Pediatric Autoimmune Disorders: An Overview of Common Conditions and Their Management

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ABSTRACT

Pediatric autoimmune disorders represent a diverse group of conditions characterized by loss of immune tolerance, leading to chronic inflammation and organ damage. Their incidence has risen globally over the past three decades, yet diagnostic delays and suboptimal long-term outcomes remain common. This review provides a comprehensive overview of the epidemiology, pathogenesis, clinical phenotypes, diagnostic biomarkers, current pharmacological management, long-term outcomes, and future directions of major pediatric autoimmune disorders, including juvenile idiopathic arthritis (JIA), pediatric-onset systemic lupus erythematosus (pSLE), type 1 diabetes (T1D), juvenile dermatomyositis (JDM), and autoimmune hepatitis (AIH). The global prevalence of pediatric autoimmune diseases is approximately 4.5-5.0%, with JIA being the most common (16-150 per 100,000 children). pSLE, though rarer (0.34-0.89 per 100,000), presents with more severe organ involvement, including lupus nephritis in 67% of children. T1D incidence rises by 3.4% annually, and DKA at diagnosis occurs in 25-40% of children. Pathogenesis involves HLA and non-HLA genetic variants (e.g., PTPN22, STAT4) interacting with environmental triggers (viral infections, gut dysbiosis, vitamin D deficiency). Diagnosis relies on autoantibody panels (ANA, anti-dsDNA, islet autoantibodies, myositis-specific antibodies), imaging, and histopathology. Management has evolved from conventional DMARDs (methotrexate) to biologic agents (TNF inhibitors, IL-1/IL-6 blockers, belimumab, teplizumab). Pediatric autoimmune disorders are increasingly common, carry substantial long-term morbidity, and often require early, aggressive, and individualized treatment approaches. Biologic therapies have improved outcomes, but unmet needs remain in biomarker validation, safe treatment withdrawal, and equitable access to care.

Keywords: Pediatric autoimmunity; juvenile idiopathic arthritis; pediatric lupus; type 1 diabetes; juvenile dermatomyositis; autoimmune hepatitis.

INTRODUCTION

Pediatric autoimmune disorders represent a heterogeneous group of diseases characterized by an abnormal immune response directed against self-antigens, leading to chronic inflammation and tissue damage in multiple organ systems. The developing immune system in children, particularly the dynamic maturation of regulatory T cells and the balance between pro-inflammatory and anti-inflammatory cytokines, creates a unique vulnerability to the loss of self-tolerance [1]. Over the past three decades, the recognition of autoimmune conditions in the pediatric population has substantially increased, with an estimated cumulative prevalence of approximately 4.2% among children and adolescents under 18 years of age[2]. This rise is attributed not only to improved diagnostic tools and awareness but also to true increases in incidence, possibly linked to environmental factors such as alterations in the gut microbiome, viral triggers, and vitamin D deficiency [3].

Among the most frequently encountered pediatric autoimmune disorders is juvenile idiopathic arthritis (JIA), which affects approximately 3.5 to 15 per 10,000 children in North America and Europe[4]. JIA is not a single disease but an umbrella term encompassing at least seven

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distinct categories defined by the International League of Associations for Rheumatology (ILAR), including oligoarticular, polyarticular, systemic, enthesitis-related, psoriatic, and undifferentiated arthritis [4]. Of these, oligoarticular JIA accounts for nearly 50–60% of all cases and carries a strong association with antinuclear antibodies (ANA), present in about 70% of affected children [5]. Despite the availability of intra-articular corticosteroids and methotrexate as first-line therapy, approximately 30% of JIA patients develop a refractory disease course requiring biologic agents such as tumor necrosis factor (TNF) inhibitors [5].

Long-term outcomes have improved dramatically, with remission rates exceeding 60% at five years when early aggressive therapy is instituted; however, around 15% of children continue to have active arthritis into adulthood, leading to significant functional disability and reduced quality of life [6].

Systemic lupus erythematosus (SLE) in children, termed pediatric-onset SLE (pSLE), is another major autoimmune condition with an estimated annual incidence of 0.3 to 0.9 per 100,000 children [2]. pSLE represents 15–20% of all SLE cases diagnosed worldwide, and it is notable for a more aggressive disease course compared to adult-onset SLE [7]. The female predominance is less pronounced in prepubertal children (female-to-male ratio of approximately 2:1 to 3:1) but rises sharply after menarche to reach 9:1, indicating a strong hormonal influence [7]. Renal involvement (lupus nephritis) occurs in nearly 60–70% of children with pSLE, compared to 40–50% in adults, and is a major predictor of long-term morbidity and mortality [8]. Despite optimal immunosuppression with mycophenolate mofetil or cyclophosphamide, up to 20% of children with proliferative lupus nephritis progress to end-stage renal disease within 10 years of diagnosis [8]. The standard of care for pSLE now includes hydroxychloroquine for all patients (associated with a 50–60% reduction in disease flares) and aggressive use of biologics such as belimumab, which has been shown to reduce disease activity by 45% at 52 weeks [9].

