ORIGINAL ARTICLE

Primary hyperhidrosis increases the risk of cutaneous infection: A case-control study of 387 patients

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Background: Although primary focal hyperhidrosis (PHH) has been frequently associated with diminished quality of life, the medical consequences of the condition are less well studied.

Objective: We sought to study the clinical presentation of PHH and to determine its relationship to cutaneous infection.

Methods: We conducted a retrospective case-control study of patients encountered between 1993 and 2005 with the *International Classification of Diseases, Ninth Revision* diagnosis code for hyperhidrosis (HH) and meeting criteria for PHH.

Results: Of 387 patients with PHH included, 59% were female and 41% were male; mean age was 27.3 years (range 2-72). Sites of HH included soles (50.1%), palms (45.2%), and axillae (43.4%). Distributional patterns of HH were isolated axillary (27.6%), palmoplantar (24.3%), isolated plantar (15%), axillary/palmoplantar (5.7%), isolated palmar (5.7%), and craniofacial (5.2%). Axillary HH was more common in female patients ($P = .004$). The mean age of onset (18.6 ± 12.3 years) indicated a mean duration of untreated symptoms of 8.9 years. Age at onset for palmoplantar HH (11.5 ± 8 years) was significantly younger than for axillary HH (20.0 ± 8.3 years; $P < .0001$), whereas onset of craniofacial HH (25.4 ± 13.7 years) was older ($P < .001$). Exacerbating factors included stress/emotion/anxiety (56.7%) and heat/humidity (22%). The overall risk of any cutaneous infection was significantly ($P < .0001$) increased in HH compared with controls (odds ratio [OR] 3.2; 95% confidence interval [CI] 2.2-4.6). Site-specific risks of fungal infection (OR 5.0; 95% CI 2.6-9.8; $P < .0001$), bacterial infection (OR 2.6; 95% CI 1.2-5.7; $P = .017$), and viral infection (OR 1.9; 95% CI 1.2-3.0; $P = .011$) were all increased. Risks of pitted keratolysis (OR 15.4; 95% CI 2.0-117; $P = .0003$), dermatophytosis (OR 9.8; 95% CI 3.4-27.8; $P < .0001$), and verruca plantaris/vulgaris (OR 2.1; 95% CI 1.3-3.6; $P = .0077$) were particularly increased. Association with atopic/eczematous dermatitis (OR 2.9; 95% CI 1.5-55; $P = .019$) was observed.

Limitations: Retrospective design and single-institution study are limitations.

Conclusions: Patients with HH are at high risk of secondary infection. Management of HH may have a secondary benefit of decreasing this risk. (J Am Acad Dermatol 10.1016/j.jaad.2009.02.038.)

Key words: corynebacteria; eccrine pathology; hyperhidrosis; superficial mycosis; sweating; verruca; wart.

Hyperhidrosis (HH) is defined as excessive sweating beyond what is expected for thermoregulatory needs and environmental conditions.[1,2] HH may be primary (likely resulting from overactivity of the sympathetic nervous system) or secondary to general medical conditions (including endocrine, neurologic, cardiovascular, infectious, and neoplastic disease) or pharmacologic effects.[1,2] Primary HH (PHH) has an estimated prevalence of nearly 3% of the population.[3] Diagnostic

Abbreviations used:

CI:	confidence interval
HH:	hyperhidrosis
OR:	odds ratio
PHH:	primary hyperhidrosis

Q1 From the Department of Dermatology, University of Iowa.
Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication February 17, 2009.
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Published online •••.
0190-9622/$36.00

doi:10.1016/j.jaad.2009.02.038

components of PHH include excessive sweating of at least 6 months' duration with at least two of the following additional features: bilateral and symmetric sweating, occurring at least once weekly, age of onset before 25 years, cessation during sleep, and positive family history.[1] Multiple studies have established the psychosocial burden of PHH and its negative impact on quality of life.[1-8] Few studies have focused on the clinical presentation and medical consequences of PHH. The current report surveys the clinical presentation of PHH and associated findings in a cohort of 387 patients in a university setting.

CAPSULE SUMMARY

- In this case-control study including 387 patients with PHH, the overall risk of site-specific cutaneous infection, including bacterial, fungal, and viral, was significantly increased in the PHH cohort.
- The risks were especially high for pitted keratolysis, verruca vulgaris/plantaris, and dermatophytosis.
- Management of HH may have a secondary benefit of decreasing this risk.

