Sarcoidosis in Johannesburg, South Africa: A retrospective study

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Background. Sarcoidosis is a multisystem granulomatous condition of uncertain aetiology that most frequently affects the lungs. Because of clinical and radiological similarities with tuberculosis (TB), particularly in high-prevalence regions, sarcoidosis is frequently misdiagnosed as TB.

Objective. To review the clinical features of sarcoidosis patients in a South African (SA) population, adding clinical information to the relatively few studies that have been conducted in SA patients with sarcoidosis.

Methods. This was a retrospective study of 102 sarcoidosis patients conducted between 2002 and 2006 at the Charlotte Maxeke Johannesburg Academic Hospital.

Results. Of 102 sarcoidosis patients, there were 69 (67.6%) females and 33 (32.4%) males. The majority (85.3%) were non-smokers. The mean age of the group was 44.6 years. One-third of patients had chronic comorbid diseases. Almost 17% had been treated initially for TB, prior to being diagnosed as having sarcoidosis. Two patients developed active TB while receiving corticosteroid treatment for sarcoidosis. The salient clinical manifestations were dry cough (the most common presenting symptom in 82.4%), dyspnoea in 53.9%, cutaneous lesions other than erythema nodosum in 33.3%, and on lung examination crackles were noted in 37.3% of patients. Raised angiotensin-converting enzyme (ACE) levels were found in 56.8% of patients. The majority (48%) of patients had stage II chest radiographic changes. Cutaneous (28.4%), mediastinal lymph node (25.5%) and transbronchial lung (25.5%) biopsies were the most frequent sites confirming granulomatous inflammation. Overall, 21.2% of patients had obstructive airway disease. Systemic corticosteroids were indicated in 87.3% of patients and the relapse rate was 60.7%.

Conclusion. Sarcoidosis is often initially misdiagnosed as TB in SA. The most common biopsy sites for histological confirmation were the skin and mediastinal lymph nodes, and transbronchial lung biopsies were also frequently taken. Stage II chest radiographic changes were most common. Overall, systemic corticosteroids were administered in 87.3% of cases and the relapse rate was 60.7%.

Keywords: sarcoidosis, clinical features, tuberculosis

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Sarcoidosis is a widespread granulomatous disease of unknown aetiology, primarily affecting the lungs and the lymphatic system. It has been reported from almost every corner of the globe, impacting all races and ethnic groups, with differing epidemiological findings from numerous reports. In Europe, the incidence of sarcoidosis varies from 1 to 64 patients per 100 000 population and in the USA it is reported as 10 - 35 per 100 000 persons, more commonly occurring in the black population.[1] The burden of sarcoidosis in South Africa (SA) is not clearly known, as accurate epidemiological data are not available. Initial studies from the beginning of the 1960s indicate that in SA sarcoidosis was rare. During the late 1960s and 1970s rates of between 3.7 and 23.2 per 100 000 patients were estimated in the different population groups within SA.[2,3] Geographical regions and referral bias play important roles in the documented incidence of sarcoidosis in various studies.[4-6]

While sarcoidosis remains an underdiagnosed disorder, doctors are alert to it, with growing understanding and increasing awareness. Owing to its similarities to tuberculosis (TB), sarcoidosis has been under-reported from developing countries. Furthermore, as the clinical and radiological features may be similar to those of pulmonary TB, patients with sarcoidosis are often initially treated as TB patients.

This study was undertaken with the main objective of studying the profile of patients with sarcoidosis in Johannesburg, SA. The study describes and analyses the clinical features of 102 sarcoidosis patients.