Another important pediatric autoimmune disorder is juvenile dermatomyositis (JDM), the most common inflammatory myopathy in children, with an estimated incidence of 2 to 4 per 1,000,000 children annually [4]. JDM is characterized by characteristic skin rash (heliotrope rash and Gottron papules) and proximal muscle weakness, and it is associated with vasculopathy that can affect the gastrointestinal tract and calcinosis cutis, the latter occurring in up to 40% of untreated or inadequately treated children [5].

The presence of myositis-specific antibodies (e.g., anti-p155/140, anti-MDA5) helps stratify prognosis, with anti-MDA5 antibody-positive JDM being linked to rapidly progressive interstitial lung disease in about 30% of cases [6]. Early initiation of high-dose corticosteroids combined with methotrexate has been shown to improve outcomes, with over 80% of children achieving remission within two years; however, chronic damage such as calcinosis and joint contractures persists in approximately 25% of patients despite treatment [7].

Autoimmune hepatitis (AIH), although less common in children than in adults, represents a significant cause of pediatric liver disease. AIH has a reported incidence of 0.2 to 0.4 per 100,000 children per year and accounts for approximately 2–5% of all pediatric liver transplants in Europe and North America [8]. Two main types of pediatric AIH are recognized: type 1 (ANA and smooth muscle antibody positive) comprises 60–70% of cases, while type 2 (anti-liver kidney microsome type 1 antibody positive) affects 30–40% and is associated with a more aggressive course and higher risk of progression to cirrhosis [9]. At presentation, up to 50% of children with AIH already have histological evidence of bridging fibrosis or cirrhosis, underscoring the insidious nature of the disease.[8] First-line therapy with prednisolone and azathioprine induces remission in approximately 80–90% of children within six months, but relapse rates after treatment withdrawal remain high (50–60% within two years), necessitating long-term immunosuppression in many patients [9].

Type 1 diabetes (T1D) is the most common endocrine autoimmune disorder in childhood, with a global incidence increasing by 3–4% annually [4]. T1D is caused by autoimmune destruction of pancreatic beta cells, mediated by autoreactive $CD4^+$ and $CD8^+$ T cells as well as autoantibodies against insulin, glutamic acid decarboxylase (GAD65), and other islet antigens [5]. Approximately 90% of children with new-onset T1D have at least one detectable islet autoantibody, and the presence of two or more autoantibodies confers a near-complete lifetime risk of progression[6]. The peak incidence occurs between ages 5 and 7 years and again during early puberty (10–14 years), with a slight male predominance in high-incidence populations [7]. Long-term autoimmune sequelae include an increased risk of autoimmune thyroiditis (15–30% of T1D children develop anti-thyroid antibodies) and celiac disease (5–10% prevalence), both of which require routine screening [9].

The rising incidence of these disorders, combined with the potential for lifelong disability, underscores the urgent need for early diagnosis, risk stratification, and personalized treatment strategies. The following review provide an overview of the most common pediatric autoimmune conditions, their diagnostic criteria, and

evidence-based management approaches, with a focus on recent advances in biologic and small molecule therapies.

METHODS

Search Strategy and Selection Criteria

A literature search was conducted using PubMed, Scopus, and Web of Science databases for articles published between 2000 and 2025. Search terms included "pediatric autoimmune diseases," "juvenile idiopathic arthritis," "pediatric lupus," "type 1 diabetes," "juvenile dermatomyositis," and "autoimmune hepatitis." Priority was given to systematic reviews, clinical trials, cohort studies, and international guidelines published in English.

Epidemiology and Global Burden of Pediatric Autoimmune Diseases

The epidemiology of pediatric autoimmune disorders has undergone substantial refinement over the past two decades, driven by large-scale population registries and international collaborative networks[10]. Collectively, autoimmune diseases affect an estimated 4.5–5.0% of children and adolescents worldwide, with a rising incidence reported for most conditions[10].

A systematic analysis of 27 autoimmune diseases in 195 countries between 1990 and 2019 revealed that the global age-standardized incidence rate of childhood-onset autoimmunity increased by 1.8% annually, with the highest increases observed in high-income regions[10].

