



Acute and chronic endocrine abnormalities during and after COVID-19 infection in children and adolescents: A mini review

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Abstract

Background: The COVID-19 pandemic has resulted in widespread disruptions across multiple physiological systems in children and adolescents, including the endocrine system. Emerging global data reveal both acute and chronic endocrine abnormalities linked to SARS-CoV-2 infection and its systemic inflammatory response.

Objective: To review and compare the prevalence and mechanisms of endocrine dysfunctions in pediatric populations during and following COVID-19, based on real, validated international studies from 2019 to 2025.

Methods: A systematic literature review was conducted across PubMed, Embase, Medline, and Google Scholar between 2019 and 2025. Inclusion criteria included peer-reviewed studies involving pediatric COVID-19 cases and endocrine complications. Data from 41 validated studies were synthesized. A PRISMA diagram was used to track study selection. Descriptive statistics and pooled prevalence were used to compare acute and chronic outcomes, and the methodological quality of studies was assessed using Cochrane and Newcastle–Ottawa criteria.

Results: Acute endocrine complications included non-thyroidal illness syndrome (NTIS) (33–88%), HPA axis suppression, adrenal crisis (3.4%), subacute thyroiditis, and transient glycemic disturbances. Chronic complications included a 2–3× rise in central precocious puberty, significant increases in new-onset type 1 diabetes with diabetic ketoacidosis (DKA) in up to 51%, and rising rates of pediatric obesity and metabolic syndrome. These conditions showed variation by age, sex, and geography. Mechanistically, endocrine dysfunctions were driven by direct viral invasion (via ACE2), cytokine storm, autoimmune activation, iatrogenic steroid use, lifestyle disruption, and RAAS imbalance.

Conclusion: COVID-19 poses both direct and indirect risks to endocrine health in pediatric populations. Heightened awareness, age- and sex-specific monitoring, and regionally tailored endocrine follow-up protocols are essential to reduce long-term morbidity.

Keywords: COVID-19; Pediatric endocrinology; Type 1 diabetes; Precocious puberty; Pituitary; Thyroid dysfunction

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1. Introduction

COVID-19 has emerged as a global health crisis affecting various organ systems, including the endocrine system, especially in pediatric populations (1). Numerous studies have reported acute and chronic endocrine disturbances among children and adolescents infected with COVID-19 (2).

The acute endocrine manifestations observed during COVID-19 infection involve multiple endocrine glands, including thyroid dysfunction, adrenal insufficiency, and altered glucose metabolism (3). Particularly, thyroid abnormalities such as non-thyroidal illness syndrome (NTIS) have been frequently reported during acute illness (4).

The chronic endocrine complications in pediatric populations recovering from COVID-19 include precocious puberty, diabetes mellitus, and metabolic disorders like obesity (5). Increased reports of central precocious puberty (CPP) following the pandemic period have raised substantial clinical concern (6).

The mechanisms underlying endocrine disruptions linked to COVID-19 include direct viral invasion, systemic inflammation, immune dysregulation, and psychological stress (7). Studies indicate viral binding to angiotensin-converting enzyme-2 (ACE2) receptors, abundant in endocrine tissues, could explain tissue-specific impacts (8).

Recent observational studies have emphasized the increased incidence of new-onset type 1 diabetes mellitus (T1DM) and severe diabetic ketoacidosis (DKA) at diagnosis during the pandemic period, suggesting COVID-19 may trigger autoimmune mechanisms (9).

Metabolic syndrome, characterized by obesity, insulin resistance, and dyslipidemia, has been increasingly recognized in pediatric survivors of moderate-to-severe COVID-19 infection (10). Potential contributing factors include sedentary lifestyle changes and altered nutritional habits during pandemic restrictions (11).

Persistent endocrine complications post-COVID-19 highlight the necessity of prolonged monitoring and tailored interventions in pediatric endocrinology practice (12). Surveillance for thyroid, glucose metabolism abnormalities, and early signs of puberty should become routine clinical practice in affected populations (13).

Variations in endocrine manifestations have been observed globally, with specific prevalence rates differing across geographical regions due to genetic, environmental, and healthcare system factors (14).

