

ORIGINAL ARTICLE

HIGH RESOLUTION CT TYPICAL PATTERNS IN PULMONARY SARCOIDOSIS: CORRELATION WITH CLINICAL SYMPTOMS AND RADIOLOGICAL STAGING

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Abstract:

Introduction: Sarcoidosis is a multisystemic and often chronic disease that can involve nearly any organ. The lungs and intrathoracic lymph nodes are the most commonly affected structures.

The aim: of the study is to classify the stages of sarcoidosis and analyze their correlation with clinical symptoms.

Material and Methods: A total of 50 patients with sarcoidosis came to our University Clinic for Pulmonology and Allergology-Skopje during 2022-2023 period - a retrospective observational study. A high-resolution computed tomography (HRCT) using a 128-slice PHILIPS INCISIVE CT scanner was performed to all patients, using a 1 mm thin-slice protocol optimized for thoracic imaging. Disease staging was conducted according to the Scadding Score System. Clinical symptoms such as smoking, dyspnea and cough were identified from the MOJ TERMIN medical records and compared with the stage of the disease.

Results: The disease stage did not significantly correlate with the patients' sex and age, but it did significantly correlate with their place of residence. There was a statistically significant difference in the distribution of former smokers across disease stages, driven by the significantly higher proportion of former smokers in stage III compared to stage II. The disease stage had a significant impact on patient hospitalization. The disease stage had a significant impact on the presence of reticular opacities in the upper and middle zones.

Key words: *HRCT; lungs; sarcoidosis; staging; symptoms.*

Introduction:

Sarcoidosis is a systemic inflammatory disease of unknown etiology, characterized by the formation of non-caseating granulomas in various organs, most commonly the lungs and intrathoracic lymph nodes. The disease may affect multiple organ systems, resulting in a broad spectrum of clinical manifestations. Diagnosis is typically established through a combination of clinical manifestation, radiologic findings, and histopathological confirmation of granulomatous inflammation.

Imaging plays a central role in both the diagnosis and monitoring of sarcoidosis. While chest radiography is often the first-line imaging modality, it has notable limitations—particularly its lower sensitivity for detecting parenchymal changes and mediastinal lymphadenopathy. In contrast, computed tomography (CT) provides greater sensitivity in identifying both pulmonary and nodal involvement (1,2).

High-resolution computed tomography (HRCT) offers even higher spatial resolution than standard CT, allowing for detailed visualization of subtle parenchymal abnormalities and fine structural changes within the lungs (3). HRCT is especially useful in differentiating active inflammatory lesions—representing potentially reversible disease—from irreversible fibrotic changes. This distinction is critical for prognosis and therapeutic decision-making. Moreover, HRCT is invaluable in evaluating atypical or ambiguous radiographic findings and is widely regarded as the gold standard for thoracic imaging in sarcoidosis (4).

This study aims to classify the stages of sarcoidosis and analyze their correlation with clinical symptoms

Material and Methods: A total of 50 patients who came to our hospital with a confirmed diagnosis of sarcoidosis were enrolled over a two-year period at the University Clinic for Pulmonology and Allergology in Skopje- a retrospective observational study. Patients, who have previously signed an informed consent, participated in the study voluntarily. The study was conducted with the consent of the Ethics Commission of the Faculty of Medicine in Skopje and was in accordance with the ethical principles of the Declaration of Helsinki of the World Medical Association for medical research involving human subjects.

A high-resolution computed tomography (HRCT) using a 128-slice PHILIPS INCISIVE CT scanner were performed to all patients, using a 1 mm thin-slice protocol and specialized reconstruction algorithm optimized for thoracic imaging. HRCT images were assessed using standard lung and mediastinal window settings. Lymph nodes were anatomically classified as hilar or mediastinal, and enlargement was defined as a maximum short-axis diameter (MSAD) greater than 10 mm. Disease staging was conducted according to the Scadding Score System: stage 0 – normal; stage I – hilar or mediastinal lymph node enlargement; stage II – lymphadenopathy with parenchymal involvement; stage III – parenchymal disease without nodal enlargement; and stage IV – advanced fibrotic changes indicating end-stage pulmonary disease. Pulmonary parenchymal abnormalities were categorized as nodules (micronodules: 1–3 mm; macronodules: >5 mm), reticular opacities, fibrotic lesions, ground-glass opacities, and confluent consolidations. Nodular distribution was further classified into perilymphatic, centrilobular, and random patterns. Additionally, the predominant localization of pulmonary lesions was documented according to lung zones: upper, middle, or lower. Clinical symptoms such as smoking, dyspnea and cough were identified from the MOJ TERMIN medical records and compared with the stage of the disease.

Results:

The statistical analysis of the data obtained from the study was performed using the statistical software SPSS version 23.0.

Categorical (attribute) variables are presented using absolute and relative frequencies. Numerical (quantitative) variables are presented with the mean, standard deviation, minimum, and maximum values.

