doi:10.36849/JDD.8401R1

February 2025 212 Volume 24 • Issue 2

BRIEF COMMUNICATION

Journal of Drugs in Dermatology

Insights Into Demographics, Comorbidities, and Risk Factors in Keloids and Hypertrophic Scars: A Retrospective Study

Ajay N. Sharma MD MBA,[a] Abhinav Birda BA,[b] Minjun Park BS,[c] Sarah Choe BS,[a] Jesse Salas BS,[a] Colin Kincaid BS,[a] Natasha A. Mesinkovska MD PhD[a]

[a]Department of Dermatology, University of California Irvine, Irvine, CA
[b]School of Medicine, Rosalind Franklin University, Chicago, IL
[c]School of Medicine, Saint Louis University, St. Louis, MO

ABSTRACT

Hypertrophic scars and keloids represent abnormal wound healing, manifesting as raised scars confined to or extending beyond the wound margin, respectively. Understanding the risk factors associated with these scarring types is crucial for prevention and management. Utilizing the TriNetX global health research network database, we analyzed the data of 6,249 patients with hypertrophic scars or keloids. We employed the ICD-10 code L91.0 for identification, generating a control cohort matched by age, sex, and race. Associations between scarring and race, ethnicity, and various comorbidities were quantified. The analysis revealed that hypertrophic scars and keloids were more commonly associated with Black/African American individuals (OR=1.74, $P<0.01$) and less so with White races and Hispanic ethnicity. Significant comorbidities associated with increased risk included scarring alopecia, rosacea, atopic dermatitis, and acne. Inadequate sample size limited analysis for conditions like vitiligo. The findings suggest a higher prevalence of these scars in Black/African American races, potentially linked to melanocyte-mediated fibroblast and extracellular matrix activities. A notable correlation with inflammatory conditions suggests shared cytokine pathways, highlighting IL-4 and IL-13 as therapeutic targets. The strong association between scarring alopecia and skin cancers may implicate chronic inflammation and treatment-related scarring. Limitations of the study include its retrospective design, possible misdiagnosis, and small sample sizes for certain comorbidities.

J Drugs Dermatol. 2025;24(1):212-215. doi:10.36849/JDD.8401R1

INTRODUCTION

Hypertrophic scars, those that are raised and confined to the wound margin, and keloidal scars, those that extend beyond the wound margin, are manifestations of abnormal wound healing.[1] In effort to better stratify and define the characteristics of those at risk for hypertrophic scars and keloids, we utilized a large global health research network database from 108 health care organizations (TriNetX) to quantify the associations between race, ethnicity, and comorbidities.

MATERIALS AND METHODS

We identified the cohort of all patients with hypertrophic scars/keloids and generated a control cohort of age, sex, and race-matched patients without those diagnoses. The ICD-10 code, L91.0, which codes both hypertrophic scars and keloids, was utilized. Despite the lack of separation with this single code, given the significant overlap in pathophysiology, clinical presentation, and management of both entities, we believe the results of this analysis still provide a novel contribution to the literature.

RESULTS

A total of 6,249 patients, roughly 1% of the total database, with hypertrophic scars and keloids (52% female, mean [SD] age 48.1 [24.2] years) were identified (Table 1). As anticipated, higher association was identified for hypertrophic scars and keloids in Black/African American races (OR=1.74, $P<0.01$), while White race and Hispanic ethnicity conferred a decreased risk (OR=0.71, $P<0.01$), (OR= 1.06, $P>0.05$), respectively (Table 1). The highest associated risk factors included history of scarring alopecia (OR=3.64), rosacea (OR=3.50), atopic dermatitis (OR=3.47), and acne (OR=3.42) (all $P<0.01$) (Table 2).

TABLE 1.

Patient Demographic Information for Keloid/Hypertrophic Scar Cohort and Control CohortAfter Propensity Score Matching for Age, Sex, and Race (left)

