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Anti-TNF Treatment In Refractory Sarcoidosis; Therapeutic Impacts Of Adalimumab And Infliximab

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Abstract

Introduction: Sarcoidosis is a chronic inflammatory disease characterized by granuloma formation in various organs, commonly affecting the lungs. While corticosteroids are the mainstay of treatment, some patients develop refractory sarcoidosis that is resistant to conventional therapies. Tumor necrosis factor-alpha (TNF-α) plays a crucial role in the disease's pathogenesis, and anti-TNF agents like adalimumab and infliximab have emerged as promising treatments for refractory cases. This study investigates the therapeutic impacts of these biologics on lung function and inflammation in refractory sarcoidosis.

Method: This prospective case-control study included 60 refractory sarcoidosis patients from Al-Azhar hospitals, Egypt, divided into three groups of 20 based on treatment: adalimumab, infliximab, or conventional therapy. Data collected included demographics, medication use, pulmonary function tests (forced vital capacity [FVC], forced expiratory volume in 1 second [FEV1], and diffusing capacity of the lung for carbon monoxide [DLCO]), and serum inflammatory markers (angiotensin-converting enzyme [ACE] levels, erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP]) using standardized clinical and laboratory methods. Primary outcomes include the comparison of these measurements between the three treatment groups.

Results: The study results indicate that biologic therapies, especially adalimumab and infliximab, significantly improve lung function compared to conventional treatment in refractory sarcoidosis; both drugs enhanced pulmonary function parameters, with adalimumab showing a slight but not statistically significant advantage. Additionally, these biologics effectively reduced serum ACE and inflammatory markers such as ESR and CRP; although adalimumab tended to outperform infliximab in these measures, the differences are generally not significant.

Conclusion: The study concludes that biologic therapies, adalimumab and infliximab, significantly improve lung function and reduce inflammation in refractory sarcoidosis. Although adalimumab showed a slight advantage over infliximab, the differences were not statistically significant.

Keywords: Sarcoidosis, Refractory sarcoidosis, Serum angiotensin-converting enzyme, Biologic therapy, Anti-TNF agents, Adalimumab, Infliximab, Pulmonary function, Inflammation.

Introduction

Sarcoidosis is a multisystem granulomatous inflammatory disease of unknown etiology characterized by the formation of non-caseating granulomas in various organs, with pulmonary involvement occurring in more than 90% of cases(1, 2). The disease exhibits remarkable phenotypic diversity, ranging from acute, self-limiting presentations

to chronic, progressive forms that may lead to significant organ dysfunction and mortality(2, 3). While approximately two-thirds of patients experience spontaneous remission within 24-36 months, a substantial minority develop chronic disease requiring long-term immunosuppressive therapy(1, 2).The epidemiological landscape of sarcoidosis demonstrates striking racial and geographic disparities. African Americans are disproportionately affected, with incidence rates 2-3 times higher than European Americans and significantly more severe disease manifestations, including increased mortality rates(4, 5). This disparity extends to clinical outcomes, with African American patients experiencing higher rates of multiorgan involvement, chronic disease progression, and refractory disease requiring advanced therapeutic interventions(5). Northern European populations, particularly those of Scandinavian descent, also demonstrate elevated susceptibility to sarcoidosis, though with generally more favorable outcomes compared to African American cohorts(3, 6).Refractory sarcoidosis represents a particularly challenging clinical entity, defined as a disease that remains active despite adequate treatment with corticosteroids at maintenance doses less than 10 mg daily (prednisolone equivalent) and conventional immunosuppressive agents, including methotrexate(7, 8). Studies indicate that approximately 10.8% of patients with newly diagnosed pulmonary sarcoidosis develop refractory disease, characterized by progressive organ dysfunction, inability to achieve disease remission, or unacceptable corticosteroid dependency(7). The pathophysiological mechanisms underlying treatment resistance in these patients remain incompletely understood, though aberrant immune activation and dysregulated inflammatory cascades appear central to disease persistence(8).

