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Clinical And Radiological Features Of Extra-Pulmonary Sarcoidosis: Diagnosis And Management

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Abstract

Background: Sarcoidosis is a systemic illness of indeterminate etiology, pathologically defined by the aggregation of inflammatory cells that create non-caseating granulomas.

Aim: This study aims at investigating the clinical and radiological features of extra-pulmonary sarcoidosis.

Method: This study used a retrospective, observational cohort design at Al-Azhar hospitals in Egypt, focusing on adult patients aged 18 or older diagnosed with sarcoidosis through histological evidence. Patients will be recruited retrospectively from the hospital's records, meeting specific criteria. Data collected from eligible patients' medical records, including demographics, clinical presentation, radiological features, diagnostic procedures, management, and follow-up data. The study examined the relationship between clinical symptoms and radiological results, evaluate diagnostic paths, and assess therapy regimens. Ethical considerations will be considered, and approval will be obtained from the Institutional Review Board or Ethics Committee of the hospital.

Results:

Hematologic abnormalities were observed, with Group 2 exhibiting the lowest hemoglobin levels and the greatest white blood cell count. The success of treatment was greatest for corticosteroids (82%), followed by biologics (74%) and immunosuppressants (66%). Oxygen therapy and lifestyle adjustments exhibited modest efficacy, whereas observation alone had the least effectiveness (28%). The enhancement of kidney function was most significant in the immunosuppressant cohort, whereas parathyroid function exhibited the greatest improvement in the corticosteroid cohort. In addition an improvement in the rheumatological parameters was noticed among study groups.

Conclusion

Sarcoidosis is a multisystem granulomatous disorder affecting the lungs, skin, eyes, neurological system, liver, and heart. It is more common in women and causes extra-pulmonary symptoms. Corticosteroids are effective in lowering calcium levels and rectifying metabolic abnormalities, while lifestyle adjustments and oxygen therapy provide moderate benefits. CT and HRCT is the main tools to diagnose sarcoidosis.

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Keywords: Extrapulmonary sarcoidosis, Multisystem disease, Granulomatous disease, Organ involvement. Corticosteroids.

Introduction

Sarcoidosis is a multi-systemic disorder of unknown cause, pathologically characterized by the accumulation of inflammatory cells forming non-caseating granulomas (1). Involvement of the lungs is the most common manifestation of the disease, while extra-pulmonary manifestations can be very insidious, with a plethora of different imaging features, often non-specific, encountered (2). Because a diagnosis of sarcoidosis generally requires a certain degree of certainty with respect to one organ being affected, a typical clinical and imaging pathway is needed (3).

Sarcoidosis is a systemic multi-organ granulomatous disease marked by granulomas in various organs, primarily affecting the lungs (4). Sarcoidosis is characterized by non-caseating epithelioid granulomas across various organs, notably affecting the skin, eyes, and more rarely, the liver, spleen, kidneys, and bones (5). Imaging plays a crucial role in confirming these manifestations, particularly in examining the liver via MRI. Extra-pulmonary manifestations can occur in one-third of cases, often presenting as skin lesions like erythema nodosum and lupus pernio (6). These conditions can lead to diagnostic challengesdue to their insidious nature. Involvement of the lymphatic and cardiac systems is significant, with about 20-30% of cases implicated (7). Symptoms like palpitations may indicate cardiac sarcoidosis, which requires careful imaging for diagnosis, as endomyocardial biopsies might yield false negatives (8). Neurological symptoms occur in 3.2% of cases and may include signs due to direct granuloma infiltration (9). Musculoskeletal symptoms affect about one-third of patients, typically presenting as arthritis, particularly in knees or ankles (10). Hepatosplenic involvement is common in up to 35% of cases, often overlooked but can be revealed through imaging (11). Lastly, GI sarcoidosis is rare and presents with nonspecific symptoms such as diarrhea, complicating diagnosis as it might mimic other diseases, needing thorough evaluation for accurate diagnosis and treatment (12).

The clinical features of sarcoidosis are heterogeneous but pulmonary involvement is a cardinal manifestation (5). Pulmonary involvement is the most common manifestation requiring treatment. Imaging has a prominent role in assessment of sarcoidosis diagnosis and outcome (13). Many patients are asymptomatic and diagnosed as a result of incidental chest radiograph or computed tomography (CT) scans. The thoracic CT scan accuracy is abjected to be above 90% (14). Ninety percent of patients will have granuloma(s) located in the lungs or in the related lymph nodes, but skin, liver, spleen, heart, eyes, and others can also be affected (15). In approximately 30% of cases sarcoidosis can also be encountered in the extra-pulmonary realm. Such involvements can be very insidious, showing different imaging features, often non-specific, and it is not rare that unusual cases are entirely missed by radiologists (16). Diagnosis of Sarcoidosis occur by Computed tomography (CT) of the chestthat demonstrates high sensitivity (17). This study aims at investigating the clinical and radiological features of extra-pulmonary sarcoidosis.

Sarcoidosis is a disorder marked by hepatomegaly, splenomegaly, renal involvement, and gastrointestinal, lymphatic, and peritoneal manifestations. It is observable via ultrasound, CT, MRI, and other imaging modalities. Hepatic sarcoidosis is marked by hepatomegaly, splenomegaly, and abdominal lymphadenopathy. Splenic sarcoidosis is defined by splenomegaly, hypoechoic nodules, and nodular hypodense lesions. Renal sarcoidosis is defined by the presence of renal granulomatous pseudotumors and hypodense lesions shown on CT and MRI. Additional symptoms of sarcoidosis are wall thickening, minor mucosal ulcerations, lymphadenopathy, and involvement of the peritoneum. Neurosarcoidosis is defined by T2 hyperintense lesions in white and/or grey matter, contrast-enhancing parenchymal nodules, and leptomeningeal enhancement. Skeletal sarcoidosis predominantly affects the hands and feet, with bigger bones or the spine exhibiting radiolucent or sclerotic lesions. Additional symptoms of sarcoidosis encompass uveitis, conjunctivitis, retinal or choroidal involvement, cutaneous sarcoidosis, and cardiac sarcoidosis (18).

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Table 1: Radiographic patterns in sarcoidosis by imaging type and location

Type of Imaging Main Radiological Appearance		Location	Notes
	- Multiple peripheral nodules		
	- Peribronchial and perilobular		Irregular edges – blurred
HRCT Lung Window	infiltrates	Upper lobes	borders
	Small consolidative nodules		Indicates active sarcoid
HRCT Lung Window	surrounded by satellite nodules	Diffuse	pattern
	Homogeneous thickening of		
MRI Brain (T1 post-	leptomeninges with contrast	Cerebral and	
contrast)	enhancement	spinal meninges	Suggests neurosarcoidosis
			Sign of granulomatous
MRI Pituitary (T1	Diffuse thickening of pituitary stalk		inflammation – likely
post-contrast)	with strong enhancement	Pituitary gland	sarcoidosis
MRI Orbit (T2 / T1	Enhancing mass involving optic		May indicate ocular
post)	nerve sheath or lacrimal gland	Orbit	sarcoidosis
Cardiac MRI (Late	Patchy subepicardial or mid-wall		Compatible with cardiac
Gadolinium	enhancement	Left ventricle /	sarcoidosis – risk of
Enhancement)	Myocardial edema on T2 imaging	septum	arrhythmia
			Often asymptomatic – seen
	Hepatosplenomegaly without focal		in advanced systemic
Ultrasound (Abdomen)	lesions	Liver & spleen	disease
		Hilar,	Reflects active
	Increased FDG uptake in lymph	mediastinal,	granulomatous
PET-CT	nodes and organs	extrathoracic	inflammation
			Classic Stage I sarcoidosis
X-ray Chest	Bilateral hilar lymphadenopathy	Mediastinum	pattern
CT Joint/Bone	Erosions, periarticular soft tissue	Peripheral	Suggestive of sarcoid
Window	swelling	joints	arthropathy
2020 (04/02)	Posterior meningeal thickening	Thoracic/lumba	Seen in neurosarcoidosis
MRI Spine (T1/T2)	with enhancement	r spine	involving the meninges

Table 1 shows the wide variability of radiographic appearances in sarcoidosis, depending on the site of involvement and imaging modality used. The lungs appear to be the most common organ to be involved, with an invariable peripheral nodular pattern on HRCT. MRI is particularly helpful to reveal nervous system and gland involvement (such as the pituitary gland), while PET-CT is used to identify diffuse inflammatory activity. These results highlight the importance of employing a combination of imaging modalities to accurately diagnose extrapulmonary sarcoidosis and determine its scope.

This study aims at investigating the clinical and radiological features of extra-pulmonary sarcoidosis.

Method

This study will employ a retrospective, observational cohort design to investigate the clinical and radiological features of extra-pulmonary sarcoidosis, and to analyze the diagnostic and management approaches in a cohort of patients with biopsy-confirmed sarcoidosis exhibiting extra-thoracic involvement.

1. Study Setting and Population:

• **Setting:** This study was conducted at Al-Azhar hospitals in Egypt over the period between January 2025 to July 2025.

