

ORIGINAL ARTICLE

A comparison between self-reported hand eczema and self-reported signs and symptoms of skin lesions indicating hand eczema

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Abstract

Background: The accuracy of self-reported hand eczema (HE) is currently unclear, and it is unknown how well self-reported signs and symptoms of skin lesions that indicate HE correlate with self-reported HE.

Objectives: To correlate self-reported signs and symptoms of skin lesions on the hands with self-reported HE, to assess the sensitivity and specificity, and to suggest a definition for HE.

Method: Seven hundred ninety-five (47.8%) of 1663 invited healthcare workers completed a digital questionnaire, and were asked to report if they experienced HE or any of the following skin signs/symptoms in past 11 months: scaling, erythema, fissures, vesicles, dryness, itch, stinging.

Results: HE during the past 11 months was reported by 11.9%. Of these, 91.4% reported at least one skin sign versus 32.3% of those without self-reported HE. The highest sensitivity and specificity were found for erythema (77.4% and 78.2%, respectively) and itch (78.5% and 78.6%, respectively), both separately and combined. The combination of ≥ 2 signs (erythema, scaling, fissures and vesicles) and itch, reached a sensitivity of 52.7% and specificity of 93.9%.

Conclusion: The marked difference between self-reported HE and signs/symptoms highlights the importance of differentiating between data based on self-reported HE and signs/symptoms. As a first step towards diagnostic HE criteria, ≥ 2 signs combined with itch could be considered, but clinical studies are needed to verify the precision.

KEYWORDS

diagnostic criteria, epidemiology, hand eczema, self-reports

1 | INTRODUCTION

Hand eczema (HE) is a prevalent inflammatory skin disease with far-reaching consequences for affected patients and society.¹ The lack of

specific criteria for a HE diagnosis challenges the comparison of prevalence estimates between epidemiological studies. The one-year prevalence is often estimated based on replies to the question, 'Have you had HE within the past 12 months?',^{2,3} and validation studies have

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confirmed a sensitivity and specificity as high as 71.4%⁴ and 99.8%,² respectively, for this question, as compared to a clinical diagnosis performed by a dermatologist.^{2,4-6} Other studies reported the HE prevalence based on self-reported signs and symptoms.⁷⁻⁹ Self-reported signs and symptoms are essential in the diagnosis and assessment of HE severity; however, discrepancies between self-reported HE and self-reported signs and symptoms have been reported. In two recent studies, 90.4% and 66% healthcare workers (HCWs), respectively, reported one or more HE-associated signs/symptoms, while only 14.9% and 33%, respectively, responded 'yes' to the question regarding having had HE.^{7,9}

The clinical diagnosis of HE is determined by the overall impression of the physicians or dermatologists, rather than on a specific set of criteria.¹⁰ Various operational definitions for the HE diagnosis have been used.^{6,8,11-13} For example, HE has been defined as the presence of vesicles or erythema in combination with scaling, fissures or papules,^{6,11} or as having more than one of the following: red swollen hands, scaling, fissures, vesicles, red papules or itch.¹² Other studies suggested that HE could be diagnosed as itching erythema, papules and/or vesicles and scaling,¹³ or as erythema and oedema, scaling and fissures, or itch and fissures.⁵ Uter et al. included additional signs such as infiltration, oozing, erosions, hyperkeratosis and lichenification.⁸ Finally, some authors added the time aspect and required a minimum duration of 3 weeks.^{4,12}

Standardized diagnostic criteria for HE, comparable to the Hanifin and Rajka criteria or the UK Working Party Criteria for atopic dermatitis (AD),^{14,15} would be helpful to differentiate HE from other skin manifestations such as dry or hardened skin, or other variations within the norm. A first step in this direction would be an improved understanding of patients' perception of signs and symptoms in relation to the self-reported HE diagnosis. In this study comprising HCWs with and without HE, we aim to correlate self-reported signs and symptoms to self-reported HE and to give suggestions for standardized diagnostic criteria for HE based on self-report.

