

A Cross Sectional Study on Clinical and Radiological Profile of Sarcoidosis in a Tertiary Care Center in India

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A B S T R A C T

Introduction:- Sarcoidosis is a global disease found in almost all continents. It is a multi-system disorder of unknown aetiology. sarcoidosis can involve almost all organs of body but lungs and the lymphatics are the common sites. Current study was done to study the clinicoradiological Profile of sarcoidosis in a tertiary care centre.

Material and Methods:- This was a cross sectional observational study, includes 56 patients diagnosed to have sarcoidosis in department of pulmonary medicine in lilavati hospital and research centre, Bandra, Mumbai during the period 2015-2017

Results:- Average age of sarcoidosis was 46.07± 6.06 years, females comprised 64.28% of the patients. Before coming to our department, 42.9% patients had been misdiagnosed to have TB. Cough (85.7%) was the most common presenting symptom; end inspiratory crepitations was seen in 50% patients. Cutaneous involvement were rarely seen. Pulmonary function testing showed restriction in 21.42% patients. The most common radiological feature was bilaterally symmetrical hilar lymphadenopathy.

Conclusions:- Sarcoidosis has clinical, radiological and serological manifestations which can vary. In developing countries with high prevalence of TB, like India, sarcoidosis is often misdiagnosed as TB. Hence, patients having chronic cough, bilateral hilar lymphadenopathy with or without infiltrates should be investigated for sarcoidosis.

Keywords: Sarcoidosis, Tuberculosis, Pulmonary Function Test.

INTRODUCTION

Sarcoidosis is a global disease found in almost all continents. It is a multi-system disorder of unknown aetiology.^{1,2} The pathognomic feature of sarcoidosis is formation of non caseating granuloma, sarcoidosis can involve almost all organs of body but lungs and the lymphatics are the common sites liver, spleen, eyes, CNS and skin are the other common organs affected by sarcoidosis.³

sarcoidosis shows epidemiological variations world wide. Important reasons of these variations are- a precise and consistent case definition is lacking, disease presentation is variable, sensitive and specific diagnostic tests are not available, because of these reasons and its resemblance with tuberculosis, sarcoidosis is under reported specially in developing countries. Also the availability of invasive diagnostic technique plays an important role in prevalence of sarcoidosis^{4,5}

Most of the studies suggest a slightly higher disease rate for women. In a population-based incidence study of sarcoidosis in the United States, rates were 5.9 per 100,000 person-years for men and 6.3 per 100,000 person-years for women In the UK, general practice data have suggested an incidence

of approximately 3 cases of sarcoidosis per 100000 people per year. In another UK study, a similar incidence of 5 cases per 100000 people per year was found^{5,6}, While study done in a tertiary care respiratory Centre, Delhi sarcoidosis (37.37%) was most common among 289 patient followed by IPF(27.68%).⁷ The true prevalence of sarcoidosis in India is not clearly known as reliable epidemiological data are not available. This study was, therefore, undertaken with the aim to study the clinicoradiological profile of pulmonary sarcoidosis in the Indian context.

Current study objective was to study the clinicoradiological Profile of sarcoidosis in a tertiary care centre.

MATERIAL AND METHODS

This was a cross sectional prospective observational study which included patients diagnosed to have sarcoidosis in department of pulmonary medicine in lilavati hospital and research centre, Bandra, Mumbai. during the period 2015-2017. The diagnosis of sarcoidosis was based upon compatible clinical, radiological, laboratory and/or histopathological features as per the joint statement of the American Thoracic Society, the European Respiratory Society and the World Association of Sarcoidosis and Other Granulomatous

Disorders (ATS/ERS/WASOG)⁵ and also exclusion of any other causes of the same. Patients who are unable to give history or critically ill were excluded from the study.

After taking clearance from ethical committee and informed consent from patients a detailed history was recorded and physical examination was performed in all the patients at the time of initial presentation. Laboratory investigations included haemogram, chest radiograph, and sputum smear examination for acid-fast bacilli (AFB), Mantoux test, pulmonary function testing (PFT), electrocardiogram, laboratory tests like serum angiotensin converting enzyme (ACE) levels. Chest radiograph and Contrast enhanced computed tomography (CECT) of chest were performed in all patients. Fibreoptic bronchoscopy (FOB) and transbronchial lung biopsy (TBLB) was performed in patient willing for the procedure and if they were physiologically fit [forced vital capacity (FVC) > 1L, arterial oxygen tension (PaO₂) > 60mm Hg on room air]. In patients who were either not fit to undergo FOB or refused to undergo the same, the diagnosis was made on the basis of clinical, laboratory and radiological features

The patients were classified based on the Siltzbach classification which defines the five stages of the sarcoidosis: Stage 0, which has normal appearance on chest radiograph; Stage 1, lymphadenopathy only; Stage 2, having lymphadenopathy and parenchymal disease; Stage 3, parenchymal disease only; and Stage 4, with parenchymal fibrosis.