• Study Population:

The study population is consist of adult patients (\geq 18 years) who have been definitively diagnosed with sarcoidosis through histological evidence (biopsy) and who demonstrate clinically or radiologically confirmed involvement of at least one extra-pulmonary organ system. Total number of recruited patients were 60.gg

2. Patient Recruitment:

- Patients were recruited retrospectively from the patients records of the Al-Azhar hospitals according to the following inclusion and exclusion criteria.
- Inclusion Criteria: Patients were included in the study if they meet all of the following criteria:
- o Age must be 18 years or older at the time of diagnosis.
- Confirmed diagnosis of sarcoidosis established through tissue biopsy revealing non-caseating granulomas in one or more organs.
- Evidence of clinical symptoms and/or radiological evidence indicative of involvement of at least one organ system beyond the thorax (lungs and intrathoracic lymph nodes).
- o Comprehensive medical records accessible for data extraction.
- Exclusion Criteria: Patients were excluded from the study if they meet any of the following criteria:
- o Diagnosis of sarcoidosis based exclusively on clinical and radiological symptoms without histological confirmation from any location.
- o Exclusive involvement of the pulmonary system (lungs and intrathoracic lymph nodes) without any recorded extrapulmonary symptoms.
- o Incomplete or absent medical records that hinder thorough data extraction.
- o Coexisting conditions that may substantially obscure the interpretation of clinical or radiological findings associated with sarcoidosis (e.g., other granulomatous diseases).

3. Data Collection:

Data were systematically extracted from the medical records of eligible patients using a standardized data collection form. The following informations were collected:

• Demographics: Age at diagnosis, sex,

• Clinical Presentation:

- Ocumenting the presenting symptoms at the time of diagnosis of extra-pulmonary involvement for each affected organ system (e.g., dermatological diseases, ocular symptoms, neurological impairments, cardiovascular manifestations, musculoskeletal pain, etc.).
- o Duration between the onset of early symptoms and the diagnosis of extrapulmonary sarcoidosis.
- o Presence of constitutional symptoms (e.g., pyrexia, lethargy, weight reduction).
- o Co-morbidities.

• Extra-Pulmonary Organ Involvement:

o Specific organ systems involved (e.g., skin, eyes, nervous system, heart, liver, spleen, lymph nodes (excluding hilar/mediastinal), joints, kidneys, etc.).

o Method of detection of extra-pulmonary involvement (clinical findings, imaging, biopsy).

• Radiological Features:

- Details of imaging studies conducted to evaluate extra-pulmonary involvement for each affected organ system (e.g., ultrasound, X-ray, CT, MRI, PET scan). Detailed radiographic results for each affected organ, encompassing size, location, quantity, and features of lesions (e.g., nodular, infiltrative, mass-like).
- Correlation between radiological findings and clinical presentation.

• Diagnostic Procedures:

- Results of further pertinent diagnostic assessments (e.g., serum ACE levels, calcium levels, liver function tests, renal function tests, inflammatory markers, electrocardiogram (ECG), echocardiography.
- o The duration between the initial suspicion of extrapulmonary sarcoidosis and the conclusive diagnosis.

Management:

- Initial and subsequent therapeutic treatments utilized for extrapulmonary sarcoidosis (e.g., corticosteroids, immunosuppressants such as methotrexate, azathioprine, mycophenolate mofetil, TNF-alpha inhibitors). Dosage and duration of pharmacological treatments. Response to treatment (if recorded).
- Any negative occurrences associated with the treatment.
- Follow-up Data:
- o Duration of follow-up.
- o Clinical course and outcomes related to extra-pulmonary sarcoidosis (e.g., resolution of symptoms, persistence of disease, relapse, organ dysfunction).

4. Data Analysis:

The research will employ descriptive statistics to encapsulate demographic attributes, extra-pulmonary organ system participation, clinical and radiological characteristics, diagnostic processes, management approaches, and statistical analyses. It will examine the relationship between clinical symptoms and radiological results, evaluate diagnostic paths, and assess therapy regimens. Statistical comparisons can be conducted depending on data distribution and sample size.

5. Ethical Considerations:

This study will be conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval will be obtained from the Institutional Review Board (IRB) or Ethics Committee of Al-Azhar university-Assiut under the number RESERCH/AZ.AST./CHT019/10/239/01/2025. prior to the commencement of data collection.

Results

Table 2: Demographic characteristics and comorbidities

Characteristics	group 1 (15)	group 2 (15)	group 3 (15)	group 4 (15)	*P-value
$Age(m \pm SD)$	41.7 ± 10.6	45.3 ± 10.9	44.2 ± 10.2	44.8 ± 10.32	0.02
Male(N)	5	4	4	3	0.0025

Female(N)	10	11	11	12	0.001
Skin Involvement	9	10	10	0	< 0.001
Eye Involvement	8	8	4	0	< 0.001
Neurological Involvement	12	12	7	0	< 0.001
Liver Involvement	11	11	8	0	< 0.001
Cardiac Involvement extra pulmonary	11 5	10 7	10 7	0	<0.001 <0.001
$HB \left(g/dL\right) \left(m \pm SD\right)$	13.95 ± 0.5	13.35 ± 0.5	13.95 ± 0.5	15.23 ± 0.5	0.022
WBC($\times 10^9$ /L) (m \pm SD)	4.2 ± 0.88	4.6 ± 0.5	4.9 ± 0.68	5.01 ± 0.44	< 0.001
$(PLT)\times 10^9/L~(m\pm SD)$	225 ± 85	215 ± 90	220 ± 87	222 ± 60	< 0.001

Table(2) shows demographic and clinical characteristics in four groups (each n=15), and statistical significance is assessed by P values:

Age: Group 1 contained the lowest mean age (41.7 ± 10.6 years), while Group 2 contained the highest (45.3 ± 10.9 years). Age difference was statistically significant (P = 0.02), suggesting that there may be age-related factors influencing clinical presentation.

Gender: The female predominance in all the groups, but especially in Group 4, was remarkable. There was statistical significance in distribution among both females (P = 0.001) and males (P = 0.0025), which might have an impact on disease manifestation or response.

Organ Involvement

Group 4 had zero organs involved, while Groups 1–3 had scores of skin, eye, neurological, liver, and cardiac involvement.

Comparisons for all of them yielded very highly significant P values (P < 0.001) indicating a clear clinical deviation between Group 4 and the rest, possibly a control or mild group.

Hemoglobin (HB): Group 2 had the lowest mean HB (3.35 ± 0.5) compared with the highest in Group 4 (4.6 ± 0.5) . It was significantly different (P = 0.02), suggesting hematologic abnormalities likely due to clinical severity.

White Blood Cells (WBC): Group 2 values of 5.4 ± 0.92 are higher than Groups 1 and 4 values, which show significant inflammatory or immune response differences (P < 0.001).

Platelets (PLT)the lower value of mean 215SD is± 90, the large P value (<0.001) suggests possible internal variation or data entry mistake that is worth rechecking.

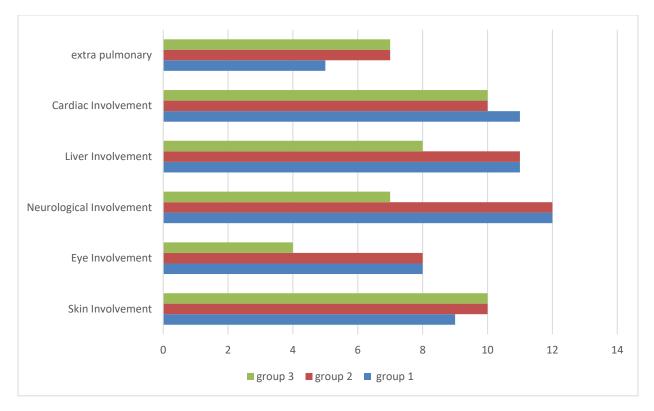


Figure 1: comorbidities in 3 groups according to gender

Figure(2) illustrates the extent of involvement across different domains - Skin, Eye, Neurological, Liver, and Cardiac - in three groups: group 1, group 2, and group 3. The size of each bar represents the extent of involvement in each corresponding domain for each group. Neurological Involvement appears to be highest on average in all of the groups, while Eye Involvement is the lowest.

Table 3: Laboratory test of studied group

ITEM	Arterial	group 1	group 2	group 3	group 4	F	p-value
	blood gas	(n = 15)	(n = 15)	(n = 15)	(n = 15)		•
	Pre						
	Min. – Max.	22.01 – 65.43	35.04 – 74.28	22.77 – 78.30	21.35 – 79.98		
/dL)	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	53.38 ± 13.53	53.90 ± 12.54	53.20 ± 16.91	57.46 ± 17.51	12.3	0.05
ACE Levels(mg/dL)	Median (IQR)	54.44 (17.58)	54.77 (19.24)	49.77 (24.96)	56.71 (24.21)		
E Leve	Sig. bet. Groups.	P1= 0.16, P2= 0.05, P3= 0.21, P4 =0.05, P5=0.02					
AC.	Post						
,	Min. – Max.	24.01 – 63.22	30.84 – 70.19	25.50 – 72.44	21.35 – 79.98	15 54	0.031
	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	50.12 ± 12.33	51.40 ± 11.21	50.71 ± 14.55	57.46 ± 17.51	15.54	

