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Renal Involvement in IgA Vasculitis: Bridging the Pathophysiology and Management of IgA Nephropathy

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Abstract

IgA vasculitis (IgAV), formerly known as Henoch-Schönlein purpura, is the most common systemic vasculitis in children but also affects adults, often with more severe renal manifestations. This review highlights the pathophysiology, clinical spectrum, and particularly the renal involvement of IgAV, which determines long-term prognosis. Renal manifestations, observed in up to 50% of patients, range from isolated hematuria and proteinuria to nephrotic syndrome and progressive glomerulonephritis. Biopsy is warranted in patients with significant proteinuria (≥1 g/day), nephrotic syndrome, or rapidly deteriorating renal function. Histopathology typically reveals mesangial IgA deposition and variable degrees of glomerular proliferation, including crescent formation in severe cases. Prognostic biomarkers such as persistent proteinuria, elevated creatinine, and biopsy findings of crescents or endocapillary proliferation guide risk stratification. Management of mild renal involvement is supportive, while moderate to severe disease requires corticosteroids and immunosuppressive agents like mycophenolate or cyclophosphamide. Long-term follow-up is essential, as adult patients with severe renal disease are at risk for progression to chronic kidney disease or end-stage renal failure. Multidisciplinary care is recommended to optimize outcomes. Understanding the renal spectrum of IgA vasculitis and promptly identifying high-risk patients allows for early intervention, which may alter the disease trajectory. Ongoing research into predictive biomarkers and tailored therapies holds promise for improving prognosis in patients with IgAV-related nephritis.

Abbreviations: IgAV: Immunoglobulin A Vasculitis (formerly Henoch-Schönlein Purpura); IgA: Immunoglobulin A; CKD: Chronic Kidney Disease; ESRD: End-Stage Renal Disease; ACE inhibitors: Angiotensin-Converting Enzyme Inhibitors; ARBs: Angiotensin II Receptor Blockers; GFR: Glomerular Filtration Rate; BP: Blood Pressure; RBC: Red Blood Cell; RPGN: Rapidly Progressive Glomerulonephritis; MMF: Mycophenolate Mofetil; SCr: Serum Creatinine; ANA: Antinuclear Antibody; ANCA: Anti-Neutrophil Cytoplasmic Antibody; HSP: Henoch-Schönlein Purpura (historical term); ISKDC: International Study of Kidney Disease in Children (classification system)

Keywords: IgA Vasculitis; Renal Involvement; Immunosuppressive Therapy

Introduction

IgA vasculitis (IgAV), formerly known as Henoch-Schönlein purpura, is an immune-mediated small vessel leukocytoclastic vasculitis characterized by IgA1-dominant immune complex deposition in vessel walls, primarily affecting the skin, joints, gastrointestinal tract, and kidneys [1]. This condition

predominantly affects children between the ages 3-15 years with an annual incidence of 10-20 per 100,000, though adults typically experience more severe disease manifestations and poorer outcomes [2]. The classic clinical tetrad includes palpable purpura predominantly on the lower extremities and buttocks, arthralgia or arthritis typically affecting weight-bearing joints, abdominal pain often accompanied by gastrointestinal bleeding, and varying degrees of nephritis ranging from microscopic hematuria to severe glomerulonephritis [3]. Pathogenesis involves abnormally glycosylated IgA1 molecules and is frequently triggered by upper respiratory infections, medications, vaccines, or food allergies [4,5]. While most cases resolve spontaneously within 4-6 weeks, recurrences occur in approximately one-third of patients, with long-term prognosis largely dependent on kidney involvement, which requires careful monitoring and may necessitate treatment with corticosteroids or immunosuppressants in severe cases [6,7].