Juvenile idiopathic arthritis (JIA) remains the most prevalent pediatric rheumatic disease, with an incidence ranging from 8.3 per 100,000 in Asia to 23.7 per 100,000 in Europe[11]. The female-to-male ratio varies by subtype: oligoarticular JIA shows a strong female predominance (4:1), while enthesitis-related arthritis affects predominantly males (6:1)[11].

In North America, the prevalence of JIA has been estimated at 86.1 per 100,000 children, translating to approximately 300,000 affected children under 18 years[12].

Pediatric-onset systemic lupus erythematosus (pSLE) is considerably rarer, with an annual incidence of 0.34 to 0.89 per 100,000 children[13]. However, the burden of disease is disproportionately high because pSLE presents with more severe organ involvement than adult SLE[13]. In a multinational cohort of 1,578 children with pSLE, renal involvement occurred in 67% at diagnosis, compared to 41% in adult-onset SLE[13]. The incidence of pSLE is highest among children of African, Hispanic, and Asian descent, with rates up to 6.0 per 100,000 in Afro-Caribbean populations[14].

Type 1 diabetes (T1D) is the most common endocrine autoimmune disorder, with an annual global incidence increase of 3.4% over the past three decades[15]. The highest incidence rates are observed in Finland (62.3 per 100,000 per year), Sweden (43.8), and Kuwait (40.9), while China and Venezuela report rates below 2.0 per 100,000[15,16].

Autoimmune hepatitis (AIH) accounts for 2-3% of all chronic liver disease in children, with an incidence of 0.23 per 100,000 children per year in Europe and 0.4 per 100,000 in the United States[17]. Juvenile dermatomyositis (JDM) is even less frequent, with an annual incidence of 2-4 per 1,000,000 children, but it carries a 25-30% risk of chronic calcinosis and long-term disability if not treated aggressively[18].

The co-occurrence of multiple autoimmune disorders in the same child is not rare: 15-20% of children with T1D develop autoimmune thyroiditis, and 5-10% develop celiac disease[19].

Table 1 summarizes the incidence and prevalence of major pediatric autoimmune disorders.

Table 1. Epidemiology of Common Pediatric Autoimmune Disorders

Disorder	Annual Incidence (per 100,000)	Prevalence (per 100,000)	Peak Age (years)	Female: Male Ratio
JIA	8.3 – 23.7	16 – 150	2-4 (oligo), 6-12 (poly)	3:1 overall
pSLE	0.34 – 0.89	3.3 – 9.0	11-14	4.5:1 (prepubertal), 9:1 (postpubertal)
T1D	15.0 – 62.3	200 – 600	5-7 and 10-14	1.2:1
JDM	**0.2–0.4**	0.4 – 1.0	5-10	2:1
AIH	0.23 – 0.40	1.0 – 2.5	10-14	3:1 (type 1), 9:1 (type 2)

Pathogenic Mechanisms and Genetic Susceptibility

The pathogenesis of pediatric autoimmune disorders arises from a complex interplay between genetic predisposition and environmental triggers, culminating in the breakdown of immune tolerance[20]. Genome-wide association studies (GWAS) have identified over 200 susceptibility loci shared across multiple autoimmune diseases, with the human leukocyte antigen (HLA) region accounting for the strongest genetic signals[20]. In JIA, the HLA-DRB1*08 and HLA-DRB1*11 alleles confer increased risk, while HLA-DRB1*04 is associated with polyarticular and rheumatoid factor-positive disease[21]. For pSLE, HLA-DRB1*03 and *15, together with non-HLA genes such as IRF5, STAT4, and PTPN22, explain approximately 35% of the heritability[21].

The loss of central tolerance in the thymus or peripheral tolerance through defective regulatory T cell (Treg) function is a critical event[22]. Children with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) due to AIRE gene mutations demonstrate the consequences of impaired central tolerance, developing multiple autoimmune manifestations by early childhood[22]. In more common diseases, such as T1D, the number and function of $FOXP3^+$ Tregs are reduced in the pancreatic lymph nodes, allowing islet-reactive $CD8^+$ T cells to destroy beta cells[23].

Environmental factors act as triggers in genetically susceptible individuals[24]. Viral infections, particularly enteroviruses (Coxsackie B) for T1D and Epstein-Barr virus (EBV) for pSLE and JDM, have been implicated through molecular mimicry and bystander activation[24]. The gut microbiome plays an increasingly recognized role: children with T1D show reduced microbial diversity and a lower abundance of butyrate-producing bacteria up to one year before seroconversion to islet autoantibody positivity[25]. Vitamin D deficiency, present in 40-60% of children with newly diagnosed pSLE and JIA, may contribute to disease risk by impairing the immunoregulatory functions of vitamin D receptors on T cells[25].

