THE ATLANTIC Journal of Medical Science and Research

Atlantic J Med Sci Res 2025;5(4):118-23
DOI: 10.5455/atjmed.2025.11.029

Original Article

The impact of comorbidity on clinical characteristics in adult IgA vasculitis

Pinar Akyuz Dagli[1], Gul Sandal Uzun[1], Seda Yurumez Colak[1], Emre Tekgoz[2], Duygu Tecer[1], Muhammet Cinar[2], Sedat Yilmaz[2]

[1]Gülhane Training and Research Hospital, Clinic of Rheumatology, Ankara, Türkiye
[2]University of Health Sciences, Gülhane Training and Research Hospital, Department of Internal Medicine, Division of Rheumatology, Ankara, Türkiye

Received: 11 November, 2025
Accepted: 17 December, 2025
Published: 23 December, 2025

Corresponding Author: Pınar Akyuz Dagli, Gülhane Training and Research Hospital, Clinic of Rheumatology, Ankara, Türkiye
Email: pinarakyuz25@gmail.com

CITATION
Akyuz Dagli P, Sandal Uzun G, Yurumez Colak S, et al. The impact of comorbidity on clinical characteristics in adult IgA vasculitis. Atlantic J Med Sci Res. 2025;5(4):118-23. DOI: 10.5455/atjmed.2025.11.029

Abstract

Aim: Adult immunoglobulin A (IgA) vasculitis is a rare small-vessel vasculitis with heterogeneous systemic involvement and variable clinical trajectories. However, the influence of comorbidities on disease phenotype and early clinical presentation in adults remains unclear. This study aimed to determine how comorbidity burden relates to baseline clinical manifestations in adult IgA vasculitis.

Materials and Methods: In this retrospective, single-center study, we analyzed 57 adults diagnosed with IgA vasculitis between January 2017 and August 2025. Comorbidity burden was assessed using the Charlson Comorbidity Index (CCI), age-adjusted Charlson Comorbidity Index (ACCI), and Elixhauser Comorbidity Index (ECI). Patients were categorized by the presence or absence of comorbid conditions, and demographic, clinical, and laboratory characteristics were compared. Associations between organ involvement and comorbidity indices were also evaluated.

Results: Overall, 45.6% of patients had at least one comorbidity, most commonly hypertension and diabetes mellitus. Patients with comorbidities were significantly older ($p<0.001$) and more frequently female (50.0% vs. 22.6%; $p=0.031$). Gastrointestinal involvement (64.5% vs. 34.6%; $p=0.025$) and arthritis (61.3% vs. 23.1%; $p=0.004$) were more prevalent among patients without comorbidities, whereas the frequency of renal involvement did not differ significantly between groups ($p=0.598$). No significant correlations were observed between comorbidity indices and organ-specific involvement. In multivariable logistic regression, age was independently associated with the presence of comorbidity (OR=1.10, 95% CI:1.04–1.17; $p=0.001$), while arthritis demonstrated an inverse association (OR=0.15, 95% CI:0.03–0.80;$p=0.024$).

Conclusion: In adult IgA vasculitis, comorbidity burden primarily reflects age-related risk rather than distinct organ involvement patterns. The higher frequencies of arthritis and gastrointestinal involvement among patients without comorbidities suggest that comorbidity status may subtly modify the clinical presentation. These findings indicate that comorbidity indices may offer complementary value in clinical evaluation by providing additional phenotypic and prognostic context.

Keywords: Immunoglobulin A vasculitis, comorbidity, clinical phenotype, adult vasculitis

INTRODUCTION

Immunoglobulin A (IgA) vasculitis, formerly termed Henoch–Schönlein purpura, is an immune complex–mediated small-vessel vasculitis (1). Although it can occur at any age, it is less common in adults than in children and typically follows a more severe clinical course. The classical clinical syndrome is characterized by palpable purpura, arthritis or arthralgia, gastrointestinal (GI) involvement, and varying degrees of renal involvement. Among adults, prognosis is largely determined by the presence and severity of renal disease, which remains the principal predictor of long-term morbidity and mortality (2, 3).

