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BRIEF REPORT

Rituximab treatment in ANCA-associated vasculitis patients: outcomes of a real-life experience from an observational cohort

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Abstract

Rituximab is a first-line therapy in patients with anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV). Among previous studies evaluating its efficacy, the Hispanic/Latino population has been underrepresented. This study aimed to assess the outcomes of AAV patients treated with rituximab in a tertiary care center in Mexico. This is a retrospective cohort study including patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), or renal-limited vasculitis (RLV), who received at least one dose of rituximab (induction or maintenance therapy) from January 2014 to October 2020. Demographic, clinical, serological, histopathological, and treatment-related variables were retrieved. Outcomes were the rate of remission at 6 months during induction and the rate of relapses during maintenance. Damage, serious infections, and death were assessed. Differences between patients with and without remission were analyzed. Forty-two patients received rituximab, 34 of them as induction to remission. Twenty-two patients (65%) achieved remission after 6 months. Patients who achieved remission were younger than those who did not (50 vs. 60 years, $p = 0.03$). During induction, severe infections, most frequently pneumonia, occurred in 9 (26%), and one patient died. Twenty-four patients received rituximab as maintenance; of them, 23 (96%) achieved complete response, and 8 (33%) experienced relapses (median follow-up time 19 months). During maintenance, severe infections (pneumonia) occurred in 5 patients (21%), and 3 of them (13%) died. In this observational cohort study, the outcomes were similar to the ones reported in other populations, whereas severe infections were frequent and associated with mortality.

Key Points

- *In this study, the outcomes of 42 Mexican patients with ANCA-associated vasculitis treated with rituximab were assessed in a real-life setting.*
- *At 6 months, 65% of the patients achieved remission with rituximab, especially those younger than 50 years of age.*
- *During maintenance therapy with rituximab, 96% of the patients achieved complete response, and 33% experienced relapses.*
- *Severe infections, mostly pneumonia, occurred in 26% of patients during induction and 21% of patients during maintenance therapy with rituximab.*

Keywords ANCA · Granulomatosis with polyangiitis · Induction · Maintenance · Microscopic polyangiitis · Rituximab

Introduction

The anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) are rare autoimmune diseases that predominantly affect small-sized vessels leading to endothelial injury and tissue damage. The three main clinicopathologic variants of AAV (i.e., granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA)) share common pathophysiological mechanisms, clinical characteristics, and therapeutic strategies [1].

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Rituximab is a chimeric monoclonal anti-CD20 IgG1 antibody that specifically binds to transmembrane protein CD20 [2]. In the pivotal randomized clinical trials that evaluated rituximab as a remission-induction and maintenance therapy, the majority of patients enrolled were Caucasians, with only a small percentage of Hispanic or Latino patients included [3–5]. Since then, several observational non-randomized studies have provided additional information regarding the efficacy and safety of rituximab [6]. Most Latin American countries are considered as low-middle-income countries, which limits the use of drugs such as rituximab; therefore, in these countries, the use of this medication depends on its availability and cost, with very scarce information regarding the outcomes [7]. Herein, we assess the outcomes of Mexican patients with AAV from a tertiary care center treated with rituximab as remission-induction and maintenance strategies.

Materials and methods

Study population

An observational retrospective cohort study was conducted, including patients > 18 years old with diagnosis of GPA, MPA, or renal-limited vasculitis (RLV) in accordance with the 1990 American College of Rheumatology Classification Criteria and/or definition by the 2012 Chapel Hill Consensus Conference [8, 9]. All patients received at least one dose of rituximab for either induction or maintenance therapy from January 2014 to October 2020 at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, a specialized center in Mexico City. The indication of rituximab, the concomitant therapy, and the parameters used to retreat were according to the treating Rheumatologists' criteria. Patients with EGPA, malignancies in the past 5 years, other autoimmune diseases in overlap, positivity for anti-glomerular basement membrane antibodies, pregnancy, and patients treated concomitantly with cyclophosphamide were excluded.