Patient with diagnosis of chronic lung diseases like asthma, bronchiectasis, Chronic Obstructive pulmonary Diseases (COPD) requiring treatment intervention and diagnosis and Patients who were not able to perform Pulmonary function test and 6 minute walk test like hemodynamically unstable patients, patients with stroke/bed ridden patients and acute coronary syndrome were excluded from the study.

STATISTICAL ANALYSIS

Nominal type of Qualitative data was represented in form of frequency and percentage. Nominal type of Qualitative data included sex of the cases, symptoms, clinical signs, CECT chest findings, etc.

RESULTS

A total of 56 patients who were diagnosed as cases of Sarcoidosis on the basis of contrast enhanced CT chest findings were studied for their clinicoradiological assessment (table 1, table 2).

Mean age of presentation was 46.07 years, among which 64.3% were female, mean duration of illness before presentation was 23.05 months. Most common presenting complaint was found to be dry cough (85.7%), followed by breathlessness (71.4%), constitutional symptoms like fever, weight loss and anorexia were seen in 21.4% patients. Arthralgia was seen in 35.7% patients. skin involvement was found in 8 (14.3%) patients, 52

Author	Year	Total no of cases	Prevalence	Age	Gender	Duration	Non smoker	Predominant symptom	Cutaneous involvement	Crepitation in Auscultation
Kumar et al ⁸	2012	146		43 year mean, 70% patients were more than 40 year	female patients 58.2%	20.5 months	129, (88.44%)	cough 131, (89.7%), SOB-102, (69.9%)	15, (10.3%)	72, (49.3%)
Mahapatra et al ⁹	2014	140	13/140	between 30-50 year - 8/13 patients	female patients 9/13					
Kumar et al ¹⁰	2014	108	37.3%	mean -43.78 year	female patients 63, (58.34%)	2.35 year	94, (87.03%)	cough 103, (95.31%), SOB- 85, (78.7%)		
Anand Kumaret al ¹¹	2016	88	14, (17.5%)	54± 4.2 years in male, 41.9 ± 4.2 years in female	female patients 12, (85.7%)					
Gupta et al ¹²	2017	150		40% cases between 40-50 year	female patients 60%		73.3%	cough 130/150, SOB-125/150	20/150 cases	
Dhooria et al ¹³	2018	803	339(42.2%)	44.8± 11.8 years	Female 51%	3-8 months	322(95%)			
Current study	2019	56		46.07± 6.06 years	female patients 36 (64.28%)	23.5± 5.02 months	52 patients (92.9%)	Cough 48(85.7%), breathlessness 40 (71.4%)	8 (14.3%)	28(50%)

Table-1: Comparison of different studies (clinical parameters)

patients (92.9%) were nonsmoker.

Crackles were found in 28 (50%) patients, all patients (100%) of sarcoidosis had abnormal chest x ray, serum ACE level was elevated in 40 (71.4%) patients, 42.9% patients were misdiagnosed as TB.

DISCUSSION

In this study mean age in sarcoidosis was 46.07 ± 6.06 years. This is in accordance with Indian literature, Kumar et al¹¹ (mean age 43.78 years) and Kumar et al¹⁰ (mean age 43 years). Kundu et al¹⁴ also gives similar results. The ATS/ERS/WASOG statement⁵ states that sarcoidosis consistently shows a predilection for adults under age 40; peaking in those aged 20-29 years. However, studies^{5,15} done in Scandinavian countries and Japan report a second peak in incidence in women aged over 50 years. Other studies from western countries also report more than 70% patients of sarcoidosis to be of less than 40 years of age.^{5,15} In this study, among 56 patients of sarcoidosis 36(64.3%) were female patients and 20(35.7%) were male patients. This is in accordance with Kumar et al¹¹ in which they found 58.34% female patients. Also, in a study done by Kumar et al¹⁰ there were 85 (58.2%) females but Sharma et al¹⁶ found only 39% females in 210 sarcoidosis patients. Most of the western literature also showed female preponderance, for example study done by Demirkok et al¹⁷ found 81% females in their study.

In this study mean duration of presentation was 23.5 ± 5.02 months in sarcoidosis, which is nearly similar to a study done by Kumar et al¹⁸, in which they found mean duration of illness in sarcoidosis to be 2.35 years. Also, in a study done by Kumar et al¹⁰ the average duration of illness was 20.5 months.