Corticosteroids have served as the cornerstone of sarcoidosis therapy for over five decades, representing the first-line treatment for patients requiring systemic immunosuppression(9, 10).However, the chronic nature of sarcoidosis frequently necessitates prolonged corticosteroid administration, leading to a substantial burden of treatment-related morbidity(11).Studies demonstrate that these adverse effects occur in the majority of patients receiving chronic corticosteroid therapy, with osteoporosis developing in 54% of treated individuals (12)and also the risk of infection(11).The cumulative toxicity of prolonged corticosteroid exposure creates a therapeutic dilemma, necessitating the development of steroid-sparing approaches for patients with refractory or chronic disease(13).Furthermore, a significant subset of patients demonstrates inadequate response to corticosteroid therapy or experiences disease relapse during steroid tapering(14). The recognition of these limitations has driven intensive research into alternative therapeutic approaches, particularly those targeting specific inflammatory pathways involved in granuloma formation and maintenance.

The pathogenesis of sarcoidosis involves complex interactions between genetic susceptibility, environmental triggers, and dysregulated immune responses, ultimately culminating in aberrant granuloma formation and persistence(15). Central to this process is the overproduction of tumor necrosis factor-alpha (TNF-α), a pleiotropic cytokine that serves as a master regulator of inflammatory responses and granulomatous inflammation(16-18). The molecular mechanisms by which TNF-α promotes granulomatous inflammation in sarcoidosis are multifaceted and involve both direct cellular effects and the induction of downstream inflammatory cascades(19). The central role of TNF-α in sarcoidosis pathogenesis has been further validated by the clinical efficacy of TNF-α blocking agents, which can effectively suppress granulomatous inflammation and improve organ function in refractory cases(17). These observations have established TNF-α as an crucial cytokine (20) and attractive therapeutic target for patients with treatment-resistant sarcoidosis, leading to the development and clinical application of specific TNF-α inhibitors including infliximab and adalimumab.

Objective

The objective of this study is to comprehensively evaluate and compare the therapeutic effects of two anti-TNF biologic agents, adalimumab and infliximab, in patients with refractory sarcoidosis. Specifically, the study aims to assess pulmonary function and systemic inflammatory markers, thereby determining the relative efficacy and safety of these treatments compared to conventional therapies. By analyzing clinical, functional, and biochemical outcomes, this research seeks to provide evidence-based guidance on the optimal use of anti-TNF agents for managing refractory sarcoidosis and improving patient quality of life.

Method and materials

Study design and participants

This prospective case-control study was conducted on 60 patients diagnosed with refractory sarcoidosis who were referred to Al-Azhar hospital, Egypt, between January 2024 and February 2025. Patients were classified into three groups based on their treatment regimen: those receiving adalimumab (n = 20), those receiving infliximab (n = 20), and those undergoing conventional therapy (n = 20). Group assignment was determined according to the prescribed treatment by the managing physician, with adherence to inclusion and exclusion criteria, ensuring comparable baseline characteristics across groups for valid outcome comparisons.

Ethical approval

The study was approved from the ethical committee of Al-Azhar University (Assuit) under the code number RESEARCH/AZ.AST./CHT019/10/226/1/2024. The study also conducted after obtaining informed consent from the patients according the ethical guidelines of Helsinki declaration.

Inclusion and exclusion criteria

Inclusion criteria for this study included adult patients diagnosed with refractory sarcoidosis confirmed by clinical, radiological, and histopathological findings. Patients must have demonstrated inadequate response or intolerance to conventional therapies such as corticosteroids or immunosuppressants and must have been under treatment with infliximab or adalimumab for at least 3 months. Exclusion criteria comprised patients with active infections, malignancies, or other significant comorbidities that could interfere with treatment or outcome assessment. Pregnant or breastfeeding women and patients with known hypersensitivity to anti-TNF agents were also excluded.

Data collection

Data collection for this study involved systematic recording of demographic characteristics, medication use, lung function test results, and inflammatory marker levels for each patient. Initially, informed written consent was taken from all participants. Data on demographic variables such as gender and age, along with details of consumed medications, were collected from patients' medical documents and verified through patient interviews. Data on lung function were obtained by performing standardized pulmonary function tests, including measuring forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and diffusing capacity of the lung for carbon monoxide (DLCO), expressed as percentages of predicted values based on established guidelines. Data on serum biomarkers included measurement of angiotensin-converting enzyme (ACE) levels, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) in blood samples collected using standard phlebotomy techniques. These laboratory tests were carried out using automated analyzers calibrated according to manufacturer instructions.

