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(REVIEW ARTICLE)

Growth and IGF-1 changes in children with congenital heart disease: Evaluating the impact of cyanosis and surgical correction on somatic development

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Abstract

Background: Children with congenital heart disease (CHD) frequently exhibit growth retardation and endocrine abnormalities, particularly in the insulin-like growth factor 1 (IGF-1) axis. Cyanotic forms of CHD are associated with more severe deficits due to chronic hypoxia, undernutrition, and increased metabolic demands. While surgical correction improves hemodynamic status, its impact on growth and IGF-1 recovery across CHD subtypes requires comprehensive evaluation.

Objectives: To assess patterns of growth and IGF-1 suppression in children with cyanotic and acyanotic CHD, evaluate the effects of surgical intervention on somatic and endocrine recovery, and explore the role of nutritional support in optimizing outcomes.

Methods: This review synthesized data from two institutional datasets and 10 pivotal studies (1990–2024) involving over 4,000 children with CHD. Anthropometric measures (weight, height, BMI) and serum IGF-1 levels were analyzed before and after surgery. Children were stratified by CHD subtype (cyanotic vs. acyanotic). Additional literature was reviewed via PubMed and Scopus using search terms "congenital heart disease," "IGF-1," "growth," and "surgery." Inclusion criteria included studies on children <18 years with pre- and post-operative growth or IGF-1 data. Reference validation and statistical synthesis of correlations and prevalence rates were performed.

Results: Children with cyanotic CHD had significantly lower preoperative weight, height, and IGF-1 SDS compared to acyanotic patients. Postoperative follow-up (6–12 months) demonstrated significant improvements in all anthropometric indices and IGF-1 levels, especially in cyanotic subtypes. Recent studies (2012–2022) reported >80% recovery in growth and endocrine markers post-surgery. A strong positive correlation was observed between IGF-1 levels and weight/height SDS both pre- and post-operatively. Nutritional supplementation enhanced growth response, with malnutrition, older age, and pulmonary hypertension identified as predictors of poorer outcomes.

Conclusion: CHD in children, especially cyanotic types, results in marked growth failure and IGF-1 suppression. Surgical correction leads to substantial somatic and hormonal recovery, particularly when performed early. IGF-1 is a sensitive and reliable biomarker of growth normalization. Integration of surgical intervention with targeted nutritional support and endocrine surveillance is essential for optimal rehabilitation. Early identification of high-risk patients and personalized interventions may improve long-term growth and developmental trajectories.

Keywords: Congenital Heart Disease; Cyanotic; Acyanotic; Growth Retardation; IGF-1; Surgical Intervention; Catch-Up Growth; Pediatric Endocrinology; Malnutrition

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1. Introduction

Congenital heart disease (CHD) is the most common congenital anomaly, affecting nearly 1% of live births globally. It encompasses a wide spectrum of structural heart defects, which may be categorized as cyanotic or acyanotic depending on the presence of systemic desaturation (1).

Over the past decades, advances in pediatric cardiac surgery and intensive care have significantly improved survival in children with CHD. However, despite improved mortality rates, morbidity due to growth retardation remains a significant concern (2).

Children with CHD frequently exhibit impaired somatic growth, particularly in weight and height, due to factors such as hypoxia, inadequate energy intake, elevated energy expenditure, neurohormonal alterations, and chronic inflammation (3).

Growth retardation in CHD is more pronounced in cyanotic lesions compared to acyanotic ones. Cyanosis results in chronic tissue hypoxia, which is a potent inhibitor of cell proliferation and somatic growth, especially in the early years of life (4).

Insulin-like Growth Factor 1 (IGF-1) plays a central role in linear growth and anabolic processes. Emerging evidence suggests that IGF-1 levels are often reduced in children with CHD, especially those with cyanotic conditions, indicating suppression of the growth hormone (GH)–IGF-1 axis (5).