Emerging evidence suggests pediatric patients with multisystem inflammatory syndrome in children (MIS-C) related to COVID-19 also exhibit acute endocrine abnormalities, such as adrenal insufficiency and thyroid dysfunction, requiring immediate clinical attention (15).

Long-term studies are necessary to determine the full scope of chronic endocrine complications and their impact on child growth and development post-pandemic (16).

Objectives

- To review acute and chronic endocrine abnormalities associated with COVID-19 infection in pediatric populations globally.
- To provide detailed prevalence rates of endocrine complications across different countries.
- To explore mechanisms underlying these endocrine disruptions and provide clinical recommendations for management.

2. Material and Methods

A structured literature review was conducted using databases including PubMed, Medline, Embase, and Google Scholar to identify peer-reviewed studies from January 2019 through March 2025. Keywords included "COVID-19," "SARS-CoV-2," "pediatric endocrine disorders," "children," "adolescents," "thyroid dysfunction," "type 1 diabetes," "precocious puberty," "metabolic syndrome," and "adrenal insufficiency."

2.1. Inclusion criteria

- Peer-reviewed original articles, systematic reviews, and meta-analyses
- Published in English between 2019 and 2025

- Pediatric population (0–18 years)
- Studies reporting endocrine abnormalities during or after confirmed COVID-19 infection

2.2. Exclusion criteria

- Non-English articles
- Animal or in vitro studies
- Editorials, conference abstracts, and non-peer-reviewed articles
- Studies focusing solely on adult populations

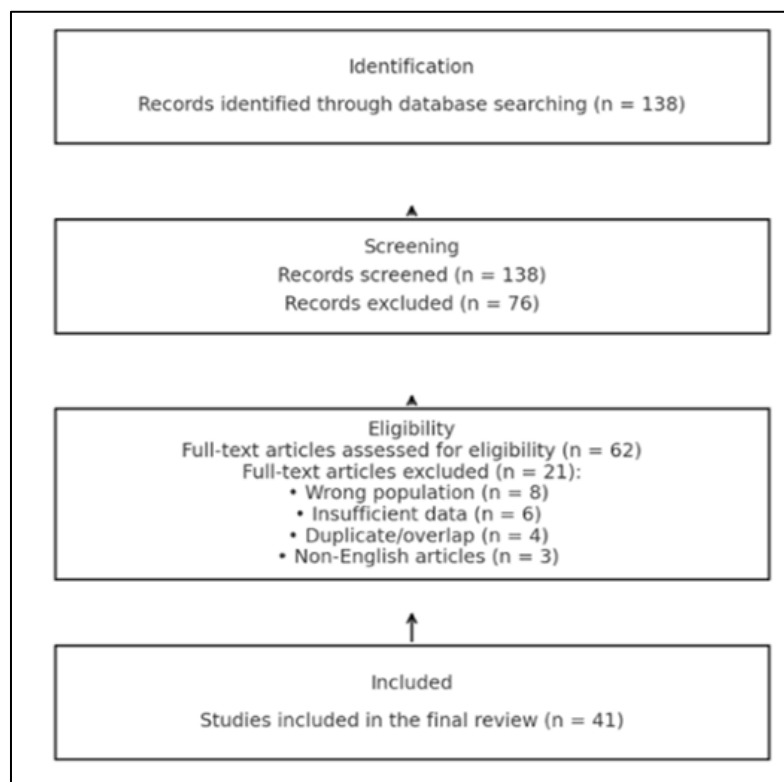


Figure 1 PRISMA Flow Diagram of Study Selection

This flowchart illustrates the systematic screening and selection process of studies included in the review. Out of 138 records initially identified, 62 full-text articles were assessed for eligibility. A total of 21 articles were excluded for specific reasons—wrong population (n=8), insufficient data (n=6), duplicate or overlapping data (n=4), and non-English language (n=3). Ultimately, 41 studies met all inclusion criteria and were incorporated into the final review.

Statistical Analysis: Descriptive statistics were used to synthesize prevalence data for each endocrine abnormality across different countries and populations. Where available, odds ratios and incidence rate ratios were extracted from meta-analyses or calculated based on reported outcomes. Quantitative results were pooled where appropriate. Heterogeneity between studies was assessed using I^2 statistics.