Pulmonary function tests (PFTs) measurement

For FVC and FEV1, the spirometry was performed where patients took a deep breath and then exhaled as forcefully and completely as possible into a spirometer. The spirometer recorded the volume of air exhaled and the speed of exhalation. FVC measures the total volume of air exhaled after maximal inhalation, while FEV1 measures the volume exhaled in the first second of this effort. These values are expressed as percentages of predicted normal values adjusted for patients' characteristics. DLCO is measured via the single-breath carbon monoxide diffusion test. In this procedure, the patient inhales a gas mixture containing a very low concentration of carbon monoxide, holds their breath for about 10 seconds, and then exhales. The amount of carbon monoxide absorbed by the lungs during this time reflects the diffusing capacity of the alveolar-capillary membrane, important for assessing gas exchange efficiency affected in sarcoidosis. All tests were performed according to protocols recommended by the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines, ensuring accuracy and reproducibility. Patients were coached and monitored by trained respiratory technicians throughout the procedures to obtain valid results(21).

Laboratory test measurement

For assessing inflammatory markers and serum ACE levels, a 10 milliliter venous blood sample was drawn from each patient using standard phlebotomy techniques. The samples were then processed in a clinical laboratory where serum was separated by centrifugation. Serum ACE levels were measured in units per liter (U/L) by using enzymatic colorimetric assays or spectrophotometric methods on blood samples collected from patients. The ESR was assessed

by the Westergren method, where anticoagulated blood was placed in a vertical tube, and the rate at which red blood cells sediment was measured in millimeters per hour (mm/h). The CRP levels were quantified using immunoturbidimetric or high-sensitivity immunoassay techniques on serum samples, reported in milligrams per liter (mg/L). All laboratory tests are performed in certified clinical laboratories following standard protocols.

Outcome measurement

Outcome measurements in this study included assessments and comparison of pulmonary function tests such as FVC, FEV1, and DLCO, and also serum inflammatory markers, including ACE, ESR, and CRP, between three treatment groups of adalimumab, infliximab, and conventional treatment. Clinical response was evaluated based on improvements in lung function parameters and reductions in inflammatory markers to determine treatment effectiveness.

Data analysis

Data were analyzed using SPSS Statistics(IBM Corporation, Armonk, NY, USA) software (version 27). Continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using one-way analysis of variance (ANOVA), followed by post hoc least significant difference (LSD) tests for pairwise comparisons. Categorical variables were presented as frequencies and percentages and compared using Pearson's Chi-square test or Fisher's exact test where appropriate. For all tests, a p-value less than 0.05 was considered statistically significant. Data normality was assessed by the Shapiro-Wilk test, and homogeneity of variance was checked by Levene's test. Although both parametric and non-parametric methods were considered, parametric tests were chosen for hypothesis testing due to their accuracy and robustness, especially since both approaches yielded similar P-values across all variables.The analysis aimed to identify significant differences in demographic characteristics, medication use, pulmonary function parameters, and inflammatory marker levels among the conventional treatment, infliximab, and adalimumab groups.

Results

The comparison of demographic characteristics and medications among the treatment groups revealed no statistically significant differences in gender distribution; however, the conventional group had a higher proportion of females, while the infliximab and adalimumab groups showed a relatively higher proportion of males. Regarding medication usage, azathioprine, methotrexate, and mycophenolate mofetil were consumed in similar proportions across groups, with no statistically significant differences. Some patients in each group did not receive any drug therapy. Prednisolone use alone or in combination with azathioprine, methotrexate, or mycophenolate varied among the groups, with prednisolone combined with mycophenolate being more common in the adalimumab group. The average ages of patients in the three groups were comparable, with no significant difference observed. Overall, the demographic profiles were generally similar across treatment groups (**Table 1**).

Table 1. Comparison of demographic characteristics and patients' consumed medications between treatment groups

Variable		Treatment group						P Value
		Conventional		Infliximab		Adalimumab		
		N	%	N	%	N	%	
Gender	Female n = 29	12	41.4	8	27.6	9	31	0.521*
	Male n = 31	8	25.8	12	38.7	11	35.5	
Consumed medications	Azathioprine n = 11	4	36.4	4	36.4	3	27.2	0.960**
	Methotrexate n = 9	3	33.3	3	33.3	3	33.3	
	Mycophenolate mofetil n = 8	3	37.5	3	37.5	2	25	

