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Original Article

# Epidemiology and clinical outcome and its main determinants among patients with inflammatory myositis

**Fatemeh Shirani[1], Ali Javadzadeh[1], Abdolreza Rahaeebakhsh Izadi[1*]**

[1] *Department of Internal Medicine, School of Medicine, Hazrat-e Rasool General Hospital, Iran University of Medical Sciences, Tehran, Iran*

***Corresponding author:** Abdolreza Rahaeebakhsh Izadi, **Address**: Department of Internal Medicine, School of Medicine, Hazrat-e Rasool General Hospital, Iran University of Medical Sciences, Tehran, Iran, **Email**: abdolrezarahaeebakhshizadiabdo@gmail.com, **Tel**: +982164351

## Abstract

***Background & Aims*:** Despite the proper understanding of pathophysiological aspects and recent development in therapeutic approaches, the outcome of patients suffering from inflammatory myositis remains unsatisfactory. In addition, there is no clinical information and a clear outlook for this disease in the community. This study aimed to evaluate the outcome of patients with inflammatory myositis (response rate to treatment) and to determine the related and predictive factors of this outcome in these patients.

***Materials & Methods*:** This historical cohort study was performed on 80 patients suffering from inflammatory myositis. By retrospectively reviewing the patient records in the hospital, basic information was extracted and through telephone calls, the outcome status of the disease, and response to treatment were assessed during follow-up and categorized as complete remission, partial remission, and no remission.

***Results*:** Within the follow-up time, 40.0% were completely treated (complete remission), 3.8% had no proper response to treatment (incomplete remission), and 13.8% did not respond to the treatment. Also, 23.8% did not refer for further treatment at least six months from the start of treatment. No death was reported within the follow-up time. We found an association between the quality of treatment response and baseline parameters, including the rate of receiving intravenous immune globulin regimen, time of symptoms onset, gender, different patterns of disease, and disease subtype.

***Conclusion*:** A notable number of inflammatory myositis patients still do not respond to routine treatment, and we, in fact, are at the forefront of managing the disease.

***Keywords*:** Clinical outcome, Inflammatory myositis, Outlook

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## Introduction

An inflammatory myositis is a group of acquired diseases whose most important features are the weakness and fatigue of the proximal muscles with sub-acute progression and infiltration of mononuclear cells in muscle tissue with degeneration and

regeneration of muscle fibers and increase in muscle enzymes (1). These diseases are divided into three main types, including dermatomyositis, polymyositis, and inclusion body myositis (2). These conditions are rare muscular disorders that occur in about 0.5 and 8 per million people (3).

Muscle biopsy is the most useful diagnostic method for inflammatory myositis, which shows inflammation and infiltration of mononuclear cells into muscles (4). However, it should be noted that inflammation is evident not only in polymyositis but also in some muscular dystrophies, including Duchenne and Becker muscular dystrophies and facioscapulohumeral, as well as some metabolic, toxic, and viral infections, which can be associated with muscle inflammation, increased muscle enzymes, and polymyositis-like clinical signs, commonly known as nonspecific myositis (5,6).

In dermatomyositis, due to complement activation, lysis of endothelial cells in the microvascular-endomysial system, vascular necrosis, microinfarction and inflammation, and finally vperivascular atrophy occurs (7, 8). In polymyositis and inclusion body myositis, endomysial lymphocyte infiltration is predominantly by CD8 T cells that attack the muscle fibers, which supply major histocompatibility class I antigens (9). In muscle pathology, except for fiber necrosis, fiber degeneration, and regeneration, one of the important characteristics is the endomysial infiltration of fibers by lymphocytes (10). In addition to these findings, the formation of vacuoles and amyloid sediments is also observed in myocytes (11). Regarding the survival of patients with inflammatory myositis, although the survival of these patients has improved significantly with the widespread use of corticosteroids as well as immunosuppressive drugs, notable mortality has been reported in the literature with a five-year survival rate of about 60% (12). In this regard, an accurate evaluation of the prognosis of these patients can provide the possibility of proper management of these patients as much as possible. Ths study aimed to evaluate the outcome of patients with inflammatory myositis (response rate to treatment) and to determine the related and predictive factors of this outcome in these patients.

