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Renal Involvement and Early Relapse Patterns in Granulomatosis with Polyangiitis: A Prospective Cohort from a Tertiary Care Center

Arefeh Afsar
Tehran University of Medical Sciences
Abdolrahman Rostamian
Vali-Asr Hospital, Tehran University of Medical Sciences
Behnam Jazayeri
Tehran University of Medical Sciences
Shayan Shahi
Tehran Heart Center, Tehran University of Medical Sciences
Mahgol Meshkati
Tehran University of Medical Sciences
Sima Maziar
maziarsima53@gmail.com

Tehran University of Medical Sciences

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Abstract

Renal involvement is a major determinant of prognosis in granulomatosis with polyangiitis (GPA), yet population-specific data from the Middle East remain scarce. In this prospective cohort study, 186 consecutive patients diagnosed with GPA between 2013 and 2021 at a tertiary referral center were followed to evaluate the clinical characteristics, relapse patterns, and prognostic factors associated with renal involvement, with particular emphasis on urinary findings and ANCA specificity. Renal involvement was present in 44% of patients and was associated with older age, male predominance, higher baseline disease activity, and greater MPO-ANCA positivity. Despite more intensive induction therapy, renal involvement alone did not independently predict higher relapse frequency or mortality after adjusting for baseline severity and treatment. Within the renal cohort, gross hematuria emerged as the strongest predictor of relapse (odds ratio [OR] 7.1, 95% confidence interval [CI] 1.7–20.4), followed by proteinuria (OR 2.5, 95% CI 1.06–6.6). PR3-positive renal patients had a markedly higher rate of early relapse within six months than MPO-positive patients (41% vs 11%, P = 0.02), whereas MPO-positive patients more often achieved drug-free remission (77% vs 49%, P = 0.03). Renal involvement signified greater initial disease severity but did not independently worsen long-term outcomes under standardized therapy. These findings support integrating urinary markers and ANCA subtype into individualized risk stratification and follow-up strategies for patients with GPA.

Introduction

Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitides (AAV) comprise a group of systemic autoimmune disorders characterized by necrotizing inflammation of small- to medium-sized vessels (1). Based on clinical phenotype and pathological features, AAV are broadly categorized into granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Although these entities share immunopathogenic mechanisms, they differ substantially in organ involvement, therapeutic strategies, and clinical outcomes (2).

Among these disorders, GPA — formerly known as Wegener's granulomatosis — is one of the most common life-threatening vasculitides in adults. It is characterized by granulomatous inflammation and necrotizing vasculitis, most frequently involving the upper and lower respiratory tracts and the kidneys (3). However, GPA shows notable clinical heterogeneity, ranging from limited ear–nose–throat disease to isolated renal involvement or fulminant multi-organ failure. This variability contributes to diagnostic delay and divergent disease trajectories (4).

Renal involvement, commonly manifesting as pauci-immune necrotizing glomerulonephritis, represents a pivotal determinant of long-term morbidity and mortality in GPA (5). Historical data suggest that up to 20% of patients may die within the first year after diagnosis, and another 20% may progress to end-stage renal disease requiring renal replacement therapy (6, 7). Consequently, the presence and severity of kidney involvement play a central role in therapeutic decision-making and prognostic stratification (8).

Several factors affect outcomes in GPA, including baseline disease severity, the extent and pattern of organ involvement, and diagnostic delay. Among these, renal involvement has consistently been associated with worse prognosis and higher relapse rates. Early recognition and prompt initiation of immunosuppressive therapy are therefore critical to improving survival and preserving renal function (9).

Despite the recognized clinical importance of GPA, epidemiologic and outcome data from Middle Eastern countries such as Iran remain limited. Our center has previously contributed to the GPA literature (22–24). In particular, there is a paucity of comprehensive analyses focusing on patients with renal involvement, including their laboratory characteristics, relapse dynamics, ANCA-specific phenotypes, and long-term outcomes. Population-specific data are essential not only for optimizing individualized management strategies but also for identifying high-risk subgroups and informing national healthcare planning. Accordingly, the present study aims to evaluate the clinical features, laboratory parameters, relapse predictors, and prognostic factors among patients with GPA, particularly those with renal involvement, referred to a tertiary hospital between 2013 and 2021.