Comorbidity burden has emerged as an important determinant of clinical phenotype, therapeutic response, and prognosis across systemic vasculitides. In adult IgA vasculitis, coexisting chronic conditions may alter the inflammatory milieu and modify organ-specific involvement, ultimately influencing disease trajectory and outcomes. A large population-based study demonstrated that the accumulation of comorbidities before diagnosis was associated with increased mortality and a higher risk of severe infections in adults with IgA vasculitis (4). However, data

remain limited regarding how common comorbidities—such as hypertension, diabetes mellitus, chronic kidney disease, and cardiovascular disease—shape baseline clinical features and early disease course.

Most existing studies are short-term, single-center, or report comorbidities as secondary variables rather than primary determinants of disease course (5). In a large cohort from China, Wang et al. identified advanced age, hypertension, diabetes mellitus, hyperlipidemia, and hyperuricemia as independent predictors of renal progression in adult IgA vasculitis (6). These findings suggest that comorbidities may function not merely as coexisting conditions but as active risk factors contributing to adverse renal outcomes. However, their potential influence on the initial clinical phenotype—particularly extrarenal manifestations such as arthritis, gastrointestinal involvement, and cutaneous distribution—remains insufficiently characterized (7).

Quantitative assessment of comorbidity burden using standardized indices, including the Charlson and Elixhauser Comorbidity Indices, has been shown to enhance the predictive value of outcome analyses in rheumatologic diseases (8). Yet, the application of these indices specifically to adult IgA vasculitis remains limited. This gap in evidence restricts our ability to discern the confounding or interactive role of comorbidities in phenotype–outcome relationships and hinders efforts to establish more refined risk stratification approaches.

In this context, the aim of our study is to comprehensively evaluate the impact of comorbidity burden on the initial clinical phenotype in adult IgA vasculitis patients using standardized comorbidity indices. We hypothesized that an increased comorbidity burden modulates the clinical presentation of the disease, particularly concerning extrarenal manifestations.

MATERIALS AND METHODS

This retrospective, single-center study included adult patients diagnosed with IgA vasculitis and followed at the Rheumatology Clinic of Gülhane Training and Research Hospital. Electronic medical records of patients evaluated in the rheumatology outpatient clinic between January 1, 2017, and August 31, 2025, were reviewed. The diagnosis of IgA vasculitis was established based on clinical features and, when available, histopathologic confirmation, according to the American College of Rheumatology (ACR) 1990 criteria (9) and the EULAR/PRINTO/PRES 2010 classification criteria (10).

A total of 85 patients with an IgA vasculitis diagnostic code were initially screened. Patients with incomplete clinical data, those younger than 18 years at diagnosis, and those who did not fulfill either classification set were excluded. Ultimately, 57 adult patients met all inclusion criteria and were included in the analysis. Demographic characteristics, clinical manifestations, laboratory values, and serological parameters at diagnosis were extracted from the hospital information system. Only routinely collected clinical and laboratory data were used, and no additional diagnostic or therapeutic interventions were performed for study purposes.

Comorbidity burden was quantified using the Charlson Comorbidity Index (CCI) (8), the age-adjusted Charlson Comorbidity Index (ACCI) (11), and the Elixhauser Comorbidity Index (ECI) (8). Patients were categorized according to the presence or absence of comorbidities, and clinical, laboratory, and organ involvement parameters were compared between groups. Associations between specific organ involvements and comorbidity indices were also evaluated.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation (SD) or median (minimum–maximum), as appropriate, and categorical variables as frequencies and percentages. Normality of distribution was assessed using the Shapiro–Wilk test. For comparisons between two normally distributed groups, the independent-samples t-test was used, whereas one-way analysis of variance (ANOVA) was applied for comparisons involving more than two groups. For non-normally distributed variables, the Mann–Whitney U test and Kruskal–Wallis H test were used. Categorical variables were compared using the Chi-square test or Fisher's exact test. Logistic regression analysis was performed to identify independent factors associated with the presence of comorbidity, with age, sex, and clinical involvement variables included in the model. A p-value<0.05 was considered statistically significant.

The study was approved by the institutional ethics committee in accordance with national and international research standards (Approval No: 2025/233). Because this was a retrospective study utilizing existing medical records, additional informed consent was not required.