In this study, cough and breathlessness were the most common presenting complains in sarcoidosis. Cough found in 48(85.7%) patients and breathlessness found in 40 (71.4%) patients. This is in accordance with Kumar et al¹¹ in which they also observed cough and breathlessness as most common presenting symptoms in sarcoidosis. Also, in a study done by Kumar et al¹⁰ the most common presenting symptom was found to be cough, which was present in 131 (89.7%) patients, followed by exertional dyspnea in 102 (69.9%). These observations are also in accordance with other Indian studies^{18,19} and with ATS statement on sarcoidosis.⁵

In this study constitutional symptoms (fever, anorexia, and weight loss) found in 12 (21.4%) patients of sarcoidosis. This is in accordance with Kumar et al¹⁰ in which they found fever in

Author	Chest xray	CECT chest	H/O ATT intake	serum ACE	PFT
Kumar et al ⁸	stage 1 - 51.4%, stage 2 - 37.1%, stage 3 - 5.7%, stage 4 - 2.8 %	mediastinal lymphadenopathy -139, (97.2%), Parenchymal involvement 104, (72.7%)	43, (29.5 %)	84 (57.7%)	restriction 86, (58.9%), obstruction 26,(17.8%), mixed 21,(14.4 %), DLCO - 104,(72.2%)
Mahapatra et al ⁹	hilar lymph node enlargement were common				
Kumar et al ¹⁰	hilar lymph node enlargement - 46, 942.59%,) reticulo-nodular pattern 76, (70.37%)	mediastinal lymphadenopa- thy-46,(42.59%), interstitial infil- trate-43,(39.815), ground glass opacities - 36,(33.33%)	24,(22.22%)	mean 82.84	mean FVC -72.71, FEV1- 66.14, FEV1/FVC- 85.37, TLC- 70.77, DLCO- 64.15
Anand Kumaret al ¹¹		GGO- 53.8%,reticular shadows23.1%, mediastinal lymph node -92.3%	53.80%		
Gupta et al ¹²	stage 1- 85, stage 2 -35, stage 3 - 25, stage 4 - 5	mediastinal Lymphadenopathy- 105/150 (70 %), peribronchovascular distribution 40/150, (26.7%), GGO-25, (16.7%)			60% restrictive, 20% obstructive, 10% mixed
Dhooria et al ¹³	stage1- 96,(28.3%) stage 2-138, (40.7%), stage 3-77,(22.7%), stage 4-11,(3.2%)		68,(20.1%)		values were higher compared to other ILDs
current study	stage 1 -16 stage2- 20 stage 3- 12 stage 4 - 8,	mediastinal lymphadenopathy 85.7 % patients (n=48) peribronchovascular thickening 78.6 % (n=44) patients	24 Patients (42.9%)	69.64	Restrictive pattern 12 patients (21.42%), obstruction 4 patients (7.1%),

25.4% patients, While Kumar et al¹¹ found fever in 11.11% patients. Old Indian literature also stated constitutional symptoms in sarcoidosis between 14 – 57%^{16,20,21,22,23}

In this study skin involvement was found in 8 (14.3%) patients of sarcoidosis, In sarcoidosis skin involvement has been reported to be affected by race, e.g., skin involvement in the form of erythema nodosum is more common in patients of northern European descent. Cutaneous involvement has been reported to occur in 25% of patients in western countries.⁵ Similarly, ACCESS study group²⁴ found prevalence of skin involvement (excluding erythemanodosum) in United States of America to be 15.9%; erythema nodosum was observed in 8.3%. In Indian study, done by Kumar et al¹⁰ cutaneous involvement was seen in 10.3% patients and none of the patients had erythema nodosum.

In this study 52 patients (92.9%) were nonsmoker among 56 sarcoidosis patients. This is in accordance with Kumar et al¹⁰ in which they found 88.4% nonsmoker, and Kumar et al¹¹ in which they found 87.04 % nonsmoker among sarcoidosis patients. Kamat et al²⁵ also finds similar findings in non smoker group. In a study done on Turkish population²⁶, 75 % patients were nonsmoker among 293 sarcoidosis patients. Negative correlation between sarcoidosis and smoking was also supported in the ACCESS study²⁷

Crackles were found in 28 (50%) patients of sarcoidosis, which is nearly in accordance with Kumar et al¹⁰ in which they found crackles in 49.3% of patients, but according to ATS statement on sarcoidosis⁵ crackles were present in fewer than 20% of patients. In later stages of sarcoidosis lung parenchymal involvement occurs more frequently. The difference observed in western literature and this study may be because current study had more number of patients with lung parenchymal involvement.