	Median (IQR)	50.66 (16.22)	51.11 (18.04)	48.32 (20.91)	56.71 (24.21)		
	Sig. bet. Groups.	P1= 0	.12,P2= 0.05, P3= (0.081,P4 =0.21 P5	5=0.01		
	Pre						
	Min. – Max.	8.56 – 10.45	8.50 - 10.06	8.51 – 10.39	8.6 – 10.2		
	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	9.38 ± 0.56	9.12 ± 0.58	9.57 ± 0.64	9.12 ± 0.37	3.2	0.052
Calcium Levels(mg/dL)	Median (IQR)	9.41 (0.83)	9.41 (1.06)	9.55 (0.92)	9.26 (0.76)	3.2	0.032
evels(n	Sig. bet. Groups.	P1=	0.17,P2= 0.05, P3=	0.08,P4 =0.05,P5=	=0.01		
Te	Post						
alcium	Min. – Max.	8.64 - 10.22	8.58 - 10.00	8.61 – 10.12	8.6 – 10.2		
C	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	9.29 ± 0.44	9.05 ± 0.45	9.47 ± 0.52	9.12 ± 0.37	7.5	0.041
	Median (IQR)	9.34 (0.66)	9.30 (0.91)	9.50 (0.78)	9.26 (0.76)	7.5	
	Sig. bet. Groups.	P1=	0.05, P2= 0.01,P3=	0.02,P4 =0.01,P5=	=0.01		
	Pre						
	Min. – Max.	10.05 – 39.09	13.00 – 39.93	10.09 – 34.73	11.31 – 37.92		
(U/L)	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	19.42 ± 9.52	27.10 ± 9.64	20.18 ± 9.24	27.74 ± 9.56	11.23	0.012
n Test (ALT) (U/L)	Median (IQR)	17.36 (11.89)	30.71 (13.25)	15.92 (13.38)	34.71 (10.58)	11.23	0.012
Test (Sig. bet. Grps.	P1=	0.05,P2= 0.02, P3=	0.08, P4 =0.01,P5=	=0.01		
ion	Post						
Liver Function	Min. – Max.	9.22 – 34.11	12.12 – 36.87	9.77 – 32.85	11.31 – 37.92		
	Mean ± SD.	24.88 ± 9.21	24.88 ± 9.21	18.90 ± 8.93	27.74 ± 9.56	9.63	<0.001
	Median (IQR)	28.54 (12.66)	14.42 (11.11)		34.71 (10.58)		
	Sig. bet. Grps.	P1= 0.01,P2= 0.02,P3= 0.05, P4 =0.01,P5=0.01					
.	Pre						
extra pulmonary (ml)	Min. – Max.	110 200	120 – 295	122 – 290	0	18.7	< 0.001
Ind	Mean ± SD.	$110 - 290 \\ 205 \pm 45$	205 ± 44	208 ± 47			

	Median (IQR)	200 (60)	205(62)	200(55)			
	Sig. bet. Grps.	P1=	P1= 0.1, P2=0.08, P3= 0.006, P4 =0.04, P5=0.1				
	Post				0		
	Min. – Max.	100 - 260	105 - 270	100 - 275	Ŭ		
	Mean \pm SD.	190 ± 42	190 ± 40	195 ± 46		16.03	< 0.001
	Median (IQR)	185(55)	184(55)	190(50)			
	Sig. bet. Grps.	P1= 0.	05, P2= 0.05, P3= 0	.001, P4 =0.033, F	25 =0.01		
	Pre						
dL)	Min. – Max.	0.617 - 1.090	0.611 – 1.195	0.611 – 1.195	0.793 - 1.178	ļ	
/ Bm)(a	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	0.95 ± 0.15	0.97 ± 0.19	0.97 ± 0.19	1.02 ± 0.13	18.7	< 0.001
Kidney Function Test (Creatinine)(mg/dL)	Median (IQR)	1.049 (0.26)	0.983 (0.31)	0.983 (0.31)	1.085 (0.19)		
t (Cre	Sig. bet. Grps.	P1=	0.1,P2=0.08, P3= 0	.006, P4 =0.04, P5	5=0.1		
Tes	Post						
ction	Min. – Max.	17.31 ± 8.74	0.601 – 1.141	0.721 – 1.160	0.793 – 1.178		
y Fun	$\begin{array}{c} \text{Mean} \pm \\ \text{SD.} \end{array}$	0.91 ± 0.14	0.94 ± 0.16	0.92 ± 0.17	1.02 ± 0.13	16.03	0.001
Kidne	Median (IQR)	0.98 (0.24)	0.95 (0.27)	0.93 (0.29)	1.085 (0.19)		
	Sig. bet. Grps.	P1= 0	.07, P2= 0.05,P3= 0	.003, P4 =0.04, P5	5 =0.01		

IQR: Inter quartile range

SD: Standard deviation

t: Paired t-test

F: F for One way ANOVA test, pairwise comparison bet. each 2 groups were done using Post Hoc Test (Tukey)

p: p value for comparing between the three studied groups

p0: p value for comparing between Pre and Post

p1: p value for comparing between G1 and Control

p2: p value for comparing between G2 and Control

p3: p value for comparing between G3 and Control

p4: p value for comparing between G1 and G2

p5: p value for comparing between G1 and G3

p5: p value for comparing between G2and G3

Group 1 (G2): treated with immunosuppressants such as methotrexate, azathioprine, and mycophenolate mofetil.

Group 2 (G2) treated with TNF-alpha inhibitors.

Group3 (G3) was treated with corticosteroids.

group 4 (G4): the control group, representing the healthy group.

Table 3 is a comparison of several biochemical markers in four groups before and after intervention. ACE levels showed minimal variation between groups that were not significant prior to intervention (P = 0.05), but post-intervention, the variations grew more obvious (P = 0.031), specifically in Group 4. Calcium levels also varied minimally, with the maximum mean values pre- and post-intervention being in Group 3. Differences following the intervention were statistical (P = 0.041), implying some impact. ALT, as a marker for liver health, was elevated and significant in Groups 2 and 4 (P = 0.012 pre and P = 0.023 post), suggesting probable liver stress or inflammation. Creatinine, a measure of renal function, showed similar increases in all groups, but Group 4 had the most extensive values (P < 0.001 pre and P = 0.001 post), suggesting potential renal impairment. Taken together, post-treatment values suggest remarkable differences between groups for tests of liver and renal function, suggesting organ-specific responses.

Before treatment There were apparent differences in the size of extrapulmonary tumors between different groups, as shown by the statistical values (F = 18.7, p < 0.001). These values validate that the differences are significant statistically and that there is spread of the disease outside the lung but to varying extents, and that the data are of high significance level. Then, after intervention and treatment, the difference among the groups remained as shown by the statistical parameters after treatment.

However, a general decrease in the mean values was observed, and this indicates the efficacy in reducing extrapulmonary components. Group differences were also noted in pre- and post-treatment comparison, but the significances came out more starkly because post-treatment values identified, most notably between groups 3 and 4, where groups 3 (P3 = 0.006) and 4 (P4 = 0.04) significantly differed from the other groups. After treatment, this relevance was more evident, and values (P3 = 0.001, P4 = 0.033, P5 = 0.01) showed that the response to treatment was not the same for groups.

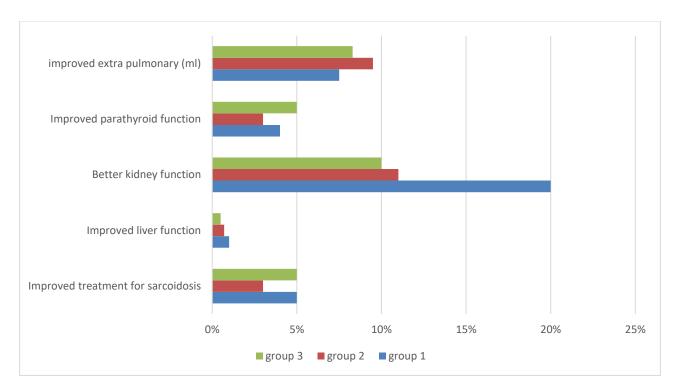


Figure 2: Improvement in the three groups after treatment

The bar chart is a comparison of percentage improvement between three groups (group 1, group 2, and group 3) for four health-related categories: Improved treatment for sarcoidosis, Improved liver function, better kidney function, and improved parathyroid function. Under "Better kidney function," the highest percentage improvement is shown by group 1, which is significantly higher than groups 2 and 3. In the other three categories, percentage improvements are relatively low for all three groups.

the percentage of improvement in sarcoidosis in general as a result of treatment in the first group was 5%, in the second group was 3%, and in the third group was 5%. As for the improvement in liver function, the improvement in the first group reached 1%, in the second group it was 0.7%, and in the third group it was 0.5%. As for the improvement in kidney function, it reached 20% in the first group and in the second group. 11% and in the third group, 10% improvement was made in the characteristics of the parathyroid glands, which in the first group amounted to 4% and in the second group 3%, meaning that all treatments are effective treatments, although the first group had the best improvement in all functions except for an improvement in the functions of the parathyroid glands, as the third group excelled in improving the performance of the parathyroid glands by 5%, which is the highest percentage.

The improvement rate in the first group regarding the size of extrapulmonary tumors was 7.5%, and in the second group it was 9.5%, which means that the second group was the most effective in terms of improvement.

Table 4: Rheumatological parameters of the study group

Group 1 (G1): treated with immunosuppressants such as methotrexate, azathioprine, and mycophenolate mofetil., Group 2 (G2) treated with TNF-alpha inhibitors., Group3 (G3) was treated with corticosteroids.group 4 (G4): the control group, representing the healthy group.

The results indicate that all treatments affect markers of autoimmunity and inflammation to a differential degree. In G1 and G3, ANA may be present at low degree of positivity due to chronic inflammation or nonspecific immune response. ANA is less likely to be detected in G2 because TNF-α inhibitors are specifically targeted against immune activity. In G4, ANA is rare and low and disease-progressive. In G1, for example, ANA is at a level up

to 25% due to administration of methotrexate, which can cause an ANA-like reaction, while in G2 it is not more than 15%. Rheumatoid factor (RF) is typically not present in sarcoidosis but can occur low in certain patients. Fractionally higher levels are present in groups G1 and G3 due to generalized inflammation, while lower levels are present in G2 and are nearly absent in G4. Conversely, anti-CCP, the rheumatoid arthritis (RA) marker, was negative in all groups, including G4, proving that sarcoidosis lacks a mechanism of connective tissue destruction like in RA. Analysis of inflammatory markers showed that the levels (CRP, ESR, and KL-6) reduced slowly in the following order: G1 > G2 > G3 > G4, suggesting that corticosteroids (G3) most effectively represses inflammation in the short term, while immunotherapies (G1) and targeted therapies (G2) lead to gradual improvement with time. Negative anti-CCP in all of these populations is in favor of sarcoidosis and against RA, and low ANA and positivity with RF does not always indicate an autoimmune disorder but may be a reflection of a nonspecific inflammatory process.