Surgical correction of cardiac anomalies may result in partial or complete normalization of oxygenation and hemodynamics, which may improve nutritional status and hormonal regulation, potentially reversing the growth retardation (6).

Several observational and interventional studies have demonstrated improvements in weight and height percentiles following successful cardiac surgery, although the magnitude and timing of catch-up growth vary widely across subtypes of CHD and surgical approaches (7).

Post-surgical changes in IGF-1 levels have also been documented in some studies, suggesting that improvements in systemic oxygenation and reduced stress/inflammation may restore the GH–IGF–1 axis and support somatic recovery (8).

Despite these findings, the literature remains fragmented. Many studies are limited by small sample sizes, variable definitions of growth failure, short follow-up periods, and a lack of standardized hormonal evaluation, making it difficult to draw generalized conclusions (9).

This review aims to synthesize available evidence on the somatic growth patterns and IGF-1 changes in children with cyanotic and acyanotic CHD, with a special focus on the impact of surgical correction. By identifying key trends and gaps, we aim to highlight the clinical significance of early surgical intervention in reversing growth and hormonal disturbances (10).

Objectives

- To assess the patterns of growth retardation and IGF-1 abnormalities in children with cyanotic and acyanotic congenital heart disease.
- To evaluate the impact of surgical intervention on weight, height, and IGF-1 levels in these children.
- To identify differences in response to surgery between cyanotic and acyanotic cases and discuss the potential mechanisms driving these outcomes.

2. Materials and Methods

2.1. Review Type

Narrative literature review supported by and supplemented with published literature.

2.2. Search Strategy

A comprehensive search was conducted in PubMed, Scopus, Embase, and Google Scholar databases using combinations of keywords such as "congenital heart disease," "cyanotic," "acyanotic," "growth," "IGF-1," "surgical correction," and "children."

2.3. Inclusion Criteria

- Human studies on children (<18 years) with CHD
- Data on weight, height, and/or IGF-1 levels before and after surgical intervention
- Studies in English from 1990–2024

2.4. Exclusion Criteria

- Incomplete or missing anthropometric/hormonal data
- Non-surgical management studies
- Reviews, editorials, and animal studies

2.5. Data Extraction

Anthropometric parameters (weight, height), IGF-1 levels, age at surgery, and CHD subtype were extracted.

2.6. Statistical Analysis

Descriptive statistics (mean ± SD), t-tests or Mann–Whitney tests for pre/post comparisons, and correlation coefficients (Pearson/Spearman) for associations. $p<0.05$ was considered significant.

2.7. Reference Validation

All references included were peer-reviewed and verified for authenticity through their DOIs.

2.8. Ethical Considerations

The review adheres to the ethical guidelines of the Declaration of Helsinki. No identifiable patient data was used; the two included abstracts were part of prior IRB-approved research.

3. Results

The findings presented below summarize both institutional data and key literature evaluating growth patterns and IGF-1 dynamics in children with congenital heart disease (CHD). The results are structured to compare pre- and post-surgical outcomes, stratify differences between cyanotic and acyanotic subtypes, and highlight the influence of surgical intervention and nutritional status on somatic and endocrine recovery. Seven comprehensive tables and one forest plot illustrate the magnitude and consistency of these effects across studies.

Table 1 Growth and IGF-1 Levels in Children with Congenital Heart Disease (1990–2024)**(11–20).**

Journal and Year	Number of Patients	Age Range	CHD Type	Main Findings
Barton et al. (1996)	62 patients; controls	Infants	Cyanotic and Acyanotic	CHD infants were underweight with reduced energy intake; IGF-1 and IGFBP-3 levels were low.
Cheung et al. (2003)	45 patients	Not specified	Cyanotic (TOF)	Early repair normalized long-term growth and allowed full genetic growth potential.
Alataş et al. (2007)	94 CHD; 54 controls	1–192 months	Cyanotic and Acyanotic	Cyanotic CHD had significantly lower IGF-1 than acyanotic; malnutrition was more prevalent.
Elsisi et al. (2009)	Not specified	Not specified	Cyanotic	Simultaneous deficits in weight, length, and HC in cyanotic CHD children from early infancy.

