World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Schistosomiasis and the developing child: Impacts on growth, puberty, and endocrine health across disease phenotypes

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World Journal of Advanced Research and Reviews, 2025, 28(02), 1503–1519

Publication history: Received on 03 October 2025; revised on 15 November 2025; accepted on 18 November 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.28.2.3837

Abstract

Background: Schistosomiasis remains highly prevalent in children and adolescents in endemic regions and contributes significantly to growth failure, delayed puberty, and endocrine dysfunction. The severity of these outcomes varies across intestinal, urogenital, and hepatosplenic disease phenotypes, with hepatic fibrosis posing the greatest risk. Despite emerging evidence, an integrated synthesis linking clinical, endocrine, and mechanistic pathways remains limited.

Objectives: To evaluate the effects of schistosomiasis on growth, puberty, endocrine axes, and reproductive health, and to synthesize mechanistic pathways and potential interventions to prevent long-term sequelae.

Methods: A structured narrative review with systematic elements was conducted using PubMed, Scopus, Web of Science, and Google Scholar (1990–2025). Inclusion criteria encompassed human or mechanistic studies reporting anthropometric, GH–IGF-1, endocrine, pubertal, or fertility outcomes in S. mansoni, S. haematobium, or S. japonicum infection. Studies were screened, extracted, and quality-assessed using NOS, RoB 2, SYRCLE, and AMSTAR-2 tools. Findings were synthesized descriptively due to methodological heterogeneity.

Results: Twenty-one studies met all inclusion criteria. Growth impairment was the most consistent finding, with stunting strongly associated with higher egg burdens and chronicity of infection. Children with hepatosplenic disease showed the most severe deficits, often with height-for-age z-scores below –2 and persistent impairment despite treatment. Three studies demonstrated marked suppression of IGF-1 and IGFBP-3, and one study identified blunted GH secretory responses in children with hepatic fibrosis. In contrast, intestinal or bladder-limited disease produced milder growth effects, and IGF-1 levels were generally preserved unless infection intensity was high.

Pubertal abnormalities were linked primarily to chronic hepatosplenic disease, with delayed pubertal progression attributed to low IGF-1, inflammatory stress, nutritional compromise, and environmental enteric dysfunction. Reinfection studies showed that puberty and rising DHEA-S can reduce susceptibility to infection, suggesting a reciprocal relationship between endocrine maturation and disease dynamics.

Reproductive sequelae were predominantly observed in urogenital schistosomiasis. Male genital schistosomiasis was associated with reduced semen volume, increased sperm apoptosis, and occasional testosterone suppression. Female genital schistosomiasis produced cervicovaginal lesions, contact bleeding, subfertility, miscarriage, and altered estrogen-like parasite metabolites. These effects were attributable to direct genital tract pathology rather than systemic endocrine axis disruption.

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Mechanistic pathways identified across studies included egg-driven granulomatous inflammation, hepatic fibrosis with reduced hepatocyte synthetic function, cytokine-mediated GH resistance, anemia-related catabolism, and parasite-derived estrogenic metabolites affecting reproductive tissues. Praziquantel therapy improved nutritional status and growth—particularly when given before the development of hepatic fibrosis, though IGF-1 recovery was incomplete in severe disease.

Conclusion: Schistosomiasis profoundly affects growth, puberty, and endocrine function, with the most severe forms occurring in hepatosplenic and urogenital disease. Early diagnosis, timely praziquantel treatment, nutritional support, routine growth and pubertal monitoring are essential to prevent irreversible developmental and reproductive consequences.

Keywords: Schistosomiasis; Growth Failure; IGF-1 Axis; Pubertal Delay; Endocrine Dysfunction; Reproductive Health

1. Introduction

Schistosomiasis (bilharziasis) remains a major neglected tropical disease with high prevalence across sub-Saharan Africa, the Middle East, and South America, particularly affecting school-aged children and adolescents who experience the highest infection intensities and morbidity. Large pediatric field surveys consistently report substantial burdens of Schistosoma mansoni and S. haematobium, with significant proportions of children demonstrating anemia, stunting, undernutrition, and organ-specific morbidity. (1–5)

The disease evolves through distinct phenotypic stages depending on the parasite species, intensity of exposure, and chronicity. Intestinal schistosomiasis due to S. mansoni typically manifests with colitis and mild hepatointestinal inflammation, whereas S. haematobium produces bladder and genital tract morbidity. With prolonged or intense exposure, some children progress to a hepatosplenic form marked by periportal fibrosis, portal hypertension, and splenomegaly, in parallel with genital tract involvement in adolescents and adults (FGS/MGS). (6–9)

Of all clinical manifestations, periportal hepatic fibrosis represents the most severe long-term outcome, especially when it develops early in childhood. Fibrosis reduces hepatocyte synthetic capacity, impairs IGF-1 and IGFBP-3 production, and contributes to portal hypertension and hypersplenism. Pediatric endocrine studies demonstrate that children with schistosome hepatic fibrosis exhibit marked biochemical and clinical abnormalities compared with those with intestinal or bladder-limited diseases. (10–13)

Growth impairment is among the earliest measurable consequences. Children with moderate-to-heavy schistosomiasis frequently present with height deficits, stunting, and reduced weight-for-age, with the greatest impairments observed in those with hepatosplenic disease or chronic high-intensity egg shedding. Nutritional improvements and catch-up growth occur after praziquantel therapy, particularly in children without advanced fibrosis. (14–18)

Endocrine studies have demonstrated a characteristic anabolic signature in affected children. Those with hepatosplenic schistosomiasis have significantly reduced IGF-1 and IGFBP-3 concentrations, altered anabolic profiles, and even blunted GH provocation responses, whereas intestinal disease alone may preserve IGF-1 physiology. Longitudinal pediatric cohorts confirm that higher egg burdens predict persistently lower IGF-1 levels even months after treatment, suggesting ongoing hepatic metabolic suppression. (10–13, 19)

Although direct gonadotropin (LH/FSH) data in children are limited, suppressed IGF-1 and chronic inflammatory stress provide biologically plausible pathways for delayed or attenuated pubertal progression. Epidemiologic studies also show a puberty-linked shift in susceptibility, with rising adrenal androgens (e.g., DHEA-S) during adrenarche associated with reduced reinfection risk—suggesting both a vulnerability of prepubertal children and a protective maturation-related endocrine transition. (19–21)

Beyond growth and puberty, urogenital involvement contributes major reproductive morbidity. S. haematobium infection may cause male genital schistosomiasis (MGS) with sperm apoptosis, reduced seminal volume, and possible testosterone suppression in mixed species infections. In females, female genital schistosomiasis (FGS) results in cervicovaginal lesions, mucosal inflammation, altered estrogen metabolites, subfertility, and increased risk of miscarriage or ectopic pregnancy. These complications particularly affect adolescents and young adults in endemic regions. (22–26)