We used Fisher's exact test to compare the HRCT findings between smokers and non-smokers, patients with and without cough, and among different disease stages.

Statistical significance was defined at a level of $p < 0.05$.

The relevant data are presented in tables and graphs.

The disease stage did not significantly correlate with the patients' sex and age ($p = 1.0$ and $p = 0.55$), but it did significantly correlate with their place of residence ($p = 0.023$). All patients in stages III and IV were from urban areas.

Current smokers did not have a significantly different distribution across the four disease stages (16.67% in stage II vs 22.22% in stage IV; $p = 0.81$). However, there was a statistically significant difference in the distribution of former smokers across disease stages ($p = 0.014$), driven by the significantly higher proportion of former smokers in stage III compared to stage II (100% vs. 25%; $p = 0.01$). A statistically significant difference in the frequency of dyspnea was confirmed between patients in stages 1 and 4 ($p = 0.026$).

The disease stage had a significant impact on patient hospitalization ($p < 0.0001$). Pairwise group comparisons showed significant differences between stages I and IV (9.09% vs. 75%, $p = 0.014$), and between stages II and IV (50% vs. 75%, $p = 0.0001$).

Only 2 out of 4 patients in stage III (50%) had a positive family history of pulmonary disease.

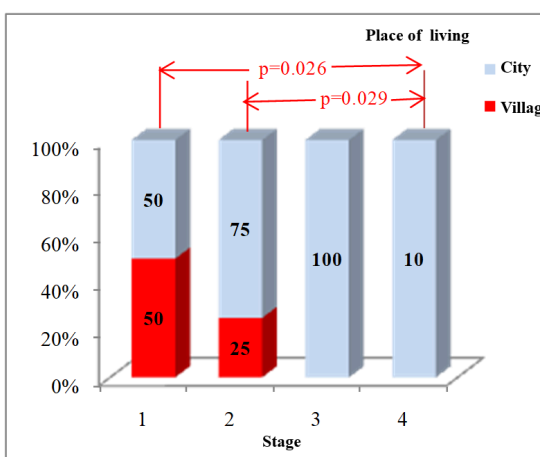
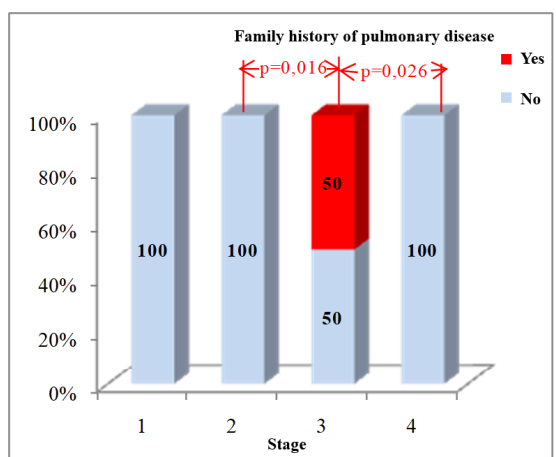
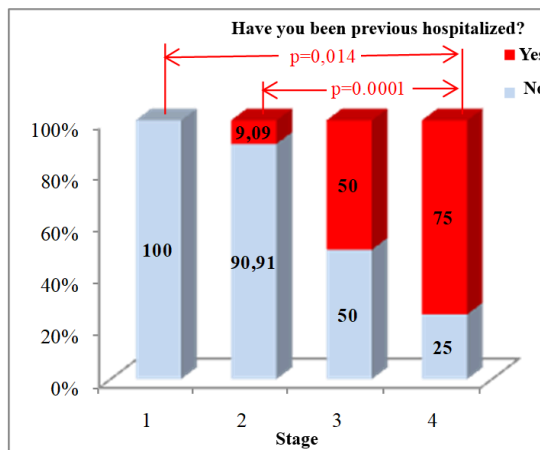
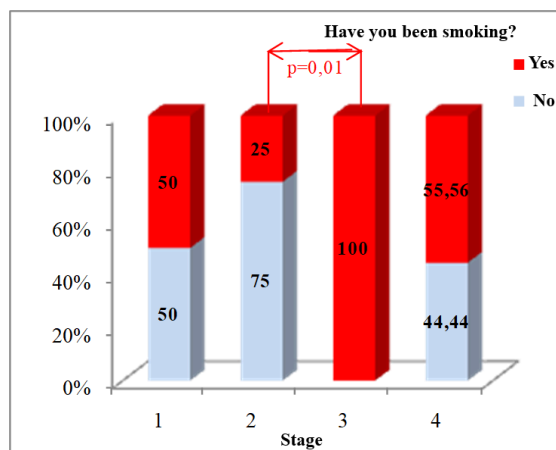
Table 1: Gender Distribution, Residence, Smoking Status, Hospitalizations, and Genetic Predisposition by Sarcoidosis Stage