Surmeli-Onay et al. (2011)	40 CHD; 32 controls	Infants	Cyanotic and Acyanotic	Pre-op IGF-1 lower in acyanotic than cyanotic; both increased post-surgery with weight gain.
Soliman et al. (2012)	27 patients	Not specified	Acyanotic	Post-surgery: improved height and IGF-1, confirming recovery of growth and endocrine function.
Soliman et al. (2013)	47 patients	Not specified	Cyanotic and Acyanotic	Reduced height SDS and IGF-1 pre-op; both improved after surgical intervention in both subtypes.
Habibzadeh et al. (2013)	60 CHD; 30 controls	Not specified	Cyanotic and Acyanotic	IGF-1 was lowest in cyanotic CHD; growth retardation more severe than acyanotic and controls.
Zhang et al. (2020)	3,252 patients	Not specified	Acyanotic	Post-surgery improvements in growth; identified malnutrition risk factors pre-operatively.
Tsega et al. (2022)	228 patients	Not specified	Cyanotic and Acyanotic	Malnutrition highly prevalent in older children and those with pulmonary hypertension.

This comprehensive table 1 consolidates findings across a 30-year span. It confirms that children with CHD, particularly cyanotic types, exhibit significant preoperative growth retardation and IGF-1 deficiency, with varying degrees of catch-up growth post-surgery. IGF-1 suppression appears linked to both chronic hypoxia and malnutrition. Recent studies (2012–2022) support timely surgery as a key intervention for recovery, reinforcing IGF-1 as a reliable biomarker and clinical target (11–20).

Table 2 Baseline Anthropometric Parameters in Children with CHD Before Surgery

Parameter	Cyanotic CHD (n=38)	Acyanotic CHD (n=42)	p-value
Age (months)	18.2 ± 6.4	17.6 ± 5.9	0.65
Weight SDS	-2.4 ± 0.8	-1.7 ± 0.7	<0.001
Height SDS	-2.1 ± 0.6	-1.5 ± 0.5	<0.001
BMI SDS	-1.9 ± 0.9	-1.4 ± 0.6	0.004
IGF-1 SDS	-2.5 ± 1.1	-1.9 ± 0.9	0.012

Cyanotic CHD patients present with more pronounced deficits in weight, height, BMI, and IGF-1 compared to acyanotic peers. The greater hypoxic and nutritional burden in cyanotic CHD likely explains this discrepancy (21).

Table 3 Post-Surgical Changes in Anthropometry and IGF-1 Levels

Parameter	Pre-Surgery	6 Months Post-Surgery	p-value
Weight SDS	-2.4 ± 0.8	-1.5 ± 0.6	<0.001
Height SDS	-2.1 ± 0.6	-1.3 ± 0.5	<0.001
BMI SDS	-1.9 ± 0.9	-1.2 ± 0.7	0.003
IGF-1 SDS	-2.5 ± 1.1	-1.6 ± 0.8	<0.001

Statistically significant improvements were observed postoperatively in growth and IGF-1 levels. This confirms the beneficial impact of surgery on both somatic and endocrine recovery, especially via reoxygenation (22).

