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# Polymyalgia rheumatica: A case series from Colombia and analysis of Latin America

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ABSTRACT

*Objective:* Polymyalgia rheumatica (PMR) is the most common inflammatory disease in patients over 50 years. Information about the disease in Latin America (LATAM) is scarce. We aimed to evaluate a group of Colombian patients with PMR and to conduct a systematic review of PMR in LATAM.
*Methods:* A multicentric retrospective study was performed. Medical records of 256 PMR patients were evaluated. Patients were divided into two groups, those fulfilling the 2012 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for PMR and those who did not (i.e., clinical diagnosis). A systematic literature review and meta regression was performed comparing Colombian vs LATAM patients.
*Results:* From 256 patients, 145 (56.6%) fulfilled the 2012 EULAR/ACR criteria, and 111 (43.3%) were classified by clinical diagnosis. Inflammatory bilateral shoulder pain, pelvic girdle aching, morning stiffness >45 min, elevated erythrocyte sedimentation rate (ESR), and C-reactive protein (CPR), and Methotrexate (MTX) prescription were more common in the 2012 EULAR/ACR group. None of the included patients presented overt polyautoimmunity (PolyA), whereas up to 24% exhibited latent PolyA. In addition, these patients showed high frequency of malignancy (7.59%). In the meta regression analysis, Colombian patients exhibited lower ESR levels, and were less likely to develop giant cell arteritis (GCA) as compared to the rest of LATAM data.
*Conclusion:* Patients with PMR in LATAM exhibit similar phenotypes from other cohorts worldwide. Malignancy, GCA and latent PolyA should be considered in the routine clinical follow-up of patients with PMR.

## 1. Introduction

Polymyalgia rheumatica (PMR) is an inflammatory disease characterized by the bilateral compromise of the shoulder and pelvic girdles, associated with morning stiffness, usually lasting more than 45 min. In addition, it is characterized by elevation of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); the latter is considered a crucial factor in diagnosis [1]. This disease is most frequent in people over 50 years of age, with a peak between the ages of 70–75, mainly affecting women in a ratio 3:1 to men [1]. In addition, PMR is closely associated with giant cell arteritis (GCA), which suggest the commonalities between these two conditions (i.e., autoimmune tautology).

PMR mostly presents in northern Europeans with an incidence of 41–113 cases per 100,000 persons, mainly in those over the age of 50.

*Abbreviations:* ACPA, Cyclic citrullinated peptide antibody.; ANAs, Antinuclear antibodies.; CART, Classification and regression trees.; CI, Confidence interval.; CRP, C-reactive protein.; DMARDs, Disease-modifying antirheumatic drugs.; ESR, Erythrocyte sedimentation rate.; EULAR/ACR, European League Against Rheumatism/American College of Rheumatology.; GCA, Giant cell arteritis; GCs, Glucocorticoids.; IQR, Interquartile range.; LATAM, Latin America.; MTX, Methotrexate.; OR, Odds ratio.; PolyA, Polyautoimmunity.; PMR, Polymyalgia rheumatica.; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.; RF, Rheumatoid factor.; SD, Standard deviation.; ts-DMARDs, Targeted-synthetic disease-modifying antirheumatic drugs..

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**Table 1**
General characteristics of patients with polymyalgia rheumatica.

| Characteristics | Patients meeting the 2012 EULAR/ACR criteria[a] n = 145 | PMR by clinical diagnosis only[a] n = 111 | P value[b] |
|---|---|---|---|
| Gender | | | 0.7703 |
| Female | 108 (74.5%) | 85 (76.6%) | |
| Male | 37 (25.5%) | 26 (23.4%) | |
| Age, years, (Median - IQR) | 76 (65–82) | 78 (68–83) | 0.2133 |
| Age of onset of symptoms, years (Median - IQR) | 72 (60–78) | 72 (61.5–77) | 0.9197 |
| Disease duration, years, (Median - IQR) | 4.38 (2.53–7) | 4.71 (2.68–7.71) | 0.3970 |
| Time of follow-up, months (Median - IQR) | 12 (4–42.75) | 6 (1–16.75) | **<0.00001** |
| Inflammatory bilateral shoulder pain | 145 (100%) | 91/110 (82.7%) | **<0.00001** |
| Pelvic girdle aching | 138 (95.2%) | 74/110 (67.3%) | **<0.00001** |
| Arthralgia | 53 (36.6%) | 46/110 (41.8%) | 0.4370 |
| Arthritis | 23 (15.9%) | 27/110 (24.5%) | 0.1107 |
| Morning stiffness | 112 (77.2%) | 73/110 (66.4%) | 0.0655 |
| Morning stiffness >45 min | 80 (55.2%) | 28/110 (25.5%) | **<0.00001** |
| Fever | 1 (0.7%) | 2/110 (1.8%) | 0.5795 |
| Weight loss | 6 (4.1%) | 3/110 (2.7%) | 0.7359 |
| Fatigue | 16 (11%) | 13/110 (11.8%) | 0.8450 |
| Night sweats | 1 (0.7%) | 0/110 (0%) | 1.0000 |
| Scalp tenderness | 3 (2.1%) | 2/110 (1.8%) | 1.0000 |
| Elevated ESR | 122 (84.1%) | 50/97 (51.5%) | **<0.00001** |
| Value ESR (Median - IQR) | 50 (33–77) | 37 (24.5–50) | 0.0069 |
| Elevated CRP | 93/139 (66.9%) | 30/89 (33.7%) | **<0.00001** |
| Rheumatoid factor | 4/137 (2.9%) | 4/63 (6.3%) | 0.2636 |
| ACPA | 2/97 (2.1%) | 2/56 (3.6%) | 0.6238 |
| ANAs | 30/111 (27%) | 12/57 (21.1%) | 0.4550 |
| Elevated CK | 9/71 (12.7%) | 1/46 (2.2%) | 0.0861 |
| Temporal artery biopsy | 1/63 (1.6%) | 1/68 (1.5%) | 1.0000 |