variable		Stage				p-level
		1 n=4 (%)	2 n=24 (%)	3 n=4 (%)	4 n=18 (%)	
Gender	femal e	4(100)	22(91.67)	4(100)	16(88.89)	p=1.0
	male	0	2(8.33)	0	2(11.11)	
Place of living	city	2(50)	18(75)	4(100)	18(100)	*p=0.023 1 vs 4 p=0.026 2 vs 4 p=0.029
	villag e	2(50)	6(25)	0	0	
Do you smoke?	yes	0	4(16.67)	0	4(22.22)	p=0.81
	no	4(100)	20(83.33)	4(100)	14(77.78)	
Have you been smoking?	yes	2(50)	6(25)	4(100)	10(55.56)	*p=0.014 2 vs 3 p=0.01
	no	2(50)	18(75)	0	8(44.44)	
Have you been previous hospitalized ?	yes	0	2(9.09)	2(50)	12(75)	***p=0.0001 0 1 vs 4 p=0.014 2 vs 4 p=0.0001
	no	4(100)	20(90.91)	2(50)	4(25)	
Family history of	yes	0	0	2(50)	0	**p=0.01 2 vs 3 p=0.016
	no	4(100)	24(100)	2(50)	18(100)	

pulmonary disease						3 vs 4 p=0.026
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p (Fisher's exact test)

*sig p<0.05, **sig p<0.01, ***sig p<0.0001



The stage of the disease was not significantly associated with cough presence or cough intensity ($p = 0.71$); all patients in stages 1 and 3 had cough, as did 75% of patients in stage 2 and 77.78% in stage 4.

Regarding the distribution of patients by stage and cough intensity: mild cough was present in patients across all stages, most commonly in stage 1 (100%). Severe cough occurred only in stage 4 patients (28.57%). There was no statistically significant difference in the distribution of mild, moderate, and severe cough among disease stages ($p = 0.06$).

Shortness of breath was reported by 50% of patients in stage 1, 58.33% in stage 2, and by all patients in stages 3 and 4. A statistically significant difference in the frequency of dyspnea was confirmed between patients in stages 1 and 4 ($p = 0.026$).

Results from the MRC (Medical Research Council) scale differed significantly across disease stages ($p < 0.0001$):

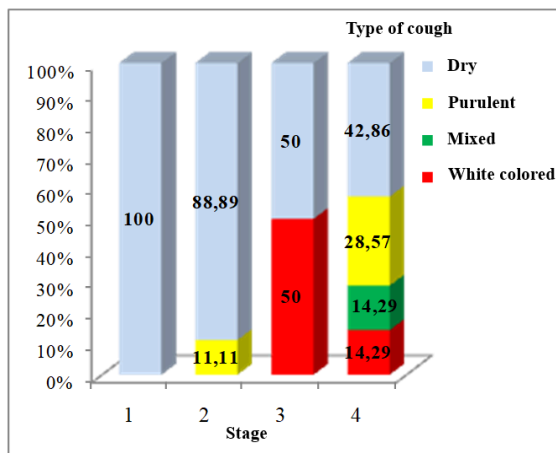
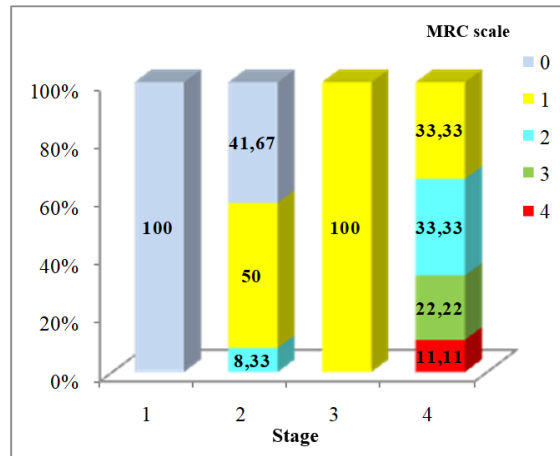
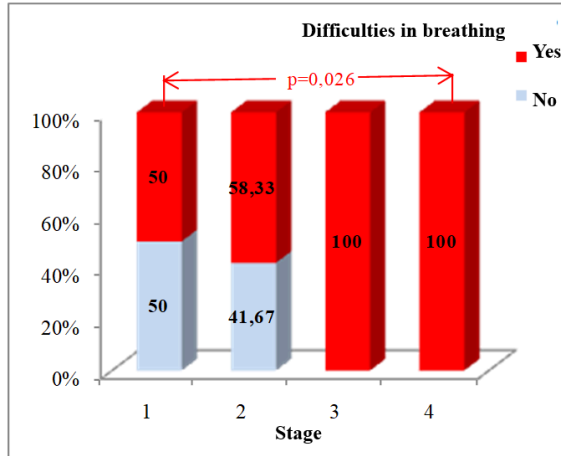
- All stage 1 patients scored MRC 0 (dyspnea only during strenuous exercise);
- Most stage 2 patients had MRC 1 (dyspnea when walking fast on flat ground or climbing a slight hill); this score was also seen in all stage 3 patients;
- Stage 4 patients frequently had MRC 1 and MRC 2 (dyspnea when walking fast on flat ground or climbing a slight hill, and when walking on flat ground for a few minutes)—33.33%.

