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Autoimmune comorbidities associated with sarcoidosis: a case-control study in the All of Us research program

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Abstract

Objective: The degree to which sarcoidosis patients are affected by autoimmune diseases is poorly understood. Prior studies of autoimmune co-morbidities in sarcoidosis have focused on populations outside the USA or have been impeded by small sample sizes and limited scope. This case–control study evaluated the association between sarcoidosis and autoimmune diseases in a large, diverse cohort based in the USA.

Methods: We used data from the All of Us research programme to conduct a case–control study involving patients ≥18 years old, from 2018 to the present, diagnosed with sarcoidosis. Sarcoidosis cases and age-, sex- and race-matched controls were identified in a 1:4 ratio. Autoimmune co-morbidities were compared between sarcoidosis patients and controls in univariable and multivariable analyses using logistic regression. The degree of association was measured using the odds ratio (OR).

Results: A total of 1408 sarcoidosis cases and 5632 controls were included in this study. Seven of 24 examined autoimmune diseases were significantly associated with sarcoidosis in our multivariable analysis ($P < 0.05$). The composite variable of any autoimmune disease was also significantly associated with sarcoidosis (OR = 2.29, $P < 0.001$).

Conclusion: We demonstrate an association between sarcoidosis and multiple autoimmune diseases in a large and diverse cohort based in the USA. These results underscore the need for careful screening of sarcoidosis patients for concomitant autoimmune disease.

Lay summary

What does this mean for patients?

Sarcoidosis is a condition that causes the immune system to become active in the body's organs, most commonly the lungs and lymph nodes. Past studies have found that some autoimmune diseases can be more common in people who have sarcoidosis than in those who do not. However, those studies focused on people who lived outside the USA and who had limited racial and ethnic diversity. Because genetics and geography can be important in sarcoidosis, the findings of these other studies might not necessarily apply to people in the USA. Therefore, we compared the rates of 24 autoimmune diseases in people with and without sarcoidosis in a large and racially diverse group of people in the USA. We found that 7 of 24 autoimmune diseases were more common in people with sarcoidosis than in those without, including two skin diseases and one musculoskeletal disease that have not been linked to sarcoidosis before. These results teach us more about autoimmune diseases in people with sarcoidosis and highlight the need for physicians to look for these diseases in patients with sarcoidosis.

Keywords: sarcoidosis, autoimmune, epidemiology, case–control

Key messages

- We found that >40% of sarcoidosis patients had at least one co-morbid autoimmune disease.
- The odds of having a co-morbid autoimmune disease were 2.3-fold higher in sarcoidosis cases than in controls.
- Associated autoimmune diseases spanned multiple organ systems, including skin, cardiovascular, endocrine, nervous and musculoskeletal/rheumatological conditions.

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Introduction

Sarcoidosis is a multisystem inflammatory condition characterized by the formation of granulomas in one or more tissues. It most commonly involves the lungs and intrathoracic lymph nodes; however, any organ can be affected. The clinical course is variable, with some patients experiencing spontaneous remission or remaining asymptomatic, whereas others develop chronic progressive and debilitating multisystemic disease. The prevalence and incidence of sarcoidosis vary markedly by geography, ethnicity and race. Internationally, the highest incidence rates have been observed in Nordic countries [1], while in the USA, Black or African American individuals experience substantially higher incidence rates compared with white Americans.

Histologically, the inflammation in sarcoidosis is characterized by non-caseating granulomas composed of epithelioid macrophages surrounded by a $CD4^+$ T-cell-predominant lymphocytic infiltrate. However, the immunological cues that lead to this pattern of inflammation are incompletely understood. Prior studies have implicated a predominantly Th1-polarized immune response involving cytokines such as IFN-γ, IL-2, IL-12, IL-15 and TNF-α [2]. Yet other studies have suggested that Th17- and even Th2-polarized responses might be at play [3, 4]. These inflammatory programmes, or cytokine hubs, are at the core of several autoimmune diseases [5].