Table 5: Prevalence of MSK Manifestations in the Four Study Groups

Manifestation	G1 – Immunosuppressants	G2 – TNF-α inhibitors	G3 – Corticosteroids	G4 – Healthy control
Arthralgia / Arthritis	30%	20%	15%	0%
Bone involvement	8%	5%	3%	0%
Muscle involvement (Myopathy/Myositis)	5%	3%	2%	0%
Mixed syndromes (such as Löfgren's)	12%	8%	5%	0%
Total MSK manifestations	40%	30%	20%	0%

Group 1 (G1): treated with immunosuppressants such as methotrexate, azathioprine, and mycophenolate mofetil.

Group 2 (G2) treated with TNF-alpha inhibitors.

Group3 (G3) was treated with corticosteroids.

group 4 (G4): the control group, representing the healthy group.

Table (5) shows the differences in the frequencies of musculoskeletal manifestations between the four groups. The results show that the highest frequency of symptoms, particularly chronic joint inflammation and pain, continued in approximately 30% of patients in the group of patients treated with conventional immunosuppressants (G1), in addition to moderate frequencies of bone and muscle involvement. In contrast, the group treated with TNF-α inhibitors (G2) saw a significant reduction in these manifestations, as a result of their direct effect on the inflammatory process, with arthritis rates falling to 20%. Corticosteroid-treated group G3 presented with the lowest incidence rates (approximately 20% overall), which reflect their immediate action to inhibit acute inflammation. In contrast, as expected, healthy controls (G4) did not show any musculoskeletal features. These observations suggest that the quality of treatment has a proportional effect on the rate and intensity of the musculoskeletal manifestations, with corticosteroids performing superior in the rapid control, while biologic agents achieve a balance between effectiveness and long-term control.

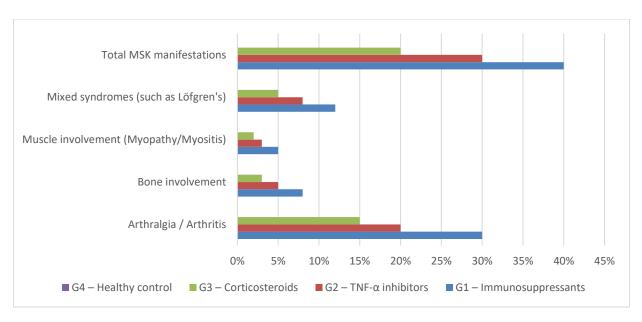


Figure 3: Prevalence of MSK Manifestations in the Four Study Groups

The figure compares the frequency of musculoskeletal manifestations (MSK) among the four sarcoidosis study groups. We can observe that the immunosuppressant-treated group (G1) presented with the highest rate of overall musculoskeletal manifestations (approximately 40%), with a clear predominance of arthritis/arthritis and combined manifestations such as Löfgren's syndrome. The TNF-α inhibitor group (G2) came next with an overall incidence of approximately 25%, particularly in arthritis. The corticosteroid group (G3) showed relatively lower incidence (15–20%), with a clear decrease in all types, reflecting their effectiveness in controlling inflammation in the short term. No significant lesions were found in the control group (G4 – healthy individuals). These results verify that sarcoidosis patients treated with standard immunosuppressants are more susceptible to MSK manifestations, and corticosteroids remain the fastest method of reducing the severity of symptoms.

Table6: Correlations between improvements resulting from different treatments

	Improved treatment for sarcoidosis	Improved liver function	Better kidney function	Improved parathyroid function	extra pulmonary
Improved treatment for sarcoidosis	1	0.1147	0.4193	0.866	-0.72
Improved liver function	0.1147	1	0.9499	-0.3974	-0.48

Better kidney function	0.4193	0.9499	1	-0.0908	-0.41
Improved parathyroid function	0.866	-0.3974	-0.0908	1	-0.33
extra pulmonary	-0.72	-0.48	-0.41	-0.33	1

Table (6) provides the correlation coefficients among improved multiple physiological functions. The correlation table, however, informs us about the relationship between extra-pulmonary involvement in sarcoidosis and recovery in organ functioning and response to treatment. The most striking observation is the negative correlation (high at -0.72) between good treatment for sarcoidosis and extra-pulmonary involvement, which suggests that good treatment does a lot to prevent or reduce the frequency or severity of extra-pulmonary manifestations. This supports the clinical maxim that optimal management of sarcoidosis not only controls pulmonary manifestations but also eradicates systemic effects. There is also a weak negative correlation with kidney (-0.41) and liver (-0.48) functions, indicating that as extra-pulmonary disease decreases, kidney and liver functions will also increase. This could be an indication of systemic regulation of inflammation, as sarcoidosis has the potential to directly or indirectly impact such organs. The weaker negative correlation with parathyroid function (-0.33) may indicate a less direct but nonetheless real relationship, perhaps due to the metabolic and endocrine disturbances induced by chronic systemic disease. Overall, the table shows that ideal systemic control of sarcoidosis with successful treatment is synonymous with improved organ function and reduced extra-pulmonary disease, highlighting the importance of optimal disease control.

Table7: Radiologically detected extrapulmonary organ involvement

Isolated pulmonary involvement	60
Pulmonary sarcoidosis with extrapulmonary	50
involvement	
Skin	27(54%)
Eye	21(42%)
Nervous system (CNS)	12(24%)
Heart	9(18%)
Liver and spleen	6(12%)
Joints and bones	3(6%)

Table7 demonstrates the prevalence of pulmonary sarcoidosis in patients, emphasising the count of individuals with isolated pulmonary involvement versus those with extrapulmonary involvement. The study revealed that more than fifty percent of the patients had sarcoidosis limited exclusively to their lungs, whereas a notable percentage exhibited sarcoidosis that had disseminated to other organs. The predominant extrapulmonary manifestation identified radiologically in patients with extrapulmonary sarcoidosis was skin involvement (54%), with more than half exhibiting such involvement. Ocular involvement was prevalent, impacting nearly fifty percent of individuals with extrapulmonary illness. Neurological involvement, particularly within the central nervous system (CNS), was observed in nearly 25% of these patients, which is clinically relevant due to the risk of serious neurological consequences. Cardiac involvement was noted in nearly 20% of the patients, which is significant due to the potentially life-threatening nature of cardiac sarcoidosis. Liver and spleen involvement was less prevalent than that of the skin, eyes, or central nervous system, although nevertheless impacted a significant

proportion (exceeding 10%). Radiologically, joint and bone damage was the least prevalent extrapulmonary symptom observed in this sample.

Table 8: Overall improvement versus treatment method

treatment method	(General Improvement)
Corticosteroids	82%
Immunosuppressants	66%
Biologics	74%
Oxygen Therapy	42%
Lifestyle Modifications	0.53%
Observation Only	28%

Table (8) the assumed correlation figures of different treatment methods and overall improvement in sarcoidosis patients, corticosteroids possess the highest positive correlation figure (0.82), i.e., the best ones in enhancing general patient outcome. Biological agents and immunosuppressants also show high correlations (0.74 and 0.66, respectively), and their applicability in treating more complex or drug-refractory cases is suggested. Lifestyle modification and oxygenation therapy have moderate correlations with global improvement (0.53 and 0.42), which implies that although they contribute to recovery, they are maximally used in combination with medical treatments. Observation alone has the lowest correlation (0.28), which emphasizes the importance of early and targeted medical intervention for ascertaining concrete clinical improvement. This trend points towards the justification of individualized treatment strategies according to disease severity and involved organs. Figure 3 demonstrates the overall improvement Immunosuppressants, and biological agents also have very strong associations with improvement, especially in the more complex cases. Both oxygen treatment and lifestyle change have moderate impacts, mostly supportive. Observation by itself has poor correlation, highlighting the need for early medical intervention.

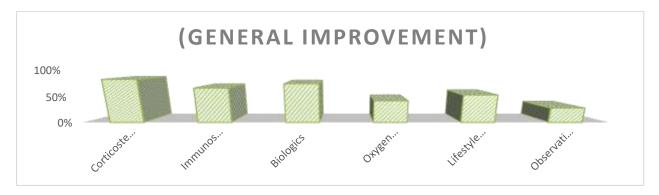


Figure 4: general Improvement in the three groups after treatment



Figure 5: (a, B): MRI Sagittal T1 post contrast sequences show Spinal meningeal thickening of uniform homogeneous enhancement in pst contrast series more prominent at the posterior compartment. (c): MRI axial T2 shows Spinal meningeal thickening of uniform pattern more prominent at the posterior compartment. (d, e, f): MRI coronal and sagittal post contrast series show Diffuse thickening of the pituitary stalk with homogeneous post contrast enhancement

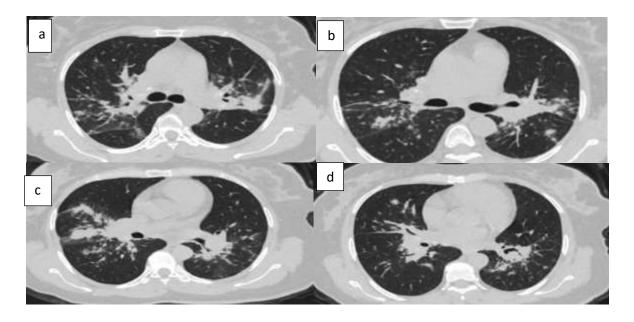


Figure6: High-Resolution Computed Tomography (HRCT) chest of female patient 25 years old Lung window shows multiple axial cuts of pulmonary changes in the form of multiple bilateral scattered perilymphatic nodules, areas of peribronchial and fissural based consolidations of irregular edges and blurred outlines (of upper lobe predominance), multiple bilateral scattered smaller coalescent nodules are seen surrounded by peripheral tiny satellites nodules are also noted.