Table 2: Clinical Characteristics of Patients According to Sarcoidosis Stage

variable		Stage				p-level
		1 n=4 (%)	2 n=24 (%)	3 n=4 (%)	4 n=18 (%)	
Do you cough	yes	4(100)	18(75)	4(100)	14(77.78)	p=0.71
	no	0	6(25)	0	4(22.22)	
Intensity of cough	mild	4(100)	10(55.56)	2(50)	4(28.57)	p=0.06
	moderate	0	8(44.44)	2(50)	6(42.86)	
	severe	0	0	0	4(28.57)	
Type of cough	dry	4(100)	16(88.89)	2(50)	6(42.86)	*p=0.032
	purulent	0	2(11.11)	0	4(28.57)	
	Mixed	0	0	0	2(14.29)	
	White colored	0	0	2(50)	2(14.29)	
Difficulties in breathing	yes	2(50)	14(58.33)	4(100)	18(100)	**p=0.003 1 vs 4 p=0.026
	no	2(50)	10(41.67)	0	0	
MRC scale	0	4(100)	10(41.67)	0	0	***p=0.000
	1	0	12(50)	4(100)	6(33.33)	
	2	0	2(8.33)	0	6(33.33)	
	3	0	0	0	4(22.22)	
	4	0	0	0	2(11.11)	

p (Fisher's exact test)

*sig p<0.05, **sig p<0.01, ***sig p<0.0001



The disease stage had a significant impact on the presence of reticular opacities in the upper and middle zones ($p = 0.023$); 8.33% of stage 2 patients and 44.44% of stage 4 patients had this finding on HRCT, with a statistically significant difference ($p = 0.01$).

In the lower lung zones, reticular opacities in peripheral and subpleural regions were found in 16.67% of stage 2 patients and 44.44% of stage 4 patients. No statistically significant difference was observed in the frequency of such findings across all four disease stages ($p = 0.096$).

A statistically significant difference in the distribution of patients with and without peribronchovascular reticular opacities in the lower zones was confirmed ($p = 0.003$). Such opacities were noted in 8.33% of stage 2 patients and 55.56% of stage 4 patients, with a statistically significant difference ($p = 0.0014$).

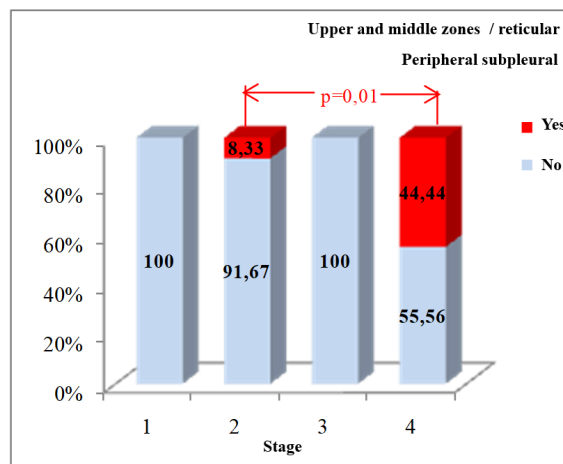
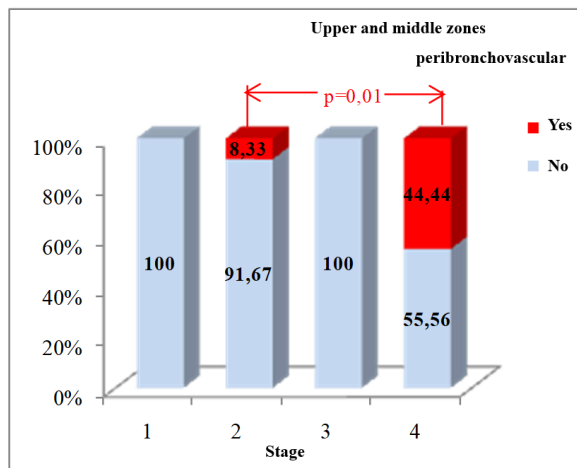
Table 3: Distribution of Reticular Changes According to Sarcoidosis Stage

