

The Association between Atopic Disorders and Keloids: A Case-control Study

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Abstract

Background:

Keloids and atopic disorders share common inducing and maintaining inflammatory pathways that are characterized by T-helper cell 2 cytokines.

Aims and Objectives:

The objective of this study was to test for associations between keloids and atopic eczema, asthma and hay fever.

Materials and Methods:

This was a case-control study with 131 patients diagnosed with keloids at our dermatology outpatient clinic between 2000 and 2012. Controls were 258 partners of keloid or sarcoidosis patients. Patient who reported life time prevalences of atopic eczema, asthma and hay fever were assessed using a questionnaire based on The European Community Respiratory Health Survey (ECRHS) and The International Study of Asthma and Allergies in Children (ISAAC).

Results:

The prevalence of asthma was lower in keloid patients (19/131 vs. 20/258, $P = 0.035$), as was being diagnosed with asthma by a physician (18/131 vs. 19/258, $P = 0.039$) and using inhalators for asthma (13/131 vs. 7/258, $P = 0.02$). After adjusting for age and non-European descent the odds ratio for having a keloid was (adjusted OR = 4.44; 95% CI 1.59–12.40) in asthmatics using inhalators. There were no clear and consistent associations found for keloids with atopic eczema or with hay fever.

Conclusion:

In conclusion, our study shows that keloids may be strongly associated with atopic asthma. Atopic eczema and hay fever do not seem to be correlated with keloid. Further studies are warranted to assess the validity of atopic asthma as a risk factor for the development of keloid scars.

Keywords: *Asthma, atopic dermatitis, atopy, fibrosis, keloid, scar*

What was known?

Keloids are common but no modifiable risk factors are known.

Introduction

Keloids are fibroproliferative dermal tumors resulting from skin trauma and subsequent abnormal scar formation.[1] Besides being a cosmetic problem, keloids are often pruritic and painful. Therefore, patients with keloids may suffer from physical impairments and a decreased health-related quality of life.[2] The life-time prevalence of keloids has been reported to be around 10% in Africans, whereas keloids are rarely seen in individuals of European genetic ancestry.[3] Besides the ancestry and young age no other risk factors for the development of keloids are known. To date, there are no effective treatments and there are no satisfactory means of prevention. On the cellular level, keloids are characterized by an overproduction of extracellular matrix and a high activity of fibroblasts during the inflammatory and remodelling phases of scar formation.[4,5] Recent experimental studies have demonstrated that keloid development is driven by three dysfunctional pathways: Altered apoptosis, altered transcription of growth factors such as transforming growth factor beta (TGF- β) and vascular endothelial growth factor (VEGF) along with deregulation of the immune system. Evidence for the involvement of the immune system in keloid formation is found in the increased numbers of mast cells in the edges of keloids and the high CD4:CD8 tissue T-lymphocyte ratio.[6] The key players in this inflammatory pathway are the T-helper 2 (Th-2) cytokines interleukin IL-13 and IL-4, which induce collagen production by the fibroblasts.[7]

Upregulation of the Th-2 cytokines is also strongly linked to atopy. Atopic disorders include atopic eczema, hay fever and asthma. Atopy results from a defect in the epidermal barrier function and a hyperactive, Th-2 skewed, immune response with increased serum IgE levels.[8] The main cytokines driving the atopic inflammation are also IL-13 and IL-4. Thus, cytokine milieu in keloids and atopic disorders appear to be similar, and therefore, patients with atopic disorders may have an increased risk of developing keloids. The objective of this case-control study was to investigate whether atopy is a risk factor for the development of keloids.

Materials and Methods

Study design and study population This case-control study was conducted at our Department of Dermatology. Cases were patients diagnosed with keloids between 2000 and 2012 at our dermatology outpatient clinic. The diagnosis of keloid was made by a dermatologist on the basis of clinical findings of a raised tumorous scar extending beyond the wound borders. The partners of the keloid patients were asked to serve as controls. In addition, available data from a similar postal survey were also included. From this data-set, partners of patients diagnosed with sarcoidosis at our hospital [Figure 1] were included as controls. This additional control group of partners of sarcoidosis patients was considered eligible because the data collection was similar and demographic characteristics ethnic background, residence, age and sex were comparable to the keloid group. Controls were excluded if they had had keloid. Both groups were approached by a postal questionnaire. The non-responders were contacted by telephone and sent a second mailing. The Local Medical Ethical Committee waived the board review because the study was single-subject and questionnaire based.