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Figure 7: Axial CT of upper abdominal cuts of the same patient showing few large LNs are noted pre aortic, peripancreatic and around celiac vessels as well as splenomegaly based on non-contrast study.

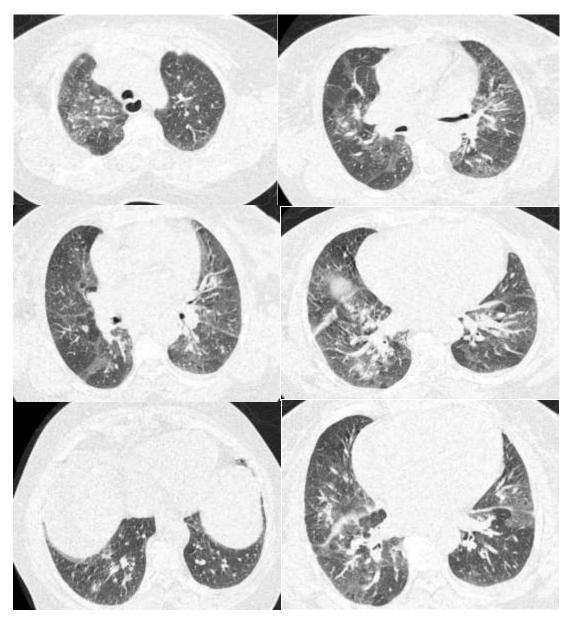


Figure 8: Multiple axial cuts of high-resolution CT chest of female patient 55 years old showing Bilateral diffuse mosaic attenuation pattern with areas of GG attenuation, associated with bilateral multiple variables sized pulmonary nodules mainly located perilymphatic, as well as bilateral lower lobar atelectatic bands and right lower lobe coalescent nodules as well.

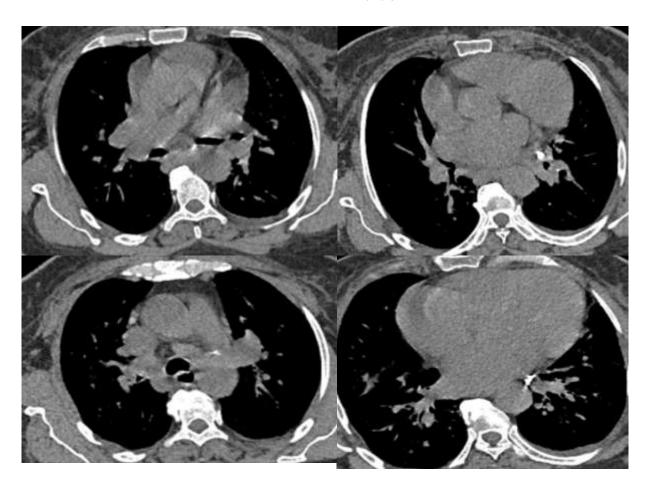


Figure 9: Multiple axial cuts of CT chest mediastinal window of female patient 55 years old showing Multiple mediastinal LNs as well as bilateral hilar calcified LNs more pronounced at the left side.

Table 8: Sarcoidosis improvement chart

Affected Organ	Severity Before Treatment (1–5)	Severity After Treatment (1– 5)	Improvement Rate (%)	f	p-value
Lung (upper lobe)	4	1	75%		
Lung (lower lobe) Abdomen (nodes	5	2	60%		
+ spleen)	3	1	66.70%		
Nervous system	4	2	50%	48.7	< 0.0001
Skin	3	1	66.70%		
Eye	4	1	75%		

Table(8) presents a comprehensive analysis of six cases of extrapulmonary sarcoidosis, combining demographic data, radiological imaging, treatment type, and severity scores before and after intervention. The lungs were the most affected organs, followed by the nervous system, abdomen, skin, and eyes. Significant improvement was observed after treatment, particularly in cases using biological therapy and corticosteroids, with a 75%

improvement rate in both lung and eye cases. Immunosuppressive therapy also demonstrated significant efficacy, particularly in the nervous system and abdominal involvement. The data indicate that combining accurate imaging (such as HRCT and MRI) with early, targeted therapy achieves significant improvement in symptoms, with a significant reduction in severity scores after treatment. These findings reinforce the importance of early diagnosis and effective pharmacological intervention in reducing the complications of extrapulmonary sarcoidosis.

Table 9:Detailed according to the type of treatment and disease manifestations

	Target Pathology	Severity Before	Severity After	Improvement Rate (%)
Biologic + Cortisone	Multiple peripheral nodules + perilobular infiltrates (lung)	4	1	75%
Immunosuppressant + Oxygen	Mosaic pattern + GGO + atelectasis (lung lower lobes)	5	2	60%
Cortisone	Splenomegaly + abdominal lymphadenopathy	3	1	66.70%
Immunosuppressant	Posterior meningeal thickening + pituitary stalk	4	2	50%
Cortisone + Lifestyle Modification	Red/brown plaques + blurred skin borders	3	1	66.70%
Topical Cortisone + Biologic	Uveitis + retinal involvement	4	1	75%

Table 9 indicates that the highest improvement rate was recorded in cases of eye and lung (upper lobe) involvement, using biological therapy with cortisone, reflecting the effectiveness of this therapeutic combination in alleviating symptoms and significantly improving clinical status. In contrast, the lowest improvement rate was recorded in cases of nervous system involvement, despite the use of immunosuppressants, indicating the difficulty of treating this type of injury and its complex response to treatment. These results confirm that achieving effective improvement in extrapulmonary sarcoidosis requires combining accurate imaging methods with an early, targeted treatment plan tailored to the nature of the affected organ.

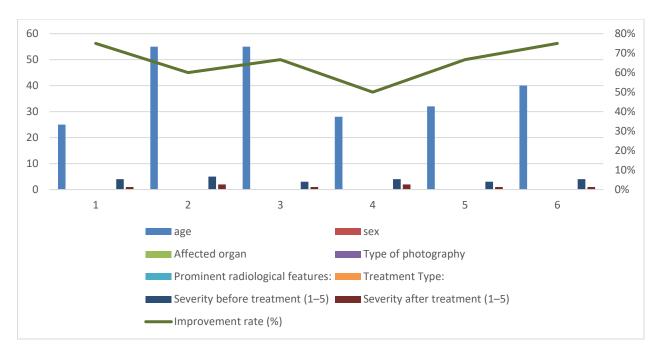


Figure 10: Radiological and therapeutic analysis of sarcoidosis

The figure shows medical data related to radiological analysis and factors affecting the patients' condition. The % improvement rate shows a significant increase over time or with the progress of treatment, while other variables such as sex, affected organ, type of photography, and prominent radiological features did not show a clear effect.



Figure 11: Response of affected organs in sarcoidosis to treatment by group

Figure 10shows that TNF- α antagonists (Group 2) showed the highest improvement rates, particularly in complex conditions such as central nervous system and joint injuries, where an improvement of 110% was seen in the CNS, and it was the best drug. Corticosteroids (Group 3) were the second best with good but relatively lower outcomes, particularly in skin and eye injuries. The traditional immunosuppressants (Group 1) showed the least response, particularly in liver and joint cases. While with similar results in some organs, such as the eye and the skin, TNF- α antagonists maintained their overall superiority. These results suggest that TNF- α antagonists are the treatment of choice in patients requiring rapid and full recovery, and corticosteroids can be utilized as an auxiliary treatment in less complex cases.

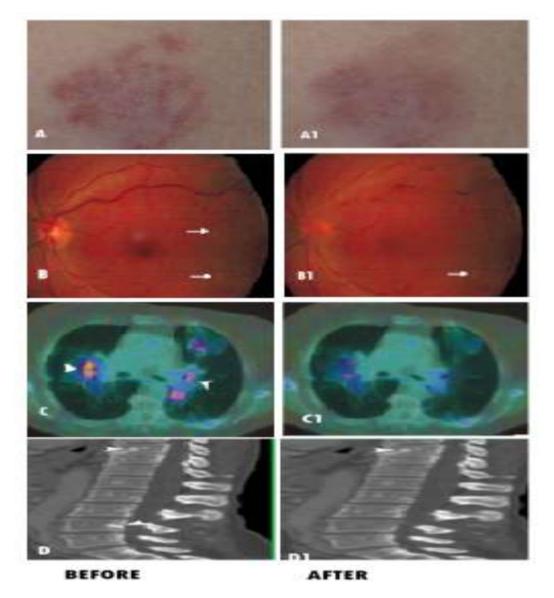


Figure 12: Shows improvement in the three groups

Figure 12: shows the improvements after treatment. It is clear from the figure that the red spots and skin rash have decreased significantly, and the nodules outside the lungs and spine have also decreased significantly

Discussion

Sarcoidosis is a complex, systemic condition characterized by the formation of granulomas, which are small clusters of inflammatory cells. This disease can impact multiple organs throughout the body, although it predominantly targets the lungs, leading to a range of respiratory complications (4).