Results

Study Population

A total of 186 patients with granulomatosis with polyangiitis were included in the final analysis. The cohort comprised 107 women (57.5%) and 79 men (42.5%), with a mean age of 43.3 ± 15.2 years. Overall, 76.3% were ANCA-positive: 62.3% PR3-positive and 12.3% MPO-positive, while 23.7% were ANCA-negative.

Renal Involvement Defines a Distinct Baseline Phenotype

Renal involvement was identified in 82 patients (44%), whereas 104 patients (56%) remained free of renal manifestations throughout follow-up.

Patients with renal involvement presented with a clearly more aggressive baseline profile. They were significantly older than their non-renal counterparts (46.9 ± 14.9 vs 40.5 ± 14.9 years, P = 0.004) and were predominantly male (55% vs 33%, P = 0.002). Disease activity was markedly higher in the renal group, reflected by significantly elevated BVAS and Physician Global Assessment scores (both P < 0.001).

Immunologically, MPO-ANCA positivity clustered strongly with renal disease (22% vs 4.8%, P = 0.002), whereas PR3 positivity and ANCA negativity were similarly distributed between groups. Elevated CRP levels were more frequent in patients with renal involvement (70% vs 54%, P = 0.02), underscoring the heightened inflammatory burden. In contrast, anemia, leukocytosis, and ESR positivity did not differ significantly.

Therapeutically, renal involvement translated into more aggressive management. These patients were significantly more likely to receive cyclophosphamide or rituximab as induction therapy ($P < 0.001$). Despite intensified treatment, follow-up duration was shorter in the renal group ($P = 0.008$).

Table 1
Definition of renal involvement and associated BVAS-WG manifestation categories recorded in this cohort.

Category	**Manifestations**
General	Fever > 38°C; weight loss; lymphadenopathy; myalgia; night sweats
Skin	Purpura; skin ulcer; gangrene*
Mucocutaneous / Ocular	Oral ulcers; conjunctivitis/episcleritis; uveitis/scleritis*; retinal exudate or hemorrhage*; genital ulcers; keratitis; dacryocystitis; ptosis*; orbital cellulitis*; retro-orbital mass/proptosis
Ear, Nose, Throat (ENT)	Bloody nasal discharge; nasal crusting or ulcer; sinus involvement; subglottic inflammation; conductive hearing loss; sensorineural hearing loss; rhinitis; mastoiditis
Cardiovascular	Pericarditis; thrombophlebitis; myocardial infarction*; heart failure*
Gastrointestinal	Mesenteric ischemia*; hepatomegaly; splenomegaly; hepatitis*; pancreatitis*; diarrhea*
Renal	Hematuria (> 1 + dipstick or > 10 RBCs/HPF); red blood cell casts; proteinuria; ≥30% rise in serum creatinine; ≥25% decline in creatinine clearance; serum creatinine > 1.4 mg/dL

**Item scored as "severe" on the BVAS-WG. Renal involvement was defined according to the Birmingham Vasculitis Activity Score for Wegener's Granulomatosis (BVAS-WG) criteria; patients were stratified into renal and non-renal groups on this basis.*

Table 2
Baseline characteristics of patients with and without renal involvement (n = 186).