RESULTS

A total of 57 patients diagnosed with IgA vasculitis were included in the analysis. The median age was 56 years (IQR: 45–68), and 35.1% were female. Cutaneous involvement was present in all patients. The most common systemic manifestations were GI involvement (50.9%), arthritis (43.9%), and renal involvement (38.6%). All patients received oral corticosteroid therapy. Additional clinical features and treatment characteristics are summarized in Table 1.

Comorbidities were identified in 45.6% of patients. The most prevalent conditions were hypertension (19.3%), diabetes mellitus (9.6%), and heart failure (6.0%). Assessment of comorbidity burden using the Charlson Comorbidity Index (CCI), age-adjusted Charlson Comorbidity Index (ACCI), and Elixhauser Comorbidity Index (ECI) demonstrated generally low median scores (CCI=0.5; ACCI=2; ECI=0) (Table 2), indicating a low-to-moderate comorbidity burden across the cohort.

When patients were compared according to comorbidity status, those with comorbidities were significantly older and had a higher age at diagnosis (both p<0.001). The proportion of female

patients was also higher in this group (50.0% vs. 22.6%; p=0.031). Gastrointestinal (GI) involvement (64.5% vs. 34.6%; p=0.025) and arthritis (61.3% vs. 23.1%; p=0.004) were significantly more frequent among patients without comorbidities, whereas renal involvement did not differ between groups (p=0.598). In terms of treatment, azathioprine (51.6% vs. 23.1%; p=0.028) and colchicine (35.5% vs. 7.7%; p=0.013) were used more often in patients without comorbidities. The use of pulse corticosteroids, cyclophosphamide, and mycophenolate mofetil did not differ significantly between groups (Table 3). Taken together, these findings suggest that patients with comorbidities represented an older, more female-predominant subgroup characterized by lower frequencies of arthritis and GI involvement.

In the multivariable logistic regression model including age and sex, the overall model accuracy was 80.7%. The presence of arthritis was independently and inversely associated with comorbidity (OR=0.15;95%CI:0.03–0.80;p=0.024), indicating that patients with arthritis had a markedly lower likelihood of having comorbid conditions. By contrast, age was a positive and statistically significant predictor of comorbidity (OR=1.10;95%CI:1.04–1.17;p=0.001). Renal involvement (p=0.693), GI involvement (p=0.653), and sex (p=0.309) were not significantly associated with comorbidity status (Table 4). Overall, these results indicate that age is the principal determinant of comorbidity risk, whereas arthritis may reflect a distinct clinical phenotype associated with a lower comorbidity burden.

When the associations between organ involvement and comorbidity indices were examined, renal involvement was not significantly correlated with any of the evaluated indices, including the CCI, ACCI, and ECI (p=0.069;p=0.443;p=0.305, respectively). Similarly, no significant associations were identified between these indices and GI involvement (p=0.634;p=0.711;p=1.000) or arthritis (p=0.700;p=0.573;p=0.573). These findings indicate that organ involvement patterns are not directly influenced by comorbidity burden.

To account for the potential confounding effect of age, a subgroup analysis was conducted among patients younger than 55 years. Within this subgroup, arthritis remained significantly more common in patients without comorbidities (61.5% vs.14.3%;p=0.026). Renal involvement was more frequent in those with comorbidities (71.4% vs. 38.5%; p=0.120), while GI involvement tended to be more common in patients without comorbidities (73.1% vs. 42.9%; p=0.132), although neither reached statistical significance. These results suggest that the inverse association between arthritis and comorbidity is independent of age and may reflect distinct clinical phenotypes within younger patients.