EULAR: European League Against Rheumatism, ACR: American College of Rheumatology, IQR: Interquartile range, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ACPA: Cyclic citrullinated peptide antibody, ANA: Antinuclear antibodies, CK: Creatine kinase, PMR: Polymyalgia rheumatica.

[a] In this retrospective study all charts of patients with PMR were reviewed and classified into two groups: those meeting the 2012 EULAR/ACR criteria, and those not fulfilling these criteria.

[b] P values for categorical variables were obtained by Fisher's exact test. Continuous variables were analyzed by Mann-Whitney-U test.

**Table 2**
Giant cell arteritis clinical characteristics in patients with polymyalgia rheumatica.

| GCA clinical characteristics | Patients meeting the 2012 EULAR/ACR criteria n = 145 | PMR by clinical diagnosis only n = 111 | P value[a] |
|---|---|---|---|
| **New onset headache** | 7 (4.8%) | 5/110 (4.5%) | 1.0000 |
| **Jaw, tongue, or limb claudication** | 3 (2.1%) | 1/110 (0.9%) | 0.6362 |
| **Visual disturbances** | 2 (1.4%) | 2/110 (1.8%) | 1.0000 |
| **Temporal artery abnormalities** | 1 (0.7%) | 2/110 (1.8%) | 0.5795 |

EULAR: European League Against Rheumatism, ACR: American College of Rheumatology, PMR: Polymyalgia rheumatica, GCA: Giant cell arteritis.

[a] P values for categorical variables were obtained by Fisher's exact test. Continuous variables were analyzed by Mann-Whitney-U test.

Asia, Africa and Latin America (LATAM) exhibit the lowest frequency of PMR [2,3]. Studies estimating the prevalence of PMR in these countries are scarce, and there is not information about the clinical differences among LATAM and other latitudes.

The diagnosis of PMR remains to be defined by clinical diagnosis based on information obtained by medical records, and clinical evaluation. Laboratory and imaging studies are essential to rule out differential diagnoses [4]. Currently, the most commonly used classification criteria are those of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) [5]. However, these criteria still present a high rate of false negative results [5].

We aimed to evaluate a group of patients with PMR, and determining those clinical characteristics associated with the fulfillment of 2012 EULAR/ACR classification criteria in four tertiary centers in Colombia. In addition, we conducted a systematic review of PMR in LATAM to develop a comparative analysis in this continent.

## 2. Materials and methods

### 2.1. Study design

A multicentric retrospective study was conducted from October 2020 to February 2021 in four tertiary specialized rheumatology centers; two were in Bogotá, Colombia including the Dermatology and Rheumatology Foundation (FUNINDERMA), and the Center for Autoimmune Diseases Research (CREA). The remaining centers were the Centro de Referencia en Osteoporosis, Reumatología & Dermatología, and Fundación Valle Del Lili, from Cali, Colombia. Records from 256 patients with clinical diagnosis of PMR were retrospectively assessed. Patients were divided in two groups: those fulfilling 2012 EULAR/ACR classification criteria (n: 145), and those diagnosed as PMR according to the clinical judgement of the treating rheumatologist (i.e., clinical diagnosis), but not meeting the 2012 EULAR/ACR classification criteria (n: 111). This was a low-risk study according to the resolution 8430 of 1993 from the Ministry of Health of Colombia.

### 2.2. Clinical variables

Medical records were reviewed using a questionnaire that sought information about demographic and clinical characteristics, including age, age of disease onset, symptoms at onset and comorbidities. Time of follow-up was defined as the time the patient was evaluated from the first time to the last medical visit in months. Inflammatory bilateral shoulder and pelvic girdle pain, were defined as the clinical compromise of these regions, characterized by morning stiffness, pain at rest and mechanical limitation. Morning stiffness was defined as struggle or impossibility to mobilize an articulation in the morning lasting ≥45 min. Elevated ESR as an elevation over 20 mm/h, and elevated CPR as the number of times the result was increased over the upper limit of each reference laboratory value.