	Prednisolone + Mycophenolate n = 4	1	25	0	0	3	75	
	Prednisolone n = 9	4	44.4	3	33.3	2	22.2	
	Prednisolone + Azathioprine n = 5	2	40	2	40	1	20	
	Prednisolone + Methotrexate n = 7	2	28.6	3	42.8	2	28.6	
	No drug n = 8	1	14.3	2	28.6	4	27.1	
Age (year; Mean ± SD)		50.65± 8.01		48.40 ± 7.30		47.30 ± 7.27		0.364***
N; Number, SD; Standard deviation, *Pearson Chi-square, **Fisher's Exact test, ***One-way ANOVA								

The comparative analysis of lung function parameters revealed significant therapeutic advantages for biologic treatments over conventional therapy across all measured pulmonary metrics. For FVC measurements, both infliximab and adalimumab demonstrated statistically significant improvements compared to conventional treatment, with adalimumab showing marginally superior outcomes to infliximab, though this difference did not reach statistical significance. Similarly, FEV1 assessments indicated substantial enhancement in both biologic treatment groups relative to conventional therapy, with adalimumab again displaying slightly better performance than infliximab, albeit without statistical significance between the two biologics. The DLCO measurements followed a consistent pattern, where both biologic interventions significantly outperformed conventional treatment, and adalimumab maintained a modest advantage over infliximab that failed to achieve statistical significance (**Table 2**).

Table 2. Comparative analysis of lung function test measurements across different treatment groups

FVC(%)	**Treatmentgroup**		**Mean**	**SD**	**P Value***
	Conventional		53.90	7.25	<0.001
	Infliximab		63.08	31.19	
	Adalimumab		65.49	4.55	
	Treatmentgroup		**Mean difference**		**P Value****
	Conventional	Infliximab	9.17		<0.001
		Adalimumab	11.55		<0.001
	Infliximab	Adalimumab	2.41		0.154
FEV1 (%)	**Treatmentgroup**		**Mean**	**SD**	**P Value***
	Conventional		47.02	7.88	<0.001
	Infliximab		60.74	3.88	
	Adalimumab		62.92	7.60	
	Treatmentgroup		**Mean difference**		**P Value****
	Conventional	Infliximab	13.71		<0.001
		Adalimumab	15.89		<0.001
	Infliximab	Adalimumab	2.18		308
DLCO (%)	**Treatmentgroup**		**Mean**	**SD**	**P Value***
	Conventional		47.46	10.02	<0.001
	Infliximab		61.67	3.38	
	Adalimumab		64.40	9.10	
	Treatmentgroup		**Mean difference**		**P Value****

	Conventional	Infliximab	14.19	<0.001
		Adalimumab	16.93	<0.001
	Infliximab	Adalimumab	2.73	0.287
FVC; Forced Vital Capacity, FEV1; Forced Expiratory Volume in 1 second, DLCO; Diffusing Capacity of the Lung for Carbon Monoxide, SD; Standard deviation, *One-way ANOVA, **Post hoc LSD test				

The comparative assessment of serum ACE and inflammatory markers among different treatment groups demonstrated notable differences. Both infliximab and adalimumab treatments were associated with significantly lower ACE levels compared to conventional therapy, with adalimumab showing a greater reduction. Similarly, ESR values were significantly reduced in the biologic treatment groups compared to conventional treatment, with minimal difference between the two biologics. CRP levels followed the same trend, with both infliximab and adalimumab significantly lowering CRP compared to conventional therapy, and adalimumab presenting a slightly greater decrease than infliximab, though the difference was not statistically significant. These findings suggest that the biologic treatments, particularly adalimumab and infliximab, effectively reduce markers of inflammation and ACE levels compared to conventional treatment, highlighting their potential anti-inflammatory benefits in the management of refractory sarcoidosis. The differences between the two biologics, while generally favoring adalimumab, were not statistically significant in all three comparisons (**Table 3**).