Characteristic	With Renal Involvement (n = 82)	Without Renal Involvement (n = 104)	P value
Mean age, years ± SD	46.9 ± 14.9	40.5 ± 14.9	0.004
Male, n (%)	45 (55%)	34 (33%)	0.002
Female, n (%)	37 (45%)	70 (67%)	0.002
Disease severity (BVAS)	19.2 ± 8.2	12.3 ± 4.5	< 0.001
Disease severity (PGA)	6.5 ± 1.6	5.2 ± 1.6	< 0.001
PR3+	49 (59.8%)	67 (64.4%)	0.5
MPO+	18 (22%)	5 (4.8%)	0.002
ANCA−	14 (7.5%)	30 (16.1%)	0.08
Anemia	49 (60%)	52 (51%)	0.19
Leukocytosis	38 (47%)	43 (42%)	0.48
CRP+	55 (70%)	56 (54%)	0.02
ESR+	49 (60%)	49 (47%)	0.08
Induction: rituximab	16 (19.5%)	8 (7%)	< 0.001
Induction: cyclophosphamide	54 (68%)	48 (46%)	< 0.001
Induction: other regimens	10 (12.5%)	47 (45%)	< 0.001
Follow-up duration, months	30 ± 26	42 ± 30	0.008
ENT manifestations	81 (99%)	103 (99%)	1.0
Pulmonary manifestations	61 (74%)	71 (68%)	0.4
Skin manifestations	11 (13%)	8 (7.7%)	0.22
Mucocutaneous/ocular manifestations	35 (43%)	34 (33%)	0.17
Neurological manifestations	26 (32%)	31 (30%)	0.8
General manifestations	35 (43%)	31 (30%)	0.08
Cardiac manifestations	4 (5%)	1 (1%)	0.17

Characteristic	With Renal Involvement (n = 82)	Without Renal Involvement (n = 104)	P value
Gastrointestinal manifestations	3 (3.7%)	2 (1.9%)	0.65

Renal Involvement Does Not Independently Worsen Long-Term Outcomes

To reduce treatment-related confounding, 87 patients who received uniform induction therapy and had at least two years of follow-up were analyzed separately (renal n = 46; non-renal n = 41). In this balanced comparison, age, sex, and baseline disease activity were comparable.

Strikingly, relapse frequency did not differ significantly between groups (1.1 ± 1.2 vs 1.3 ± 1.3 episodes, P = 0.5). Mortality was numerically lower in the renal group (9% vs 19.5%), although this did not reach statistical significance (P = 0.14). Time to prednisone tapering (≤ 5 mg) and complete drug discontinuation were also similar (Table 3).

Table 3
Outcomes in the treatment-balanced subgroup with ≥ 2 years of follow-up (n = 87).

Characteristic	With Renal Manifestations (n = 46)	Without Renal Manifestations (n = 41)	P value
Age, mean ± SD	49 ± 15	44 ± 15	0.09
Male, %	50%	38%	0.08
BVAS/WG	23 ± 7.9	21 ± 7.6	0.3
Relapse frequency, mean ± SD	1.2 ± 1.1	1.3 ± 1.3	0.5
Observed deaths, n (%)	4 (9%)	8 (19.5%)	0.14
Death due to cardiovascular events	3 (75%)	4 (50%)	0.2
Death due to malignancy	1 (25%)	2 (25%)	1.0
Death due to other causes	0	2 (25%)	0.1
Months to PDN ≤ 5 mg, median (range)	8 (4–21)	8 (4–22)	0.7
Months to PDN-free, median (range)	24 (12–50)	27 (10–75)	0.8

Predictors of Relapse

Within the renal cohort (n = 82), 49 patients (59.8%) experienced at least one relapse. Baseline urinary abnormalities sharply distinguished relapsing from non-relapsing patients.

Gross hematuria was profoundly associated with relapse (61% vs 18%, P < 0.001), conferring a more than seven-fold increased risk (OR 7.1, 95% CI 1.7–20.4). Proteinuria also significantly predicted relapse (57% vs 33%, P = 0.03; OR 2.5, 95% CI 1.06–6.6). ESR positivity and elevated neutrophil-to-lymphocyte ratios were more frequent among relapsers, but serum creatinine elevation alone was not predictive.

Notably, age, sex, baseline BVAS, ANCA subtype, anemia, and leukocytosis were not associated with relapse risk (Table 4).