Methods

This was a retrospective record review undertaken between 1 January 2002 and 31 December 2006, involving 102 patients seen at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) pulmonology facilities. During this time, the Hillbrow Hospital was closed owing to reorganisation of medical services in Johannesburg, with some patients (together with their charts), and some medical staff, being transferred to CMJAH. The study included the transferred patients from Hillbrow Hospital and those attending CMJAH. The diagnosis of sarcoidosis was determined on the basis of compatible clinical signs, radiological features, together with biopsy evidence of non-caseating epithelioid granulomas, and by the exclusion of all established causes of granulomatous inflammation as described in the joint declaration of the American Thoracic Society (ATS), the European Respiratory Society (ERS), and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG).[4] Three patients in the study did not have biopsies performed. These

patients without histological confirmation of granulomas were deemed to have sarcoidosis if they had compatible clinical, laboratory and radiological features, with an appropriate response to corticosteroids, and/or spontaneous resolution, and no evidence of TB or other cause for their clinical features. The demographic, clinical, laboratory and radiographic treatment and outcome data of all patients were collected.

Statistical analysis was carried out with Student's *t*-test, the Mann-Whitney *U*-test for continuous variables, and the χ^2 test, or Fisher's exact test (2-tail), for categorical variables, as appropriate. The GraphPad Prism version 4.0 (GraphPad Software Inc., USA) was used to perform the statistical analysis and for graphic representations of the data. Statistical significance was at *p*<0.05.

The research was approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (ref. no. M110752).

Results

Between January 2002 and December 2006, 102 patients with sarcoidosis were seen by the pulmonology services at CMJAH. There were 69 (68%) females and 33 (32%) males. The mean age (standard deviation (SD)) was 44.6 (12.1) years, ranging from 22 to 77 years. The current cohort did not show the described classic bimodal age distribution (Fig. 1).

Table 1 indicates the common comorbid conditions and the clinical profile reported in the sarcoidosis patients. Coexisting illnesses were present in 30% of these patients, most commonly hypertension, renal dysfunction (estimated glomerular filtration rate (eGFR) <90 mL/min/m²), obesity and diabetes mellitus. Most patients were non-smokers (85.3%). Almost 17% of patients had initially been treated for TB empirically, without response, at the local community clinic. Two patients developed active pulmonary TB while receiving corticosteroid therapy for sarcoidosis. These patients did not receive isoniazid (INH) prophylaxis. Four (3.9%) patients developed HIV infection during their follow-up treatment for sarcoidosis, and their mean CD4 count was 233 cells/μL; 3 patients had CD4 counts <200 cells/μL and 1 patient had a CD4 count of 933 cells/μL. These patients were referred to the Infectious Disease HIV Clinic.

The presenting clinical features of the patients are shown in Table 2. The most common symptom was cough. Erythema nodosum occurred in 8 (7.8%) patients and other non-erythema nodosum cutaneous manifestations occurred in 27 (26.5%). Haemoptysis occurred in 2 patients – one patient had post-TB bronchiectasis and the other endobronchial sarcoidosis.

Histological confirmation of the diagnosis was made in 99 (97.1%) patients. The most common biopsy sites were skin (28.4%), followed by mediastinal lymph nodes via mediastinoscopy (25.5%) and transbronchial lung biopsy via fibreoptic bronchoscopy (25.5%) (Table 3).

Organ manifestations of sarcoidosis were wide and varied (Table 4). Thoracic manifestations, including hilar lymphadenopathy and parenchymal lung involvement, were present in >70% of the patients. Cutaneous manifestations included papulonodular rash, erythema nodosum, disfiguring facial lesions, lupus pernio and psoriasis-like rash, which were confirmed on histological examination. Ocular manifestations included anterior uveitis, posterior uveitis, retrobulbar neuritis and pan-uveitis, which were confirmed by slit-lamp examination by an ophthalmologist. Bone and joint manifestations included reported arthralgias, clinical arthritis and dactylitis, confirmed as cystic bone lesions on radiographic examination.

Most patients (*n*=49; 48%) had stage II chest radiographic features at the time of diagnosis. i.e. evidence of hilar and/or mediastinal lymphadenopathy, together with pulmonary nodules or reticulonodular infiltrates, followed by stage I in 24 (23.5%) patients. A stage III chest radiograph was seen in 16 (15.7%) patients, stage IV in 10 (9.8%) and 3 (2.9%) had a normal chest radiograph.