## Materials & Methods

This historical cohort study was performed on 80 patients with inflammatory myositis referred to Rasoul Akram Hospital in Tehran, Iran. The exclusion criteria were the existence of any patient dissatisfaction in participating in the study, the lack of access to the patient for any reason, or the lack of part of the diagnostic tests in the hospital files.

By retrospectively reviewing the patient records in the hospital, basic information including demographic characteristics, clinical manifestations, underlying diseases, medications received, the pattern of organ and visceral involvement, a phasic pattern of disease, and frequency of underlying risk factors such as heart or lung diseases, malignancy, infection and intake of corticosteroids and immunosuppressive drugs were collected and recorded in a checklist. Through telephone calls, the outcome status of the disease, and response to treatment, were assessed during follow-up and categorized as complete remission, partial remission, and no remission. The study endpoint was to assess and compare the baseline parameters between survived and non-survived subgroups to ultimately determine the prognostic factors of survival in such patients. This study was approved by the Ethical committee of the Iran University of Medical Sciences, Tehran (ethical code: IR.IUMS.FMD.REC.1401.297).

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. All data were analyzed using the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York). Continuous variables were compared using t-test or Mann-Whitney test whenever the data did not appear to have normal distribution, or when the assumption of equal variances was violated across the study groups. P values of $\leq 0.05$ were considered statistically significant.

## Results

Overall, 80 patients (mean age 41.83 ± 14.62 years, ranged 14-83 years, 65.0% female) were included in the study. The average age of men and women was 40.75 ± 15.79 years and 43.68 ± 12.62 years, respectively with no difference (p = 0.39). The results of the study showed that the mean time interval between the onset of symptoms and referral was 628.9 ± 611.118 days (423.55 ± 1055 days in men and 728.98 ± 1135 days in women), which statistically showed no difference between the two genders (p = 0.29). The pointed time according to underlying disorders is shown in Table 1. In 14.5% of patients, the symptoms had occurred 90 days before the visit, which was the most common in terms of the duration of symptoms in patients until the visit to the clinic. The maximum time interval was 4380 days and the minimum was 1 day. It was also observed that in almost 80% of patients, the time interval between the onset of symptoms and visit to the clinic was more than 30 days. The mean levels of laboratory biomarkers in men and women, summarized in Table 2, indicate no difference between men and women. A review of a biopsy report of patients showed a myopathy pattern in 53.8% of patients 34.88% of males and 65.12% of female patients (p = 0.23). Also, 33.8% had inflammatory myositis patterns, of which 31% were men and 69% were women (p = 0.36). In total, 47.4% had dermatological symptoms without difference between men and women (p = 0.57). Also, none of the patients had Calcinosis Cutis. Regarding underlying disorders, 30 patients had one or more comorbidities, and 21 did not report a specific history. In those with such underlying disorders, the most common included hypertension in 6.3%, cancers in 6.3%, cardiac disorders in 2.5%, and hypothyroidism in 2.5%. In this study, 28.8% were treated with intravenous immune globulin (IVIG), of which 30.4% were men and 69.6% were women (p = 0.82). In the two groups with and without IVIG treatment protocols, there was no difference in inflammatory myositis pattern (26.1% versus 41.4, p = 0.81) as well as in myopathy pattern (33.3% versus 48.7%, p = 0.53). In total, disease-modifying antirheumatic drugs (DMARDs) regimen was prescribed in 12.5% (14.3% in men and 11.5% in women), while synthetic DEMARD was considered in 72.5% (67.9% in men and 75.0% in women). The most common type included dermatomyositis (DM) in 47.5%, followed by polymyositis (PM) in 21.3% and inclusion body myositis (IBM) in 2.5%. No difference was found between the type of disease and patient gender (Table 3). Dermatological symptoms were found only in those with the DM disease subtype (78.9%), but not in other disease subtypes. Also, regarding the difference in laboratory parameters, the mean level of alanine aminotransferase (ALT) was significantly higher in the subgroup with PM than in other subgroups (p = 0.007) (Table 3). We also found no difference in the IVIG treatment regimen across the different disease subgroups (p = 0.06).