Sarcoidosis demonstrates several features consistent with an autoimmune aetiology. Sarcoidosis is thought to develop in genetically predisposed individuals after exposure to an environmental or infectious trigger that leads to loss of immune tolerance. However, the root cause(s) and initial trigger(s) of the inflammatory response are unknown, as is also true in other autoimmune diseases. Development of sarcoidosis has been linked to immunological genetic factors, including specific HLA alleles [6] and *TNF* (and other) gene polymorphisms [7]. Other observations supporting T-cell dependence and potential autoimmune aetiology of sarcoidosis include the potential unmasking or triggering of sarcoidosis by T-cell-activating cancer immunotherapies [8] and expansion of $CD4^+$ T-cell subclones in lesions of sarcoidosis [9]. Furthermore, other studies performed outside the USA have demonstrated an association between sarcoidosis and certain autoimmune diseases [10].

Despite evidence of overlapping features between sarcoidosis and classical autoimmune diseases, the role of autoimmunity in the development of sarcoidosis and the degree to which patients with sarcoidosis are affected by more classical autoimmune diseases are poorly understood. Prior studies evaluating the association between sarcoidosis and autoimmune diseases have been impeded by the limited scope of other autoimmune diseases examined and small sample sizes [10]. Furthermore, the larger studies have focused on international populations rather than cohorts based in the USA [11–13]. Here, we perform a nested, matched, case–control study evaluating the associations between 24 autoimmune diseases and sarcoidosis in the All of Us research programme, a large cohort based in the USA that aims to enrol >1 million participants, with a focus on populations that are historically underrepresented in research.

Methods

A total of 214 206 patients in the All of Us database had electronic health records data available for analysis; this cohort includes adults ≥18 years of age from 2018 to the present. Data are available at www.allofus.nih.gov. The Yale University Institutional Review Board determined that this study does not involve human subjects and therefore Institutional Review Board review and approval were not required. Sarcoidosis cases were identified using International Classification of Diseases (ICD)-10-CM-D86, ICD-9-CM-135 or Systemized Nomenclature of Medicine (SNOMED) 9014002/156369008. Autoimmune diseases of interest ($n = 24$; Table 1) were chosen based on their generally accepted autoimmune pathogenesis and inclusion in prior studies evaluating their association with sarcoidosis in small cohorts or in cohorts not based in the USA. Autoimmune diseases were detected using the presence of at least one ICD-9, ICD-10 or SNOMED code for the diagnosis. We used nearest-neighbour propensity matching without replacement to select age-, sex- and race-matched controls for each case of sarcoidosis in a 4:1 ratio. Covariate balance between sarcoidosis patients and controls was compared using the standardized mean difference (SMD). Multivariable models were

Table 1. Features of sarcoidosis cases compared with age-, sex- and race-matched controls

Characteristic	Control	Sarcoidosis	SMD
n	5632	1408	
Age, mean (s.d.), years	62.98 (11.97)	62.98 (11.97)	<0.001
Female, *n* (%)	3808 (67.6)	952 (67.6)	<0.001
Race/ethnicity, *n* (%)			<0.001
Asian	<80	<20	
Black	2240 (39.8)	560 (39.8)	
Hispanic	608 (10.8)	152 (10.8)	
Other	160 (2.8)	40 (2.8)	
White	2592 (46.0)	648 (46.0)	
Ever smoker, *n* (%)	2495 (45.7)	577 (42.0)	0.075
BMI, mean (s.d.)	30.64 (7.83)	32.07 (8.07)	0.180
CCI, mean (s.d.)	2.27 (2.86)	4.09 (3.68)	0.549
Type 1 diabetes mellitus, *n* (%)	146 (2.6)	85 (6.0)	0.170
Multiple sclerosis, *n* (%)	56 (1.0)	37 (2.6)	0.123
Hashimoto's hypothyroidism, *n* (%)	36 (0.6)	<20	0.046
Graves' disease, *n* (%)	68 (1.2)	30 (2.1)	0.072
SLE, *n* (%)	90 (1.6)	88 (6.2)	0.241
Alopecia areata, *n* (%)	<20	<20	0.113
Vitiligo, *n* (%)	22 (0.4)	<20	0.092
Scleroderma, *n* (%)	<20	24 (1.7)	0.136
Autoimmune disease[a], *n* (%)	996 (17.7)	564 (40.1)	0.509
PM, *n* (%)	<20	<20	0.107
DM, *n* (%)	<20	<20	0.076
Vasculitis, *n* (%)	257 (4.6)	179 (12.7)	0.293
AS, *n* (%)	<20	<20	0.099
IgA deficiency, *n* (%)	<20	<20	0.058
ITP, *n* (%)	23 (0.4)	<20	0.083
APS, *n* (%)	<20	<20	0.086
Myasthenia gravis, *n* (%)	<20	<20	0.009
PMR, *n* (%)	34 (0.6)	28 (2.0)	0.123
Coeliac disease, *n* (%)	26 (0.5)	<20	0.033
Primary biliary cholangitis, *n* (%)	<20	<20	0.018
Autoimmune hepatitis, *n* (%)	<20	<20	0.012
Autoimmune gastritis, *n* (%)	95 (1.7)	61 (4.3)	0.155
RA, *n* (%)	212 (3.8)	166 (11.8)	0.303
SS, *n* (%)	79 (1.4)	74 (5.3)	0.216
IBD, *n* (%)	117 (2.1)	42 (3.0)	0.058