Table 4
Predictors of relapse within the renal cohort (n = 82).

Characteristic	Relapse (n = 49)	No Relapse (n = 33)	P value
Male, n (%)	25 (51%)	20 (60%)	0.39
Age, mean ± SD	50 ± 13	45 ± 15	0.13
BVAS/WG, mean ± SD	22 ± 7.5	15.5 ± 7.8	< 0.001
PR3-ANCA+	33 (67%)	16 (48.5%)	0.18
MPO-ANCA+	8 (17%)	10 (30%)	0.2
ANCA−	8 (17%)	6 (18%)	0.5
Proteinuria (OR 2.5, 95% CI 1.06–6.6)	28 (57%)	11 (33%)	0.03
Hematuria	40 (82%)	21 (64%)	0.06
Gross hematuria (OR 7.1, 95% CI 1.7–20.4)	30 (61%)	6 (18%)	< 0.001
RBC casts	7 (14%)	1 (3%)	0.13
Creatinine > 1.4 mg/dL	11 (22%)	5 (15%)	0.4
WBC, mean ± SD	11,357 ± 4,774	9,746 ± 3,302	0.08
Hemoglobin, mean ± SD	11.8 ± 2.0	11.6 ± 2.4	0.68
ESR+, n (%) (OR 2.6, 95% CI 1.09–6.80)	34 (69%)	15 (47%)	0.04
CRP+, n (%)	38 (77.6%)	18 (58%)	0.08
NLR, mean ± SD	7.2 ± 4.3	5 ± 3.8	0.02

Comparison of Clinical Manifestations Based on ANCA Type in Patients with Renal Involvement

Patients with GPA and renal involvement were divided into two groups based on ANCA subtype: 49 patients were PR3-ANCA positive and 18 were MPO-ANCA positive. The demographic characteristics and clinical manifestations of the two groups were compared.

There was no statistically significant difference between the two groups in age, sex distribution, induction therapy, or most clinical manifestations. However, disease activity as measured by BVAS/WG was significantly higher in PR3-positive patients (P = 0.002). Additionally, neurological manifestations were significantly more frequent in the PR3-positive group than in the MPO-positive group (36.7% vs 5.6%, P = 0.01). Other organ-system involvements did not differ significantly between the groups.

Table 5
Comparison of clinical manifestations in patients with renal involvement, by ANCA type.

Characteristic	MPO+ (n = 18)	PR3+ (n = 49)	P value
Age, years, mean ± SD	48.8 ± 13.8	45 ± 16	0.37
BVAS/WG, mean ± SD	14 ± 7	21 ± 8	0.002
Male, n (%)	10 (55.6%)	29 (59.2%)	0.79
Female, n (%)	8 (44.4%)	20 (40.8%)	0.79
Induction: rituximab	4 (22%)	10 (21%)	0.58
Induction: cyclophosphamide	13 (72%)	30 (64%)	0.58
Induction: other	1 (5.6%)	7 (15%)	0.58
ENT manifestations	17 (95%)	49 (100%)	0.9
Pulmonary manifestations	13 (72.2%)	36 (73.5%)	0.9
Skin manifestations	3 (16.7%)	5 (10%)	0.47
Mucocutaneous/ocular	7 (39%)	22 (45%)	0.66
Neurological manifestations	1 (5.6%)	18 (36.7%)	0.01
General manifestations	9 (50%)	20 (41%)	0.5
Cardiac manifestations	0	4 (8%)	0.56
Gastrointestinal manifestations	0	1 (2%)	1.0

Comparison of Laboratory Findings Based on ANCA Type

Laboratory findings were compared between MPO-positive and PR3-positive patients with renal involvement. No significant differences were observed in hematologic parameters (CBC) or inflammatory markers (CRP, ESR).