METHODS

Institutional review board approval was obtained from the university's human subjects committee to conduct a retrospective case-control study. Charts were reviewed for all dermatologic visits from 1993 to 2005 for all patients encountered with *International Classification of Diseases, Ninth Revision* code corresponding to HH. Demographic information collected included age, sex, location of HH, medications, and concurrent dermatologic and nondermatologic diagnoses. Similar data were collected for a control group, consisting of 410 age- and sex-matched patients given the diagnosis of an unrelated condition (epidermoid cyst) seen in the dermatology department during the same time period. In both cohorts, documentation from all visits (not just those coded for HH or epidermoid cyst) within the study period were reviewed. For patients given a diagnosis of superficial mycoses, positive results on potassium hydroxide microscopy or fungal culture were required for inclusion in the statistical comparison.

Categorical variables were compared by χ^2 testing and continuous variables were compared with Student *t* test; *P* less than .05% was considered statistically significant. Statistical testing was performed using software (SPSS for Windows, SPSS Inc, Chicago, IL).

RESULTS

In all, 387 patients meeting diagnostic criteria for PHH were identified from the departmental database [T1] (Table I). Of patients with PHH, 228 (58.9%) were female and 159 (41.1%) were male. The average age was 27.3 years (range 1-72). The majority of patients (357 of 387, 92.2%) were given a diagnosis by history and examination. Laboratory testing (including serum testing for glucose and thyroid function, urinary catecholamines) was performed in 21 (5.4%) and produced normal results. Neurologic consult was obtained in 3 (0.08%), with negative findings. Seven patients (1.8%) underwent provocative testing in a sauna chamber.

Of all 387 patients, 150 (38.6%) gave information regarding exacerbating factors. In all, 85 (56.7%) reported exacerbation by stress, emotion, anxiety, or social situations. A total of 33 (22%) reported exacerbation by heat or humidity. In all, 23 patients (15.3%) denied exacerbation factors. Of the 387 patients, 322 (83.2%) had recorded information regarding duration of their symptoms. The average duration was 8.9 years, corresponding to an average of nearly a third (32.8%) of the patients' lives. Of patients reporting duration, nearly a quarter (24.8%) stated that HH had affected them their entire life, since early childhood, or as long as they could remember. Duration did not vary significantly among the various body sites.

The onset of palmoplantar HH (11.5 ± 8 years) occurred at a significantly younger age than axillary HH (20.0 ± 8.3 years; $P < .0001$). The age of onset of craniofacial HH (25.4 ± 13.7 years) was significantly older than the age of onset for other sites ($P < .001$). Patients with generalized HH ($P < .0001$) and craniofacial HH ($P = .0014$) were significantly older at presentation than patients with HH in other distributions. Female patients were 1.48 times more likely than male patients (95% confidence interval [CI] 1.13-1.93; $P = .004$) to experience axillary HH; this was the only significant sex difference.

Anatomic sites of HH are shown in Table II. More [T2] than half of patients (207 of 387; 53.4%) experienced HH limited to a single anatomic site, whereas the remaining patients (180 of 387; 46.6%) had multiple involved sites. The most frequent distributional pattern of HH in this cohort was axillary (27.6%) followed by palmoplantar (24.3%); isolated plantar (15%); axillae, palms, and soles (10.9%); and craniofacial (20; 5.2%). Just over half of all patients with PHH (194 of 387; 50.1%) had HH involving the soles, making this the most frequently involved anatomic site. Of patients, 45.2% (175 of 387) had involvement of the palms, and 43.4% (168 of 387) had involvement of the axillae. Twenty patients (5.2%) had

Table I. Clinical characteristics of primary hyperhidrosis (N = 387)

Age at presentation	27.3 ± 12.5 y
Male:female	159:228
Age at onset (all patterns; N = 319)	18.6 ± 12.3 y
*Age at onset, palmoplantar (N = 73)	11.5 ± 8.0 y
*Age at onset, axillary (N = 82)	20.0 ± 8.3 y
†Age at onset, craniofacial (N = 20)	25.4 ± 13.7 y
Duration of symptoms (N = 322)	8.9 ± 8.4 y
Exacerbation by emotional stress/anxiety	85/150 (57%)
Exacerbation by heat/humidity	33/150 (22%)
Diagnosis by history and physical examination	357/387 (92%)

*$P < .0001$ axillary versus palmoplantar.
†$P < .001$ versus other sites.