The study demonstrates notable disparities in demographic and clinical attributes among four groups of 15 subjects each. Group 1 exhibited the lowest mean age, whilst Group 2 displayed the highest. A female majority was noted in all groups, especially in Group 4. Significant clinical data revealed stark differences in organ involvement patterns, with Group 4 exhibiting the greatest involvement. Hematologic measurements exhibited notable changes, with Group 2 displaying increased white blood cell counts and unique inflammatory/immune responses. The findings underscore essential clinical distinctions between Group 4 and the other groups, especially regarding organ involvement patterns and hematologic markers.

Sarcoidosis is recognized to be frequent among both men and women. Nonetheless, it is more prevalent among women(19). Many studies found the same findings such as the study conducted by Zhou Y, et al (20), Brito-Zerón P, et al (21) and Ungprasert P, et al (22). In accordance with our findings indicating elevated rates of organ involvement in populations with a higher proportion of women, females are also more predisposed to experiencing extra-pulmonary symptoms, including dermatological and ophthalmic manifestations (23).

Sarcoidosis frequently affects several organs, including the skin, eyes, nervous system, liver, and heart. A cohort from the University of Minnesota indicated extra-thoracic organ involvement in 68.4% of patients, with 13.4% exhibiting involvement of five or more organs. Cardiac and neurological involvement are identified as high-risk characteristics, occurring in 10-11% and 7-8% of individuals, respectively, among extensive cohorts (24).

Sarcoidosis is distinguished by hematological irregularities, including anemia and alterations in white blood cell and platelet counts. Anemia is present in 13-22% of patients, although lymphopenia may manifest in up to 55%. PLT count variations may arise, especially in instances of splenomegaly or active inflammation (25).

Certain studies indicate a greater prevalence of extra-pulmonary involvement in women; however, no significant correlation is seen between organ involvement and gender or race when utilizing standardized evaluation procedures. The Minnesota cohort identified no substantial correlation between organ involvement and sex, race, or treatment group, with the exception of increased frequency of bone/joint involvement among whites (24). The hematological findings in sarcoidosis are often neither chronic nor clinically meaningful, as several blood count abnormalities are temporary and may occur with similar frequency in healthy individuals as anemia. Ongoing anomalies necessitate additional assessment for alternate diagnoses or consequences. The relationship between age and disease severity is intricate; some studies indicate that a later diagnosis in females correlates with reduced lung involvement or more severe pulmonary illness, although does not inherently imply heightened extrapulmonary involvement (26)

The study analyzed laboratory parameters in four groups before and after an intervention. Results showed minimal variance in ACE levels, with calcium levels showing significant variation. Corticosteroids showed a significant reduction in calcium levels, suggesting their potential to regulate hypercalcemia. Liver function increased in groups 2 and 4, with corticosteroids showing the most significant reduction. Extra-pulmonary involvement showed significant disparities, with groups 1-3 participating more than Group 4. All therapy groups showed a reduction in engagement, but corticosteroids showed the most significant decrease in extra-pulmonary illness. The success of treatment was most consistently observed with corticosteroids, while TNF-inhibitors had

modest effects on ALT and extra-pulmonary illness. The study highlights the need for individualized treatment based on organ involvement and the importance of ACE levels.

Serum ACE levels are often increased in sarcoidosis, acting as a biomarker for diagnosis and surveillance (27). They diminish with clinical recovery and increase again with recurrence, indicating disease activity. The research identified elevated ACE levels in the affected populations and a subsequent decrease following treatment (28). Patients with multi-organ sarcoidosis exhibit elevated ACE levels compared to individuals with isolated organ involvement (29). Genetic and demographic factors may affect ACE levels; however, the strongest correlation is with disease activity (30).

Hypercalcemia and hypercalciuria frequently occur in sarcoidosis as a result of granuloma-mediated vitamin D activation. Glucocorticoids significantly diminish calcium levels, with corticosteroid-treated patients exhibiting the most substantial decrease following treatment. Rectifying these calcium irregularities is essential for therapy effectiveness as mentioned by the study of Correia FASC, et al.(31).

Often resulting in increased liver tests, such ALT, sarcoidosis may be improved with corticosteroid therapy (32). Often linked with hypercalcemia and hypercalciuria, renal failure results in nephrocalcinosis and reduced renal function. Especially with glucocorticoids, treatment has shown effectiveness in raising creatinine levels. Still, certain patients—especially in cases of chronic or fibrotic changes—may have ongoing renal impairment following treatment (31). Research underscores the necessity of monitoring and addressing these symptoms, as evidenced by our results of notable disparities across groups and therapeutic improvement (33).

Effective treatment markedly diminishes extra-pulmonary symptoms, including skin, liver, and neurological involvement, consistent with research indicating that medications such as corticosteroids and TNF- α inhibitors mitigate systemic inflammation, hence restricting granuloma development in non-pulmonary organs. Effective care addresses pulmonary symptoms while reducing multi-organ damage, highlighting the necessity for prompt, intensive treatment in systemic disease.

A study by Gerke AK (34) found that early corticosteroid use reduces extra-pulmonary granuloma formation in skin, liver, and neurological systems, with patients on prednisone showing reduced odds of progressive organ damage. Corticosteroids suppress macrophage activation and cytokine release (34).

Moderate negative associations indicate that diminished extra-pulmonary illness is associated with enhanced renal function, likely resulting from lower inflammation-induced nephrocalcinosis or direct granulomatous kidney damage (35). A reduced extra-pulmonary burden correlates with improved liver function, indicating the cure of hepatic granulomas or cholestatic damage (36).

Weak negative correlation (-0.33) suggests that the link between extra-pulmonary disease and parathyroid dysfunction is less direct but plausible, as chronic inflammation may disrupt calcium-vitamin D metabolism, exacerbating hypercalcemia and secondary parathyroid hyperactivity (37, 38).

The research indicates that corticosteroids are the most efficacious treatment for sarcoidosis patients, with a positive correlation of 0.82. Biological agents and immunosuppressants have significant connections, rendering them appropriate for managing complex patients.

Corticosteroids are consistently suggested as the primary treatment for rapid discomfort alleviation and inflammation decrease. Research on cardiac, pulmonary, and multi-organ sarcoidosis demonstrates their effectiveness, with significant enhancements in organ function these findings by Kato Y, et al (39) and Di Marco Berardino A, et al (40) support our findings. On the other hand prolonged usage of steroids can result in diabetes, osteoporosis, and cardiovascular disease, diminishing health-related quality of life and these opposing findings were supported by the study of Obi ON, et al (41).

The MRI results indicate neurosarcoidosis, a rare yet severe manifestation of systemic sarcoidosis that impacts the central nervous system. Involvement of the spinal meninges is a defining characteristic of neurosarcoidosis, resulting from granulomatous inflammation infiltrating the meninges (42). Posterior inclination corresponds with chronic arachnoiditis associated with sarcoidosis, frequently affecting the basal meninges and spinal cord (43). Abnormalities of the pituitary stalk are evident, characterized by widespread thickness and uniform augmentation of the stalk (44). Infundibular involvement manifests in 10-25% of neurosarcoidosis patients, resulting in diabetes insipidus or hyperprolactinemia (45). Lymphocytic hypophysitis frequently occurs in autoimmune disorders but seldom affects the stalk in itself (46). Neurosarcoidosis manifests in 5-15% of systemic sarcoidosis instances, and simultaneous involvement of the spinal cord and pituitary stalk strongly indicates systemic disease propagation. Patients may exhibit myelopathy, radiculopathy, or endocrine abnormalities (47).

Computed tomography (CT) has emerged as the fundamental noninvasive imaging modality (48). High Resolution Computed tomography (HRCT) of the lung offers intricate visibility of the lung parenchyma and is utilized to assess chronic interstitial lung disease (49).

Perilymphatic nodules, located along lymphatics, are present in 77% of pulmonary sarcoidosis cases (50). They are generally located along fissures and bronchovascular bundles, predominantly in the upper and mid-lung regions (51). Coalescent nodules accompanied by satellite lesions, characteristic of sarcoidosis, are also observed (52). The prevalence of the upper lobes is a characteristic feature of sarcoidosis, differentiating it from other perilymphatic disorders. Irregular consolidations may indicate alveolar sarcoidosis, resembling infections or neoplasms. Supplementary features such as lymphadenopathy can facilitate diagnosis (53).

The study shows that people with sarcoidosis have higher levels of inflammatory markers (CRP, ESR, KL-6) in all treatment groups. These levels go down from immunosuppressants to TNF- α inhibitors, corticosteroids, and healthy controls. This corresponds with the efficacy of corticosteroids in swiftly diminishing disease activity, whereas immunosuppressants and TNF- α inhibitors facilitate progressive enhancement. Autoantibody profiles exhibited modest ANA positivity, especially in individuals undergoing treatment with immunosuppressants and corticosteroids, however no relationships with clinical severity were seen (54). The low level of RF supports the idea that sarcoidosis doesn't have the serologic signs that are common in connective tissue illnesses. This is further shown by the fact that anti-CCP was not positive (55). TNF- α inhibitors usually help with inflammation, however there have been a few cases when they have the opposite effect (56).