The coexistence of two or more ADs with classification criteria was termed *"Overt polyautoimmunity (PolyA)"*, whereas the presence of autoantibodies unrelated to the index AD, without criteria fulfillment, was named *"Latent PolyA"*. Malignancy was registered as diagnosed by an oncologist. Association with GCA, was defined as patients with PMR, who developed clinical manifestations of GCA and received a final diagnosis of this disease. Likewise, association to rheumatoid arthritis (RA) was defined as patients who fulfilled 2010 EULAR/ACR classification criteria after an initial diagnosis of PMR [6]. Relapse was defined as the return of symptoms and the need to restart or increase the glucocorticoids (GCs) or any other treatment for disease control [7]. Concerning pharmacological therapy, the current or prior use of GCs, methotrexate (MTX), antimalarials, azathioprine, biological therapy, and targeted-synthetic disease-modifying antirheumatic drugs (ts-DMARDs) were also documented.

### 2.3. Information sources and search strategy for systematic review

A systematic review of the literature was done following the

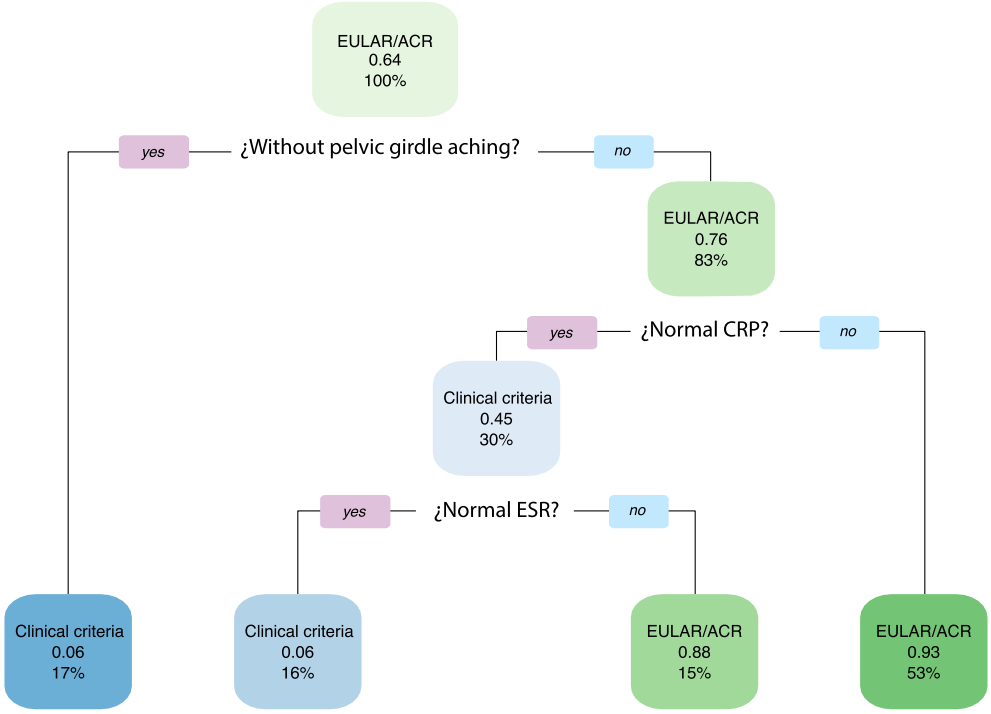


**Fig. 1.** Classification and decision tree for PMR classification criteria. The figure shows the decision rules for classification of patients according to pelvic girdle aching, CRP, and ESR. Each box contains the probability of fulfillment of PMR classification criteria, as well as the proportion of patients inside each node. PMR: Polymyalgia rheumatica; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate. See text for further explanations.

Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline [8]. LILACS, SciELO and PubMed were systematically searched for published and unpublished studies. Additional manual searches of the references cited in the articles were done.

The search included articles up to March of 2021. No restrictions were placed on study period or sample size. Other information sources such as personal communications and author's repositories were included. Terms used for this search were: ("Polymyalgia rheumatica" OR "Rheumatic polymyalgia" OR "Polimialgia reumatica") AND ("Latin America" OR "Mexico" OR "Belice" OR "Costa Rica" OR "El Salvador" OR "Guatemala" OR "Honduras" OR "Nicaragua" OR "Panama" OR "Cuba" OR "Haiti" OR "Dominican Republic" OR "Puerto Rico" OR "Caribbean Antilles" OR "Colombia" OR "Peru" OR "Ecuador" OR "Venezuela" OR "Bolivia" OR "Paraguay" OR "Chile" OR "Argentina" OR "Brazil" OR "Uruguay" OR "Guyana" OR "French Guyana" OR "Surinam"). Articles in Spanish and English were included.

### 2.4. Eligibility criteria

Studies meeting the following criteria were included: (a) Studies about PMR in LATAM, (b) studies describing clinical characteristics, treatment, and outcomes, (c) case reports, case series, cross-sectional, case-control, cohort, or clinical trial studies were also included. Studies from other regions were excluded.