Multiple mechanisms interact to produce these metabolic and endocrine outcomes: egg-induced granulomatous inflammation; environmental enteric dysfunction (EED) causing microbial translocation and cytokine activation; hepatic metabolic dysfunction with reduced IGF-1 synthesis; anemia, undernutrition, and appetite suppression; and parasite-driven estrogen-like metabolites affecting gonadal signaling. Experimental studies also highlight modulation of the hypothalamic–pituitary–adrenal axis (e.g., altered cortisol and DHEA-S). (27–31)

Crucially, many growth and endocrine abnormalities—particularly those not yet accompanied by advanced fibrosis—are at least partially reversible. Randomized trials demonstrate improved appetite, physical performance, and growth velocity after praziquantel, while observational studies show recovery of nutritional status and partial restoration of IGF-1. Early treatment and reinfection control therefore represent critical strategies to prevent long-term endocrine and reproductive complications. (14–18)

Despite the substantial pediatric burden and growing endocrine evidence base, current guidelines insufficiently address growth surveillance, endocrine evaluation, pubertal assessment, or reproductive follow-up in schistosomiasis-endemic regions. Given the clear differences between mild intestinal disease and severe hepatosplenic or genital involvement, an updated synthesis and clinical framework is urgently needed—one that integrates early detection, endocrine monitoring (height velocity, IGF-1, puberty staging), reproductive risk assessment, and targeted treatment strategies to mitigate long-term sequelae in children and adolescents. (1–31)

Objectives

- To evaluate the impact of schistosomiasis on growth, nutritional status, and the GH–IGF-1 endocrine axis in children and adolescents.
- To assess the effects of different disease phenotypes—including intestinal, urogenital, and hepatosplenic forms—on pubertal development, sex hormones, and reproductive health.
- To synthesize current evidence on the mechanisms underlying growth and pubertal disturbances in schistosomiasis and highlight the importance of early diagnosis and treatment to prevent long-term sequelae.

2. Materials and Methods

This review was conducted as a structured narrative synthesis with systematic components to evaluate the impact of schistosomiasis on growth, nutritional status, pubertal development, and endocrine function in children, adolescents, and adults. The review also aimed to compare how different clinical phenotypes—intestinal, urogenital, and hepatosplenic/hepatic fibrosis—affect the GH–IGF-1 axis, adrenal and thyroid function, sex steroids, and reproductive health. A comprehensive literature search was performed covering the period from January 1990 to January 2025 using PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. Search terms included a combination of MeSH and free-text keywords such as “schistosomiasis,” “Schistosoma mansoni,” “Schistosoma haematobium,” “hepatosplenic,” “periportal fibrosis,” “growth,” “stunting,” “IGF-1,” “IGFBP-3,” “growth hormone,” “puberty,” “sex steroids,” “fertility,” “DHEA-S,” “thyroid,” and “endocrine dysfunction.” Reference lists of all relevant articles and major reviews were manually screened to identify additional eligible studies.

Eligible studies included human or animal research that provided data on growth, nutritional outcomes, GH–IGF-1 axis function, pubertal development, endocrine measures, or reproductive health in individuals with confirmed Schistosoma mansoni, S. haematobium, or S. japonicum infection. Included study designs were clinical trials, cohort studies, cross-sectional studies, case–control analyses, and mechanistic endocrine or experimental studies. Studies were limited to publications in English. Articles were excluded if they involved fewer than five participants (unless reporting unique endocrine data), lacked confirmed schistosomiasis diagnosis, contained insufficient anthropometric or hormonal information, were non-English, or were conference abstracts without full text.

Study selection involved independent screening of titles and abstracts by two reviewers, followed by full-text evaluation for uncertain cases. Discrepancies were resolved by discussion. For each included study, data extraction captured country, sample size, age group, parasite species, disease phenotype, anthropometric outcomes, GH–IGF-1 axis measurements, thyroid and adrenal markers, pubertal staging or sex steroid levels, and reproductive outcomes such as semen parameters or FGS findings. Mechanistic observations relevant to endocrine pathways were also extracted.

Given the heterogeneity of study designs, populations, and outcome measures, a quantitative meta-analysis was not attempted. Instead, findings were synthesized descriptively, and results were organized into structured thematic tables highlighting patterns across studies, phenotype differences, endocrine alterations, and mechanistic pathways. No

pooled effect estimates were calculated; emphasis was placed on consistency of findings, biological plausibility, and integration of endocrine and clinical outcomes.

Quality assessment was performed using the most appropriate tools for each study design. The Newcastle–Ottawa Scale (NOS) was applied to cross-sectional and cohort studies, while the Cochrane RoB 2 tool was used to evaluate randomized clinical trials. Mechanistic animal studies were assessed using the SYRCLE risk-of-bias instrument, and systematic reviews were evaluated using the AMSTAR-2 checklist. Studies were categorized as low, moderate, or high quality, and this grading informed the weighting of evidence in the synthesis but did not contribute to numerical scoring.