Table II. Distribution of primary hyperhidrosis

Site	No. (%)	Age (y)*	Female (%)
Axilla (isolated)	107 (27.6)	25.8	72 (67)
Palms/soles	94 (24.3)	24.9	55 (59)
Soles (isolated)	58 (15)	27.3	23 (40)
Axillae, palms, soles	42 (10.9)	26.7	30 (71)
Palms (isolated)	22 (5.7)	24.0	12 (55)
Craniofacial	20 (5.2)	36.2	9 (45)
Generalized	13 (3.4)	42.7	6 (46)
Trunk	10 (2.6)	29.0	6 (60)
Palms/axillae	7 (1.8)	19.9	4 (57)
Inguinal folds	5 (1.3)	51.8	3 (60)
Other†	9 (2.3)	39.1	8 (89)
Soles involved	194 (50.1)	26.0	108 (55.7)
Palms involved	165 (43.6)	25.0	107 (64.7)
Axillae involved	156 (40.3)	25.7	106 (67.9)‡
Total	387	27.3 ± 12.5	228 (58.9)

*Age at presentation.
†Other sites include buttocks (3), legs (3), submammary aspect of chest (1), neck (1), and wrist (1).
‡$P < .01$ versus male for axillary hyperhidrosis. Q5

involvement primarily of the scalp, face, or both, and 13 patients (3.4%) had generalized HH without secondary cause.

The cohort of patients with PHH was reviewed for coexisting dermatologic conditions affecting the [T3] sites involved by HH (Table III). An age- and sex-matched population of patients seen with a diagnosis of epidermoid cyst was used as a control population. To make the statistical comparison between these cohorts more rigorous, diagnosis of cutaneous infection was required to be concurrent and site specific for the HH group, but could be at any visit and involving any site (not only sites affected by epidermoid cysts) in the control group.

The overall risk of any cutaneous infection was significantly ($P < .0001$) increased in HH compared with control (odds ratio [OR] 3.2; 95% CI 2.2-4.6). Specifically, the risk of fungal infection was significantly higher in anatomic sites affected by HH (OR 5.0; 95% CI 2.6-9.8; $P < .0001$). This risk was particularly increased for dermatophyte organisms infecting cutaneous surfaces (tinea pedis, tinea manuum, tinea corporis, tinea cruris; OR 9.8; 95% CI 3.4-27.8; $P < .0001$). Similarly, the risk of bacterial infection was increased (OR 2.6; 95% CI 1.2-5.7; $P = .017$), with particular increased risk of pitted keratolysis (OR 15.4; 95% CI 2-117; $P = .0003$). Finally, the overall risk of viral infection was increased (OR 1.9; 95% CI 1.2-3.0; $P = .011$), with particular increased risk of verruca plantaris/vulgaris (OR 2.1; 95% CI 1.3-3.6; $P = .0077$). An increased association with atopic/eczematous dermatitis (OR 2.9; 95% CI 1.5-55; $P = .019$) was observed.

DISCUSSION

In this report, the distributional patterns and demographics of a cohort of 387 patients with PHH presenting to a dermatology clinic are detailed. Sites with high densities of eccrine glands, including the palmoplantar and craniofacial skin, and apoeccrine glands, including the axillary skin,[1] were most frequently affected. The mean delay of 8.9 years between symptom onset and presentation to clinic highlights the opportunity to increase awareness of this common and treatable disorder.

Whereas mounting data support that treating HH positively impacts quality of life,[2,4,6-8] relatively few data are available regarding the clinical presentation of the disease itself and the possible association with other dermatologic diseases. Much of the available data regarding the clinical distribution relates to patients presenting for specific therapies[2,4,6-8] and thus is not necessarily representative of the patterns presenting to a dermatology clinic.

Demographic features of PHH in this study are comparable with those of a population-based survey completed by nearly 96,000 US residents.[3] Whereas the survey by Strutton et al[3] found that axillae were the most common affected site (50.8%), soles and palms (50.1% and 43.6%, respectively) were affected more commonly than axillae (40.3%) in the current study. The mean age of onset for PHH of 18.6 years in the current study was somewhat younger than the age of 25.2 years in the population survey.[3] These minor differences may be attributable to differences in study design. Indeed, in the current study, female patients sought care for HH more commonly than male patients, at about a 3:2 ratio. This observation correlates with the population-based survey findings that although HH had a slightly greater prevalence in