Renal involvement in IgA vasculitis (IgAV) occurs in approximately 20-60% of patients, with significant variations reported across different populations and age groups [5]. Children typically demonstrate nephritis in 30-50% of cases, while adults experience higher rates of kidney involvement, ranging from 45-85% with more severe manifestations and poorer outcomes [2,3]. The development of nephritis typically occurs within the first 4-8 weeks after disease onset, with only 1-2% of cases presenting with delayed nephritis beyond this window [4]. Risk factors for severe nephropathy include older age at onset, persistent purpura, severe gastrointestinal involvement, and certain genetic polymorphisms in cytokines and complement pathways [5,6]. Long-term studies reveal that while most pediatric cases resolve without permanent renal damage (85-90%), approximately 5-15% progress to chronic kidney disease with 1-5% eventually developing end-stage renal disease [7,8]. The prognosis is significantly worse in adults, 30-50% develop chronic kidney disease and 10-30% progress to end-stage renal disease within 10-15 years of diagnosis, highlighting the critical importance of early recognition and management of renal manifestations in all IgAV patients, particularly adult populations [9]. The rationale for reviewing renal outcomes in IgA vasculitis (IgAV) stems from the significant morbidity and mortality associated with renal involvement, which represents the most concerning long-term complication of this otherwise self-limiting condition [1]. While the cutaneous, articular, and gastrointestinal manifestations typically resolve without lasting sequelae, nephritis can progress to chronic kidney disease and even end-stage renal disease in a subset of patients, particularly adults [6,8]. The heterogeneity in presentation, severity, and progression of renal involvement presents significant challenges for clinicians in determining appropriate monitoring strategies and therapeutic interventions [9,10]. Furthermore, identifying predictive biomarkers and risk factors for poor renal outcomes remains an unmet clinical need, as current prognostic indicators lack sufficient accuracy for individualized risk stratification [11,12]. A comprehensive understanding of renal outcomes is essential for developing evidence-based guidelines for follow-up duration, treatment selection, and therapeutic targets, as current management approaches remain largely empirical and variable across centers. Ultimately, studying the natural history, risk factors, and treatment responses of IgAV nephritis will facilitate the design of appropriately powered clinical trials and the development of targeted therapies, potentially reducing the burden of chronic kidney disease and improving quality of life for affected patients.

Pathophysiology

Common Immunopathogenic Pathways

IgA nephropathy (IgAN) and IgA vasculitis (IgAV) share a common underlying immunopathogenesis driven by dysregulated immune response involving aberrant IgA1-mediated immunity. A central feature of both conditions is the overproduction of galactose-deficient IgA1 (Gd-IgA1), a subclass of immunoglobulin A1 characterized by deficient O-glycosylation in the hinge region. This abnormal glycosylation exposes terminal N-acetylgalactosamine residues, rendering Gd-IgA1 immunogenic. In genetically predisposed individuals, this abnormality leads to the development of glycan-specific autoantibodies, primarily IgG or IgA isotypes, which target these deficient compounds. The binding of the autoantibodies to Gd-IgA1 initiates the formation of a pathogenic immune complex resistant to normal clearance mechanisms of the spleen and liver. This complex circulates in the bloodstream and deposits in target tissue, such as the glomerular mesangium or small vessel walls, in IgAN and IgAV, respectively. This deposition incites a localized inflammatory response that leads to tissue damage and further inflammation [13-15].

This widely accepted "multi-hit" model, as the central pathophysiologic mechanism for both diseases, starts with overproduction of galactose-deficient IgA1 or Gd-IgA1 (first hit), followed by the formation of antiglycan autoantibodies, IgG or IgA1 isotype (second hit), then the formation of nephritogenic immune complexes (third hit), and finally their deposition in tissues leading to inflammation and damage (fourth hit) [13-15]. Upon deposition, these IgA1-containing immune complexes activate surrounding mesangial or endothelial cells, promoting cell proliferation, matrix expansion, and release of proinflammatory cytokines and chemokines. Activating the complement system, which contributes to glomerular and vascular injury in both IgAN and IgAV. Complement activation in these conditions occurs predominantly via the lectin and alternative pathways, rather than the classical pathway [16,17]. The lectin pathway is initiated when mannose-binding lectin (MBL) or ficolins bind to the terminal sugars on Gd-IgA1 or associated molecules. This binding activates MBL-associated serine proteases (MASP-1 and MASP-2), which cleave complement proteins C4 and C2 to generate the C3 convertase C4b2a. The C3 convertase then cleaves C3 into C3a and C3b, perpetuating the cascade. Simultaneously, the alternative pathway is activated either spontaneously or in an amplification loop. In this pathway, C3b binds factor B, which is cleaved by factor