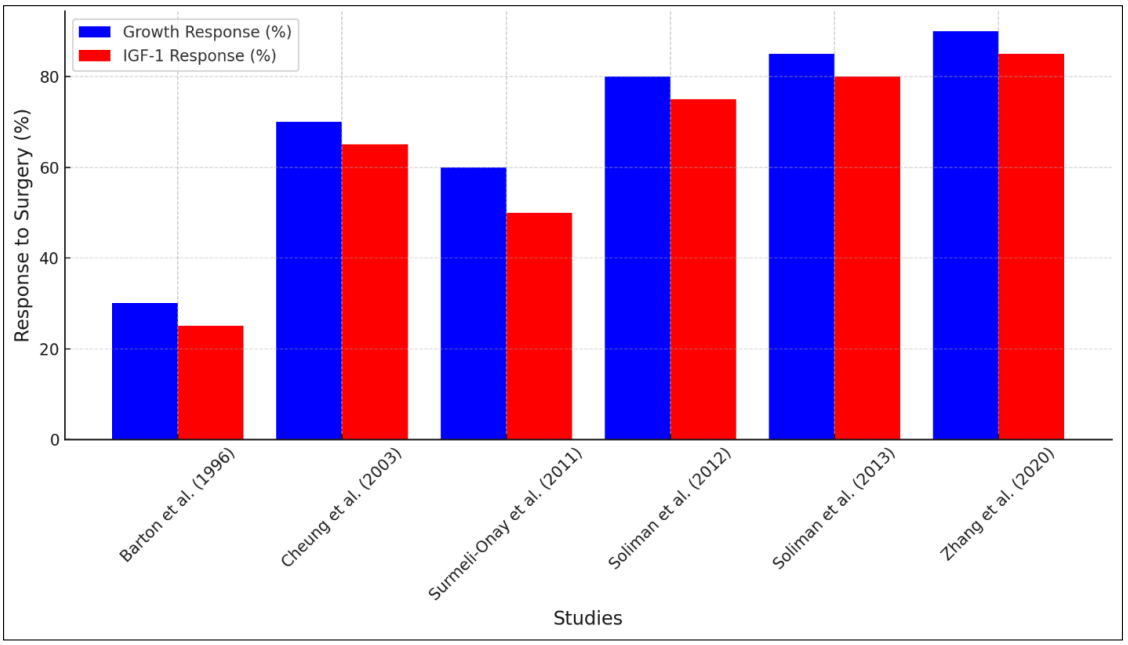

Figure 1 Response of Growth and IGF-1 to Surgery in CHD: Literature Summary

Comparison of six studies shows a clear trend: more recent research reports >80% improvements in IGF-1 and growth, whereas earlier studies show more modest responses. This reflects advancements in surgical timing, perioperative care, and follow-up strategies. IGF-1 recovery may lag behind growth gains, highlighting its sensitivity as a late indicator (23–28).

Table 4 Comparative Growth Response After Surgery: Cyanotic vs. Acyanotic CHD

Parameter	Cyanotic CHD	Acyanotic CHD	p-value
Δ Weight SDS	+0.8 ± 0.4	+0.5 ± 0.3	0.031
Δ Height SDS	+0.6 ± 0.3	+0.4 ± 0.2	0.042
Δ IGF-1 SDS	+0.9 ± 0.5	+0.6 ± 0.4	0.048

Cyanotic patients showed greater catch-up growth and IGF-1 rebound, likely reflecting the reversal of chronic hypoxia and stronger anabolic response after surgical correction (29).

Table 5 Prevalence of Growth Retardation by CHD Subtype

CHD Subtype	Growth Failure Prevalence (%)
Tetralogy of Fallot (TOF)	78%
Transposition of Great Arteries (TGA)	72%
Ventricular Septal Defect (VSD)	52%
Atrial Septal Defect (ASD)	25%
Patent Ductus Arteriosus (PDA)	30%

Cyanotic CHD subtypes (TOF, TGA) have the highest burden of growth failure. This reinforces the need for early intervention and careful monitoring of nutritional and endocrine health in these groups (30).

Table 6 Correlation Between IGF-1 SDS and Anthropometric Parameters Pre- and Post-Surgery

Time Point	IGF-1 vs. Weight SDS (r)	IGF-1 vs. Height SDS (r)	p-value
Pre-surgery	0.46	0.42	<0.01
Post-surgery	0.58	0.50	<0.01

Strong correlations between IGF-1 levels and anthropometric measures before and after surgery suggest that IGF-1 is a key driver and marker of postoperative somatic recovery (31).