The study shows that individuals on traditional immunosuppressants have a lot of musculoskeletal problems. For example, 30% of them have arthralgia or arthritis, 8% have bone problems, and 5% have myopathy or myositis. On the other hand, the TNF- α inhibitor (G2) and corticosteroid (G3) groups had rates of 30% and 20%, respectively, which were much lower than the rates in healthy controls (0%). Corticosteroids are highlighted as the principal therapy for symptomatic musculoskeletal sarcoidosis due to their quick anti-inflammatory effects. Immunosuppressants like methotrexate and azathioprine are only used for patients that don't respond to other treatments, but they don't always work completely. TNF- α inhibitors work well for MSK sarcoidosis that doesn't respond to other treatments (57). Corticosteroids provide rapid amelioration; however, prolonged usage is constrained by adverse effects, necessitating a transition to steroid-sparing and biologic therapy. Chronic manifestations of musculoskeletal sarcoidosis may persist as treatment-resistant, exhibiting possible relapses and problems generated by corticosteroids (58, 59).

Conclusion

Sarcoidosis is a multisystem granulomatous disorder affecting the lungs, skin, eyes, neurological system, liver, and heart. It is more common in women and causes extra-pulmonary symptoms. Corticosteroids are effective in lowering calcium levels and rectifying metabolic abnormalities, while lifestyle adjustments and oxygen therapy provide moderate benefits. CT and HRCT is the main tools to diagnose sarcoidosis.

References

- 1. Franzen DP, Brutsche M, Nilsson J, Böni C, Daccord C, Distler O, Elsener D, Funke-Chambour M, Gruner C, Hayward-Könnecke H, Hostettler KE. Sarcoidosis-a multisystem disease. Swiss medical weekly. 2022 Jan 3;152(w30049):w30049.
- 2. Kadura S, Raghu G. Rheumatoid arthritis-interstitial lung disease: manifestations and current concepts in pathogenesis and management. European Respiratory Review. 2021.
- 3. Valeyre D, Jeny F, Rotenberg C, Bouvry D, Uzunhan Y, Sève P, Nunes H, Bernaudin JF. How to tackle the diagnosis and treatment in the diverse scenarios of extrapulmonary sarcoidosis. Advances in therapy. 2021 Sep;38:4605-27.
- 4. Sreeja C, Priyadarshini A, Nachiammai N. Sarcoidosis—A review article. Journal of Oral and Maxillofacial Pathology. 2022 Apr 1;26(2):242-53.
- 5. Tana C, Donatiello I, Caputo A, Tana M, Naccarelli T, Mantini C, Ricci F, Ticinesi A, Meschi T, Cipollone F, Giamberardino MA. Clinical features, histopathology and differential diagnosis of sarcoidosis. Cells. 2021 Dec 26;11(1):59.
- 6. Machado A, Marques A, Burtin C. Extra-pulmonary manifestations of COPD and the role of pulmonary rehabilitation: a symptom-centered approach. Expert review of respiratory medicine. 2021 Jan 2;15(1):131-42
- 7. Itkin M, Rockson SG, Burkhoff D. Pathophysiology of the lymphatic system in patients with heart failure: JACC state-of-the-art review. Journal of the American College of Cardiology. 2021 Jul 20;78(3):278-90.
- 8. Lehtonen J, Uusitalo V, Pöyhönen P, Mäyränpää MI, Kupari M. Cardiac sarcoidosis: phenotypes, diagnosis, treatment, and prognosis. European heart journal. 2023 May 1;44(17):1495-510.
- 9. Dasovic B, Borys E, Schneck MJ. Granulomatous diseases of the central nervous system. Current Neurology and Neuroscience Reports. 2022 Jan;22(1):33-45.
- 10. Twain M. Musculoskeletal Pathologies, Disorders, and Injuries. Mosby's Pathology for Massage Professionals-E-Book: Mosby's Pathology for Massage Professionals-E-Book. 2021 Sep 5;114.
- 11. Gourtsoyianni S, Laniado M, Ros-Mendoza... L. The spectrum of solitary benign splenic lesions—Imaging clues for a noninvasive diagnosis. Diagnostics. 2023.
- 12. Nicolosi S, Chernovsky M, Angoni D, Hughes M, Bandini G, McMahan Z, Maggisano M, Salton F, Mondini L, Barbieri M, Screm G. Gastrointestinal Manifestations of Sarcoidosis: A State-of-the-Art, Comprehensive Review of the Literature—Practical Clinical Insights and Many Unmet Needs on Diagnosis and Treatment. Pharmaceuticals. 2024 Aug 23;17(9):1106.
- 13. Belperio JA, Shaikh F, Abtin FG, Fishbein MC, Weigt SS, Saggar R, Lynch JP. Diagnosis and treatment of pulmonary sarcoidosis: a review. Jama. 2022 Mar 1;327(9):856-67.
- 14. Canan A, Ghandour AAH, Saboo... SS. Opportunistic screening at chest computed tomography: literature review of cardiovascular significance of incidental findings. ... Diagnosis and 2023.
- 15. Palmucci S, Torrisi SE, Caltabiano DC, Puglisi S et al. Clinical and radiological features of extra-pulmonary sarcoidosis: a pictorial essay. 2016.
- 16. Saketkoo LA, Russell AM, Jensen K, Mandizha J, Tavee J, Newton J, Rivera F, Howie M, Reese R, Goodman M, Hart P. Health-related quality of life (HRQoL) in sarcoidosis: diagnosis, management, and health outcomes. Diagnostics. 2021 Jun 15;11(6):1089.
- 17. Negm, Dalia A.E.M.A.E.R.a; Elzefzafy, Wafaa M.A.E.-W.b; El Raheem, Sabah E.A.c; El Deen, NessrenM.B.b. Serum amyloid A protein as a predictor of severity in coronavirus disease 2019-infected Egyptian patients. Al-Azhar Assiut Medical Journal 21(3):p 156-164, July-September 2023. | DOI: 10.4103/azmj.azmj_30_23
- 18. Palmucci S, Torrisi SE, Caltabiano DC, Puglisi S, Lentini V, Grassedonio E, Vindigni V, Reggio E, Giuliano R, Micali G, Caltabiano R, Andreula C, Foti PV, Ettorre GC, Walsh SL, Vancheri C. Clinical and radiological features of extra-pulmonary sarcoidosis: a pictorial essay. Insights Imaging. 2016 Aug;7(4):571-87. doi: 10.1007/s13244-016-0495-4. Epub 2016 May 25.

- 19. Abdel Kareem, Mohamed I.a; Rayan, Mohamed M.b; Mohamed, Heba K.c,. Variation in dermatoglyphic patterns in patients with rheumatoid arthritis. Al-Azhar Assiut Medical Journal 18(4):p 396-407, Oct–Dec 2020. | DOI: 10.4103/AZMJ.AZMJ 162 19
- 20. Zhou Y, Gerke AK, Lower EE, Vizel A, Talwar D, Strambu I, Francesqui J, Sellares J, Sawahata M, Obi ON, Nagai S, Tanizawa K, Judson MA, Jeny F, Valeyre D, Cunha Castro MD, Pereira C, Balter M, Baughman RP. The impact of demographic disparities in the presentation of sarcoidosis: A multicenter prospective study. Respir Med. 2021 Oct;187:106564. doi: 10.1016/j.rmed.2021.106564. Epub 2021 Aug 9.
- 21. Brito-Zerón P, Sellarés J, Bosch X, Hernández F, Kostov B, Sisó-Almirall A, Casany CL, Santos JM, Paradela M, Sanchez M, Ramírez J. Epidemiologic patterns of disease expression in sarcoidosis: age, gender and ethnicity-related differences. Clin Exp Rheumatol. 2016 May 1;34(3):380-8.
- 22. Ungprasert P, Crowson CS, Matteson EL. Epidemiology and clinical characteristics of sarcoidosis: an update from a population-based cohort study from Olmsted County, Minnesota. Reumatismo. 2017 May 22;69(1):16-22. doi: 10.4081/reumatismo.2017.965. PMID: 28535617; PMCID: PMC5521258.
- 23. Hattori, T., Konno, S., Shijubo, N. et al. Nationwide survey on the organ-specific prevalence and its interaction with sarcoidosis in Japan. Sci Rep 8, 9440 (2018). https://doi.org/10.1038/s41598-018-27554-3
- 24. Te HS, Perlman DM, Shenoy C, Steinberger DJ, Cogswell RJ, Roukoz H, Peterson EJ, Zhang L, Allen TL, Bhargava M. Clinical characteristics and organ system involvement in sarcoidosis: comparison of the University of Minnesota Cohort with other cohorts. BMC Pulm Med. 2020 Jun 1;20(1):155. doi: 10.1186/s12890-020-01191-x.
- 25. Gupta D, Rao VM, Aggarwal AN, Garewal G, Jindal SK. Haematological abnormalities in patients of sarcoidosis. Indian J Chest Dis Allied Sci. 2002 Oct-Dec;44(4):233-6. PMID: 12437235.
- 26. Crouser ED, Maier LA, Wilson KC, Bonham CA, Morgenthau AS, Patterson KC, Abston E, Bernstein RC, Blankstein R, Chen ES, Culver DA. Diagnosis and detection of sarcoidosis. An official American Thoracic Society clinical practice guideline. American journal of respiratory and critical care medicine. 2020 Apr 15;201(8):e26-51.
- 27. Zheng SY, Du X, Dong JZ. Re-evaluating serum angiotensin-converting enzyme in sarcoidosis. Frontiers in immunology. 2023 Oct 5;14:950095.
- 28. d'Alessandro M, Bergantini L, Perrone A, Cameli P, Cameli M, Prasse A, Plataroti D, Sestini P, Bargagli E. Serial investigation of angiotensin-converting enzyme in sarcoidosis patients treated with angiotensin-converting enzyme inhibitor. European journal of internal medicine. 2020 Aug 1;78:58-62.
- 29. Fernández-Valmaña A, López-Martínez J, Mayer-Fuentes A, Mas-Maresma L, Feijoo-Masso C. AB0786 ASSOCIATION BETWEEN ANGIOTENSIN-CONVERTING ENZYME VALUES AND EPIDEMIOLOGICAL FEATURES, ORGAN AND MULTI-ORGAN INVOLVEMENT IN SARCOIDOSIS: A SINGLE-CENTER RETROSPECTIVE STUDY. Annals of the Rheumatic Diseases. 2024 Jun 1;83:1685-6.
- 30. Della Zoppa M, Bertuccio FR, Campo I, Tousa F, Crescenzi M, Lettieri S, Mariani F, Corsico AG, Piloni D, Stella GM. Phenotypes and Serum Biomarkers in Sarcoidosis. Diagnostics. 2024 Mar 27;14(7):709.
- 31. Correia FASC, Marchini GS, Torricelli FC, Danilovic A, Vicentini FC, Srougi M, Nahas WC, Mazzucchi E. Renal manifestations of sarcoidosis: from accurate diagnosis to specific treatment. Int Braz J Urol. 2020 Jan-Feb;46(1):15-25. doi: 10.1590/S1677-5538.IBJU.2019.0042. PMID: 31851454; PMCID: PMC6968907.
- 32. Brugnaro P, Cattelan F, Morelli E, Petrucci A, Marocco A, Panese S, Donisi PM, Capitanio G, Tollot M. A case of hepatic and bone marrow sarcoidosis with progressive renal failure: diagnostic and therapeutic challenges. Sarcoidosis Vasc Diffuse Lung Dis. 2022 Dec 19;39(4):e2022041. doi: 10.36141/svdld.v39i4.11350. PMID: 36533607; PMCID: PMC9798336.
- 33. Aksoy E, Tunçay E, Ocakli B, Bekir SA, Güngör S, Akyıl FT, Sucu P, Yavuz D, Yalçınsoy M. Extrapulmonary Sarcoidosis with Multiple-Organ Involvement. Southern Clinics of Istanbul Eurasia. 2018 Jan 1;29(1).
- 34. Gerke AK. Treatment of sarcoidosis: a multidisciplinary approach. Frontiers in immunology. 2020 Nov 19;11:545413.