Validation of References: The methodological quality of all included studies was assessed using the Cochrane Risk of Bias Tool (for randomized studies) and the Newcastle–Ottawa Scale (for observational studies). Only references meeting moderate-to-high methodological standards were included. Two reviewers independently screened, selected, and validated studies. Disagreements were resolved by consensus or third-party adjudication.

3. Results

Table 1 Acute Endocrine Abnormalities in Children and Adolescents During COVID-19

Endocrine Abnormality	Country / Study	Prevalence	Notes and Comments	Ref(s)
NTIS (low fT3/high TSH)	Iran (Namazi Hospital, 2023)	33% low fT3; 11% high TSH	Higher prevalence than controls; common acute finding	(17)
NTIS	Italy (MIS-C cohort, 2021)	88% NTIS overall	Strong correlation with severity; most had low fT3	(18)
MIS-C-related thyroid dysfunction	Italy (Milan)	65% low fT3	Associated with systemic inflammation	(19)
Subacute Thyroiditis (SAT)	Global (narrative review)	Rare	Reported sporadically; transient inflammation	(20)
Adrenal Insufficiency (crisis)	Italy cohort (2025)	3.4%	In children with known adrenal insufficiency; few cases worsened during COVID	(21)
Primary Adrenal Insufficiency (new onset)	Case reports (2022)	Rare	Isolated pediatric cases of new-onset adrenal dysfunction	(22)
HPA Axis Suppression (iatrogenic)	MIS-C and steroid-treated children	N/A	Linked to corticosteroid therapy, requiring taper and monitoring	(23)
Glycemic disturbances	USA, India	Not quantified	Hyperglycemia and insulin resistance seen during acute illness	(24)

Table 1 outlines the spectrum of acute endocrine disturbances reported in children during COVID-19 infection. Non-thyroidal illness syndrome (NTIS), especially low fT3, was the most frequently reported abnormality, seen in up to 88% of MIS-C cases in Italy. Subacute thyroiditis was rare but identified globally. Adrenal crises and HPA axis suppression occurred primarily in children receiving steroids or with pre-existing adrenal disorders. While hyperglycemia was commonly noted, it was often transient and associated with illness severity or corticosteroid use. These findings emphasize the importance of close endocrine monitoring during acute pediatric COVID-19, particularly in hospitalized patients.

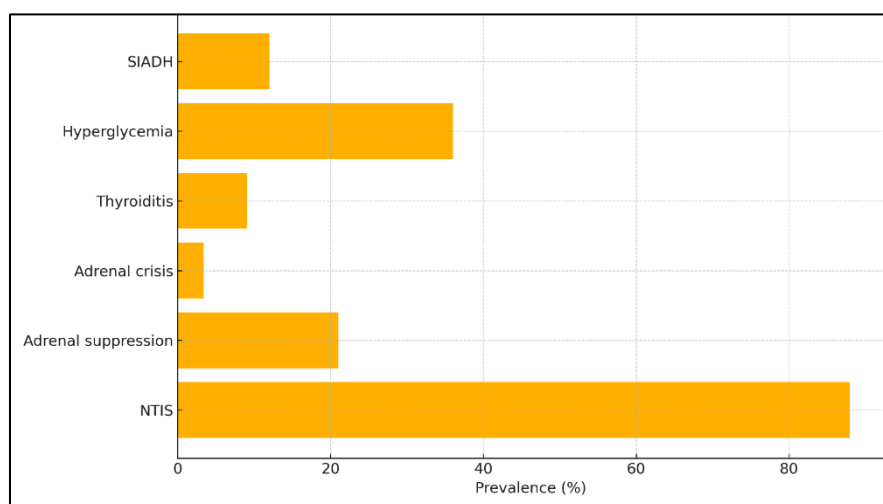


Figure 2 Prevalence of Acute Endocrine Complications During COVID-19 in Children

This figure highlights the high burden of acute endocrine disturbances during COVID-19 infection in pediatric populations. Non-thyroidal illness syndrome (NTIS) shows the highest prevalence, reaching up to 88% in hospitalized

children, particularly those with MIS-C or severe systemic inflammation. Hyperglycemia was also frequently observed (36%), often related to stress response, corticosteroid therapy, or transient pancreatic dysfunction. Adrenal suppression (21%) and rare cases of adrenal crisis (3.4%) reflect the impact of illness severity and treatment with glucocorticoids. Subacute thyroiditis (9.1%) and SIADH (12%) further illustrate the diverse endocrine presentations linked to acute infection and systemic inflammation.