Patient reported atopic features Atopic status was established through a validated questionnaire comprising questions from the European Community Respiratory Health Survey (ECRHS) and International Study of Asthma and Allergies in Children (ISAAC) protocol.[9,10] Patients were considered to have atopic eczema, asthma or hay fever if they reported having one of these conditions. However, the diagnoses were further explored by inclusion of questions on physician-made diagnoses and physician prescribed medication. Thus, patients reporting eczema were questioned about the use of topical corticosteroids, asthma patients were asked about the use of inhalators, and patients with hay fever were asked about their use of anti-histamine drugs. Patients were also questioned about the key-symptoms of these conditions. Family history was positive for these disorders if one first-degree relative had been reported to have either eczema, asthma or hay fever.

Ancestry Non-European ancestry and darker skin phenotypes are important determinants of the risk of keloids.[1] The ancestry was established by documenting the birth country of both parents and

self-identification by the subject. Patients were classified to be either of African, Asian or European ancestry. If one of the parents was born in an African or Asian country, the subject was considered to be of African or of Asian descent, respectively. Considering that all ethnicities other than the European confer a higher risk of keloids, we dichotomized the ancestry to European or non-European in the final multivariate model.

Keloid properties Patients were asked to report the number of keloids and anatomical location of their keloids. The modes of induction of the keloid were predefined: Surgery, acne, spontaneous, piercing, burns and other. Patients also graded on a visual analogue scale (VAS) on pain and pruritus symptoms caused by their keloids. Both symptoms highly correlate with physical impairment and loss of quality of life.^[2] In order to further assess the symptom severity and its effect on quality of life, we used the validated Skindex-29 questionnaire to measure dermatology-specific health-related quality of life.^[11] These measurements were collected in order to test for a correlation between the keloid severity and the presence of atopy.

Statistical analysis For sample size calculations, we assumed a prevalence of 10% for patient-reported asthma and 14% for patient reported hay fever in our control group, as found previously.^[12] This would make up for an estimated prevalence of about 20% of any atopic disorder in controls. We expected at least twice this percentage in keloid patients.^[13] For a power of 80% and an alpha level of 0.05, a sample size of 126 cases and 252 controls was required. The Chi-squared test was used to test for statistical differences in proportions and the Mann Whitney-U test for non-parametric testing. Multivariate logistic regression models were used to calculate adjusted odds ratios (OR) and 95% confidence intervals (95% CI). Ancestry was considered a confounder in the possible association between atopy and keloids. Therefore we also performed analyses with stratification by ancestry. In the multivariate analysis, atopic eczema, asthma and hay fever were analyzed separately. However, additional analyses were done with a composite variable where subjects were considered atopic if they had reported either eczema, asthma or hay fever. No additive or multiplicative interactions were found between asthma and non-European descent. Values of $P < 0.05$ were considered significant. All data were analyzed using IBM SPSS version 19.0 (Chicago, Illinois, 2011).

Results

Patient characteristics We identified 207 keloid patients through medical records diagnosed between 2000 and 2012. Of the 207 patients, 131 (response rate 63%) sent back the questionnaire. Eighty-one (81) partners of keloid patients also replied [\[Figure 1\]](#). One hundred and seventy-seven (177) partners of sarcoidosis patients were added to the control group which totalled 258 controls. The 76 non-responder keloid patients had an average age of 42 years (SD 17) and 36% of them were male. The keloid patients were on average younger than the controls (41 vs. 48 years, $P < 0.001$) [\[Table 1\]](#). The cases did not differ significantly from the controls in terms of sex distribution and a positive family history of atopy. However, the cases with keloid were significantly more frequently of non-European ancestry (81% vs. 51%, $P < 0.001$) [\[Table 1\]](#). Keloids were most frequently found on the chest (44%) and on the back and the shoulders (16%). The most frequently self-reported cause of keloid was surgery (40%) followed by spontaneous that is unprovoked onset (17%).

Atopic asthma Both self-reported and physician-diagnosed asthma were more prevalent among keloid patients than in controls (15% vs. 8%, $P = 0.035$ and 14% vs. 7%, $P = 0.039$) respectively. This observation was confirmed by the increased use of inhalators in the keloid patients (10% vs. 3%, $P = 0.002$). This difference was observed in the European subjects but not in the non-Europeans.

In the univariate analysis only asthma was associated with keloids (crude OR 2.03; 95% CI 1.04–3.96) [\[Table 2\]](#) but this association did not remain statistically significant in the model adjusted for age and ancestry (adjusted OR 1.91; 95% CI 0.92–3.93). Being treated for asthma with inhalators was significantly associated with keloids in both the crude (crude OR 4.00; 95% CI 1.56–10.30) and the adjusted model (adjusted OR 4.44; 95% CI 1.59–12.40). Having any atopic feature also increased the risk of developing a keloid (crude OR 1.64; 95% CI 1.07–2.50). This positive association remained after adjusting for age and ancestry (adjusted OR 1.34; 95% CI 0.85–2.12) but was no longer statistically significant. In the stratified

analysis of only European subjects, the effect of treated asthma remained significant after adjusting for age; patients on inhalants had a seven-fold increased odds of having a keloid (adjusted OR 7.08; 95% CI 2.00–25.25). The percentage of subjects reporting any atopic feature was higher in keloid patients (54% vs. 42%, $P = 0.023$) and having both hay fever and asthma was more frequently found in keloid patients (3% vs 8%, $P = 0.034$) [Table 3].

