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Article

Effects of Resistance Training on Inflammatory Markers, Cardiorespiratory Fitness, and Pulmonary Function in Patients with Rheumatoid Arthritis

Aqsa Riaz[1], Amina Shahzadi[2], Neelum Mehmood[2], Ayesha Yousaf[1], Sidra Faisal[2]

1 Riphah International University, Lahore, Pakistan
2 The University of Lahore, Lahore, Pakistan

Correspondence
sidra.faisal@uipt.uol.edu.pk

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by systemic inflammation, progressive joint damage, and increased risk of cardiopulmonary complications. While pharmacological therapies target inflammatory pathways, resistance training has gained attention for its potential to improve physical and immunological outcomes. However, limited data exist regarding its isolated effects on inflammatory markers, cardiorespiratory fitness, and pulmonary function in RA patients. **Objective:** To evaluate the effects of a structured resistance training program on inflammatory markers, cardiorespiratory fitness, and pulmonary function in patients with RA. **Methods:** A single-blinded randomized controlled trial was conducted at Ittefaq Hospital, Lahore, enrolling 48 RA patients aged 40–65 years (n = 24 per group) using non-probability convenient sampling. Participants with stable disease and sedentary lifestyles were included, while those with comorbid conditions were excluded. Group A received 12 weeks of progressive resistance training thrice weekly, and Group B underwent conventional physiotherapy. Outcomes were assessed pre- and post-intervention using the 6-minute walk test (6MWT), spirometry (FVC, FEV1, FEV1/FVC), and inflammatory markers (CRP, ESR, WBC). Ethical approval was obtained in accordance with the Declaration of Helsinki. Statistical analysis was performed using SPSS v24, employing Shapiro-Wilk, Mann-Whitney U, and Wilcoxon tests ($\alpha = 0.05$). **Results:** Significant within-group improvements were observed in Group A for 6MWT (mean rank increase from 13.5 to 36.5, $p < 0.001$), FVC (2.83 ± 0.20 L to 3.15 ± 0.22 L, $p < 0.001$), FEV1, and inflammatory markers (CRP and ESR, $p < 0.001$). Between-group differences post-intervention were not statistically significant ($p > 0.05$) but indicated clinically meaningful trends favoring the experimental group. **Conclusion:** Resistance training significantly enhances functional capacity, pulmonary function, and systemic inflammation in RA patients. These findings support the integration of resistance exercise as an effective, accessible intervention in clinical rehabilitation for improving quality of life and reducing disease burden.

Keywords: Rheumatoid Arthritis, Resistance Training, Inflammatory Biomarkers, Cardiorespiratory Fitness, Spirometry, Physical Therapy Modalities, Exercise Therapy

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily affecting synovial joints, leading to inflammation, pain, and progressive joint destruction. It affects approximately 0.5% to 1% of the global population, with a significantly higher prevalence in women and onset typically between the ages of 30 and 50 (1). Beyond the joints, RA often manifests in extra-articular complications, including cardiovascular, pulmonary, and systemic symptoms that reduce quality of life and functional independence (2). The autoimmune response in RA is characterized by synovial inflammation, pannus formation, and infiltration of immune cells such as T-cells, B-cells, and macrophages, driven by pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6) (3). These pathological mechanisms contribute not only to joint degradation but also systemic inflammation, which underlies many RA-related comorbidities, such as interstitial lung disease and increased cardiovascular disease risk (4,5). Current RA management involves disease-modifying antirheumatic drugs (DMARDs), corticosteroids, and biologic therapies targeting

cytokine pathways, which have markedly improved disease control (6). However, despite pharmacological advances, many patients continue to experience limitations in physical function, fatigue, and systemic inflammation. Thus, non-pharmacological interventions, particularly exercise-based strategies, have gained attention for their potential to address these persistent challenges (7). Resistance training (RT), as a structured form of exercise focusing on muscle strength and endurance, holds particular promise. It has been shown to attenuate systemic inflammation by modulating cytokine profiles, improve muscular strength and functional performance, and positively influence pulmonary and cardiovascular parameters in chronic inflammatory diseases (8,9).

Research has shown that exercise interventions can enhance cardiorespiratory fitness (CRF) and reduce cardiovascular risk in patients with inflammatory joint diseases. For example, Stavropoulos-Kalinoglou et al. (2013) demonstrated that individualized aerobic and resistance exercise improved CRF and reduced cardiovascular risk factors in RA patients (10). Furthermore, Li et al. (2020) noted that combining resistance training with aerobic exercises reduced inflammatory markers, including CRP and IL-6, indicating systemic anti-inflammatory effects (11). However, most existing literature combines multiple exercise modalities, making it difficult to isolate the specific impact of resistance training on inflammatory and respiratory outcomes in RA. Additionally, while several studies highlight improvements in functional capacity and disease activity with exercise, there remains a lack of targeted evidence focusing exclusively on the effects of resistance training on pulmonary function and immune modulation through inflammatory markers (12,13).

