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Comorbidities associated with discoid lupus erythematosus: A case-control study in the All of Us research program

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Introduction

- Lupus erythematosus (LE) is a chronic autoimmune disorder that frequently involves the skin and predominantly affects women.[1]
- While the most common chronic cutaneous lupus subtype is discoid LE (DLE),[1] its common comorbidities are undercharacterized.[2] Prior research has demonstrated several cardiovascular comorbidities exist within the DLE population,[4] yet other domains have been relatively underexplored.
- We sought to explore the **potential comorbidities associated with DLE patients** using electronic health record (EHR) data from the All of Us Research Program, a National Institutes of Health database that strives to **include participants from groups historically underrepresented in biomedical research.**

Methods

Overview:

- We conducted **a nested, case-control study** on adults (aged 18+) within the **All of Us research program** from **May 2018 to July 2022**.
- The Mass General Brigham IRB deemed the study to be non-human subjects' research. Cases of DLE were identified using Observational Medical Outcomes Partnership (OMOP) Common Data Model code 4066824, including ICD-10CM code L93.0 and SNOMED diagnostic code 200938002. Each DLE case was matched with four controls of the same age, race/ethnicity, and gender (all P = 1.000). Comorbidities were assessed using OMOP (please see Table 1 for complete list).

Data Analysis Procedure:

- **Pearson χ2** was used to compare data between cases and controls.
- **Conditional logistic regression** was used to calculate odds ratios (ORs) to evaluate DLE-associated comorbidities. Data analysis was performed using Python version 3.7.12. Significance was determined with two-sided P < .05.

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Results

Table 1. Characteristics of DLE patients and Control group in All of Us

	DLE, No. (%) (n= 919)	Control, No. (%)(n=3676)	p-value*
Race/Ethnicity			1.00
White	339 (36.9)	1356 (36.9)	
Black or African American	300 (32.6)	1200 (32.6)	
Hispanic	200 (21.8)	800 (21.8)	
Asian	30 (3.3)	120 (3.3)	
Other	50 (5.4)	200 (5.4)	
Gender			1.00
Male	103 (11.2)	412 (11.2)	
Female	798 (86.8)	3192 (86.8)	
Other	18 (2.0)	72 (2.0)	
Age (y)			1.00
Average	55.2	55.2	
Standard Deviation	14.7	14.7	