Atopic eczema Of the atopic eczema related outcomes only flexural itching rash was significantly more frequently reported by the keloid patients compared to the controls (24% vs. 12%, $P = 0.004$) [Table 3]. Keloid patients reported having had eczema more frequently but this difference was only borderline significant (31% vs. 24%, $P = 0.125$). The prevalence of the physician made diagnosis of atopic eczema was similar in both groups (26% vs 23%, $P = 0.568$). No difference was found in the use of topical corticosteroids. Atopic eczema was not associated with keloids in the adjusted model (adjusted OR 1.27; 95% CI 0.76–2.13) [Table 2].

Hay fever and keloids The prevalence of self-reported hay fever was similar in keloid patients and controls (33% vs. 29%, $P = 0.463$). The prevalence of physician diagnosed hay fever was higher in keloid patients (26% vs. 20%, $P = 0.173$) but this difference was borderline significant. Keloid patients reported having a congested runny nose without having a cold more frequently than the controls (51% vs. 39%, $P = 0.019$). Nevertheless, no association between hay fever and keloids was found in the multi multivariate model (adjusted OR 1.04 95% CI 0.63–1.17) [Table 2].

Atopic versus non-atopic keloid patients The atopic keloid patients did not differ from the non-atopic keloid patients in terms of family history, ancestry, age, and age at onset of keloids [Table 4]. The visual analogue scale scores for itch (6.4 vs. 5.4 $P = 0.615$) and pain (1.2 vs. 0.9, $P = 0.838$) as well as the Skindex-29 scores (45 vs 45, $P = 0.962$) were similar across the groups.

Discussion

Keloids and atopic disorders share common inducing and maintaining inflammatory pathways that are characterized by T-helper cell 2 (Th-2) cytokines. In this case control study, we assessed the association between atopic disorders and keloids. Of the three atopic disorders, asthma was significantly, consistently and strongly associated with keloids. However, there were no consistent associations found for keloids with atopic eczema or with hay fever. There seems to be no difference in clinical presentation and disease impact between atopic and non-atopic keloid patients. In addition, this study has confirmed the traditional risk factors young age and non-European ancestry.

Possible mechanism to explain the association between keloids and atopic asthma is the shared inflammatory (Th-2) pathway but also the activity of fibrocytes in the injured tissues which play a role in tissue remodelling.[14,15] The Th-2 cytokine pathway may interact similarly with fibrocytes in asthma and keloids. The interleukins 4 and 13, which are archetypical Th-2 cytokines, are of paramount importance in atopic disorders, mostly so in atopic asthma.[16,17] They are also known to play a pivotal role in fibrosis.[18] They augment collagen formation in lung fibroblasts in asthma and in conjunctival fibroblasts.[19,20] In human skin, mechanical damage polarizes skin dendritic cells towards a Th-2 cytokine secreting profiles where IL-13 and IL-4 are known to induce chemotaxis and collagen production in fibroblasts.[21,22,23] It is also possible to induce alpha-smooth muscle activity in skin fibroblasts through sensitization with allergens. This is mediated by TGF- β and IL-13 mainly secreted by eosinophils.[24]

Of all atopic disorder, asthma embodies the most inflammatory and the only one where remodelling of tissue plays a role. This may also explain the lack of an association of keloids with atopic eczema and hay fever. The common denominator of atopic asthma and keloids is that both disorders start out with an inflammatory phase followed by untameable and inadequate tissue remodelling. If our findings represent a true association, asthma could be considered a very important risk factor for keloids and could have clinical relevance as it helps stratify the risk better.

Two observational studies have suggested the existence of an association between keloids and atopy. In a small ($N = 38$) questionnaire-based case control study from 1987, the authors found a prevalence of 85% of atopic and allergic symptoms in keloid patients versus 49% in healthy controls.[13] Another study by the

same group observed that 6 out of 18 (33%) keloid patients had serum IgE levels above 150 ng/mL.[25] This study was uncontrolled but the authors expected 5% of the patients to have increased IgE levels based on previous measurements. Both studies were conducted at the time when the concept of atopy was not yet fully developed.[13,25] The authors hypothesized that increased mast cell activity in allergic individuals may predispose them to keloids.