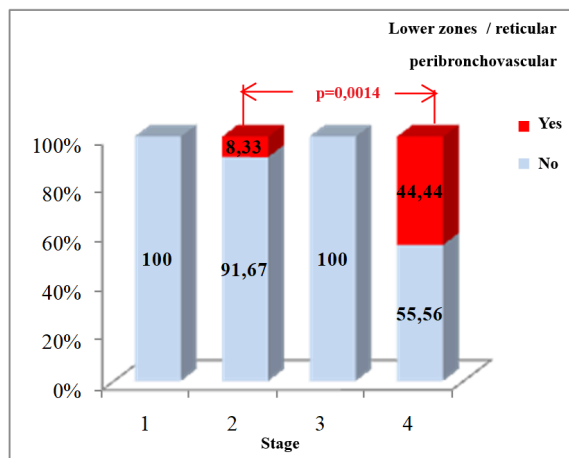
variable	Stage				p-level
	1 n=4 (%)	2 n=24 (%)	3 n=4 (%)	4 n=18 (%)	
Upper and middle zones					

reticular	Peripheral subpleural	yes	0	2 (8.33)	0	8(44.44)	*p=0.023 2 vs 4 p=0.01	
		no	4 (100)	22(91.67)	4(100)	10(55.56)		
	peribronchovascular	yes	0	2 (8.33)	0	8(44.44)		
		no	4 (100)	22(91.67)	4(100)	10(55.56)		
Lower zones								
reticular	Peripheral subpleural	yes	0	4(16.67)	0	8(44.44)	p=0.096	
		no	4(100)	20(83.33)	4(100)	10(55.56)		
	peribronchovascular	yes	0	2 (8.33)	0	10(55.56)		**p=0.003 2 vs 4 p=0.0014
		no	4(100)	22(91.67)	4(100)	8(44.44)		

p (Fisher's exact test)

*sig p<0.05, **sig p<0.01, ***sig p<0.0001





No statistically significant difference was found in the frequency of micronodular changes sized 1–3 mm and >3 mm in the upper and middle lung zones across disease stages ($p > 0.05$). Peribronchovascular micronodular opacities 1–3 mm were most common in stage 2 patients (25%), perilymphatic micronodular opacities 1–3 mm in peribronchovascular regions were most common in stage 4 patients (33.33%), perilymphatic micronodular changes 1–3 mm in subpleural regions were most frequently detected in stage 3 patients (50%), and these stage 3 patients also most often showed micronodular changes >3 mm in peripheral and subpleural regions (50%). Micronodular opacities >3 mm in peribronchovascular regions were most often seen in stage 2 patients (33.33%). In the lower lung zones, peribronchovascular micronodular opacities 1–3 mm were detected in 50% of stage 3 patients and 11.11% of stage 4 patients; this HRCT finding showed a statistically significant difference across disease stages ($p = 0.018$). Other localizations of micronodular changes in the lower lung zones

Table 4: Distribution of Micronodular Changes by Sarcoidosis Stage

Micronodular opacities		Stage				p-level	
		1 n=4 (%)	2 n=24 (%)	3 n=4 (%)	4 n=18 (%)		
Upper and middle zones							
Micronodular opacities (1-3 MM)	Centrilobular	yes	0	0	0	0	p=0.46
		no	4(100)	24(100)	4(100)	18(100)	
	Peribronchovascular	yes	0	6(25)	0	2(11.11)	
		no	4 (100)	18(75)	4(100)	16(88.89)	
Micronodular opacities (1-3 MM) Perilymphatic	Peribronchovascular	yes	0	6(25)	2(50)	6(33.33)	p=0.45
		no	4 (100)	18(75)	2(50)	12(66.67)	

	Subpleural	yes	0	4(16.67)	2(50)	4(22.22)	p=0.33	
		no	4 (100)	20(83.33)	2(50)	14(77.78)		
Micronodular opacities (>3 MM)	Periferal and subpleural	yes	0	6(25)	2(50)	2(11.11)	p=0.21	
		no	4 (100)	18(75)	2(50)	16(88.89)		
	Peribronchovascular	yes	0	8(33.33)	0	2(11.11)	p=0.18	
		no	4 (100)	16(66.67)	4(100)	16(88.89)		
Lower zones								
Micronodular opacities (1-3 MM)	Centrilobular	yes	0	0	0	0		
		no	4(100)	24(100)	4(100)	18(100)		
	Peribronchovascular	yes	0	0	2(50)	2(11.11)		*p=0.018 2 vs 3 p=0.016
		no	4(100)	24(100)	2(50)	16(88.89)		
Micronodular opacities (1-3 MM) perilymphatic	Peribronchovascular	yes	0	2 (8.33)	0	0	p=0.65	
		no	4(100)	22(91.67)	4(100)	18(100)		
	Subpleural	yes	0	2 (8.33)	0	0	p=0.65	
		no	4(100)	22(91.67)	4(100)	18(100)		
Micronodular opacities (>3 MM)	Peripheral and subpleural	yes	0	0	0	2(11.11)	p=0.65	
		no	4(100)	24(100)	4(100)	16(88.89)		
	Peribronchovascular	yes	0	2 (8.33)	0	0	p=0.65	
		no	4(100)	22(91.67)	4(100)	18(100)		

p (Fisher's exact test)