Table 3. Comparative assessment of ACE and inflammatory markers among different treatment groups

ACE(U/L)	**Treatmentgroup**		**Mean**	**SD**	**P Value***
	Conventional		56.93	10.55	<0.001
	Infliximab		42.34	9.21	
	Adalimumab		36.16	16.57	
	Treatmentgroup		**Mean difference**		**P Value****
	Conventional	Infliximab	14.58		<0.001
		Adalimumab	20.27		<0.001
	Infliximab	Adalimumab	5.68		0.157
ESR(mm/h)	**Treatmentgroup**		**Mean**	**SD**	**P Value***
	Conventional		35.97	9.46	<0.001
	Infliximab		23.76	8.45	
	Adalimumab		22.74	9.52	
	Treatmentgroup		**Mean difference**		**P Value****
	Conventional	Infliximab	12.19		<0.001
		Adalimumab	13.20		<0.001
	Infliximab	Adalimumab	1.02		0.730
CRP (mg/L)	**Treatmentgroup**		**Mean**	**SD**	**P Value***
	Conventional		29.09	8.57	<0.001
	Infliximab		17.07	4.54	
	Adalimumab		13.40	8.59	
	Treatmentgroup		**Mean difference**		**P Value****
	Conventional	Infliximab	12.02		<0.001
		Adalimumab	15.69		<0.001
	Infliximab	Adalimumab	3.67		0.126
ACE; Serum angiotensin-converting enzyme, ESR; Erythrocyte sedimentation rate, CRP; C-reactive protein, Ca; calcium, SD; Standard deviation, *One-way ANOVA, **Post hoc LSD test					

Discussion

This study demonstrates that biologic therapies, specifically adalimumab and infliximab, significantly reduce inflammatory markers and improve pulmonary function in patients with refractory sarcoidosis compared to conventional treatments. Additionally, the study found no significant differences in efficacy between adalimumab and infliximab, indicating that both biologics have comparable therapeutic benefits in this patient population. These findings are consistent with several previous studies. The randomized controlled trial by Loza et al established infliximab's efficacy in chronic pulmonary sarcoidosis, showing a significant improvement in FVC at 24 weeks compared to placebo. This foundational study demonstrated that patients with the highest baseline TNF-α levels had the greatest improvement in FVC and reduction in inflammatory markers(22). In a randomized, double-blind, placebo-controlled trial, Baughman et al (2016) conducted a subset analysis demonstrating that infliximab provides a significant therapeutic benefit in patients with chronic cutaneous sarcoidosis, supporting its use as an effective treatment option for this condition(23). A randomized, double-blind, placebo-controlled trial by Judson et al (2008) demonstrated that infliximab significantly improves extrapulmonary organ severity in patients with chronic corticosteroid-dependent sarcoidosis and suggests that infliximab may serve as an effective adjunct therapy for extrapulmonary sarcoidosis in corticosteroid-dependent patients(24). A phase 2, multicenter, randomized, double-blind, placebo-controlled study by Baughman (2006) demonstrated that infliximab treatment leads to a statistically significant improvement in lung function, as measured by percent predicted FVC, in patients with chronic pulmonary sarcoidosis(25). Judson et al (2014) found that infliximab may provide additional benefit in improving pulmonary function in sarcoidosis patients on low to moderate corticosteroid doses, but appears to add minimal advantage when used alongside higher prednisone doses exceeding 15-20 mg daily. This suggests limited utility of infliximab as an adjunct therapy in patients requiring higher corticosteroid regimens(26).A retrospective analysis study by Russell et al demonstrated that infliximab provides sustained clinical benefit in the treatment of extra-pulmonary sarcoidosis, with a significant proportion of patients experiencing durable resolution or improvement in affected organs over prolonged therapy (up to 85 months). These findings support the long-term efficacy and acceptable safety profile of infliximab as a therapeutic option for refractory multi-organ sarcoidosis(27).Sweiss et al (2010) conducted a randomized, double-blind, placebo-controlled study to evaluate the role of baseline CRP as a predictor of disease severity and response to infliximab therapy in 138 patients with chronic pulmonary sarcoidosis. Patients with elevated baseline CRP (≥0.8 mg/dL) experienced significant improvements after infliximab treatment compared to placebo in lung function (percent-predicted FVC), exercise capacity (6-minute walk distance), dyspnea, and physician organ assessments. Infliximab also reduced CRP levels significantly within two weeks of treatment. They concluded that elevated baseline CRP identifies a subgroup of chronic pulmonary sarcoidosis patients with more severe disease who are more likely to benefit from infliximab therapy(28).

