Cardiometabolic Risk in Individuals with Down Syndrome and Psoriasis
A Retrospective Cohort Study Using the Epic Cosmos Data Set

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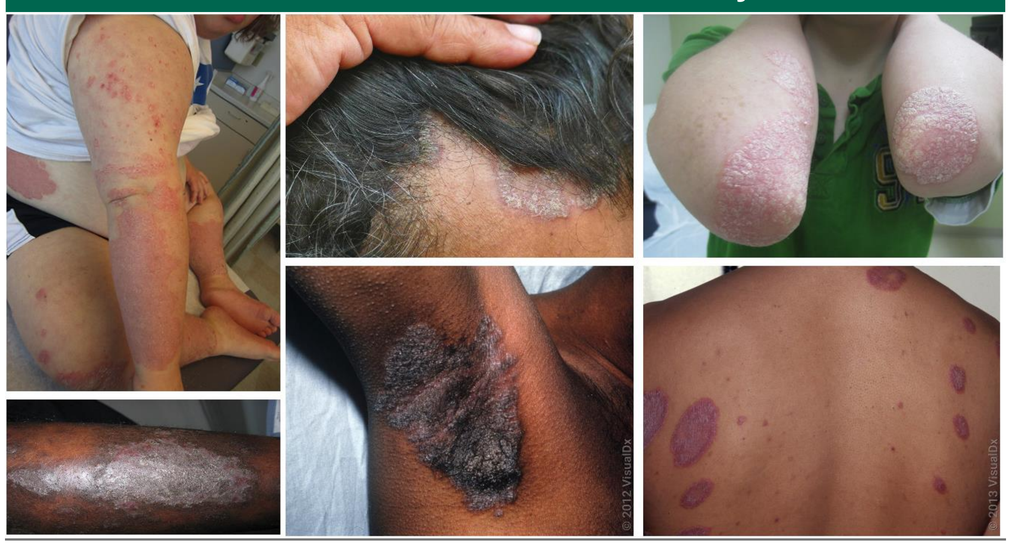
BACKGROUND

Psoriasis is common in individuals with Down syndrome (DS), **yet the association of psoriasis with cardiometabolic disease in DS is unknown** (**Figure 1**).[1] In the neurotypical population, psoriasis is associated with increased risk of metabolic and cardiovascular disease.[2] In contrast, individuals with DS exhibit a distinct cardiometabolic phenotype characterized by lower baseline blood pressure and reduced atherosclerotic cardiovascular disease.[3] **Whether psoriasis alters the unique cardiometabolic profile of DS remains unclear.**

OBJECTIVE

Assess cardiometabolic and cardiovascular comorbidities in individuals with DS and psoriasis.

FIGURE 1. Psoriasis in individuals with Down syndrome



METHODS

A retrospective cohort study using the United States Epic Cosmos dataset was performed from January 1, 2017, to December 31, 2024. Inclusion criteria included **≥1 encounter with an ICD-10 diagnosis code for DS, ≥2 encounters for cutaneous psoriasis, and ≥1 medical encounter ≥365 days after the first psoriasis diagnosis**. Patients with DS and psoriasis were matched 1:4 to individuals with DS by age and sex. Cardiometabolic comorbidities were identified using ICD-10 codes. The prevalence of each comorbidity was compared between psoriasis and controls with chi-square tests. Obesity was explored as a mediator of the association between psoriasis and cardiometabolic comorbidities.

RESULTS

2,582 patients with DS and psoriasis were matched to 10,328 controls (**Table 1**). Compared to controls, individuals with DS and psoriasis had a statistically significantly higher prevalence of overweight/obesity, dyslipidemia, type 2 diabetes, sleep apnea, and metabolic dysfunction–associated fatty liver disease (**Table 2**). There were no differences between cohorts in hypertension, atherosclerosis, myocardial infarction, or stroke. Mediation analysis demonstrated that obesity had a significant indirect effect on dyslipidemia, type 2 diabetes, sleep apnea, and MAFLD

LIMITATIONS

Diagnoses were based on ICD-10 codes, which are subject to diagnostic inaccuracies. Data on psoriasis severity, anthropometric measurements, laboratory values, and diagnostic studies were not available. Since the life expectancy of individuals with DS is increasing, long-term cardiovascular risk may be incompletely captured.

