

A Prospective Study of Clinical Characteristics of Patients with Sarcoidosis from Punjab

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Abstract

Background and objectives. There is wide variation in clinical presentations of sarcoidosis across different ethnic groups and geographical areas.

Methods. Ninety-six patients with histopathologically proven sarcoidosis from Punjab were studied during the period January 2012 to January 2016 at the teaching hospital attached to our medical college.

Results. Their mean age was 46.6±10.6 years; there were 51 (53.1%) females. All the patients were symptomatic at the time of presentation; 64.6% presented with predominantly respiratory symptoms while 35.4% had prominent extra-pulmonary symptoms. The various extra-pulmonary features presenting as the initial manifestations of sarcoidosis in the present study included prolonged pyrexia (13.5%); acute kidney injury (5.2%); neurological (5.2%); salivary gland (5.2%) and ocular (3.1%) involvement. About 10% of our patients had presented with life threatening manifestations as the sole presentation of the disease. The chest radiograph at presentation revealed stage 0 in 5.2%; stage 1 in 51.1%; stage 2 in 26% and stage 3 in 17.7% patients.

Conclusions. In our study female preponderance was noted and the disease peaked during the late fourth decade of life. All the patients were symptomatic at the time of presentation and extra-pulmonary manifestations were the presenting feature in around one-third of the patients. Prolonged pyrexia, anicteric cholestasis, salivary gland involvement and AKI were uncommon, but important salient clinical manifestations in patients presenting with sarcoidosis from Punjab. [*Indian J Chest Dis Allied Sci* 2018;60:61-68]

Key words: Sarcoidosis, Ethnicity, Clinical, Punjabi, Pulmonary.

Introduction

Sarcoidosis is a chronic, multi-system disorder of unknown aetiology characterised histopathologically by the presence of non-caseating granulomas. The diagnosis of sarcoidosis is established when clinico-radiological findings are corroborated by histological evidence of non-caseating compact epithelioid cell granulomas after exclusion of known causes for granulomatous diseases, like mycobacterial and fungal infections, malignancy, and berylliosis.¹ It usually affects young, apparently healthy persons. Sarcoidosis can practically affect any organ of the body; however lung and thoracic lymph nodes are the most commonly involved. The liver, skin, and eye are the other commonly affected organs.

Sarcoidosis occurs throughout the globe, with variable incidence and epidemiologic features, probably related to differences in environmental exposures, genetic susceptibility and surveillance methods. In United States, the annual incidence of sarcoidosis for black population is 35.5 cases per 100,000 as compared

with 10.9 per 100,000 among whites.²⁻³ In Europe, the prevalence of sarcoidosis is highest for Swedish (64 per 100,000),⁴ and is lowest for Spanish (0.2 per 100,000) population.⁵ The occurrence of sarcoidosis is less common in Asian countries with an incidence of 1-2 per 100,000 inhabitants.⁶

Sarcoidosis has been under-reported from India due to lack of awareness about the disease, non-availability of diagnostic modalities and its close resemblance with other more commonly recognised granulomatous diseases like tuberculosis, leprosy and fungal infection.⁷ But now it is being recognised more frequently all over the country. A study by Respiratory Unit at Kolkata estimated incidence of 10 to 12 cases/1,000 for sarcoidosis.⁸

There is wide variation of clinical presentations of sarcoidosis across different ethnic groups and geographical areas.^{9,10} There is paucity of literature describing the clinical characteristics of patients with sarcoidosis from Punjabi ethnic populations. The present study was intended to recognise the clinical

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characteristics of sarcoidosis patients among single ethnic population of Punjab, North India.

Material and Methods

We prospectively evaluated all consecutive newly diagnosed, histopathologically proven, cases with sarcoidosis seen in the teaching hospital attached to our medical college in Punjab. The study was carried out in an 1100 bedded tertiary care teaching hospital in North India between January 2012 and January 2016. Patients who had received glucocorticoid treatment in the previous three months, sero-positive for human immunodeficiency virus (HIV) or had any associated cardio-pulmonary disease were excluded. The diagnosis of sarcoidosis was made on the basis of following criteria: (i) compatible clinico-radiological profile; (ii) demonstration of non-caseating epithelioid cell granulomas on histopathology; (iii) exclusion of other granulomatous diseases, such as tuberculosis, hypersensitivity pneumonitis or fungal infection. The site of biopsy/fine needle aspiration cytology (FNAC) for the diagnosis was based on the symptomatic organ system involvement, ease of access and minimum risk associated with the procedure. The study was approved by the Institutional Ethics Committee and a written informed consent was taken from all the subjects.