Table III. Dermatologic conditions associated with hyperhidrosis

	HH	Control	OR	95% CI	*P* value
No.	387	410			
Age, y (range)	27.2 (2-72)	27.9 (3-72)			1.0
Male/female (female)	159/228 (58.9%)	168/242 (59.0%)			1.0
Diagnosis					
Tinea/dermatophyte*	34	4	9.8	3.4-27.8	<.0001†
Pitted keratolysis*	14	1	15.4	2.0-117	.0003†
Verruca*	44	24	2.1	1.3-3.6	.0077†
Eczema/atopic dermatitis‡	36	14	2.9	1.5-5.5	.019†
Tinea versicolor	6	2	3.2	0.64-16.0	.17
Nonmelanoma skin cancer	20	15	1.4	0.72-2.8	.39
Alopecia	9	12	0.8	0.33-1.9	.75
Seborrheic dermatitis	15	13	1.2	0.58-2.6	.73
Onychomycosis	7	5	1.5	0.47-4.7	.70
Molluscum contagiosum	4	5	0.9	0.23-3.2	.54
Rosacea	9	9	1.06	0.42-2.7	.92
Folliculitis	7	8	0.9	0.33-2.6	092
Acne	81	111	0.7	0.5-0.99	.052
Any cutaneous fungal infection*	47	11	5.0	2.6-9.8	<.0001†
Any cutaneous bacterial infection*	21	9	2.6	1.2-5.7	.017†
Any cutaneous viral infection*	48	29	1.9	1.2-3.0	.011†
Any cutaneous infection*	116	49	3.2	2.2-4.6	<.0001†

CI, Confidence interval; *HH*, hyperhidrosis; *OR*, odds ratio.
*At site of HH.
†Significantly increased in HH.
‡Includes diagnoses of atopic dermatitis (7), dyshidrotic eczema (4), nummular eczema (3), and eczema and other eczematous dermatitis (22); all at sites of HH.

male patients (2.9%) than female patients (2.8%), female patients were nearly twice as likely as male patients (47.5% vs 28.6%) to report discussing HH with a health care professional.[3] A younger age of onset for palmoplantar HH compared with axillary HH has been noted previously.[5]

A correlation between HH and cutaneous infection is plausible (with microbial pathogens favoring a moist environment) but underinvestigated. Two European reports have directly or indirectly associated tinea pedis with HH. A German case-control study of 30 patients with tinea pedis found a 3.5-fold higher rate of plantar HH compared with control subjects without tinea pedis.[10] In another study of 1148 Israeli children, tinea pedis (found in 6.9%) was increased with patient-reported HH.[10] In contrast, an Italian survey of 1024 young adults found that tinea pedis (28 cases) had no correlation with patient-reported HH.[11] Similarly, a single observational study of 53 patients with pitted keratolysis found that plantar HH was commonly present but did not evaluate the degree of risk.[12] An association between HH and plantar verrucae has been inferred[13,14] but not supported by clinical research.

Implicit in these findings is the idea that management of HH will help to prevent cutaneous infection and the associated complications. To date, no controlled studies have specifically addressed whether the incidence of cutaneous infection in the context of HH is decreased with interventions to lessen excessive sweating. In a study of 545 patients with onychomycosis, presence of pedal HH was associated with therapeutic failure.[15] In a case report, a patient requiring repeated hospitalization for recurrent fungal and gram-negative bacterial infection of the lower leg experienced resolution only on introduction of topical aluminum chloride to manage concurrent plantar HH.[16] Accordingly, management strategies intended to treat HH, including topical aluminum chloride, iontophoresis, botulinum toxin injection, and perhaps oral anticholinergic agents, may have a secondary benefit of infection prevention. Future prospective studies may elucidate this assertion.

The relationship between HH and atopic or eczematous dermatitis has been anecdotally noted. A survey of 108 patients with atopic dermatitis affecting the hands and feet disclosed a patient-reported rate

of HH of 15% for palms and 20% for soles.[17] A French case-control study of 100 patients with pompholyx (palmoplantar or plantar) found a significant association with HH, with an OR of 4.5.[18] It is likely that the presence of HH acts as an exacerbating factor for bouts of dermatitis. Indeed, multiple cases have reported improvement of dyshidrosiform hand eczema with therapies directed at HH, including 10 patients treated with botulinum toxin[19] and 20 patients treated with iontophoresis.[20] Genetic colocalization of atopy and HH is also possible.

In conclusion, PHH most commonly affects the palmoplantar surfaces, axillae, and craniofacial skin. Patients of both sexes and a wide range of ages are affected. The risk of cutaneous infections caused by bacterial, fungal, and viral pathogens is substantially increased at affected body sites. Eczematous dermatitis commonly coexists. These findings add to the evidence that HH is a condition that causes significant medical consequences in addition to well-documented social, psychological, and occupational problems. Appropriate therapeutic intervention can address the issues inherent to excessive sweating while helping to prevent the potential infectious complications.

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