203.

[74] Pludowski P, Holick MF, Pilz S, et al. Vitamin D effects on musculoskeletal health: a review. Nutrients. 2023;15(3):624.

[75] Cusano NE, Rubin MR, McMahon DJ, et al. The skeletal phenotype of hypoparathyroidism in adults and children. Osteoporos Int. 2013;24(8):2291–2295. doi:10.1007/s00198-013-2373-6.

[76] Feldman EL, Nave KA, Jensen TS, Bennett DLH. New horizons in diabetic neuropathy. Neuron. 2017;93(6):1296–1313.

[77] Jaiswal M, Larkin ME, Martin CL, et al. Association of symptoms of diabetic neuropathy with glycemic control and cardiovascular risk factors in youth with diabetes. J Diabetes Complications. 2018;32(9):866–872. doi:10.1016/j.jdiacomp.2018.06.001.

[78] Sakkal-Alkaddour H, Albaradie R, El Shanti H. Neurologic manifestations of hypoglycemia in children. Front Pediatr. 2020;8:579763.

[79] Kress JP, Hall JB. ICU-acquired weakness and recovery from critical illness. N Engl J Med. 2014;370(17):1626–1635.

[80] Vanhorebeek I, Latronico N, Van den Berghe G. ICU-acquired weakness. Intensive Care Med. 2020;46(4):637–653.

[81] Chen J, Zhou B, Wu M, et al. ICU-acquired weakness: recent insights. J Intensive Med. 2024;4(4):240–254.

[82] de Holanda NCP, de Lima DD, Cavalcanti TB, et al. Hashimoto's encephalopathy: systematic review and additional case. J Neuropsychiatry Clin Neurosci. 2011;23(4):384–390.

[83] Brandi ML, Bilezikian JP, Shoback D, et al. Management of hypoparathyroidism: summary statement and guidelines. J Clin Endocrinol Metab. 2016;101(6):2273–2283.

[84] De Luca C, Kowalski K, Nocera MF, et al. Obesity-related myosteatosis: endocrine and inflammatory links. Nat Rev Endocrinol. 2023;19(2):101–118.

[85] Naidoo K, Wiles CM. Muscle disorders associated with endocrine disease. Pract Neurol. 2021;21(4):294–303.

[86] Aragón-Vela J, Romero-Trejo D, Torrens-Mas M, et al. The role of molecular and hormonal factors in obesity and physical exercise: a review. Int J Mol Sci. 2022;23(24):15706

[87] Breton MD, Kanapka LG, Beck RW, et al. A randomized trial of closed-loop control in children with type 1 diabetes. N Engl J Med. 2020;383(9):836–845.