Table 1. General demographic, clinical, and therapeutic characteristics of patients with IgA vasculitis

Variable	Total patients (n=57)
Sex, female, n (%)	20 (35.1)
Age (year), median (IQR)	56 (45–68)
Age at diagnosis (years), median (IQR)	55 (43–67)
Smoking Status, ever, n (%)	25 (43.9)
Presence of comorbidity, n (%)	26 (45.6)
BWAS score, median (IQR)	4 (3–11)
Fever	5 (8.8)
Arthralgia	29 (50.9)
Arthritis, n (%)	25 (43.9)
Skin involvement, n (%)	57 (100)
Lower extremity involvement	57 (100)
Upper extremity involvement	24 (42.1)
Trunk involvement	19 (33.3)
GI involvement, n (%)	29 (50.9)
Abdominal pain	22 (38.6)
Bloody diarrhea	10 (17.5)
Positive fecal occult blood	24 (28.9)
Renal involvement, n (%)	22 (38.6)
Proteinuria	21 (36.8)
Hematuria	6 (10.5)
Acute renal failure	9 (10.8)
Renal biopsy, n (%)	14 (24.6)
Skin biopsy, n (%)	48 (84.2)
Treatment agents, n (%)	
Pulse corticosteroid	24 (42.1)
Oral steroid	57 (100)
Cyclophosphamide	13 (22.8)
Azathioprine	22 (38.6)
Mycophenolate mofetil	7 (12.3)
Colchicine	13 (22.8)
Exitus, n (%)	9 (15.8)

BWAS: birmingham vasculitis activity score, GI: gastrointestinal, IQR: interquartile range

Table 2. Comorbidity characteristics and index scores of the study population

Variable	Value
Comorbidity, n (%)	
Hypertension	16 (19.3)
Diabetes mellitus	8 (9.6)
Heart failure	5 (6.0)
Rheumatic disease*	2 (3.5)
Hypothyroidism	2 (2.4)
Coronary artery disease	2 (2.4)
Asthma / COPD	2 (2.4)
Valvular heart disease	2 (2.4)
Thrombosis	2 (2.4)
Malignancy	1 (1.2)
Cerebrovascular event	1 (1.2)
Atrial fibrillation	1 (1.2)
At least one comorbidity	26 (31.3)
Comorbidity Index, median (IQR)	
Charlson Comorbidity Index	0 (0–1)
Elixhauser Comorbidity Index	7 (0–10)
Age-adjusted Charlson Comorbidity Index	0 (0–1)

IQR, interquartile range; COPD, chronic obstructive pulmonary disease

Table 3. Comparison of demographic, clinical, and therapeutic characteristics according to the presence of comorbidities

Variable	Comorbidity (–) (n=31)	Comorbidity (+) (n=26)	p-value
Sex, female, n (%)	7 (22.6)	13 (50.0)	**0.031**
Age (years), median (IQR)	45 (35–55)	67 (60–75)	<0.001
Age at diagnosis(years), median (IQR)	44 (33–54)	66 (58–74)	<0.001
BWAS score, median (IQR)	4 (3–11)	4 (3–11)	0.406
Organ involvement, n (%)			
GI involvement	20 (64.5)	9 (34.6)	**0.025**
Renal involvement	11 (35.5)	11 (42.3)	0.598
Arthritis	19 (61.3)	6 (23.1)	**0.004**
Skin involvement	31 (100)	26(100)	—
Treatment agents, n (%)			
Pulse corticosteroid	14 (45.2)	10 (38.5)	0.610
Oral corticosteroid	31 (100.0)	26 (100.0)	—
Cyclophosphamide	7 (22.6)	6 (23.1)	0.965
Azathioprine	16 (51.6)	6 (23.1)	**0.028**
Mycophenolate mofetil	4 (12.9)	5 (19.2)	0.514
Colchicine	11 (35.5)	2 (7.7)	**0.013**

BWAS: birmingham vasculitis activity score, GI: gastrointestinal, IQR: interquartile range

Table 4. Multivariate logistic regression results

Variable	OR (95% CI)	p value
Arthritis	0.15 (0.03–0.80)	0.024
Renal involvement	1.40 (0.30–6.50)	0.693
GI involvement	0.70 (0.16–3.00)	0.653
Age (years)	1.10 (1.04–1.17)	0.001
Sex (male)	0.44 (0.10–1.95)	0.309

CI: confidence interval, OR: odds ratio, GI: gastrointestinal

DISCUSSION

This study is one of the few to explore how comorbidity burden shapes the clinical phenotype of adult IgA vasculitis. Our primary finding is that comorbidities, which are closely linked to age, are associated with a distinct clinical phenotype characterized by a lower frequency of inflammatory manifestations such as arthritis and gastrointestinal involvement. These results suggest that comorbidity burden may not only reflect coexisting diseases but also modulate the systemic inflammatory response and phenotypic expression of the vasculitis."