Detailed history, occupational exposure, physical and ophthalmological examination were recorded on a structured performa. The laboratory investigations, including complete blood counts, erythrocyte sedimentation rate, liver function test, serum calcium, serum creatinine, sputum smear examination for acid-fast bacilli (AFB), tuberculin skin test (Mantoux test), pulmonary function testing, serum angiotensin-converting enzyme (ACE) levels, chest radiograph and thoracic computed tomography (CT) (where ever possible), were recorded. The chest radiograph were evaluated and classified based on radiological classification recommended in the guidelines established jointly by the American Thoracic Society (ATS), European Respiratory Society (ERS) and World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG). Stage 0, normal lungs and mediastinum; Stage 1, hilar adenopathy with clear lung fields; Stage 2, hilar adenopathy with lung infiltrates; Stage 3, normal hilum with lung infiltrates and Stage 4, lung fibrosis.¹ Pulmonary function tests were done using a dry rolling seal spirometer (Spiroflow, PK Morgan Ltd, Kent UK) as per the standard ATS guidelines. The measurements included forced expiratory volume in the first second (FEV₁), forced vital capacity (FVC), and the ratio of FEV₁ to FVC. The abnormalities on spirometry were categorised into normal, obstructive and restrictive pattern.

Statistical Analysis

Data are presented as percentage or mean \pm standard deviation (SD). Groups were compared using Chi-square test, z-test of proportions, student's t-test and Mann Whitney U-test as appropriate. A p-value <0.05 was considered as statistically significant. Statistical analysis was done using Statistical Package for the Social Sciences software (SPSS, version 20.0).

Results

During the study period 96 histopathologically proven patients with sarcoidosis were studied. All the patients belonged to the state of Punjab (3 generations), and hence, represented single ethnicity. The subjects included 51 (53.1%) females. The mean age of the patients was 46.6 \pm 10.6 years (range, 23-70 years). There was no statistically significant gender-based difference in age ($p = 0.506$) (Table 1); however, women were slightly older than men at the time of presentation. Only 28 (29.2%) patients in the present study were less than 40 years of age. Family history of sarcoidosis was present in three (3.1%) patients.

Table 1. Characteristics of the sarcoidosis patients

Variable	Total (n=96)	Male (n=45)	Female (n=51)	p-value
Age <40 years*	28 (29.2)	14 (13.1)	14 (27.4)	0.693
Age (years)†	46.6 \pm 10.6	45.8 \pm 10.1	47.2 \pm 10.6	0.506
Smoking*	12 (12.5)	12 (26.6)	0 (0)	—
Familial sarcoidosis*	3 (3.1)	1 (2.2)	2 (3.9)	0.645
Delay in diagnosis†	16.3 \pm 7.6	15.2 \pm 6.5	17.4 \pm 8.5	0.162
No. of physicians visited†	3.5 \pm 1.5	3.6 \pm 1.6	3.5 \pm 1.4	0.734
Prior empirical ATT*	30 (31.1)	12 (26.6)	18 (35.3)	0.36

*=Data are presented as No. (%); †=Data are presented as mean \pm standard deviation

Definition of abbreviation: ATT=Anti-tuberculosis treatment

With regard to occupation, there was predominance of home makers (31.2%) and agriculturist (24%). Twelve (12.5%) patients in the study population were smokers (current and reformed). Thirty (31.3%) patients had already received empirical anti-tuberculosis treatment before tissue diagnosis of sarcoidosis was confirmed.

The mean number of physicians consulted was 3.5 (range 1-9). In our study, all the patients were symptomatic at the time of presentation. The mean duration of symptoms prior to presentation was 16.3 \pm 7.6 weeks (range, 4 weeks – 44 weeks).