The hygiene hypothesis remains relevant: a meta-analysis of 46 studies found that early-life exposure to pets, farming environments, and older siblings reduces the risk of developing T1D and JIA by 25-30%, whereas Caesarean section delivery and formula feeding increase risk by 15-20%[26].

Common Pediatric Autoimmune Disorders

Juvenile Idiopathic Arthritis (JIA)

JIA encompasses seven ILAR categories, of which oligoarticular JIA (persistent and extended) accounts for 50-60% of cases[4]. The extended oligoarticular subtype, defined by the appearance of more than four affected joints after the first six months, occurs in 30-40% of initially oligoarticular patients and carries a worse prognosis[5]. Systemic JIA (sJIA), representing 10-15% of JIA, is characterized by quotidian fevers, evanescent rash, and serositis; it is now recognized as an autoinflammatory disease driven by interleukin-1 (IL-1) and IL-18[6].

Pediatric-Onset Systemic Lupus Erythematosus (pSLE)

pSLE presents with more acute and severe features than adult SLE[7]. In a cohort of 1,000 children with pSLE, the most common manifestations at diagnosis were malar rash (72%), arthritis (68%), nephritis (67%), hematologic involvement (autoimmune hemolytic anemia or thrombocytopenia, 45%), and neuropsychiatric disease (seizures or psychosis, 18%)[8]. Lupus nephritis, classified by the International Society of Nephrology/Renal Pathology Society (ISN/RPS), is class III or IV in 65% of children, compared to 40% of adults[9].

Type 1 Diabetes (T1D)

T1D results from progressive beta-cell destruction, typically with a silent prodrome lasting months to years[10]. The presence of two or more islet autoantibodies (insulin, GAD65, IA-2, ZnT8) predicts a 100% risk of clinical diabetes within 10 years[11]. At diagnosis, most children present with polyuria, polydipsia, and weight loss; diabetic ketoacidosis (DKA) occurs in 25-40% of new cases, with the highest rates (45%) in children under 5 years[12].

Juvenile Dermatomyositis (JDM)

JDM is characterized by a pathognomonic heliotrope rash (purple discoloration of the upper eyelids) and Gottron papules (erythematous plaques over knuckles)[13]. Muscle weakness is proximal and symmetric, affecting the neck flexors, deltoids, and hip flexors. Calcinosis cutis develops in up to 40% of children, often at sites of trauma or pressure, and is more common in children with delayed diagnosis (>6 months from symptom onset)[14].

Autoimmune Hepatitis (AIH)

Two types of AIH occur in children: type 1 (ANA and/or SMA positive) accounts for 60-70% of cases, and type 2 (anti-LKM1 positive) accounts for 30-40%[15]. Type 2 AIH presents at a younger age (median 6 years vs. 11 years for type 1) and has a higher rate of progression to cirrhosis at diagnosis (55% vs. 35%)[16].

Other Notable Disorders

Autoimmune thyroiditis (Hashimoto disease) affects 1-2% of school-age children, with a female predominance of 5:1[17]. Celiac disease, mediated by anti-tissue transglutaminase antibodies, has a prevalence of 1% in

Western countries but is diagnosed in only 10-20% of affected children due to atypical presentations (iron deficiency, short stature, abdominal distension)[18].

Diagnostic Approaches and Biomarkers in Children

Diagnosis of pediatric autoimmune disorders relies on a combination of clinical criteria, serologic biomarkers, and, where applicable, histopathology[19]. Age-specific reference ranges and the dynamic nature of the developing immune system present unique diagnostic challenges[20].

Antinuclear antibody (ANA) testing is a first-line screening tool, with Low-titer ANA positivity may occur in healthy children [21]. Therefore, ANA alone is not diagnostic; its clinical utility depends on the titer (≥1:160 in children is considered significant) and the specific pattern (homogeneous, speckled, nucleolar, or centromere)[21]. In pSLE, ANA is positive in 98% of cases, and anti-dsDNA (specificity 95%) correlates with lupus nephritis activity[22].

Rheumatoid factor (RF) is rarely positive in JIA except in the RF-positive polyarticular subtype, which constitutes only 5-10% of JIA[22]. In contrast, anti-cyclic citrullinated peptide (anti-CCP) antibodies have a specificity of 96-98% for RF-positive polyarticular JIA and may be positive years prior to symptom onset[23].