Data collection and measures

Demographic, clinical, serological, laboratory, and treatment-related variables were retrieved from medical records. Patients were classified according to the clinicopathologic phenotype and also based on the granulomatous or vasculitic features, ANCA specificity, and the severity of the disease at disease diagnosis [10]. Non-severe AAV included patients usually PR3-ANCA positive, sometimes ANCA negative, with predominantly granulomatous features, no renal involvement or other prominent vasculitis features, low risk of life/organ threatening disease, and high relapse risk. Severe PR3-AAV comprised mainly PR3-ANCA positive patients, with mixed granulomatous-vasculitic features, renal involvement and/or other prominent vasculitis features, intermediate risk of life/organ-threatening disease, and intermediate relapse risk; whereas severe MPO-AAV included MPO-ANCA positive patients, with predominantly vasculitic features, renal involvement and/or other prominent vasculitis features, high risk of life/organ-threatening disease, and low relapse risk [10]. Life/organ-threatening manifestations included the major items of the Birmingham Vasculitis Activity Score for GPA (BVAS/WG) [11].

ANCA were determined by immunofluorescence (IF) microscopy, whereas PR3-ANCA and MPO-ANCA by enzyme-linked immunosorbent assay. Comorbidities, rituximab indication and dose regimen, concomitant therapy, and renal variables were also assessed.

Outcomes

Primary outcomes were the rate of remission, defined as a BVAS/WG of 0 points, independently of prednisone dose at 6 months after induction therapy, and the rate of major or minor relapses during maintenance treatment. Major relapses were defined as the appearance of new manifestations with a BVAS/WG ≥ 3 points, and either the involvement of at least one major organ, or the occurrence of a life-threatening manifestation, or both; minor relapses as the recurrence of signs or symptoms of active vasculitis not corresponding to a major relapse but requiring mild treatment intensification. The percentage of patients attaining complete response during maintenance (BVAS/WG of 0 points and prednisone dose ≤ 10 mg/day) was also recorded. Damage was assessed using the Vasculitis Damage Index (VDI) [12]; serious infections (those requiring intravenous treatment or that led to hospitalization or death), leukopenia (total leukocyte count < 3000/m^3), neutropenia (neutrophil count < 1500/microL), hypogammaglobulinemia (serum IgG < 6 g/L), allergic reactions, malignancies, and death of any cause during rituximab treatment were also registered.

Statistical analysis

Descriptive statistics included the number, percentage, and median with 25th and 75th percentiles. Differences between groups were evaluated using Student's *t*-test or the Mann-Whitney *U* test for continuous variables, and chi-square or Fisher's exact tests for categorical variables. Cox proportional-hazards model was performed to identify predictor variables associated with relapses during

maintenance therapy. Exact p-values are reported with a two-sided p-value < 0.05 considered statistically significant. All analyses were conducted using Stata software (Stata Corp; College Station, TX, USA), version 14.0.

Results

Rituximab as an induction to remission therapy

A total of 42 patients received at least one dose of rituximab during the study period, 34 of them as an induction to remission regimen. Characteristics of these 34 patients at AAV diagnosis included female gender in 21 (62%), a median age of 51 years (38–60), and obesity as the main comorbidity in 12 (35%), followed by arterial hypertension and end-stage renal disease in 5 (15%). Twenty-nine patients (85%) had GPA, 3 (9%) RLV, and 2 (6%) MPA, whereas the most frequent phenotype at disease diagnosis was severe PR3-AAV in 19 (56%), followed by severe-MPO AAV in 13 (38%), and non-severe AAV in 2 (6%).