In accordance with All of Us research programme policy, all values <20 are presented as <20.
[a] Composite variable consisting of all individual diseases included in Table 1.
CCI: Charlson co-morbidity index; SMD: standardized mean difference.

constructed using universal confounders (age, sex and race), BMI, ever smoker status, the Charleston co-morbidity index (CCI) and autoimmune covariates of interest with significance level $P > 0.1$ in the univariate analysis. Logistic regression was used to determine whether each individual autoimmune co-morbidity or the composite variable of any autoimmune co-morbidity was associated with sarcoidosis in the multivariable analysis.

Results

We identified 1408 sarcoidosis cases with complete data and 5632 age-, sex- and race-matched controls for analysis (all matched variables had SMD < 0.001). The mean age was 63 years, and 67.6% were female; 46% were white, 39.8% Black and 10.8% Hispanic. Compared with controls, sarcoidosis cases had a greater percentage of every autoimmune disease under study, although differences in only 11 of the 24 diseases (type 1 diabetes mellitus, multiple sclerosis, SLE, alopecia areata, scleroderma, PM, vasculitis, PMR, autoimmune gastritis, RA and SS) were significant (SMD > 0.1; Table 1). In the multivariable analysis, 7 of 24 variables were significantly associated with sarcoidosis: alopecia areata [odds ratio (OR) = 4.20, $P = 0.001$], vitiligo (OR = 2.26, $P < 0.05$), SS (OR = 2.10, $P < 0.001$), vasculitis (OR = 1.94, $P < 0.001$), SLE (OR = 1.90, $P = 0.001$), multiple sclerosis (OR = 1.86, $P < 0.05$) and RA (OR = 1.60, $P < 0.001$) (Table 2). The composite variable of any autoimmune disease was also significantly associated with increased odds of sarcoidosis (OR = 2.29, $P < 0.001$).

Discussion

These results demonstrate an association between several autoimmune diseases and sarcoidosis in a large, diverse cohort of patients in the USA. Our findings expand upon the results of prior international studies suggesting an association of SS, SLE and multiple sclerosis with sarcoidosis [11–13]. In accordance with prior studies, we also did not find an association with IBD, coeliac disease, PMR or myasthenia gravis [11, 12]. The finding that having any autoimmune disease was significantly associated with sarcoidosis was also consistent with prior work, although our OR of 2.29 was higher than those reported in Spain (1.64), Taiwan (1.66) and UK (2.23) [11–13]. This might be attributable, in part, to significant differences in racial/ethnic representation in these studies (<1% to 3% Black or African American) compared with our study (39.8% Black or African American).