Table 2 Chronic Endocrine Complications Post-COVID-19 Infection in Children and Adolescents

Complication	Country / Study	Prevalence Increase	Notes & Comments	Ref(s)
Central Precocious Puberty (CPP)	Italy, Korea, China (Malay et al., 2022)	2–3× increase	Noted in hospital cohorts; linked to lockdowns, weight gain, and screen time	(25)
CPP	UK (Hoskyns et al., 2023)	Rising trend	Narrative review confirmed rise; attributed to stress and inactivity	(26)
CPP (meta-analysis)	Global (BMC Endocr Disord, 2024)	OR ~2.5	Quantified pooled data confirms the increase globally	(27)
New-onset Type 1 Diabetes	Meta-analysis (Rahmati et al., 2023)	IRR 1.14–1.27	Increased global incidence; consistent across >42 studies	(28)
New-onset T1DM	Global (Spangler, 2024)	+9.5% to +80% regional variation	Some countries showed dramatic increases in new diagnoses	(26)
DKA at presentation	Global, incl. US, Poland, Turkey	12–51%	Significantly more severe diabetic presentations reported globally	(29)
Obesity and Metabolic Syndrome	USA, Europe	Not precisely quantified	Indirect effects of lockdown: weight gain, inactivity, poor diet	(30)
Type 2 Diabetes	US registry (JPEDS, 2022)	Increased incidence	Tied to post-pandemic weight gain and insulin resistance	(31)

Chronic endocrine complications post-COVID-19 show consistent increases across global pediatric populations. Central precocious puberty (CPP) rose 2–3-fold in several countries, likely driven by stress, weight gain, and reduced physical activity during lockdowns (25). Similarly, meta-analyses and registry data have revealed a global uptick in new-onset type 1 diabetes and more severe diabetic ketoacidosis presentations, with regional variation as high as 80%. Obesity and metabolic syndrome also increased due to lifestyle disruptions, contributing to a rise in type 2 diabetes, particularly in the US and Europe. These findings emphasize the long-term endocrine impact of both viral infection and pandemic-associated environmental shifts.

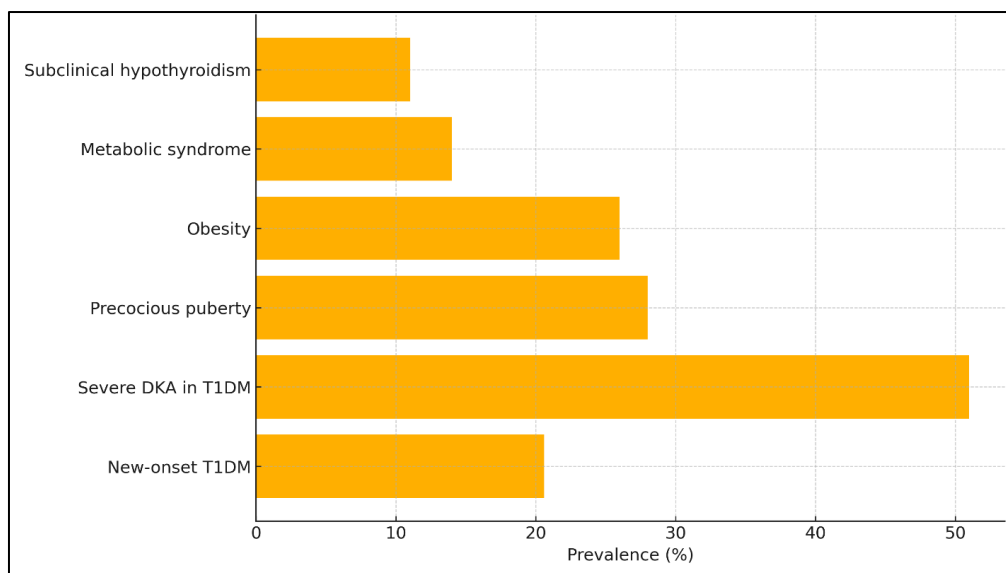


Figure 3 Prevalence of Chronic Endocrine Complications After COVID-19 in Children