*sig p<0.05

Enlarged lymph nodes were detected in patients at stages 1, 2, and 4. A statistically significant difference was confirmed among the four disease-stage groups in the prevalence of bilateral hilar lymphadenopathy (p = 0.003), right paratracheal lymphadenopathy (p = 0.001), and other nodal stations (p < 0.0001). Bilateral hilar lymphadenopathy was detected in 100% of stage 1 patients 83, 33% of stage 2 patients and 55, 56% of stage 4 patients with pairwise comparisons showing

statistically significant differences between stages 1 and 3 ($p = 0.019$) and between stages 2 and 3 ($p = 0.0034$). Right paratracheal lymphadenopathy was seen in 100% of stage 1 patients 91, 67% of stage 2 patients and 77, 78% of stage 4 patients with significant differences found between stages 1 and 3 ($p = 0.019$), stages 2 and 3 ($p = 0.007$), and stages 3 and 4 ($p = 0.0096$).

Table 5: Distribution of Lymphadenopathy, Calcified Lymph Nodes, and Additional Findings by Sarcoidosis Stage

variable			Stage				p-level
			1 n=4 (%)	2 n=24 (%)	3 n=4 (%)	4 n=18 (%)	
Lymphadenopathy	Bilateral hilar	yes	4(100)	20(83.33)	0	10(55.56)	**p=0.003 1vs3 p=0.019 2vs3 p=0.0034
		no	0	4(16.67)	4(100)	8(44.44)	
	Right paratracheal	yes	4(100)	22(91.67)	0	14(77.78)	**p=0.001 1vs3 p=0.019 2vs3 p=0.0007 3vs4 p=0.0096
		no	0	2(8.33)	4(100)	4(22.22)	
	Other nodal stations	yes	4(100)	22(91.67)	0	10(55.56)	***p=0.000 1 vs 3 p=0.0014 2 vs 3 p=0.0007 2 vs 4 p=0.01
		no	0	2(8.33)	4(100)	8(44.44)	
	Conglomerate lymphnodes	yes	2(50)	6(25)	0	2(11.11)	p=0.21
		no	2(50)	18(75)	4(100)	16(88.89)	
Calcified lymphnodes	Focal calcificates	yes	0	10(41.67)	0	2(11.11)	p=0.053
		no	4(100)	14(58.33)	4(100)	16(88.89)	
	Punctiform	yes	0	2(8.33)	0	0	p=0.65
		no	4(100)	22(91.67)	4(100)	18(100)	
	Scaly	yes	0	2(8.33)	0	0	p=0.65
		no	4(100)	22(91.67)	4(100)	18(100)	
Additional finding	Pneumocyst/bullae	yes	0	4(16.67)	0	8(44.44)	p=0.096
		no	4(100)	20(83.33)	4(100)	10(55.56)	

	Traction bronchiectasis	yes	0	0	0	14(77.78)	***p=0.000
		no	4(100)	24(100)	4(100)	4(22.22)	
	Fibrosis	yes	0	0	0	16(88.89)	***p=0.000
		no	4(100)	24(100)	4(100)	2(11.11)	
	Honeycombing	yes	0	0	0	2(11.11)	p=0.42
		no	4(100)	24(100)	4(100)	16(88.89)	

p (Fisher's exact test)

*sig p<0.05, **sig p<0.01, ***sig p<0.0001

Discussion:

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. Pulmonary involvement is the most common manifestation of the disease, with interstitial and granulomatous changes of varying location, intensity, and expression, depending on the stage of the disease. Staging of the disease is still performed according to established radiological criteria based on conventional chest radiography, despite the high sensitivity of HRCT (high-resolution computed tomography) in detecting subtle changes in the lungs that are not visible on standard radiographs. According to Lynch, conventional chest radiography detects only 50–60% of enlarged lymph nodes and 30–40% of parenchymal abnormalities found with HRCT. Only in a few cases have patients with biopsy-confirmed sarcoidosis shown a normal HRCT scan. (5)

Involvement of the hilar and mediastinal lymph nodes is observed in 50–90% of patients, most commonly bilaterally. The disease affects both sexes, with a slight predominance in women, in whom a second incidence peak may be seen after the age of 50 (notably in Japan). Although the etiology remains unknown, certain occupations appear to increase the predisposition to this disease. These include nurses, cleaning staff, administrators in the chemical industry, dispatchers, and firefighters. It primarily occurs in non-smokers and typically manifests symptoms of dry cough and dyspnea. Perilymphatic distribution of pulmonary granulomas is consistently detected on HRCT.