Within the follow-up time, 40.0% were completely treated (complete remission), 3.8% had no proper response to treatment (incomplete remission), and 13.8% did not respond to the treatment. Only 18.8% were discharged with good clinical condition. Also, 23.8% had not been referred for further treatment at least six months from the start of treatment. No death was reported within the follow-up time. We found no difference in the rate of receiving IVIG regimen and the quality of treatment response (33.3 in the group with complete remission, 50.0 in the group with incomplete remission, and 40.0% in those without response to treatment; p = 0.97). We indicated also no difference in the time between symptoms onset and admission between the three response groups. Also, there was no significant association of gender, different patterns of disease, and disease subtype with the response to treatment.

**Table 1.** Time interval between the onset of symptoms and referring to the hospital

| Diagnosis | Mean | SD |
|---|---|---|
| PM+ dystrophy | 3650.00 | 1256.12 |
| DM | 308.71 | 689.177 |
| DM+PM | 365.00 | 520.34 |
| IBM | 372.00 | 506.288 |
| Myopathy | 65.00 | 77.782 |
| Myositis | 450.00 | 546.23 |
| Overlap syndrome | 425.00 | 431.335 |
| PM | 749.07 | 1265.910 |

PM: polymyositis, DM: polymyositis, IBM: inclusion body myositis

**Table 2.** The mean levels of laboratory biomarkers according to gender

| Biomarker | Total, mean ± SD | Men, mean ± SD | Women, mean ± SD | p value |
|---|---|---|---|---|
| ESR | 28.29±21.76 | 29.21±26.25 | 27.75±19.06 | 0.82 |
| CPK | 2584.45±3864.46 | 2669.26±3017.42 | 2538.00±4291.84 | 0.93 |
| ALT | 84.07±90.08 | 75.48±77.44 | 77.93±97.21 | 0.39 |
| AST | 113.32±151.82 | 125.50±113.73 | 106.36±170.73 | 0.57 |

ESR: erythrocyte sedimentation rate, CPK: creatine phosphokinase, ALT: alanine aminotransferase, AST: aspartate aminotransferase

**Table 3.** Comparing baseline characteristics according to the disease subtypes

| Variable | | DM | PM | IBM | p value |
|---|---|---|---|---|---|
| Laboratory parameters | ESR, mean ± SD | 28.74±20.61 | 20.10±16.96 | 41.50±33.23 | 0.007 |
| | CPK, mean ± SD | 1687.83±2633.93 | 3859.69±3250.69 | 1357.50±767.21 | |
| | ALT, mean ± SD | 67.18±50.26 | 139.07±100.85 | 49.50±12.02 | |
| | AST, mean ± SD | 125.03±147.62 | 120.71±112.05 | 87.00±74.57 | |
| Gender | Male, % | 34.0 | 32.2 | 33.7 | 0.63 |
| | Female, % | 66.0 | 67.8 | 66.3 | |
| Dermatological symptoms, % | | 78.9 | - | - | 0.001 |
| IVIG receiving, % | | 32.3 | 66.7 | - | 0.06 |

IVIG: Intravenous immune globulin, ESR: erythrocyte sedimentation rate, CPK: creatine phosphokinase, ALT: alanine aminotransferase, AST: aspartate aminotransferase, PM: polymyositis, DM: polymyositis, IBM: inclusion body myositis

## Discussion

Despite a proper understanding of pathophysiological aspects and recent development in therapeutic approaches, the outcome of patients suffering from inflammatory myositis remains unsatisfactory. In this regard and according to our observations, one-third of patients could completely be treated by common therapeutic regimens, while about 40% of patients remained untreated. Given the fact that most patients may not respond to typical medications, using the combination of glucocorticoids and adjunctive immunosuppressive agents is now recommended. Numerous synthetic and biological immunosuppressive agents are currently available to treat inflammatory myositis, sometimes in combination; however, it should also be pointed out that personalized medicine has a central role to determine the treatment choice in these patients but with considering disease phenotype, patient's characteristics, and using supplement interventions such as exercise (13, 14).