WHY THIS RESEARCH MATTERS

These findings suggest that psoriasis in individuals with DS is associated with increased metabolic disease burden without a corresponding increase in hypertension or cardiovascular outcomes. Obesity appears to also be a primary driver for this increased metabolic disease burden. These observations highlight potential differences in immune and vascular biology. Individuals with DS exhibit chronic immune dysregulation, including overactivation of type I interferon signaling, which may predispose to both psoriasis and metabolic dysfunction.[4] However, genes encoded on chromosome 21, including *RCAN1* and *DYRK1A*, may provide vascular protection by dampening calcineurin–NFAT signaling, a central pathway in vascular inflammation and atherogenesis.[5] **Collectively, these findings suggest that the effects of psoriasis in DS may be mediated predominantly through metabolic rather than vascular pathways, supporting a potential decoupling of systemic inflammation from cardiovascular risk in this population.**

FUNDING

National Institutes of Health INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome (INCLUDE) Project R03 - RFA-OD-22-008

AFFILATIONS

REFERENCES

FIGURE 2. Study Flowchart

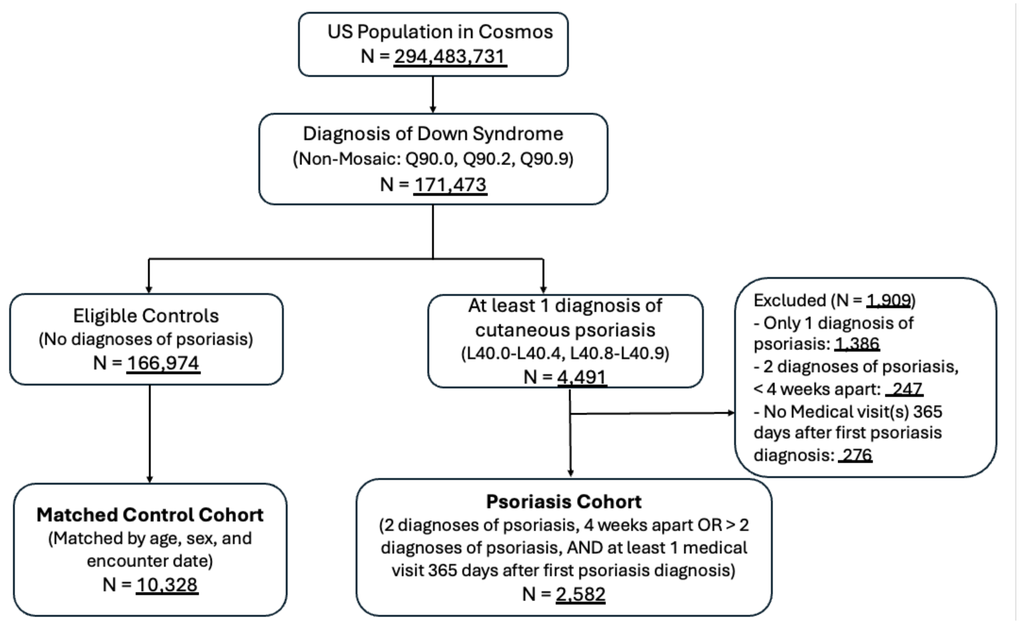


TABLE 1. Demographics Characteristics

Group		Psoriasis cases	Control population
Overall population		2,582	10,328
Sex			
	Female	1,189 (46.1%)	4,756 (46.1%)
	Male	1,393 (53.9%)	5,572 (53.9%)
Age at first psoriasis diagnosis (years), Mean (SD)		31.1 (14.9)	-
Age range, years			
	0 – 12	226 (8.8%)	904 (8.8%)
	13 – 17	296 (11.5%)	1,184 (11.5%)
	18 – 29	813 (31.5%)	3,252 (31.5%)
	30 – 39	499 (19.3%)	1,996 (19.3%)
	40 – 49	351 (13.6%)	1,404 (13.6%)
	50 - 59	311 (12.0%)	1,244 (12.0%)
	60+	86 (3.3%)	344 (3.3%)
Race and Ethnicity			
	Hispanic	353 (13.7%)	1,364 (13.2%)
	Non-Hispanic Asian	113 (4.4%)	308 (3.0%)
	Non-Hispanic Black or African American	117 (4.5%)	1,124 (10.9%)
	Non-Hispanic Other (including multiracial)	51 (2.0%)	181 (1.8%)
	Non-Hispanic White	1,802 (69.8%)	6,778 (65.6%)
	Unknown	146 (5.7%)	573 (5.6%)
United States Census Region			
	Midwest	828 (32.5%)	3,261 (31.6%)
	Northeast	532 (20.6%)	2,103 (20.4%)
	South	831 (32.2%)	3,470 (33.6%)