The 2010 study by Herreaz, notes that the most common characteristic finding is the presence of small, well-defined nodules ranging in size, from 2 to 5 mm, with a lymphangitic distribution. Although these lesions are seen in the central lung zones—typically with a peribronchovascular and centrilobular distribution—they are more frequently observed in the peripheral lung fields, commonly showing a centrilobular and subpleural distribution, along the fissures. (6)

The 2005 study by Akira et al., which included 40 patients with a 7-year follow-up period, reports that additional findings in sarcoidosis, such as ground-glass opacities and consolidations, most commonly progress into cystic lung changes. In contrast, abnormalities in the form of micro- and macronodular changes typically resolve or decrease in size. Fibrotic changes do not disappear and are associated with a worse prognosis, as well as increased mortality and morbidity (7). Traction bronchiectasis, architectural distortion of the lungs, and cystic lung changes are irreversible alterations.

In this study, the patients were predominantly female—46 (92%) compared to 4 (8%) male—aged between 30 and 73 years, most of whom lived in urban areas. Regarding smoking status, 8 patients (16%) declared themselves as current smokers, while 42 (84%) were non-smokers; however, 28 (56%) of the non-smokers had a history of smoking.

Regarding the distribution of patients by sarcoidosis stage, 4 patients (8%) were in stage 1, 24 (48%) in stage 2, 4 (8%) in stage 3, and 18 (36%) were diagnosed with stage 4 sarcoidosis.

In the study by Peeyush (8), analyzed a group of predominantly male 40 patients with pulmonary sarcoidosis, with most cases detected in stages 2 and 3 of the disease. In contrast, our patients were predominantly female, most commonly in stages 2 and 4. Bilateral hilar lymphadenopathy was present in 76% of our patients, with calcifications detected in 17%. Lesion distribution was predominantly in the upper and middle lung zones (78%), while diffuse distribution affecting the lower zones was seen in 22% of patients (8).

Clinically, cough was present in 80% of the patients, most often of mild intensity, and predominantly dry in 56% of cases.

Breathing difficulties were reported in 76% of the patients, with dyspnea lasting between 3 and 24 months, while fatigue was reported by 14 patients (28%).

Overall, reticular opacities were detected in 44 (88%) patients, similarly distributed in the upper/middle and lower lung zones—20 (40%) and 24 (48%) respectively—which corresponds to the larger number of patients diagnosed in stage 4 of the disease.

The stage of the disease was not significantly associated with the presence or intensity of cough. Regarding cough intensity, mild cough was reported by patients across all stages, most frequently in stage 1, while severe cough was observed only in patients with stage 4 disease.

As previously noted, sarcoidosis is a multisystem granulomatous disease of unknown etiology, with pulmonary involvement being the most common presentation. According to general literature, most patients are in stage 1, followed by stage 2, which includes pulmonary involvement and lymphadenopathy. In this study, most patients were found in stages 2 and 4. This variation, as well as the predominance of female patients, is likely due to the relatively small sample size, as well as the socioeconomic status of patients in our country, where health awareness is generally low.

Involvement of the hilar and mediastinal lymph nodes is seen in 50–90% of patients. (9)

The study by Miller BH et al. found that up to 90% of patients with sarcoidosis have pulmonary involvement at some stage of the disease, where lung imaging plays a key role in disease

detection, diagnosis, and management. In the same study, thoracic lymphadenopathy was present in over 85% of patients, with bilateral lymph node involvement seen in up to 95% of those with thoracic nodal disease (10). Parenchymal involvement includes perilymphatic micronodules (up to 5 mm), larger nodules, ground-glass opacities, consolidations, reticulations, and fibrosis (11).

Lymphadenopathy in sarcoidosis is non-necrotizing and typically bilateral and symmetrical—this is a classic pattern of sarcoidosis and is consistent with our findings. Symmetrical lymphadenopathy is an important diagnostic marker for sarcoidosis, as symmetry is uncommon in many differential diagnoses, such as tuberculosis or lymphoma (12). In a high percentage of cases, the lymph nodes may appear conglomerated.

According to Nishino M. and colleagues, as well as Ors F. and colleagues, perilymphatic micronodules on HRCT are found in more than 90% of patients, typically distributed symmetrically in the middle and upper lung zones.

The perilymphatic distribution of micronodules is a characteristic feature of sarcoidosis. These nodules are usually well-defined, with bilateral and generally symmetrical distribution, predominantly involving the upper and middle lung fields (9, 13, 14).