	Hypertrophic Scars/Keloids and Control Cohorts			Prevalence of Comorbidities in Hypertrophic Scars/Keloids Cohort						
	Hypertrophic Scars/Keloids (n=6,249)	Controls (n=6,249)	*P*-value	Acne (n = 621)	Dermatitis/ Eczema (n = 2,624)	Rosacea (n = 404)	Scarring Alopecia (n=371)	Melanoma and other malignancy of the skin (n=2,303)	Nicotine Dependence (n=1,071)	Diabetes (n=885)
Age, mean [SD] years	48 (24)	48 (25)	0.85	45 (22)	54 (24)	66 (16)	55 (20)	69 (13)	63(17)	64 (16)
Sex, no (%)										
Female	3,214 (51)	3,214 (51)	1	382 (62)	1,327 (51)	241 (60)	301 (81)	1,069 (47)	469 (44)	403 (47)
Male	2,944 (47)	2,946 (47)	0.97	214 (35)	1,228 (48)	152 (38)	63 (17)	1,192 (52)	565 (53)	444 (51)
Race, no (%)										
White	3,946 (63)	3,961 (63)	0.78	368 (60)	1,826 (71)	342 (85)	249 (67)	2,039 (89)	769 (72)	545 (63)
Black/AA	1,200 (19)	1,200 (19)	1	130 (21)	378 (15)	10 (2)	60 (16)	19 (1)	145 (13)	190 (22)
Asian	192 (3)	177 (3)	0.43	20 (3)	56 (15)	10 (2)	13 (4)	10 (0)	21 (2)	23 (3)
Other	279 (4)	279 (4)	1	27 (4)	110 (4)	10 (2)	14 (4)	37 (2)	18 (2)	29 (3)
Unknown	586 (9)	586 (9)	1	60 (10)	203 (8)	39 (9)	29 (8)	176 (8)	103 (9)	67 (7)
Ethnicity, no (%)										
Not Hispanic	5,031 (81)	5,030 (81)	0.98	509 (83)	2,201 (85)	359 (90)	314 (85)	2,073 (91)	909 (85)	747 (84)
Hispanic	564 (9)	565 (9)	0.98	48 (8)	193 (7)	16 (4)	25 (7)	31 (1)	39 (4)	62 (7)
Unknown	654 (10)	654 (10)	1	55 (9)	196 (8)	25 (6)	32 (9)	177 (8)	117 (11)	76 (9)

	Hypertrophic Scars/Keloids and Control Cohorts			Prevalence of Comorbidities in Hypertrophic Scars/Keloids Cohort						
	Hypertrophic Scars/Keloids (n=6,249)	Controls (n=6,249)	*P*-value	Inflammatory Polyarthropathies (n = 806)	Hypothyroid (n=740)	Hypertension (n=2,408)	Neoplasms (n=3,848)	Fibroids (n = 215)	Alopecia Areata (n= 35)	Vitiligo (n = 19)
Age, mean [SD] years	48 (24)	48 (25)	0.85	68 (15)	64 (17)	64(17)	60 (19)	56 (13)	54 (20)	52 (19)
Sex, no (%)										
Female	3,214 (51)	3,214 (51)	1	407 (51)	203 (28)	1,086 (46)	2,135 (56)	212 (100)	27 (77)	10 (52)
Male	2,944 (47)	,2946 (47)	0.97	380 (47)	521 (70)	1,237 (52)	1,662 (43)	0 (0)	10 (28)	10 (52)
Race, no (%)										
White	3,946 (63)	3,961 (63)	0.78	599 (74)	564 (76)	1,638 (69)	2,903 (75)	112 (52)	19 (54)	11 (57)
Black/AA	1,200 (19)	1,200 (19)	1	101 (13)	64 (9)	422 (18)	426 (11)	60 (27)	10 (28)	10 (52)
Asian	192 (3)	177 (3)	0.43	17 (2)	18 (2)	47 (2)	64 (2)	15 (6)	10 (28)	0 (0)
Other	279 (4)	279 (4)	1	16 (2)	21 (3)	58 (2)	105 (3)	10 (4)	10 (28)	10 (52)
Unknown	586 (9)	586 (9)	1	62 (8)	65 (9)	183 (8)	312 (8)	17 (7)	10 (28)	0 (0)
Ethnicity, no (%)										
Not Hispanic	5,031 (81)	5,030 (81)	0.98	722 (90)	625 (84)	2,050 (87)	3,324 (87)	184 (85)	32 (91)	14 (73)
Hispanic	564 (9)	565 (9)	0.98	34 (4)	48 (7)	118 (5)	206 (5)	19 (9)	10 (28)	10 (52)
Unknown	654 (10)	654 (10)	1	50 (6)	67 (9)	197 (8)	318 (8)	12 (6)	10 (28)	10 (52)

Overall prevalence of risk factors in keloid/hypertrophic scar cohort and each subgroup's respective demographic information (right).The following ICD-10 codes used to identify the prevalence of prior reported comorbidities in both the study and control populations: diabetes=E08-E13, hypertension=I10-I16, nicotine dependence=Z87.891, neoplasm=C00-D49, melanoma and other malignancies of the skin=C43-C44, hypothyroid=E03, dermatitis/eczema=L20-L30, inflammatory polyarthropathies=M05-M14, acne=L70, rosacea=L71, scarring alopecia=L66, fibroids=D25, alopecia areata=L63, vitiligo=L80. AA, African American.

TABLE 2.