	West	374 (14.5%)	1,474 (14.3%)
	US Territories	2 (0.1%)	2 (0.02%)
	Unknown	5 (0.2%)	18 (0.2%)
Insurance at first psoriasis diagnosis			
	Medicaid	553 (21.4%)	2,097 (20.3%)
	Medicare	835 (32.3%)	2,979 (28.8%)
	Commercial (Miscellaneous other)	1,005 (38.9%)	3940 (38.2%)
	Uninsured (self-pay)	6 (0.2%)	37 (0.4%)
	Unknown	177 (6.9%)	1,253 (12.1%)
	Not Applicable	6 (0.2%)	22 (0.2%)

Table 2. ICD-10–Defined Cardiometabolic and Cardiovascular Comorbidities in Individuals with Down Syndrome with and without Psoriasis

	Psoriasis Cohort (N = 2,582)	Control Cohort (N = 10,328)	P-value
ICD-10 Cardiometabolic Risk Factors			
E66* - Overweight, obese	1342 (52.0%)	4359 (42.2%)	<.0001
I10 - Essential (Primary) hypertension	365 (14.1%)	1556 (15.1%)	0.2476
E78* - Disorders of lipoprotein metabolism and other lipidemias	1013 (39.2%)	3619 (35.0%)	<.0001
E11* - Type 2 diabetes mellitus	368 (14.3%)	1261 (12.2%)	0.0057
G47.3* - Sleep apnea	1000 (38.7%)	3302 (32.0%)	<.0001
K76.0 - Metabolic Associated Fatty Liver Disease (MAFLD)	243 (9.4%)	650 (6.3%)	<.0001
ICD-10 Codes – Cardiovascular Disease			
I70*- Atherosclerosis	32 (1.2%)	98 (0.9%)	0.2255
I20* - Ischemic chest pain without acute MI	11 (0.4%)	45 (0.4%)	0.9999
I21* - Acute Myocardial Infarction	35 (1.4%)	181 (1.8%)	0.1865
I22* - Subsequent myocardial infarction	2 (0.1%)	2 (0.0%)	0.3815
I24* - Other acute ischemic heart diseases	25 (1.0%)	93 (0.9%)	0.8352
I25* - Chronic ischemic heart disease	81 (3.1%)	346 (3.4%)	0.6313
G45.9 – Transient cerebral ischemic attack, unspecified	10 (0.4%)	54 (0.5%)	0.4712
I60* - Nontraumatic subarachnoid hemorrhage	8 (0.3%)	46 (0.4%)	0.4330
I61* - Nontraumatic intracerebral hemorrhage	13 (0.5%)	46 (0.4%)	0.8194
I62*- Other and unspecified nontraumatic intracranial hemorrhage	12 (0.5%)	62 (0.6%)	0.5026
I63* - Cerebral infarction	63 (2.4%)	268 (2.6%)	0.7070
I64* - Stroke, not specified as hemorrhagic or infarction	0 (0%)	0 (0%)	-
I65* – Occlusion and stenosis of precerebral arteries	17 (0.7%)	79 (0.8%)	0.6633
I66* – Occlusion and stenosis of cerebral arteries	3 (0.1%)	37 (0.4%)	0.0748
I67* – Other cerebrovascular diseases	44 (1.7%)	186 (1.8%)	0.8030
I68* – Cerebrovascular disorders in diseases classified elsewhere	5 (0.2%)	14 (0.1%)	0.6879