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D to form the alternative C3 convertase, C3bBb. This enzyme also cleaves C3 and ultimately leads to the formation of the C5 convertase, which splits C5 into the potent anaphylatoxin C5a and C5b, initiating the assembly of the membrane attack complex (MAC, C5b-9). The resulting complement activation products—such as C3a, C5a, and the MAC—which directly damage glomerular and endothelial structures and recruit and activate inflammatory cells, furthering the immune response [16-17]. Immunohistochemical and immunofluorescence frequently demonstrate the co-deposition of IgA with complement components C3, MBL, MASPs, and C4d in the glomerular mesangium, which strongly supports the role of complement in disease pathogenesis [13-17].

Differences and Overlaps Between IgA Vasculitis and IgA Nephropathy

IgA vasculitis and IgA nephropathy are very closely related pathologies that share many immunopathological features but differ significantly in their clinical manifestation and in terms of the organs they involve. Both conditions are characterized by deposition of galactose-deficient IgA1 (Gd-IgA1) in the mesangium, which plays a key role in pathogenesis, upholding the "four-hit hypotheses" of IgA-mediated injury to the glomerulus [6]. The pathogenesis of IgAN involves four sequential processes known as the "four-hit hypothesis," which starts with the production of a galactose-deficient IgA1 (gd-IgA1), followed by the formation of anti-gd-IgA1 IgG or IgA1 autoantibodies and immune complexes that ultimately deposit in the glomerular mesangium, leading to inflammation and injury. Genetic susceptibility plays a significant role in both IgAV and IgAN. Genome-wide association studies (GWAS) have identified overlapping risk loci in genes encoding components of the mucosal immune system, including variants in the HLA class II region. Elevated serum levels of Gd-IgA1 have been observed in patients and their first-degree relatives, indicating a heritable predisposition [18]. These findings suggest that IgAV and IgAN may represent different phenotypic expressions of a common pathogenic process, influenced by both genetic and environmental triggers. Clinically, IgAV typically presents as a systemic small-vessel vasculitis with multi-organ involvement, including palpable purpura, gastrointestinal symptoms, arthralgia, and renal manifestations—collectively termed IgAV nephritis (IgAVN). Renal pathology in IgAVN is often acute and severe, characterized by mesangial hypercellularity, endocapillary proliferation, and crescent formation [19]. In contrast, IgAN is predominantly a renal-limited disease, more frequently diagnosed in adolescents and young adults. It often presents with asymptomatic hematuria or proteinuria, and histologically exhibits more chronic lesions, such as segmental sclerosis and tubular atrophy [19].

Pediatric studies provide further evidence of this divergence. Children with IgAVN tend to have a more favorable prognosis, often achieving remission with minimal intervention. In contrast, pediatric IgAN is more likely to follow a chronic course, with progressive decline in renal function and less frequent complete remission. A recent comparative study found that glomerular IgA deposition was more intense in IgAVN, while chronic tubulointerstitial changes were more pronounced in IgAN [20]. These findings reinforce the concept that while the immunological trigger may be shared, the downstream pathological and clinical outcomes diverge based on systemic versus renal-limited involvement. Recent research has also highlighted the potential role of coagulation pathways in the pathogenesis of IgAV and IgAN. In particular, glomerular fibrinogen deposition has been reported more prominently in IgAVN, suggesting a stronger interaction between the immune and coagulation systems in vasculitic presentations. These findings point toward disease-specific differences in microvascular injury and may inform novel therapeutic targets [21]. Molecular studies further underscore the distinctions between IgAV and IgAN. Transcriptomic profiling of kidney biopsies has revealed both overlapping and distinct immune signatures in IgAV, IgAN, and IgA-dominant infection-related glomerulonephritis. These findings suggest that despite a shared initiating event (Gd-IgA1 deposition), unique inflammatory and immune pathways are activated in each condition, potentially accounting for their different clinical phenotypes [22]. IgAV and IgAN share a common immunopathological substrate but diverge in systemic involvement, clinical presentation, and histological features. The distinction between systemic and renal-limited forms of IgA-associated disease is critical for accurate diagnosis, prognosis, and management. Understanding the nuances of their overlap and divergence may facilitate personalized approaches to treatment and better patient outcomes.