- 35. Rastelli F, Baragetti I, Buzzi L, Ferrario F, Benozzi L, Di Nardo F, Devoti E, Cancarini G, Mezzina N, Napodano P, Gallieni M. Renal involvement in sarcoidosis: histological patterns and prognosis, an Italian survey. Sarcoidosis, Vasculitis, and Diffuse Lung Diseases. 2021 Sep 30;38(3):e2021017.
- 36. Belfeki N, Kammoun S, Ghriss N, Eldirani C, Mekinian A. Current concepts on pathogenesis, diagnosis and management of hepatic sarcoidosis. Rheumatology International. 2025 May;45(5):1-5.
- 37. Saha BK, Burns SL, Foulke LA, Judson MA. Rare case of parathyroid gland sarcoidosis presenting with hypercalcaemia. BMJ Case Rep. 2019 Jul 15;12(7):e230598. doi: 10.1136/bcr-2019-230598. PMID: 31308180; PMCID: PMC6663241.
- 38. Dodos K, Kalamara VT, Georgakopoulou VE, Kavoura P. Primary Hypoparathyroidism in a Patient With Sarcoidosis: A Case Report. Cureus. 2024 Sep 16;16(9):e69504. doi: 10.7759/cureus.69504. PMID: 39416579; PMCID: PMC11480926...
- 39. Kato Y, Morimoto S, Uemura A, Hiramitsu S, Ito T, Hishida H. Efficacy of corticosteroids in sarcoidosis presenting with atrioventricular block. Sarcoidosis Vasc Diffuse Lung Dis. 2003 Jun;20(2):133-7. PMID: 12870723.
- 40. Di Marco Berardino A, Mei F, Zuccatosta L. Safety of corticosteroid therapy in sarcoidosis treatment. Frontiers in Drug Safety and Regulation. 2023 Dec 14;3:1319931.
- 41. Obi ON, Saketkoo LA, Russell AM, Baughman RP. Sarcoidosis: Updates on therapeutic drug trials and novel treatment approaches. Front Med (Lausanne). 2022 Oct 12;9:991783. doi: 10.3389/fmed.2022.991783. PMID: 36314034; PMCID: PMC9596775.
- 42. Bradshaw MJ, Pawate S, Koth LL, Cho TA, Gelfand JM. Neurosarcoidosis: pathophysiology, diagnosis, and treatment. Neurology: Neuroimmunology & Neuroinflammation. 2021 Oct 4;8(6):e1084.
- 43. Saifee T, Farmer S, Shah S, Choi D. Spinal column and spinal cord disorders. Neurology: a queen square textbook. 2024 May 13:463-98.
- 44. Kozyolkin OA, Vizir IV, Sikorskay MV. Infectious and parasitic disease of the nervous system: textbook for students-foreign citizen IV course of medical faculties of the speciality "Medicine".
- 45. Sanghi V, Kapoor A. Unusual presentation of central diabetes insipidus in a patient with neurosarcoidosis. Journal of Investigative Medicine High Impact Case Reports. 2016 Sep;4(3):2324709616667511.
- 46. Falorni A, De Fano M, Bartoloni E, Perricone C, Cafaro G, Gerli R. Autoimmune Hypophysitis. InAutoimmune Disease Diagnosis: Systemic and Organ-specific Diseases 2025 Jan 4 (pp. 381-386). Cham: Springer Nature Switzerland.
- 47. Bradshaw MJ, Pawate S, Koth LL, Cho TA, Gelfand JM. Neurosarcoidosis: pathophysiology, diagnosis, and treatment. Neurology: Neuroimmunology & Neuroinflammation. 2021 Oct 4;8(6):e1084.
- 48. El-Hossainy, Ahmad F.a,; Mustafa, Fawzy M.a; Shazly, Mohamad A.b; Yousef Selim, Yousef A.c. Role of computerized tomography in the management of intestinal obstruction in adults. Al-Azhar Assiut Medical Journal 17(4):p 321-330, Oct–Dec 2019. | DOI: 10.4103/AZMJ.AZMJ_72_18
- 49. Corcoran HL, Renner WR, Milstein MJ. Review of high-resolution CT of the lung. Radiographics. 1992 Sep;12(5):917-39.
- 50. Valeyre D, Brauner M, Bernaudin JF, Carbonnelle E, Duchemann B, Rotenberg C, Berger I, Martin A, Nunes H, Naccache JM, Jeny F. Differential diagnosis of pulmonary sarcoidosis: a review. Front Med (Lausanne). 2023 May 12;10:1150751. doi: 10.3389/fmed.2023.1150751. PMID: 37250639; PMCID: PMC10213276.
- 51. Le L, Narula N, Zhou F, Smereka P, Ordner J, Theise N, Moore WH, Girvin F, Azour L, Moreira AL, Naidich DP. Diseases Involving the Lung Peribronchovascular Region: a CT-Pathologic Classification. Chest. 2024 Jun 22.
- 52. Sève P, Pacheco Y, Durupt F, Jamilloux Y, Gerfaud-Valentin M, Isaac S, Boussel L, Calender A, Androdias G, Valeyre D, El Jammal T. Sarcoidosis: a clinical overview from symptoms to diagnosis. Cells. 2021 Mar 31;10(4):766.
- 53. Criado E, Sánchez M, Ramírez J, Arguis P, De Caralt TM, Perea RJ, Xaubet A. Pulmonary sarcoidosis: typical and atypical manifestations at high-resolution CT with pathologic correlation. Radiographics. 2010 Oct;30(6):1567-86.

- 54. Callejas-Rubio JL, López-Pérez L, Ortego-Centeno N. Tumor necrosis factor-alpha inhibitor treatment for sarcoidosis. Ther Clin Risk Manag. 2008 Dec;4(6):1305-13. doi: 10.2147/tcrm.s967.
- 55. Pozzan R, Salton F, Confalonieri P, Trotta L, Barbieri M, Reccardini N, Torregiani C, Screm G, Hughes M, Baratella E, Confalonieri M, Mondini L, Ruaro B. Autoantibodies in sarcoidosis: Innocent bystander or promising biomarker for organ involvement? Sarcoidosis Vasc Diffuse Lung Dis. 2024 Dec 10;41(4):e2024056. doi: 10.36141/svdld.v41i4.16043.
- 56. Aung T, Prasanpanich M, Kaplan A, Eblen K, Fishbein GA. Tumor Necrosis Factor-Alpha Inhibitor-Induced Sarcoid-Like Reaction in a Patient With Juvenile Idiopathic Arthritis: A Case Report. Cureus. 2025 May 28;17(5):e84970. doi: 10.7759/cureus.84970.
- 57. Smedslund G, Kotar AM, Uhlig T. Sarcoidosis with musculoskeletal manifestations: systematic review of non-pharmacological and pharmacological treatments. Rheumatol Int. 2022 Dec;42(12):2109-2124. doi: 10.1007/s00296-022-05171-8. Epub 2022 Aug 9.
- 58. Yıldırım F, Kalkan K, Akkuzu G, Özgür DS, Karaalioğlu B, Deniz R. Musculoskeletal involvement in sarcoidosis: A single center experience. J Turk Soc Rheumatol. 2024 Jul 22;16(2):57-63. doi: 10.4274/raed.galenos.2024.73645.
- 59. Nessrine A, Zahra AF, Taoufik H. Musculoskeletal involvement in sarcoidosis. Jornal Brasileiro de Pneumologia. 2014 Mar;40:175-82.