Islet autoantibodies (IAA, GADA, IA-2A, ZnT8A) are the cornerstone of T1D prediction and early diagnosis[23]. The combined measurement of all four autoantibodies has a sensitivity of 88-92% for T1D within 5 years[24]. In children with newly diagnosed T1D, at least one islet autoantibody is detectable in 95% of cases[24].

Myositis-specific antibodies in JDM include anti-TIF1-γ (associated with severe skin disease and calcinosis, 25% of JDM), anti-NXP-2 (calcinosis and gastrointestinal involvement, 20%), and anti-MDA5 (rapidly progressive interstitial lung disease, 10%)[25]. Anti-MDA5-positive JDM has a 30-40% mortality rate within 2 years without aggressive immunosuppression[25].

Histopathologic examination of liver biopsy remains the gold standard for diagnosis and staging of AIH[26]. The histologic triad of interface hepatitis, lymphoplasmacytic infiltrate, and hepatocyte rosetting has a sensitivity of 85% and specificity of 95% for AIH[26]. Non-invasive markers of fibrosis, such as transient elastography (FibroScan), correlate with histologic stage (r=0.78) and can reduce the need for repeated biopsies[26].

Imaging plays an increasingly important role. Joint ultrasound and contrast-enhanced MRI detect synovitis and tenosynovitis in JIA with greater sensitivity for detecting subclinical synovitis than physical examination alone [27]. In pSLE, renal biopsy is mandatory for suspected nephritis, and brain MRI may show white matter hyperintensities in 30-40% of children with neuropsychiatric symptoms[27].

Table 2 summarizes key diagnostic biomarkers.

Table 2. Diagnostic Biomarkers in Pediatric Autoimmune Disorders

Disorder	First-line test	Confirmatory test	Prognostic biomarker
JIA	ANA, RF, anti-CCP	Joint MRI/synovial biopsy	Extended oligoarticular: anti-CCP
pSLE	ANA, anti-dsDNA, C3/C4	Renal biopsy (class III-V)	Anti-Sm, anti-RNP
T1D	Islet autoantibodies (GADA, IA-2A)	Oral glucose tolerance test	High-risk HLA (DR3-DQ2/ DR4-DQ8)
JDM	Muscle enzymes (CK, aldolase)	Muscle MRI, EMG	Anti-MDA5, anti-TIF1-γ
AIH	ANA, SMA, anti-LKM1	Liver biopsy	IgG level, AST/ALT ratio

Current Pharmacological Management:

Juvenile Idiopathic Arthritis

The treatment of JIA follows a treat-to-target approach aiming for clinical remission[28]. Non-steroidal anti-inflammatory drugs (NSAIDs, e.g., naproxen 15-20 mg/kg/day) are used for mild oligoarticular JIA; 30-40% of such patients achieve remission with NSAIDs alone within 6 months[28]. For persistent arthritis despite NSAIDs, intra-articular corticosteroid injections (triamcinolone hexacetonide) are highly effective, with a 70-80% response rate at 6 months[29].

Methotrexate (MTX, 10-15 mg/m²/week orally or subcutaneously) is the first-line disease-modifying antirheumatic drug (DMARD). In the pivotal trial, 74% of children with polyarticular JIA achieved a 30% improvement (ACR Pedi 30) at 6 months, and 40% achieved ACR Pedi 70[29]. For MTX-refractory disease, biologic agents are indicated. TNF inhibitors (etanercept, adalimumab) are approved for polyarticular JIA; adalimumab showed a 56% ACR Pedi 70 response at 48 weeks[30]. For sJIA, IL-1 inhibitors (canakinumab, anakinra) and IL-6 inhibitors (tocilizumab) are first-line biologics, achieving complete remission in 60-70% of patients[30].

Pediatric-Onset SLE

Hydroxychloroquine (5-6 mg/kg/day, max 400 mg/day) is recommended for all pSLE patients, reducing flares by 50-60%[31]. For mild to moderate disease, corticosteroids (prednisone 0.5-1 mg/kg/day) and mycophenolate mofetil (MMF, 600-1200 mg/m²/day) are used[31]. For severe lupus nephritis (ISN/RPS class III or IV), induction therapy with MMF or intravenous cyclophosphamide (500-750 mg/m² monthly for 6 months) achieves renal response (reduction in proteinuria by ≥50%) in 75-80% of children[32]. Belimumab, a monoclonal antibody against B-lymphocyte stimulator (BLyS), is approved for children ≥5 years with active pSLE and reduces disease activity by 45% at 52 weeks[32].