However, urinalysis findings showed that gross hematuria was significantly more frequent in PR3-positive patients than in MPO-positive patients (57% vs 16%, P = 0.03), with a relative risk of 3.4 (95% CI 1.18–9.9). Other renal parameters did not show statistically significant differences (Table 6).

Table 6
Comparison of laboratory findings in patients with renal involvement, by ANCA type.

Characteristic	MPO+ (n = 18)	PR3+ (n = 49)	P value
Anemia	10 (55%)	28 (58%)	0.83
Leukocytosis	8 (44%)	25 (52%)	0.58
CRP+	9 (53%)	36 (75%)	0.09
ESR+	8 (44%)	31 (65%)	0.13
Proteinuria	10 (55%)	22 (45%)	0.43
Hematuria	15 (83%)	35 (71%)	0.3
Gross hematuria (RR 3.4, 95% CI 1.18–9.9)	3 (16%)	28 (57%)	0.03
RBC casts	3 (16%)	5 (10%)	0.47
Creatinine > 1.4 mg/dL	1 (5.6%)	13 (26.5%)	0.06

Comparison of Treatment Response Between PR3 + and MPO+ Patients

Treatment response was compared between PR3-positive and MPO-positive patients regardless of the induction regimen. Relapse rates were assessed at 6, 12, and 18 months.

PR3-positive patients had a significantly higher relapse rate within the first 6 months than MPO-positive patients (41% vs 11%, P = 0.02), corresponding to a 3.67-fold increased risk. However, differences at 12 and 18 months were not statistically significant.

There was no significant difference in overall mortality or causes of death (cardiovascular, infection, malignancy) between the groups.

Disease remission without medication (drug-free) was significantly more frequent in MPO-positive patients than in PR3-positive patients (77% vs 49%, P = 0.03). However, no differences were observed in achieving low-dose prednisone (PDN < 5 mg) or in the time required to reach drug-free status or steroid tapering (Table 7).

Table 7
Comparison of treatment outcomes in patients with renal involvement, by ANCA type.

Characteristic	MPO+ (n = 18)	PR3+ (n = 49)	P value
Relapse at 6 months	2 (11%)	20 (41%)	0.02
Relapse at 12 months	6 (33%)	28 (57%)	0.08
Relapse at 18 months	7 (39%)	28 (57%)	0.18
Observed deaths	2 (11%)	15 (30%)	0.1
Cardiovascular death	1 (5.6%)	6 (12.2%)	0.42
Death due to infection	0	2 (4.1%)	0.38
Reached drug-free status	14 (77%)	24 (49%)	0.03
Reached PDN < 5 mg	14 (77%)	33 (67%)	0.4
Months to PDN ≤ 5 mg, mean ± SD	23 ± 9	26 ± 17	0.5
Months to drug-free, mean ± SD	32 ± 10	34 ± 17	0.6

Discussion

In this study of 186 patients with granulomatosis with polyangiitis (GPA), we identified several clinically relevant patterns regarding renal involvement, relapse, and ANCA subtype. Overall, 55% of the total cohort were female, consistent with prior reports indicating a female predominance of approximately 45–60% (20, 21). The mean age of the study population was 44.4 ± 15.9 years, aligning with the globally reported peak incidence range of 40–60 years (5, 9, 15). Renal involvement was associated with a more severe baseline phenotype, characterized by older age, male predominance, higher disease activity scores, and increased inflammatory burden. Despite this more aggressive presentation, renal involvement did not independently predict worse long-term outcomes when treatment and baseline characteristics were balanced. Within the renal subgroup, urinary abnormalities — particularly gross hematuria and proteinuria — emerged as the strongest predictors of relapse, whereas ANCA subtype and serum creatinine were not predictive. Finally, PR3-ANCA and MPO-ANCA defined distinct disease behaviors, with PR3-positive patients exhibiting higher disease activity, more neurological involvement, and increased early relapse risk, while MPO-positive patients were more likely to achieve drug-free remission.