The initial laboratory data of the group of patients showed a mean (SD) Hb of 14.2 (1.83) g/dL, ranging from 9.0 to 19.1 g/dL; white cell count 6.90 (3.0) × 10⁹/L, with a range of 1.2 - 23.5 × 10⁹/L, and platelet count 295 (103) × 10⁹/L, ranging from 99 to 653 × 10⁹/L. The erythrocyte sedimentation rate (ESR) was 24 (27) mm/h, with a range of 0 - 125 mm/h. The serum angiotensin-converting enzyme (sACE) concentration was elevated at 116 (307) U/L, ranging from 9 to 3 000 U/L. The serum calcium level was 2.39 (0.21) mmol/L; the liver function test results were: total bilirubin 12 (18) μmol/L, direct bilirubin 4 (12) μmol/L, alkaline phosphatase (AP) 126 (145) IU/L, gamma-glutamyl transferase (GGT) 79 (100) IU/L, alanine transaminase 43 (115) IU/L, aspartate transaminase 36 (58) IU/L, including albumin 42 (5) g/dL, and globulin 79 (7) g/dL – all within the normal range. The serum electrolytes were: sodium 139 (10) mmol/L, potassium 4.0 (0.4) mmol/L, chloride 104 (4) mmol/L, urea 5.3 (2.1) mmol/L and creatinine 91 (32) μmol/L.

Abnormal laboratory data of the patients are shown in Table 5. Five patients had anaemia (Hb <11 g/dL), 6 had leukopenia (white cell count <4 × 10⁹/L) and 2 had platelets <150 × 10⁹/L. A raised (≥20 mm/1st h) ESR (49 (29)) was found in 36 (40.4%)
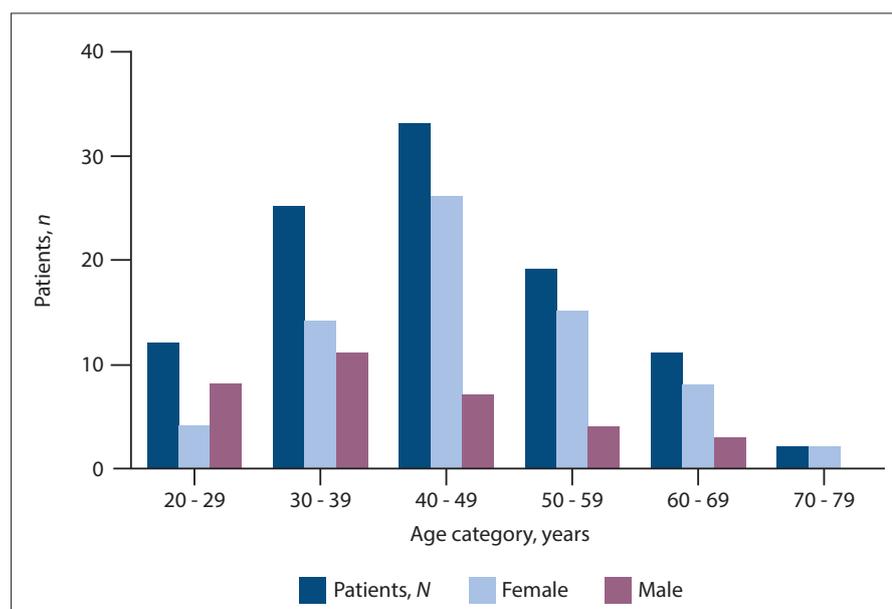

Fig. 1. Age category of patients with sarcoidosis.

Table 1. Common comorbid conditions and clinical profile of 102 patients with sarcoidosis

Comorbid conditions and clinical profile	n (%)*
Comorbid diseases	
Hypertension	33 (32.4)
Renal dysfunction (eGFR <90 mL/min/m²)	17 (19.5)
eGFR between 60 and 89	8 (7.8)
eGFR between 30 and 59	7 (6.9)
eGFR between 15 and 29	2 (2.0)
Overweight	18 (17.6)
Diabetes mellitus	16 (15.7)
Asthma	12 (11.8)
Gastroesophageal reflux disease	12 (11.8)
Clinical profile	
Family history of sarcoidosis	3 (2.9)
Non-smokers	87 (85.3)
Smokers (current/ex), n	8/7
Previous history of tuberculosis treatment	17 (16.7)
HIV positive, n (%) (mean CD4 count, cells/μL)	4 (3.9) (233)

eGFR = estimated glomerular filtration rate.
*Except where otherwise indicated.