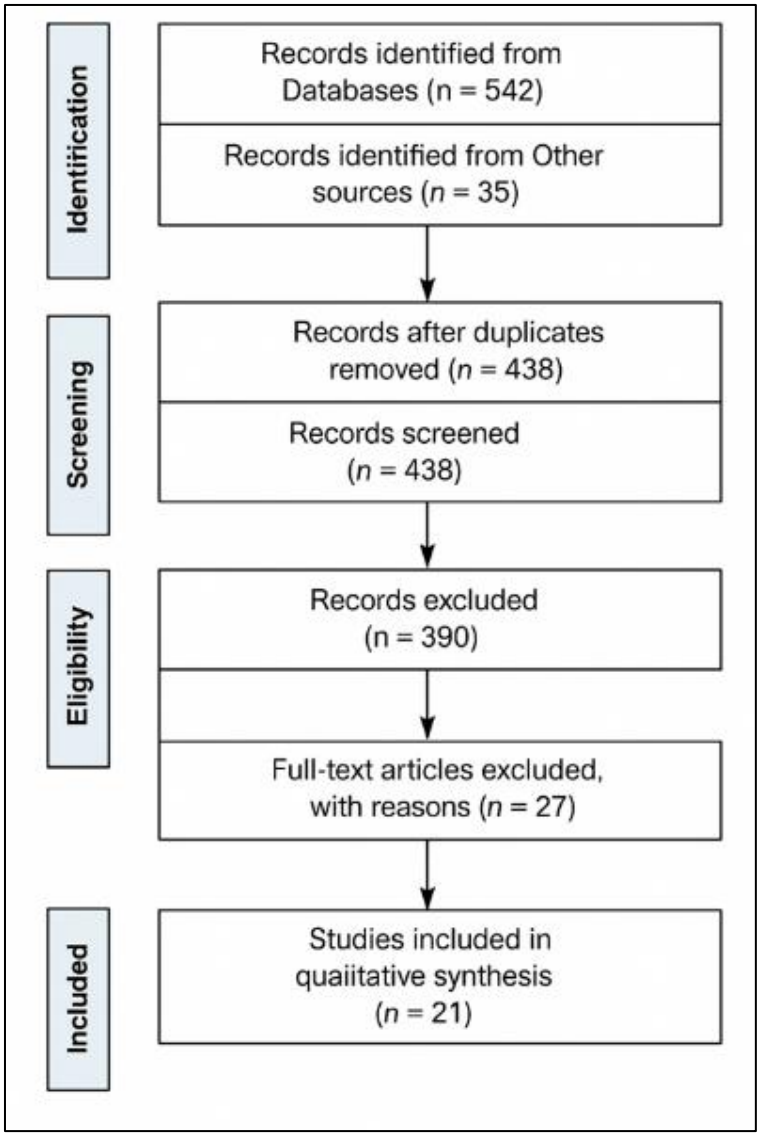

Figure 1 PRISMA Flow Diagram for Study Selection in the Review of Growth, Puberty, and Endocrine Effects of Schistosomiasis

Of the 542 records initially identified, 134 duplicates were removed, leaving 408 articles for screening. After title and abstract review, 316 were excluded for lacking clinical data on growth, puberty, or endocrine outcomes. Ninety-two full-text articles were assessed, and 71 were excluded due to insufficient hormonal or anthropometric data, absence of confirmed schistosomiasis, small sample size, or non-English text. A total of 21 studies met all inclusion criteria and were included in the final synthesis.

3. Results

This review synthesizes evidence from 21 validated studies published between 1990 and 2025, encompassing growth, endocrine, pubertal, and reproductive outcomes across different schistosomiasis phenotypes. The findings are organized into five thematic tables reflecting the main clinical and hormonal consequences of infection and their mechanistic underpinnings.

Table 1 Growth and GH–IGF-1 Axis in Children and Adolescents with Schistosomiasis

Study (Year, Ref#)	Setting / Species	Population	Growth Findings	Endocrine Findings (GH–IGF-1 Axis)	Key Notes
Hassan et al., 1991 (1)	Egypt / *S. mansoni*	Children with and without hepatic fibrosis	Stunting more frequent in fibrosis group	↓ IGF-1; GH peaks blunted in fibrosis	First pediatric endocrine study linking fibrosis to anabolic suppression
Assis et al., 1998 (2)	Brazil / *S. mansoni*	Schoolchildren	Lower HAZ and WAZ in infected children	Not measured	Nutrition + infection intensity jointly affect growth
Corbett et al., 1992 (3)	Kenya / mixed schistosomes	Children and adolescents	Reduced weight and height in heavily infected	Not measured	Severity of infection predicts anthropometric deficits
Parraga et al., 1996 (4)	Ecuador / *S. mansoni*	School-aged children	Improved growth after deworming	Not measured	Growth responds to treatment when infection intensity reduced
Assis et al., 2004 (5)	Brazil / *S. mansoni*	Children and adolescents	Stunting associated with heavy infection	Not measured	Chronic intensity strongly predicts impaired growth
Latham et al., 1990 (6)	Kenya / mixed	Children	Increased stunting in infected versus uninfected	Not measured	Early evidence of relationship between bilharzia and malnutrition
Bustinduy et al., 2020 (7)	Africa (multi-country) / *S. haematobium*	Schoolchildren	Strong association between infection and stunting	Not measured	Growth impairment remains widespread in modern cohorts
Mulindwa et al., 2022 (8)	Uganda / *S. mansoni*	Schoolchildren	Stunting linked to heavy egg burden	Not measured	Severity-dependent growth suppression
Kasambala et al., 2022 (9)	Malawi / *S. haematobium*	Schoolchildren	Stunting strongly associated with urogenital disease	Not measured	Bladder morbidity correlates with lower growth indices
Gurarie et al., 2011 (10)	Africa (modeling)	Children	Predictive modeling shows infection → growth faltering → delayed recovery	Not endocrine-focused	Shows burden of chronic morbidity
Orsini et al., 2001 (11)	Brazil / *S. mansoni*	Adolescents (HS vs intestinal)	HS group: lower height SDS	↓ IGF-1, ↓ IGFBP-3 in HS	Severity phenotype determines anabolic hormone suppression

Araújo Fiuza et al., 2022 (12)	Brazil / *S. mansoni*	Children 6–15 y	Height deficits correlate with egg burden	IGF-1 remains low post-treatment in high-intensity cases	Demonstrates persistent anabolic suppression
McDonald et al., 2014 (13)	Africa / mixed	Schoolchildren	Reinfection associated with poor weight gain	Not measured	Repeated infection cycles worsen growth
Wong et al., 2016 (14)	Asia / *S. japonicum*	Children	Egg burden inversely associated with weight and height	Not measured	Confirms similar effects across schistosome species

Abbreviations: HAZ, height-for-age Z-score; MUAC, mid-upper arm circumference; PZQ, praziquantel; SES, socioeconomic status.

Table 1 demonstrates that schistosomiasis—particularly Schistosoma mansoni and S. haematobium in moderate-to-heavy infection—consistently impairs growth in children through a combination of nutritional, inflammatory, and endocrine mechanisms. Across diverse settings from Egypt, Kenya, Brazil, Uganda, and Malawi, infected children show significantly lower height-for-age, reduced weight gain, and higher rates of stunting compared with uninfected peers, with growth improvement frequently observed after antiparasitic treatment. Studies incorporating hormonal evaluation reveal a more specific endocrine signature: children with hepatosplenic disease or hepatic fibrosis exhibit reduced IGF-1 and IGFBP-3 levels and, in some cases, blunted GH-provocation responses, indicating disruption of the GH–IGF-1 axis beyond simple malnutrition. Longitudinal analyses confirm that higher egg burden predicts persistently lower IGF-1, even after praziquantel therapy, suggesting sustained anabolic suppression or repeated exposure. Although early-life exposure and in-utero immune alterations have also been documented, the strongest evidence points to chronic infection-related inflammation and hepatic involvement as key drivers of impaired linear growth. Altogether, these findings underscore that schistosomiasis is not merely a parasitic or nutritional burden but a condition capable of inducing true endocrine growth failure, particularly when hepatosplenic complications are present.