2 | METHODS AND MATERIALS

2.1 | Study design and population

This is a questionnaire-based study conducted at four hospitals in Greater Copenhagen area in February 2021. The study was a follow-up study to a previous survey from April–May 2020¹⁶ (Figure S1). A total of 1663 participants comprising nurses, auxiliary nurses, physicians, and a mixed group of biotechnicians, midwives and physiotherapists, were invited to respond to a digital questionnaire using SurveyXact (Aarhus, Denmark) (Figure S1). In this study, skin changes during the COVID-19 pandemic were evaluated. Therefore, all retrospective questions were referring to the period March 2020 to February 2021.¹⁷

All participants were asked to report if they experienced any of the following signs and symptoms in the past 11 months (i.e. since the 1st of March 2020): scaling, erythema, fissures, vesicles, dryness, and

itch or stinging. In line with other studies, we did not include the signs 'papules' and 'lichenification' due to a lack of specific Danish words covering these symptoms.^{5,9} Self-reported HE was defined as participants responding 'yes' to having had HE in the past 11 months ('Have you had HE since 1st of March 2020?').³ Participants who reported a history of HE but responded 'no' to the aforementioned question were categorized as participants with previous self-reported HE. Data on sex, age and profession were obtained from the Department of Human Resources, Capital Region, Denmark. History of AD was self-reported ('Have you ever had childhood eczema?').¹⁸ Self-reported HE severity was assessed on a visual analogue scale (VAS) from 0 to 10 with 10 indicating very severe HE. Since this survey was a follow-up questionnaire,¹⁶ information on self-reported HE and AD was collected from the baseline-survey to characterize the respondents and non-respondents.

2.2 | Statistical analysis

Descriptive statistics were used to characterize the study population, respondents and non-respondents, and self-reported signs and symptoms. Participants with self-reported HE within the past 11 months and participants with no history of HE were included in the analyses, while participants with previous self-reported HE were excluded from analyses on sensitivity and specificity and analyses on the number of self-reported signs and symptoms. The chi-square test was used to compare categorical data. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) together with Youden's Index were calculated for signs and symptoms separately and combined using self-reported HE as the gold standard (Appendix).¹⁹ The sensitivity refers to the proportion of participants with self-reported HE reporting signs/symptoms, while PPV evaluates whether the proportion of participants reporting the signs/symptoms also have self-reported HE (Appendix). The specificity evaluates whether the proportion of participants without self-reported HE are also without the sign/symptom (Appendix), while NPV evaluates whether the proportion of participants without signs/symptoms are also without self-reported HE. Finally, Youden's Index (0%–100%) is a value that incorporates both the sensitivity and specificity, with a value of minimum 50% considered acceptable when evaluating the usefulness of a diagnostic test (e.g. a sign). Thus, high sensitivity and high specificity result in a high Youden's Index (Appendix). A post-hoc analysis showed that 'dryness' had a low specificity for self-reported HE. Therefore, we excluded 'dryness' from the calculations based on sensitivity, specificity, PPV and NPV of combined signs/symptoms, to avoid skewing of the results. Spearman's correlation analysis was used for estimation of inter-item correlations. *p*-values <0.05 were considered statistically significant.

2.3 | Ethical considerations

The study was approved by the local ethics committee (H-20007169) and the Danish Data Protection Agency (P-2020-222).

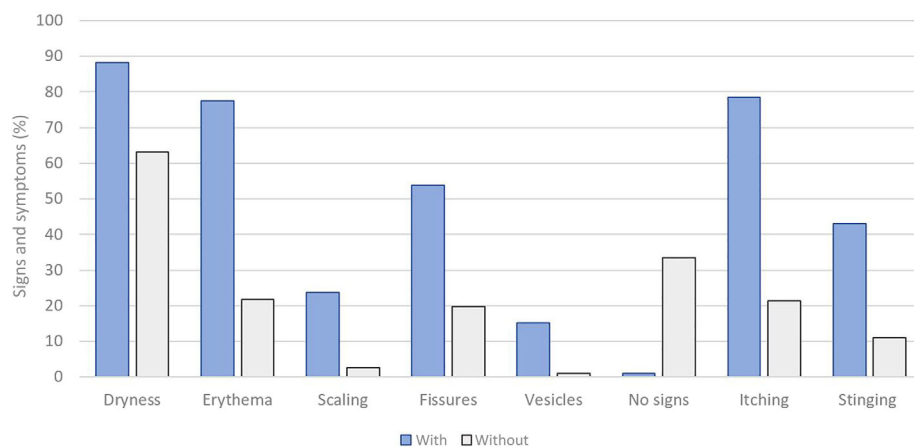


FIGURE 1 Signs and symptoms in participants with and without self-reported hand eczema (HE). Bar plot illustrating the percentage of participants with ($n = 93$) and without ($n = 524$) self-reported HE reporting signs (dryness, erythema, scaling, fissures, vesicles) and symptoms (itch, stinging). Statistically significant differences were found between participants with and without self-reported HE for each sign and symptom ($p < 0.001$) (Chi-square test and Fisher's exact test).