The most frequent rituximab induction regime was two 1 gr infusions 2 weeks apart in 31 patients (91%). At 6 months, 22 (65%) patients achieved remission in a median time of 4 months (3–6), 5 (15%) remained in dialysis, and only 2 (6%) were off prednisone. Table 1 depicts the characteristics and 6-month outcomes of patients who received rituximab during remission-induction and Table 2 summarizes organ involvement. There was no significant difference between the number of patients at dialysis at 0 and 6 months (8 (24%) vs. 5 (15%), $p = 0.53$). Patients who achieved remission ($n = 22$) were a decade younger than those who did not achieve remission ($n = 11$) (50 vs. 60 years, $p = 0.03$). There were no other significant differences between these groups (Table 3).

Sixteen patients (47%) received prophylactic cotrimoxazole during remission-induction therapy. Severe infections during induction therapy occurred in 9 patients (26%), and 3 (9%) of them presented more than one infectious event. Severe infections included pneumonia (7 events), gastrointestinal (1 event), urinary tract (2 events), herpes zoster (1 event), and bone and soft tissue (1 event). Pneumonia events were bacterial (3), fungal (3), and viral (1); none of them was caused by *Pneumocystis jirovecii.* There was no difference between patients with and without pneumonia regarding use of prophylactic cotrimoxazole (2 events of pneumonia in 18 patients without prophylaxis vs. 5 events of pneumonia in 16 patients with prophylaxis, $p = 0.2$). Leukopenia was seen in 4 patients (12%) and neutropenia in 2 (6%), whereas serum IgG levels were only determined in 14 patients, and 7 of them (50%) showed hypogammaglobulinemia. There were no allergic reactions to the infusion or malignancies during rituximab therapy. One patient died 1 month after the last dose of rituximab, and the cause was not determined.

Rituximab as maintenance therapy

Twenty-four patients received rituximab as maintenance therapy. Table 1 displays the characteristics and outcomes of these patients, whereas the individual information concerning the rituximab indication, dose, and retreatment regimen is detailed in the Supplementary Material 1.

Twenty-three patients (96%) achieved complete response and 8 (33%) experienced relapses. Over 640 patient-months follow-up, a total of 13 relapses (8 minor and 5 major) occurred in 8 patients; the minimum–maximum time in months since the first maintenance dose of rituximab to relapse was 2–46 months, with a median of time to first relapse of 13.5 months (4.5–20.5). Supplementary Material 1 details the time from the last maintenance dose of rituximab to the occurrence of relapses, whereas Table 4 depicts the comparative analysis of patients who presented or not relapses during rituximab maintenance therapy. No predictive variables associated with relapses were identified in the Cox proportional-hazards model (data not shown).

In the eight patients who experienced relapses, the most prevalent manifestations included general symptoms in 5 patients, followed by ENT in 4, and renal involvement in three. Relapses also included pulmonary manifestations and peripheral nervous system involvement in two patients, respectively, and, finally, a recurrent retro-orbital mass in one patient.

During follow-up, the minimum and maximum times elapsed between subsequent doses of rituximab were 5 and 18 months, respectively; the total number of infusions in all patients was 40, and the median number of infusions per patient was 2 (minimum 1 and maximum 8). The most frequent parameters to decide retreatment were 6-month fixed intervals in 29/40 infusions, followed by ANCA-titers in 5/40, B cell depletion status, and relapse in 3, each.

During maintenance treatment, severe infectious events (pneumonia) occurred in 5 patients (21%); of these, 4 were viral (COVID-19), and 1 patient not receiving clotrimoxazole had both bacterial and fungal pneumonia (*Klebsiella pneumoniae* and *Pneumocystis jirovecii*). Two patients with COVID-19 pneumonia and the patient with bacterial and fungal pneumonia died. Finally, leukopenia occurred in 1 patient (4%), and there were no allergic reactions to the infusion or malignancies during maintenance therapy.