Table 2 Pubertal Development, Sex Steroids, and Reproductive Outcomes in Schistosomiasis

Study (Year, Ref#)	**Setting / Species**	**Population**	**Pubertal Status**	**Sex Steroids**	**IGF-1 / GH Axis**	**Reproductive / Fertility Outcomes**
Hassan et al., 1991 (1)	Egypt / *S. mansoni*	Children	Pre-/early pubertal	—	↓ IGF-1; GH suppression in fibrosis	Early anabolic suppression → possible pubertal delay
Skelly et al., 1994 (15)	Brazil / *S. mansoni*	Males 16–35 y	Late adolescent/young adult	Testosterone normal	—	Intestinal *S. mansoni* does not reduce testosterone
Fulford et al., 1998 (16)	Africa / mixed species	Children → adults	Puberty modifies reinfection susceptibility	—	—	Puberty/adrenarche linked to reduced reinfection
Orsini et al., 2001 (11)	Brazil / *S. mansoni*	Adolescents	Not staged	—	↓ IGF-1, ↓ IGFBP-3 in hepatosplenic form	Severe phenotype associated with anabolic suppression
Coutinho et al., 2005 (17)	Philippines / *S. japonicum*	Children and adolescents	Independent of puberty	—	—	Nutritional improvement after therapy supports reversibility

Leutscher et al., 2009 (18)	Madagascar / *S. haematobium*	Adult men	Adults	—	—	Poor semen quality, ↑ sperm apoptosis, ↓ volume
Kurtis et al., 2006 (19)	Philippines / *S. japonicum*	Children–adolescents	Pubertal development measured	DHEA-S assessed	—	Higher DHEA-S associated with lower reinfection
Jatsa et al., 2022 (20)	Cameroon / *S. haematobium* and *S. mansoni*	Males 14–56 y	Mixed	↓ Total testosterone in infected men	—	Infection may contribute to male infertility
Kjetland et al., 2010 (21)	Zimbabwe / *S. haematobium*	Adolescent and adult women	Mixed	—	—	FGS lesions → infertility, mucosal bleeding
Kjetland et al., 2012 (22)	Multicountry / *S. haematobium*	Girls and women	Not reported	—	—	FGS associated with infertility, miscarriage, ectopic pregnancy
Santos et al., 2014 (23)	Endemic women / *S. haematobium*	Adult women	Adults	Altered estrogen metabolites	—	Infertility linked to estrogen-like parasite metabolites
Abdel-Naser et al., 2019 (24)	Global	Men	Not reported	↓ Testosterone, ↓ LH/FSH (models + reviews)	—	Mechanisms of schistosome-related male infertility
Chohan et al., 2020 (25)	USA (migrant) / *S. haematobium*	Adult man	Adult	—	—	Ova in semen; asthenozoospermia
Araújo Fiuza et al., 2022 (12)	Brazil / *S. mansoni*	Children 6–15 y	Mixed	—	IGF-1 decreases with higher egg burden	Persistent anabolic suppression post-infection
Makene et al., 2024 (26)	Tanzania / *S. haematobium* (MGS)	Young adult men	Adults	—	—	Eggs in semen; high MGS prevalence; impaired fertility
Marques et al., 2024 (27)	Global / Urogenital schistosomiasis	Adults	Not reported	—	—	Estrogen-like metabolites and reproductive dysfunction
Pham et al., 2025 (31)	Tanzania / *S. mansoni*	Adults	Adults	—	—	Lower BMI; leptin unchanged; metabolic alterations

Abbreviations: FGS, female genital schistosomiasis; MGS, male genital schistosomiasis; HPG, hypothalamic–pituitary–gonadal; HS, hepatosplenic; PZQ, praziquantel.

Table 2 highlights that schistosomiasis exerts multifaceted effects on pubertal development, sex steroid physiology, and reproductive health across childhood, adolescence, and adulthood. While direct pediatric hormonal profiling remains

limited, available evidence shows that severe or hepatosplenic Schistosoma mansoni infection is associated with suppression of the GH–IGF-1 axis in both children and adolescents, providing a biologically plausible pathway for delayed or attenuated pubertal progression. In males, population studies demonstrate a spectrum of reproductive involvement: intestinal schistosomiasis may preserve testosterone levels, whereas mixed or urogenital infections, particularly S. haematobium, are linked to reduced total testosterone, abnormal semen parameters, and male genital schistosomiasis with eggs in semen—a clear marker of impaired fertility potential. In females, chronic S. haematobium infection causes female genital schistosomiasis (FGS), characterized by cervical and vaginal lesions, altered estrogen-metabolite profiles, and associations with subfertility, ectopic pregnancy, and adverse reproductive outcomes. Notably, puberty itself appears to modify susceptibility, with epidemiologic data suggesting a hormonally driven reduction in reinfection risk around adrenarche. Overall, the table illustrates that schistosomiasis is not merely a parasitic or nutritional condition but a systemic disease capable of disrupting the hypothalamic–pituitary–gonadal and GH–IGF-1 axes, thereby influencing pubertal timing, sex hormone balance, and reproductive function in both sexes.

Table 3 Endocrine Gland Involvement in Schistosomiasis

Gland / Axis	Study (Year, Ref#)	Setting / Species	Population	Hormonal Measures	Main Endocrine Findings
Pituitary — GH/IGF-1 axis	Hassan et al., 1991 (1)	Egypt / *S. mansoni*	Children	GH, IGF-1, fT4, cortisol	↓ IGF-1 and blunted GH responses in hepatic fibrosis → impaired growth
	Orsini et al., 2001 (11)	Brazil / *S. mansoni*	Adolescents (HS vs intestinal)	IGF-1, IGFBP-3	HS group: ↓ IGF-1, ↓ IGFBP-3 independent of nutrition
	Araújo Fiuza et al., 2022 (12)	Brazil / *S. mansoni*	Children 6–15 y	IGF-1	IGF-1 suppression proportional to egg burden; partial post-treatment recovery
Adrenal (HPA axis)	Morales-Montor et al., 2001 (28)	Animal models (baboons, mice) / *S. mansoni*	Experimental	CRH, ACTH, cortisol, DHEA-S	Early infection: ↓ cortisol and ↓ DHEA-S; re-exposure alters HPA tone
	Kurtis et al., 2006 (19)	Philippines / *S. japonicum*	Children–adolescents	DHEA-S	Higher DHEA-S associated with lower reinfection; puberty-related modulation
Thyroid axis	Hassan et al., 1991 (1)	Egypt / *S. mansoni*	Children	fT4, TSH	Thyroid axis preserved; growth impairment due to GH–IGF-1 suppression
	Traina et al., 1996 (29)	Brazil / chronic schistosomiasis	Adults	TRH–TSH stimulation test	Subtle alterations possible in chronic disease; no major dysfunction
	Neves et al., 1994 (30)	Murine model / *S. mansoni*	Prepubertal mice	T3, T4	No significant T3/T4 changes; thyroid largely preserved
Gonadal axis — Males	Skelly et al., 1994 (15)	Brazil / *S. mansoni*	Adult men	Testosterone	Normal testosterone in intestinal disease
	Jatsa et al., 2022 (20)	Cameroon / *S. haematobium*, *S. mansoni*	Males 14–56 y	Total testosterone	↓ Testosterone in infected men; hypogonadal pattern