Although our keloid patients did not report having eczema or hay fever more often, they did report symptoms compatible with these diagnoses (itchy flexural rash and congested or runny nose in the absence of common cold). This may reflect underdiagnosing of these conditions in keloid patients of whom most are immigrants. Patients with asthma may suffer less from this phenomenon because of the more severe symptomatology which may prompt them to seek medical attention. The retrospective study design is the main limitation of our study. In addition, the questionnaire-based reporting may have led to information bias with subsequent underdiagnosing of eczema and hay fever but this bias is of non-differential type. Finding a suitable control group is a challenge because keloids are mostly seen in non-Europeans. To our surprise, the vast majority of their partners were actually of European ancestry causing a mismatch in ethnicity between cases and controls. We suspected ancestry to be the greatest confounder in the association between atopy and keloids. The prevalence of asthma has been shown to be higher in immigrants from Suriname when compared to the Dutch in a study based on administrative data (5.9% vs. 4.2%, $P < 0.001$ for all ages).[26] The prevalence of dermatologist diagnosed atopic eczema is also higher in Caribbean immigrant children in the UK than in their white counterparts (16.3% vs. 8.7%, OR 2.1 95% CI 1.1–3.9).[27] As a way of a sensitivity, analysis we explored the distribution of atopic features across subjects of European and non-European descent in the total study population. No difference was observed in the distribution of reported asthma and eczema related features in our groups. Also, the ancestry stratified analysis showed that the association between keloid and asthma is strongest in European subjects completely excluding mixing of effects by more prevalent asthma in non-European keloid patients.

This is to our knowledge the first study to assess the association between atopic features and keloids with validated questionnaires in dermatologist-diagnosed keloid patients and comparing it to a control group. We found that keloids are strongly associated (4–5-fold increased odds) with physician treated atopic asthma. Further exploring of this association necessitates confirmation in a larger study population preferably in an ethnically homogenous group or with matched controls. The ascertainment of atopy should be accomplished with more robust methods such as serum IgE-measurements or skin prick testing.

What is new?

Atopic asthma may be an easily identifiable risk factor for keloids.

Footnotes

Source of support: Nil

Conflict of Interest: Nil.

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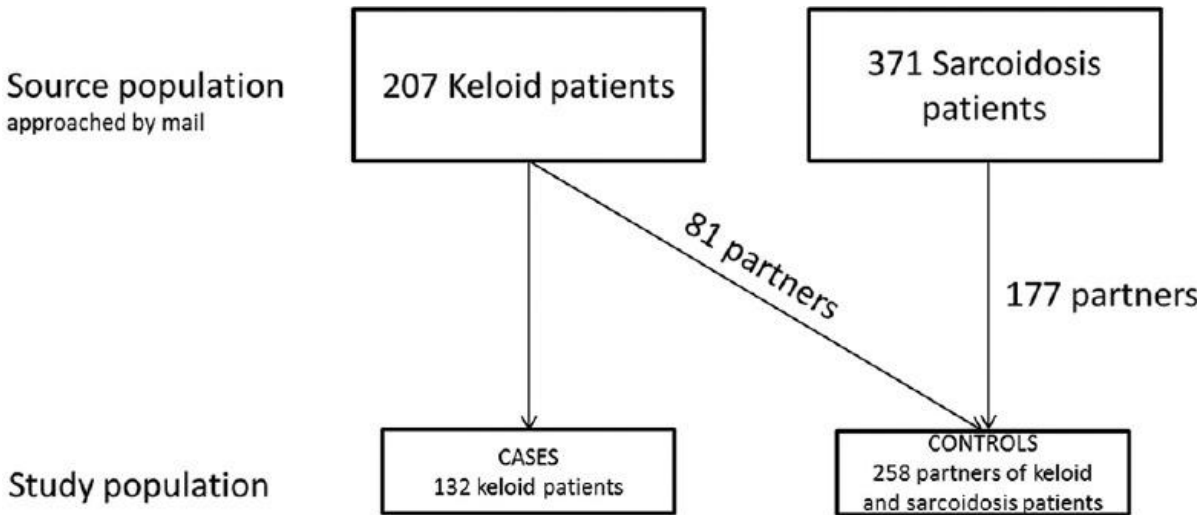
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Figures and Tables

Figure 1



Study population

Table 1

	Keloid patients N=132	Controls N=258	P
Mean age in years (SD)	40 (15)	48 (15)	<0.001
Males	60 (46%)	131 (52%)	0.283
Family history of atopy	58 (44%)	110 (54%)	0.063
Ancestry			
European	67 (51%)	209 (81%)	<0.001
African	32 (24%)	33 (13%)	<0.001
Asian	33 (25%)	16 (6%)	<0.001
Family history of keloid	35 (27%)	N/A	
Anatomical site of keloid			
Chest	56 (44%)		
Back and shoulders	21 (16%)		
Head and ears	20 (16%)		
Other	31 (24%)		
Provocation			
Surgery	52 (40%)		
Acne	20 (15%)		
Spontaneous	23 (17%)		
Piercing	10 (8%)		
Other	26 (20%)		