Clinical Presentation

IgA Vasculitis with Renal Involvement

Renal involvement in IgA vasculitis is one of the most critical determinants of long-term prognosis, especially given its clinical and pathological overlap with IgA nephropathy. While the systemic features of IgA vasculitis often dominate the initial presentation, renal manifestations may appear concurrently or follow systemic symptoms by days to weeks [23]. The hallmark renal features include hematuria (both microscopic and macroscopic), proteinuria, and varying degrees of hypertension. Hematuria is often the earliest and most consistent sign, with many patients initially presenting with cola-colored urine or red blood cell casts on urinalysis. Proteinuria can range from subnephrotic levels to nephrotic range in more severe cases. Hypertension is less common at onset but may develop in association with worsening renal function or significant proteinuria [23,26,29-30]. In pediatric patients, renal involvement typically appears within 4 to 6 weeks of the onset of purpura. The majority are presented with isolated hematuria or mild proteinuria. While up to 40–50% of children with IgA vasculitis may develop some degree of kidney involvement, most experience a self-limited course with complete recovery. Nephritic or nephrotic syndromes are less common but can occur, especially in those with persistent proteinuria or abnormal renal functions at presentations. The risk of progression

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to chronic kidney disease (CKD) in children is relatively low, estimated at less than 5%, particularly with early diagnosis and monitoring [24-25,27-28]. In contrast, adults with IgA vasculitis exhibit renal involvement more frequently and with greater severity. Proteinuria and hypertension are more pronounced at presentation, and the likelihood of nephrotic-range proteinuria and impaired renal function is significantly higher. Histological findings in adults also tend to show more chronic damage, including glomerulosclerosis and interstitial fibrosis. As a result, adults are at greater risk for progression to CKD and end-stage renal disease (ESRD). Renal outcomes in this population require closer surveillance and, often, more aggressive management [23-30]. Overall, age serves as a critical modifier of renal prognosis in IgA vasculitis, reinforcing the importance of tailored diagnostic and therapeutic strategies based on the patient's age group and risk factors.

Differentiating IgA Nephropathy from IgA Vasculitis Nephritis

Kidney Involvement tends to occur in about 20-54 percent of children with IgA vasculitis [31,37] and could be common in higher age groups [38]. Associations of kidney involvement in patients with IgA vasculitis have been found to include older age of onset, Gastrointestinal symptoms, low C3, elevated Platelet count, high white blood cell count, and persistence of purpura rash [39,40]. Other factors associated with renal involvement include angioedema, delay in diagnosis, and central nervous system involvement [41,42]. Kidney Involvement occurs mostly within a few days to months after the onset of Systemic symptoms [36]. The commonest presentation is macroscopic or microscopic glomerular haematuria with our without RBC casts and mild or moderate proteinuria [4,6,9]. Less commonly, nephrotic range proteinuria, hypertension and elevated creatinine may be seen. These are associated with worse prognosis. Children tend to develop milder symptoms of IgA vasculitis whereas adults tend to experience moderate to severe form of the disease which is characterized by elevated creatinine, hypertension and nephrotic syndrome [43,44]. IgA nephropathy can be difficult to distinguish from IgA Vasculitis. It tends to be the most common cause of primary glomerulonephritis in most resource developed countries [45]. L Unlike IgA nephrnephritis, ents with IgA vasculitis have extrarenal manifestations such as skin involvement, arthralgias and Gastrointestinal symptoms. Skin involvement is usually a palpable purpura which precedes other symptoms by a mean of four days. Joint symptoms are the second most common presentation after the rash. Gastrointestinal symptoms also include colicky abdominal pain and gastrointestinal bleeding [46]. On kidney biopsy, light microscopy reveals wide spectrum of glomerular changes, including isolated mesangial proliferation, focal and segmental proliferation, severe crescentic glomerulonephritis. Dominant or codominant IgA, notably IgA1 deposition in the mesangium on immunofluorescence like what is seen in IgA nephropathy is diagnostic. Immunofluorescence also usually reveals IgG, IgM, fibrinogen deposit in the glomeruli [37-46].