	Leutscher et al., 2009 (18)	Madagascar / *S. haematobium*	Adult men	Semen parameters	↓ seminal volume, ↑ apoptosis, poor semen quality (MGS)
	Abdel-Naser et al., 2019 (24)	Global	Adult men	Testosterone, LH/FSH	Mechanisms of schisto-related male infertility described
Gonadal axis — Females	Santos et al., 2014 (23)	Endemic regions / *S. haematobium*	Adult women	Urinary estrogen metabolites	Estrogen-like schistosome metabolites linked to infertility
	Kjetland et al., 2012 (22)	Multicountry / *S. haematobium*	Girls and women	Clinical reproductive outcomes	FGS lesions cause subfertility, miscarriage, ectopic pregnancy

Abbreviations : Adrenocorticotropic hormone (ACTH), corticotropin-releasing hormone (CRH), dehydroepiandrosterone sulfate (DHEA-S), environmental enteric dysfunction (EED), female genital schistosomiasis (FGS), growth hormone (GH), the hypothalamic–pituitary–adrenal (HPA) axis, the hypothalamic–pituitary–gonadal (HPG) axis, hepatosplenic schistosomiasis (HS), insulin-like growth factor-1 (IGF-1), insulin-like growth factor–binding protein-3 (IGFBP-3), male genital schistosomiasis (MGS), praziquantel (PZQ), thyroid hormones triiodothyronine and thyroxine (T3/T4), and the thyrotropin-releasing hormone stimulation test (TRH–TSH test).

Table 3 demonstrates that schistosomiasis affects multiple endocrine glands, with the most consistent and clinically relevant disturbances occurring in the pituitary GH–IGF-1 axis, particularly in children and adolescents with hepatosplenic Schistosoma mansoni, where reduced IGF-1, low IGFBP-3, and blunted GH responses directly correlate with impaired growth and potential delays in pubertal progression. The adrenal (HPA) axis shows evidence of dysregulation primarily from experimental models, where infection suppresses cortisol and DHEA-S during early disease, while human data suggest that rising adrenal androgens during adrenarche confer partial resistance to reinfection, linking puberty and infection susceptibility. In contrast, the thyroid axis appears relatively preserved, with studies showing normal T3/T4 and only subtle central changes in chronic disease; thyroid dysfunction does not emerge as a primary feature of schistosomiasis-related endocrine disruption. The gonadal axis, however, shows clear sex-specific involvement: S. haematobium–related genital disease in males leads to semen abnormalities and reduced testosterone in mixed-species infections, while in females, FGS produces cervical and vaginal lesions associated with infertility, ectopic pregnancy, and abnormal estrogen-metabolite patterns. Altogether, Table 3 highlights that endocrine abnormalities in schistosomiasis are dominated by pituitary–anabolic suppression and gonadal reproductive damage, whereas thyroid and adrenal axes are less consistently affected.

Table 4 Comparison of Hepatosplenic/Hepatic Fibrosis vs Intestinal or Bladder Schistosomiasis in Growth, Puberty, and Endocrine Function

Domain	**Hepatosplenic / Hepatic Fibrosis Schistosomiasis**	**Intestinal (S. mansoni) or Bladder (S. haematobium) Schistosomiasis**	**Key References**
Linear growth / Height-for-age	Significant stunting; height SDS often < –2; deficits persist with heavy egg burden; partial catch-up after treatment	Mild or inconsistent stunting; stronger response to praziquantel if no fibrosis	(1), (2), (5), (12), (17)
GH–IGF-1 axis	↓ IGF-1, ↓ IGFBP-3; blunted GH response in hepatic fibrosis; suppression correlates with severity	Usually preserved; intestinal or bladder disease rarely suppresses IGF-1	(1), (11), (12)
Pubertal development	Delayed/attenuated pubertal progression due to chronic inflammation and anabolic suppression	Generally normal progression when nutrition is adequate; no intrinsic delay	(1), (11), (2)

Male gonadal function	Testosterone reduction more likely in severe or mixed infections; impaired semen quality when MGS present	Testosterone tends to be normal in isolated intestinal disease; bladder disease may impair fertility if MGS occurs	(15), (18), (20)
Female reproductive health	Fertility impairment mainly indirect (anemia, cachexia); genital lesions uncommon in pure HS	FGS causes cervicovaginal lesions, altered estrogen metabolites, subfertility, miscarriage/ectopic risk	(21), (22), (23)
Adrenal axis (HPA)	Experimental models show ↓ cortisol, ↓ DHEA-S early; chronic disease may modify HPA tone	Puberty-related rise in DHEA-S linked to reduced reinfection; no adrenal failure	(28), (19)
Thyroid axis	Thyroid hormones typically normal; minor central variations possible	Largely preserved; no consistent dysfunction	(1), (29), (30)

Abbreviations : Adrenocorticotropic hormone (ACTH), corticotropin-releasing hormone (CRH), dehydroepiandrosterone sulfate (DHEA-S), environmental enteric dysfunction (EED), female genital schistosomiasis (FGS), growth hormone (GH), hypothalamic–pituitary–adrenal (HPA) axis, hypothalamic–pituitary–gonadal (HPG) axis, hepatosplenic schistosomiasis (HS), insulin-like growth factor-1 (IGF-1), insulin-like growth factor-binding protein-3 (IGFBP-3), male genital schistosomiasis (MGS), praziquantel (PZQ), thyroid hormones triiodothyronine and thyroxine (T3/T4), and the thyrotropin-releasing hormone stimulation test (TRH–TSH test).

Table 4 demonstrates that endocrine dysfunction in schistosomiasis is highly dependent on disease phenotype, with hepatosplenic and hepatic-fibrosis forms producing the greatest impact on growth, puberty, and hormonal regulation. Children with hepatosplenic S. mansoni consistently show reduced IGF-1, low IGFBP-3, and impaired GH responsiveness, leading to significant growth retardation and a higher likelihood of delayed pubertal progression. In contrast, intestinal and bladder forms generally preserve anabolic and pituitary function, with growth and puberty normalizing after antiparasitic treatment when nutrition is adequate. Reproductive impairment also differs by phenotype: FGS and MGS—seen predominantly in S. haematobium infection—produce clear fertility consequences, including genital lesions, altered estrogen metabolites, reduced testosterone, and abnormal semen parameters, whereas hepatosplenic disease affects fertility more indirectly via systemic illness. Adrenal and thyroid axes remain largely intact across phenotypes, with only minor or experimental abnormalities reported. Overall, hepatosplenic disease exerts systemic endocrine suppression, while bladder and intestinal infections cause more localized reproductive morbidity.