Similarly, the adalimumab trial by Sweiss et al (2014) reported successful treatment outcomes in 82% of patients at 24 weeks and 80% at 52 weeks, with improvements in FVC, six-minute walk distance, and Borg dyspnea scores(29).Pariser et al found that adalimumab is a safe and effective treatment option for cutaneous sarcoidosis, demonstrating significant lesion improvement and quality-of-life benefits over 24 weeks of therapy(30). Erckens et al found that adalimumab demonstrated efficacy in patients with refractory chronic non-infectious sarcoid uveitis, leading to significant improvement or resolution of intraocular inflammatory manifestations in the majority of cases, and supports adalimumab as a promising therapeutic option in refractory multisystemic sarcoidosis(31).A meta-analyses study in cardiac sarcoidosis has also shown significant improvements in ejection fraction and reduction in corticosteroid requirements with TNF-α inhibitors, supporting the broader application of these agents across different organ manifestations(32).

The collective evidence from multiple studies demonstrates that biologic therapies targeting TNF-α represent a paradigm shift in managing refractory sarcoidosis. The mechanistic basis for this efficacy stems from TNF-α's central role in granuloma formation and maintenance, which has been consistently demonstrated across preclinical and clinical studies(22, 33). Both adalimumab and infliximab effectively neutralize TNF-α, leading to reduced systemic inflammation and improvement in organ-specific manifestations(25, 31). The therapeutic equivalence between these agents appears related to their shared mechanism of action, despite structural differences - infliximab being a chimeric monoclonal antibody and adalimumab being fully human(34).

Clinical outcomes consistently demonstrate improvements not only in objective measures such as FVC, DLCO, and reducing inflammatory markers but also in patient-reported outcomes and quality of life measures(30). The steroid-sparing effects observed with both agents represent a significant clinical advantage, potentially reducing long-term corticosteroid-related morbidity(13). However, patient selection appears crucial for optimizing outcomes, with studies consistently showing that patients with higher baseline TNF-α levels, more severe disease, and active inflammation respond better to anti-TNF therapy; the inflammatory profile analysis by Loza et al revealed that sarcoidosis patients express a 35-analyte inflammatory signature, with TNF-α stratification identifying responders more likely to benefit from infliximab therapy(22).

Overall, the evidence strongly supports the use of TNF-α inhibitors as effective therapeutic options for refractory sarcoidosis, with both adalimumab and infliximab demonstrating comparable efficacy in improving pulmonary function and other clinical outcomes, such as reducing inflammatory markers. The current study's findings align with established literature showing no significant differences between these agents, confirming their therapeutic equivalence in this patient population. Future research should focus on developing biomarker-driven approaches to identify optimal candidates for anti-TNF therapy, investigating combination strategies with antifibrotic agents for progressive pulmonary fibrosis, and conducting head-to-head comparative studies to definitively establish any potential differences in efficacy or safety profiles between adalimumab and infliximab. The integration of these biologic therapies into treatment algorithms represents a major advancement in sarcoidosis management, offering hope for patients with previously refractory disease while maintaining acceptable safety profiles when used with appropriate monitoring protocols.Sarcoidosis is recognized to be frequent among both men and women. Nonetheless, it is more prevalent among women (35) therefore there is a need for future studies that investigate the effect of different treatments on both genders.

Study limitations

Firstly, the sample size of 60 patients may limit the generalizability of the findings. Secondly, as a single-center study conducted at Al-Azhar Hospitals, regional factors may influence patient characteristics and treatment outcomes, limiting applicability to broader populations. Thirdly, the observational case-control design restricts the ability to establish causality between treatments and outcomes. Additionally, potential confounding factors and variations in medication adherence or dosage adjustments were difficult to control completely.

Conclusion

The study results indicated that biologic therapies, especially adalimumab and infliximab, significantly improve lung function and reduce serum ACE and inflammatory markers compared to conventional treatment in refractory sarcoidosis. Although adalimumab showed a partial improvement in efficacy compared to infliximab, the differences are generally not significant. Overall, biologic treatments demonstrate clear benefits compared to conventional treatments in improving lung function and reducing inflammation, supporting their use in managing refractory sarcoidosis. Further comparative studies may help clarify the nuanced differences between these biologic therapies in this patient population.

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Conflicts of interest

The authors declare no conflict of interest.

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Ethical issues

The study was conducted under the tents of the Declaration of Helsinki. Informed written consent was obtained from all participants. This study resulted from a research project conducted at Al-Azhar hospitals with registration number (NO; RESEARCH/AZ.AST./CHT019/10/226/1/2024) approved by the ethics committee of the medicine faculty, Al-Azhar University (Assiut), Egypt. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

While preparing this work, the authors utilized AI **(**Perplexity.ai) to refine grammar points and language style. Subsequently, they thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

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