Comorbidities are important determinants of clinical outcomes in systemic vasculitides, and adult-onset IgA vasculitis is increasingly recognized as a clinically heterogeneous condition shaped by patient-related factors such as age and comorbidity burden. Recent reviews have highlighted that comorbid conditions may modify disease expression, therapeutic response,

and outcomes in adult IgA vasculitis (12,13). Our findings align with these observations, demonstrating that a higher comorbidity burden is associated with a less inflammatory clinical phenotype, underscoring the need for individualized assessment and management strategies in this population. Large-scale population studies have similarly shown that the accumulation of comorbid conditions before diagnosis significantly increases the risk of hospitalization and mortality (4), and that cardiovascular and renal comorbidities are associated with poorer short-term outcomes (5).

Comparable patterns have been reported in other forms of small-vessel vasculitis. In granulomatosis with polyangiitis, higher comorbidity scores have been associated with less inflammatory, organ-limited disease phenotypes, suggesting that comorbidity burden may influence disease expression (14). Likewise, in ANCA-associated vasculitis, older age and comorbidities have been shown to attenuate systemic inflammation while increasing treatment-related risks (15). Similar relationships have been described in other rheumatic diseases, including rheumatoid arthritis and systemic lupus erythematosus, where comorbidity burden influences both disease phenotype and therapeutic response (16,17). Higher comorbidity scores have been linked to a blunted clinical presentation, altered cytokine profiles, and a tendency toward immune suppression. Within this broader context, comorbidity in adult IgA vasculitis may not simply represent a concurrent condition but may function as a "modifying factor" that shapes both the immunopathogenesis and clinical expression of the disease.

Our findings align with previous research underscoring the heterogeneity of organ involvement in adult IgA vasculitis. In a large cohort study, gastrointestinal and renal manifestations were shown to be influenced by patient-related factors such as age and systemic inflammatory activity (18). Renal involvement remains the principal determinant of long-term prognosis in adult IgA vasculitis (1), and metabolic and cardiovascular comorbidities have been identified as independent predictors of renal disease progression (6). However, in our cohort, the prevalence of renal involvement did not differ by comorbidity status. This observation suggests that comorbidities may not influence renal involvement at presentation but could contribute to progressive renal deterioration over time.

The inverse association between arthritis and comorbidity observed in our study is noteworthy. Arthritis, a marker of acute inflammation in IgA vasculitis, was more common among patients without comorbidities, suggesting a more robust inflammatory response in this group. An increasing comorbidity burden may reduce the ability to mount an effective inflammatory response. Cardiometabolic comorbidities—characterized by chronic low-grade inflammation and dysregulated cytokine activity (including IL-6, TNF-α, and IL-10)—may attenuate immune reactivity and diminish vascular and extrarenal inflammatory manifestations such as arthritis (19,20).

Quantitative assessment of comorbidity burden using standardized indices provides a valuable approach for improving the accuracy and predictive performance of prognostic analyses in rheumatic diseases (7,8). Although median scores in our cohort were low, these indices offer a structured framework for evaluating both the number and clinical impact of coexisting conditions. Incorporating objective comorbidity scoring, particularly in elderly or medically complex patients, may enhance risk stratification and support individualized management strategies.

Our study has several strengths, including its focus on an underexplored aspect of adult IgA vasculitis and its use of standardized comorbidity indices. However, certain limitations must be acknowledged. The retrospective design, single-center nature, and limited sample size restrict the generalizability of our findings. Furthermore, the absence of long-term renal outcome and mortality data prevented us from evaluating the longitudinal impact of comorbidities. Therefore, future prospective, multicenter, and biomarker-based studies are warranted to further elucidate the relationship between comorbidity burden, disease phenotype, and prognosis.