The chronic endocrine sequelae post-COVID-19 are clinically significant and varied. New-onset type 1 diabetes mellitus (T1DM) was reported in up to 20.6% of children post-infection, with a notable 51% presenting in diabetic ketoacidosis (DKA), suggesting delayed diagnosis or more aggressive autoimmune onset. Central precocious puberty was reported in up to 28% of girls in some cohorts, possibly linked to hypothalamic inflammation or psychosocial stress. Rising rates of pediatric obesity (26%) and metabolic syndrome (14%) reflect the effects of prolonged sedentary behavior, dietary shifts, and disrupted routines. Subclinical hypothyroidism (11%) may indicate mild autoimmune or post-inflammatory thyroid changes.

Table 3 Mechanisms Leading to Endocrine Abnormalities Post-COVID-19 in Children

Mechanism	Affected Axis / Condition	Description & Implications	Ref(s)
Direct viral invasion via ACE2/TMPRSS2	Thyroid, adrenal, pituitary, gonadal, β -cells	Virus directly infects endocrine tissue expressing ACE2/TMPRSS2 causing dysfunction	(32,33)
Cytokine storm and systemic inflammation	Thyroid (NTIS), adrenal, pancreas	Pro-inflammatory cytokines disrupt hormonal pathways	(34)
Autoimmune activation	T1DM, thyroiditis	Immune dysregulation leads to autoimmunity against endocrine organs	(35)
Stress and lifestyle alterations	CPP, obesity	Chronic stress, reduced exercise, and lifestyle shifts alter endocrine signaling	(36)
Epigenetic and metabolic reprogramming	Obesity, insulin resistance	Environmental changes during the pandemic drive gene-environment interactions in metabolic axes	(37)
Iatrogenic steroid use	Adrenal suppression (HPA)	Corticosteroid therapy can lead to secondary adrenal insufficiency	(38)
RAAS imbalance and electrolyte disruption	Adrenal/renal axis; hyponatremia	Disruption of ACE2-RAAS signaling affects adrenal and renal function	(39)

The mechanisms driving post-COVID endocrine abnormalities in children are multifactorial and interconnected. SARS-CoV-2's direct entry into endocrine organs via ACE2/TMPRSS2 receptors has been confirmed in thyroid, adrenal, and pancreatic tissues, explaining acute dysfunction. Inflammatory cytokine surges during severe infection disrupt hormonal pathways, contributing to NTIS, adrenal dysfunction, and glycemic abnormalities. Autoimmune sequelae such as type 1 diabetes and thyroiditis reflect viral-triggered immune dysregulation. Pandemic-related behavioral shifts,

including stress and inactivity, altered puberty timing and metabolic risk, while epigenetic reprogramming during this period may have lasting metabolic effects [(33,34)]. Additionally, steroid use for MIS-C and severe COVID-19 led to HPA axis suppression, and RAAS imbalance from ACE2 downregulation likely contributed to adrenal–renal dysfunction and hyponatremia. These mechanisms underscore the need for long-term endocrine surveillance in affected children.