Table 2. Presenting clinical features of 102 patients with sarcoidosis

Presenting clinical features	n (%)
Respiratory	
Cough	84 (82.4)
Dyspnoea	54 (53.9)
Chest pain	28 (27.5)
Haemoptysis	2 (2.0)
Crackles	38 (37.3)
Skin	
Erythema nodosum	8 (7.8)
Other cutaneous manifestations	27 (26.5)
Ocular	19 (18.6)
Nervous system	3 (2.9)
Constitutional	
Weight loss	25 (24.5)
Fever	10 (9.8)
Night sweats	20 (19.6)
Malaise or fatigue	31 (30.4)
Arthralgia	10 (9.8)
Jaundice	1 (1.0)
Asymptomatic	1 (1.0)

Table 3. Biopsy sites for histological confirmation in patients with sarcoidosis

Histological confirmation and biopsy sites	n (%)
Histological confirmation	99 (97.1)
Biopsy sites (multiple sites at times)	
Skin	29 (28.4)
Mediastinoscopy and lymph node	26 (25.5)
Transbronchial lung biopsy	26 (25.5)
Peripheral lymph node	9 (8.8)
Surgical lung biopsy	8 (7.8)
Clinical	3 (2.9)
Liver	3 (2.9)
Bone marrow and trephine	2 (2.0)
Lacrimal gland	2 (2.0)
Salivary gland	1 (1.0)
Nasal	1 (1.0)

Table 4. Organ involvement in patients with sarcoidosis

Organ involvement	n (%)
Lung parenchyma	74 (72.5)
Hilar lymphadenopathy	72 (70.6)
Skin	35 (34.3)
Papulonodular rash	20 (19.6)
Erythema nodosum	8 (7.8)
Disfiguring facial lesions	4 (3.9)
Lupus pernio	2 (2.0)
Psoriasiform rash	1 (1.0)
Peripheral lymphadenopathy	23 (22.5)
Ocular	19 (18.6)
Uveitis (anterior, posterior, pan-uveitis, retrobulbar)	18 (17.6)
Lacrimal gland enlargement	1 (1.0)
Bone and joints	12 (11.8)
Arthralgia	3 (2.9)
Arthritis	8 (7.8)
Dactylitis	1 (1.0)
Hepatomegaly	10 (10.0)
Splenomegaly	9 (8.8)
Hepatosplenomegaly	7 (6.9)
Cardiac	
Dilated cardiomyopathy	3 (2.9)
Cor pulmonale	2 (2.0)
Complete heart block	1 (1.0)
Neurological	3 (2.9)
Aseptic meningitis	2 (2.0)
Cerebrovascular accident	1 (1.0)
Renal stones	2 (2.0)
Parotid enlargement	2 (2.0)
Clubbing	2 (2.0)
Jaundice	1 (1.0)
Asymptomatic	1 (1.0)

patients. The sACE level was >52 IU in 56.8% of patients and the serum calcium was elevated (>2.5 mmol/L) in 20 (22.7%) cases. Hypercalciuria (>300 g/24 h) was observed in 4 (11.1%) of 36 patients in whom it was tested. Raised GGT (>78 IU/L) and AP (>128 IU/L) were observed in 28 (31.8%) and 19 (21.6%) patients, respectively. A decreased eGFR (<90 mL/min/m²) was noted in 17 (19.5%) patients.