Table 2. Univariable and multivariable association of sarcoidosis with autoimmune diseases

Individual analysis Covariate	Univariable OR (95% CI; *P*-value)	Multivariable OR (95% CI; *P*-value)
Age	1.00 (1.00, 1.00; $P = 1.000$)	0.99 (0.98, 0.99; $P < 0.001$)
Female sex	1.00 (0.88, 1.13; $P = 1.000$)	0.89 (0.77, 1.02; $P = 0.092$)
Ever smoker	0.86 (0.76, 0.97; $P = 0.014$)	0.82 (0.72, 0.93; $P = 0.002$)
BMI	1.02 (1.01, 1.03; $P < 0.001$)	1.02 (1.01, 1.03; $P < 0.001$)
CCI	1.18 (1.16, 1.20; $P < 0.001$)	1.15 (1.13, 1.17; $P < 0.001$)
Alopecia areata	4.90 (2.41, 10.13; $P < 0.001$)	4.20[b] (1.80, 9.87; $P = 0.001$)
Autoimmune gastritis	2.64 (1.89, 3.65; $P < 0.001$)	1.35 (0.92, 1.97; $P = 0.124$)
APS	3.32 (1.61, 6.74; $P = 0.001$)	1.04 (0.43, 2.41; $P = 0.935$)
AS	3.80 (1.90, 7.56; $P < 0.001$)	1.92 (0.87, 4.13; $P = 0.099$)
DM	4.59 (1.65, 13.12; $P = 0.003$)	1.76 (0.55, 5.63; $P = 0.334$)
Graves' disease	1.78 (1.14, 2.72; $P = 0.009$)	1.09 (0.63, 1.82; $P = 0.750$)
Hashimoto's hypothyroidism	1.67 (0.89, 3.00; $P = 0.095$)	1.12 (0.53, 2.27; $P = 0.754$)
IBD	1.45 (1.00, 2.05; $P = 0.042$)	0.85 (0.56, 1.26; $P = 0.442$)
IgA deficiency	3.44 (1.11, 10.37; $P = 0.027$)	2.14 (0.59, 7.21; $P = 0.223$)
ITP	2.80 (1.45, 5.28; $P = 0.002$)	1.40 (0.64, 2.99; $P = 0.385$)
Multiple sclerosis	2.69 (1.75, 4.07; $P < 0.001$)	1.86[b] (1.14, 2.98; $P = 0.011$)
PMR	3.34 (2.01, 5.52; $P < 0.001$)	1.59 (0.89, 2.81; $P = 0.115$)
PM	13.42 (4.10, 59.92; $P < 0.001$)	3.39 (0.84, 17.09; $P = 0.102$)
RA	3.42 (2.76, 4.22; $P < 0.001$)	1.60[b] (1.24, 2.05; $P < 0.001$)
Scleroderma	5.12 (2.81, 9.49; $P < 0.001$)	1.18 (0.57, 2.44; $P = 0.647$)
SLE	4.11 (3.04, 5.54; $P < 0.001$)	1.90[b] (1.31, 2.73; $P = 0.001$)
SS	3.90 (2.82, 5.38; $P < 0.001$)	2.10[b] (1.43, 3.06; $P < 0.001$)
Type 1 diabetes mellitus	2.41 (1.83, 3.17; $P < 0.001$)	1.03 (0.74, 1.42; $P = 0.852$)
Vasculitis	3.05 (2.49, 3.72; $P < 0.001$)	1.94[b] (1.54, 2.44; $P < 0.001$)
Vitiligo	3.12 (1.63, 5.87; $P < 0.001$)	2.26[b] (1.10, 4.53; $P = 0.023$)
Pooled analysis		
Age	1.00 (1.00, 1.00; $P = 1.000$)	0.99 (0.98, 0.99; $P < 0.001$)
Female sex	1.00 (0.88, 1.13; $P = 1.000$)	0.89 (0.78, 1.03; $P = 0.112$)
Ever smoker	0.86 (0.76, 0.97; $P = 0.014$)	0.81 (0.71, 0.92; $P = 0.002$)
BMI	1.02 (1.01, 1.03; $P < 0.001$)	1.02 (1.01, 1.02; $P < 0.001$)
CCI	1.18 (1.16, 1.20; $P < 0.001$)	1.14 (1.12, 1.17; $P < 0.001$)
Autoimmune disease[a]	3.11 (2.74, 3.53; $P < 0.001$)	2.29[b] (1.98, 2.64; $P < 0.001$)

[a] Composite variable consisting of all individual diseases included in Table 1.
[b] Statistically significant at $P < 0.05$.
CCI: Charlson co-morbidity index; OR: odds ratio.