Sixty-two (64.6%) patients presented with predominate respiratory symptoms, and 34 (35.4%) with prominent

extra-pulmonary symptoms at the time of initial presentation. The various symptoms observed among our patients at presentation are shown in table 2. Cough (58.3%) and dyspnoea (44.8%) were the most common respiratory symptoms. Arthralgia (21.9%) was the most common extra-pulmonary symptom.

The various extra-pulmonary features presenting as the initial manifestations of sarcoidosis in the present study included prolonged pyrexia (fever lasting longer than 6 weeks) in 13 (13.5%); acute renal failure 5 (5.2%); salivary glands involvement 5 (5.2%); ocular symptoms 3 (3.1%); meningismus 3 (3.1%); facial palsy 2 (2.1%) and acute pancreatitis 1 (1%).

Hepatomegaly, peripheral lymphadenopathy, and splenomegaly (reticulo-endothelial system) were observed in 20.8%, 19.8% and 13.5% cases, respectively. Thirteen (13.5%) patients presented with prolonged pyrexia as the initial and sole manifestation of sarcoidosis. Five (5.2%) patients had various oral symptoms, like unilateral painless swelling of the parotid/sub-mandibular glands, dysgeusia, oral burning and xerostomia.

Around 10% of our patients had presented with life-threatening manifestations as the sole presentation of the disease. The various potentially life-threatening conditions presenting as the initial manifestations of sarcoidosis in the present study included acute renal failure in five (5.2%), encephalopathy with meningismus in three (3.1%) and acute pancreatitis and acute respiratory failure in one (1.04%) patient each.

Table 3 depicts the laboratory tests done in patients with sarcoidosis. High serum ACE levels (>60 U/L) were observed in 59 (61.5%) patients. Tuberculin skin test was negative in all patients. Thirteen (13.5%) patients had abnormal liver function test reflected by anicteric cholestasis. The mean alkaline phosphatase of these patients was 308.38±45.31 IU/mL which was around three times the normal (normal range 35-104 IU/L). This was associated with mild increase in transaminases (<2 times the normal). All these patients underwent liver biopsy which showed non-caseating granulomas. Eleven (11.5%) patients had hypercalcaemia. Five (5.2%) patients had serum creatinine >1.6 mg/dL and three (3.1%) had pancytopenia at the time of presentation.

The chest radiograph done at the time of presentation revealed stage 0 in 5 (5.2%); stage 1 in 49 (51.1%); stage 2 in 25 (26%) and stage 3 in 17 (17.7%) patients. Hilar and mediastinal lymphadenopathy were the most common CT chest findings seen in 87.7% and 83.7% cases, respectively. Lung function tests were normal in 64.7% while 26.2% had restrictive and 9.1% had obstructive defect (Table 4).

There was no significant gender-based difference in the clinical presentation except that chest pain and shortness of breath were more common in males and

Table 2. Symptoms and signs in patients with sarcoidosis at the time of diagnosis