### 2.5. Study selection

Study selection was done independently by two reviewers (i.e., CT and MR) who evaluated studies for eligibility in a two-step procedure. In the first phase, all identified titles and abstracts were evaluated to ensure the relationship with PMR. The potentially relevant articles were subsequently selected and evaluated again in the second phase. Here, a full-text review was done to determine whether the studies effectively reported the data about the clinical features of PMR. Retrieved articles were rejected if the eligibility criteria were not met, and a third reviewer (i.e., JMA) was consulted in cases in which the eligibility criteria were not clear.

### 2.6. Data extraction and quality assessment

Data were extracted using a standardized form to include the following variables: author, country, region, age, gender, time of follow-up, clinical features (as specified for our clinical study), inflammatory markers, autoantibodies, treatments, and comorbidities. A single author (i.e., CT) extracted the information, and a second reviewer (i.e., MR) verified the extracted information. Any discrepancies or missing information were resolved by consensus. Evaluation of quality of the eligible studies was not performed. The PRISMA checklist for systematic reviews is presented in Appendix 1.

### 2.7. Statistical analysis

Univariate descriptive statistics were performed. Categorical variables were analyzed using frequencies, and quantitative continuous variables were expressed as the mean and standard deviation (SD) or the median and interquartile range (IQR). The Kruskal-Wallis, Mann–Whitney *U* test, or Fisher's exact tests were used based on the results.

The comparisons between Colombia and LATAM, were done by means of meta regression fixed effect model, using Metafor R package (http://www.jstatsoft.org/v36/i03/). For quantitative variables, the effect size used was the raw mean, and to compare among regions the mean difference was estimated using the fixed effects meta regression model. For qualitative variables, effect size used was the logit-transformed proportion, and to compare among regions the logarithm of the odds ratio (OR) was estimated using the fixed effects meta regression model. For mean difference and odds ratio, 95% confidence intervals (CIs) are reported.

Classification and regression trees (CART) were used to evaluate the relationship between 2012 EULAR/ACR classification criteria and disease. Variables with p value $\leq$ 0.25 in the bivariate analysis were

**Table 3**
Treatment, comorbidities, and outcomes of patients with polymyalgia rheumatica.

| Characteristics | Patients meeting the 2012 EULAR/ACR criteria n = 145 | PMR by clinical diagnosis only n = 111 | P value* |
|---|---|---|---|
| Glucocorticoid | 138 (95.2%) | 101/109 (92.7%) | 0.4304 |
| GC average dose, (Median - IQR) | 7.5 (5–12.5) | 6.8 (5–10) | 0.5521 |
| Methotrexate | 66 (45.5%) | 31 (27.9%) | **0.0043** |
| MTX average dose, (Median - IQR) | 10 (10–15) | 10 (10–15) | 0.3745 |
| Antimalarials | 33 (22.8%) | 21 (18.9%) | 0.5369 |
| Azathioprine | 3 (2.1%) | 4 (3.6%) | 0.4712 |
| Azathioprine average dose, (Median - IQR) | 50 (50–50) | 50 (50–62.5) | 0.6171 |
| Biological therapy | 2 (1.4%) | 3 (2.7%) | 0.6551 |
| Ts-DMARD | 3 (2.1%) | 2 (1.8%) | 1.0000 |
| Arterial hypertension | 54 (37.2%) | 40 (36%) | 0.8962 |
| Diabetes mellitus | 26 (17.9%) | 15 (13.5%) | 0.3920 |
| Dyslipidemia | 32 (22.1%) | 18 (16.2%) | 0.2682 |
| Glaucoma[a] | 3 (2.1%) | 2 (1.8%) | 1.0000 |
| Anemia | 9 (6.2%) | 7 (6.3) | 1.0000 |
| Hypothyroidism[b] | 35 (24.1%) | 19 (17.1%) | 0.2163 |
| Autoimmune/ Autoinflammatory disease | 5 (3.4%) | 5 (4.5%) | 0.7503 |
| Malignancy | 11 (7.6%) | 3 (2.7%) | 0.1028 |
| Breast Cancer | 4 (2.8%) | 0 (0.0%) | |
| Skin cancer | 0 (0.0%) | 1 (0.9%) | |
| Chronic Myeloid Leukemia | 1 (0.7%) | 0 (0.0%) | |
| Colorectal Cancer | 1 (0.7%) | 1 (0.9%) | |
| Prostate Cancer | 2 (1.4%) | 0 (0.0%) | |
| Lung cancer | 0 (0.0%) | 1 (0.9%) | |
| Prostate Cancer and Basal Cell Carcinoma[c] | 1 (0.7%) | 0 (0.0%) | |
| Stomach Cancer | 1 (0.7%) | 0 (0.0%) | |
| Thyroid Cancer | 1 (0.7%) | 0 (0.0%) | |
| Association with GCA | 4 (2.8%) | 0 (0%) | 0.1353 |
| Criteria fulfillment for GCA | 2 (1.4%) | 0 (0%) | 0.5069 |
| Association with RA | 10 (6.9%) | 8 (7.2%) | 1.0000 |
| RA, time after PMR, months (Median - IQR) | 3 (1–9) | 27 (3–58.8) | 0.2339 |
| Overt PolyA | 0 (0.0%) | 0 (0.0%) | – |
| Latent PolyA | | | |
| Latent RA[d] | 3/137 (2.2%) | 1/64 (1.6%) | 1.0000 |
| Latent ANAs | 30/111 (27.0%) | 12/57 (21.1%) | 0.4550 |
| Overall latent PolyA | 33/138 (23.9%) | 13/67 (19.4%) | 0.5927 |
| Relapses | 42 (29%) | 20 (18%) | 0.0553 |
| Relapses, n (Median - IQR) | 1 (1–2) | 1 (1–1) | 0.4249 |