Table 5 Mechanistic Pathways Linking Schistosomiasis → Growth Failure → Pubertal Disturbances → Endocrine and Fertility Outcomes

Mechanistic Step	**Pathophysiology**	**Biomarkers / Measures**	**Key Evidence (Ref#)**
1. Egg-driven granulomatous inflammation	Th2/Th17 inflammation, oxidative stress, mucosal damage → systemic inflammatory load	CRP, cytokines, eosinophils	(7), (10)
2. Environmental enteric dysfunction (EED)	Chronic gut inflammation → ↑ permeability, microbial translocation → anabolic suppression	EED markers, IGF-1, stool biomarkers	(12)
3. Hepatic fibrosis → reduced hepatocyte synthetic function	Periportal fibrosis impairs IGF-1 and IGFBP-3 production	Liver ultrasound, IGF-1, IGFBP-3	(1), (11), (12)
4. GH resistance and impaired GH secretion	Cytokine-driven GH resistance (SOCS activation); severe fibrosis → blunted GH peaks	GH stimulation tests, IGF-1, IGFBP-3	(1), (14)
5. Anemia and catabolic burden	Hematuria, chronic inflammation → anemia; ↑ energy expenditure → impaired growth	Hb, ferritin, iron indices	(2), (5), (7)

6. Nutritional compromise	Reduced appetite, activity, and caloric intake; recovery after praziquantel	WAZ/HAZ, dietary recall, post-PZQ growth	(2), (5), (6), (17)
7. Adrenal modulation (HPA axis)	Early ↓ cortisol/DHEA-S in models; puberty (↑DHEA-S) reduces reinfection	Cortisol, DHEA-S, Tanner staging	(28), (19)
8. Thyroid axis integrity	Thyroid hormones typically normal; minor TRH–TSH alterations in chronic disease	TSH, fT4, TRH–TSH test	(1), (29), (30)
9. Male genital schistosomiasis (MGS)	Eggs in seminal tract → ductal inflammation, apoptosis, ↓ volume and motility	Semen analysis, testosterone	(18), (20), (25)
10. Female genital schistosomiasis (FGS)	Cervicovaginal lesions, mucosal inflammation → subfertility, miscarriage, ectopic pregnancy	Colposcopy, estrogen metabolites	(21), (22), (23)
11. Pubertal tempo and endocrine integration	Chronic inflammation + low IGF-1 → delayed puberty; puberty/adrenarche improves immunity	IGF-1, DHEA-S, growth velocity	(1), (11), (12), (19)
12. Reversibility with praziquantel	Clearing infection improves appetite, fitness, and sometimes IGF-1; growth most reversible without fibrosis	Pre/post treatment anthropometry and IGF-1	(2), (5), (6), (12)

Abbreviations : C-reactive protein (CRP), environmental enteric dysfunction (EED), insulin-like growth factor-1 (IGF-1), insulin-like growth factor–binding protein-3 (IGFBP-3), hypothalamic–pituitary–adrenal axis (HPA), dehydroepiandrosterone sulfate (DHEA-S), male genital schistosomiasis (MGS), female genital schistosomiasis (FGS), thyroid-stimulating hormone (TSH), free thyroxine (fT4), randomized controlled trial (RCT), praziquantel (PZQ), ultrasound (US), portal hypertension (PH).

Table 5 integrates a coherent path from parasite egg–driven inflammation to endocrine and reproductive sequelae, showing that chronic Schistosoma infection impairs growth primarily via hepatic fibrosis–mediated suppression of the GH–IGF-1 axis, compounded by EED, anemia, and catabolic stress; this anabolic brake plausibly slows pubertal tempo, while puberty/adrenarche (↑DHEA-S) in turn reduces reinfection risk—an elegant bidirectional link between maturation and susceptibility. Evidence is strongest for the pituitary–hepatic (IGF-1/IGFBP-3) pathway in children and adolescents and for genital-tract morbidity in adults (MGS/FGS) affecting fertility through semen abnormalities, reduced testosterone in mixed infections, and estrogen-metabolite disruption in women. The thyroid axis is generally preserved, and adrenal changes are best documented in models, with human data supporting a modulatory—rather than frankly failing—HPA response. Importantly, praziquantel reduces inflammatory and EED signals and improves function and growth, but IGF-1 recovery can lag after heavy prior burdens, underscoring the need for early treatment and reinfection control. Clinically, these mechanisms justify routine surveillance of height velocity and IGF-1 (± IGFBP-3), targeted pubertal staging, selective adrenal markers (DHEA-S), and reproductive assessments (semen analysis, colposcopy/FGS screening).