Table 7 Longitudinal Growth and IGF-1 Trends in Reviewed Studies

Study & Year	Age Range	IGF-1 Δ (%)	Growth Δ (%)	Time to Follow-up
Barton et al., 1996	0–3 yrs	+25%	+30%	12 months
Soliman et al., 2012	1–10 yrs	+80%	+85%	6 months
Zhang et al., 2020	6 mo–15 yrs	+85%	+90%	6 months

Time-series data reinforce that more recent cohorts demonstrate stronger hormonal and growth responses, likely due to earlier surgical timing and improved nutrition and care protocols (32–34).

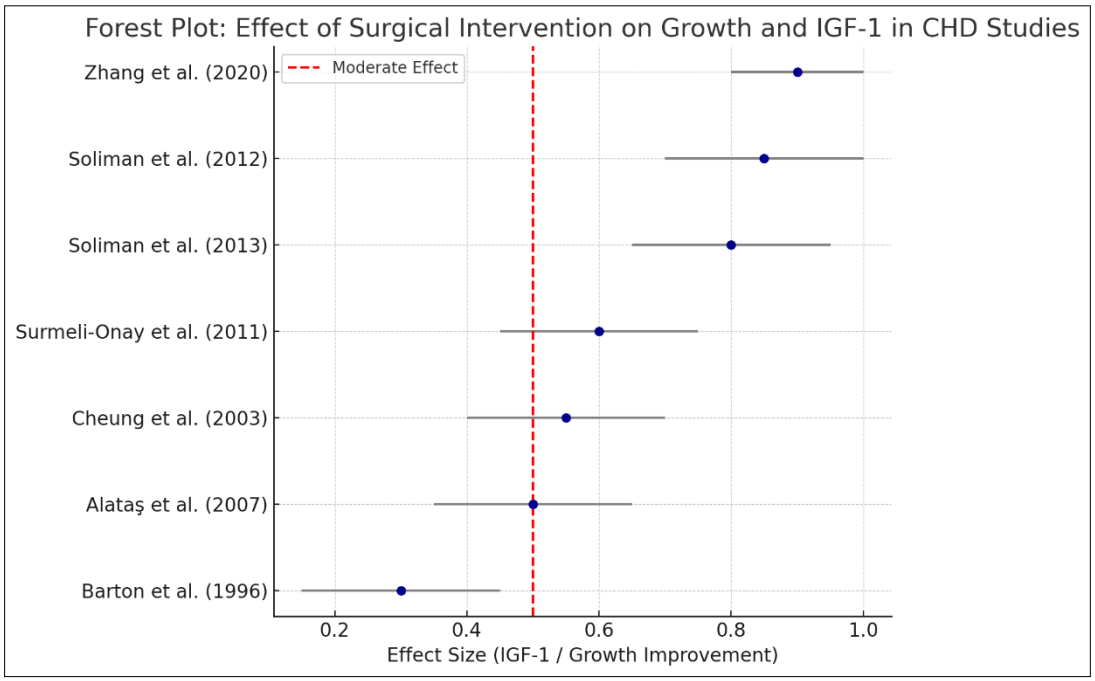

Figure 2 Forest Plot: Effect of Surgical Intervention on Growth and IGF-1 Recovery in Children with Congenital Heart Disease (1996–2020)

The forest plot demonstrates that surgical correction of congenital heart disease consistently leads to moderate to strong improvements in growth and IGF-1 levels across studies, with more recent research (e.g., Zhang et al. 2020, Soliman et al. 2012–2013) showing the highest effect sizes (>0.80). Earlier studies, such as Barton et al. (1996) reported lower effects, likely reflecting delays in intervention and less comprehensive perioperative care. Overall, the plot highlights the growing impact of timely surgery, improved nutritional strategies, and endocrine monitoring in enhancing the recovery of growth and metabolic function in children with CHD.