MTX: Methotrexate, GC: Glucocorticoid, ts-DMARD: Targeted synthetic disease modifying antirheumatic drugs, PMR: Polymyalgia rheumatica, EULAR: European League Against Rheumatism, ACR: American College of Rheumatology, GCA: Giant cell arteritis, RA: Rheumatoid Arthritis, PolyA: Polyautoimmunity; n: number, IQR: Interquartile range.
*P values for categorical variables were obtained by Fisher's exact test. Continuous variables were analyzed by Mann-Whitney-U test.
[a] Diagnosis by clinical suspicion.
[b] No autoantibodies were performed.
[c] One patient presented with synchronous neoplasia.
[d] Positivity for rheumatoid factor or cyclic citrullinated peptide antibodies.

included in the model [9]. These account for age, bilateral shoulder pain, pelvic girdle aching, arthritis, morning stiffness ≥45 min, ESR, CRP, creatin kinase (CK) levels, and hypothyroidism. Briefly, CART is a non-parametric approach in which a series of recursive subdivisions separate the data by dichotomization. The aim is to identify, at each partition step, the best predictive variable and it is best corresponding splitting value while optimizing a statistical criterion. The significance level of the study was set to 0.05. Statistical analyses were done using R software version 4.0.1.

## 3. Results

### 3.1. General characteristics

General characteristics of patients are shown in Table 1. From 256 patients, 145 (56.6%) fulfilled the 2012 EULAR/ACR criteria, and 111 (43.4%) were classified by clinical diagnosis. Most of patients in both groups were women. Age, age at onset, duration of disease, rheumatoid factor (RF), and cyclic citrullinated peptide antibody (ACPA) were similar between groups. Patients fulfilling the 2012 EULAR/ACR classification criteria were followed by a longer time than those with clinical diagnosis. In addition, inflammatory bilateral shoulder pain, pelvic girdle aching, morning stiffness >45 min, elevated ESR and CRP, were also most common in the 2012 EULAR/ACR group. Some patients exhibited clinical manifestations of GCA, but these were not different between groups (Table 2).

Next, we conducted a CART analysis to evaluate those factors associated with the classification of patients into 2012 EULAR/ACR criteria or clinical diagnosis by the clinician (Fig. 1). At this respect, we found that pelvic girdle aching, elevated CRP and ESR are the most critical factors used by clinicians and useful to classify patients into 2012 EULAR/ACR criteria. In clinical practice, the pelvic girdle aching was the most relevant symptom to classify patients with PMR, followed by CRP and the ESR.

### 3.2. Treatment and comorbidities

Almost all patients were treated with GCs (Table 3). Patients fulfilling the 2012 EULAR/ACR criteria were more likely to receive MTX. Administration rate of antimalarials, azathioprine, and biologicals was similar in both groups. Hypertension was the most common comorbidity, followed by hypothyroidism and dyslipidemia. The frequency of additional comorbidities was lower than 18%. Interestingly, eleven patients fulfilling the 2012 EULAR/ACR criteria showed malignancies (Table 3). Malignancy was associated with a later onset of disease (83 vs 72 years; P = 0.0190). In addition, none of the patients presented overt PolyA. However, about 24% of patients had latent PolyA, mostly represented by antinuclear antibodies (ANAs).

### 3.3. Outcomes

Only 4 patients developed overt GCA (Table 3). RA, relapses, and hospitalizations were slightly more common in those patients fulfilling the 2012 EULAR/ACR criteria. Intragroup analysis showed that relapses were associated with a longer duration of disease (4 years vs 7 years; P < 0.001), female gender (85.7%; P = 0.0480), arthritis (26.2%; P = 0.0300), fatigue (21.4%; P = 0.0110), a higher use of disease-modifying antirheumatic drugs (DMARDs) (7.1%; P = 0.0060), and the presence of hypothyroidism (40.5%; P = 0.0030). Interestingly, patients presenting relapses exhibited a higher rate of GCA (7.1%; P = 0.0400) and RA (14.3%; P = 0.0250).