To improve treatment response to current therapies in patients with inflammatory myositis, identifying the main factors affecting treatment response and the disease-related final prognosis is the first line. In this comtext, different studies have attempted to introduce the main outcome determinants. Some other studies have pointed to old age, non-white race, bulbar involvement, delayed treatment, and cardiovascular and pulmonary involvement as the main disease-related prognostic factors leading complete remission (15). To achieve a good prognosis, three steps must be taken.

First, an individualized treatment regimen should be selected considering the patient's clinical condition. Second, the main goals for selecting such treatment regimens should be considered improving muscle strength, stabilizing clinical and hemodynamic conditions, and improving long-term quality of life (16-18). The last step is to monitor the treatment response using different arms such as serial monitoring muscle enzymes, inflammatory biomarkers, and other hematological tests. It has been indicated that almost all biomarkers are nonspecific or even unpredictable; however, some markers such as CK level are now used to assess disease activity levels (19, 20).

Reviewing the literature showed unfortunately poor outcomes for patients suffering from inflammatory myositis, even by employing novel treatment regimens. In a study by van de Vlekkert et al. (20), after a three-year follow-up, it was found that the mortality of these patients was 15%. The course of the monophasic disease was determined in 27%, 35% had a chronic subacute disease, and 35% had a recurrent phase of the disease. Additionally, 33% of patients did not receive medication and treatment for one year. During the follow-up, 68% were disabled. Malignancy was reported to be the leading cause of death. Three patients had malignancy at the beginning of the disease, and seven patients developed malignancy during follow-up, which was mainly in the DM group (20). In another study by Amaral (21), within a mean follow-up time of nine years, survival at 5, 10, 15, and 20 years was 94.6%, 82.2%, 72.1%, and 66.1%, respectively. Mortality was 24.7%, which was mainly due to the underlying infection, pulmonary involvement, infection, and simultaneous involvement of the upper and lower limbs. These studies show that we are at the forefront of managing the disease.

The disease response to treatment may be affected by some baseline factors such as demographics, clinical conditions, the type of disease, or the regimen selected for treatment. However, in our study, none of the baseline variables such as gender, the pattern of disease, disease subtype, and receiving IVIG regimen could predict the complete regimen. Our findings might be influenced by several factors. First, a small sample size of study led to partially low study power leading insignificance of some study relationships or the impossibility of identifying prognostic factors. Second, the choice of treatment will be based on the decision and clinical judgment of the physician and therefore due to the lack of study design in the form of clinical trial and randomization between intervention groups, it was impossible to assess the factors affecting the prognosis.

## Conclusion

While myositis is a treatable disease, most patients present with multiphasic or chronic disease and require maintenance treatment, as do most other immune disorders, such as myasthenia gravis. The negative effects on the performance and quality of life in this disease are significant, and the lack of further progress after 18 months of treatment is disappointing. We hope that new treatments in the future will not only greatly reduce inflammation but also reduce the risk of disease damage and improve the quality of life and function of these patients. Therefore, according to studies, the need for malignant screening for this disease is emphasized. Based on the results of the present study as well as the review of previous studies, it is suggested that screening should be performed at the time of diagnosis and at least annually.

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None declared.

## Ethical statement

This study was approved by the Ethical committee of the Iran University of Medical Sciences, Tehran (ethical code: IR.IUMS.FMD.REC.1401.297).

## Conflict of interest

None declared.

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## Data availability

The raw data supporting the conclusions of this article are available from the authors upon reasonable request.

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