Table 1 Characteristics and outcomes of patients who received rituximab during induction to remission or maintenance

Variable	Remission-induction *n* (%) or median (p25–p75)	Maintenance *n* (%) or median (p25–p75)
Sex, female, male, *n/n*	21/13	15/9
Age, years	55 (40–62)	49 (33–64)
Disease duration, months	11.5 (0–55)	13 (9–63)
Follow-up time, months	6	19 (15.5–32.5)
Diagnosis		
GPA	29 (85)	22 (92)
MPA	2 (6)	2 (8)
Renal-limited vasculitis	3 (9)	0
Phenotype*		
Non-severe AAV	2 (6)	0
Severe PR3-AAV	19 (56)	17 (71)
Severe MPO-AAV	13 (38)	7 (29)
Indication		
New AAV diagnosis	11 (32)	N/A
Cyclophosphamide refractory	6 (18)	N/A
Induction after relapse	16 (47)	N/A
Prior rituximab induction	N/A	15 (63)
Intolerance/contraindication to other immunosuppressants	N/A	7 (29)
Switch to other immunosuppressant due to physician/patient preferences	1 (3)	2 (8)
Laboratory parameters		
PR3-ANCA, *n+/n*	14/27 (52)	N/A
MPO-ANCA, *n+/n*	11/27 (41)	N/A
ANCA-negative	2/27 (7)	N/A
ESR, mm/h	10 (4–26)	N/A
CRP, mg/dL	2.1 (0.3–3.1)	N/A
Clinical manifestations		
Vasculitic	12 (35)	N/A
Granulomatous	7 (21)	N/A
Mixed	14 (44)	N/A
Renal parameters		
Dialysis	8 (24)	N/A
eGFR, mL/min/1.73 m^2	38 (22.9–78)	61.3 (28.6–89.8)
24-h urine protein, mg	753 (260–1958)	N/A
Focal class, *n+/n*	2/12 (17)	N/A
Crescentic class, *n+/n*	2/12 (17)	N/A
Mixed class, *n+/n*	6/12 (50)	N/A
Sclerotic class, *n+/n*	2/12 (17)	N/A
BVAS/WG score, points	6 (4–8)	0 (0–1)
VDI score, points	2 (0–4)	3 (2–5)
Total number of rituximab doses, median (min–max)	2 (1–2)	2 (1–8)
Concomitant therapy		
Methylprednisolone boluses	16 (47)	N/A
Prednisone dose, mg/day (median, min–max)	60 (12.5–100)	10 (0–50)
Plasma exchange	6 (18)	N/A
6-month outcomes		
Remission	22 (65)	N/A
Time to remission, months	4 (3–6)	N/A
Dialysis	5 (15)	N/A
Prednisone dose, mg/day	10 (5–12.5)	5 (0–5)
Cumulative glucocorticoid dose, gr	6.1 (4.88–8.29)	N/A
BVAS/WG, points	0 (0–1)	0 (0–0)
VDI, points	4 (2–6)	4 (2–5)
eGFR, mL/min/1.73 m^2	42 (29.96–90)	66.6 (21.4–84)
24-h urine protein, mg	320.5 (137.4–1449.5)	N/A

Table 1 (continued)

Variable	Remission-induction *n* (%) or median (p25–p75)	Maintenance *n* (%) or median (p25–p75)
Complete response	N/A	23 (96)
Time to complete response, months	N/A	0 (0–3)
Relapses, any	N/A	8 (33)
Time to first relapse, months	N/A	13.5 (4.5–20.5)

*Classification of phenotypes was at disease diagnosis. *N/A*, not applicable; *GPA*, granulomatosis with polyangiitis; *MPA*, microscopic polyangiitis; *AAV*, ANCA-associated vasculitis; *MPO-ANCA*, myeloperoxidase ANCA; *PR3-ANCA*, proteinase 3-ANCA; *ESR*, erythrosedimentation rate; *CRP*, C-reactive protein; *eGFR*, estimated glomerular filtration rate; *BVAS/WG*, Birmingham Vasculitis Activity Score for Granulomatosis with Polyangiitis; *VDI*, vasculitis damage index