Clinical Findings	Total (n=96)	Male (n=45)	Female (n=51)	p-value
Symptoms				
Cough	56 (58.3)	29 (64.4)	27 (52.9)	0.253
Shortness of breath	43 (44.8)	26 (57.7)	17 (33.3)	0.016
Fever	37 (38.5)	14 (31.1)	23 (45.1)	0.159
Weight loss	32 (33.3)	14 (31.1)	18 (35.3)	0.664
Fatigue	26 (27.1)	15 (33.3)	11 (21.6)	0.195
Anorexia	23 (23.9)	11 (24.4)	12 (23.5)	0.916
Arthralgia	21 (21.9)	10 (22.2)	11 (21.6)	0.938
Chest pain	10 (10.4)	8 (17.8)	2 (3.9)	0.026
Skin lesion	10 (10.4)	4 (8.9)	6 (11.8)	0.645
Abdominal discomfort	10 (10.4)	5 (11.1)	5 (9.8)	0.834
Myalgia	7 (7.3)	2 (4.4)	5 (9.8)	0.313
Dry eye	6 (6.3)	0 (0)	6 (11.8)	—
Jaw swelling	6 (6.3)	2 (4.4)	4 (7.8)	0.492
Blurring of vision	6 (6.3)	1 (2.2)	5 (9.8)	0.125
Dryness of mouth	5 (5.2)	2 (4.4)	3 (5.9)	0.7489
Abnormal taste	5 (5.2)	3 (6.6)	2 (3.9)	0.5485
Red eye	4 (4.2)	1 (2.2)	3 (5.9)	0.370
Facial deviation	4 (4.2)	1 (2.2)	3 (5.9)	0.370
Arthritis	3 (3.1)	2 (4.4)	1 (1.9)	0.485
Hoarseness of voice	3 (3.1)	1 (2.2)	2 (3.9)	0.632
Headache	3 (3.1)	1 (2.2)	2 (3.9)	0.632
Altered sensorium	3 (3.1)	2 (4.4)	1 (1.9)	0.485
Diplopia	1 (1.0)	0 (0)	1 (1.9)	—
Jaundice	1 (1.0)	0 (0)	1 (1.9)	—
Signs				
Hepatomegaly	20 (20.8)	9 (20)	11 (21.6)	0.850
Lymphadenopathy	19 (19.8)	8 (17.8)	11 (21.6)	0.641
Splenomegaly	13 (13.5)	6 (13.3)	7 (13.7)	0.955
Crepitation	10 (10.4)	4 (8.9)	6 (11.8)	0.645
Uveitis	8 (8.3)	1 (2.2)	7 (13.7)	0.041
Ronchi	6 (6.3)	1 (2.2)	5 (9.8)	0.125
Skin plaques	6 (6.3)	2 (4.4)	4 (7.8)	0.492
Pallor	5 (5.2)	1 (2.2)	4 (7.8)	0.216
Skin nodules	4 (4.2)	2 (4.4)	2 (3.9)	0.898
Parotid enlargement	4 (4.2)	1 (2.2)	3 (5.9)	0.370
Facial nerve palsy	4 (3.1)	1 (2.2)	3 (5.9)	0.370
Nephrolithiasis	3 (3.1)	3 (6.7)	0 (0)	—
Conjunctivitis	3 (3.1)	0 (0)	3 (5.9)	—
Orbital swelling	3 (3.1)	0 (0)	3 (5.9)	—
<i>Erythema nodosum</i>	3 (3.1)	0 (0)	3 (5.9)	—
Meningitis	3 (2.1)	1 (2.2)	2 (3.9)	0.632
Icterus	1 (1.0)	0 (0)	1 (1.9)	—
Digital clubbing	0 (0)	0 (0)	0 (0)	—

Data are presented as No. (%)

Table 3. Laboratory findings in patients with sarcoidosis

Laboratory Findings	Total (n=96)	Male (n=45)	Female (n=51)	p-value
Haemoglobin (g/dL)	12.9±2.3	13.4±1.7	12.5±2.6	0.059
TLC (10 ³ /μL)	8.8±3.6	9.2±3.5	8.5±3.6	0.290
Platelet (10 ³ /μL)	239.3±82.0	238.2±89.6	240.1±75.7	0.911
Blood urea (mg/dL)	19.6±6.7	20.8±8.5	18.5±4.3	0.085
Serum creatinine (mg/dL)	1.09±0.54	1.16±0.77	1.04±0.1	0.299
Serum calcium (mg/dL)	9.51±0.98	9.53±1.23	99.45±0.92	0.710
Serum total bilirubin	1.06±0.28	1.02±0.15	1.10±0.36	0.192
SGOT (IU/L)	34.82±16.23	33.07±13.59	36.37±18.24	0.322
SGPT (IU/L)	41.07±21.97	39.51±20.29	42.45±23.47	0.516
ALP (IU/L)	163.45±75.53	160.04±66.49	166.45±83.24	0.681
ACE levels (IU/L)	75.42±36.4	114.89±25.64	115.12±23.89	0.964

Definition of abbreviations: TLC=Total lung capacity; SGOT=Serum glutamic-oxaloacetic transaminase; SGPT=Serum glutamic-pyruvic transaminase; ALP=Alkaline phosphatase; ACE=Angiotensin-converting enzyme

uveitis was more common in females. Similarly, there was no significant gender-based difference in the laboratory findings. Histopathology of representative extra-pulmonary sites is shown in the figure.