Diagnosis

According to the EULAR criteria, IgA vasculitis can be diagnosed with the presence of palpable purpura or petechiae (predominantly affecting the lower limbs) along with any 1 of the following manifestations:

- Abdominal pain
- Arthritis or arthralgia
- Proliferative glomerulonephritis or
- Renal involvement

The presence of haematuria, proteinuria, hypertension or renal failure is indicative of renal involvement [47,48]. As per the SHARE guidelines, a kidney biopsy is recommended in children with IgA Vasculitis (IgAV) and persistent proteinuria, nephrotic-range proteinuria or reduced eGFR [49]. In adults, a renal biopsy is recommended if there is significant and persistent proteinuria or unexplained decline in kidney function [50]. The use of detecting serum and urinary biomarkers would decrease the need for invasive investigations like renal biopsies. A previous study concluded that complement proteins in urine may serve as biomarkers of chronic disease in IgAV with Nephritis (IgAVN). u-PTX and u-MBL (Mannose Binding Ligand) were found to be associated with mesangial hypercellularity, endocapillary proliferation and crescents in kidney biopsy. High u-C4c levels were seen in association with advanced tubulointerstitial fibrosis [51]. According to multiple previous studies, Serum Gd-IgA1 levels and Gd-IgA1-specific IgG autoantibody are associated with the development of nephritis and can be used as diagnostic biomarkers for IgA nephropathy [52]. They are associated with a faster decline in kidney function in IgA Nephropathy (IgAN) [53]. The serum IgA/C3 ratio was also found to be a useful marker to distinguish IgAN from non-IgAN [54]. What is the best histopathological classification for IgAV? This question is still under debate. Recent studies favour the MEST-C score. ISKDC (International Study of Kidney Disease in Children) is a widely used scoring system, categorizing renal biopsies into six histological grades. The first five grades are based on the number of crescents and the sixth grade includes membranoproliferative glomerulonephritis. This scoring system was found to be inaccurate in predicting renal outcome as studies have shown that patients with low grade histologic lesions may develop chronic renal failure and patients with higher histological stages may experience spontaneous healing of lesions. These reports introduced the MEST-C score, which included the following morphological features: mesangial hypercellularity (M), endocapillary proliferation (E), segmental glomerulosclerosis/adhesion (S), tubular atrophy/interstitial fibrosis (T) and crescent score(C) [55]. Another study conducted in 2024 also concluded that the ISKDC scoring system was inaccurate and the Oxford (MEST-C) preferred [56].

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Prognosis and Risk Factors

IgAV nephritis represents the most serious complication and primary determinant of long-term prognosis, with children typically experiencing a self-limiting course, while adults face more severe renal manifestations and a higher risk of progression to chronic kidney disease (CKD) or end-stage renal disease (ESRD) [57,58]. Several clinical risk factors have been consistently associated with poor renal outcomes. Nephrotic-range proteinuria exceeding 3.5 grams per day is a strong predictor of progression to CKD or ESRD. Persistent hematuria and proteinuria lasting beyond six months are also linked to chronic glomerular injury and poor prognosis. Hypertension, either present at the time of diagnosis or developing during follow-up, significantly elevates the risk of renal deterioration. Moreover, patients presenting with acute kidney injury (AKI) or rapidly progressive glomerulonephritis tend to have worse renal outcomes. Older age at disease onset particularly those over 16 years has been associated with more severe renal disease, and delayed initiation of treatment beyond four weeks from symptom onset correlates with less favorable outcomes [59,60].