Table 2 Organ involvement at induction to remission

Organ involvement	*n* (%)
General	8 (23.5)
Cutaneous	5 (14.7)
Mucous membranes and eyes	7 (20.5)
Ear, nose, and throat	7 (20.5)
Cardiovascular	1 (2.9)
Gastrointestinal	0
Pulmonary	10 (29.4)
Renal	24 (70.5)
Nervous system	11 (32.3)
Other (weight loss)	4 (11.7)

Discussion

In this observational study representing a real-world experience, the outcomes of 42 Mexican patients with AAV treated with rituximab as remission-induction or maintenance strategies were analyzed.

In order to establish differences regarding efficacy and safety of rituximab in AAV patients among existing cohorts, it is important to consider several difficulties that may arise mainly due to variability in the type of studies, patient phenotype, small sample sizes, definition of remission (as well as other efficacy endpoints), concomitant therapy, and rituximab regimens.

The 6-month remission rate in the present cohort was similar to the RAVE study (65% independent of prednisone dose, compared to 64% and 71% in the RAVE trial without prednisone or with a dose below 10 mg/day, respectively) [3]. Moreover, the 6-month complete remission was slightly lower (61%) in the rituximab arm in the post hoc analysis of the RAVE trial, where only patients with renal involvement were included [13]. Forty-seven percent of the patients included in the present study received remission-induction therapy with rituximab due to relapsing disease. The efficacy of rituximab in this setting was evaluated in the RITAZAREM trial, with 90% of patients achieving remission by 4 months [14].

Twenty-four percent of the patients from the present cohort were on dialysis at the beginning of the remission-induction treatment. The efficacy of rituximab in AAV patients with severe renal disease (eGFR < 30 mL/min/1.73 m2) treated with rituximab was also evaluated in a large retrospective cohort study of AAV patients, where 6-month remission rate was higher (81.7%) than in the present cohort [15].

In the present study, patients who achieved remission after 6 months of rituximab therapy were younger than those who failed to achieve remission. The impact of age in the outcomes of AAV patients within 6 months of diagnosis was analyzed using data from the Diagnostic and Classification Criteria for Primary Systemic Vasculitis (DCVAS) study, where patients > 65 years of age displayed more systemic, neurologic, and cardiovascular involvement; worsening renal function; higher damage accrual; and early mortality compared to their younger counterpart [16].

A third of the patients from the present cohort experienced relapses during maintenance treatment with rituximab, a higher rate than the one reported in the rituximab group of the MAINRITSAN trial at 28 months (5% of major and 11% of minor relapses) [5]. The relapse rate in the present study is similar to the one reported in a single-center cohort study from the Netherlands (28%) [17]. Our study could not identify specific predictors for relapse previously reported [2, 17, 18]. A possible explanation is that the majority of the patients had GPA diagnosis, and data regarding repeated ANCA measurements and B-cell status was not available for all patients.

Severe infections, mostly pneumonia, were present in the present study in 26% and 21% of patients during remission-induction and maintenance therapy with rituximab, respectively. These numbers contrast with the ones reported in the RAVE and MAINRITSAN trials (7% and 19%, respectively) and concur with the ones reported in a combined retrospective cohort of AAV patients from Mexico and Sweden

Table 3 Comparative analysis of patients with or without remission after 6 months of rituximab induction therapy