Table 2. Comorbidities of DLE patients and Control group in All of Us

	OMOP Code	DLE, No. (%) (n=919)	Control, No. (%) (n=3676)	Odds Ratio (95% CI)	p-value*
Dermatological Comorbidities					
Acne	141095	110 (12.0)	300 (8.2)	1.57 (1.24-1.98)	<0.001
Alopecia areata	141933	24 (2.6)	≤20 (≤0.5)	7.56 (3.83-14.9)	<0.001
BCC of skin	4112752	24 (2.6)	78 (2.1)	1.32 (0.83-2.11)	0.239
Contact dermatitis (Allergic)	4031019	27 (2.9)	69 (1.9)	1.56 (0.99-2.45)	0.053
Contact dermatitis (Irritant)	4004352	24 (2.6)	47 (1.3)	2.07 (1.26-3.4)	0.004
Dermatomyositis	80182	≤20 (≤2.2)	≤20 (≤0.5)	15.5 (5.77-41.62)	<0.001
Eczema	133835	152 (16.5)	357 (9.7)	1.88 (1.53-2.31)	<0.001
Hidradenitis suppurativa	4241223	25 (2.7)	40 (1.1)	2.42 (1.47-3.99)	<0.001
Lichen planus	132703	21 (2.3)	22 (0.5)	4.07 (2.21-7.49)	<0.001
Localized scleroderma	441928	24 (2.6)	24 (0.7)	4.45 (2.49-7.98)	<0.001
Melanoma of skin	141232	≤20 (≤2.2)	23 (0.6)	1.57 (0.72-3.41)	0.253
Psoriasis	140168	56 (6.1)	104 (2.8)	2.14 (1.54-2.99)	<0.001
SCC of skin	4111921	≤20 (≤2.2)	24 (0.6)	2.53 (1.32-4.83)	0.005
Seborrheic dermatitis	137053	126 (13.7)	190 (5.2)	2.95 (2.32-3.74)	<0.001
Vitiligo	138502	≤20 (≤2.2)	22 (0.6)	2.22 (1.06-4.64)	0.035
Non-dermatological Comorbidities					
Alcoholism	4218106	61 (6.6)	282 (7.7)	0.88 (0.66-1.17)	0.380
Anxiety	441542	477 (51.9)	1358 (36.9)	1.86 (1.61-2.15)	<0.001
Cardiovascular disorder	134057	836 (91.0)	2531 (68.9)	4.61 (3.64-5.84)	<0.001
Celiac disease	194992	**≤20 (≤2.2)	21 (≤0.6)	3.83 (1.97-7.46)	<0.001
Depressive disorder	440383	480 (52.2)	1324 (36.0)	1.97 (1.7-2.28)	<0.001
Diabetes mellitus (Type 1)	201254	37 (4.0)	90 (2.4)	1.67 (1.13-2.47)	0.010
Diabetes mellitus (Type 2)	201826	259 (28.2)	821 (22.3)	1.38 (1.18-1.63)	<0.001
End stage renal disease	193782	70 (7.6)	65 (1.8)	4.97 (3.49-7.07)	<0.001
Gingivitis	4281516	32 (3.5)	94 (2.6)	1.52 (1.01-2.3)	0.046
Hypertensive disorder	316866	636 (69.2)	1698 (46.2)	2.62 (2.25-3.06)	<0.001
Hyperthyroidism	4142479	69 (7.5)	145 (3.9)	1.92 (1.43-2.58)	<0.001
Hypothyroidism	140673	265 (28.8)	586 (15.9)	2.15 (1.82-2.54)	<0.001
Inflammatory bowel disease	4074815	25 (2.7)	29 (0.8)	3.4 (1.99-5.81)	<0.001
Interstitial lung disease	4119786	109 (11.9)	93 (2.5)	5.24 (3.93-6.99)	<0.001
Lung cancer	443388	≤20 (≤2.2)	32 (0.9)	1.83 (0.99-3.39)	0.054
Lymphoma	432571	33 (3.6)	35 (1.0)	3.57 (2.22-5.72)	<0.001
Nephritis	193253	243 (26.4)	127 (3.5)	10.38 (8.23-13.09)	<0.001
Rheumatoid arthritis	80809	247 (26.9)	134 (3.6)	9.87 (7.87-12.38)	<0.001
Seizure	377091	148 (16.1)	208 (5.7)	3.17 (2.53-3.97)	<0.001
Sjögren syndrome	254443	171 (18.6)	57 (1.6)	14.02 (10.32-19.04)	<0.001

Discussion

- **Our case-control study reports on several comorbidities of DLE, which remain under-characterized in the literature,** and reinforces a known link between DLE and cardiovascular disease in a dataset enriched with individuals from diverse backgrounds historically underrepresented in biomedical research.[3,4]
- **Cardiovascular risks in DLE** are hypothesized to arise from skin-specific inflammation (i.e., chronic elevation of pro-inflammatory cytokines like interleukin-17).[4]
- Significant associations were also found between DLE and several other **autoimmune conditions** noted in patients with CLE without concurrent SLE,[5] which may be explained by overlapping genetic and environmental factors.
- The increased odds of **depression and anxiety** may reflect severe quality-of-life impairments from chronic autoimmune diseases like DLE.
- **Limitations** include reliance on EHR and lack of DLE severity data. Clinical similarities between dermatomyositis, lichen planus, and DLE may contribute to their respective increased odds of concurrent diagnosis with DLE and warrant further analyses in settings with detailed chart reviews and clinical images.
- Our study underscores the need for further DLE research to enhance disease pathophysiology understanding, patient management, and avenues for DLE-specific treatment, particularly among individuals from diverse backgrounds.

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