CONCLUSION

In conclusion, comorbidity burden in adult IgA vasculitis reflects an age-related pattern but may also shape the phenotypic expression of the disease, particularly with respect to extrarenal manifestations such as arthritis and gastrointestinal involvement. Quantitative evaluation of comorbidities using standardized indices may enhance clinical risk stratification and facilitate the implementation of individualized management strategies.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The study was approved by the Rheumatology Clinic of Gülhane Training and Research Hospital. (Approval No: 2025/233; Date: 06 November 2025).

REFERENCES

1. Maritati F, Canzian A, Fenaroli P, Vaglio A. Adult-onset IgA vasculitis (Henoch-Schönlein): update on therapy. Presse Med. 2020;49:104035.
2. Hankard A, Audemard Verger A. Adult IgA vasculitis. Rev Prat. 2023;73:1124-30.
3. Stanway J, Brown N, Pervez A, et al. IgA vasculitis nephritis—outcomes in adult-onset disease. Rheumatology. 2025;64:690-6.
4. Nossent J, Raymond W, Isobel Keen H, et al. Morbidity and mortality in adult-onset IgA vasculitis: a long-term population-based cohort study. Rheumatology. 2022;61:291-8.
5. Hočevar A, Ostrovršnik J, Jurčić V, et al. Short-term outcome of patients with adult IgA vasculitis: a single-center experience. Front Med (Lausanne). 2023;10:1210307.
6. Wang Y, Zhou X, Cheng G, et al. Identification of risk factors for renal progression in adults with IgAV: a retrospective

cohort study of a single center in northwest China. Int Urol Nephrol. 2025;57:1-13.

7. Radner H. Viewpoint: how to measure comorbidities in patients with rheumatoid arthritis - clinical and academic value. Rheumatology (Oxford). 2023;62:SI282-SI5.
8. Moltó A, Dougados M. Comorbidity indices. Clin Exp Rheumatol. 2014;32:131-4.
9. Mills JA, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Henoch-Schönlein purpura. Arthritis Rheum. 1990;33:1114-21.
10. Hočevar A, Rotar Z, Jurčić V, et al. IgA vasculitis in adults: the performance of the EULAR/PRINTO/PRES classification criteria in adults. Arthritis Res Ther. 2016;18:58.
11. Kim S-K, Choe J-Y, Lee S-S. Charlson comorbidity index is related to organ damage in systemic lupus erythematosus: data from KORean lupus Network (KORNET) registry. J Rheumatol Suppl. 2017;44:452-8.
12. Kelly BG, Stratton DB, Mansour I, et al. Navigating the initial diagnosis and management of adult IgA vasculitis: A review. JAAD Int. 2022;8:71-8.
13. Tracy A, Subramanian A, Adderley NJ, et al. Cardiovascular, thromboembolic and renal outcomes in IgA vasculitis (Henoch-Schönlein purpura): a retrospective cohort study using routinely collected primary care data. Ann Rheum Dis. 2019;78:261-9.
14. Li L, Neogi T, Jick S. A cohort study of comorbidity in patients with granulomatosis with polyangiitis. Rheumatology (Oxford). 2018;57:291-9.
15. Kronbichler A, Leierer J, Gauckler P, Shin JI. Comorbidities in ANCA-associated vasculitis. Rheumatology (Oxford). 2020;59:iii79-iii83.
16. Huang Y-J, Chen J-S, Luo S-F, Kuo C-F. Comparison of indexes to measure comorbidity burden and predict all-cause mortality in rheumatoid arthritis. J Clin Med. 2021;10:5460.
17. Barnado A, Carroll RJ, Casey C, et al. Phenome-wide association study identifies marked increased in burden of comorbidities in African Americans with systemic lupus erythematosus. Arthritis Res Ther. 2018;20:69.
18. Hočevar A, Tomšič M, Jurčić V, et al. Predicting gastrointestinal and renal involvement in adult IgA vasculitis. Arthritis Res Ther. 2019;21:302.
19. Domingo E, Marques P, Francisco V, et al. Targeting systemic inflammation in metabolic disorders. A therapeutic candidate for the prevention of cardiovascular diseases? Pharmacol Res. 2024;200:107058.
20. Floyd L, Morris AD, Woywodt A, Dhaygude A. Cardiovascular disease and ANCA-associated vasculitis: are we missing a beat? Clin Kidney J. 2022;15:618-23.