Table 6 indicates the results of pulmonary function tests in patients with sarcoidosis. Lung function studies were performed on initial

Table 5. Abnormal laboratory results of patients with sarcoidosis

Parameter	n (%)	Mean (SD)
Anaemia (Hb <11 g/dL) (n=94)	5 (5.3)	10.2 (0.7)
Leukopenia (WCC <4 × 10⁹/L) (n=94)	6 (6.4)	3.1 (0.9)
Thrombocytopenia (Plt <150 × 10⁹/L) (n=91)	2 (2.2)	105 (5)
Raised ESR (≥20 mm/1st h)	36 (40.4)	49 (29)
Raised ACE (>52 IU) (n=95)	54 (56.8)	180 (396)
Raised serum Ca++ (>2.50 mmol/L) (n=88)	20 (22.7)	2.62 (0.19)
Hypercalciuria (>300 g/24 h) (n=36)	4 (11.1)	n/a
Raised GGT (>78 IU/L) (n=88)	28 (31.8)	173 (135)
Raised AP (>128 IU/L) (n=88)	19 (21.6)	287 (251)
eGFR <90 (mL/min/m2) (n=87)	17 (19.5)	54 (20)

SD = standard deviation; Hb = haemoglobin; WCC = white cell count; Plt = platelets; ESR = erythrocyte sedimentation rate; ACE = angiotensin-converting enzyme (normal 8 - 52 IU); Ca++ = calcium (normal 2.15 - 2.50 mmol/L); n/a = not applicable; GGT = gamma-glutamyl transferase (normal 0 - 78 IU/L); AP = alkaline phosphatase (normal 0 - 128 IU/L); eGFR = estimated glomerular filtration rate.

Table 6. Pulmonary function tests in patients with sarcoidosis

Pulmonary function tests	n (%)
FEV1 (n=99)	
≥80% predicted	56 (56.6)
<80% predicted	43 (43.4)
FVC (n=99)	
≥80% predicted	73 (73.7)
<80% predicted	26 (26.3)
FEV1/FVC (n=99)*	
75 - 82	34 (34.3)
<70	21 (21.2)†
TLC (n=78)	
≥80% predicted	66 (84.6)
<80% predicted	12 (15.4)
DLCO (n=78)	
<80% predicted	29 (37.2)

FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; TLC = total lung capacity; DLCO = diffusion capacity for carbon monoxide.
*75 - 82 considered normal.
†16 patients had a normal FVC and 5 a reduced FVC.

Table 7. Treatments received and relapse rate in patients with sarcoidosis

Treatments received	n (%)
CS	89 (87.3)
CQ	27 (26.5)
MTX	10 (9.8)
AZA	4 (3.9)
COL	2 (2.0)
CYC	1 (1.0)
Combination therapy	
CS + CQ	20 (19.6)
CS + MTX	4 (3.9)
CS + CQ + MTX	3 (2.9)
CS + CQ + MTX + AZA	2 (2.0)
CS + CQ + MTX + AZA + CYC	1 (1.0)
CS + CQ + COL	1 (1.0)
CS + COL	1 (1.0)
CS + AZA	1 (1.0)
Other	
Inhaled steroids	34 (33.3)
Nasal steroids	15 (14.7)
Relapse rate	54 (60.7)

CS = corticosteroids; CQ = chloroquine; MTX = methotrexate; AZA = azathioprine; COL = colchicine; CYC = cyclophosphamide.

merely observed, as they did not have an indication for therapy, all had a spontaneous clinical response; however, 54 patients of the cohort (60.7%) had a relapse, ~2 - 5 years after initiation of corticosteroids. Chloroquine was prescribed in 27 (26.5%) patients, methotrexate (MTX) in 10 (9.8%), azathioprine (AZA) in 4 (3.9%), colchicine (COL) in 2 (2.0%) and cyclophosphamide (CYC) in 1 patient. Almost always, MTX, AZA, COL and CYC were used in addition to steroids simultaneously and as steroid-sparing agents, or when patients had a poor response to corticosteroid therapy alone. Prophylaxis with INH was not used and co-trimoxazole was administered if patients were receiving ≥2 immunosuppressive agents. Nasal steroids were used to treat associated chronic rhinitis.