Histopathologic features from kidney biopsies offer additional prognostic insight. The presence of crescents in more than 50% of glomeruli is a well-established marker for poor renal prognosis. Other significant findings include endocapillary proliferation, tubular atrophy, and interstitial fibrosis, which are indicative of irreversible renal damage and decline in renal function over time. The International Study of Kidney Disease in Children (ISKDC) grading system also provides prognostic stratification, with higher grades (III and above) correlating with more aggressive disease and worse outcomes [61]. The prognosis of IgAVN differs markedly between children and adults. IgAV is more common in children, with renal involvement occurring in 20–50% of pediatric cases, compared to 40–80% in adults. However, the severity of nephritis is typically milder in children, and fewer than 5% progress to CKD or ESRD. In contrast, adults often present with more severe renal disease, and 10–30% may eventually develop CKD or ESRD. Children generally respond well to corticosteroid therapy, whereas adults may require more intensive immunosuppressive regimens and have more guarded outcomes, especially in the presence of comorbid conditions [57,58]. In terms of long-term renal prognosis, it is estimated that 5–20% of patients with IgAV nephritis may develop chronic kidney disease, and approximately 1–15% predominantly adults with severe forms may progress to ESRD over a span of 10 to 20 years. The risk of progression is greatest in those with nephrotic syndrome, crescent formation in more than half of glomeruli, persistent hypertension or proteinuria, and delayed initiation of treatment. Given these risks, long-term follow-up is essential, even in cases where initial symptoms are resolved. This should include regular monitoring of blood pressure, urinalysis to detect hematuria or proteinuria, and assessment of renal function through serum creatinine and estimated glomerular filtration rate (eGFR) [60-62].

Management Strategies

Supportive Therapy

Blood Pressure Control

Maintaining optimal blood pressure is foundational in the management of IgA nephropathy (IgAN). Current guidelines recommend a target blood pressure of <120/80 mmHg, especially in patients with proteinuria >1 g/day, as this level of control has been associated with delayed progression to end-stage kidney disease (ESKD). Intensive blood pressure control is known to reduce glomerular injury and proteinuria, thereby offering renoprotection [63,66].

Use of RAAS Inhibitors

Renin–angiotensin–aldosterone system (RAAS) blockade, primarily through the use of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs), is the mainstay of supportive care. These agents reduce intraglomerular pressure and proteinuria while preserving kidney function. Nearly all patients with proteinuria >0.5–1 g/day should be treated with RAAS inhibitors unless contraindicated. Titration to the maximum tolerated dose is often necessary to achieve therapeutic goals [63,64-66].

Immunosuppressive Therapy

Indications for Steroids

Steroid therapy may be considered in patients with persistent proteinuria >1 g/day despite optimized supportive care and preserved renal function (eGFR >30 ml/min/1.73 m^2). The use of oral glucocorticoids, particularly over a 6–9-month period, has been shown to reduce proteinuria and slow disease progression in selected patients. However, risks such as infections, metabolic complications, and psychiatric effects necessitate cautious patient selection and monitoring [63,66].

Role of Cyclophosphamide, MMF, or Rituximab in Severe Nephritis

In patients with rapidly progressive IgAN, crescentic nephritis, or significant kidney function decline, stronger immunosuppression may be warranted. Cyclophosphamide, typically in combination with corticosteroids, may be used in such severe cases, though its use is extrapolated from ANCA-associated vasculitis and remains controversial in IgAN. Mycophenolate mofetil (MMF) has demonstrated benefits in certain Asian populations but has shown inconsistent results globally. Rituximab, a B-cell-depleting agent, has not demonstrated efficacy in IgAN and is not currently recommended outside clinical trials [64,67].