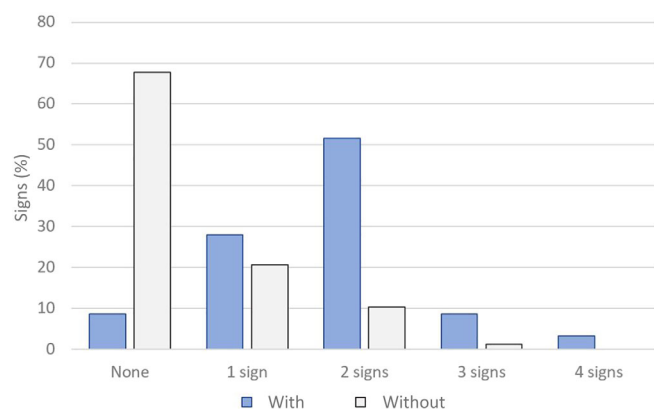


FIGURE 2 Number of signs (erythema, scaling, fissures, vesicles) in participants with and without self-reported hand eczema (HE). The percentage of signs in participants with self-reported HE is illustrated by the blue bars, while the number of signs in participants without self-reported HE is shown with grey bars. The sign 'dryness' was excluded from the calculations.

3 | RESULTS

Out of 1663 participants, 795 (47.8%) responded to the questionnaire (83.4% females, 16.6% males). A total of 11.9% reported HE within the past 11 months, 20.8% had previous self-reported HE, while 67.3% reported no history of HE (Table S1). We found no significant difference between respondents and non-respondents with respect to sex, profession and a history of self-reported HE (28.4% vs. 25.6%) and a history of AD (17.3% vs. 16.0%).¹⁷ The respondents were significantly older than the non-respondents ($p < 0.001$).¹⁷ The mean self-reported HE severity (VAS) during the study period was 3.5 points with no significant difference between the sexes.

3.1 | Signs and symptoms in participants with and without self-reported HE

Participants with self-reported HE reported signs (dryness, erythema, scaling, fissures, vesicles) and symptoms (itch and stinging)

significantly more often than participants without self-reported HE, Figure 1.

Dryness was reported by 88.2% participants with self-reported HE and by 63.2% participants without self-reported HE, indicating a low specificity of this sign. When not including dryness, one sign or more were reported by 91.4% as compared to 32.3% participants with and without self-reported HE, respectively (Figure 2). Of the participants with previous self-reported HE, 47.5% reported one sign or more (excluded dryness).

While no significant differences were found between sexes and age groups, we found that physicians (25.0%) and the mixed group of biotechnicians, midwives and physiotherapists (33.3%) with self-reported HE reported ≥ 3 signs more often than nurses (7.9%) and auxiliary nurses (0%) ($p = 0.06$) (Table S2).

Regarding the correlations between signs and symptoms, the strongest correlation was found between erythema and itch (Figure S2).

3.2 | Sensitivity and specificity of signs and symptoms

The sensitivity, specificity, Youden's Index, PPV and NPV of the signs and symptoms are given in Table 1. Regarding signs, the highest sensitivity and specificity was found for erythema (77.4% and 78.2%) with a Youden's Index of 55.6% and PPV of 38.7%. For symptoms, itch showed the highest sensitivity and specificity of 78.5% and 78.6%, respectively, and a Youden's Index of 57.1% and PPV of 39.5%.

In an attempt to assess the criteria for a standardized HE diagnosis based on signs and symptoms, we combined signs and symptoms based on their level of sensitivity and specificity, as evaluated by Youden's Index, and PPV (Table 1). The combination of erythema and itch had a sensitivity of 66.7%, specificity of 89.1% and PPV of 52.1%. When assessing the combination ≥ 2 signs (erythema, scaling, fissures, vesicles), we found a sensitivity of 63.4%, specificity of 88.4%, and PPV of 49.2%. After including 'itch' in the calculation, the sensitivity was reduced to 52.7%, while the specificity and PPV increased to 93.9% and 60.5%, respectively (Table 1).