The main indications (sometimes multiple) for corticosteroid therapy in the 89 patients were their respiratory symptoms (90%) or their chest radiographic features and/or pulmonary function test abnormalities. In 13 (14.6%) patients, posterior uveitis or pan-uveitis was the indication for therapy. The other indications include disfiguring facial lesions (n=4; 4.5%) and lupus pernio (n=2; 2.2%), generalised lymphadenopathy (n=4; 4.5%), cardiac disease (3 with dilated cardiomyopathy and 1 with complete heart block), hepatosplenomegaly and generalised lymphadenopathy (n=3; 3.4%) and constitutional symptoms (n=3; 3.4%). Hypercalcaemia, renal calculi and meningitis were indications for steroids in 2 patients (2.2%) each. There was 1 (1.1%) patient each with an indication of jaundice, splenomegaly and neutropenia, parotidomegaly, superior vena cava obstruction and dactylitis. When combination therapy was used, it was almost always as additional therapy to corticosteroids, as steroid-sparing agents or if there was a poor response to corticosteroid therapy.

presentation in 99 of the 102 cases. Of the parameters tested, the forced expiratory volume in 1 second (FEV₁) was normal in 56 (56.6%) patients and the forced vital capacity (FVC) was normal in 73 (73.7%). The total lung capacity (TLC) was decreased in 12 (15.4%) cases. Airway obstruction (FEV₁/FVC ratio <70) was documented in 21 (21.2%) cases, and a reduced diffusion capacity for carbon monoxide (DL_CO) was noted in 29 (37.2%) patients.

The treatments received by the patients are shown in Table 7. Most had an indication for corticosteroids, which were prescribed in 89 (87.3%) patients. Patients were treated and followed up in the Respiratory Outpatient Department, together with the other subspecialties as needed. Duration of follow-up ranged from 3 months to >10 years. There was a good initial clinical response to therapy in most patients, and the few (13; 12.7%) who were

Discussion

The clinical characteristics of 102 patients with sarcoidosis have been described, of whom >97% had a histopathologically confirmed diagnosis. There was a female gender predominance, a high prevalence of comorbidities, an extremely high proportion of symptomatic disease and a high relapse rate. This study adds to the knowledge of the demographic, clinical and laboratory features of sarcoidosis patients on presentation, as well as the treatment of patients with sarcoidosis in SA.

The current study revealed that the median age of the sarcoidosis patients was 44.6 years and 64% were >40 years old. Comparable observations have been made in other SA studies.[2,3] The ATS, ERS and WASOG statement expresses that sarcoidosis consistently shows a predilection for adults <40 old, peaking at 20 - 29 years of age.[7,8] Scandinavian nations and Japan report a second peak in incidence in women >50 years old.[9] Studies in India have highlighted the older age of onset of sarcoidosis.[10,11] The diagnostic age was 47 years in males and 54 years in females in Italy.[12] In other countries, such as in Spain, the age gap is not as large (men – 44 years v. women – 49 years).[13] In an Estonian study the average age for men was 34 years and for women 43 years.[14] The claim quoted in the literature that the onset of sarcoidosis peaks between the ages of 20 and 45 years,[4] is not endorsed by the more recent reports, with peak ages closer to 30 - 55 years.

In this study, there were twice as many females (67.6%), similar to the previous study from Johannesburg (64.6%),[3] although there were somewhat fewer females in the Cape Town study.[2] Globally, it has been reported that there is a slight female preponderance in sarcoidosis,[4,15] even though a male preponderance has been reported in Indian studies.[10,11] In a worldwide study,[16] there was no definite gender predominance. There are signs that gender plays a part in the manifestation of the disease. In A Case Control Etiologic Study of Sarcoidosis (ACCESS),[15] women were more likely to have ocular and neurological involvement and erythema nodosum, and men were more likely to be hypercalcaemic.