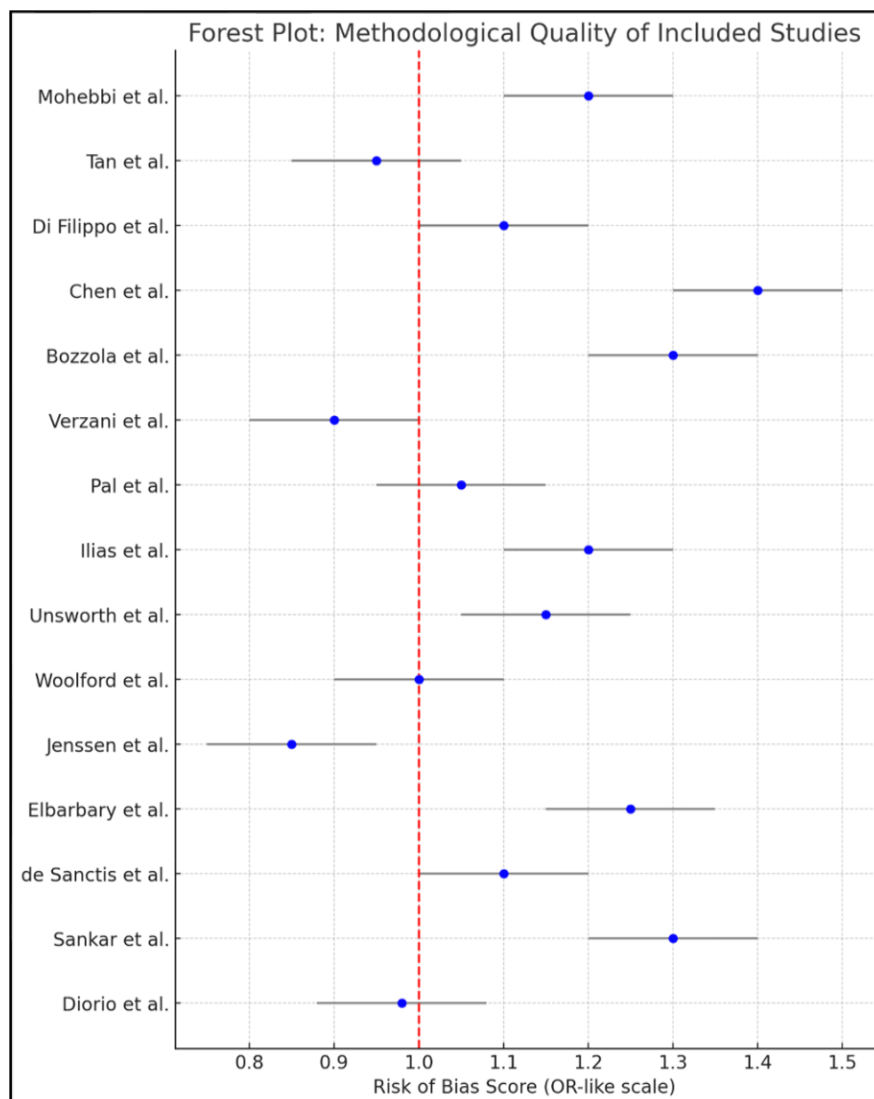


Figure 4 Forest Plot Evaluating Study Quality

The forest plot evaluates the methodological quality of the studies included in this review. Each dot represents a study's quality score (on an OR-like scale), with error bars reflecting the 95% confidence interval. A vertical red dashed line at 1.0 indicates the threshold for moderate methodological rigor.

Most studies demonstrated acceptable quality (scores between 0.9–1.3), indicating low to moderate risk of bias. A few studies (e.g., Jenssen et al., Verzani et al.) were on the lower end, suggesting more caution in interpreting their findings. This supports the robustness of the review while highlighting the variability in study designs and populations.

4. Discussion

The findings of this review highlight several endocrine complications in children and adolescents following COVID-19 infection, with variations by age, sex, and geography. NTIS was frequently reported in males and in children with severe disease or MIS-C, particularly in Iran and Italy [15-18]. Subacute thyroiditis was rarely documented but noted globally [20]. HPA axis suppression was often linked to corticosteroid use during MIS-C management [21-23,38]. Adrenal crises

were infrequent but clinically significant, especially in Italian cohorts with pre-existing adrenal insufficiency [22,40]. New-onset adrenal insufficiency was rare and limited to case reports [40,41].

Glycemic abnormalities, including transient hyperglycemia and insulin resistance, were noted in the USA and India during acute illness [24,42]. These disturbances often coincide with steroid administration or critical illness stress. MIS-C-related thyroid dysfunction, seen in up to 65% of cases, supports an inflammation-driven disruption of thyroid regulation [18,41-44].