TABLE 1 Sensitivity and specificity of signs and symptoms for self-reported hand eczema (HE)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's Index
Signs					
Dryness	88.2	36.8	19.9	94.6	25.0
Erythema	77.4	78.2	38.7	95.1	55.6
Scaling	23.7	97.3	61.1	87.8	21.0
Fissures	53.8	80.3	32.7	90.7	34.1
Vesicles	15.1	98.9	70.0	86.8	14.0
Symptoms					
Itch	78.5	78.6	39.5	95.4	57.1
Stinging	43.0	89.1	41.2	89.8	32.1
Number of signs (excluded dryness)					
1 sign	28.0	79.4	19.4	86.1	7.4
2 signs	51.6	89.7	47.1	91.3	41.3
≥2 signs	63.4	88.4	49.2	93.2	51.8
≥3 signs	11.8	98.7	61.1	86.3	10.5
Signs and itch combined (excluded dryness)					
1 sign and itch	21.5	92.7	34.5	86.9	14.2
≥2 signs and itch	52.7	93.9	60.5	91.8	46.6
Signs and symptoms combined					
Erythema and itch	66.7	89.1	52.1	93.8	55.8
Erythema and fissures	46.2	89.7	44.3	90.4	35.9
Erythema and scaling	19.4	98.7	72.0	87.3	18.1
Erythema and vesicles	10.8	99.4	76.9	86.3	10.2
Vesicles and itch	10.8	99.2	71.4	86.2	10.0
Scaling and itch	19.4	99.0	78.3	87.4	18.4
Fissures and itch	44.1	92.2	50.0	90.3	36.3
Erythema, scaling and fissures	8.6	99.2	66.7	86.0	7.8
Erythema, scaling and itch	16.1	99.2	78.9	87.0	15.3

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

Since the sensitivity and specificity of the combination of ≥2 signs together with itch were high, we evaluated whether the sensitivity and specificity could be influenced by the sex, age, and profession of the participants as well as AD and self-reported HE severity. The sensitivity and specificity were higher in females, younger participants and in physicians and nurses as compared to males, older participants and other professions (i.e. auxiliary nurses and mixed group of biotechnicians, midwives, physiotherapists), Table 2. Furthermore, we found a higher sensitivity in participants with a history of AD and in participants with severe HE as compared to those without AD and those with mild HE, respectively.

4 | DISCUSSION

We assessed self-reported signs and symptoms in HCWs with and without self-reported HE, and showed that although more than 90% of participants with self-reported HE reported at least one sign (erythema, scaling, fissures, vesicles), this was also the case in more than

30% of those without self-reported HE. As emphasized in previous studies,^{4,20} this comprises an important problem when comparing prevalence estimates from studies based on self-reported HE versus self-reported signs of HE. When assessing the sensitivity and specificity for signs and symptoms in relation to self-reported HE, erythema and itch showed the highest sensitivity and specificity, both separately and in combination. We found, however, that ≥2 signs (any of the following: erythema, scaling, fissures and vesicles) combined with itch yielded a fair sensitivity of 52.7%, high specificity of 93.9% as well as a high PPV of 60.5%, suggesting that this combination of signs and symptoms may be helpful when constructing a future set of diagnostic criteria for HE. Importantly, future research efforts on diagnostic criteria should also include clinical diagnoses of HE.

The majority of the study population had no history of self-reported HE; however, more than 30% of these participants reported signs and more than 20% reported symptoms related to HE. This may be partly explained by the fact that our participants were HCWs, and they may be more exposed due to the high amount of wet work as compared to healthy controls. Moreover, 47% of participants with

TABLE 2 Sensitivity and specificity of ≥ 2 signs (excluded dryness) and itch for self-reported hand eczema (HE) stratified by sex, age, profession, atopic dermatitis (AD) and HE severity

	≥ 2 signs and itch	
	Sensitivity (%)	Specificity (%)
Sex		
Female	53.6	93.4
Male	44.4	96.0
Age groups		
≤ 29 years	60.0	92.6
≥ 30 years	51.3	94.0
Profession		
Physician	56.3	99.3
Nurse	54.0	91.6
Auxiliary nurse	37.5	93.5
Mixed group	50.0	92.1
Self-reported AD ($n = 565^a$)		
Yes ($n = 98$)	57.1	92.9
No ($n = 467$)	50.0	94.9
Self-reported HE severity (0–10) ($n=91^b$)		
Mild (0–5) ($n = 65$)	44.6	n/a
Moderate–severe (6–10) ($n = 26$)	73.1	n/a

Note: The sensitivity and specificity of ≥ 2 signs (excluded dryness) and itch may depend on the sex, age, profession, AD status and HE severity of included participants.