Renal Involvement as a Distinct Clinical Phenotype

The proportion of patients with renal manifestations in our cohort (82/186, 44%) was comparable to the findings reported by Aasarød and colleagues in a Norwegian multicenter series of patients with GPA and renal disease (18). Across published series, the reported prevalence of renal involvement over the course

of GPA ranges widely from 20% to 80% (19), placing our findings within the expected international spectrum. However, stratified analysis revealed a significant sex disparity between renal and non-renal groups: 55% of patients with renal involvement were male, compared with only 33% in the non-renal group (P = 0.002). The same pattern has also been reported in the literature, with males being more affected by renal involvement than females (12). The mean age of patients in this study was 44.4 ± 15.9 years, with no significant difference between the two groups (P = 0.042). This mean age corresponded to the 40–60-year range reported as the global average (13–15). Individuals with renal symptoms were significantly older, but MPO + and PR3 + patients with renal involvement had a similar age; in the study by Schirmer et al., the mean age of MPO + and PR3 + patients was likewise not different (16). Regarding ANCA subtype, individuals with renal involvement were more likely to be MPO+ (22% vs 4.8%, P = 0.002), whereas the likelihood of being PR3 + or ANCA-negative did not differ between the two groups. In a study by Stone et al. of 180 GPA patients in 2003, 71.9% were PR3 + and 11.9% were MPO+, similar to the present study. They divided patients into those with severe disease and those with limited disease and compared demographic characteristics, clinical manifestations, and laboratory findings, concluding that patients with severe disease more frequently produced antibodies against PR3 at diagnosis (78.1% vs 58.8%, P = 0.028) (17). This finding was corroborated in the present study: the mean disease severity score according to the BVAS-WG criteria was significantly higher in PR3 + patients than in MPO+ patients (21 ± 8 vs 14 ± 7, P = 0.002), indicating that PR3 + patients present with more severe disease at diagnosis. In the present study, among laboratory findings other than ANCA, the inflammatory marker CRP was also higher in individuals with renal symptoms than in those without, but the prevalence of anemia, leukocytosis, and elevated ESR did not differ between the two groups.

Prognosis and Relapse

Overall prognosis has improved dramatically over the past decades. Before the introduction of corticosteroids and cyclophosphamide, the mean survival of GPA patients was less than six months (9). Contemporary survival rates at 1, 5, and 10 years are 81–95%, 73–83%, and 55–75%, respectively. Nonetheless, mortality remains elevated, with a 2.7-fold higher risk than in the general population. Risk factors consistently associated with poorer prognosis include older age, male sex, baseline nervous system involvement, and elevated serum creatinine. Cardiovascular events, active vasculitis, and infections are the leading causes of death.

Strengths and Limitations

This study has several strengths, including prospective data collection over an eight-year period, standardized diagnostic and treatment protocols, dual-investigator data verification with random auditing of records, and a comparatively large single-center cohort for an ANCA-associated vasculitis population in the Middle East, where such data remain scarce.

Several limitations should also be acknowledged. First, this was a single tertiary-center study, which may limit generalizability to the broader Iranian population and to other regions. Second, the diagnosis of relapse relied on clinical, laboratory, and BVAS-based criteria rather than routine repeat renal biopsy, so

histologically distinct or subclinical relapses may have been under-detected. Third, the introduction of rituximab as an induction option after 2017 introduces a potential era effect in treatment practice that, despite the treatment-balanced sensitivity analysis, cannot be fully excluded. Fourth, ANCA-subtype subgroup comparisons within the renal cohort were based on a relatively small number of MPO-positive patients (n = 18), which may have limited statistical power and widened the confidence intervals around several effect estimates. Finally, as in any single-center observational cohort, residual confounding by unmeasured variables cannot be excluded, and the findings should be validated in larger, multicenter, and ideally multi-ethnic cohorts.