Discussion

All our patients were natives of Punjab (minimum three consecutive generations) and represented single ethnicity. Most of the patients in the present study were in the fourth and fifth decade of life with a mean age of 46.5 years. In the present study 70% of the patients were above 40 years of age in contrast to studies from the western countries where more than 70% of the sarcoidosis patients were less than 40 years.^{11,12} Similar observations on age distribution of sarcoidosis have been reported in other Indian studies.¹³⁻¹⁷

In our study there was female predominance among sarcoidosis cases in contrast to male dominance reported in various Indian studies.^{13-15,18,19} However, worldwide there is female preponderance of sarcoidosis across all racial and ethnic groups.^{20,21} The female preponderance of sarcoidosis amongst patients of Punjabi ethnic origin may partly be explained by the lower threshold of the cases to seek medical advice due to better socio-economic status.

In the present study from Punjab, all the patients were symptomatic at the time of presentation which is concordant with studies from other Indian states.^{7,13-15,18,19} In the West where routine chest radiograph screening is done, 20% to 30% of sarcoidosis cases are detected while they are asymptomatic.²² In India, there is no concept of annual health check-up which may be the reason that here we see only symptomatic disease.

Table 4. Radiological and spirometry findings in patients with sarcoidosis

	Total (n=96)	Male (n=45)	Female (n=51)	p-value
Radiological staging at diagnosis (n=96)*				
Stage 0	5 (5.2)	3 (6.7)	2 (3.9)	0.545
Stage 1	49 (51.1)	23 (51.1)	26 (50.9)	0.989
Stage 2	25 (26.0)	13 (28.9)	12 (25.5)	0.550
Stage 3	17 (17.7)	6 (13.3)	11 (21.6)	0.291
Computed tomography of chest (n=49)*				
Hilar lymph nodes	43 (87.7)	22 (91.7)	21 (84)	0.461
Mediastinal lymph nodes	41 (83.7)	21 (87.5)	20 (80)	0.448
Perilymphatic nodules	20 (40.8)	8 (33.3)	12 (48)	0.488
Septal and nonseptal lines	20 (40.8)	6 (25)	14 (56)	0.089
Ground glass opacity	8 (16.3)	3 (12.5)	5 (20)	0.578
Lung mass/ Nodule	5 (10.2)	2 (8.3)	3 (12)	0.751
Diffuse nodules	5 (10.2)	2 (8.3)	3 (12)	0.751
Consolidation	3 (6.1)	1 (4.1)	2 (8)	0.632
Spirometry findings (n=88)				
FVC (%)†	79.31 (12.27)	80.07 (12.03)	78.67 (12.44)	0.840
FEV ₁ (%)†	75.64 (13.37)	76.67 (12.57)	74.77 (13.94)	0.956
FEV ₁ /FVC	77.07 (9.88)	77.03 (9.69)	77.10 (10.05)	0.545
Normal*	57 (64.7)	28 (70)	29 (60.4)	0.593
Restrictive*	23 (26.2)	9 (22.5)	14 (29.2)	0.393
Obstructive*	8 (9.1)	3 (7.5)	5 (10.4)	0.578

*=Data are presented as No. (%), †=Data are presented as mean±standard deviation

Definition of abbreviations: FVC=Forced vital capacity; FEV₁=Forced expiratory volume in one second

In our patients, respiratory symptoms were the initial presenting feature in around two-third (65%) of the patients. However, radiographic evidence of thoracic involvement was seen in 95% cases. While in most of the Indian studies respiratory symptoms were the initial presenting feature in 80% to 90% of the patients with sarcoidosis (Table 5).¹³⁻¹⁹ This may partly be explained by the fact that most of these studies were carried out in respiratory units rather than in a general hospital. In the West, respiratory symptoms were the initial presenting manifestation in 40% to 60% of patients with sarcoidosis.²²