### 3.4. Systematic review

Initially, 116 records were found through the database search. One additional study was identified by other sources. After duplicate studies were excluded, a total of 104 studies were obtained. After the first records were screened by title and abstract, 73 articles were fully assessed for eligibility. Of these, 61 articles were excluded, 3 because they were focused on population other than LATAM, 23 because they were review articles, and finally 35 articles because they were primarily focused on GCA and other related diseases. This procedure left 12 articles that fulfilled the inclusion criteria, and they were included in the quantitative and qualitative synthesis (Fig. 2) (Appendix 2).

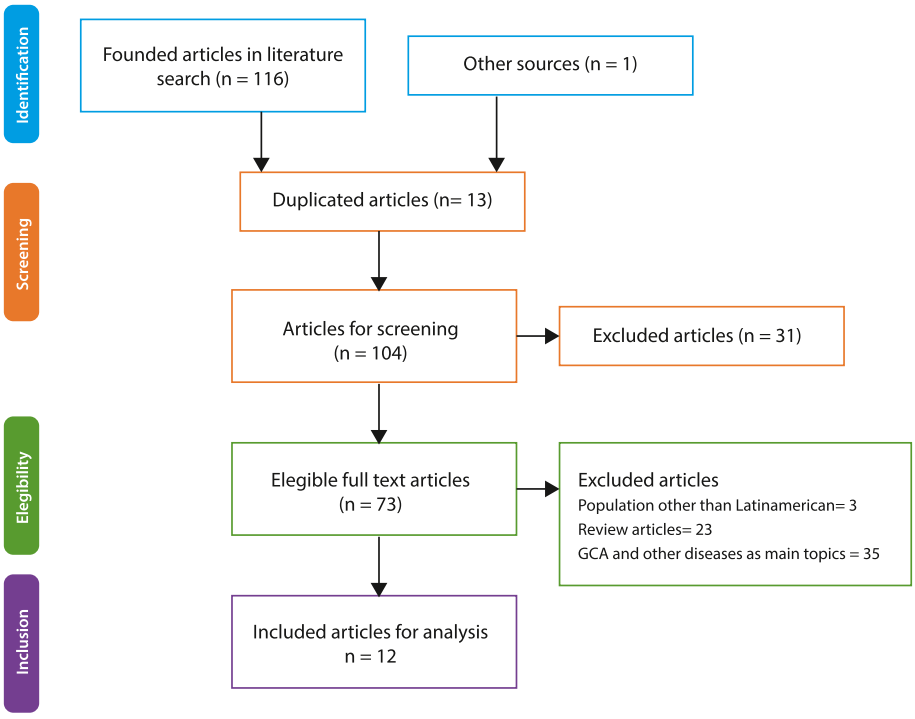


**Fig. 2.** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow chart.

### 3.5. Studies characteristics

Out of 12 studies included in the systematic review, 3 were case-control studies, 1 was a cohort study, 3 case series, 2 were descriptive, 2 case reports and 1 was a cross-sectional study (Appendix 2). No clinical trials were included in this systematic review.

### 3.6. Colombia vs Latin America

Patients with PMR from Colombia were less likely to present morning stiffness, elevated ESR, association with GCA and fulfill GCA criteria (Table 4). On the other hand, Colombian patients were more likely to exhibit jaw, tongue, or limb claudication, and visual disturbances than patients from other countries, however, despite all these clinical characteristics of GCA, this entity was not diagnosed as such. Other clinical parameters such as age, sex, clinical features, autoantibodies, treatment, overt PolyA, and comorbidities did not differ between Colombia and the rest of LATAM.

## 4. Discussion

In this case series, patients fulfilling the 2012 EULAR/ACR criteria were more prone to exhibit inflammatory bilateral shoulder pain, pelvic girdle aching, morning stiffness >45 min, elevated ESR and CRP than those patients with clinical diagnosis of PMR (not fulfilling 2012 EULAR/ACR criteria). In addition, the former group were also followed by a longer period. Conversely, age, age at onset of symptoms, duration of disease and other clinical and laboratory features such as arthralgia, arthritis, fever, weight loss, fatigue, night sweats, scalp tenderness, RF, ACPA, antinuclear antibody and elevated CK were similar between groups. This in line with recent meta-analysis, in which Twohig et al. [10] showed that systemic inflammation was the most frequently assessed outcome, followed by pain and stiffness.

There was also no difference when analyzing the small group of patients who were associated to GCA. Interestingly, pelvic girdle aching, elevated CRP and elevated ESR were the most critical factors used by clinicians to classify patients as PMR according to 2012 EULAR/ACR classification criteria as shown in Fig. 1. Our data add further knowledge about PMR in non-Caucasian populations [11,12]..

As mentioned by June and Aggarwal "classification criteria are not designed to be used for clinical diagnosis or applied to individual patients but instead used to further research of the population. They are defined as a set of disease characteristics used to group individuals into a well-defined relatively homogenous population with similar clinical disease features" [13]. "Classification criteria are essential for understanding disease pathogenesis and assessing treatment response. Classification criteria increase the specificity for underlying disease by creating a homogenous population while at times losing sensitivity" [13]. Symptoms of PMR can also be present as the initial manifestation of other diseases, such as RA, GCA, malignancy and miscellaneous diseases [11].