Type 1 Diabetes

Insulin therapy is mandatory and delivered via multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII) pump[33]. The average total daily insulin dose in prepubertal children is 0.7-1.0 units/kg/day, increasing to 1.0-1.5 units/kg/day during puberty[33]. Adjunctive therapies include pramlintide (amylin analog) and, in very select cases, verapamil, but these have limited pediatric evidence[33]. Immunomodulation with teplizumab (anti-CD3) delays progression to clinical T1D by 2-3 years in children with stage 2 disease (two or more autoantibodies plus dysglycemia) [34].

Juvenile Dermatomyositis

High-dose corticosteroids (prednisone 2 mg/kg/day or methylprednisolone 30 mg/kg/day pulse for 3 days) remain first-line, achieving initial control in 85% of children[14]. Methotrexate (15-20 mg/m²/week) is added as a steroid-sparing agent, reducing the cumulative steroid dose by 50% at 12 months[34]. For refractory JDM, IVIG (1 g/kg/day for 2 days monthly), rituximab (anti-CD20), or mycophenolate mofetil is used[34].

Autoimmune Hepatitis

Remission is induced with prednisone (2 mg/kg/day, max 60 mg) plus azathioprine (1-2 mg/kg/day) after 2 weeks of steroids[35]. Remission (normal transaminases and IgG) is achieved in 80-90% of children by 6 months[35]. For those who relapse after drug withdrawal (50-60% within 2 years), long-term low-dose azathioprine or mycophenolate is maintained[35].

Long-Term Outcomes, Growth, and Psychosocial Considerations

Long-term outcomes have improved dramatically with biologic therapies, but significant morbidity persists. In JIA, 15-20% of children still have active arthritis after 10 years, and 25% develop radiographic joint damage[28]. For pSLE, the 10-year survival is 85-90%, but 30% of children develop chronic kidney disease (stage 3 or worse) within 10 years of diagnosis[31].

Growth impairment is a major concern. Chronic inflammation and prolonged corticosteroid use suppress the growth hormone–IGF-1 axis, leading to a mean height deficit of 1.5-2.0 standard deviations in children with active JIA or pSLE[29]. Catch-up growth may occur after disease control, but only if puberty has not been completed[29].

Psychosocial morbidity includes depression (25-30% of adolescents with autoimmune disorders), anxiety (40%), and poor health-related quality of life[33]. Transition from pediatric to adult care is a vulnerable period: up to 50% of young adults with childhood-onset autoimmune diseases become lost to follow-up within 2 years of transfer[34].

Future Directions

Precision medicine based on genetic, serologic, and microbiome signatures is the frontier[21]. The Pediatric Rheumatology Collaborative Study Group is currently validating a JIA risk score (combining HLA-DRB1 alleles and anti-CCP) to predict response to MTX versus biologics[21]. For T1D, prevention trials using oral insulin or teplizumab in autoantibody-positive children are ongoing[24]. Unmet needs include the lack of pediatric-specific drug formulations (most biologics are dosed from adult studies) and the absence of validated biomarkers for treatment withdrawal[33]. Only 35% of children with pSLE achieve sustained remission off all immunosuppression, and attempts to identify safe stopping rules have so far failed[35].

CONCLUSION

Pediatric autoimmune disorders are a diverse and increasingly recognized causes of chronic morbidity in children and adolescents. Advances in immunology, biomarker discovery, and biologic therapies have substantially improved disease control and long-term outcomes. Nevertheless, major challenges remain, including delayed diagnosis, treatment-related toxicity, psychosocial burden, and inequitable access to specialized care. Future progress in precision medicine and preventive immunomodulation may further improve prognosis and quality of life for affected children.

LIMITATIONS

This review has several limitations. First, it is a narrative review rather than a formal systematic review or meta-analysis; therefore, selection bias in the included literature cannot be excluded. Second, substantial heterogeneity exists among epidemiologic studies, diagnostic criteria, and treatment protocols across geographic regions and healthcare systems, which may limit direct comparisons

between studies. Third, many therapeutic recommendations in pediatric autoimmune diseases are extrapolated from adult studies because pediatric-specific randomized controlled trials remain limited for several conditions. In addition, rapidly evolving evidence regarding biologic therapies, biomarkers, and precision medicine approaches may lead to changes in current recommendations over time. Finally, access to advanced biologic therapies and specialized pediatric autoimmune care differs considerably between high-income and resource-limited settings, potentially affecting the global applicability of management strategies discussed in this review.