In the present study of sarcoidosis patients from Punjab, extra-pulmonary symptoms were the initial presenting feature in around one-third of the patients. However, all these patients had radiographic evidence of thoracic involvement. A higher number of patients presenting with extra-pulmonary features at the time of initial presentation

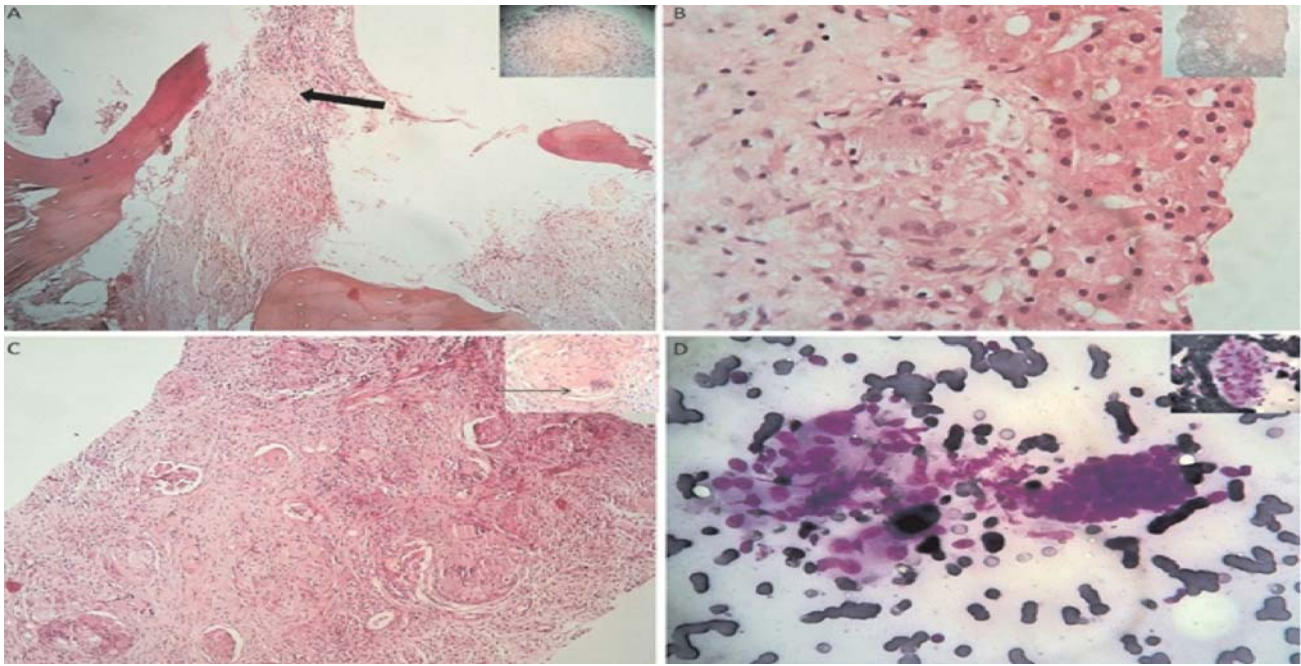


Figure. Photomicrograph showing (A) bone-marrow granuloma; small compact granuloma-black arrow (inset) (Haematoxylin and eosin, $\times 100$); (B) liver parenchymal infiltration by small granuloma; reticulin accentuation around granuloma (inset) (Haematoxylin and eosin $\times 400$); (C) granuloma in renal parenchyma; asteroid body-small arrow (inset) (Haematoxylin and eosin, $\times 100$) and (D) fine needle aspiration cytology smear from parotid swelling showing granuloma along with ductal cells; tiny naked granuloma (inset) (Giemsa $\times 400$).

may partly be related to differences in the ethnic background of the cohort.

The various initial presenting extra-pulmonary manifestations of sarcoidosis in the present study included prolonged pyrexia (fever lasting longer than 6 weeks) in 13 (13.5%); acute kidney injury in 5 (5.2%); salivary gland involvement in 5 (5.2%); ocular symptoms in 3 (3.1%); meningism in 3 (3.1%); facial palsy in 2 (2.1%) and acute pancreatitis in 1 (1%).