Abbreviations: AD, atopic dermatitis; HE, hand eczema.

^aParticipants answering, 'Don't know' to the question on AD were excluded.

^bMissing $n = 2$.

previous (and not within the past 11 months) self-reported HE reported at least one sign indicating a greater awareness of signs in participants with previous HE compared to those without. Notably, some participants may also have *filaggrin* gene mutations, that often lead to skin fissures on the hands and fingers in individuals without a history of AD.²¹ Several factors including skin protective campaigns during the pandemic may explain why we found a relatively low prevalence of self-reported HE in this group of HCWs.¹⁷ Taken together, our findings suggest that prevalence estimates for HE should be interpreted and compared carefully since both the population and the method used to identify HE may strongly impact the results.

In a Swedish study,⁶ erythema and fissures were the most commonly reported signs by HE-patients, which is in line with our findings. Regarding erythema, we also found a high sensitivity; however, since 21.8% of the participants without self-reported HE reported erythema, this resulted in a low PPV of 38.7%, indicating that not all HCWs consider erythema as HE, but rather as a work-related stigma. Notably, high sensitivity and PPV values are important when the signs/symptoms are used for identification of HE in a population. Concerning fissures, we found sensitivity, Youden's Index and PPV

markedly lower than for erythema, indicating that fissures do not supersede erythema with respect to identifying self-reported HE. Likewise, scaling and vesicles showed low levels of sensitivity, Youden's Index and PPV questioning the usefulness of the individual signs. Nevertheless, the participants might have confused dryness with scaling, and they might have difficulties with identifying the vesicles, particularly those that are small and deeply seated. Importantly, these signs or symptoms are not exclusive to HE and may be associated with other less common diseases such as id reactions due to tinea and scabies, or even hepatitis giving itchy skin. A clinical set-up with a physician diagnosing the HE would have enabled us to exclude such cases. HE is a dynamic disease; thus, we chose to evaluate signs/symptoms related to HE in the past 11 months rather than only current HE.

With respect to itch and stinging sensation in relation to self-reported HE, we found itch to be more sensitive than stinging. In qualitative study including 20 HE-patients, itch was reported by all patients as a symptom related to HE,²² and in a recent multicentre study, the prevalence of itch was 82.3% in HE-patients as compared to 8.0% healthy controls,²³ underscoring that itch is a core symptom of HE.

Although the question used for self-reported HE has shown fair to high levels of sensitivity in some validation studies,^{2,4,6} it is still subjective and relies on the patient's perception and knowledge of HE. In our study, the participants were HCWs, suggesting a higher level of medical knowledge than the general population. In validation studies based on farmers²⁴ and industrial workers,⁵ the sensitivity of the self-reported HE was markedly lower compared to a study comprising nurses only.⁴ In accordance, we found a higher sensitivity of ≥ 2 signs and itch in physicians and nurses as compared to other professions, for example, auxiliary nurses and biotechnicians, with lower educational levels. Importantly, a history of AD increased the sensitivity suggesting that previous experience of dermatitis influences the awareness of signs/symptoms. As anticipated, having severe HE increased the sensitivity of ≥ 2 signs and itch, since severe HE may be linked to increased knowledge of HE owing to frequent consultations with dermatologists and HE treatment. Taken together, signs and symptoms associated with HE should be evaluated in a diverse population to increase the generalizability of the results.

In a previous study in HE-patients, females reported more impaired quality of life as compared to males although the females had less severe HE.²⁵ Despite having the same HE severity as assessed by VAS, the females with self-reported HE in our study had fewer signs to report as compared to the males. This may also explain why nurses and auxiliary nurses (i.e. female-dominated professions) with self-reported HE reported fewer signs as compared to physicians and the mixed group.