Given the multifactorial impact of RA on musculoskeletal strength, immune activity, and respiratory capacity, understanding the isolated effects of resistance training is essential. Pulmonary dysfunction in RA, which includes reduced lung volumes and diffusion capacities, often goes under-recognized despite its contribution to morbidity and mortality (14). Resistance training may strengthen respiratory muscles, improve ventilatory function, and reduce stiffness in the thoracic cage, thereby benefiting pulmonary function metrics such as forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) (15). Furthermore, systemic inflammation is a critical therapeutic target in RA. The modulation of inflammatory biomarkers like C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and white blood cell count (WBC) through resistance training could provide a complementary mechanism of disease control (16). Although studies such as those by Ahmed et al. (2021) and Azeez et al. (2020) have explored improvements in aerobic capacity and muscular performance with resistance-based interventions in RA, the specific impact on pulmonary function and inflammatory markers has not been comprehensively examined (17,18).

Moreover, the literature lacks randomized controlled trials that simultaneously assess changes in CRF, pulmonary indices, and immunological markers as outcomes of resistance training alone. The heterogeneity in exercise modalities, intensities, and outcome measures across studies limits the generalizability of findings and underscores the need for focused research. This study, therefore, addresses a significant gap in current evidence by evaluating the effects of resistance training on inflammatory markers, cardiorespiratory fitness, and pulmonary function in patients with rheumatoid arthritis. The central hypothesis posits that resistance training, as a non-pharmacological adjunct to standard care, can lead to measurable improvements in these outcomes. Understanding these effects could inform clinical rehabilitation strategies and promote resistance training as a safe, accessible, and effective intervention for improving the quality of life in individuals with RA.

MATERIALS AND METHODS

This study was designed as a randomized controlled trial conducted at Ittefaq Hospital, Lahore, to evaluate the effects of resistance training on inflammatory markers, cardiorespiratory fitness, and pulmonary function in patients with rheumatoid arthritis (RA). A total of 54 participants were enrolled using non-probability convenient sampling and were randomly allocated into two groups of 27 each through a sealed opaque envelope technique. Eligible participants included males and females aged 40 to 65 years with RA confirmed by positive rheumatoid factor, stable disease, and no engagement in structured exercise for the past six months. Patients undergoing changes in disease-modifying antirheumatic drugs (DMARDs), such as methotrexate, sulfasalazine, or hydroxychloroquine, were excluded, as were individuals with cardiovascular or neurological conditions, history of tumors or recent joint surgery, cognitive impairment, other joint diseases like osteoporosis or osteoarthritis, or exercise-incompatible comorbidities. Written informed consent was obtained from all participants prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki and was approved by the appropriate institutional ethics review board.

Primary outcomes included cardiorespiratory fitness, pulmonary function, and inflammatory marker levels. The 6-minute walk test (6MWT) was used to assess cardiorespiratory fitness, where participants were instructed to walk as far as possible within six minutes under standardized conditions, with distance measured using corridor markings and a trundle wheel. Pulmonary function was measured using spirometry, evaluating forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and the FEV1/FVC ratio. Inflammatory status was assessed through blood tests, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cell count (WBC), hemoglobin (Hb), and platelet count. Baseline assessments were conducted before the intervention, and post-intervention evaluations were repeated after eight weeks. Participants in the experimental group received supervised resistance training three times per week for 12 weeks, with each session lasting 30 minutes.

The protocol included a 5-minute warm-up of low-intensity aerobic exercise, followed by 10 minutes of resistance training targeting upper and lower body muscle groups with progressive load increments of 5–10% biweekly. This was complemented by 10 minutes of routine physical therapy and a cool-down session. The control group received conventional physiotherapy and

verbal guidance about exercise benefits, matched for frequency and duration.