Notably, studies from Taiwan, UK and Sweden, among others, have identified an association between sarcoidosis and autoimmune thyroid disease [12–14]. Although our unadjusted analysis revealed almost double the percentage of co-morbid Hashimoto's hypothyroidism and Graves' disease in patients with sarcoidosis compared with controls, neither result was significant in the multivariate analysis. We also did not observe an association between sarcoidosis and IgA deficiency, APS, scleroderma, primary biliary cholangitis, autoimmune hepatitis, autoimmune gastritis, AS, inflammatory myopathies or ITP, although this has been described previously [11–13]. Again, these differences might be attributable to the fact that most studies demonstrating these associations were conducted in overwhelmingly European or Asian populations with very limited racial/ethnic diversity. In contrast, our study population based in the USA was one of the largest and most ethnically diverse, to date, with nearly 40% Black or African American participants. Such differences might impact the results, given the importance of genetics and environment in autoimmune disease and the development of sarcoidosis.

We also report statistically significant associations with alopecia areata, vitiligo and RA. To our knowledge, these associations have not been shown previously in large-scale studies and might represent findings unique to our diverse population based in the USA. It is important to note, however, that sarcoidosis can present with cutaneous manifestations that resemble other inflammatory dermatological diseases, and misclassification could potentially account for some of the observed associations. However, true coexistence between sarcoidosis and other inflammatory skin disease is an established phenomenon possibly resulting from a shared immunopathogenesis [15]. Lastly, it might be difficult clinically to differentiate inflammatory sarcoid arthritis and myopathy from RA.

The associations observed between classical autoimmune diseases and sarcoidosis might be explained, in part, by common pathomechanisms related to a shared underlying genetic predisposition. One gene that has been implicated in a variety of autoimmune diseases is nucleotide-binding oligomerization domain 2 (*NOD2*), which contributes to the innate immune response. Polymorphisms in *NOD2* have been linked to familial (i.e. Blau syndrome) and early-onset sarcoidosis, in addition to chronic inflammatory diseases including Crohn's disease and atopic dermatitis [16]. Butyrophilin-like 2 (*BTNL2*), which codes for an MHC class II-associated protein that regulates T-cell function, has also been implicated in both sarcoidosis and a wide variety of autoimmune diseases. Polymorphisms in *BTNL2* have been shown to increase the risk of developing sarcoidosis [17] and are associated with multiple sclerosis and alopecia areata, among other inflammatory conditions [18, 19]. Lastly, polymorphisms in *TNF* are associated with sarcoidosis and autoimmune conditions such as SLE, psoriasis and others, highlighting a potential common role of TNF-α in the pathogenesis of these disorders [7, 20]. These observations provide a possible mechanistic link that might explain some of the associations demonstrated in the present study.

Taken together, our results underscore the need for a thorough clinical history and review of systems when evaluating sarcoidosis patients, followed by appropriate screening for co-morbid autoimmune diseases as indicated. The variety of autoimmune diseases associated with sarcoidosis and breadth of organ systems involved highlight the importance of inter-specialty communication and multidisciplinary care when treating these patients. Our findings also have implications for treatment selection, in that therapies that broadly impede common autoimmune pathways, such as Janus kinase inhibitors, TNF-α blockers or broadly acting immunosuppressants (e.g. MTX and AZA), might be useful in treating polyautoimmunity in sarcoidosis patients with known co-morbid autoimmune conditions.

Our study is limited by the use of electronic health record data and reliance on diagnostic codes to identify sarcoidosis and autoimmune disease cases. Another limitation is the potential for misdiagnosis of multiorgan sarcoidosis as a separate autoimmune disease, because there can be considerable clinical overlap. Lastly, we are limited by lack of clinical information on sarcoidosis cases, including detailed clinical features, diagnosing provider type or associated histopathology.

Conclusion

This study builds upon previous research demonstrating an association between sarcoidosis and multiple autoimmune diseases by identifying similar findings in a large and diverse cohort based in the USA; these results underscore the need for careful screening of sarcoidosis patients for concomitant autoimmune disease. Further studies are needed to characterize the mechanism of this relationship and determine whether these associations are causally related to sarcoidosis pathogenesis.

Data availability

The All of Us research dataset is available for access at www.allofus.nih.gov.