Statistically significant *P* values are <0.05. Controls consisted of 81 keloid patients' partners and 177 partners of patients with sarcoidosis

Subject characteristics

Table 2

<i>N</i> =389	Crude OR (95% CI)	Adjusted* OR (95% CI)
Age (per 10 years)	0.70 (0.60-0.81)	0.69 (0.59-0.81)
Non-European descent	3.90 (2.42-6.12)	3.89 (2.40-6.31)
Atopic features		
Eczema ever	1.42 (0.89-2.27)	1.27 (0.76-2.13)
Asthma ever	2.03 (1.04-3.96)	1.91 (0.92-3.93)
Hay fever ever	1.19 (0.75-1.87)	1.04 (0.63-1.17)
Combined variables		
Asthmatics on inhalants	4.00 (1.56-10.30)	4.44 (1.59-12.40)
Any atopic feature	1.64 (1.07-2.50)	1.34 (0.85-2.12)
Ancestry stratified analysis Europeans only <i>N</i> =276		
Age (per 10 years)	0.56 (0.45-0.69)	Adjusted for age
Asthma ever	2.50 (1.10-5.70)	2.30 (0.94-5.80)
Asthmatics on inhalants	6.30 (2.03-19.53)	7.08 (2.00-25.25)

Analysis of total and European subjects only. Statistically significant values are in bold. *Adjusted for age and non-European descent. OR: odds ratio, CI: Confidence interval

Univariate and multivariate logistic regression analysis of keloid risk factors

Table 3

	Total			European			Non-European		
	Keloid N=132 (%)	Controls N=258 (%)	P	Keloid N=67 (%)	Control N=209 (%)	P	Keloid N=65 (%)	Control N=49 (%)	P
Atopic eczema									
Ever had eczema	40 (31)	61 (24)	0.125	19 (28)	52 (25)	0.661	21 (32)	9 (18)	0.068
Flexural itching rash	32 (24)	31 (12)	0.002	18 (27)	23 (11)	0.003	14 (22)	8 (16)	0.442
Physician diagnosed	33 (26)	59 (23)	0.568	16 (24)	50 (24)	0.932	17 (26)	9 (19)	0.263
Current topical corticosteroid use	21 (17)	44 (16)	0.822	10 (15)	38 (18)	0.736	11 (17)	6 (12)	0.348
Family history	36 (30)	76 (30)	0.967	19 (28)	61 (29)	0.934	17 (26)	15 (31)	0.865
Asthma									
Ever had asthma	19 (15)	20 (8)	0.035	11 (16)	15 (7)	0.028	8 (12)	5 (10)	0.661
Physician diagnosed	18 (14)	19 (7)	0.039	10 (15)	14 (7)	0.039	8 (12)	5 (10)	0.661
Current use of inhalators	13 (10)	7 (3)	0.002	9 (13)	5 (2)	<0.001	4 (6)	2 (4)	0.583
Family history	28 (23)	56 (22)	0.781	14 (21)	46 (22)	0.986	14 (22)	10 (20)	0.650
Hay fever									
Ever had hay fever	42 (33)	75 (29)	0.463	19 (28)	56 (27)	0.870	23 (35)	19 (39)	0.962
Congested or runny nose, not during a common cold	66 (51)	99 (39)	0.019	32 (48)	77 (37)	0.118	34 (52)	22 (45)	0.349
Physician diagnosed	33 (26)	50 (20)	0.173	14 (21)	37 (18)	0.629	19 (29)	13 (27)	0.604
Current use of nasal spray/antihistaminics	31 (24)	50 (20)	0.335	13 (19)	33 (16)	0.565	18 (28)	17 (35)	0.524
Family history	42 (34)	91 (36)	0.669	21 (31)	70 (33)	0.746	21 (32)	21 (43)	0.390
Combinations									
Any atopic feature ever	70 (54)	107 (42)	0.023	33 (49)	84 (40)	0.238	37 (60)	23 (47)	0.181
Asthma and eczema	6 (5)	6 (2)	0.222	3 (4)	5 (2)	0.392	3 (5)	1 (7)	0.432
Asthma and hay fever	11 (8)	9 (3)	0.034	5 (7)	6 (3)	0.102	6 (9)	3 (6)	0.464
Eczeema and hay fever	17 (13)	30 (12)	0.650	9 (13)	25 (12)	0.791	8 (12)	5 (10)	0.616
Asthma, eczema and hay fever	3 (2)	5 (2)	0.796	1 (1)	4 (2)	0.808	2 (3)	1 (2)	0.682