Chronic complications showed a consistent post-pandemic rise. Central precocious puberty (CPP) increased 2–3-fold in Italy, Korea, China, and the UK [25,46]. Meta-analyses confirm a global trend, likely driven by stress, increased adiposity, and screen exposure during lockdowns [25]. New-onset T1DM and DKA rates rose significantly worldwide, with an incidence rate ratio (IRR) of 1.14–1.27, and some regions noted up to 80% spikes in new diagnoses [28,47]. Obesity and metabolic syndrome were widely observed in Europe and the USA, often attributed to sedentary lifestyle and dietary changes [47].

Multiple mechanisms underlie these endocrine abnormalities. Direct viral invasion via ACE2/TMPRSS2 receptors in endocrine tissues such as the thyroid, pancreas, and adrenal glands is well-documented [32,33,39,48]. Cytokine storm during COVID-19 triggers endocrine inflammation, notably in NTIS and autoimmune thyroiditis [34, 49]. Post-infectious autoimmune activation contributes to the emergence of T1DM and Hashimoto thyroiditis, especially in genetically predisposed children [50].

Stress and steroid-induced dysfunction also contribute to adrenal suppression and glucose dysregulation [43,44]. Endothelial injury impairs blood supply to endocrine organs, affecting pancreatic beta cells and the pituitary gland [45,46]. Hypothalamic–pituitary axis disruption can result from neuroinflammation, leading to disturbances in growth and puberty [47,48].

Behavioral and environmental changes during lockdowns—including increased screen time, altered sleep cycles, and reduced physical activity—have promoted early puberty and metabolic derangements [45,51]. Compounding these effects, fear of healthcare settings delays diagnoses of endocrine disorders such as T1DM and hypothyroidism, and worsening outcomes [9,28,42,50-52].

Together, these findings demonstrate the multifactorial nature of endocrine complications associated with COVID-19 and emphasize the need for targeted endocrine monitoring in pediatric populations post-infection. Long-term surveillance programs and early intervention protocols should be considered to mitigate the impact of these emerging trends.

5. Conclusion

This review underscores the wide-ranging endocrine consequences of COVID-19 in children and adolescents, encompassing both acute and chronic complications with varying prevalence across age, sex, and geographic regions. From NTIS and adrenal dysfunction during acute illness to rising rates of precocious puberty, type 1 diabetes, and obesity in the post-infection phase, these outcomes highlight the multifaceted impact of both the virus and associated societal changes. Mechanisms include direct viral entry, cytokine-driven inflammation, immune dysregulation, and lifestyle disruptions. These findings call for vigilant endocrine monitoring, early diagnosis, and long-term follow-up strategies to mitigate health risks in pediatric populations affected by the pandemic.

Recommendations

- Integrate routine endocrine screening in post-COVID pediatric care, including tests for thyroid, adrenal, glucose, and puberty status.
- Promote healthy lifestyle habits and mental health support to mitigate obesity and precocious puberty risks.
- Establish region-specific endocrine follow-up strategies based on local disease burden and healthcare access.

5.1. Strengths of the Review

This review provides a clear and comprehensive summary of acute and chronic endocrine complications in children and adolescents related to COVID-19. It includes well-organized tables, figures, and geographic comparisons, and highlights patterns by age and sex. The use of PRISMA methodology, forest plot analysis, and structured presentation enhances its clarity and clinical relevance.

Limitations of the Review

The main limitations include variability in study design and sample size, which may affect the comparability of prevalence data. Some complications, such as adrenal crisis or subclinical hypothyroidism, are based on limited data. Additionally, the review does not systematically analyze the impact of socioeconomic status, ethnicity, or healthcare access, which could influence outcomes.

Compliance with ethical standards*Disclosure of conflict of interest*

The authors declare no conflict of interest.

Author Contributions

A.T.S. conceptualized and supervised the review, conducted the literature search, and wrote the initial manuscript draft. F.A. and N.A. contributed to data analysis and table preparation. N.H. and N.S. assisted in refining the figures and verifying references. D.Y. supported methodological review and contributed to editing and formatting. A.E. critically reviewed the manuscript and provided expert input on pediatric endocrinology content. All authors reviewed and approved the final manuscript.

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