In this study, clinical features of GCA were similar between the PMR 2012 EULAR/ACR criteria and the PMR clinical diagnosis groups. These clinical characteristics of GCA (i.e., headache 4.5%, claudication 2.1%, visual disturbances 2.1% and altered temporal artery 0.7%), were lower than the reported in Medellín, Colombia (11%, 2.9%, 7.4% and 8.8%, respectively) [14]. This could be secondary to a population difference in clinical presentation, but still there is not enough data to draw a conclusion about it. GCA is a large and medium-sized blood vessel systemic vasculitis characterized by the granulomatous involvement of the aorta and it is major branches [15]. GCA and PMR are inflammatory diseases with a close relationship between them [16].

Classically, patients with PMR have been treated with GCs [17]. In fact, response to GCs has been considered as a clinical hallmark of the disease in the Jones and Hazleman [18], and Healey [19] classification criteria. In our cohort, most of patients were treated with GCs regardless of 2012 EULAR/ACR criteria fulfillment. These results confirm that rheumatologists still consider GCs as the first line of management in PMR [17].

Treatment with MTX is commonly considered in patients with relapsing disease, or in high risk of adverse events related to long term GCs management. However, it is still unknown whether early initiation or long-term management with GCs could reduce relapses or associated PMR complications [17]. In this study, patients fulfilling 2012

**Table 4**
Meta-analysis and meta regression of systematic review.

| Characteristics | Colombia[a] | Latin America[a] | Colombia vs. Rest of Latin America[b] |
|---|---|---|---|
| Gender | | | |
| Female | 77.61% (60.03–88.89) | 74.33% (71.62–76.62) | 1.19 (0.75–2.46) |
| Male | 22.58% (11.26–40.13) | 25.67% (23.13–28.38) | 0.86 (0.54–1.37) |
| Age, years, (mean) | 72.11 (68.99–75.23) | 73.60 (71.40–75.80) | −1.49 (−5.30 to 2.33) |
| Inflammatory bilateral shoulder pain | 93.87% (72.10–98.91) | 93.43% (85.56–97.15) | 0.99 (7.51–7.51) |
| Pelvic girdle aching | 79.69% (74.06–84.37) | 87.69% (73.94–94.70) | 0.72 (0.13–3.88) |
| Arthralgia | 39.31% (33.51–45.42) | – | – |
| Arthritis | 26.18% (11.89–48.24) | 19.06% (8.18–38.36) | 1.43 (0.41–5.31) |
| Morning stiffness | **74.88% (69.71 to 79.45)** | **98.68% (73.19 to 99.95)** | **0.044 (0.01 to 0.36)** |
| Morning stiffness >45 min | 60.20% (19.13–90.63) | 94.21% (65.51–99.29) | 0.1 (0.00–2.89) |
| Fever | 11.79% (1.15–60.66) | 7.53% (2.88–18.27) | 1.59 (0.05–49.5) |
| Weight loss | 10.07% (0.62–66.68) | 11.78% (6.89–19.43) | 0.36 (0.13–0.97) |
| Fatigue | 22.24% (6.91–52.41) | 27.32% (0.37–97.41) | 1.28 (0.06–27.4) |
| Scalp tenderness | 3.38% (1.43–7.82) | – | – |
| Elevated ESR | **63.90% (58.05 to 69.35)** | **88.67% (81.52 to 92.53)** | **0.24 (0.09 to 0.67)** |
| Elevated CRP | 58.95% (39.64–75.85) | 68.09% (58.03–76.70) | 0.71 (0.06–8.94) |
| Rheumatoid factor | 5.22% (2.15–12.12) | 1.20% (0.17–8.05) | 4.52 (0.42–48.5) |
| ACPA | 3.39% (0.97–11.11) | – | – |
| ANAs | 18.94% (10.86–90.94) | – | – |
| Temporal artery biopsy | 1.51% (0.57–3.96) | – | – |
| New onset headache | 6.54% (3.56–11.72) | 2.16% (0.64–42.91) | 2.36 (0.11–49.9) |
| Jaw, tongue, or limb claudication | **2.02% (0.91 to 4.41)** | **0.06% (0.00 to 0.96)** | **34 (1.89 to 610)** |
| Visual disturbances | **3.03% (1.1 to 8.03)** | **0.06% (0.00 to 0.96)** | **50.3 (1.74 to 1455)** |
| Temporal artery abnormalities | 1.34% (0.51–3.53) | – | – |
| Glucocorticoids | 93.38% (80.86–97.92) | 97.01% (89.20–99.22) | 0.43 (0.06–2.91) |
| Methotrexate | 36.67% (21.64–54.83) | 18.69% (1.51–77.53) | 2.05 (0.18–23.4) |
| Antimalarials | 22.23% (16.64–26.70) | – | – |
| Azathioprine | 2.85% (1.37–5.86) | 4.55% (0.64–26.15) | 0.62 (0.07–5.25) |
| Arterial hypertension | 28.71% (15.26–47.37) | 14.89% (9.02–23.59) | 2.31 (0.49–10.8) |
| Diabetes mellitus | 13.32% (7.95–21.48) | 19.64% (7.06–44.04) | 0.73 (0.28–1.87) |
| Dyslipidemia | 14.18% (6.35–28.70) | 16.44% (1.82–67.63) | 1.19 (0.22–6.59) |
| Glaucoma | 1.96% (0.82–4.63) | – | – |
| Anemia | 8.47% (4.81–14.48) | 3.45% (1.30–8.83) | 2.59 (0.62–10.8) |
| Hypothyroidism | 14.87% (6.29–31.27) | – | – |
| Malignancy | 6.83% (0.59–47.15) | – | – |
| Association with GCA | **2.94% (0.59 to 13.46)** | **7.78% (4.10 to 14.28)** | **0.34 (0.12 to 0.95)** |
| Criteria fulfillment for GCA | **1.4% (0.45 to 4.26)** | **7.44% (3.59 to 14.81)** | **0.18 (0.45 to 0.70)** |
| Association with RA | 7.27% (4.90–10.66) | 2.17% (0.13–26.81) | 3.53 (0.21–60) |
| Overt polyautoimmunity (RA + GCA) | 1.41% (0.19–9.62) | 0.53% (0.03–7.85) | 2.70 (0.05–145.50) |
| Relapses | 27.97% (17.53–41.50) | 33.43% (3.98–85.88) | 0.75 (0.10–5.52) |