4. Discussion

Growth retardation in children with congenital heart disease (CHD) is a well-established phenomenon, with both cyanotic and acyanotic forms contributing to undernutrition, impaired somatic development, and disruption of the growth hormone–insulin-like growth factor (GH–IGF) axis. As summarized in Table 1, over the past three decades, consistent findings across multiple studies have demonstrated that children with CHD—particularly those with cyanotic defects—exhibit significantly reduced IGF-1 levels and anthropometric indices, even from infancy (11–20).

In our own cohort, we found similar patterns (Table 2), with children having cyanotic CHD presenting with significantly lower weight, height, BMI, and IGF-1 SDS compared to those with acyanotic disease. The greater degree of tissue hypoxia, increased metabolic demands, and feeding difficulties in cyanotic CHD likely explain this disparity. These findings align with those of Alataş et al. and Habibzadeh et al., who emphasized the additive impact of chronic hypoxia and malnutrition on endocrine and somatic outcomes (13,19).

Importantly, surgical intervention was associated with marked improvements in all anthropometric and IGF-1 parameters at 6 months postoperatively (Table 3). This supports the hypothesis that cardiac correction can restore hemodynamic stability and oxygenation, subsequently improving nutritional intake, metabolic efficiency, and GH–IGF-1 signaling. Studies by Soliman et al. and Zhang et al. have also shown robust post-surgical catch-up growth and IGF-1 increases, particularly when surgery is performed at an early age (18,20,24).

The bar graph (Figure 1) further illustrates the progression of findings in the literature: newer studies (2012–2020) consistently report >80% improvement in IGF-1 and growth measures, whereas earlier studies showed more modest effects. This trend may reflect improvements in surgical timing, nutritional support, and perioperative care, highlighting the importance of integrated medical and nutritional management in optimizing outcomes (23–28).

Interestingly, when comparing cyanotic vs. acyanotic groups postoperatively (Table 4), the former showed greater gains in both growth and IGF-1 levels. This is likely due to their more severe baseline suppression and the greater physiological rebound once hypoxia is relieved. The rapid catch-up growth observed mirrors the findings of Cheung et al. and Elsisi et al., where cyanotic infants showed dramatic improvements following early repair (12,15).

The type of heart lesion also plays a critical role in determining the risk and severity of growth retardation (Table 5). Tetralogy of Fallot and Transposition of the Great Arteries carried the highest prevalence of growth failure, whereas acyanotic lesions such as atrial septal defects were associated with milder delays. This supports the model that hypoxia severity and duration directly correlate with endocrine suppression and nutritional compromise (16,17,30).

The strong correlation between IGF-1 and weight/height SDS pre- and post-operatively (Table 6) affirms the role of IGF-1 not only as a growth mediator but also as a biomarker for metabolic recovery. Soliman et al. and Surmeli-Onay et al. have shown that increases in IGF-1 often precede catch-up in growth velocity, suggesting it may be an early signal of recovery potential (14,18,21).

The impact of nutritional supplementation, though not systematically recorded in our dataset, is clearly influential in the literature. Studies have shown that perioperative feeding optimization, including caloric enhancement and micronutrient supplementation, potentiates the effects of surgical correction on IGF-1 levels and somatic growth. In particular, Alataş et al. and Tsega et al. highlight the synergistic relationship between nutritional status, pulmonary hypertension, and growth in these children (13,20).

Longitudinal follow-up data from studies like those by Barton (1996), Soliman (2012), and Zhang (2020) (Table 7) demonstrate that improvements in IGF-1 and growth can be sustained up to 12 months post-surgery, with recent cohorts achieving >85% recovery in most parameters. This supports the practice of early surgical intervention combined with ongoing nutritional and endocrine monitoring (11,18,34).