Statistically significant *P*-values are in bold

Atopic features in keloid patients and controls stratified according to ancestry

Table 4

Keloid patients N=126	Any atopic feature N=71	Without atopic features N=60	P
Positive family history for keloid	17 (24%)	15 (25%)	0.966
Non-European descent	35 (50%)	22 (37%)	0.153
Age, mean (SD)	42 (14)	39 (14)	0.281
Age at onset mean (SD)	21 (13)	18 (14)	0.376
Median (IQR)			
VAS for itch	6.4 (3.3-7.8)	5.4 (0.6-8.2)	0.615
VAS for pain	1.2 (0.2-5.1)	0.9 (0.2-5.2)	0.838
SKINDEX-29	45 (38-56)	45 (32-61)	0.962

SD: Standard deviation, IQR: Interquartile range, VAS: Visual analogue scale

Comparison of atopic with non-atopic keloid patients

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A Relationship between Physical Activities and Hand Dermatitis: An Epidemiology Study of the USA Population

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Abstract

Background:

Hand dermatitis is a common, chronic relapsing skin disease, resulting from a variety of causes including endogenous predisposition and environmental exposures to irritants and allergens. Physical activities have been reported to be beneficial for patients with hand dermatitis.

Objectives:

We aim to evaluate the association between self-reported physical activities and hand dermatitis using the 2003-2004 National Health and Nutrition Examination Survey (NHANES) database.

Methods:

Information regarding 2,688 participants aged 20 to 59 years from the 2003-2004 NHANES cycle were retrieved and analyzed. Diagnosis of hand dermatitis was based on standardized photographs of the hands read by two dermatologists. Physical activity during leisure time for the prior 30 days was assessed using standardized questionnaire. Based on the suggested MET scores provided for each response in the questionnaire section of the NHANES methodology, the MET scores for average level of physical activities, walking/bicycling, and performing tasks around home/yard for the past 30 days was calculated.

Results:

There were 42 (1.56%) diagnosed cases of active hand dermatitis among the 2,688 participants. Those who reported recent vigorous or moderate physical activities were less likely to have a diagnosis of active hand dermatitis (OR: 0.436, 95% CI: 0.200 to 0.947, $P = 0.036$ and OR: 0.489, 95% CI: 0.261 to 0.916, $P = 0.025$, respectively). This negative association remained statistically significant even after adjusting for age, gender, ethnic groups and atopic diathesis.

Conclusions:

Moderate and vigorous levels of physical activities appeared to be beneficial for hand dermatitis. Therefore, it is important to advise patients with active hand dermatitis to remain physically active. However, clinicians should also be cognizant of the fact that the heat and sweat generated from physical activities might also exacerbate the condition.

Keywords: *Epidemiology, hand dermatitis, physical activities*

What was known?

Hand dermatitis is a known inflammatory condition that is associated with endogenous and exogenous factors. Lifestyle factors such as smoking and physical exercise have been implicated in mediating the course of hand dermatitis.

Introduction

Hand dermatitis is a common, chronic relapsing skin disease resulting from a variety of causes including atopic diathesis, contact with irritants/allergens, and wet works.[1,2,3,4] Lifestyle factors such as physical exercise have been implicated to be negatively associated with hand dermatitis, which is an inflammatory condition of unknown mechanism.[5,6] Physical activity has been shown to modulate inflammatory processes by influencing granulocytes, lymphocytes, monocytes, as well as cytokines.[7,8,9] Few studies, however, evaluate the relationship between exercise and hand dermatitis. In this study, we aim to evaluate the association between physical activity and hand dermatitis using the National Health and Nutrition Examination Survey (NHANES) database.

Methods

Study population NHANES is a periodic, annual population survey that targets the civilian, noninstitutionalized USA population. It utilizes a stratified multistage probability sampling design. In our analysis of interest, randomly selected individuals aged 20–59 years are interviewed in their homes about the below-mentioned variables of interest. A total of 2688 participants subsequently completed health examinations. Data on hand dermatitis diagnosis, and information on physical activity during leisure time in the cycle year 2003–2004 were retrieved and analyzed.

Outcome Diagnoses of active hand dermatitis were identified from the 2003 to 2004 NHANES examination data. All study participants had standardized photographs of dorsal and palmar views of the hands. These photographs were read by two dermatologists for the presence of hand dermatitis. When the findings of the two dermatologists disagreed, the image reading software program required a third consensus reading. For the consensus readings, both dermatologists reviewed the image simultaneously and came to a unified decision.