The chest radiographs reveal abnormalities in more than 90 per cent of the patients with sarcoidosis at presentation¹⁶ Hilar lymphadenopathy was found in three-fourth cases of sarcoidosis. In this study all patients (100%) of sarcoidosis had abnormal chest x ray. Predominant finding in Chest x ray in sarcoidosis in this study was hilar lymphadenopathy found in 44(78.6%) patients while only 32 (57.1%) patients has abnormal lung parenchyma in chest x ray. According to literature the classic radiographic feature of sarcoidosis is bilateral hilar lymphadenopathy and is reported to be present in nearly three quarters of patients.⁵ In study done by Kumar et al¹⁰ Radiographic evidence of bilateral hilar lymphadenopathy was noted in 130 (89%) patients. Parenchymal infiltrates were seen in 68 (46.6%) patients with or without lymphadenopathy. This observation is not in accordance with Kumar et al¹¹ who found hilar lymphadenopathy in 42.59%patients and Reticular/reticulo-nodular shadow in 70.37% patients.

Among patients of sarcoidosis in this study most common CECT finding was mediastinal lymphadenopathy found in 48(85.7%) patients, followed by parenchymal involvement in the form of peribronchovascular nodule (44 patients, 78.6%) associated with few reticulations (40 patients,71.4%) ground glass opacities(24 patients, 42.9%) while fibrosis and traction bronchiectasis found in only (8 patients, 14.3%). These observations are in accordance with Kumar et al¹⁰ in

which they also found mediastinal lymphadenopathy as most common finding in 139 (97.2%) patients, followed by parenchymal involvement in 104 (72.7%)patients. In western literature, study done by Avital et al²⁸ thoracic lymphadenopathy was the most common finding detected in 89% patients. Lung parenchyma involvement was seen in 60% patients. These changes were variable and included: ground-glass attenuation (n=39), multiple small nodules typically in a peribronchovascular distribution (n= 44), irregular thickening of the interlobular septa (n=16).

In this study among patients of sarcoidosis mean FEV1% (mean % predicted) was 69.14 ± 6.31, FVC% (mean % predicted) was 72.36 ±6.84, FEV1/FVC% (mean) was 75.5± 8.16 and TLC% (mean % predicted) was 74.21 ± 5.47 This is in accordance with Indian study Kumar et al¹¹ FEV1% (mean % predicted) 66.14, FVC% (mean % predicted) 72.71, FEV1/FVC% (mean) 85.37, TLC% (mean % predicted) 70.77. while study done by Shorr et al²⁹ showed FVC % predicted 42.6 ± 13.8 and FEV1 % predicted 36.0 ± 14.4. The difference between this study and study done by Shorr et al may be because; they performed their study on those advance sarcoidosis patients who were waiting for lung transplantation.

Elevated levels of serum ACE (angiotensin converting enzyme) have been observed in 40 to 90 per cent of patients with sarcoidosis^{18,20,30} and is considered to be a marker of disease activity in reports from the West. In this study serum ACE level was elevated in 40 (71.4%) patients of sarcoidosis. Kumar et al¹⁰ also found high serum ACE levels (>40 U/L) in 84 (57.5%) patients. There was no significant difference in the SACE activity among different stages in patients with active sarcoidosis.³¹ One of the reasons for these differences could be differences in the protocols followed for ACE level estimation, lack of uniform laboratory standards, and non-availability of a definitive — gold-standard for the confirmation of the diagnosis of sarcoidosis. However, serum ACE has limited utility as a diagnostic test, due to poor sensitivity (false negative results) and insufficient specificity (almost a 10 percent rate of false positive results³²

On account of high prevalence of tuberculosis in India, many patients with interstitial lung disorders are misdiagnosed to be with tuberculosis, and receive ant tubercular drugs., sarcoidosis was frequently (42.9%) misdiagnosed as TB. This is nearly similar to study done by Kamat et al²⁵ who found history of ATT intake in 31 % of patients, while Kumar et al¹¹ found history of ATT intake only in 14.87% patients with sarcoidosis as most common entity (22.22%). In contrary, Kundu et al¹⁴ found 64 patients among total 112 patients (57%), who received ATT.

CONCLUSION

Sarcoidosis has clinical, radiological and serological manifestations which can vary. Both, clinical and radiological features of sarcoidosis can resemble TB. In developing countries with high prevalence of TB, like India, sarcoidosis is often misdiagnosed as TB. Hence, patients having chronic cough, bilateral hilar lymphadenopathy with or without infiltrates should be investigated for sarcoidosis.

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