Almost 17% of the current study patients had been treated for TB before being diagnosed as having sarcoidosis. Two patients developed confirmed active TB while being treated with corticosteroids. Four patients contracted HIV infection while receiving treatment for sarcoidosis; 3 patients had CD4 counts <200 cells/μL and 1 patient had a CD4 count >900 cells/μL. Patients with advanced HIV and low CD4 counts who receive antiretroviral therapy (ART) can develop sarcoidosis with immune reconstitution.[17]

Sarcoidosis is known to occur more frequently in non-smokers; the majority (87%) of patients in this study were non-smokers. One of the strongest negative associations to arise from the ACCESS analysis was a 35% lower chance of sarcoidosis among smokers than never smokers,[18] a result that is consistent with earlier reports.[19-22] Smoking seems to have a protective role in the occurrence of sarcoidosis, while smoking has no impact on the degree, course or outcome of the illness.[23] Familial sarcoidosis has been well described[24,25] and in the current study, familial association was seen in 3 patients.

There was a high prevalence of comorbidities in this cohort, most of which are common conditions in the general population and need to be diagnosed and treated promptly to improve the patients' overall quality of life (QoL). Comorbidities affecting QoL are more prevalent in sarcoidosis patients than in the general population[26-28] and add to the complexity of their disease and its treatment.[27,28] The occurrence of new comorbidities, whether linked to corticosteroid use, to sarcoidosis itself or to other factors, is independently and strongly correlated with adverse outcomes, including poorer QoL, hospitalisation risk and financial impacts.[29-31] Therefore, the occurrence of comorbidities during the disease course should be carefully evaluated, monitored and managed.

The most common symptom in the current study was dry cough (82%), followed by dyspnoea on exertion (52%), similar to previous studies.[7] Overall, 35 (34.3%) patients had cutaneous involvement and 8 patients had erythema nodosum. In patients of northern European descent with sarcoidosis, erythema nodosum as cutaneous involvement is more common.[32] The ACCESS study found that the prevalence of skin involvement (excluding erythema nodosum) was 15.9%, and of erythema nodosum 8.3%.[15] Lung crackles were noted in 32% of the study patients, and crackles have been reported in 20% and 50% of patient cohorts worldwide.[7] Two patients presented with haemoptysis, in 1 case due to post-TB bronchiectasis and the other patient having endobronchial sarcoidosis. Other possible mechanisms for haemoptysis include an associated mycetoma, coexistent cavitating TB or a possible viral bronchitis. Only 1 patient was asymptomatic and was diagnosed incidentally. Arthralgias were seen in 9% of patients in the current study. Joint symptoms have been recorded to occur in 25 - 39% of patients.[33,34] Hypercalcaemia was found in 23% and hypercalciuria in 11% (tested in 36 patients). The ACCESS study[35] found hypercalcaemia in 10 - 20% of patients and hypercalciuria in 40 - 62%. Raised creatinine levels and a decreased eGFR were noted in 17 (19.5%) patients; however, only 2 had renal calculi. Although the frequency of occurrence of renal involvement in sarcoidosis remains unclear, clinically significant renal involvement occurs occasionally.[36,37]

In the current study, leukopenia was seen in 6%, anaemia in 5% and 2 patients had thrombocytopenia. A raised ESR was noted in 36 (40.4%) patients. Previously, in the Johannesburg study, the ESR was noted to be elevated in 89% of patients. In the Cape Town study, 50% of patients had mild anaemia, 2 had leukopenia and 1 patient had thrombocytopenia. The ESR was commonly elevated, but rarely >90 mm/1st hour. Practically any haematological abnormality may be seen in sarcoidosis, including raised ESR, eosinophilia, leukopenia, anaemia, haemolytic anaemia, peripheral lymphopenia and thrombocytopenia.[4,33]

In this study, elevated levels of sACE were observed in 56.8% of patients. Elevated sACE levels occurred in 30 - 80% of sarcoidosis patients and may be a surrogate marker of the burden of granulomas.[38] In a previous SA study from Johannesburg,[3] elevated sACE levels were documented in 77.5% of patients.