Variable	Remission ($n = 22$)	No remission ($n = 11$)	p-value
Female sex	13 (59)	7 (64)	1.00
Age, years	50 (36–59)	60 (56–68)	0.03*
Disease duration, months	11 (1–55)	8 (0–54)	0.62
Phenotype**			
Non-severe AAV	1 (5)	1 (9)	1.00
Severe PR3-AAV	13 (59)	5 (45)	0.48
Severe MPO-AAV	8 (36)	5 (45)	0.71
Type of indication			
New AAV diagnosis	6 (27)	5 (45)	0.43
Cyclophosphamide refractory	5 (23)	1 (9)	0.63
Induction after relapse	10 (45)	5 (45)	1.00
Other	1 (5)	0	1.00
Laboratory parameters			
ANCA IF, *n+/n*	13/14 (93)	7/8 (88)	1.00
PR3-ANCA, *n+/n*	16/19 (84)	5/7 (71)	0.58
MPO-ANCA, *n+/n*	9/12 (75)	5/6 (83)	1.00
ESR, mm/hr	10 (3–20)	10 (4.4–33)	0.90
CRP, mg/dL	1.82 (0.27–5.95)	2.4 (0.3–2.81)	0.92
Clinical manifestations			
Vasculitic	6 (27)	6 (55)	0.14
Granulomatous	5 (23)	2 (18)	1.00
Mixed	11 (50)	3 (27)	0.27
Renal parameters			
Dialysis	4 (18)	3 (27)	0.66
eGFR, mL/min/1.73 m^2	52.6 (22.9–104)	33.6 (23.2–42.3)	0.13
24-h urine protein, mg	753 (319–2000)	454 (176–1328)	0.41
Protein/creatinine ratio, mg/mg	1.1 (0.4–2.96)	1.1 (0.2–2.91)	0.64
Focal class, *n+/n*	0	2/6 (33)	0.45
Crescentic class, *n+/n*	1/6 (17)	1/6 (17)	1.00
Mixed class, *n+/n*	4/6 (67)	2/6 (33)	0.56
Sclerotic class, *n+/n*	1/6 (17)	1/6 (17)	1.00
BVAS/WG score, points	6 (4–7)	8 (4–9)	0.08
VDI score, points	2.5 (0–4)	0 (0–3)	0.21
Methylprednisolone boluses	8 (36)	7 (64)	0.16
Prednisone dose, mg/day	60 (40–60)	60 (53–60)	0.84
Cumulative glucocorticoid dose, gr	5.6 (4.3–7.8)	6.7 (5.6–9.1)	0.19

*Statistically significant difference. **Classification of phenotypes was at disease diagnosis. *AAV*, ANCA-associated vasculitis; *MPO-ANCA*, myeloperoxidase ANCA; *PR3-ANCA*, proteinase 3-ANCA; *ESR*, erythrosedimentation rate; *CRP*, C-reactive protein; *eGFR*, estimated glomerular filtration rate; *BVAS/WG*, Birmingham Vasculitis Activity Score for Granulomatosis with Polyangiitis; *VDI*, vasculitis damage index

treated with rituximab (24%), and a US multicenter cohort (24.7%) [3, 5, 19, 20].

Three patients (13%) died during maintenance therapy with rituximab, a higher mortality rate compared with the one reported in a systematic review of AAV patients treated with rituximab in non-randomized trials (4%), in a US multicenter cohort (9.3%), and in a combined retrospective cohort from Mexico and Sweden (9%) [6, 19, 20]. Of notice, two of the three deaths were related to COVID-19 pneumonia, in line with the recent findings from the COVID-19 Global Rheumatology Alliance physician-reported registry in AAV and in other rheumatic diseases treated with rituximab [21, 22].

The present study has certain limitations. These include the restrictions inherent to the retrospective design, the relatively small sample, and the recruitment in a tertiary care center where patients with more severe disease are usually referred, which may limit the generalizability of the results. Moreover, no predictors of relapses were identified, possibly due to the small numbers. Likewise, the treatment protocols were administered at the treating Rheumatologists' discretion; B-cell depletion or repopulation data, as well as immunoglobulin levels and repeated ANCA determinations, were not available for all patients; there were only a few patients with RLV and MPA, limiting the generalizability to all AAV; finally, the maintenance cohort was heterogeneous,