Thirteen (13.5%) patients presented with prolonged prexia as the initial and sole clinical feature of sarcoidosis in our cohort of sarcoidosis. Several previous studies from India have failed to identify prolonged pyrexia as the initial presenting feature of sarcoidosis.^{7,13-15,17-19} Sharma *et al*¹⁶ reported PUO as the initial presenting feature of sarcoidosis in 0.6% of their patients (Table 5).

All these 13 patients had palpable hepatosplenomegaly, abnormal liver function test reflected by anicteric cholestasis (raised alkaline phosphatase ~ 3 times the normal) without other usual manifestations of systemic sarcoidosis. Except for one patient who had mild icterus, all others had clinically asymptomatic liver involvement. Though, hepatomegaly has been reported in 14% to 45% of the patients with sarcoidosis in various Indian studies,^{7,13-15,17-19} but none have recognised this anicteric cholestatic variant of sarcoidosis. This anicteric cholestatic variant of sarcoidosis among Punjabi ethnic population may partly be explained

by genetic susceptibility or environmental and immunologic factors.

Oral symptoms, such as dysgeusia, oral burning and xerostomia, as the initial manifestation of sarcoidosis was observed in 5% cases in the present study from Punjab. None had Sjögren's syndrome as anti-nuclear antibodies were negative. Oral involvement in sarcoidosis is rare in the World²³ as well as Indian literature.^{7,13-19}

Interestingly 10 patients, in our cohort of sarcoidosis patients of Punjabi ethnic origin, had presented with life-threatening manifestation as the initial presentation of sarcoidosis. Five patients had acute kidney injury; three had aseptic meningitis, one each had acute pancreatitis secondary to severe hypercalcaemia and acute hypoxaemic respiratory failure due to acute alveolar sarcoidosis. This may be related to differences in the ethnic background or the prospective evaluation or relatively sicker patients coming to us, as ours is a tertiary care referral centre.

Acute kidney injury was due to hypercalcaemia in three and granulomatous involvement of the tubulo-interstitium in two patients. Other causes of acute kidney injury with hypercalcaemia, like multiple myeloma, hyper-parathyroidism and malignancy with bony metastasis were ruled out in these patients. Several studies from India have failed to identify renal involvement as the presenting feature of sarcoidosis in their patients.¹³⁻¹⁹

Table 5. Comparison of characteristics of sarcoidosis patients in present study with other Indian studies

	Indian Studies								Western Studies		
	Present study	Bambery <i>et al</i> ¹⁷	Kashyap <i>et al</i> ¹⁵	Sharma <i>et al</i> ¹⁴	Jindal <i>et al</i> ⁷	Sharma <i>et al</i> ²¹	Kumar <i>et al</i> ¹³	South India	East India	Baughman <i>et al</i> ¹⁸	James <i>et al</i> ²⁶
Year		1987	1997	2001	2002	2012	2012	1999	1990	2001	1976
Place	Ludhiana	Chandi-garh	Himachal	Delhi	Chandi-garh	New Delhi	Delhi	Chennai	Calcutta	US	Global
Number	(n=96)	(n=40)	(n=29)	(n=106)	(n=155)	(n=164)	(n=146)	(n=22)	(n=125)	(n=736)	(n=3676)
Symptoms											
Pulmonary symptoms	65	80	90	83	61	90	90	80	91	60	21
PUO	14*	—	0	0	—	1	0	0	6	—	—
Arthralgia	22	30	35	44	27*	41	29	27	59	0.5	3
Oral symptoms	5	—	—	1	—	1	0	0	0	0	0
Signs											
Hepatomegaly	21	37	14	45	15	31	0	0	42	12*	—
Peripheral	20	42	35	45	41	34	0	0	23	15	22
Lymphadenopathy	15	40	21	18	16	19	—	9	20	12	7
Ocular involvement											
Splenomegaly	14	17	7	16	8	17	0	0	27	7	6
Skin lesions	11	0	24	37	10	24	10	32	18	16	4
Neurological involvement	8	13	3	8	1	8	0	4	12	5	4
Acute kidney injury	5	0	0	0	0	11	0	0	0	1	—
Parotid involvement	4	8	0	12	3	6	0	0	3	4	4
<i>Erythema nodosum</i>	3	20	7	6	0	5	0	0	4	8	16*
Cardiac involvement	0	7	0	7	0	0	0	0	11	2	—
Clubbing	0	0	7	3	0	0	12	0	0	—	—
Investigations											
Radiothoracic involvement	95	97	97	98	61	96	97	95	62	95	87
Ancicteric cholestasis	13	0	0	0	0	0	0	0	0	0	0
Hypercalcaemia	12	18	0	16	—	12	0	0	40	4	11
Nephrocalcinosis	3	0	0	0.9	0	0.6	0	0	0	—	—