Exposure Physical activity during leisure time for the past 30 days was assessed using questionnaire data in NHANES. The participants were asked the following questions to determine their level of physical activity, frequency, as well as the duration of each exertion. The participants were asked if they were doing any vigorous activities for at least 10 min that caused heavy sweating or a significant increase in breathing or heart rate. Examples of these activities included running, lap swimming, aerobics classes, or fast bicycling. Similarly, they were asked if they did any moderate activities for at least 10 min that cause only light sweating or a slight to moderate increase in breathing or heart rate. Examples of such activities included brisk walking, bicycling for pleasure, or dancing. They were also asked to rate their average level of physical activity each day by choosing one of the following four descriptions of their usual daily activities: (1) Sits during the day and does not walk about very much, (2) stand or walk about a lot during the day but does not have to carry or lift things very often, (3) lift light load or has to climb stairs or hills often, and (4) do heavy work or carries heavy loads. Since the frequency of the activities and the time spent during each session were provided, the total time spent in walking/bicycling for the past 30 days could be determined. Based on the suggested metabolic equivalent (MET) scores provided for each response in the questionnaire section of the NHANES methodology, separate MET scores for average level of physical activities and walking/bicycling for the past 30 days were calculated.

Questionnaire data variables Demographic variables such as age, gender, and ethnic groups were included for analysis as possible confounding factors.

Ethnic groups were categorized as “Mexican American,” “other Hispanic,” “non-Hispanic white,” “non-Hispanic black,” and “other race.” As there were no direct questions about any personal history of atopic diatheses, a positive response to any one of the following: a personal or family history of asthma or a recent history of hay fever was assigned a positive history of atopic diathesis.

Data analysis The analysis of the association between hand dermatitis and physical activity during the leisure time was done using Chi-square or Fisher exact tests. Using two sample *t*-test and Mann–Whitney U-test, the total amount of time spent in walking/bicycling and performing tasks around home/yard were compared between those with and without hand dermatitis. In order to examine the potential confounding effect of selected variables, we performed multivariate logistic regression with hand dermatitis as the dependent variable and aforementioned confounding factors as the independent variables.

The statistical package for social sciences (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was utilized to perform the analysis. Odds ratio (OR), 95% OR confidence interval (CI), and *P* values were calculated to test the null hypotheses of the association between physical activities with a diagnosis of hand dermatitis.

Clinical information and questionnaire data of the 2003–2004 NHANES cycle were available from the publicly accessible U.S. Centers for Disease Control and Prevention database. The NHANES was approved by the Institutional U.S. National Center for Health Statistics Ethics Review Board and documented consent was obtained from participants.

Results

A total of 2688 participants were included in the analysis. There were 42 (1.56%) diagnosed cases of active hand dermatitis. Among cases of active hand dermatitis, there was a strong male predominance (90.5%). Those who were diagnosed with active hand dermatitis had a slightly older mean age, compared to those who did not, however, this did not reach statistical significance (*P* = 0.129). Other characteristics of patients with and without hand dermatitis are summarized in [Table 1](#).

The participants who reported moderate and vigorous physical activities for at least 10 min for the past 30 days were less likely to have a diagnosis of active hand dermatitis (OR: 0.489, 95% CI: 0.261–0.916, *P* = 0.025 and OR: 0.436, 95% CI: 0.200–0.947, *P* = 0.036, respectively). However, those who described their average daily activities as doing heavy work or carrying heavy loads were more likely to have active hand dermatitis, compared to those who reported sitting around and not walking about (OR 4.351, 95% CI: 1.473–12.857, *P* = 0.008). The mean MET scores for average daily activities were also significantly higher in participants with active hand dermatitis. The amount of time spent in walking/bicycling did not differ significantly between those with and without active hand dermatitis. The mean MET scores for walking/bicycling also did not differ significantly between the two groups.

To adjust for possible confounding factors such as age, gender, ethnic groups, and atopic diathesis; multivariate logistic regression was performed. The negative association between recent moderate or vigorous physical activities and active hand dermatitis remained statistically significant even after adjusting for the aforementioned confounders (adjusted OR: 0.515, *P* = 0.043 and adjusted OR: 0.396, *P* = 0.011, respectively). The significant association between level of average daily activities and hand dermatitis, however, became attenuated after adjusting for confounders. The results of adjusted ORs from the logistic regression models are summarized in [Table 2](#).

Discussion

In this study, the risk of having active hand dermatitis was significantly lower in participants who reported moderate or vigorous physical activities in the past 30 days. The activities examined in NHANES database mostly involved aerobic exercises and typically would not cause friction over the hands. The beneficial effects of physical activities on hand dermatitis have been documented in various epidemiological studies. [\[1,2,3,10\]](#) A study by Wrangsjö *et al.* suggested that physical exercise was associated with a lower prevalence of hand eczema. [\[11\]](#) A Sweden study similarly reported that the prevalence of hand eczema was lower in individuals with high levels of physical exercise. [\[10\]](#) The physical exercise has been postulated to

promote muscle fibers' production of interleukin-6 (IL-6), which stimulates the production of anti-inflammatory cytokines, such as IL-1 receptor antagonist and IL-10, and inhibits the production of pro-inflammatory cytokines like tumor necrosis factor- α (TNF- α).^[12] Alterations in cytokines such as IL-1, IL-2, IL-8, IL-10, and TNF- α were suggested to be responsible for the pathogenesis of hand dermatitis.^[10] Therefore, it is likely that physical exercise influences hand dermatitis through the modulation of inflammatory cytokines.