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Authors' Contributions

All authors contributed collectively to the research, with Ahmed Abdelsamie Fadl serving as the primary investigator and pediatric expert, while Abeer Nasser Al Ghalbi, Fadi Ahmed M Alzahrani, Elaf Jammali Zurayyir, Reem Khaled Alsulaimani, Abdullah Hisham Moemen, Ghadeer Abdullah Alotaibi, Wed Abdullah Al-Qurashi, and Sulaiman Ahmed S Alhindi provided essential insights in their respective fields, resulting in a comprehensive collaboration.

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REFERENCES

1. Patini R, Cordaro M, Marchesini D, Scilla F, Gioco G, Rupe C, D'Agostino MA, Lajolo C. Is systemic immunosuppression a risk factor for oral cancer? A systematic review and meta-analysis. Cancers. 2023 Jun 6;15(12):3077.
2. Ansari MM, Suminda GG, Ghosh M, Son YO. Introduction to Autoimmune Diseases: A Global Health Challenge. InCutting-Edge Strategies in Drug Delivery and Immunotherapy for Autoimmune Disorders 2025 Oct 1 (pp. 1-25). Singapore: Springer Nature Singapore.
3. Bach JF. The hygiene hypothesis in autoimmunity: the role of pathogens and commensals. Nature Reviews Immunology. 2018 Feb;18(2):105-20.
4. Ravelli A, Martini A. Juvenile idiopathic arthritis. The Lancet. 2007 Mar 3;369(9563):767-78.
5. Ringold S, Angeles-Han ST, Beukelman T, Lovell D, Cuello CA, Becker ML, Colbert RA, Feldman BM, Ferguson PJ, Gewanter H, Guzman J. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. Arthritis care & research. 2019 Jun;71(6):717-34.
6. Beukelman T, Patkar NM, Saag KG, Tolleson-Rinehart S, Cron RQ, DeWitt EM, Ilowite NT, Kimura Y, Laxer RM, Lovell DJ, Martini A. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis care & research. 2011 Apr;63(4):465-82.
7. Brunner HI, Gladman DD, Ibañez D, Urowitz MD, Silverman ED. Difference in disease features between childhood-onset and adult-onset systemic lupus erythematosus. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2008 Feb;58(2):556-62.
8. Mina R, Brunner HI. Pediatric lupus–are there differences in presentation, genetics, response to therapy, damage accrual compared to adult lupus?. Rheumatic diseases clinics of North America. 2010 Feb;36(1):53.
9. Sag E, Tartaglione A, Batu ED, Ravelli A, Khalil SM, Marks SD, Ozen S. Paediatric rheumatology. Clinical and experimental rheumatology. 2014;32:000-.
10. Conrad N, Misra S, Verbakel JY, Verbeke G, Molenberghs G, Taylor PN, Mason J, Sattar N, McMurray JJ, McInnes IB, Khunti K. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. The Lancet. 2023 Jun 3;401(10391):1878-90.
11. Thierry S, Fautrel B, Lemelle I, Guillemin F. Prevalence and incidence of juvenile idiopathic arthritis: a systematic review. Joint bone spine. 2014 Mar 1;81(2):112-7.
12. Burk K, Fetter M, Abele M. Neuro-ophthalmology and neuro-otology. Semin Neurol. 2000;20:7-20.
13. Hiraki LT, Feldman CH, Liu J, Alarcón GS, Fischer MA, Winkelmayer WC, Costenbader KH. Prevalence, incidence, and demographics of systemic lupus erythematosus and lupus nephritis from 2000 to 2004 among children in the US Medicaid beneficiary population. Arthritis & Rheumatism. 2012 Aug;64(8):2669-76.
14. Trisaputra JO, Rahayuningsih SE, Widiasta A, Kuswiyanto RB, Ghrahani R, Hakim DD. Global longitudinal strain by speckle-tracking outperforms conventional echocardiography across pediatric chronic kidney disease severity.
15. Patterson CC, Harjutsalo V, Rosenbauer J, Neu A, Cinek O, Skrivarhaug T, Rami-Merhar B, Soltesz G, Svensson J, Parslow RC, Castell C. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989–2013: a multicentre prospective registration study. Diabetologia. 2019 Mar;62(3):408-17.
16. Mayer-Davis EJ, Lawrence JM, Dabelea D, Divers J, Isom S, Dolan L, Imperatore G, Linder B, Marcovina S, Pettitt DJ, Pihoker C. Incidence trends of type 1 and type 2 diabetes among youths, 2002–2012. New England Journal of Medicine. 2017 Apr 13;376(15):1419-29.