In the current study, 1 patient presented with jaundice, and elevated GGT and AP were seen in 32% and 22%, respectively. Hepatic involvement in sarcoidosis is common in up to 70% of patients; however, most patients with liver involvement are asymptomatic.[39,40]

The chest radiograph was abnormal in >97% of patients. Stage II (48%) was found to be the most common radiographic stage of sarcoidosis identified in the current study. Significant variability exists regarding the chest radiographic findings in different studies. Several series found that stage I was the most common radiographic stage, but in most reports from Scandinavia, radiographic stages I and II were recorded to be predominant.[41] The classic sarcoidosis radiographic

finding is bilateral hilar lymphadenopathy and is believed to be present in nearly three-quarters of patients.[42] However, some US and British Isles studies[43] show a disproportionate incidence of radiographic stage III and IV disease. Previous SA studies[2,3] report that most of the abnormalities on chest radiography were stages II and III.

Pulmonary function tests in sarcoidosis showed an obstructive pattern in 21.2% of patients. This could be due to endobronchial involvement, large thoracic nodes compressing the airways and the coexistence of asthma. Other studies reported between 30% and 50% of patients having airway obstruction.[33,44,45] In this study, impaired diffusion was noted in 29 (37.2%) patients tested. Typical lung function anomalies in sarcoidosis include reduced lung volumes and decreased diffusion capacity.[38] DL_{CO} is the most sensitive of the lung function test parameters.[46]

The most frequent sites confirming granulomatous inflammation in the current study were: the skin (28%), mediastinal lymph nodes (26%) and in transbronchial lung biopsies (26%), with the latter being performed if no other simpler available site for biopsy was accessible. A transbronchial lung biopsy diagnostic yield varies from 40% to >90%, depending on the clinician's experience.[47]

In the current study, a biopsy was not performed in 3 (2.9%) patients with highly suggestive clinical, radiographic and laboratory features and response to corticosteroid therapy. These features may be diagnostic, particularly for sarcoidosis stage I (98% reliability) and stage II (89%).[48] Winterbauer et al.,[49] in an asymptomatic individual, observed that the presence of bilateral hilar and right paratracheal lymphadenopathy on chest radiography was specific for sarcoidosis. This approach has proven to be correct in >95% of cases of asymptomatic individuals and remains cost-effective, particularly in developing countries with limited resources.[50]

In the current study, 87.3% of patients had an indication for corticosteroid treatment. When uveitis, hypercalcaemia or constitutional symptoms were the indication for treatment, the response was invariably good. Forty-five patients were treated because of a pulmonary abnormality. Some patients with abnormal pulmonary function did not show objective evidence of improvement, although some felt better. Those with disfiguring facial lesions and lupus pernio also improved, as well as those with a high burden of disease with generalised lymphadenopathy and hepatosplenomegaly. The patients with parotidomegaly and dactylitis also responded favourably to therapy.

The duration of follow-up ranged from 3 months to >10 years, and 54 (60.7%) patients of the cohort had a relapse 2 - 5 years after initiation of corticosteroids. Relapse is likely when antisarcoidosis drugs are being tapered or discontinued. Reported sarcoidosis relapse rates range from 13% to 75%, occurring 1 - 12 months after treatment tapering or withdrawal.[51]

Study limitations

The current study has certain limitations that should be addressed in future research. As the facility in which the study was conducted is a tertiary care and referral centre and a single-centre site, the findings may not be generalisable to other institutions or the broader population. The data are dated and it is possible that if the study were to be performed currently, the findings may not be the same; however, more current research is planned to involve multiple study sites. Furthermore, the study population is heavily biased towards patients with sarcoidosis who have mainly pulmonary manifestations, and therefore does not necessarily reflect the findings in a general sarcoidosis population. Lastly, there were insufficient data to determine possible reason(s) for, and circumstances surrounding the high relapse rate, which need further investigation.

Conclusion

In countries with a high prevalence of TB, such as SA, sarcoidosis is often misdiagnosed as TB, as both diseases may look very similar in many ways. Therefore, patients with bilateral hilar lymphadenopathy with or without pulmonary infiltrates should be evaluated for the possibility of sarcoidosis, particularly if there are additional characteristics that suggest this possibility or if the patients are placed empirically on TB treatment and do not respond appropriately.

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