Though physicians' assessment of standardized photographs is a very specific screening method, it may be less sensitive to detect cases of hand dermatitis that were mild or relapsing infrequently. Instead of identifying past diagnoses of hand dermatitis, the photographs would likely reflect a more current condition of the hands. Therefore, the cases of hand dermatitis identified in this study likely represented a more severe and persistent form. Although study participants who were engaged in heavy work or carried heavy loads were more likely to have active hand dermatitis, compared to those who have sedentary lifestyles, this relationship was attenuated after adjusting for confounding factors. However, it is also conceivable that participants who used their hands to carry heavy loads as part of their usual daily activity were more likely to have hand dermatitis because of the mechanical stress and friction involved in these activities, despite a beneficial effect of physical activities on hand dermatitis. The total amount of time spent and means MET scores were calculated in order to evaluate a potential dose-response relationship between physical activity and hand dermatitis. In our analysis, however, the amount of time spent and mean MET scores for walking/bicycling did not differ significantly between those with or without hand dermatitis. In contrast, Anveden Berglind *et al.* demonstrated a significant negative dose-response relationship between hand dermatitis and physical exercise in men.^[10] More research would be needed to further explore this relationship.

One of the strengths of this study is the specific screening method for hand dermatitis among a representative general population. The diagnosis of hand dermatitis was made from standardized photographs by at least one dermatologist. However, there was no information on the type of hand dermatitis and the duration of the condition for each case. Given that the more severe and persistent forms of hand dermatitis were identified, the results of this study may be more generalizable to those with more chronic and occupation-related hand dermatitis. Given the cross-sectional nature of this study, it was not possible to establish any causal relationship between physical activity and hand dermatitis. There might be reverse causation such that participants with significant hand dermatitis avoid performing physical activities. The participants were also asked to self-report their recent physical activities for the past 30 days. This can lead to recall bias and potential over- or under-reporting of their physical activities. Other possible confounding variables like contact allergies, and the habits of frequent hand washing were also not available in the database.

Conclusion

Moderate and vigorous levels of physical activities had significant negative associations with hand dermatitis. However, those with severe and persistent forms of hand dermatitis may be more likely to avoid physical exercise due to pain or sweating. An observational longitudinal cohort study with objective assessments of physical activity and hand dermatitis severity would be useful to evaluate a possible dose-dependent association. It is important to advise patients with active hand dermatitis to remain physically active while being cognizant of the fact that resulting heat and sweat can also exacerbate the condition.

Financial support and sponsorship Nil.

Conflicts of interest There are no conflicts of interest.

What is new?

Moderate and vigorous physical activities may be beneficial for hand dermatitis. However, the patients with severe hand dermatitis may avoid physical activities due to pain or sweating.

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Figures and Tables

Table 1

Characteristics	Hand dermatitis		OR	P
	Yes	No		
Age (years) (n=2688)	40.36	37.72	1.021	0.129
Gender (n=2688)				
Male	38	1263	10.40	<0.001
Female	4	1383	1.00	
Ethnic groups (n=2688)				
Mexican American	9	510	1.306	0.517
Other Hispanic	0	97	0	0.997
Non-Hispanic black	13	586	1.642	0.177
Other race	2	121	1.223	0.789
Non-Hispanic white	18	1332	1.000	
Atopic diathesis (n=2688)				
Yes	7	852	0.421	0.032
No	35	1794	1.000	

OR: Odds ratio

Characteristics of patients with and without hand dermatitis

Table 2

Characteristics	Hand dermatitis		Crude OR	P	Adjusted OR*	P
	Yes	No				
Vigorous physical activity (n=2628)						
Yes	8	925	0.436	0.036	0.396	0.011
No	33	1662	1.000		1.000	
Moderate physical activity (n=2687)						
Yes	16	1474	0.489	0.025	0.515	0.043
No	26	1171	1.000		1.000	
Average daily activity (n=2686)						
Sit a lot	5	570	1.000		1.000	
Walk a lot	18	1360	1.509	0.418	1.501	0.430
Lift light weights	9	452	2.270	0.144	2.152	0.178
Lift heavy weights	10	262	4.351	0.008	2.743	0.075
Total time spent (h) on						
Walking/cycling (n=719)	15.5	18.2	0.999	0.858	0.997	0.688
Mean MET scores (n=2688)						
Average daily activities	47.5	45.8	1.135	0.008	1.088	0.042
Walking/cycling	19.2	19.4	1.000	0.992	1.000	0.790

*Adjusted for age, gender, ethnic groups, and atopic diathesis. OR: Odds ratio, MET: Metabolic equivalent

Univariate and multivariate logistic regression of physical activity with hand dermatitis

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