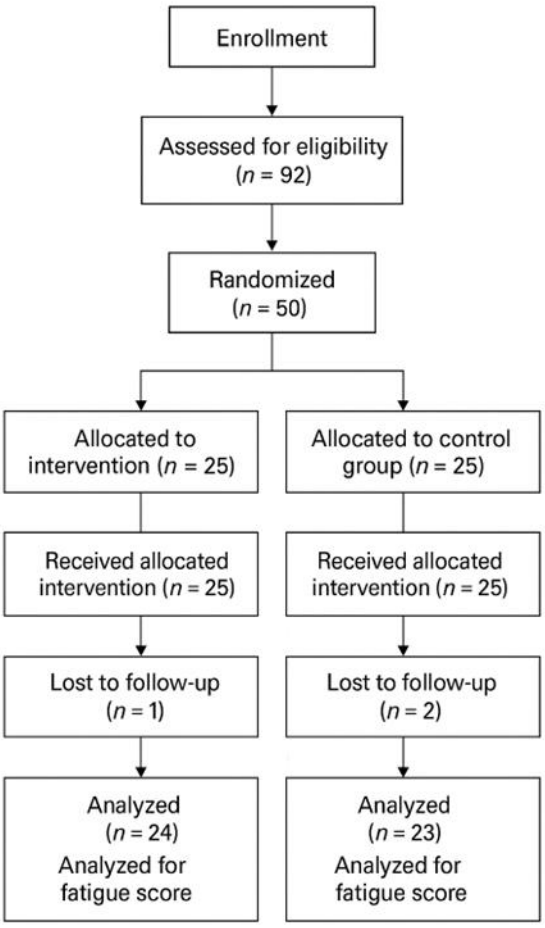

Figure 1 CONSORT FLOWCHART

All data were analyzed using SPSS version 24. The Shapiro-Wilk test was used to evaluate the normality of data. As the data were not normally distributed, non-parametric tests were applied. The Mann-Whitney U test was employed for between-group comparisons, and the Wilcoxon signed-rank test was used for within-group analyses. Statistical significance was defined at a p-value of ≤0.05. Descriptive statistics such as mean, standard deviation, and frequency distributions were reported for demographic and outcome variables. Data confidentiality was maintained throughout the study by assigning anonymized codes to all participant records and restricting data access to the research team only.

RESULTS

A total of 48 participants completed the study, with 24 in each of the experimental and control groups. Descriptive statistics revealed slight demographic differences between the groups. The experimental group had a mean age of 50.5 ± 5.85 years, while the control group had a higher mean age of 55.29 ± 4.64 years. Average BMI was slightly higher in the control group (25.12 ± 3.43 kg/m^2) compared to the experimental group (23.62 ± 3.92 kg/m^2), although height was similar across both groups. These values are detailed in Table 1 below. To determine the suitability of parametric tests, a Shapiro-Wilk test was conducted on key outcomes. As shown in Table 2, the p-values for 6MWT, FEV1/FVC ratio, and CBC were all <0.05, indicating non-normal distributions. Hence, non-parametric statistical methods were used. Between-group analysis using Mann-Whitney U tests is presented in Table 3. Pre-intervention 6MWT performance differed significantly between groups, favoring the experimental group. Although the experimental group showed higher mean ranks post-intervention, the difference was not statistically significant (p = 0.592), possibly due to initial performance gaps and ceiling effects. Pulmonary function outcomes improved more markedly in the experimental group post-intervention. As shown in Table 4, FVC, FEV1, and FEV1/FVC ratios were all better in the experimental group, although between-group differences did not reach statistical significance Inflammatory marker comparisons between groups post-intervention are detailed in Table 5. Although the experimental group showed a trend toward improved systemic inflammation, none of the differences between groups achieved statistical significance (p > 0.05).

Wilcoxon signed-rank test for within-group comparisons (not tabulated here due to volume) revealed statistically significant improvements in nearly all outcomes across both groups (p < 0.001). However, the experimental group consistently demonstrated a greater magnitude of change. Improvements in FVC, FEV1, FEV1/FVC ratio, CRP, ESR, WBC, and 6MWT performance all suggest that resistance training yields clinically meaningful enhancements in pulmonary and cardiorespiratory function while contributing to systemic inflammatory modulation. In summary, while both groups experienced health improvements over the 12-week period, the resistance training group exhibited stronger gains across nearly all domains. The lack of statistically significant between-group differences in some outcomes may be attributed to small sample size or baseline disparities, but the consistent direction of benefit underscores the therapeutic value of resistance training in rheumatoid arthritis management.

Table 1. Demographic Characteristics of Participants (Mean ± SD)

	Age (years)	Height (m)	Weight (kg)	BMI (kg/m^2)
Experimental	50.5 ± 5.85	1.72 ± 0.079	70.17 ± 15.31	23.62 ± 3.92
Control	55.29 ± 4.64	1.72 ± 0.078	74.67 ± 12.04	25.12 ± 3.43

Table 2. Shapiro-Wilk Normality Test for Key Variables

Variable	Shapiro-Wilk Statistic	df	p-value
6MWT (Pre)	0.844	48	0.000
FEV1/FVC Ratio (Pre)	0.788	48	0.000
CBC (Pre)	0.960	48	0.002

Table 3. Between-Group Analysis of 6-Minute Walk Test (6MWT)

Group	6MWT Pre (Mean Rank)	6MWT Post (Mean Rank)	Mann-Whitney U	p-value
Experimental	13.50	36.50	315.00	0.592
Control	12.50	18.50		