All values expressed are percentages rounded to the nearest digit.

*=Prolonged pyrexia; PUO=Pyrexia of unknown origin

Three patients presented with encephalopathy and meningism. Neurological involvement is typically seen within two years of the initial diagnosis of sarcoidosis.^{24,25} All these patients had chest radiograph abnormality and had undergone transbronchial lung biopsy (TBLB) to support the histopathological diagnosis of sarcoidosis.

Three (3.1%) patients presented with progressive fatigue, exercise intolerance and pancytopenia on initial complete blood count. They had hepatosplenomegaly and few scattered mediastinal lymph nodes on contrast-enhanced computed tomography (CECT) thorax and abdomen. Bone

marrow biopsy revealed hyper cellular marrow in the background of granulomatous inflammation. Several studies from India have failed to identify pancytopenia as the presenting feature of sarcoidosis in their patients.^{7,13-19} Bone marrow involvement has been reported in 3.9% cases of patients in the ACCESS study (A Case Control Etiologic Study).²⁰

Arthralgia, mostly affecting the larger joints, was most frequent (22%) extra-pulmonary symptom, in our patients. However, the occurrence of arthralgia was relatively less than that reported in other Indian studies.^{7,13-16,18,19} Joint manifestations occur in 14% to 38% of patients with sarcoidosis in the West.²⁶

Peripheral lymphadenopathy and splenomegaly was observed in 19.8% and 13.5% cases, respectively. However, the occurrence of peripheral lymphadenopathy was relatively less than that reported in other India studies.^{7,14-16} The finding of splenomegaly on clinical examination in the present study was similar to that reported by other Indian authors.^{7,13-18} However, Gupta and Gupta¹⁹ reported a higher figure of splenomegaly in their study from East India which may be partly related to endemicity of malaria at the time of study.

Ocular involvement was seen in 15% cases while it was the presenting manifestation in 3% cases, similar observations have been reported from India.^{7,14,16-19} However, a higher number of subjects had ocular presentations in the form of Heerfordt syndrome and Lofgren syndrome were uncommon, similar observations have been reported from India.^{7,13-19} None of our patients had clubbing or cardiac involvement at the time of presentation. In our study all the patients had a negative Mantoux test. Tuberculin anergy in sarcoidosis has been observed in 60% to 91% of the patients in various Indian studies.^{14-16,19}

In the present study 95% of the patients had abnormal chest radiograph at the time of presentation. We seldom classify the patients as stage 4 at the time of presentation as it is not possible to establish the exclusivity of the fibrotic component at that time.

In the present study around one-third (31.3%) of patients were misdiagnosed to have tuberculosis and there was a delay in diagnosis by a mean of 16 weeks. This misdiagnoses and delay in diagnosis may be related to non-specific presentation, lack of awareness among patients and physicians and non-availability of invasive diagnostic tests in the periphery.

Conclusions

In the present study, there was female preponderance and the disease incidence peaked in the late fourth decade of life. All the patients were symptomatic at the time of presentation. Around one-third of the patients in our study presented with extra-pulmonary manifestation at the time of initial diagnosis. A high suspicion of sarcoidosis is warranted in patients of Punjabi ethnic origin presenting with prolonged pyrexia, anicteric cholestasis, and unexplained acute kidney injury to allow for the early diagnosis and prompt institution of steroids to reduce the mortality and morbidity.

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