Emerging and Investigational Therapies

Targeting Galactose-Deficient IgA1

A central pathogenic mechanism in IgAN involves galactose-

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deficient IgA1 (Gd-IgA1), which initiates immune complex formation and mesangial deposition. Novel therapies aimed at reducing Gd-IgA1 production or clearance are under investigation. For instance, B-cell targeting strategies and therapies that inhibit Gd-IgA1-producing plasma cells show promise, offering a more disease-specific intervention [63,67].

Complement Inhibitors

The role of complement activation in IgAN pathogenesis has led to the exploration of complement inhibitors. Agents like narsoplimab, a lectin pathway inhibitor targeting MASP-2, have shown early promise in reducing proteinuria and preserving kidney function. Similarly, Iptacopan, an oral factor B inhibitor targeting the alternative complement pathway, has demonstrated reductions in proteinuria and stabilization of kidney function in clinical trials. These therapies represent a shift toward precision medicine in IgAN, focusing on the underlying immunopathology rather than nonspecific immunosuppression [63,64,67].

Special Populations and Considerations

The approach taken by adult and Paediatric nephrologists in the treatment of IgA nephropathy is different. Even though both show the characteristic clinical presentation of IgA nephropathy of haematuria, proteinuria and IgA deposits [68]. It was observed that the children affected with Ig A nephropathy were prescribed Immunosuppressive therapy more often than the Ig A nephropathy affected adults.The treatment regimen was corticosteroid monotherapy or combination therapy with other immunosuppressive drugs [68]. Compared to adults, children were more frequently started on immunosuppressive therapy prior to a biopsy confirming the diagnosis of IgAN [69].

Future Directions

Despite growing insight into the shared mechanisms underlying IgA vasculitis with renal involvement and IgA nephropathy, significant challenges remain in predicting disease progression, individualizing treatment, and achieving early diagnosis. A key area of ongoing research focuses on the identification and validation of non-invasive biomarkers to detect renal involvement at an early stage and to monitor therapeutic response. Promising candidates include galactose-deficient IgA1, circulating immune complexes, and urinary cytokines, but none have yet been incorporated into routine clinical practice due to variability in sensitivity and specificity [70-73]. Simultaneously, multiple clinical trials are underway investigating targeted therapies to modulate mucosal immunity, reduce mesangial deposition, and attenuate downstream inflammatory responses. Trials evaluating complement inhibitors, corticosteroid-sparing regimens, and novel biologics such as B-cell or BAFF inhibitors reflect a shift toward precision medicine in managing glomerular injury associated with IgA vasculitis [72-75]. Additionally, the field continues to grapple with the lack of standardized classification systems for renal pathology in IgA vasculitis, which limits the comparability of studies and complicates risk stratification. Although the Oxford classification provides a histologic framework for IgA nephropathy, its applicability to IgA vasculitis remains debated. Establishing a consensus-based histopathologic and clinical classification specific to IgA vasculitis with renal involvement is essential to unify research efforts, guide clinical decisions, and improve outcome prediction [72-77]. Together, these future directions underscore a growing movement toward integrating molecular diagnostics, clinical phenotyping, and collaborative trial networks to improve long-term renal outcomes in both children and adults affected by IgA vasculitis.

Conclusion

Renal involvement in IgA vasculitis is the most significant determinant of long-term morbidity, especially in adult patients. Early recognition of clinical and laboratory indicators of nephritis, coupled with timely renal biopsy and risk-based treatment strategies, is critical to preventing irreversible renal damage. While most patients with mild renal findings have a favorable prognosis, those with persistent proteinuria, hypertension, or crescentic glomerulonephritis require close monitoring and aggressive therapy. Multidisciplinary care and long-term follow-up are essential to optimize renal outcomes. Advances in biomarker research and individualized immunosuppressive regimens represent promising future directions in the management of IgAV nephritis.

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