A clear definition of HE based on signs and symptoms is needed for a more accurate diagnosis in clinical settings as well as in studies. We therefore evaluated the usefulness of each sign and symptom by the sensitivity and specificity, measured by Youden's Index, and PPV. Owing to the low specificity and PPV, dryness was not helpful as a sign to identify self-reported HE in our study, although it may be

considered an important precursor of HE. According to Svensson et al., the minimum criteria for the HE diagnosis were either erythema and papules/vesicles or erythema, scaling and fissures,⁶ which, however, showed low levels of sensitivity, Youden's Index and PPV in our study. Uter et al. defined HE as a combination of minimum erythema and scaling,⁸ and while the sensitivity of erythema alone was high in our study, the combination with scaling yielded a sensitivity of only 19.4%, though, with a PPV of 72%. In some previous studies, HE was suggested to be defined as a minimum of two signs,^{4,11,26} which our data confirms as a possible, useful definition for HE with a high sensitivity, Youden's Index, and PPV. The PPV further increased to 60.5% by adding the symptom itch to the calculation; however, Youden's Index decreased to 46.6%. Although Youden's Index may not be >50% (i.e. the cut-off value), the combination of signs and itch is still considered useful, since the sensitivity, specificity and PPV showed acceptable values. Itch has not routinely been considered a main criterion in the operational definitions for HE,¹¹ but with increasing focus on patient-reported outcomes, the attention to itch has been growing. Our data supports that itch is highly prevalent among participants with self-reported HE stressing the importance of including this symptom in the diagnostic criteria for HE. Alternatively, erythema and itch in combination could also be interpreted as indicative of self-reported HE with its high sensitivity and specificity. However, the sign 'erythema' is receiving increasing scepticism in dermatology owing to its lacking representability in darker skin tones.²⁷ Accordingly, HE cases would be overlooked if the definition of HE was based on erythema and itch alone. We have no data on the skin tone of our participants; however, assuming that the majority has lighter skin tones,²⁸ our suggestions may only be applicable to comparable populations.

Taken together, restricting a heterogenous disease like HE into a set of criteria is challenging. However, a minimum of two signs (i.e. erythema, scaling, fissures, vesicles) combined with itch seems to incorporate the disease into one definition for HE and could be considered as a first step towards a standardized set of diagnostic criteria for HE.

4.1 | Strengths and limitations

With no difference between respondents and non-respondents with respect to self-reported HE and AD, selection bias was considered unlikely to be a problem in our study. While our data gives valuable insight into signs and symptoms linked to self-reported HE within the past 11 months, the long period may, however, also increase the risk of recall bias and the likelihood of participants without HE experiencing signs or symptoms. The participants in our study reported relatively low HE severity which may affect the results. Since data on the skin type of the participants was not available, our findings may not be transferable to all skin types. Measures on sensitivity, specificity and predictive values are important, but these are also influenced by the prevalence, knowledge, and psychological focus on HE including coping and resilience strategies in the participants, and since our population comprised HCWs, an expected high awareness of signs and symptoms

may have influenced the results. Thus, participants with other educational levels or professions may report signs and symptoms differently, indicating that our findings might apply to HCWs only. It may be considered a limitation that the participants' HE was not clinically examined by a physician; however, the aim of this study was not to validate the sign/symptom-based HE diagnosis, but to explore the self-reported signs and symptoms in relation to self-reported HE.

5 | CONCLUSION

To conclude, our data emphasizes the importance of differentiating between studies assessing the HE prevalence based on self-reported HE versus self-reported signs. For a specific set of diagnostic criteria for HE, we consider two signs or more combined with itch as a promising first step. Future steps should include expert panel discussions and a clinical diagnostic accuracy study with dermatologist-diagnosed HE followed by external validation for determination of a final set of standardized diagnostic criteria for HE.

CONFLICT OF INTEREST

None to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX

Sign(s)/symptom(s)	Self-reported hand eczema		Total
	Yes	No	
Yes	a	b	a + b
No	c	d	c + d
Total	a + c	b + d	N
Calculation			
Sensitivity	[a/(a + c)] * 100		
Specificity	[d/(b + d)] * 100		
PPV	[a/(a + b)] * 100		
NPV	[d/(c + d)] * 100		
Youden's Index	Sensitivity + Specificity – 1		

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.