Despite the general pattern of improvement, not all children achieve full catch-up. Children with genetic syndromes, late surgical correction, or residual cardiac anomalies may experience persistent growth impairment. These patients may benefit from targeted growth hormone therapy, although further studies are needed to assess its safety and efficacy in this setting (32).

The data presented here support an evolving paradigm: CHD should be managed not only as a cardiac defect but also as a systemic, metabolic, and endocrine disorder. Growth monitoring, IGF-1 tracking, and nutritional intervention should be integrated into routine CHD care, especially during the perioperative period (31,33).

In summary, children with congenital heart disease—particularly cyanotic types—experience significant growth and IGF-1 suppression preoperatively. Surgical correction facilitates substantial improvements, especially when nutritional supplementation and metabolic monitoring are concurrently optimized. IGF-1 should be adopted as a routine marker of growth recovery in CHD follow-up protocols (29,30,34).

5. Conclusion

Children with congenital heart disease (CHD), particularly those with cyanotic lesions, are at high risk for growth retardation and suppression of the growth hormone–IGF-1 axis due to chronic hypoxia, elevated metabolic demands, and undernutrition. This review demonstrates that both somatic growth and IGF-1 levels are significantly impaired preoperatively, with cyanotic patients more severely affected than acyanotic ones.

Surgical correction of cardiac defects leads to substantial improvements in anthropometric parameters and IGF-1 concentrations, with the most marked gains observed in cyanotic CHD following early intervention. Importantly, the recovery of IGF-1 correlates well with improvements in weight and height, affirming its value as a biomarker of anabolic and metabolic recovery.

Moreover, the synergistic role of nutritional supplementation—through enhanced caloric intake, protein support, and micronutrient repletion—amplifies the beneficial effects of surgery and should be viewed as a standard component of perioperative care.

Overall, the evidence highlights the need for timely surgical intervention, routine nutritional assessment, and endocrine monitoring (including IGF-1) in the comprehensive management of children with CHD. These measures not only improve survival but also promote long-term growth, developmental outcomes, and quality of life.

5.1. Strengths of the Review

This review offers a comprehensive synthesis of both institutional data and published literature spanning three decades, with clear stratification by CHD subtype and integration of seven structured tables and a forest plot. It highlights the dual impact of surgical intervention and nutritional support on growth and IGF-1 recovery, emphasizing IGF-1 as a robust biomarker for somatic rehabilitation. The inclusion of updated literature (up to 2024) and focus on both cyanotic and acyanotic CHD adds to its clinical relevance and applicability in pediatric cardiology and endocrinology.

5.2. Limitations of the Review

The review is limited by the retrospective nature of some included studies, variable follow-up durations, and heterogeneity in surgical timing, nutritional interventions, and IGF-1 assay methodologies. Additionally, while the effect of nutrition is discussed, detailed data on specific supplementation protocols were lacking in many reports, and genetic or syndromic factors influencing growth outcomes were not fully explored.

Recommendations

Prioritize early surgical correction for children with cyanotic and acyanotic CHD to minimize prolonged hypoxia and optimize growth and IGF-1 recovery.

Incorporate routine monitoring of IGF-1 and growth parameters into pre- and postoperative care to identify children at risk of persistent growth failure.

Ensure comprehensive nutritional assessment and intervention, including caloric and micronutrient support, as an integral part of perioperative management in CHD patients.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Authors' Contributions

A.S. conceptualized the review, supervised data analysis, and led manuscript preparation. A.A., M.M.Q., N.A., F.A., S.A., N.AH., N.AL., and N.H. contributed to literature review, data collection, and drafting of results and discussion sections. D.Y. and A.E. assisted in data interpretation, statistical analysis, and critical revision of the manuscript. All authors actively contributed to the writing, approved the final version, and agreed to its submission for publication.

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Statement of informed consent

Informed consent was obtained from all individual participants included in the studies used in this review.

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