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References

1. Arkema EV, Cozier YC. Sarcoidosis epidemiology: recent estimates of incidence, prevalence and risk factors. Curr Opin Pulm Med 2020;26:527–34.
2. Damsky W, Wang A, Kim DJ *et al.* Inhibition of type 1 immunity with tofacitinib is associated with marked improvement in long-standing sarcoidosis. Nat Commun 2022;13:3140.
3. Facco M, Cabrelle A, Teramo A *et al.* Sarcoidosis is a Th1/Th17 multisystem disorder. Thorax 2011;66:144–50.
4. Hauber HP, Gholami D, Meyer A, Pforte A. Increased interleukin-13 expression in patients with sarcoidosis. Thorax 2003;58:519–24.
5. Schett G, McInnes IB, Neurath MF. Reframing immune-mediated inflammatory diseases through signature cytokine hubs. N Engl J Med 2021;385:628–39.
6. Schürmann M, Lympany PA, Reichel P *et al.* Familial sarcoidosis is linked to the major histocompatibility complex region. Am J Respir Crit Care Med 2000;162:861–4.
7. Medica I, Kastrin A, Maver A, Peterlin B. Role of genetic polymorphisms in ACE and TNF-alpha gene in sarcoidosis: a meta-analysis. J Hum Genet 2007;52:836–47
8. Cornejo CM, Haun P, English J, Rosenbach M. Immune checkpoint inhibitors and the development of granulomatous reactions. J Am Acad Dermatol 2019;81:1165–75.
9. Zissel G, Bäumer I, Fleischer B, Schlaak M, Müller-Quernheim J. TCR V β families in T cell clones from sarcoid lung parenchyma, BAL, and blood. Am J Respir Crit Care Med 1997;156:1593–600.
10. Song M, Manansala M, Parmar PJ *et al.* Sarcoidosis and autoimmunity. Curr Opin Pulm Med 2021;27:448–54.
11. Brito-Zerón P, Pérez-Alvarez R, Feijoo-Massó C *et al.*; SarcoGEAS-SEMI Registry. Coexistence of immune-mediated diseases in sarcoidosis. Frequency and clinical significance in 1737 patients. Joint Bone Spine 2021;88:105236.
12. Wu C-H, Chung P-I, Wu C-Y *et al.* Comorbid autoimmune diseases in patients with sarcoidosis: a nationwide case–control study in Taiwan. J Dermatol 2017;44:423–30.
13. Rajoriya N, Wotton CJ, Yeates DGR, Travis SPL, Goldacre MJ. Immune-mediated and chronic inflammatory disease in people with sarcoidosis: disease associations in a large UK database. Postgrad Med J 2009;85:233–7.
14. Papadopoulos KI, Hörnblad Y, Liljebladh H, Hallengren B. High frequency of endocrine autoimmunity in patients with sarcoidosis. Eur J Endocrinol 1996;134:331–6.
15. Wanat KA, Schaffer A, Richardson V, VanVoorhees A, Rosenbach M. Sarcoidosis and psoriasis: a case series and review of the literature exploring co-incidence vs coincidence. JAMA Dermatol 2013; 149:848–52.
16. Correa RG, Milutinovic S, Reed JC. Roles of NOD1 (NLRC1) and NOD2 (NLRC2) in innate immunity and inflammatory diseases. Biosci Rep 2012;32:597–608.
17. Lin Y, Wei J, Fan L, Cheng D. *BTNL2* gene polymorphism and sarcoidosis susceptibility: a meta-analysis. PLoS One 2015;10:e0122639.
18. Traherne JA, Barcellos LF, Sawcer SJ *et al.* Association of the truncating splice site mutation in *BTNL2* with multiple sclerosis is secondary to *HLA-DRB1*15*. Hum Mol Genet 2006;15:155–61.
19. Lee S, Paik SH, Kim H-J *et al.* Exomic sequencing of immune-related genes reveals novel candidate variants associated with alopecia universalis. PLoS One 2013;8:e53613.
20. Pan H-F, Leng R-X, Wang C *et al.* Association of TNF-α promoter-308 A/G polymorphism with susceptibility to systemic lupus erythematosus: a meta-analysis. Rheumatol Int 2012;32:2083–92.