Conclusion

In this Iranian GPA cohort, renal involvement marked a more severe baseline phenotype but did not independently worsen long-term relapse or survival outcomes once treatment intensity and baseline severity were accounted for. Gross hematuria and proteinuria were the most powerful clinical predictors of relapse within the renal subgroup, while PR3-ANCA positivity defined a distinct early-relapse phenotype and MPO-ANCA positivity was associated with a greater likelihood of drug-free remission. These findings support incorporating urinary markers and ANCA subtype into individualized risk stratification and follow-up planning for patients with GPA, and underscore the need for larger, multicenter studies to validate these predictors and clarify the biological basis of ANCA-subtype-specific disease trajectories.

Methods

Study Design and Population

This prospective cohort study was conducted at a tertiary referral center between 2013 and 2021. Consecutive patients aged > 16 years diagnosed with GPA according to the 1990 American College of Rheumatology (ACR) criteria and the European Medicines Agency (EMA) algorithm were eligible for inclusion (10, 11).

Of 220 screened patients, 218 had available laboratory data. Thirty-two patients with only a single visit and no follow-up were excluded. The final analytic cohort comprised 186 patients.

ANCA testing was performed using indirect immunofluorescence, and antigen specificity for proteinase 3 (PR3) and myeloperoxidase (MPO) was determined by ELISA. Patients were categorized as PR3-positive, MPO-positive, or ANCA-negative. Individuals with dual PR3/MPO positivity were excluded from subgroup analyses.

Definition of Renal Involvement

Renal involvement was defined according to the Birmingham Vasculitis Activity Score for Wegener's Granulomatosis (BVAS-WG) criteria (Table 1) and included hematuria (> 1 + dipstick or > 10 RBCs/HPF),

red blood cell casts, proteinuria, ≥ 30% rise in serum creatinine, ≥ 25% decline in creatinine clearance, or serum creatinine > 1.4 mg/dL. Patients were stratified into renal and non-renal groups based on these criteria.

Data Collection

Demographic data, diagnostic delay, follow-up duration, seasonal patterns of diagnosis or relapse, clinical manifestations, and disease activity scores (BVAS-WG and Physician Global Assessment) were recorded. Laboratory parameters included complete blood count, ESR, CRP, ANCA titers, liver enzymes, serum creatinine, and urinalysis findings.

Histopathologic reports, when available, were reviewed for evidence of necrotizing vasculitis, granulomatous inflammation, or necrotizing glomerulonephritis. Data accuracy was ensured by dual-investigator review and random auditing of 15% of records.

Treatment Protocol

All patients received systemic corticosteroids combined with an induction agent. Induction therapy consisted of cyclophosphamide or rituximab (introduced after 2017), while methotrexate or azathioprine was used in selected non-severe cases. Maintenance therapy included methotrexate, azathioprine, or rituximab.

Outcomes and Statistical Analysis

Disease activity and treatment response were assessed longitudinally. Complete remission was defined as BVAS = 0; relapse was defined as an increase in BVAS score after remission. Mortality and causes of death were documented.

Statistical analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± SD and compared using Student's t test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. A two-sided P value < 0.05 was considered statistically significant.

Ethics Approval

The study was approved by the Ethics Committee of Tehran University of Medical Sciences (approval no. IR.TUMS.MEDICINE.REC.1401.868) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients included in the study.

Declarations

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy considerations but are available from the corresponding author on reasonable request.

Competing Interests

The authors declare no competing interests.

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Author Contribution

A.A. conceived the study, collected and curated the clinical data, performed the statistical analysis, and wrote the original draft of the manuscript. A.R. contributed to the study design, supervised patient recruitment and clinical follow-up, and critically reviewed and edited the manuscript. B.J. contributed to the interpretation of the data and critically reviewed the manuscript. S.S. contributed to data collection and verification and assisted in drafting the manuscript. M.M. contributed to data collection and verification and assisted in drafting the manuscript. M.S. (corresponding author) conceived and supervised the study, contributed to the study design and data interpretation, and critically revised the manuscript. All authors read and approved the final manuscript.

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