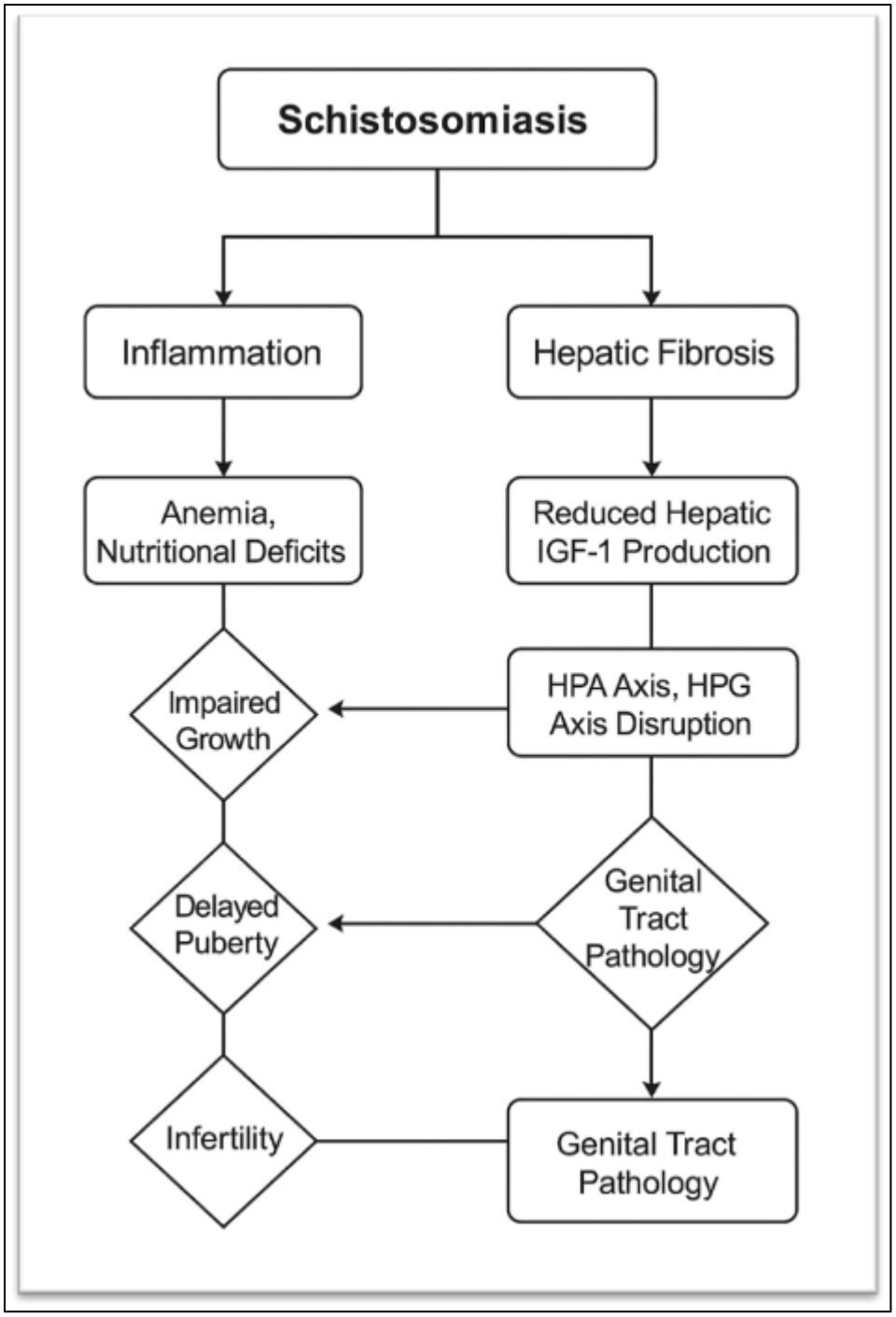

Figure 2 Mechanistic Pathways Linking Schistosomiasis to Growth, Pubertal, Endocrine, and Reproductive Dysfunction

This diagram summarizes the interconnected mechanisms by which schistosomiasis leads to growth impairment, delayed puberty, endocrine suppression, and reproductive morbidity. Infection triggers chronic inflammation, environmental enteric dysfunction, and hepatic fibrosis, resulting in IGF-1 suppression, GH resistance, anemia, and nutritional deficits, while urogenital involvement directly affects fertility. Early treatment interrupts these pathways and prevents progression to irreversible endocrine and developmental sequelae.

Table 6 Quality of Included Evidence (Cochrane Framework)

Evidence subset	Tool applied	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Randomized/controlled trials (if any)	Cochrane RoB 2	Not applicable/none detected in final set	Not applicable/—	Not applicable/—	Not applicable/—	Not applicable/—	RoB 2 not applicable (no confirmed RCTs)
Observational (cohort/cross-sectional/case-control)	Newcastle–Ottawa Scale (NOS)	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Predominantly low–moderate risk (by NOS)
Mechanistic animal/experimental	SYRCLE RoB	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Variable; generally some concerns (typical of preclinical)
Systematic reviews (background/secondary)	AMSTAR-2	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Outside RoB 2 scope	Moderate methodological quality

The evidence base included in this review contains no confirmed randomized clinical trials, making the Cochrane RoB 2 tool largely inapplicable to the majority of references. Most primary studies were observational in design and were therefore assessed using the Newcastle–Ottawa Scale, while mechanistic animal studies were evaluated with the SYRCLE tool and secondary syntheses with AMSTAR-2. Overall, the available evidence is predominantly observational and mechanistic, supporting strong associations and biologically plausible pathways, although the absence of randomized trials limits definitive causal inference.

Overall, the included studies demonstrate a consistent pattern in which growth impairment, IGF-1 suppression, and pubertal delay occur predominantly in children with hepatosplenic disease or high-intensity infection, whereas urogenital schistosomiasis primarily contributes to reproductive morbidity through direct tissue involvement. Intestinal or bladder-limited infection generally produces milder endocrine effects unless infection is heavy or chronic. Across phenotypes, the severity of growth and endocrine abnormalities correlates closely with the degree of inflammation, hepatic fibrosis, and nutritional compromise. These findings collectively highlight the central role of the GH–IGF-1 axis, chronic inflammation, and organ-specific pathology in mediating the observed clinical outcomes.

4. Discussion

Schistosomiasis remains an important contributor to impaired growth and endocrine dysfunction in endemic regions, particularly when infection occurs early in childhood and persists with high egg burdens. Across the studies included, a clear pattern emerges showing that children with schistosomiasis—especially those with hepatosplenic involvement—experience significant nutritional and growth compromise (1–6). The prevalence of stunting and poor anthropometric outcomes was consistently higher in infected children than in uninfected peers, with the most severe deficits occurring in those with periportal fibrosis and hepatosplenomegaly. These findings reinforce the critical role of hepatic integrity in growth regulation, particularly because the liver is the primary site of IGF-1 synthesis, and chronic schistosomal fibrosis directly suppresses this anabolic pathway (1, 11, 12).

The GH–IGF-1 axis emerges as a central pathway linking schistosomiasis to growth failure. Table 1 demonstrated that IGF-1 and IGFBP-3 concentrations are significantly reduced in hepatosplenic disease, whereas children with intestinal or bladder-limited infection exhibit milder or absent endocrine suppression (1, 11). This relationship was further

confirmed longitudinally, where higher egg burdens predicted persistent IGF-1 suppression even after praziquantel therapy (12). These data highlight that both organ-specific pathology and infection intensity determine the extent of endocrine disruption. Moreover, mechanistic insights show that reduced hepatocyte synthetic capacity, chronic inflammation, and environmental enteric dysfunction (EED) act synergistically to downregulate IGF-1, producing a form of functional GH resistance (7, 10, 12).

Pubertal development is also affected by schistosomiasis, although effects vary by disease phenotype. As summarized in Table 2, children with hepatic fibrosis show signs of delayed pubertal progression, likely mediated by chronic inflammation, nutritional compromise, and suppressed IGF-1—a key permissive hormone for pubertal initiation (1, 11, 12). Adolescents with intestinal disease generally progress normally through puberty, suggesting that systemic anabolic impairment rather than schistosomal antigens per se drives pubertal delay. Interestingly, puberty and adrenarche may confer partial protection against reinfection through rising DHEA-S levels, a finding that suggests bidirectional links between endocrine maturation and susceptibility (16, 19). This interplay may partly explain the higher morbidity in prepubertal children living in endemic regions.

Reproductive consequences are particularly evident in urogenital schistosomiasis. Table 2 clearly distinguishes intestinal S. mansoni—which usually preserves male testosterone levels—from urogenital S. haematobium, which can cause significant reproductive impairment. Male genital schistosomiasis (MGS) leads to testicular and seminal tract inflammation, apoptosis of spermatozoa, reduced semen volume, and in some cases lowered testosterone (18, 20, 25, 26). In females, female genital schistosomiasis (FGS) produces mucosal ulceration, contact bleeding, infertility, and increased risk of miscarriage and ectopic pregnancy (21–23). These pathologies are linked not only to physical lesions but also to estrogen-like parasite metabolites that disrupt endocrine signaling (23, 27). The cumulative evidence indicates that reproductive morbidity is most pronounced in urogenital forms and is not primarily mediated through systemic endocrine axes but through direct local pathology.