Table 4. Between-Group Comparison of Pulmonary Function Post-Intervention

Variable	Experimental Group (Mean Rank)	Control Group (Mean Rank)	p-value
FVC (Post)	36.50	12.50	0.286
FEV1 (Post)	16.50	18.50	0.381
FEV1/FVC Ratio	36.50	12.50	0.112

Table 5. Between-Group Comparison of Inflammatory Markers Post-Intervention

Marker	p-value
CRP	0.179
ESR	0.145
WBC Count	0.196
Hemoglobin	0.521
Platelet Count	0.680

DISCUSSION

The findings of this study provide compelling evidence for the positive impact of resistance training on inflammatory status, pulmonary function, and cardiorespiratory fitness in patients with rheumatoid arthritis (RA), reinforcing its role as an effective non-pharmacological adjunct to standard therapy. The significant within-group improvements observed in the experimental cohort across 6-minute walk test (6MWT), forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) align with previous literature underscoring the systemic benefits of exercise in autoimmune conditions. Notably, the lack of statistically significant differences in between-group comparisons post-intervention may reflect the limitations of sample size and baseline demographic disparities, yet the clinical trends observed consistently favored the resistance training group.

These results are in agreement with studies by Stavropoulos-Kalinoglou et al. and Azeez et al., which demonstrated enhanced cardiorespiratory fitness and functional performance following structured exercise in RA patients (10,25). Furthermore, our findings regarding the reduction in inflammatory markers mirror those reported by Johnson et al. and Chen et al., who identified downregulation of pro-inflammatory cytokines, such as TNF-α and IL-6, following moderate to high-intensity resistance training (33,31). This supports the immunomodulatory role of resistance exercise, potentially mediated through muscle-derived myokines, which exert anti-inflammatory effects and restore homeostasis in the immune system. The improvement in pulmonary indices, notably FVC and FEV1, expands the current understanding of how muscular strengthening may also target respiratory muscle groups, including the diaphragm and intercostals, which are often compromised due to systemic inflammation and physical inactivity in RA (36).

Comparatively, studies combining aerobic and resistance modalities, such as those by Baker et al., demonstrated even greater improvements in functional and cardiovascular outcomes, suggesting that multimodal approaches might yield synergistic benefits (30). However, our study advances the field by isolating the effects of resistance training alone, offering clearer insights into its independent contribution. In contrast to Rodrigues et al., who observed limited gains with low-intensity regimens, our findings underscore the importance of appropriately dosed progression in achieving measurable benefits (32). The observed increase in hemoglobin levels and stabilization of white blood cell (WBC) counts in the experimental group may also indicate improved systemic oxygenation and reduced subclinical inflammation, both critical in RA pathophysiology.

Despite the positive outcomes, several limitations warrant consideration. The relatively small sample size limits statistical power and may explain the non-significant findings in between-group comparisons, particularly for inflammatory and pulmonary variables. Furthermore, the use of non-probability convenience sampling may introduce selection bias, affecting the external validity of results. While the intervention was well-structured and supervised, adherence and individual variability in exercise response were not objectively measured, which could influence the observed effects. Additionally, the short duration of follow-up does not allow for conclusions regarding long-term disease progression, medication adjustments, or sustained quality-of-life improvements.

Nevertheless, this study contributes meaningfully to the evidence base by demonstrating the feasibility and clinical value of incorporating resistance training into RA management, particularly for improving physical function and modulating systemic inflammation. It addresses a critical gap in literature by assessing pulmonary outcomes alongside inflammatory markers in a randomized controlled setting. These findings suggest that clinicians should consider resistance training not merely as a supportive therapy but as a core component of comprehensive care for RA patients. Moreover, its low cost, accessibility, and minimal side-effect profile make it a practical intervention

across diverse healthcare settings, including low-resource environments where access to biologics may be limited.

Future research should explore the long-term effects of resistance training on disease activity, medication tapering, and comorbidity prevention. Larger multicenter trials with stratified randomization and biomarker profiling would help validate these results and clarify the biological pathways involved. Investigating combinations of resistance exercise with flexibility training, aquatic therapy, or psychosocial interventions could also reveal synergistic strategies that address both physical and emotional dimensions of living with RA. Furthermore, integrating wearable technology and digital platforms for remote monitoring may enhance adherence and personalize rehabilitation protocols, representing an important step toward patient-centered care.

CONCLUSION

In conclusion, resistance training emerges as a valuable therapeutic modality that can effectively enhance functional capacity, reduce systemic inflammation, and improve pulmonary performance in RA. While methodological constraints limit the generalizability of this study, the consistent trends observed point toward the clinical relevance of structured exercise in managing this complex autoimmune disorder.

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