ESR: Erythrosedimentation rate, CRP: C-reactive protein, ACPA: Cyclic citrullinated peptide antibody, ANAs: Antinuclear antibodies, GCA: Giant cell arteritis, RA: Rheumatoid arthritis.

[a] Data from systematic review and meta-analysis. Estimated prevalence or mean for each population group is presented with the corresponding confidence interval.

[b] Data shows odds ratios (OR), mean differences and 95% confidence intervals (95% CI) from meta-regression analysis.

EULAR/ACR criteria were more likely to receive MTX. Interestingly, these patients exhibited a trend to present a higher frequency of relapses and hospitalizations. Other medications such as azathioprine, biologics and ts-DMARDs were uncommon.

Most of the patients with PMR exhibit high burden of diseases, given by comorbid conditions including cardiovascular diseases, and cancer [20]. In a recent systematic review, it was described that patient with PMR showed a high frequency of hematogenous cancers compared to healthy controls. Hodgkin's and non-Hodgkin's lymphoma were the most common. In our study, less than 10% of patients with PMR were diagnosed with cancer. Cardiovascular and thyroid diseases are more common in patients with PMR when compared with healthy controls [20]. We found that approximately a quarter of patients fulfilling or not the 2012 EULAR/ACR criteria exhibited hypertension, dyslipidemia, and hypothyroidism. These conditions should be considered in the routine assessment of PMR.

Cancer was observed in 14 (5.5%) patients (Table 3). Muller et al. [21] using a data base from England and Wales found a 69% increased risk in PMR patients of developing cancer in the first 6 months after the diagnosis of PMR. In a similar study, Ji, et al. [22] observed an increased risk of developing cancer, after a year of hospitalization and additionally they found that skin cancer, prostate cancer and leukemias were the most common in PMR patients. In some cases, PMR symptoms could be result from a paraneoplastic syndrome, this situation should be considered when there is not response to GCs or the acute phase reactants persist elevated spite a pharmacological treatment [23,24].

When comparing clinical and laboratory features of patients with PMR from Colombia and LATAM, Colombian patients presented less frequently with morning stiffness, elevated ESR, association with GCA and fulfilling of GCA criteria (Table 4). On the contrary, Colombian patients were more prone to develop jaw, tongue or limb claudication, and also visual disturbances than patients from other countries of LATAM [25–30]. However, it is unknown if these differences are related to different variables definition or if these are true differences related to ancestry or environmental factors.

On the other hand, other features such as age, age at onset of symptoms, sex, inflammatory biomarkers, autoantibodies, and comorbidities were not different between Colombia and LATAM. Finally, there was also not difference in the management of patients with PMR between Colombia and the rest of LATAM.

Limitations of this study must be acknowledged. This was a retrospective study that could have been susceptible to selection bias. In addition, when performing the systematic literature review, there were a few studies on PMR in LATAM. Hypothyroidism was a frequent comorbidity exhibited in our patients. However, specific autoantibodies (i.

e., anti-thyroglobulin or Anti-thyroid peroxidase) were not tested in all cases.

## 5. Conclusions

Patients with PMR in LATAM exhibit similar phenotypes from other cohorts worldwide. Clinicians must be aware of the clinical differences among LATAM countries. Malignancy, GCA and latent PolyA should be considered in the routine clinical follow-up. Further analyses including other populations from LATAM are critical to evaluate the geographic differences in thisregion.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtauto.2021.100115.

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