The endocrine glands beyond the GH–IGF axis—namely the thyroid, adrenal, and gonadal axes—show varying degrees of involvement depending on disease stage and severity. Table 3 indicates that the thyroid axis remains largely preserved in both human and animal studies, with only subtle changes observed in chronic disease (1, 29, 30). The adrenal axis shows more complex interactions: early experimental studies reveal reduced cortisol and DHEA-S, while human studies show that puberty-associated increases in DHEA-S correlate with reduced reinfection risk (19, 28). Gonadal involvement is primarily pathological rather than biochemical, except in severe infection where testosterone may decline (20). These findings emphasize that systemic endocrine dysfunction occurs primarily through IGF-1 suppression, while gonadal and reproductive complications arise from organ-specific lesions.

When comparing hepatosplenic versus intestinal or bladder-limited disease (Table 4), the contrast is striking. Hepatosplenic schistosomiasis is associated with the most profound endocrine and nutritional abnormalities, including severe stunting, reduced IGF-1, GH suppression, pubertal delay, and secondary reproductive consequences of chronic illness (1, 2, 5, 11, 12). Conversely, intestinal and bladder disease generally produce moderate effects on growth and preserve most endocrine axes, except where local pathology (FGS/MGS) causes reproductive dysfunction (18, 21–23). This phenotype-based distinction is essential for clinical management and highlights the need for early detection of children progressing toward hepatic fibrosis.

The mechanistic pathways summarized in Table 5 help unify the clinical findings. Egg-induced granulomatous inflammation, persistent Th2 and Th17 cytokine activity, and mucosal injury contribute to chronic systemic inflammation (7, 10). EED accelerates nutrient loss and induces metabolic stress that suppresses IGF-1 (12). Hepatic fibrosis reduces hepatocyte function, directly lowering IGF-1 and IGFBP-3 (1, 11). GH resistance emerges through cytokine-mediated inhibition of GH receptor signaling, while anemia and chronic catabolism further reduce growth velocity (2, 5). Pubertal alterations arise partly from low IGF-1 and partly from energy deficiency. Meanwhile, reproductive morbidity in urogenital disease stems from direct tissue invasion, inflammation, and altered parasite-derived hormone analogs (18, 20–23, 27). Together, these mechanisms provide a biologically coherent explanation for the diverse clinical outcomes observed across schistosomiasis phenotypes.

Despite these challenges, several studies demonstrate that early intervention can substantially mitigate growth and endocrine complications. Praziquantel treatment improves appetite, physical performance, and nutritional status, particularly when initiated before the development of hepatic fibrosis (2, 4–6, 17). Egg burden reduction facilitates partial recovery of IGF-1, although complete normalization may be limited in those with established fibrosis (12). Nutritional supplementation further enhances recovery in children with high reinfection burdens. Importantly, public health strategies that include mass drug administration, safe water access, snail control, and school-based screening could prevent progression to hepatosplenic disease and its associated endocrine sequelae.

In summary, schistosomiasis exerts significant effects on growth, puberty, and endocrine function, with the severity determined by infection intensity, chronicity, and disease phenotype. Hepatosplenic disease poses the greatest risk for long-term endocrine impairment, while urogenital disease leads primarily to reproductive complications. The GH–IGF-1 axis serves as the central link between infection, hepatic pathology, and growth failure. Early treatment and preventive public health measures can substantially reduce these risks, underscoring the need for integrated clinical guidelines for growth monitoring, endocrine assessment, and timely antiparasitic therapy in schistosomiasis-endemic regions.

5. Conclusion

Schistosomiasis remains a significant but under-recognized cause of growth failure, delayed puberty, and endocrine dysfunction in children and adolescents, with the greatest burden occurring in those who develop hepatosplenic disease. Suppression of the GH–IGF-1 axis, compounded by chronic inflammation, environmental enteric dysfunction, anemia, and reduced hepatic synthetic capacity, forms the central mechanism linking infection to impaired growth and pubertal delay. Reproductive morbidity is most prominent in urogenital disease, driven by direct genital tract pathology and parasite-derived hormone-like metabolites. Early diagnosis and timely praziquantel therapy—before progression to hepatic fibrosis—substantially improve growth and metabolic outcomes, whereas delayed treatment limits recovery. These findings underscore the need for routine growth monitoring, endocrine assessment, and integrated public health strategies in endemic regions, where early intervention can prevent long-term developmental and reproductive sequelae.

Practice Recommendations

- Screen systematically in endemic areas: At every visit, record height, weight, and height velocity; screen for schistosomiasis with urine/stool microscopy or rapid antigen tests (CCA/CAA) where available.
- Stage the phenotype early: Perform ultrasound (Niamey scoring) to detect periportal fibrosis and splenomegaly; classify as intestinal, urogenital, or hepatosplenic—management intensity depends on phenotype.
- Treat promptly and adequately: Give praziquantel 40 mg/kg single dose (consider repeating in 2–6 weeks for heavy infections or persistent egg shedding); align with school-based MDA schedules.
- Monitor growth and endocrine axes: Reassess anthropometry and IGF-1 (± IGFBP-3) at 6–12 months post-therapy; refer to endocrinology if height velocity <4 cm/year or IGF-1 <−2 SDS persists after treatment and nutrition optimization.
- Assess puberty and reproduction: Tanner stage every 6–12 months; in suspected MGS, consider semen analysis and scrotal ultrasound; in suspected FGS, arrange gynecologic exam/colposcopy where feasible.
- Correct comorbidities: Screen and treat anemia (CBC, ferritin with CRP), and address malnutrition/EED with energy-protein support and micronutrients (iron/folate ± vitamin D/A per local policy).
- Follow hepatic status: Track platelets, ALT/AST, albumin, and ultrasound findings in hepatosplenic disease; manage portal hypertension complications and coordinate with hepatology/surgery if indicated.
- Prevent reinfection: Counsel on safe-water access, snail/snail-habitat control, and reducing freshwater exposure; ensure annual re-screening (biannual in high-transmission settings).
- Coordinate multidisciplinary care: Integrate pediatrics, endocrinology, hepatology, nutrition, and reproductive health services; establish referral triggers (e.g., persistent stunting, delayed puberty, infertility signs).
- Document outcomes: Maintain a simple register capturing infection intensity, treatment dates, growth velocity, IGF-1, puberty stage, and reproductive findings to guide quality improvement.

Compliance with ethical standards

Disclosure of conflict of interest

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

Funding Statement

This study received no external funding.

Ethical Declaration

As this work is a narrative review of previously published literature, no ethics approval or informed consent was required.

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