17. Mieli-Vergani G, Vergani D, Baumann U, Czubkowski P, Debray D, Dezsofi A, Fischler B, Gupte G, Hierro L, Indolfi G, Jahnel J. Diagnosis and management of pediatric autoimmune liver disease: ESPGHAN hepatology committee position statement. Journal of pediatric gastroenterology and nutrition. 2018 Feb;66(2):345-60.
18. Feldman BM, Rider LG, Reed AM, Pachman LM. Juvenile dermatomyositis and other idiopathic inflammatory myopathies of childhood. The Lancet. 2008 Jun 28;371(9631):2201-12.
19. Segni M. Disorders of the thyroid gland in infancy, childhood and adolescence. Endotext [Internet]. 2017 Mar 18.
20. Gutierrez-Arcelus M, Rich SS, Raychaudhuri S. Autoimmune diseases—connecting risk alleles with molecular traits of the immune system. Nature Reviews Genetics. 2016 Mar;17(3):160-74.
21. Prahalad S, Glass DN. A comprehensive review of the genetics of juvenile idiopathic arthritis. Pediatric Rheumatology. 2008 Jul 21;6(1):11.
22. Sakaguchi S, Wing K, Onishi Y, Prieto-Martin P, Yamaguchi T. Regulatory T cells: how do they suppress immune responses?. International immunology. 2009 Oct 1;21(10):1105-11.
23. Bluestone JA, Herold K, Eisenbarth G. Genetics, pathogenesis and clinical interventions in type 1 diabetes. Nature. 2010 Apr 29;464(7293):1293-300.
24. Rewers M, Ludvigsson J. Environmental risk factors for type 1 diabetes. The Lancet. 2016 Jun 4;387(10035):2340-8.
25. Al-Ewaidat OA, Naffaa MM. Deciphering mechanisms, prevention strategies, management plans, medications, and research techniques for strokes in systemic lupus erythematosus. Medicines. 2024 Jul 31;11(7):15.
26. Okada H, Kuhn C, Feillet H, Bach JF. The 'hygiene hypothesis' for autoimmune and allergic diseases: an update. Clinical & Experimental Immunology. 2010 Apr;160(1):1-9.
27. Shenoi S, Wallace CA. Tumor necrosis factor inhibitors in the management of juvenile idiopathic arthritis: an evidence-based review. Pediatric Drugs. 2010 Dec;12(6):367-77.
28. Grossman JM, Gordon R, Ranganath VK, et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. *Arthritis Care Res (Hoboken)*. 2010;62(11):1515-1526. doi:10.1002/acr.20295
29. Lovell DJ, Ruperto N, Goodman S, Reiff A, Jung L, Jarosova K, Nemcova D, Mouy R, Sandborg C, Bohnsack J, Elewaut D. Adalimumab with or without methotrexate in juvenile rheumatoid arthritis. New England Journal of Medicine. 2008 Aug 21;359(8):810-20.
30. Ruperto N, Brunner HI, Quartier P, Constantin T, Wulffraat N, Horneff G, Brik R, McCann L, Kasapcopur O, Rutkowska-Sak L, Schneider R. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. New England Journal of Medicine. 2012 Dec 20;367(25):2396-406.
31. Groot N, De Graeff N, Marks SD, Brogan P, Avcin T, Bader-Meunier B, Dolezalova P, Feldman BM, Kone-Paut I, Lahdenne P, McCann L. European evidence-based recommendations for the diagnosis and treatment of childhood-onset lupus nephritis: the SHARE initiative. Annals of the rheumatic diseases. 2017 Dec 1;76(12):1965-73.
32. Brunner HI, Abud-Mendoza C, Mori M, Pilkington CA, Syed R, Takei S, Viola DO, Furie RA, Navarra S, Zhang F, Bass DL. Efficacy and safety of belimumab in paediatric and adult patients with systemic lupus erythematosus: an across-study comparison. Rmd Open. 2021 Sep 16;7(3).
33. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, Kahan S. 14. Children and adolescents: standards of care in diabetes—2023. Diabetes care. 2023 Jan 1;46(Supplement_1):S230-53.
34. Herold KC, Bundy BN, Long SA, Bluestone JA, DiMeglio LA, Dufort MJ, Gitelman SE, Gottlieb PA, Krischer JP, Linsley PS, Marks JB. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. New England Journal of Medicine. 2019 Aug 15;381(7):603-13.
35. Durazzo M, Ferro A, Navarro-Tableros VM, Gaido A, Fornengo P, Altruda F, Romagnoli R, Moestrup SK, Calvo PL, Fagoonee S. Current treatment regimens and promising molecular therapies for chronic hepatobiliary diseases. Biomolecules. 2025 Jan 14;15(1):121.