Incidence of Risk Factors in Hypertrophic Scars/Keloids Cohort Compared to Control Cohort

Risk Factor, no (%)	Hypertrophic Scars/Keloids (n=6,249)	Control (n=6,249)	OR
Comorbidity**			
Scarring Alopecia	278 (4%)	79 (1%)	3.64*
Rosacea	388 (6%)	116 (2%)	3.50*
Atopic Dermatitis	2,365 (38%)	934 (15%)	3.47*
Acne	585 (9%)	183 (3%)	3.42*
Skin Cancer (NMSC and Melanoma)	2,231 (36%)	1,016 (16%)	2.86*
Alopecia Areata	32 (1%)	13 (0%)	2.47*
History of Neoplasm	3,569 (57%)	2,324 (37%)	2.25*
Anticonvulsant Use	2,129 (34%)	1,203 (19%)	2.17*
Race			
Black/AA	1,200 (19.2)	751 (12.0)	1.74*
White	3,946 (63.1)	4,423 (70.7)	0.71*
Asian	192 (3.1)	215(3.4)	0.89
Other	279 (4.5)	215 (3.4)	1.31*
Unknown	586	590	0.99
Ethnicity			
Not Hispanic	5,031 (80.5)	4,700 (75.2)	1.36*
Hispanic	564 (9.0)	533 (8.5)	1.06
Unknown	654 (10.5)	1,016 (16.3)	0.6*

AA, African American; NMSC, Non-Melanoma Skin Cancer; OR, odds ratio;
Age, sex, race, and ethnicity held constant for comorbidity analysis. Age, sex, and comorbidities held constant for race and ethnicity analysis.
*=*P*-values <0.05
** The following comorbidities did not a statistically significant odds ratios and were therefore omitted from the table: nicotine dependence, diabetes, inflammatory polyarthropathies, hypothyroid, hypertension, fibroids, and vitiligo

DISCUSSION

While distinct in their definition, histologic morphology, and cellular basis for development, hypertrophic scars and keloids both represent excessive dermal fibrosis and cutaneous scarring. The higher incidence in Black/African American individuals is also supported in our study, the pathogenesis of which remains undetermined and speculatively related to melanocyte stimulation of growth and proliferation of fibroblasts and extracellular matrix processes.[1,2] Due to inadequate sample size, however, analysis related to vitiligo patients was constrained.

The high correlation with inflammatory conditions such atopic dermatitis, acne, rosacea, and hypertrophic scars/keloids may be attributed to common cytokine pathways, specifically the overactivity of interleukin-4 (IL-4) and interleukin-13 (IL-13). These cytokines are instrumental to the inflammatory response, subsequent fibroblast activation, and eventual keloid pathology. This insight has led to targeted therapeutic strategies, such as dupilumab, a monoclonal antibody that inhibits IL-4 and IL-13, offering a novel approach to potentially reduce or prevent keloid formation in individuals with these conditions.[3-5] Interestingly, scarring alopecia revealed the highest association with hypertrophic scars and keloids, with many cicatricial presentations, including dissecting cellulitis and acne keloidalis nuchae, commonly presenting with thickened scarred nodules. The observed association between hypertrophic scars/keloids and skin cancers (OR = 2.86, $P<0.01$) and may stem from prolonged cytokine infiltration, with common elevation of factors such as nuclear factor-kappa B and transforming growth factor-β.[6] It is also possible that this relation could be related to necessary surgical treatments leading to abnormal scarring. Limitations of this study include the retrospective nature of data collection, the potential for misclassification of diagnoses using ICD-10 codes, and the small sample sizes of certain comorbidities.

DISCLOSURES

The authors have no conflicts of interest to disclose.

REFERENCES

1. Chike-Obi CJ, Cole PD, Brissett AE. Keloids: pathogenesis, clinical features, and management. *Semin Plast Surg.* 2009;23(3):178-184. doi:10.1055/s-0029-1224797.
2. Gao FL, Jin R, Zhang L, et al. The contribution of melanocytes to pathological scar formation during wound healing. *Int J Clin Exp Med.* 2013;6(7):609-613.
3. Shi C, Zhu J, Yang D. The pivotal role of inflammation in scar/keloid formation after acne. *Dermatoendocrinol.* 2018;9(1).doi:10.1080/19381980.2018.1448327.
4. Zhang X, Wu X, Li D. The communication from immune cells to the fibroblasts in keloids: Implications for immunotherapy. *Int J Mol Sci.* 2023;24:15475. doi:10.3390/ijms242015475.
5. Wong AJS, Song EJ. Dupilumab as an adjuvant treatment for keloid-associated symptoms. *JAAD Case Rep.* 2021;13:73-74. doi:10.1016/j.jdcr.2021.04.034.
6. Lu YY, Tu HP, Wu CH, et al. Risk of cancer development in patients with keloids. *Sci Rep.* 2021;11(1):9390. doi:10.1038/s41598-021-88789-1.

AUTHOR CORRESPONDENCE

Ajay Nair Sharma MD MBA
E-mail:..... ajayns@uci.edu