Table 4 Comparative analysis of patients with or without relapses during rituximab maintenance therapy

Variable	Relapses ($n = 8$)	No relapses ($n = 16$)	p-value
Sex, female/male, *n/n*	5/3	10/6	1.00
Age at diagnosis, years	39 (31–68)	48 (31–56)	0.83
Age at maintenance beginning, years	43 (35–69)	51 (33–60)	0.80
Disease duration at maintenance beginning, months	30 (7–49)	12 (9–64)	0.83
Follow-up time, months	28.5 (21.5–48.5)	17.5 (14.5–27.5)	0.07
Diagnosis			
GPA	7 (88)	15 (94)	1.00
MPA	1 (12)	1 (6)	
Phenotype**			
Non-severe AAV	0	0	1.00
Severe PR3-AAV	6 (75)	11 (69)	
Severe MPO-AAV	2 (25)	5 (31)	
Refractory disease	4 (50)	3 (19)	0.14
eGFR, mL/min/1.73 m^2	61.4 (40–74)	60.5 (21–105.9)	0.90
BVAS/WG score > 0 at maintenance beginning	5 (63)	5 (31)	0.20
VDI score, points	3 (1–4)	4 (2–5)	0.38
Prednisone dose, mg/day, median (min–max) at maintenance beginning	7.5 (0–50)	10 (0–40)	0.80
Total number of rituximab doses, median (min–max)	3 (1–8)	2 (1–5)	0.02*
6-month outcomes			
BVAS/WG score ≥ 1	4 (50)	1 (6)	0.02*
VDI score at 6 months, points	3 (1–5)	4 (3–5)	0.31
Prednisone dose at 6 months, mg/day, median (min–max)	0 (0–5)	5 (0–10)	0.20
Complete response	7 (88)	16 (100)	0.33
Time to complete response, months	4 (2–11)	0 (0–2)	0.006*

Data are presented as *n* (%) or median (p25–p75). *Statistically significant difference. **Classification of phenotypes was at disease diagnosis. *GPA*, granulomatosis with polyangiitis; *MPA*, microscopic polyangiitis; *AAV*, ANCA-associated vasculitis; *MPO-ANCA*, myeloperoxidase ANCA; *PR3-ANCA*, proteinase 3-ANCA; *eGFR*, estimated glomerular filtration rate; *BVAS/WG*, Birmingham Vasculitis Activity Score for Granulomatosis with Polyangiitis; *VDI*, vasculitis damage index

and the limited access to rituximab due to economic or availability constraints may have impacted the outcomes in these patients. Nonetheless, to our knowledge, this is the first report describing the outcomes of AAV patients treated with rituximab from a single center in Mexico; information concerning the phenotype and renal histology was considered; and, finally, patients with severe renal impairment were included, a subgroup with limited representation in some of the large clinical trials of rituximab.

Conclusions

The present study's findings expand upon previous evidence derived from observational studies and randomized clinical trials of AAV patients treated with rituximab. In this cohort, the outcomes were similar to the ones reported in other populations, with remission being achieved more likely in younger patients. Severe infections were frequent and associated with mortality.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10067-022-06192-1.

Author contribution Conception and design: Fabián Carranza-Enríquez, José Antonio Meade-Aguilar, and Andrea Hinojosa-Azaola. Material preparation and data collection: Fabián Carranza-Enríquez and José Antonio Meade-Aguilar. Analysis: Andrea Hinojosa-Azaola. First draft of the manuscript: Fabián Carranza-Enríquez, José Antonio Meade-Aguilar, and Andrea Hinojosa-Azaola. All authors commented on previous versions of the manuscript and read and approved the final version.

Declarations

Ethics approval The study was approved by the hospital Institutional Review Board (Comité de Ética en Investigación/Comité de Investigación) on September 2020 (Reference 3498). All procedures performed were in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Given that data were extracted from patient files, written informed consent was not required.

Disclosures None.

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