According to Starshinova et al. It has been hypothesized that components of atmospheric particulate matter or infectious causes could serve as immunogenic triggers, causing a systemic granulomatous response. In our study, as well as in the study in USA by Hannah H. Nam et.al, a significantly higher proportion of sarcoidosis patients was found to live in urban areas. (15)

A recent case-control study from India examining 100 newly diagnosed sarcoidosis patients reported that the study showed no change in the clinical presentation or the severity of disease in sarcoidosis patients with a history of smoking.(16) In our study, current smokers did not have a significantly different distribution across the four disease stages, but there was a statistically significant difference in the distribution of former smokers across disease stages, driven by the significantly higher proportion of former smokers in stage III compared to stage II . It is uncertain whether nicotine or other components of cigarette smoke alone or in combination change the clinical manifestation of sarcoidosis.(17)

In our study, the disease stage had a significant impact on the patient hospitalization. Pairwise group comparisons showed significant differences between stages I and IV. This is because in stage 4 of the disease, where pronounced fibrotic changes affect the lung parenchyma, dyspnea and fatigue become the dominant clinical symptoms, significantly impacting the patients' daily activities, and in the most severe cases, necessitating oxygen support and hospitalization.

Conclusion:

Although the radiological staging of sarcoidosis is traditionally based on the Scadding Score System, High-Resolution Computed Tomography (HRCT) is the imaging modality of choice and represents the gold standard for evaluating thoracic sarcoidosis. It accurately depicts the characteristic features of parenchymal nodules and lesions, their distribution, associated changes, as well as atypical findings. Moreover, HRCT plays a crucial role in guiding appropriate therapy by distinguishing active inflammatory lesions from irreversible fibrotic changes. Although sarcoidosis generally occurs predominantly in non-smokers, the role of nicotine in patients with

sarcoidosis is still not fully understood. Cough is a common and prominent clinical symptom in sarcoidosis patients, although the precise mechanism behind its development remains unclear.

References:

1. American Thoracic Society. Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society(ATS) and the European Respiratory Society(ERS). *Am J Respir Crit Care Med* 2000; 161; 646-664
2. Hochegger B, Marchiorri E, Zanon M, et al. Imaging in idiopathic pulmonary fibrosis; diagnosis and mimics. *Clinics (Sao Paulo)* 2019; 74.
3. Lynch DA, Sverzellati N, Travis WD, et al. Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper. *Lancet Respir Med* 2018;6(2):138-153.
4. Mohning MP, Richards JC, Huie TJ. Idiopathic pulmonary fibrosis; the radiologists role in making the diagnosis. *Br J Radiol* 2019;92(1099).
5. Wuyts WA, Cavazza A, Rossi G, Bonella F, Sverzellati N, Spagnolo P. Differential diagnosis of usual interstitial pneumonia: when is it truly idiopathic? *Eur Respir Rev.* 2014 Sep;23(133):308-19. doi: 10.1183/09059180.00004914.
6. Oliviera SD, Filho JAA, Paiva AFL, Ikari ES, Chate RC, Nomura CH. Interstitial pneumonias: review of the latest American thoracic society/European society classification. *Radiol Bras.*2018 Sept-Oct;5195): 321-32.
7. Chae JK, Jin YG, Goo MJ, Chung JM. Interstitial lung abnormalities: what radiologists should know: thoracic imaging, *Korean J Radiol* 2021;22(3): 454-463.
8. Dhagat PK, Singh S, Jain M, Singh SN, Sharma RK. Thoracic sarcoidosis: imaging with high-resolution computed tomography. *J Clin Diagn Res.* 2017 Feb;11(2):TC15–TC18. doi: 10.7860/JCDR/2017/24165.9459.
9. Criado E, Sanchez M, Ramirez J, Arguis P et al. Pulmonary sarcoidosis: Manifestation of high resolution CT with pathologic correlation, chest imaging, 2010, 1567- 1569.
10. Baughman RP, Culver DA, Judson MA: A concise review of pulmonary sarcoidosis, *Am J Respir Crit Care Med* 2011; 183:573-581.
11. Nishino M, Lee KS, Itoh H, et al: The spectrum of pulmonary sarcoidosis: Variations of high- resolution CT findings and clues for specific diagnosis. *Eur J Radiol* 2010;73:66-73.
12. Wilson AG, Hansel DM. immunologic diseases of the lung. In: Armstrong P, Wilson AG, Dee P, Hansell DM, editors. *Imaging of the diseases of the chest.*3rd ed. NW, London: Mosby; 2000.p. 637-88.

13. Avital M, Halpern IH, Deeb M, Izbicki G. Radiological findings in sarcoidosis. *IMAJ*.2008;10: 572-574.
14. Ortega IH, Gonzales LL. Update thoracic sarcoidosis. *Radiologia*2011;53(5): 443-448.
15. Nam HH, Washington A, Butt M, et al. The prevalence and geographic distribution of sarcoidosis in the United States. *JAAD Int*. 2022 Aug 5; 9:30-32. doi: 10.1016/j.jdin.2022.07.006. PMID: 36089937; PMCID: PMC9449733.
16. Jindal SK, Singh A, Joshi K, et al. Is tobacco smoking protective for sarcoidosis? A case-control study from North India. *Chest* 2006;130(4):128S.
17. Maier LA. Is smoking beneficial for granulomatous lung diseases? *Am J Resp Crit Care Med* 2004;169(8):893–895.